21st Congress of the European Society for Organ Transplantation
17 September - 20 September 2023. Athens, Greece
esotcongress.org
About the European Society for Organ Transplantation

The European Society for Organ Transplantation (ESOT) was founded nearly 40 years ago and has been dedicated to pursuing excellence in organ transplantation ever since.

Facilitating a wealth of international clinical trials and research collaborations over the years, ESOT remains committed to its primary aim of improving patient outcomes in transplantation.

With a community of transplant professionals from around the world, ESOT is an influential international organisation and the facilitator of the biennial ESOT Congress. ESOT attracts the foremost transplantation experts to work in its committees and sections. It has an impressive track record in supporting research, extensive education and promoting changes in European policy.

Our Mission

To improve outcomes for patients with terminal organ disease through transplantation, organ regeneration and substitution.

Our Vision

To promote sustainable scientific advancement through multidisciplinary communities of healthcare professionals

To deliver first-class education, training and career advancement opportunities to all healthcare professionals, with specific training programmes for low-income countries

To work with partner organisations, professional bodies and competent authorities to improve public and institutional awareness of the latest research in the field

To develop and promote policies for equitable access to transplantation and related therapeutic strategies
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ESOT LEONARDO DA VINCI TRANSPLANTATION RESEARCH INNOVATION AWARD

LDV1

BCL-6 INHIBITORS POTENTLY INHIBIT ALLOGENIC T CELL ACTIVATION - A NOVEL MECHANISM OF IMMUNOSUPPRESSION?

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Background: Bcl6i is a key transcription factor regulating T cell fate. We explored the potential of novel Bcl6i inhibitors (Bcl6i) as immunosuppressants in transplantation.

Methods: First, we determined Bcl6 expression in T cells in KTx biopsies (10 TCMR; 10 non-rejection) using multiplex immunofluorescence ISH. To test the effects and mechanism of Bcl6i on T cell activation, we performed mixed lymphocyte reactions (MLR) using healthy donor PBMC. Briefly, CFSE-labeled responder PBMC, or sorted CD4 naïve (Tr), central (Tcm) or effector (Tem) memory T cells were cocultured with irradiated third party stimulator PBMC in the presence of different Bcl6i (79.6 or F1X), the Bcl6 degrader BI-3802, and the vehicle control. After 5 days, CD4 and CD8 T cell proliferation and expression of cytokines, granzyme B and perforin were measured. In addition, we tested Bcl6i action in PBMC from KTx patients with (n=9) and without rejection (n=7).

Results: Indeed, we found pronounced Bcl6i expression in T cells during TCMR. Next, we studied the immunosuppressive effects of Bcl6i, which potently inhibited proliferation and function (IFN-γ, GrB, Per) of CD4 and CD8 T cells compared to vehicle (max. 90% inhibition) without affecting viability. This appeared to be a class effect, since F1X, 79.6 and BI-3802 showed similar effects. Bcl6i interfered with early (d0-3) rather than late (d4-6) activation and Tr, Tcm and Tem were equally inhibited by Bcl6i. Q-PCR gene expression analyses indicated that Bcl6i affected T cell fate, since canonical Th subset makers were differentially regulated (up: GATA3, IL-4, down: IFN-γ, IL-17, IL-21), while the T cell factor Tcf-1 and inhibitory receptor TIGIT were upregulated. To test whether alloreactive T cells from KTx patients would also respond to Bcl6i and be more responsive during rejection, KTx patients’ PBMC were stimulated with donor cells. T cells from rejecting patients showed increased proliferation, Tcm and Tem subsets and cytokine (IFN-γ, IL-2) expression than those from non-rejecting patients, but these parameters were significantly reduced by Bcl6i.

Conclusions: We found that Bcl6i potently inhibit the proliferation and function of T cells, especially during rejection. Since Bcl6 is markedly expressed by T cells, especially during rejection. Since Bcl6 is markedly expressed by T cells, and correlates with poor graft outcome, Bcl6i may have potential as novel immunosuppressants.

LDV2

ENGINEERED T CELLS OVERCOMING REJECTION BY ANTIBODIES (CORA-T CELLS): SELECTIVE TARGETING OF ALLOGENEIC B CELLS IN SOLID ORGAN TRANSPLANTATION

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Background: One major complication after solid organ transplantation (SOT) is antibody-mediated rejection (AMR) by anti-donor HLA antibodies as the B-cell alloimmune response is only indirectly affected by modern immunosuppression. Unselective B-cell depletions protocols are inefficient in preventing AMR and associated with an increased infection risk, emphasizing the need for a more precise targeting of alloreactive B cells.

Methods: B cells with anti-donor HLA specifically characterized by expressing the corresponding B-cell receptors (BCRs). Using BCRs against a distinct HLA molecule as target, we redirected T cells towards alloreactive B cells by introducing a novel chimeric receptor comprising the respective HLA molecule fused to intracellular 4-1BB/CD3ξ signaling domains to generate T cells overcoming rejection by antibodies (CORA-T cells). CORA-T cells harbouring a receptor with an extracellular truncated HLA-A*02 molecule were further modified to abrogate CD8 binding and confer resistance to immunosuppression. Their ability to recognize and selectively eliminate anti-HLA-A*02 B cells to limit antibody release was tested in vitro as well as in vivo.

Results: Upon co-cultivation with B-cell lines expressing and releasing anti-HLA-A*02 antibodies, CORA-T cells were specifically activated (expression of CD154, CD137), released pro-inflammatory cytokines (e.g. IFN-γ, granzyme B), and exhibited strong cytotoxicity resulting in an effective reduction of the anti-HLA-A*02 antibody release. In a xenograft mouse model, CORA-T cells significantly reduced growth of anti-HLA-A*02 B cells. Modification of the HLA-A*02 a3-domain abrogated T-cell sensitization against the CORA receptor. Additionally, CRISPR/Cas9-mediated knockouts of selected binding proteins endowed CORA-T cells with the ability to resist immunosuppressive treatment.

Conclusions: Our results demonstrate that CORA-T cells are able to specifically recognize and eliminate alloreactive B cells, having the potential to selectively prevent the formation of anti-HLA antibodies even under immunosuppressive conditions. This suggests CORA-T cells as a potent novel approach to specifically combat AMR and to improve long-term graft survival in SOT patients while preserving their overall B-cell immunity.

LDV3

COMBINATION OF TCR-DEFICIENT CAR-TREGS AND ANTI-CDS1 MONOCLONAL ANTIBODIES TO PROMOTE TRANSPLANT TOLERANCE

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Background: Solid organ transplantation remains the best therapeutic option for life-threatening organ failure, yet is associated with severe complications inherent to life-long immunosuppressive regimen. In this respect, CAR-Treg therapy is a very promising strategy to get rid of immunosuppressive drugs through the induction and maintenance of transplant tolerance. We are developing a powerful tolerogenic strategy, meant to debulk alloreactive T cells, while tipping the balance toward donor-specific CAR-Tregs. We hypothesize that T Cell Receptor Alpha Constant (TRAC)-deleted CAR-Tregs would act synergistically with anti-CD3 therapy.

Methods: TRAC-deficient HLA-A2-targeted CAR Tregs were manufactured through subsequent lentiviral transduction and Crispr-Cas9 gene editing over 7 days of culture. For the in vivo model, NSG mice were intravenously injected with HLA-A2+ peripheral blood cells at day 0 and then with a mix of two populations of HLA-A2-targeted CAR-T, either mCherry+ Luciferase+ TRAC+ or GFP+ TRAC-, cotransferred at a 1:1 ratio, the following day.

Results: We first confirmed that TRAC-deficient T cells lost surface CD3 expression. We next established the ability to stimulate CAR-Tregs, as assessed by CD25, 4-1BB and HLA-DR expression, in a HLA-A2-specific manner, irrespective of the presence of TCR. Notably, hallmark Treg markers, including FOXP3 and HELIOS, were maintained regardless the disruption or not of the TRAC gene. In order to evaluate the selective in vivo deletion of TRAC-sufficient CAR-T cells, we administered a mix of TRAC-sufficient and TRAC-deficient HLA-A2-targeted CAR T cells, along with HLA-A2+ PBMCs into NSG mice. Strikingly, TRAC- cells, unlike their TRAC- counterparts, were wiped out from the blood upon anti-CD3. Moreover, bioluminescent cell tracking showed a dramatic reduction of TRAC+ cells in the lymphoid organs of animals treated with anti-CD3 vs saline solution (control). We further demonstrated that current strategies used for CAR-Treg differentiation are insufficient to achieve the desired CAR-Treg tumor control in vivo.

Conclusions: Together, our data show that anti-CD3 therapy can provide an in vivo life-advantage to TRAC-deficient CAR-T regens, over resident TRAC-sufficient T cells. This combo strategy will reduce the number of CAR-Tregs needed to produce a cell product.

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FcγR3A influences the severity of AMR and suggests that patients at high risk can provide useful information, but often do not reach the stage of clinical implementation. Previous studies have demonstrated the diagnostic potential of the urinary chemokines CXCL9 and CXCL10 for rejection. However, before clinical application can begin, the relationship with rejection subtypes and clinical confounders, the context of use, and the added benefit of these markers must be demonstrated.

Methods: In this single-center prospective cohort study, we analyzed 1559 biopsy-paired urinary samples from 622 kidney transplantations performed between April 2013 and July 2019. We quantified urinary CXCL9 and CXCL10 using an automated immuno-assay platform and normalized the values to urinary creatinine. The latter in vitro therapeutic results were confirmed in a second independent clinical cohort of kidney transplant patients treated with IVIg.

Conclusions: Our results demonstrate that an integrated score of urine chemokines, integrated in a multivariate model with routine clinical markers (eGFR, donor-specific antibodies and polyoma viremia) had high diagnostic value for detection of acute rejection (AUC 81.3%, 95% CI 77.6-85.0). With the integrated score, 59 patients (30 ranging from 73.0% to 91.3%), finally, we showed that the race-free KSR GFR equation performed well in a series of kidney transplant recipients stratified by race, sex, age, body mass index, donor type, therapies, creatinine and GFR measurement methods and timing. Based on these results we developed an online application that estimates GFR based on recipient's age, sex and creatinine: https://transplant-prediction-system.shinyapps.io/eGFR_equation_KTX/

Conclusions: Using multiple, international cohorts of kidney recipients, we developed and validated a new race-free KSR GFR equation that demonstrated high accuracy and outperformed the race-free CKD-EPI-2021 equation developed in individuals with native kidneys.

Background: There is growing interest in the potential utility of donor-derived cell-free DNA (dd-cfDNA) as a non-invasive biomarker for surveillance of acute cellular rejection (ACR) in heart transplant (HT) recipients, thus allowing avoidance of repeated endomyocardial biopsies (EMB).

Methods: Prospective study performed between 2019 and 2022 (NCT 04973943). All patients underwent surveillance EMB at 0.5, 1, 2, 3, 4, 6 and 12 months post-HT. Dd-cfDNA levels were determined prior to each EMB, using Next Generation Sequencing technology (Allongenx, Eurofins Genome). The primary end-point was the association between dd-cfDNA levels and the presence of ACR (defined as grade ≥2R) in EMB. The correlation between dd-cfDNA and NTproBNP levels was also studied.

Results: A total of 206 patients from 12 HT centers were included (mean age 54 ± 11 years, 73% male). We analyze here the first 848 pairs of EMB and dd-cfDNA determinations. ACR was present in 35 EMB (4.1%) and AMR ≥1

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Background: Antibody-mediated rejection (AMR) is the first cause of kidney graft failure but its heterogeneous prognosis makes difficult to assess the risk of graft loss and to choose a therapeutic strategy at the time of diagnosis. The binding of anti-donor antibodies (DSA) to the surface of graft endothelial cells induces the recruitment of innate immune effectors via their Fcy receptors (depending on the cell type: FcγR2A, FcγR2B, FcγR2C, FcγR3A and FcγR3B), for which many SNPs modulating their affinity for IgG Fc have been described. The aim of this ransalitarian study was to determine which polymorphism(s) in recipient FcγRs were associated with poor prognosis at the diagnosis of AMR and the possible therapeutic consequences.

Methods and Results: Among 1682 kidney transplant recipients at Lyon University Hospital who underwent graft biopsy between 2004 and 2017, 135 (8%) were diagnosed with AMR. Of the 5 functional FcγR polymorphisms described in the literature, only FcγR III (rs3686991; p<0.005) was statistically associated with graft survival. Global and single-cell transcriptomic analyses of AMR biopsies demonstrated that non-classical monocytes and NKs are the only innate effectors expressing FcγR3A. In vitro cocultures between these human purified innate effectors and allogeneic endothelial cells covered with DSA confirmed that effector cells with high-affinity FcγR3A i activated more strongly and caused more damage to target, but ii) that these same effectors were also more effectively controlled by the addition of IgG in the culture medium. The latter in vitro therapeutic results were confirmed in a second independent clinical cohort of kidney transplant patients treated with IVIg.

Conclusions: Our results demonstrate that patients at high risk are also those who respond the best to IVIg treatment.
LONG-TERM OUTCOMES AFTER HYPOTHERMIC OXYGENATED MACHINE PERFUSION (HOPE) AND TRANSPLANTATION OF 1291 DONOR LIVERS USING REAL-WORLD DATA

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Background: Benefits of hypothermic oxygenated perfusion (HOPE) over cold storage of donor livers on short-term outcomes after transplantation have been confirmed by several randomized controlled trials. According to the IDEAL-D (Idea, Development, Exploration, Assessment, Long-term study-Framework for Devices), scientific evidence for HOPE has currently reached stage 3. We aimed to assess outcomes after transplantation of donor livers preserved by HOPE based on real-world data (IDEAL-D stage 4).

Methods: In this international, multicenter, observational cohort study, we included adult recipients of a HOPE-preserved liver transplanted between January 2012 and December 2021. Analyses were stratified for donation after brain death (DBD) and circulatory death (DCD) liver grafts. DBD grafts were classified as benchmark (primary transplant, lab MELD<20, BAR-score<9), standard, or extended criteria (ECD, according to EASL). DCD livers were classified according to the UK-DCD-risk score as low-risk (0-5 points), high-risk (6-10 points), or futile (>10 points). The primary study outcome was death-censored graft survival. Secondary outcomes included the incidence of primary non-function (PNF) and ischemic cholangiopathy (IC).

Results: We included 1291 transplantations (65% DBD) performed at 20 centers, with a median follow-up of 23 (IQR:13-42) months. For DBD, a total of 113 benchmark (13%), 211 standard (25%), and 515 ECD (61%) cases were recorded. For DCD, 163 transplants were classified as low-risk (36%), 170 as high-risk (38%), and 119 as futile (26%), with significant risk profile variations among centers (Fig. 1A). Actuarial 1-, 3-, and 5 year graft survival for DBD and DCD was 95%, 91% and 87% vs. 90%, 85% and 80%, respectively (Logrank p<0.004, Fig. 1B). Within DBD and DCD strata, graft survival was similar among risk groups (Logrank p>0.50; Fig. 1C, p=0.13, Fig. 1D). Graft loss due to PNF or IC was 3% and 0.7% (DBD), and 5.1% and 5.8% (DCD).

Conclusions: This study shows excellent 5 year graft survival after transplantation of HOPE-treated DBD and DCD livers with low rates of graft loss due to PNF or IC, despite considerably high rates of ECD DBD and high-risk/futile DCD grafts. HOPE-treatment has now reached IDEAL-D stage 4, which further supports implementation of HOPE in routine clinical practice.
OS1_1

TOWARDS DECODING HLA IMMUNOGENICITY - ONE STEP FORWARD

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Background: Development of de-novo HLA-donor-specific-antibody (dnDSA) posttransplantation is associated with increased risk for rejection and poor allograft outcome. Molecular Mismatch Load (MML) analysis was proposed as means to predict risk to develop dnDSA, yet some patients develop dnDSA despite low MML, whereas others, with high MML, do not develop dnDSA for many years. We used alternative approaches to gain insight into HLA immunogenicity.

Methods: 239 kidney transplant recipients from our center and 460 patients from the International Histocompatibility Epitope Working-Group, with high resolution HLA typing and HLA antibody testing data, were enrolled. CRISPR/Cas9 site directed mutagenesis and human HLA-DQ monoclonal antibodies were used for adsorption/elution (ad/el) studies. Electrostatic Mismatch Score (EMS) evaluation and Molecular Evolutionary Genetic Analysis (MEGA) were performed.

Results: About 25% of the two cohorts consisted of patients who received donor organs with 2 HLA-DQ mismatches but with dnDSA development only against one of the mismatches (2MM1DSA). Analysis of this unique patient group demonstrated almost complete segregation of the HLA-DQ heterodimers into high/low immunogenicity groups; validated also in the larger cohorts. Evaluation of molecular mismatches in the 2MM1DSA cohort further demonstrated that not all molecular mismatches contribute equally to formation of dnDSA. MML, whereas others, with high MML, do not develop dnDSA for many years.

Conclusions: Increased immunogenicity is not a consequence of increased MML, and epitopes should not be considered "functional epitopes". Increased immunogenicity is likely a consequence of increased evolutionary divergence. Functional studies understanding the immunobiology of allorecognition are required to decipher immunogenicity to improve transplant outcome.

OS1_2

SOLVENT-ACCESSIBLE AMINO ACID MISMATCHES ON DONOR HLA ARE ASSOCIATED WITH KIDNEY DRAFT OUTCOMES; A STEP TOWARDS PERSONALIZING POST-TRANSPLANT CARE?

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Background: Current guidelines advise the use of HLA antigenic mismatches to assess the risk of alloimmunity in kidney transplant recipients (KTR). This approach is however too crude to allow personalization of post-transplant care. Recently, the HLA epitope mismatch algorithm (HLA-EMMA) was developed to quantify solvent-accessible amino acid (saAA) mismatches that could interact with B cell receptors responsible for the humoral allo-immune response. Until date, HLA-EMMA has only been associated with graft outcomes in relatively small cohorts with a limited number of events. This observational study aimed to examine the relationship between HLA-EMMA and transplant outcomes in a large and deeply phenotyped cohort of 1580 KTR by cox regression analyses.

Methods: Outcomes of interest were patient death, death-censored graft failure (DCGF), biopsy-proven acute rejection (BPAR), overall de novo donor-specific antibody (dnDSA) development, and dnDSA development per HLA locus (A, B, C, DQ, and DR). Hazard ratios (HR) and confidence intervals (CI) were adjusted for type of transplantation, recipient and donor age/gender, number of prior transplantations, and pre-transplant DSAs.

Results: During a median follow-up of 5.5 years (IQR: 2.9-9.0), 270 (17%) patients died, 185 (12%) suffered from graft failure, 302 (19%) suffered from DCGF, 272 (17%) developed dnDSA, dnDSA against HLA-DQ were most common (n=164). Multivariable analysis showed that HLA-EMMA (total, class I, and class II saAA) mismatch scores were independently and significantly associated with patient death, DCGF, BPAR, overall dnDSA occurrence as well as HLA-specific dnDSA formation as shown in Figure 1. For locus-specific dnDSA, HR for per 10 saAA mismatches was highest for HLA-A, -B, -C, -DQ, and -DR, respectively.

Conclusions: This is the first study to investigate the association between saAA mismatches and kidney transplant outcomes calculated by HLA-EMMA in a large and deeply phenotyped cohort of KTR. These findings suggest that HLA-EMMA may be a useful tool to stratify immunological risk to potentiate personalized surveillance and immunosuppression after transplantation.

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OS1_1

TOWARDS DECODING HLA IMMUNOGENICITY - ONE STEP FORWARD

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OS1_2

SOLVENT-ACCESSIBLE AMINO ACID MISMATCHES ON DONOR HLA ARE ASSOCIATED WITH KIDNEY DRAFT OUTCOMES; A STEP TOWARDS PERSONALIZING POST-TRANSPLANT CARE?

Soufian Meziyervich*1,2, Suzanne Bezstarosti*1,2, Jesper Kers4, Teun van Gelder5, Danny van der Helm5, Paul van der Boog5, Johan de Fijter*1,2, Dirk Jan Moes5, Dave Roelen5, Geert Haasnoot5, Aiko De Vries1,2, Sebastiaan Heidt3

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Methods: Outcomes of interest were patient death, death-censored graft failure (DCGF), biopsy-proven acute rejection (BPAR), overall de novo donor-specific antibody (dnDSA) development, and dnDSA development per HLA locus (A, B, C, DQ, and DR). Hazard ratios (HR) and confidence intervals (CI) were adjusted for type of transplantation, recipient and donor age/gender, number of prior transplantations, and pre-transplant DSAs.

Results: During a median follow-up of 5.5 years (IQR: 2.9-9.0), 270 (17%) patients died, 185 (12%) suffered from graft failure, 302 (19%) suffered from DCGF, 272 (17%) developed dnDSA, dnDSA against HLA-DQ were most common (n=164). Multivariable analysis showed that HLA-EMMA (total, class I, and class II saAA) mismatch scores were independently and significantly associated with patient death, DCGF, BPAR, overall dnDSA occurrence as well as HLA-specific dnDSA formation as shown in Figure 1. For locus-specific dnDSA, HR for per 10 saAA mismatches was highest for HLA-A, -B, -C, -DQ, and -DR, respectively.

Conclusions: This is the first study to investigate the association between saAA mismatches and kidney transplant outcomes calculated by HLA-EMMA in a large and deeply phenotyped cohort of KTR. These findings suggest that HLA-EMMA may be a useful tool to stratify immunological risk to potentiate personalized surveillance and immunosuppression after transplantation.

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Kosmoliaptsis 1

Conclusions: demonstrates the importance of antibody abundance and affinity in clinically KD sera from healthy (n=15) and immunocompromised (n=15) patients, anti-RBD Ab immune-monitoring post-transplantation. In SARS-CoV-2, MAAP showed wide donor-specific-alloantibodies that lead to rejection from those that were tolerated, signal. In HLAi transplants, MAAP was able to differentiate clinically significant antibody-HLA interactions were functionally insignificant despite high SAB.

Methods: Using a microfluidic diffusional sizing-based strategy, we developed microfluidic antibody affinity profiling (MAAP), a novel in-solution immunoassay that simultaneously determines antibody Kd and [Ab] directly in serum. MAAP was developed and validated using the HLA-αβ-antibody system and applied in HLA Ab-incompatible (HLAi) transplantation and in anti-SARS-CoV-2 immunity. Results: MAAP also enabled quantification (Kd and [Ab]) of alloantibody-HLA interactions in purified and Ab-spiked sera. We showed single-antigen-bead (SAB), and cellular (FC, CDC) HLA immunossays were avidity and [Ab]-dependent, but antibody-mediated cytotoxicity is proportional to Ab-HL-AKd. Micromolar antibody-HLA interactions were functionally insignificant despite high SAB signal. In HLAi transplants, MAAP was able to differentiate clinically significant donor-specific-alloantibodies that lead to rejection from those that were tolerated, despite similar SAB output, and provided insights into memory re-activation and immune-monitoring post-transplantation. In SARS-CoV-2, MAAP showed wide variation in anti-RBD Ab Kd, which showed good correlation with neutralisation capacity (p<0.001). In convalescent sera (n=32), evidence of avidity maturation was seen 3-months post-infection, despite a reduction in Ab. In post-vaccine sera from healthy (n=15) and immunocompromised (n=15) patients, anti-RBD Ab Kd was significantly weaker against Omicron than wild-type (p=0.001), where the anti-RBD response in the immunocompromised cohort was significantly reduced.

Conclusions: This work outlines a path towards in-depth antibody profiling and demonstrates the importance of antibody abundance and affinity in clinically relevant humoral immunity.

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Background: Antibody-mediated rejection (ABMR) is a major complication after transplantation that is associated with poor graft prognosis. The presence of donor-specific anti-HLA antibodies (DSA) class I and II, especially class II, increases the risk of developing ABMR. Current therapies are aimed at controlling the immune response, but there is no specific therapy to selectively reduce the generation of DSA. The objective was to establish a new therapeutic tool to specifically eliminate anti-HLA-DQ*03:01 antibody-producing B cells by generating cytotoxic lymphocytes transduced with chimeric HLA-DQ*03:01 antibody receptors (DQB1*03-CHAR). Methods: This is a pre-clinical trial, using human cells, specifically cytotoxic T lymphocytes (CTL) generated from healthy volunteers who do not have HLA-DQ*03:01. The design, generation and production of DQ*03:01-CHAR will be carried out, with subsequent evaluation of their cytotoxic action and cytokine production, through an in-vitro model. Results: We have identified and cloned the genetic sequence corresponding to HLA class II, specifically HLA-DQ*03:01 (both the α DQA1*0501 domain and the β DQB1*0301 domain). The DQ*03:01-CHAR construct has been generated from domain binding; leader peptide (PL), extracellular domain (HLA-DQ*03:01) and intracellular domains (from A2-CHAR, generated in our laboratory), producing lentiviral particles with the construct in HEK-293T cells. After isolation of CD3+ cells from a voluntary donor, transduction and production of DQ*03:01-CHAR-Tc is performed. Conclusions: We are developing a new selective and specific therapy against B lymphocytes producing anti-HLA class II antibodies. With the development of this therapy, we will have a new tool for the desensitization of hypersensitized patients as well as for the control of ABMR, improving the results of graft survival, without increasing the infectious complications associated with conventional immunosuppressive therapy.
CHARACTERISTICS AND FUNCTION OF DONOR AND RECIPIENT TISSUE RESIDENT LYMPHOCYTES IN KIDNEY TRANSPLANTS

Daphne Hulreich-Peelen1,2, Hector Tejeda Mora1,2, Dennis Hesselink1,2, Eric Bindels3, Thierry van den Bosch4, Marian Claessens-van Groningen1,4, Marjolein Dietrich1,2, Sebastiaan Heidt1, Robert Minne1,4, Georges Verjans1, Martin Hoogduijn1, Carla Baan1,2

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Background: resident tissue lymphocytes (TRL) are key players in local immune surveillance. In immunosuppressed transplant recipients, however, the function and characteristics of TRL are less well defined. The current study aims 1) to investigate which TRL populations are present in kidney transplants, 2) to examine the frequencies and characteristics of donor and recipient TRL populations and 3) to unravel the function of TRL.

Methods: Renal lymphocytes were obtained by enzymatic digestion of kidney transplantectomy specimens (n=24) and were subsequently examined by flow cytometry to identify TRL populations and their origin (donor or recipient). The molecules CD99, CD103 and CD44a were used to define tissue residency and HLA-discrepancies between donor and recipient to define the origin of TRL.

In-depth analysis of donor and recipient TRL functionality was performed using single-cell transcriptome sequencing, single-cell T cell receptor (TCR) sequencing and virus dextramer staining.

Conclusions: Our study provides new insights in the role of the different innate immune cell populations and their interactions with the kidney structural cells and unarrives inflammatory cytokine signaling between FCGR3A+ cells and endothelial cells. Inhibition of the Syk pathway completely dampens such signaling, suggesting its potential interest as therapeutic target for kidney transplant rejection.

A NOVEL BI-SPECIFIC FUSION PROTEIN WITH CTLA4/IG/PDL2 AS A NOVEL IMMUNOSUPPRESSANT MOLECULE MODULATING ALLOIMMUNE RESPONSES

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Background: The CD28-CD80/86 cosignal is mandatory for CD28+ T cells to respond to alloantigens. CTLA4/IG regulates the CD28/CD80/86 signal and CTLA4/IG/pDL2 fusion protein has been shown to improve mouse and human allograft survival in animal models. In the present study we report the evaluation of a novel bi-specific fusion protein carrying an IgG2a molecule (Hybri) and an IgG1 molecule (Bela) that simultaneously targets human CTLA4 and PDL2.

Methods: A mouse model of kidney allograft transplantation was used to assess the efficacy of the novel bi-specific fusion protein (Hybri) vs single anti-PDL2 (Bela). The cell surface expression of PDL2 was measured on human and mouse peripheral blood mononuclear cells using flow cytometry. The fusion protein Hybri was also tested on human peripheral blood mononuclear cells.

Conclusions: this novel bifunctional protein (Hybri) efficiently abrogates the alloimmune response in the mouse model of kidney transplantation. Further studies are necessary to determine the potential of Hybri in human allograft transplantation.
Kazunobu Shinoda*1

Kidney graft samples in an acute phase (2 hours after operation) were collected to measure creatinine clearance. Neutrophil gelatinase-associated thrombospondin-1 (TM) expression in kidney grafts from long cold ischemia reperfusion injury. It is known that the expression of TM decreases. We investigated whether perfusate solution saturated with recombinant TM alpha (rTM) can protect the kidney from long cold ischemia reperfusion injury. 

Methods: To study 79-6's effect on T-B cell synapse formation, stimulated T cells and B cells before and after polyclonal stimulation.

Conclusions: Using imagestream technology, we were able to show that direct and indirect pathways of DSA generation in preclinical models are double-edged swords protecting against microvascular lesions and resulting from the generation of DSA through the inverted direct pathway, while allograft rejection is a double-edged sword that protects against the microvascular lesions of allograft rejection. We analysed the effect of NAMPT inhibition on different T cells and could observe a cytotoxic effect and a reduction in the mRNA and protein expression of Interferon-γ after NAMPT inhibition. Additionally, we isolated CD4+ and CD8+ T cells from human peripheral blood, to perform a viability assay and measure cytokine expression in T-cell receptor stimulated and unstimulated T cells with or without NAMPT inhibition. We analysed the effect of NAMPT inhibition on different T cells and could observe a cytotoxic effect and a reduction in the mRNA and protein expression of Interferon-γ after NAMPT inhibition. We confirmed our HTx model is well suited to investigate acute allograft rejection, as we observed a significantly higher number of infiltrating cells and upregulation of pro-inflammatory cytokines in the allogeneic group.

Results: We confirmed that our HTx model is well suited to investigate acute allograft rejection, and that perturbing NAMPT is effective in suppressing activation of alloactive T cells without affecting regulatory T cells. These data suggest NAMPT as a promising treatment target in acute allograft rejection.

Conclusions:

Visualizing the Effect of BCL6 Inhibition on B and T Lymphocytes by the Small Molecule Compound 79-6 by Means of Imaging Flow Cytometry

Kazunobu Shinoda1, Satoshi Tamaki2

Background: BCL6 is essential for germinal center formation and maintenance, which is critical for antibody formation. Therefore, targeting BCL6-expressing T and B cells might prevent humoral alloreactivity. Using imaging flow cytometry, which combines conventional flow cytometry with single cell fluorescence images, we were able to study the effect of a small molecule BCL6 inhibitor (79-6) on immunological T-B cell synapse formation and activation, and the expression of BCL6 on T and B cells before and after polyclonal stimulation.

Methods: To study 79-6's effect on T-B cell synapse formation, stimulated T cells and B cells before and after polyclonal stimulation.

Conclusions: Using imaging flow cytometry, we were able to show that direct and indirect pathways of DSA generation in preclinical models are double-edged swords protecting against microvascular lesions and resulting from the generation of DSA through the inverted direct pathway, while allograft rejection is a double-edged sword that protects against the microvascular lesions of allograft rejection. We analysed the effect of NAMPT inhibition on different T cells and could observe a cytotoxic effect and a reduction in the mRNA and protein expression of Interferon-γ after NAMPT inhibition. Additionally, we isolated CD4+ and CD8+ T cells from human peripheral blood, to perform a viability assay and measure cytokine expression in T-cell receptor stimulated and unstimulated T cells with or without NAMPT inhibition. We confirmed our HTx model is well suited to investigate acute allograft rejection, as we observed a significantly higher number of infiltrating cells and upregulation of pro-inflammatory cytokines in the allogeneic group.

Results: We confirmed that our HTx model is well suited to investigate acute allograft rejection, as we observed a significantly higher number of infiltrating cells and upregulation of pro-inflammatory cytokines in the allogeneic group. We unveiled an increased NAMPT expression in the serum of allograft transplanted mice, indicating NAMPT's involvement during allograft rejection. We analysed the effect of NAMPT inhibition on different T cells and could observe a cytotoxic effect and a reduction in the mRNA and protein expression of Interferon-γ after application of the inhibitor, which was more prominent in CD8+ T cells than CD4+ cells and had little effect on regulatory T cells. We characterized the effect of our NAMPT inhibitor on primary rat cardiomyocytes, and observed no effects on proliferation, cell size and cell number after up to 72 hours of treatment.

Conclusions: We could show that NAMPT is upregulated during allograft rejection and that perturbing NAMPT is effective in suppressing activation of alloactive T cells without affecting regulatory T cells. These data suggest NAMPT as a promising treatment target in acute allograft rejection.

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Conclusions: We could show that NAMPT is upregulated during allograft rejection and that perturbing NAMPT is effective in suppressing activation of alloactive T cells without affecting regulatory T cells. These data suggest NAMPT as a promising treatment target in acute allograft rejection.
Background: Directly alloreactive CD8 T cells recognise epitopes formed by an allogeneic MHC I molecule loaded with an endogenous peptide. We have identified over 40 immunogenic peptides presented by H-2Kb. We are now profiling the T cell receptor (TCR) repertoire of CD8 T cells responding to a subset of these epitopes to deepen our understanding of the molecular basis of alloreactivity.

Methods: An enriched population of alloreactive CD8 T cells was isolated from B10.BR (H-2d) or Balb/c (H-2b) mouse liver following a prime-boost against H-2Kb. B10.BR samples were stained with a panel of 12 oligonucleotide-barcoded Kb-peptide dextramers, single cells were captured for parallel analysis of paired TCR sequences, specificity and gene expression (BD Rhapsody). Results were integrated with TCR repertoires obtained from sorted populations positive for single pMHC dextramers.

Results: TCR alpha variable (TRAV) segments 13, 14 and 16 were over-represented among alloreactive T cells recognising Kb-SNYLFTKL, Kb-RTYTYEKL and Kb-VGPRYTNL from both recipient strains, and within the global alloreactive population (Figure 1a). This differs markedly from the segment usage for self-restricted CD8 T cells recognising Kk-SNYLFTKL. A family of closely-related clonotypes (metaclonotype) recognising the abundant epitope Kb-SNYLFTKL has been detected in 12/12 B10.BR mice examined (Figure 1b). Within this public metaclonotype, the sequence of the beta chain complementarity-determining region 3 (CDR3b) confers fine specificity for the peptide binding of CDR3b (Table 1, Figure 1c-d). Conclusions: Recognition of H-2Kb by alloreactive TCR is linked to the expression of particular TRAV segments, while fine specificity for the peptide is conferred by the CDR3b sequence.

OS2 7 MAPPING THE CELLULAR AND MOLECULAR LANDSCAPE OF ADAPTIVE IMMUNE RESPONSES IN KIDNEY ALLOGRAFT REJECTION

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Background: Although the clinical and histological differences between anti-body-mediated rejection (ABMR) and T-cell mediated rejection (TCMR) are well established, in-depth analyses of cellular and molecular determinants that contribute to such allograft responses are sparse. Methods: In a cohort of 76 kidney transplant recipients (stable, N=41; ABMR, N=23; TCMR, N=12) and 16 healthy controls (HC), we used high dimensional flow cytometry and single-cell RNA seq to deeply profile blood CD4 T cells and B cells. Additionally, we assessed 55 plasma cytokines.

Results: Compared to HC and stable subjects, ABMR patients displayed significantly expanded cell populations of activated ICOS+ IL-21R+ T follicular helper cells (Thf) and effector CD11c+ IL-21R+ B cells. TCMR patients showed specific expansion of Th1/Th17 CD28+ CD4 T cells and naive B cells. Plasma from ABMR patients displayed elevated IL-21, IL-8 and ICAM-1, while those from TCMR patients were enriched for IFN-g, TNF-a and IL-17A. At the single-cell transcriptional level, ABMR was characterized by elevated transcripts related to antigen receptor activation and IL2RG-STAT3 pathways in both Thf and B cells, while TCMR was associated with enrichment in cell-mediated cytotoxicity, type-1 interferon and FcγR signaling pathways in effector memory CD4 T cells.

Conclusions: We identified predominant IL-21-driven Thf and B cell effector differentiation and activation during ABMR, while TCMR was characterized by type-1 inflammatory and cytotoxic CD4 T cell changes. Thus, our study highlights novel cellular pathomechanisms associated with ABMR and TCMR, and therefore identifies novel therapeutic targetable pathways to tackle kidney allograft rejection.

Table 1.

<table>
<thead>
<tr>
<th>TRAV/TRAJ</th>
<th>CDR3a</th>
<th>TRBV/TRBJ</th>
<th>CDR3b</th>
<th>Peptide binding</th>
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<tr>
<td>16/27/V21/49</td>
<td>CAMRENTGQYQNTFY</td>
<td>13-2*01/2-4</td>
<td>CASGTCQGKNL</td>
<td>SNYLFKTKL only</td>
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<tr>
<td>16/27/V21/49</td>
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<td>SNYLFKTKL</td>
</tr>
</tbody>
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Figure 1.

a. CIRCOS plots of paired TCR β-δ segment usage showing strong bias towards TRAV/16/16 among pMHC-restricted alloreactive TCRs. This bias is also evident in the global Kb-reactive population for each group = n ≥ 3 mice.
Moumita Paul-Heng1, Martina Denkova1, Eric Taeyong Son1, Mario Leong2, Thomas Ashhurst1, Chuanmin Wang3, David Bowen4, Patrick Bertolino5, Anthony Purcell5, Nicole Lagrute6, Nicole Mifsud7, Alexandre Sharland8

1The University of Sydney, Faculty of Medicine and Health, Sydney, Australia, 2The University of Sydney, Sydney Cytometry, Sydney, Australia, 3Centenary Institute, Liver Immunobiology Laboratory, Sydney, Australia, 4Monash University Biomedical Discovery Institute, Biochemistry and Molecular Biology, Melbourne, Australia

Background: Expression of allogeneic donor MHC class I in recipient hepatocytes using adenovirus-associated viral (AAV) vectors induces tolerance to subsequent skin grafts bearing the same mismatched MHC, even in the presence of pre-existing immune memory against the donor strain. The mechanisms underlying tolerance induction are incompletely understood.

Methods: B10.BR (H-2b) mice were primed with an H-2Kb-bearing skin graft. 30 days after rejection of the primary graft, they were inoculated with AAV-Kb, followed by secondary skin grafting. Liver leukocytes were isolated at intervals between d5 and d100 following vector administration – paired TCR sequence, specificity and gene expression were determined for single alloreactive and bystander CD8 T cells (BD Rhapsody).

Results: Alloreactive T cells exposed to their cognate antigens in the liver sequester into several clusters based on gene expression. One major cluster recapitulates a published signature of deletional tolerance, while the other expresses liver-residency markers and receptors typically associated with gamma-delta, NK, and innate lymphoid cells (Figure 1a). Projection of timecourse data onto the public Kb-specific TCR, and gene expression were determined for single alloreactive and bystander CD8 T cells (BD Rhapsody).

Conclusions: Taken together, these data support roles for both deletion and exhaustion in tolerance induction of the microcirculation of the first two pig-to-human kidney xenografts by peritubular capillary (H). Control densities were below the limit of quantification. The proportions of CD15+ glomerular tufts were 98.7% in xenograft 1, 78.4% in xenograft 2, 3.0% in xenograft before implantation, and 5.5% in xenograft 1, 3.0% in xenograft before implantation, and 2.0% in wild-type pig kidney (p<0.0001, A). The proportions of CD15+ peritubular capillaries were 56.1% in xenograft 1, 3.0% in xenograft 2, 1.7% in xenograft before implantation and 5.5% in wild-type pig kidney (p<0.0001, B). The proportions of CD68+ glomerular tufts were 96.9% in xenograft 1, 97.8% in xenograft 2, 3.0% in xenograft before implantation, and 4.3% in wild-type pig kidney (p=0.0001, A). The proportions of CD68+ peritubular capillaries were 77.4% in xenograft 1, 43.3% in xenograft 2, 0.4% in xenograft before implantation and 2.0% in wild-type pig kidney (p<0.0001, B). For xenograft 1 and 2, respectively, median densities of CD68+ cells were 5.5 [IQR, 2–8.2] and 9.5 [IQR, 5–14] per glomerular tuft (C), and 2 [IQR, 1–3] and 0 [IQR, 0–0] per peritubular capillary (D). Control densities were below the limit of quantification. The proportions of CD15+ glomerular tufts were 98.7% in xenograft 1, 78.4% in xenograft 2, 6.8% in xenograft before implantation, and 5.5% in wild-type pig kidney (p<0.0001, E). The proportions of CD15+ peritubular capillaries were 56.1% in xenograft 1, 3.0% in xenograft 2, 1.7% in xenograft before implantation, and 1.6% in wild-type pig kidney (p<0.0001, F). For xenograft 1 and 2, respectively, median densities of CD15+ cells were 11.5 [IQR, 6–18.2] and 3 [IQR, 1–6] per glomerular tuft (G) and 1 [IQR, 0–0] and 0 [IQR, 0–0] per peritubular capillary (H). Control densities were below the limit of quantification.

Conclusions: Taken together, these data support roles for both deletion and immune exhaustion in tolerance mediated by liver-specific expression of donor MHC class I in skin graft recipients.

Figure 1.
Background: Genetic modifications have revolutionized xenotransplantation.

Methods: We performed a complete phenotyping of the two-world premiere successful kidney xenografts transplanted to decedent humans. We used a multimodal strategy combining i) morphological evaluation, ii) multiplex immunophenotyping, iii) ultrastructural assessment, iv) gene expression profiling, v) whole-transcriptome digital spatial profiling and cell deconvolution (Figure 1). Xenografts before implantation as well as wild-type pig kidneys were used as controls.

Results: Xenografts revealed early signs of antibody-mediated rejection, circulating IgM and IgG xenoreactive antibodies, and microvascular inflammation with linear capillary deposits of IgM and IgG. Capillary inflammation was mainly composed of intravascular CD68+ and CD15+ innate immune cells, as well as NKp46+ cells. Both xenografts displayed intense von Willebrand factor staining in capillary deposits of IgM and IgG xenoantibodies, and microvascular inflammation with linear IgM and IgG deposits.

Conclusions: This study shows for the first time the evidence for ongoing antibody-mediated rejection in pig kidney xenografts transplanted to humans. These results open avenues for further refinement of pig constructs and pathways to optimize the control of the humoral harm of rejection, for improving xenotransplant outcomes and next-generation clinical trials.
**FULL ORALS**

**O3S_4 BIOENGINEERING OF VASCULARIZED INSULIN-SECRETING ORGANOIDS FOR TYPE 1 DIABETES CELL THERAPY**

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1University of Geneva, Laboratory of Tissue Engineering and Organ Regeneration, Department of Surgery, Geneva, Switzerland; 2Geneva University Hospitals, Cell Isolation and Transplantation Center, Department of Surgery, Geneva, Switzerland; 3University of Geneva School of Medicine, Faculty of Medicine, Geneva, Switzerland; 4Geneva University Hospitals, Division of Transplantation, Department of Surgery, Geneva, Switzerland; 5Institute of Medical Research, Ilia State University, Tbilisi, Georgia, 6University of Geneva, Geneva, Switzerland

**Background:** Lack of donor organs, inflammation and poor vascularization hamper long term outcomes of intraportal islet transplantation. Based on our previous experience with generating islet organoids, we propose an improved strategy to engineer pre-vascularized islet organoids (PVO) composed of dissociated insulin-secreting cells, human amniotic epithelial cells (hAECs) and blood outgrowth endothelial cells (BOECs). PVOs are easily obtained from recipients’ peripheral blood, making them an ideal source of autologous endothelial cells.

**Methods:** PVOs were generated on microwell platforms by combining different ratios of insulin-secreting cells, human amniotic epithelial cells (hAECs) and blood outgrowth endothelial cells (BOECs). BOECs are obtained from recipients’ peripheral blood, making them an ideal source of autologous endothelial cells.

**Results:** Generated PVOs displayed good viability and function, indicating that supporting cells did not impair insulin secretion. 6 out of 7 mice transplanted with the marginal mass of PVOs reversed diabetes and the median time to resolution with normoglycemia was 7 days. PVOs were generated with a survival range of 3 months and IPGTT at 1- and 3-months post-transplant were similar to non-diabetic controls. In contrast, transplantation of the same mass of ICs or Nis did not reverse diabetes. Removal of the PVO grafts led to recurrence of hyperglycaemia within 24h. PVO retrieved grafts presented a bigger β-cell mass and vascularization compared to controls.

**Conclusions:** Here we demonstrate that adding hAECs and BOECs in the islet organoids significantly improved engraftment, leading to prompt reversal of diabetes, indicating that our strategy has the potential to solve the problem of scarcity of donor supply and poor islet engraftment. Furthermore, our approach could be a primordial step toward the engineering of a bioartificial pancreas.

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**O3S_5 EXTRAHEPATIC BILE DUCT ORGANOIDS AS A MODEL TO STUDY ISCHEMIA/REPERFUSION INJURY DURING LIVER TRANSPLANTATION**

Elke Eggenshofer1, Philipp Kreiner1, Hans Schilt1, Edward Geissler2, Stefan Brunner1, Henrik Junger3

1University Medical Center Regensburg, Surgery, Regensburg, Germany

**Background:** Biliary complications are still a major cause for morbidity and mortality after liver transplantation. Ischaemia/reperfusion injury (IRI) leads to disruption of the biliary epithelium. Yet little is known about the underlying molecular mechanism. We introduce a novel model to study the effect of IRI on human cholangiocytes using extrahepatic cholangiocyte organoids (ECOs) cultured organoids. Extrahepatic bile duct tissue was collected during liver transplantation (n=15), and control sections after cholecystectomy (n=5) and stained using in situ-hybridization. ECOs were cultured and expanded from extrahepatic biliary tissue. Multiplex immunofluorescence, in situ-hybridization and qRT-PCR were performed to identify and verify cells being of cholangiocytic phenotype in cultured organoids. IRI was induced by introducing cells to a hypoxic chamber (1% O2) for 48h, followed by reoxygenation. In situ-hybridization and qRT-PCR were performed to study markers of programmed cell death induced by IRI.

**Results:** ECOs formed circular structures recreating a tubular structure similar to that found in the extrahepatic bile duct. Analysis revealed a cholangiocyte phenotype with high expression of EpCam, Sox9, LGR5 & C19R and low expression of albumin & AHH. After hypoxia and even more pronounced after re-oxygenation, ECOs showed increased expression of ADO, HIF-1α and VEGF-α. Expression patterns were similar to those found in the bile duct biopsies.

**Conclusions:** ECOs are in vitro cellular systems that self-organize through mechanisms like those found in vivo. They recapitulate the structure and exhibit similar expression patterns of ADO, HIF-1α and VEGF-α to expression as extrahepatic bile duct during liver transplantation and thus provide a suitable model to study IRI in cholangiocytes after liver transplantation.

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**O3S_6 GENERATION OF 'UNIVERSAL' LOW-IMMUNOGENIC HUMAN PRIMARY CHOLANGIOCYTE ORGANOIDS FOR TREATMENT OF BILE DUCT DISORDERS**

Sandra Petrus-Reuget1, Adrian Baez-Ortega2, Inigo Martincorena2, Kourosh Saeb-Parsy2

1University of Cambridge, Cambridge, United Kingdom, 2Wellcome Trust Sanger Institute, Hinxton, United Kingdom

**Background:** Other than complex surgery or transplantation, there are no current curative therapies for bile duct diseases/cholangiopathies affecting the intra- or extrahepatic biliary tree. We have previously shown that human bile duct epithelial cells can be cultured as 3D organoids to generate mature primary cholangiocyte organoids (PCOs) for the treatment of cholangiopathies. Since the generation of autologous PCOs is likely to remain logistically and economically prohibitive for the foreseeable future, human injection of allogeneic PCOs remains a key outstanding barrier to their clinical translation. We thus aimed to develop ‘universal’ low-immunogenic cholangiocyte organoids for regenerative medicine applications.

**Methods:** After systemic testing of numerous conditions, human leukocyte antigen (HLA) I and II double knock out (DKO)-edited PCOs were generated using CRISPR-Cas9 by dissociating PCOs into single cells, electroporation with the guide-Cas9 complex and sorting for the specific double negative cells. Assessment comparing to parental wild-type (WT) cells was carried out by flow cytometry, functional readouts, co-culture with human peripheral blood mononuclear cells (PBMCs) in vitro, and by engraftment under kidney capsule of immunodeficient mice. Mutational load and CRISPR-driven off-target genetic mutations of parental vs ePCOs was quantified using whole genome sequencing and Nanoseq techniques.

**Results:** The HLA I and II DKO ePCOs generated a mature PCO phenotype demonstrated by flow cytometry and functional analyses. Immunomodulation in vitro by co-culture with PBMC experiments show that ePCOs have a reduced immunogenicity compared to WT cells. Additionally, off-target analysis and mutagenesis burden of parental vs ePCOs do not show CRISPR-driven off-target sites nor excess mutation in ePCOs. Additional experiments are ongoing to assess the immune response in vivo using humanized mouse models.

**Conclusions:** Human PCOs lacking HLA I and HLA II can be successfully generated using a CRISPR-Cas9 approach. ePCOs retain the phenotypic characteristics of mature PCOs and are reduced immunogenically when co-cultured with PBMC compared to parental cells. Genomic data show no CRISPR-driven off-target mutational burden in ePCOs.

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**O3S_7 MODELING KIDNEY FIBROSIS AND EXPLORING THE ANTI-FIBROTIC ACTIVITY OF MEMBRANE PARTICLES GENERATED FROM MESENCHYMAL STROMAL CELLS IN KIDNEY ORGANOIDS**

Shanghai Li1,2, Zhaoyu Du1, Sander Korevaar1, Amanda Bas-Cristóbal Menéndez1, Hui Liu1, Quincy Nlandu2, Thierry van den Bosch3, Carla Baan1, Marlies Reinders1, Martin Hoogduin2

1transplant institute, Rotterdam, Netherlands, 2transplant institute, Rotterdam, Netherlands, 3Department of Pathology, Rotterdam, Netherlands

**Background:** Ischemia, inflammation and aging drive kidney fibrosis, which leads to loss of function. Human induced pluripotent stem cell (iPSC) derived kidney organoids may represent a tool for studying fibrosis and the development of anti-fibrotic medicines. Mesenchymal stromal cells (MSC) have anti-fibrotic properties, but use of these cells has some challenges such as poor biodistribution and short life-span after administration. Nanosize membrane particles (MP) generated from the membranes of MSC could be an alternative. Hence, the aim of this study was to set up a kidney organoid fibrosis model and explore the anti-fibrotic activity of MSC-derived MP.

**Methods:** Kidney organoids were exposed to 1% O2 for 48h and 100ng/ml IL-1β for 9 days at day 12 of differentiation. Subsequently, organoids were cultured under standard conditions for 14 days. MP generated from 0.5-106 MSC were added to the medium concurrently with fibrosis-inducing stimulations for 4 days or added until the end of the experiments for 14 days.

**Results:**
**FULL ORALS**

### Transplant Plus: Regenerative therapies and Xenotransplantation

**Results:** Immunohistochemistry confirmed that kidney organoids developed PDL1+ glomeruli, Vimentin+ proximal and Ecad+ distal tubular structures. After fibrosis-inducing stimulations, collagen type 1A1+ (COL1A1) and transforming growth factor beta (TGF-β) mRNA were upregulated, and kidney structures were partly replaced by COL1A1+ and α-smooth muscle actin+ (α-SMA) fibrosis-driving cells. Early treatment with MP inhibited fibrosis processes through inhibition of TGF-β expression. Treatment at later phases was not effective.

**Conclusions:** We developed an in vitro human kidney organoid fibrosis model that recapitulates the key features of kidney fibrosis. MP demonstrated an anti-fibrotic effect at the early phase of the fibrosis process.

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### OS3_8

**HLA-DQ EPLET MISMATCH LOAD MAY IDENTIFY KIDNEY TRANSPLANT PATIENTS ELIGIBLE FOR TACROLIMUS WITHDRAWAL WITHOUTDSA FORMATION AFTER MSC THERAPY**

Suzanne Bezstarosti1,2, Soufian Meziyeh3, Marlies Reinders3, Kim Bakker4, Koen Groeneweg5, Dave Roelen6, Jesper Kers7, Johan de Fijter7, Sebastiaan Heid5

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**Background:** Recently, the randomized Triton study demonstrated that mesenchymal stromal cell (MSC) therapy could facilitate early tacrolimus withdrawal in living donor kidney transplant (KTx) recipients. Here, we analyzed de novo donor-specific HLA antibody (dnDSA) formation in context of the degree of HLA eplet mismatches (MM).

**Methods:** All patients underwent a first, living-donor KTx and received alentumumab induction, steroids, tacrolimus and everolimus. Despite excess dnDSA formation in the MSC-arm of the study, the evolution of eGFR (CKD-EPI) and proteinuria were comparable 2 years post-Tx. All dnDSA were complement-binding and three of them died, one was re-transplanted. 21 recipients of kidney grafts (22 %) showed delayed graft function, three more showed primary non-function. In all other recipients immediate organ function was good, there was no indication that organ function was negatively impacted by the SARS-CoV-2 infection of the donor.

**Conclusions:** These findings support the early experience from other countries that such organs do not pose a major immediate risk for the transplant recipients. Nevertheless, a close follow-up is needed and experiences especially regarding lung transplantation with SARS-CoV-2 positive grafts are still lacking.

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### OS4_1

**SHORT-TERM OUTCOME OF TRANSPLANT RECIPIENTS WITH SARS-COV-2-POSITIVE ORGAN DONORS IN GERMANY**

Ana Paula Barreiros1, Klaus Böhler2, Axel Rahmel3

1Deutsche Stiftung Organtransplantation, Frankfurt, Germany

**Background:** The SARS-CoV-2 pandemic had a major impact on solid organ transplantation in many countries. A significant decline of performed transplantations was described e.g. in Spain and Italy. Until March 2022, SARS-CoV-2-positive organ donors were excluded from organ donation in Germany because of the uncertainty regarding the transmission of the virus from the donor to the recipients. First results from other countries indicated that organs from carefully selected SARS-CoV-2-positive donors could be transplanted with acceptable risk for the recipients.

**Methods:** From February 25th to December 31st 2022 all SARS-CoV-2-positive donors from whom at least one organ was successfully transplanted to a recipient were identified. An organ donor was identified as SARS-CoV-2 positive, if at least one PCR test from the lower or upper airways was positive in the 14 days prior to organ removal. The follow-up was done within the framework of the vigilance and surveillance system of the German procurement organization (Deutsche Stiftung Organtransplantation/DSO).

**Results:** During the study period, 163 organs (22 hearts, 3 lungs, 44 livers and 94 kidneys) were transplanted from 57 SARS-CoV2-PCR-positive donors to 162 recipients. In none of the cases a transmission of the virus from the donor to any of the recipients was detected in a follow-up period of 14 days. One patient developed an acute pulmonary failure after heart transplantation and died, four recipients of a liver graft suffered a primary non-function of the liver, three of them died, one was re-transplanted. 21 recipients of kidney grafts (22 %) showed delayed graft function, three more showed primary non-function. In all other recipients immediate organ function was good. There was no indication that organ function was negatively impacted by the SARS-CoV-2 infection of the donor.

**Conclusions:** These findings support the early experience from other countries that such organs do not pose a major immediate risk for the transplant recipients. Nevertheless, a close follow-up is needed and experiences especially regarding lung transplantation with SARS-CoV-2 positive grafts are still lacking.

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### OS4_2

**KIDNEY TRANSPLANT RECIPIENTS BECOME LESS ADHERENT TO PREVENTIVE MEASURES AFTER SARS-COV-2 VACCINATION AND AFTER AWARENESS OF ANTIBODY RESPONSE**

Sophie Frölich1,2, Pim Bouwmans3, A. Lianne Messchendorp1, Heanne Verwoert1, Pietrya Nieuwkerk1, Marc Hemmelder4, Ron Gansevoort5, Luuk Hilbrands1, Marlies Reinders1, Jan-Stephan Sanders5, Frederike Bemmann1, Suzanne Geerlings1

1Amsterdam UMC, location AMC, Amsterdam, Netherlands, 2UMC+, Maastricht, Netherlands, 3University Medical Center Groningen, Groningen, Netherlands, 4Radboud University Medical Center, Nijmegen, Netherlands, 5Erasmus MC, Rotterdam, Netherlands

**Background:** Kidney transplant recipients (KTRs) were advised to tightly adhere to government recommendations to curb the spread of SARS-CoV-2 because of a high risk of morbidity and mortality and decreased immunogenicity after vaccination. The aim of this study was to analyze the change in adherence to preventive measures after vaccination and awareness of antibody response, and to evaluate its effectiveness.

**Methods:** Questionnaires were sent to 3531 KTRs enrolled in the Dutch RECOVAC studies, retrospectively asking for adherence to nine preventive measures on a 5-point Likert scale before and after SARS-CoV-2 vaccination and after awareness of antibody response. Blood samples were collected 28 days after the second vaccination. Antibody response was categorized as non-responder (≤50 BAU/mL), low-responder (>50 ≤300 BAU/mL) or high-responder (>300 BAU/mL) and shared with participants as a correlative of protection. Adherence before and after vaccination were compared by the Wilcoxon signed rank sum test. Logistic regression analysis was performed to estimate the association between antibody response and adherence, and adherence on acquiring SARS-CoV-2 infection.

**Results:** In 2939 KTRs (83%) who completed the first questionnaire on adherence to preventive measures, adherence was higher than before after SARS-CoV-2 vaccination (4.56, IQR 4.11-4.78 and 4.22, IQR 3.67-4.67, p<0.001). Adherence after awareness of antibody response was analyzed in 2399 KTRs (82%) of whom also blood samples were available, containing 949 non-responders, 500 low-responders and 950 high-responders. Compared to non-responders, low- and high-responders reported lower adherence (Figure 1). Higher adherence was associated with lower infection rates before and after vaccination (OR 0.67 [0.51-0.91], p=0.008 and OR 0.48 [0.28-0.86], p=0.010).

**Conclusions:** To the best of our knowledge, we are the first to show that adherence decreased after SARS-CoV-2 vaccination and in KTRs who were aware of a subsequent antibody response compared to those without. Moreover, preventive measures in this vulnerable group are effective, regardless of vaccination status.
Risk of transmission of infectious disease and prevention

Figure 1. Forest plot for non-adherence to preventive measures after awareness of antibody response by group, taking the non-responder group as reference (N=949).

**Result:**

- **Conclusions:**
  - Our national experience to date indicates that organs other than lungs can be considered for transplantation from appropriately assessed SARS-CoV-2 NAT-positive deceased donors. There is no evidence of graft-related transmission of infection. A complete data set for recipients of all organ types, with follow-up to or beyond 2 years is being collated; available data does not indicate there is a cause for concern in terms of graft and recipient outcome. It is hoped that such data will help consolidate guidance and increase organ utilization as we transition to the recovery phase of the COVID-19 pandemic.

OS4_4 TWO-YEAR FOLLOW-UP OF LIVER GRAFTS FROM COVID-19 DONORS

**Background:**

SARS-CoV-2 infections complicated by thrombosis and secondary sclerosing cholangitis were reported; however, solid non-lungs transplantation from COVID-19 donors showed excellent early results, but medium- to long-term data are lacking. We aimed to describe the outcome of our LT patients (pts) who received a graft from COVID-19 donors.

**Methods:**

We consecutively enrolled all pts transplanted in our Center from 11/2020 to 03/2022 who received a liver graft from COVID-19 donors. Pts underwent preoperative liver biopsy and magnetic resonance cholangiopancreatography (MRCP) at least 1 year from LT. Follow-up was closed in January 2023.

**Results:**

In the study period, among 213 adult LTs, 12 (5.6%) received a COVID-19 donor (11 active and 1 resolved COVID-19)1. Recipients’ and donors’ characteristics are reported in Table 1. None of the pts developed COVID-19 after LT. Two recipients tested SARS-CoV-2 RNA positive in nasopharyngeal swab immediately before LT and one was treated with sotrovimab on day-1 after LT. Eleven pts underwent end-to-end biliary anastomosis and 1 bile duct discrepancy, and 2 caliber changes <50% at anastomotic level (without cholestasis and which were not treated). Ten pts underwent liver biopsy (median time from LT 573 days, IQR 290-648) which showed no visible abnormalities in 8, 1 donor-recipient’s bile duct size discrepancy, and 2 caliber changes <50% at anastomotic level. One pt underwent successful hepatic artery thrombectomy at day-1. Eleven pts underwent protocol MRCP (median time from LT 573 days, IQR 290-648) which showed no visible abnormalities in 8, 1 donor-recipient’s bile duct size discrepancy, and 2 caliber changes <50% at anastomotic level.

**Conclusion:**

After a median time from LT of 1.8 years, 11/12 pts who received a liver graft from COVID-19 donors are alive, without evidence of SARS-CoV-2 RNA transmission. Protocol MRCP and liver biopsy did not show signs of biliary or fibrosis supporting the safe utilization of COVID-19 donors to expand the donor pool and reduce the waiting list mortality.

Peghin M, Grossi PA. J Hepatol. 2022

<table>
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<tr>
<th>Table:</th>
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<tr>
<td><strong>Recipient s n = 12</strong></td>
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<tr>
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<tr>
<td>Sex, male</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Model for end stage liver disease at LT</td>
</tr>
<tr>
<td>SARS-CoV-2 vaccination before LT</td>
</tr>
<tr>
<td>SARS-CoV-2 IgG positive before LT</td>
</tr>
<tr>
<td>SARS-CoV-2 RNA swab positive at LT</td>
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<tr>
<td>SARS-CoV-2 RNA BAL positive at LT</td>
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<tr>
<td>Donor risk index</td>
</tr>
<tr>
<td>SARS-CoV-2 RNA PCR negative on liver biopsy</td>
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<tr>
<td>Hypothemic machine perfusion</td>
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<td>Normothermic machine perfusion</td>
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Table 1. Pts and donors’ characteristics at liver transplant. *The COVID-19 resolved donor was not tested.
**OS4_5** CELLULAR HUMORAL MEMORY PROTECTS TRANSPLANT RECIPIENTS FROM EMERGING SARS-COV-2 VARIANTS OF CONCERN THAT RESIST CIRCULATING NEUTRALIZING ANTIBODIES

Maxime Espié1, Xavier Charmetant1, Ilies Benotmane1, Floriane Gallais2, Katia Lefsihane1, Veronique Barateau1, Thierry Defrance, Emmanuel Morelon1, Samira Fafi Kremer1, Sophie Caillaud1, Olivier Thauvat1
1Lyon University Hospital-INSERM U1111, Lyon University Hospital-INSERM U1111, Lyon, France, 2CHRU Strasbourg, Strasbourg, France

**Background:** The protection of vaccinated KTRs against COVID-19 depended upon the generation of neutralizing antibodies (Nabs). However, the decrease of antibody titers with time as well as the emergence of variants of concern (VOC) create a situation in which even KTRs that responded to vaccine are left without serological protection after a few months.

**Methods & Results:** The severity of 211 infections with the Omicron BA.1 VOC, diagnosed in a cohort of vaccinated KTRs, was stratified according to i) the peak of Nabs, and ii) the Nabs status immediately prior the omicron infection. As expected, responders to the vaccine who maintained high titers of NABs at the time of BA.1 infection never (0/22) developed severe disease, while patients who did not respond to vaccination (never had detectable Nabs) developed severe infections in 31/110 (28%). Surprisingly, among the 59 patients who initially responded to vaccination but had undetectable Nabs at the peak of Nabs, and immediately prior the omicron infection, 14/59 (24%) developed severe infections in 31/110 (28%).

**Conclusion:** We concluded that in contrast with the humoral serological memory that goes fading due to a decrease in Nabs titer and a narrowing of the Ig repertoire, a diverse pool of memory B cells persists over time offering an efficient long term protection to KTRs against VOC.

**OS4_6** THE HUMORAL RESPONSE TO COVID-19 VACCINATION IS PREDICTIVE OF SURVIVAL AFTER SARS-COV-2 INFECTION

Markus Hovda1, Karsten Midtvedt1, Fridjof Lund-Johansen2, Kristian Heldal1, John Torgils Vaage1, Ludvig Munthe1, Anders Asberg1
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**Background:** Kidney transplant recipients (KTR) are more susceptible to infections and prior to introduction of SARS-CoV-2 vaccines had a very high mortality from COVID-19. The coronavirus vaccination programme aimed to reduce the spread and severity of COVID-19, especially in high-risk groups. KTR had a reduced humoral vaccine induced response and repeated vaccinations were warranted. In a national cohort, we here evaluate the monitored effect of humoral vaccine response on risk of SARS-CoV-2 infection and COVID-19 related death and complications.

**Methods:** All KTR in Norway who were alive with a functioning graft at the beginning of the pandemic (February 20, 2020) were included in the analysis. Event history analysis of vaccination, monitored vaccine response, infection with SARS-CoV-2, COVID related and unrelated death was analysed using a multi-state, competing risk model approach combined with Cox proportional hazard regression. Events after November 11, 2022 were right-censored. Vaccine response was determined towards the receptor binding domain (RBD) of SARS-CoV-2 RBD BAU/mL above threshold was evaluated within the range of 5 to 5000 BAU/mL.

**Results:** A total of 3607 KTR (64% male, aged 58±14 years) were included, of which 38% had received a kidney from a living donor. During the study period, 26% (n = 1018) of KTR developed breakthrough infection. In total 7% (n = 74) died due to COVID-19 (63 following vaccination). Cumulative incidence of severe and mild breakthrough infection was 28% (n = 1018) of vaccinated KTR developed breakthrough infection. In total 7% (n = 74) died due to COVID-19 (63 following vaccination). Cumulative incidence of severe and asymptomatic BTI, respectively; mBc [21-104.75], p=0.001 for severe and asymptomatic BTI, respectively; mBc [15.75-88.38], p=0.004) for severe and mild BTI, respectively.

**Conclusions:** In KTR, humoral vaccine response does not protect against infection with SARS-CoV-2. Increased vaccine response, assessed by IgG anti-RBD BAU/mL level after vaccination, protected against COVID-related death. No excess post-COVID mortality was detected in KTR.
FULL ORALS

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Conclusions: Our data has relevant clinical implications for immune-risk stratification against COVID-19 and may guide preventive strategies in SOT. Here we show the particular relevance of measuring mBC and memory T cells producing IL-2 to identify patients more likely to respond to a booster vaccine and those at high risk of developing severe forms of COVID-19.

Managing myself after transplantating— a fulltime job

OS1 SYMPTOM BURDEN IN KIDNEY TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL STUDY

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1University Medical Center Groningen, Nephrology, Groningen, Netherlands
2University Medical Center Groningen, Health Sciences, Groningen, Netherlands

Background: Kidney transplant recipients (KTR) often report a poor health-related quality of life (HRQoL), which may partly be attributable to symptoms caused by kidney disease or treatment after kidney transplantation. We therefore aimed to assess symptom prevalence, symptom distress, and symptom burden, which is a combination of prevalence and distress, in a large cohort of KTR. Furthermore, we aimed to assess associations of symptom burden with clinical outcomes, such as HRQoL, medication adherence, depression, and societal participation.

Methods: Data of KTR at least 6 months after transplantation, enrolled in the TransplantLines Biobank and Cohort Study between June 2015 and February 2022, were used. Symptoms were assessed using the revised Modified Transplant Symptom Occurrence and Distress Scale (MTSOSD-59R). RIDIT analyses, an effective technique to analyse ordered categorical data, was performed to calculate RIDIT scores of symptom prevalence and symptom distress.

Results: We included 936 KTR (39% female; mean age 56 ± 13 years) among 3172 KTR. Tiredness, bruises, and lack of energy were the most prevalent symptoms (Figure 1). Menstrual problems (female), impotence (male), and joint pain were the most distressful symptoms. Bruises, lack of energy and tiredness were the most burdensome symptoms. In linear regression analyses, higher burden scores were associated with both lower mental and physical HRQoL (β-2.29, 95% CI -3.32 to -2.76, p<0.001; β-2.29, 95% CI -2.96 to -2.03, p<0.001; respectively; Table 1). In regression analyses, higher burden scores were strongly associated with medication non-adherence, depression, and less societal participation. All results remained significant after adjustment for potential confounders.

Conclusions: Symptoms after transplantation are a major clinical problem among KTR, and the burden of symptoms is strongly associated with lower HRQoL, less medication adherence, more depression, and less societal participation. Our findings highlight the need to reduce symptom burden in KTR, for instance by individualizing immunosuppression.

Table 1 | Linear regression analyses of squared root symptom burden with health-related quality of life as dependent variable in 740 kidney transplant recipients

<table>
<thead>
<tr>
<th>Model</th>
<th>Physical component scale</th>
<th>Mental component scale</th>
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<tr>
<td></td>
<td>B (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Crude</td>
<td>-3.00 (2.32 to -2.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 1</td>
<td>-3.03 (2.30 to -2.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>-3.00 (2.32 to -2.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 3</td>
<td>-2.94 (2.32 to -2.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 4</td>
<td>-2.93 (2.39 to -2.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 5</td>
<td>-2.91 (2.35 to -2.58)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: 95% CI 95% confidence interval. Model 1: adjusted for age and sex; model 2: model 1 + time since transplantation; model 3: model 2 + psychological factors, physical health, and adherence; model 4: model 3 + haemoglobin, WFR, albumin and NT-proBNP; model 5: model 4 + tacrolimus use, cyclosporine use, prednisone or prednisolone use and protein-pump inhibitor use.

Figure 1 | RIDIT scores of symptom prevalence and symptom distress at 60 symptoms of the MTSOSD-59R

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OSS_2 THE LONGITUDINAL DEVELOPMENT OF TRANSPANT SPECIFIC WELL-BEING AND SYMPTOMS FROM PRE-TRANSPLANT TO FIVE YEARS AFTER HEART TRANSPLANTATION

Marita Dalvindt1,2, Annika Kisch1, Shahab Nozhoor1, Anna Forsberg1
1Lund University, Health Science, Lund, Sweden, 2Lund University, Thoracic surgery, Lund, Sweden

Background: The Swedish multicentre “Self-management after thoracic transplant” study (SMATT) has until now produced 23 papers, two doctoral theses and numerous master theses, and the main outcome was to identify symptom patterns and barriers for self-management among heart and lung recipients. Findings have revealed that the post-transplant adaptation is challenging involving an extensive symptom burden, fatigue, and chronic pain. The design has either been cross-sectional or qualitative and longitudinal. Now it is time to present the first data from the longitudinal cohorts. Thus, the aim of this study was to analyse and present prospective data on chronic pain, fatigue and transplant specific wellbeing from pre-transplant to five years after heart transplantation (HTX).

Methods: This prospective study involves the first 31 heart recipients, 80 % men and 20 % women, followed for five years from pre-transplant to five years after heart transplantation. The inclusion criteria were being a heart or lung recipient transplanted at either of the two Thoracic transplant centres in Sweden performing thoracic transplantation. Swedish speaking, not hospitalised nor in treatment of on-going acute rejection and mentally lucid. We used non-parametric statistics to analyse the Organ Transplant Symptom and Well-being Instrument, the Pain-O-Meter and the MF1-19 measuring fatigue.

Results: Chronic pain for two years after HTX compared to pre-bx (p=0.054) and even worse after three years (p=0.017) involving severe joint and muscle pain and foot pain. There were no differences in transplant specific well-being after three and four years compared to pre-bx. It takes one year to experience decreased mental fatigue. The level of mental fatigue is then reman stable until five years post-transplant when the fatigue is equal to pre-transplant again.

Conclusions: The findings confirm previous results from the SMATT-study showing that chronic pain is a major concern after HTX along with fatigue. It is obvious that the pain problems accelerate two-four years post-transplant.

Transplant specific well-being is the same as pre-transplant three to four years after HTX. Chronic pain and fatigue remain the most prominent concerns up to five years after heart transplantation and needs specific attention from the transplant professionals.

OSS_3 QUANTITATIVE FINDINGS FROM THE COMPASSIONATE MINDFUL RESILIENCE PROGRAMME IN ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE (THE COSMIC STUDY)

Anna Wilson1, Clare Mckeaveney1, Claire Carswell1, Karen Atkinson1, Stephanie Julie Burton1, Clare Mcveigh1, Lisa Graham-Wiseman1, Erika Jaakskelainen1, William Johnstone1, Daniel O’Rourke1, Joanne Reid1, Soham Raj1, Ian Walsh2, Helen Noble1
1Queen’s University Belfast, Belfast, United Kingdom, 2MindfulnessUK, Taunton, United Kingdom, 3University of Oulu, Oulu, Finland, 4Northern Ireland Kidney Patients Association, Belfast, United Kingdom, 5Northern Ireland, Kidney Patients Association, Belfast, United Kingdom

Quantitative findings from the Compassionate Mindful Resilience Programme in Adult Patients with Chronic Kidney Disease (The COSMIC Study)

Background: People with advanced kidney disease face multiple challenges associated with the disease and associated treatments including difficult symptomst such as anxiety and depression1. This study aimed to examine the initial effects of the Compassionate Mindful Resilience (CMR) programme for patients with stage 4 or 5 chronic kidney disease including those who had received a kidney transplant, in collaboration with Kidney Care UK (KCUK).

Methods: A single group, quasi-experimental study was conducted. Participants with stage 4 or 5 chronic kidney disease, or post-transplant, were recruited to take part in the CMR programme via a KCUK email newsletter and their patient support Facebook group. Power analysis was used to estimate an adequate sample size of 75 participants. 84 participants completed the programme. Most were female (66%) and post-transplant (63%). As compared to pretest scores, participants reported a reduction in anxiety and depression and improvement in self-com- passion, mindfulness, resilience, and wellbeing.

Conclusions: Our findings suggest that the CMR programme had the potential to improve psychological outcomes among people with advanced kidney disease.


OSS_4 MEDITERRANEAN DIET AND METABOLIC SYNDROME: A DIETARY INTERVENTION STUDY TO REDUCE METABOLIC SYNDROME RISK AFTER HEART TRANSPLANTATION

Michelle Marinoni1, Verónica Ferrara1, Giulia Valdi2, Chiara Nalli1, Concetta Di Nola2, Sandro Spongì2,3, Giovanni Benedetti4, UgoLívi5,6, Maria Parpigno, 7Igor Vendramin8
1University of Udine, Cardiothoracic Department, Udine, Italy, 2University of Udine, Department of Medicine , Udine, Italy

Background: heart-transplant (HTx) patients are inclined to develop the Metabo-litic Syndrome (MetS), mainly due to the side effects of immunosuppressive therapy. The Mediterranean Diet (MD) has proven to be effective preventing MetS in general population. Thus, the aim of the study was to assess the impact of a dietary intervention based on MD principle in HTx patients with high risk of MetS.

Methods: at baseline (T0), after 6 (T1), and 12 months (T2) patients were invited to complete a 4-day dietary record (AdDR) to bring at the scheduled visits. During the meetings, a nutritionist detected dietary habits and provided personalized nutritional advices, monitoring the improvement during the follow-ups. At each timepoint clinical, anthropometric and body composition data were assessed. To estimate nutrient intakes from 4-dDR was used The Italian Food Composition Database (BDA). The study was approved by the Regional Ethics Committee.

Results: at T0, 50 patients were enrolled, 30 of them have reached the T1, and 17 the T2. The mean age of the subjects was 57 ± 13 years (males: 87%). During the study period, dietary habits showed: a significant increase of the MD score [T0=4.5 (3.0 – 5.0) vs. T2=6.0 (4.0 – 7.0); p=0.004]; a significant decrease of daily total energy intake and, in particular, of total fats and saturated fatty acids [T0=18.5 (15.6 – 24.8) g/day vs. T1=16.3 (12.6 – 18.9) g/day; p=0.001]; a significant increase of fiber, vitamin E, and DHA intakes between T0 and T2. Together with the improvement of dietary habits, body composition showed already at T1 a significant decrease of fat mass (%) [T0=22.3 ± 7.7 vs. T1=18.3 ± 7.8; p<0.001], and a significant decrease of fat free mass [T0=7.7 ± T1=81.4±8.2; p=0.002]. Furthermore, MetS diagnosis criteria improved at each timepoint and its prevalence showed a important reduction from 50% at T0, to 37% at T1, to 29% at T2.

Conclusions: the dietary intervention providing personalized dietary advices exerted multiple beneficial effects on MD adherence, body composition, and MetS criteria of HTx patients.

OSS_5 THE EFFECT OF SYSTEMCHANGE™ ON MEDICATION ADHERENCE IN KIDNEY TRANSPLANT RECIPIENTS: A RANDOMIZED CLINICAL TRIAL

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Background: The SystemCHANGE™ intervention harnesses patients’ established daily routines/habits, environment, and important others, as possible solutions that are reocurring and thus reliable systems that could support medication taking to become a dependable routine/habit. The aim of this study was to evaluate the effect of a six-month SystemCHANGE™ intervention compared to a six-month attention-control education intervention on medication adherence and quality of life in kidney transplant recipients. A six-month maintenance phase where the intervention was withdrawn was also evaluated.

Methods: A randomized controlled trial single-blind (participants) study design was used. After screening for 3 months using electronic monitoring, participants with medication adherence (>85) were excluded from the study while those with medication nonadherence (<85) were randomized, the intervention group (n=42) received the 6-month SystemCHANGE™ intervention and the attention control group (n=42) received the 6-month patient education intervention. The maintenance phase continued for six months afterwards. Electronic monitoring was used to assess adherence.

Results: At the completion of the six-month intervention phase, there was a statistically significant difference in medication adherence between the SystemCHANGE™ group (median 0.97, IQR 0.93 -0.98) and attention control (median 0.81, IQR 0.71-0.87) groups (U=2.843, p<0.004, Table 1, Figure 1). There was no difference in the quality of life between groups (p>0.05).

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Managing myself after transplanting—a fulltime job

Conclusion: This study, which had a strong research design, showed that the SystemCHANGE™ intervention was effective in improving patients' medication adherence and outcomes.

Table 1. Comparison of in-group and intergroup adherence levels

<table>
<thead>
<tr>
<th>SystemChange™</th>
<th>Attention control</th>
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<tbody>
<tr>
<td>N X ± SD</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Baseline</td>
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</tr>
<tr>
<td>6 months</td>
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</tr>
<tr>
<td>12 months</td>
<td>20</td>
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</table>

Test value: 31.924, p = 0.105

Conclusions: Selection bias appears to have occurred in recruitment of the experimental group. This group benefited from the intervention self-management skills improved. Preliminary results suggest that among recipients who have difficulties with self-management this intervention may be of added value.

NURSE-LED SELF-MANAGEMENT SUPPORT AFTER ORGAN TRANSPLANTATION — A MULTICENTER, MULTI-ORGAN STEPPED WEDGE RANDOMIZED CONTROLLED TRIAL

Regina van Zanten1, Monique van Dijk1, Joost van Rosmalen2, Denise Beck1, Robert Zietse1, Anneloes van Staa1, Emma Massey3

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Background: After organ transplantation effective self-management skills are essential to deal with medical, emotional and role challenges and for optimal clinical outcomes. However, effective interventions to support post-transplant self-management outcomes are lacking. The aim of this study was to implement and test effectiveness of a nurse-led intervention to promote self-management skills among heart, kidney, liver and lung transplant recipients in comparison to standard care.

Methods: This multi-centre stepped-wedge randomized controlled trial was performed at 6 departments of 5 University Medical Hospitals between September 2020 and November 2022. All departments started in the control phase and after the departments were randomly assigned to a start date to commence the experimental group. Before starting the experimental phase the nurse practitioners were trained in delivering the intervention. Patients in the control group received care as usual and completed questionnaires at baseline (T0) and after 6 months (T1). Patients in the experimental group received standard care plus the ZENN intervention and the same questionnaires at T0 and T1. The primary outcome was the Skills and technique acquisition scale of the Medcare Telemonitoring and treatment at home during the pandemic, we implemented the SelfCare after Renal Transplantation (SeCReT-box) and a smartphone application (Luscii®) with a custom made protocol and integration to the electronic patient file (HXK® by Chirop). In this study we evaluated uptake and use of this home-monitoring system after kidney transplantation.

Methods: We performed a retrospective analysis of enrollment into the home-monitoring program. The SeCReT-box contained medically certified devices such as a thermometer, pulse-oximeter, weighing scale and blood pressure monitor. All de novo kidney transplant recipients were considered eligible for inclusion, without upfront exclusion criteria. The protocol in Luscii® included measurements (SeCReT-box), questionnaires (on wound healing, pain, skin frequency, smoking, sexual problems, adherence via BAASIS®) and a non-inferiority confirmed, superiority not significant). Medical time dedicated to medical workload, economic saving and quality of life.

Results: Six hundred and fifty eight KTR have been randomized so far with 330 of them having a follow-up of 2 years. Among all KTR approached to participate in the study, 37% were not included mainly due to the impossibility to access Internet (44%) or to masterize the app (36%). After randomization, 27% of KTR were considered as non compliant in adequately using Ap'Telecare®. Over the 2 years study duration, graft dysfunction occurred in 16% and 18% of KTR in the control (Ap'Telecare®) and conventional arm, respectively (RR 0.87 (0.56 ; 1.38), non-inferiority confirmed, superiority not significant). Medical time dedicated to handling daily lab results was decreased by a factor 3 for KTR using Ap'Telecare®. Rates of unplanned consultations and hospitalisations were reduced by 26% (p<0.003) for patients using Ap'Telecare® respectively (p<0.003).

Conclusions: This preliminary report of Ap'Tx suggest that a partial and reasonable remote follow-up of selected KTR is feasible, safe and logistically beneficial. Determining the nature of factors associated with a wider implementation of Ap'Telecare® is underway.

UPTAKE OF HOME-MONITORING AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE ANALYSIS

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Background: Innovations in telemedicine, such as teleconsultations and home-monitoring of clinical parameters, are rapidly developing in the field of transplantation, accelerated by the COVID-19 pandemic. In order to facilitate monitoring and treatment at home during the pandemic, we implemented the SelfCare after Renal Transplantation (SeCReT-box) and a smartphone application (Luscii®) with a custom made protocol and integration to the electronic patient file (HXK® by Chirop). In this study we evaluated uptake and use of this home-monitoring system after kidney transplantation.

Methods: We performed a retrospective analysis of enrollment into the home-monitoring program. The SeCReT-box contained medically certified devices such as a thermometer, pulse-oximeter, weighing scale and blood pressure monitor. All de novo kidney transplant recipients were considered eligible for inclusion, without upfront exclusion criteria. The protocol in Luscii® included measurements (SeCReT-box), questionnaires (on wound healing, pain, skin frequency, smoking, sexual problems, adherence via BAASIS® and/or Luscii®) and a non-inferiority confirmed, superiority not significant). Medical time dedicated to medical workload, economic saving and quality of life.

Results: A total of 177 patients underwent kidney transplantation of which 167 (94% of all recipients) initiated the home-monitoring program, of which 155 used both the SeCReT-box and Luscii®. 12 patients used only the SeCReT-box, mainly due to digital illiteracy or lack of a smartphone, and wrote their measurements on paper. Of the 167 recipients that initiated home-monitoring, only 4 (2.4%) stopped using the SeCReT-box and/or Luscii® deliberately. Currently, there are 142 active users, 8 recipients stopped due to graft failure, 3 recipients died and 10 recipients stopped because they were referred back to their local hospital. In all, 9 of 177 recipients (5.1%) could not start, or stopped home-monitoring deliberately. An in-depth analysis of usage is ongoing.

Conclusions: Uptake and continued use of home-monitoring was very high (95%) among this varied group of kidney transplant recipients. Further analysis is needed on barriers and facilitators of its use, in order to reach a more widely adopted use.
**FULL ORALS**

**OS6.1** Improving outcomes of end-stage heart: instead of MCS to the long-term

**5-YEAR OUTCOME AFTER CONTINUOUS FLOW LVAD WITH FULL-MAGNETIC VS HYBRID LEVITATION SYSTEM: RESULTS OF AN ALL-COMERS MULTICENTER REGISTRY**

Alessandra Francica1*, Antonio Loforte2, Matteo Attisani1, Massimo Maiani1, Attilio Isacovi3, Teodora Nisi4, Marina Comisso5, Amedeo Terzi5, Michele De Bonis1, Igor Vrendamini5, Massimo Boffini6, Francesco Musumeci1, Davide Pacini1, Francesco Onorati1

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**Background**: Despite its withdrawal, hundreds of patients are still supported with HeartWare(HW) and a consensus about the long-term management of these patients is still questioned. Published data have focused on short-term outcome. It is the aim of this study to analyse mid-term survival and freedom from major complications in a real-world population supported with HW and HeartMate3 (HM3).

**Methods**: From 2010 to 2022, the MIRAMACS Italian Registry enrolled all-comer patients requiring third generation LVAD support (HM3 or HW) at seven Cardiac Surgery Centers. Adverse events were defined according to INTERMACS definitions. A Cox-regression analysis adjusted for preoperative and postoperative confounders was performed to compare survival and freedom from major adverse events at 5 years of follow-up.

**Results**: A total of 447 patients were implanted with LVAD because of end-stage heart failure: 214 HM3 and 233 HW. The two populations differed in age, heart failure etiology, body surface area, renal and hepatic dysfunctions, degree of pulmonary hypertension. Periprocedural mortality (14% vs 9% for HM3 vs HW; p=0.1) and most of post-operative complications rates were similar between the two groups. The overall survival at 5 years was higher in HM3 patients (64.1% vs 42.6% for HM3 vs HW; p=0.004) (Figure). The Cox-regression analysis adjusted for major confounders showed an almost doubled risk for mortality (HR 1.5 [1.2-1.9]; p=0.031), and a more than doubled risk for both ischemic stroke (HR 2.08 [1.06-4.08]; p=0.033) and hemorrhagic stroke (HR 2.6 [1.3-4.9]; p=0.005) in patients supported by HW. Moreover, HW patients experienced a higher rate of pump thrombosis (3.9% vs 0.5%; p<.001). Subanalysis in Bridge-to-Transplant reported similar cumulative survival and freedom from adverse events, though time to transplant was shorter in HW (32.2 vs 49.1 months; p=0.001). In Destination Therapy, 5-years cumulative survival (61.8% vs 34.5% p=0.038) reflecting a change in medical practice (Figure 1A). At transplant, recipients had a worse kidney function (estimated glomerular filtration rate ≤ 60 mL/min/1.73 m2: old scheme = 28.6%; new scheme: 45%, p < 0.001), and were more likely to be on ECMO support (33.5% compared to 28.1%; p = 0.038), reflecting the prioritization of more severe patients (Figure 1B). Post-transplant outcomes were not significantly influenced by the allocation system.

**Conclusions**: The implementation of the 2018 French allocation scheme had a limited impact on the profiles of HTx candidates but selected more severe patients for HTx without significant impact on post-transplant outcomes.

**OS6.2** IMPACT OF THE 2018 FRENCH ALLOCATION SCHEME ON THE PROFILE OF HEART TRANSPLANTATION CANDIDATES AND RECIPIENTS: INSIGHTS FROM A HIGH-VOLUME CENTER

Guillaume Coutance1*, Eva Desire1, Mickael Lescoat1, Guillaume Lebreton1, Shaida Varnous1, Leprince Pascal1

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**Background**: In 2018, a new cardiac allograft allocation scheme based on an individual scoring system considering the risk of death both on the waitlist and after heart transplantation (HTx), was implemented in France. We aimed to assess the impact of this new scheme on the profile of HTx candidates and recipients.

**Methods**: In this single-center retrospective study, we included consecutive patients listed and/or transplanted between 01/01/2012 and 09/30/2021 at La Pitié-Salpêtrière Hospital. Baseline characteristics of patients were retrieved from the national CRISTAL registry and were compared according to the type of allocation scheme (before or after 2018).

**Results**: A total of 1098 newly listed HTx candidates and 855 HTx recipients were included: One-year post-listing and post-transplant mortality was 12.4% and 20%, respectively. At listing, the proportion of candidates on inotropes significantly declined following the scheme update (26.3% compared to 20.9%; p = 0.038), reflecting a change in medical practice (Figure 1A). At transplant, recipients had a worse kidney function (estimated glomerular filtration rate ≤ 60 mL/min/1.73 m2: old scheme = 28.6%; new scheme: 45%, p < 0.001), and were more likely to be on ECMO support (33.5% compared to 28.1%; p = 0.038) under the new scheme, reflecting the prioritization of more severe patients (Figure 1B). Post-transplant outcomes were not significantly influenced by the allocation system.

**Conclusions**: The implementation of the 2018 French allocation scheme had a limited impact on the profiles of HTx candidates but selected more severe patients for HTx without significant impact on post-transplant outcomes.
RESULTS FROM OVER 800 TRANSPLANT RECIPIENTS ENROLLED IN THE GUARDIAN-HEART REGISTRY: CHALLENGING THE STANDARD OF CARE

Andreas Zuckermann*, Yasuhiro Shudo, Dan Meyer, Scott Silvestry, Marzia Leachče, Christopher Sciroitno, Maria Rodrigo, Si Pham, Jeffrey Jacobs, Koji Takeda1, Hannah Copeland, Andržej Víode, Masashi Kawabori, Jacob Schroder, David D’alesandro
1Medical University of Vienna, Cardiac Surgery, Vienna, Austria, 2Stanford University School of Medicine, Stanford, United States, 3Baylor University Medical Center, Dallas, United States, 4AdventHealth Transplant Institute, Orlando, United States, 5Corewell Health, Grand Rapids, United States, 6Sentara Norfolk General Hospital, Norfolk, United States, 7MedStar Heart and Vascular Institute, Washington DC, United States, 8Mayo Clinic Jacksonville, United States, 9UF Health Shands Hospital, Gainesville, United States, 10Columbia University, New York, United States, 11Lutheran Health, Fort Wayne, United States, 12University of Kansas Medical Center, Kansas City, United States, 13Tufts Medical Center, Boston, United States, 14Duke University Medical Center, Durham, United States, 15Massachusetts General Hospital, Boston, United States

Background: The decades long gold standard for preservation of donor hearts in ice appears to be rapidly shifting to advanced hypothermic preservation. In 2022, almost in 3 donor hearts in the US were transported in a Paragain SherpaPak Cardiac Transport System (CTS). This controlled hypothermic technology is both FDA approved and CE Marked and has been in clinical use since 2018 preserving organ temperatures between 4 – 8°C. Real-world evidence on the clinical benefits of using CTS compared to conventional ice storage (ICE) is evaluated in the GUARDIAN-Heart Registry to assess whether improved outcomes are achieved with this technology.

Methods: Data from 877 adults at 16 US centers receiving donor hearts preserved and transported in either CTS (n=487) or ICE (n=390) between October 2015-August 2022 were analysed in the GUARDIAN-Heart registry. Propensity matching on donor age, gender, era, ischaemic time, and baseline durable ventricular assist device (VAD) utilization was performed to balance baseline differences to further evaluate outcomes between cohorts (see Table). Summary statistics were used for comparisons, and Kaplan Meier method was used to estimate survival.

Results: The CTS cohort demonstrated reduced severe primary graft dysfunction (PGD) compared to ICE in the unmatched cohort (p=0.08). Table. When propensity matched, CTS had significantly lowered severe PGD compared to ICE by 65% (92.0% vs 95.6%, ICE vs CTS, respectively). Kaplan-Meier survival was similar to ICE by 60% (10.0% vs 4.0%, p=0.01), and overall MCS utilization by 37% (32.1% vs 20.1%, ICE vs CTS, respectively). Kaplan-Meier survival was similar (one year, ICE = 91.9%, SCTS = 95.6%, p=0.12). Further analysis on a larger dataset with ongoing enrolment in this live registry will be available for presentation.

Conclusions: Utilization of the Paragain CTS for organ preservation is associated with lower rates of severe PGD. This finding continues to fundamentally challenge the decades-long status quo of using ice for transporting donor hearts.

Table: Baseline Demographics and Post-transplant Outcomes

OS6_5 MOLECULAR DIAGNOSTIC CLASSIFICATION OF HEART ALLOGRAFT REJECTION BASED ON THE TARGETED BANFF HUMAN ORGAN TRANSPLANT GENE EXPRESSION PANEL

Alessia Giarraputo1,2,3, Guillaume Coutance1, Marny Fedrigo1, Olivier Aubert1, Jessy Dagobert1, Blaise Robin1, Ilaria Barison1, Chiara Casarini1, Fariza Mezine1,2, Stéphanie Combes1, Patrick Bouvier1, Jon Kobashigawa1, Jignesh Patel1, Jean-Paul Duong van Huyen1, Annalisa Angelini4, Alexandre Loupy1
1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, France, 2Cardiovascular Pathology, Department of Cardiovascular, Thoracic, Vascular Sciences, University of Padua, Padua, Italy, 3Department of Cardiovascular and Thoracic Surgery, Cardiology Institute, Pitié Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), Sorbonne University Medical School, Paris, France, 4Pitié Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, Italy, 5Cedars-Sinai Smidt Heart Institute, Los Angeles, United States, 6Kidney Transplant Department, Necker Hospital, Assistance Publique - Hôpitaux de Paris, Paris, France

Background: Endomyocardial biopsies (EMB) gene expression profiling is a promising companion tool of the pathology diagnosis of rejection. While the routinization of panenomic approaches is limited, targeted molecular profiling combined with reproduce formalin-fixed paraffin-embedded (FFPE) EMB-based technology has the potential to change the current paradigm of cardiac rejection diagnosis. We aimed to develop and validate targeted gene expression diagnostic system of cardiac rejection.

Methods: We performed a multicenter, retrospective study, building a reference set of 810 FFPE-EMB collected between 2001 and 2021 and representative of the landscape of rejection (antibody-mediated rejection-AMR, n=188; acute cellular rejection-ACR, n=281; chronic rejection-CR, n=341). Nanostring Counter Technology with BHOT panel, a consensus-based panel of 770 genes, was used to analyze tissue gene expression. Differential expression and elastic net approaches were applied to identify key AMR and ACR-related transcripts. A supervised machine learning model was used to build molecular classifiers of AMR and ACR. Their performance was evaluated in an independent validation set (n=117).

Results: Overall, the molecular analysis of 592 (97%) biopsies successfully passed all quality control and normalization steps. The molecular profiles of both ACR and AMR included typical transcripts reflecting the rejection-related pathophysiology. In the validation cohort, the AMR and ACR models accu-
Alessia Giarraputo1,2, Guillaume Coutineux3, Olivier Aubert1, Marny Fedrigo1, Dina Zielinski1, Fariza Mezine1, Michael Mengel1, Patrick Brunevol1, Jean-Paul Duong van Huyen1,2, Annalisa Angelini5, Alexandre Loupy1,2
1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, 2Department of Cardiovascular Pathology, Department of Cardiac, Thoracic, Vascular Sciences, University of Padua, Padua, Italy, 3Department of Cardiovascular Pathology, Department of Cardiac, Thoracic, Vascular Sciences, University of Padua, Padua, Italy, 4Department of Cardiovascular Pathology, Department of Cardiac, Thoracic, Vascular Sciences, University of Padua, Padua, Italy, 5Department of Cardiac and Thoracic Surgery, Cardiology Institute, Pitié-Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), Sorbonne University Medical School, Paris, France.

**Background:** Tissue-based gene expression approaches have been developed as a companion tool of routine pathology to refine the diagnosis of cardiac rejection. Whole-transcriptome profiling defined molecular phenotypes of rejection, but its clinical application remains limited by several hurdles. The consensus Banff Human Organ Transplant (BHOT) panel is developed to facilitate cost-effective and reproducible expression analysis of solid organ allografts. We aimed at validating the targeted panel as a proxy to whole-transcriptome analysis.

**Methods:** To assess the BHOT panel reliability in detecting gene expression pattern associated with antibody-mediated rejection (AMR), we performed in silico analysis and projected the BHOT panel on already published microarray data of 142 heart transplant biopsies (PMID:28148598). We compared the targeted and whole-transcriptome molecular profiles in AMR-biopsies (n=71) and non-AMR matched-control (non-rejection or acute cellular rejection, n=71) by performing differential expression, pathway, and network analyses.

**Results:** Out of the 30 most differentially expressed genes (FDR<0.05) between AMR and non-AMR identified in whole-transcriptome analysis, two-thirds (n=19) were included in the BHOT panel (Figure). These genes covered major immune pathways and key cells involved in the physiology of AMR, including IFNG-inducible genes, NK-cells, monocytes-macrophages, injury and B-cells. The remaining genes not targeted in the BHOT were related to unspecific immune response. Major pathways related to AMR and graft injury identified in the targeted panel were associated with: antigen processing cross presentation (q=2.86E-15), lymphoid and non-lymphoid immune interaction (q=1.00E-22), and Immunoregulatory interaction in adaptive immune system (q=1.01E-22).

**Conclusions:** We developed and validated robust molecular-based models, showing high diagnostic performance to detect heart rejection profiles in transplanted patients. These results support the clinical utility of BHOT-based diagnostic model to improve diagnostic and follow-up procedure in heart transplantation.
**FULL ORALS**

### Improving outcomes of end-stage heart: instead of MCS to the long-term

**Methods:** We performed a single-center, single-arm, open-label trial (DUET trial, NCT02013037). Patients with panel reactve antibodies (PRA) ≥70% and pre-formed donor-specific antibodies (DSA) ≥ 5,000 MFI were eligible. In addition to standard of care, patients received 9 infusions of eculizumab during the first two months post-transplant. The primary composite endpoint was antibody-mediated rejection (AMR) ≥ pAMR2 and/or left ventricular dysfunction during the first year. Secondary endpoints included hemodynamic compromise, allograft rejection and patient survival. A matched control group at equivalent immunologic risk and treated with perioperative plasmapheresis and intravenous immunoglobulins was retrieved from the Paris Transplant Group reference set (propensity score matching).

**Results:** Twenty patients were included in the treatment group. Median post-transplant follow-up was 4.8 years. Beyond the first year post-transplant, there were no episodes of pAMR2 or greater and no LV dysfunction. Primary endpoint free-survival was 79.0% at 3- and 5-year post-transplant. Overall survival was 90% and 83.1% at 3- and 5-year post-transplant. Beyond the first year post-transplant, one episode of pAMR1 was diagnosed and one patient had minimal de novo cardiac allograft vasculopathy. Compared to a matched-control group, we observed a non-statistically significant benefit of eculizumab with a lower incidence of primary endpoint or death (primary endpoint: HR=0.50, 95%CI=0.15-1.67, p=0.26; mortality: HR=0.51, 95%CI=0.13-2.07, p=0.35, Figure 1A and 1B).

**Conclusions:** We report favorable 5-year outcomes of a complement inhibition-based strategy for the management of immunologically high-risk HTx. Chronic antibody-mediated allograft injuries were uncommon. Our results support the utility of complement inhibition for immunologically high-risk heart transplantation.

### Molecular monitoring of lung allograft rejection

**Methods:** We performed a single-center, single-arm, open-label trial (DUET trial, NCT02013037). Patients with panel reactive antibodies (PRA) ≥70% and pre-formed donor-specific antibodies (DSA) ≥ 5,000 MFI were eligible. In addition to standard of care, patients received 9 infusions of eculizumab during the first two months post-transplant. The primary composite endpoint was antibody-mediated rejection (AMR) ≥ pAMR2 and/or left ventricular dysfunction during the first year. Secondary endpoints included hemodynamic compromise, allograft rejection and patient survival. A matched control group at equivalent immunologic risk and treated with perioperative plasmapheresis and intravenous immunoglobulins was retrieved from the Paris Transplant Group reference set (propensity score matching).

**Results:** Twenty patients were included in the treatment group. Median post-transplant follow-up was 4.8 years. Beyond the first year post-transplant, there were no episodes of pAMR2 or greater and no LV dysfunction. Primary endpoint free-survival was 79.0% at 3- and 5-year post-transplant. Overall survival was 90% and 83.1% at 3- and 5-year post-transplant. Beyond the first year post-transplant, one episode of pAMR1 was diagnosed and one patient had minimal de novo cardiac allograft vasculopathy. Compared to a matched-control group, we observed a non-statistically significant benefit of eculizumab with a lower incidence of primary endpoint or death (primary endpoint: HR=0.50, 95%CI=0.15-1.67, p=0.26; mortality: HR=0.51, 95%CI=0.13-2.07, p=0.35, Figure 1A and 1B).

**Conclusions:** We report favorable 5-year outcomes of a complement inhibition-based strategy for the management of immunologically high-risk HTx. Chronic antibody-mediated allograft injuries were uncommon. Our results support the utility of complement inhibition for immunologically high-risk heart transplantation.

*Figure 1*

#### A: Primary endpoint-free survival

- **HR** = 0.50
- 95% CI = 0.15-1.67
- p = 0.26

**Number at risk**

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**Time post-transplant (years)**

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#### B: Post-transplant survival

- **HR** = 0.51
- 95% CI = 0.13-2.07
- p = 0.35

**Number at risk**

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**Time post-transplant (years)**

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IVIG, intravenous immunoglobulins; PP, plasmapheresis.
Molecular monitoring of lung allograft rejection

on the median value for PIRCHE-II. There was no significant difference in the two groups regarding probability of dnDSA development. However, there was a clear trend towards a reduced five-year survival rate in the group that showed a high-PIR CHE-II score and developed dnDSA post-TX (p = 0.076).

Conclusions: Taking the current shortage of donor organs into consideration, PIRCHE may be able to identify acceptable mismatches to optimize donor-recipient compatibility, help improve long-term survival and reduce the rate of graft failures. However, as pre-TX HLA-matching, in contrast to other forms of solid organ transplantation (SOT), currently plays no role in general in the allocation of lung allografts, adjustments in the PIRCHE-II thresholds may be needed in order to better reflect epitope load and DSA development.

Background: CLAD is the leading cause of mortality after lung transplantation. Emerging evidence suggests that the balance of effector and regulatory lymphocytic responses determines lung allograft outcomes favouring rejection or tolerance. However, the molecular mechanisms controlling these responses remain largely unknown. Recently we demonstrated that the expression of lymphocyte-specific transcriptional co-activator BOB1 in the lung recipients' blood predicts CLAD development. In this study, we aimed to explore the role of BOB1 in the pathophysiology of CLAD.

Methods: The imaging mass cytometry was performed on lung tissue obtained from patients with CLAD through transbronchial biopsy and stained with a panel of 36-heavy-metal-tagged antibodies. BOB1-specific inhibitors were developed through a classical medicinal chemistry approach via virtual library screening. The effect of BOB1 targeting was assessed on: 1) B-cell proliferation, apoptosis, activation, and immunoglobulin production in the model of T-dependent B-cell differentiation; 2) B-cell regulatory capacity in the co-cultures with activated effector T cells; 3) primary and secondary T-cell responses.

Results: We identified multiple immune cell subsets in the lung allograft, the target tissue of CLAD, and observed the massive infiltration of plasma cells expressing high levels of BOB1. Targeting BOB1 abrogates B-cell proliferation, activation and differentiation into antibody-secreting plasmablasts in vitro. This phenotype and the arrest of isotype-switched immunoglobulin production was accompanied by the down-modulation of plasma cell differentiation and class-switching genes, such as IRF4, PRDM1, AICDA, IgH1, and IgH3. In addition, targeting BOB1 suppressed proliferation and IL-17A production by T cells during recall responses. In sharp contrast, the interference with BOB1 function did not affect the regulatory function of B cells.

Conclusions: The presence of BOB1+ lymphocytes in CLAD lungs and the notion that attenuation of biological activity of BOB1 in vitro dampens activated lymphocytic responses without compromising the immunosuppressive potential, support the role of BOB1 in CLAD pathogenesis, laying a solid rationale for the investigation of its targeting in relevant experimental models in vivo.

Full Orals

OS7_3 TRANSCRIPTİONAL CO-ACTİVATOR BOB1 AS THE KEY REGULATOR OF PATHOGENİC LYMPHOCYTİC RESPONSES IN CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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Background: CLAD is the leading cause of mortality after lung transplantation. Developing non-invasive biomarkers would allow to prevent lung allograft damage. We previously identified three B-cell related genes with blood expression associated with CLAD, namely BLK, POU2AF1 and TCL1A. The purpose of this study was to validate this signature in an independent cohort of 293 lung transplanted recipients.

Methods: The expression of the 3 genes was measured by quantitative PCR at 12, 18 or 24 months after transplantation in the blood samples of lung transplanted patients of the multicenter COLT cohort. Theses samples include samples from patients with CLAD (n=56) and patients with good graft function at least 5 years after transplantation (n=102). Blood from patients with lung infection. These results confirm the ability of these 3 genes to predict the development of CLAD in lung transplantation.

Conclusions: The downregulation of these three B cells-related genes suggests a B cell imbalance in favour of an alloimmune reaction. Combined with clinical parameters, these genes may help identifying patients likely to develop CLAD and to benefit from therapy to prevent development of the pathology.

OS7_4 VALIDATION OF A BLOOD GENE SIGNATURE TO PREDICT CHRONIC ALLOGRAFT DYSFUNCTION IN LUNG TRANSPLANTATION

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Background: Since chronic lung allograft dysfunction (CLAD) is the major limitation to long-term survival after lung transplantation, identifying patients at risk of CLAD using non-invasive biomarkers would allow to prevent lung allograft damage. We previously identified three B-cell related genes with blood expression associated with CLAD, namely BLK, POU2AF1 and TCL1A. The purpose of this study was to validate this signature in an independent cohort of 293 lung transplanted recipients.

Methods: The expression of the 3 genes was measured by quantitative PCR at 12, 18 or 24 months after transplantation in the blood samples of lung transplanted patients of the multicenter COLT cohort. Theses samples include samples from patients with CLAD (n=56) and patients with good graft function at least 5 years after transplantation (n=102). Blood from patients with lung infection. These results confirm the ability of these 3 genes to predict the development of CLAD in lung transplantation.

Conclusions: The downregulation of these three B cells-related genes suggests a B cell imbalance in favour of an alloimmune reaction. Combined with clinical parameters, these genes may help identifying patients likely to develop CLAD and to benefit from therapy to prevent development of the pathology.
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**Background:** Non-specific histopathologic findings and a lack of accurately defined phenotypes pose a barrier in diagnosing rejection in lung allografts. We hypothesized that new rejection phenotypes could be identified using probabilistic unsupervised analysis of gene expression data.

**Methods:** 121 formalin-fixed paraffin-embedded transbronchial biopsies were included and classified according to ISHLT criteria to three categories: anti-body-mediated rejection (AMR, n=42), acute cellular rejection (ACR, n=50) or non-rejection (n=29). Histological, clinical and immunological data were gathered and biopsies were sequenced using the Banff Human Organ Transplant panel. Archetypal analysis was applied to normalized gene counts to identify distinct phenotypes. The final archetypal model was chosen using the elbow method on the residual sum of squares. We performed differential expression analysis comparing each archetype vs. all other archetypes.

**Results:** We identified four distinct histological, immunological and molecular archetypes. Archetype 1 (n=21 biopsies) was characterized by capillary lesions and circulating anti-HLA DSA. Differentially expressed genes captured B- and T-cells activation (CD45, CD3D, JAK3) and interferon signalling (STAT1, CXCL11). Archetype 2 (n=46) was predominantly defined by perivascular mononuclear cell infiltrates. Its upregulated transcripts were associated with cell-extracellular matrix interactions, angiogenesis (COL4A3, VEGFA) and cell injury (AGER). Archetype 3 (n=35) and archetype 4 (n=18) were histologically similar but distinguished by capillary lesions, perivascular mononuclear cell infiltrates and circulating anti-HLA DSA occurring at low frequencies. Molecularly the archetypes differed with top transcripts of archetype 3 being mainly involved in cellular processes while archetype 4 captured anti-inflammatory responses (IL1R2, IL4R) and interferon signalling (IFNGR1, JAK1, STAT3).

**Conclusions:** Unsupervised archetypal analysis of gene expression data identified lung allograft phenotypes with distinct histological, immunological and molecular profiles. This approach has the potential to refine rejection-related diagnoses in lung allografts and improve the shortcoming of the current diagnostic classification system.

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**Molecular monitoring of lung allograft rejection**

**OS7.5 - UNSUPERVISED ANALYSIS OF LUNG TRANSPLANT PHENOTYPES USING GENE EXPRESSION DATA**

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**Background:** Survival after lung transplantation (LT) is hampered by the development of chronic lung allograft dysfunction (CLAD). There is no treatment available to reverse CLAD once diagnosed, but early intervention could modify the progressive lung function decline. Thus, biomarkers are needed for early detection of CLAD. High levels of donor-derived cell-free DNA (ddcfDNA) have been described to precede acute cellular rejection and antibody mediated rejection diagnosis. The aim of this study is to assess if there is any association between ddcfDNA and chronic lung allograft dysfunction (CLAD).

**Methods:** This is a longitudinal study in which ddcfDNA levels were determined in 100 LT recipients at the 3rd, 6th, 9th, 12th, 24th and 36th month after LT. Firstly, real-time PCR was performed to detect an informative INDEL polymorphism for each donor/recipient pair. Secondly, levels of ddcfDNA were determined by quantifying the informative INDEL by digital PCR in the plasma of the recipient. Clinical data was collected during a three years follow-up to determine infections, antibody mediated and acute cellular rejection, and CLAD.

**Results:** Globally, we noted an upward trend of ddcfDNA levels at 1, 2 and 3 years of follow-up when referred to 3 months. Levels of ddcfDNA were determined compared between CLAD and no CLAD patients at different time points, and a cut-off value of 1.86% at 12 months could identify those patients with higher probability of developing CLAD (Figure 1).

**Conclusions:** Determine ddcfDNA levels in plasma could be a useful non-invasive biomarker for CLAD prediction. This study was partially funded by ISCIII (‘PI17/01485’), co-funded by ERDF and SEPAR (552/2017).
FULL ORALS

Molecular monitoring of lung allograft rejection

**OS7_7** DONOR-DERIVED CELL-FREE DNA AND CELL-FREE RNA LEVELS USING A COST-EFFECTIVE LIQUID BIOPSY TECHNIQUE MONITORING LUNG ALLOGRAFT REJECTION

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**Background:** Donor-derived cell-free DNA (dd-cfDNA) and cell-free RNA are non-invasive tests that look for donor-specific DNA/RNA markers in recipient plasma. Next Generation Sequencing (NGS), droplet digital PCR (ddPCR), and massively multiplexed PCR (mmPCR) platforms, which are currently available to diagnose allograft rejection, are not economically viable in developing countries. To address this problem, we created a real-time PCR-based donor-derived cell-free DNA (dd-cfDNA) and cell-free RNA (dd-cfRNA) assay.

**Methods:** We used a novel PCR assay to measure donor-derived cell-free DNA (dd-cfDNA) and donor-derived cell-free RNA (dd-cfRNA) in 123 plasma samples from 60 lung transplant recipients to diagnose acute rejection. Preoperative, intraoperative, and postoperative risk factors were subjected to regression analysis.

**Results:** The majority of the patients (61.2%) were male, with a mean age of 47.37 years (range: 14-72 years) and a BMI of 22.84. (range: 14.1- 33.7). The most common pre-transplant diagnosis was idiopathic pulmonary fibrosis (47.37%), followed by chronic hypoxemia pneumonitis (15.4%) and connective tissue-related interstitial disease (8.6%). Our key findings are as follows: 1. When compared to the stable organ (median 8.3 ng/mL), dd-cfDNA level was higher in acute rejection (median 21.7 ng/mL, interquartile range (IQR): -0.0- 46.8 ng/mL). 2. The dd-cfRNA level was higher in acute rejection (median 13.75 ng/mL, interquartile range (IQR): 0.0- 46.8 ng/mL) than in stable organ (median 2.3 ng/mL, IQR: -0.0- 17.3 ng/mL). Data analysis of dd-cfDNA levels revealed a rejection sensitivity of 56.7% and specificity of 79.7%, whereas dd-cfRNA levels revealed a rejection sensitivity of 33% and specificity of 77.1%. However, the positive predictive values for dd-cfDNA and dd-cfRNA were only 28.8% and 33%, respectively, while the negative predictive values were 89.68% and 87.1%, respectively.

**Conclusions:** dd-cfRNA, like dd-cfDNA, has good negative predictive values in detecting rejection that histopathology may have missed.

Figure 1: Median cfDNA & cfRNA in relation to rejection

Kidney allocation to improve outcomes

**OS8_1** KIDNEY TRANSPLANTATION FROM UNCONTROLLED DONATION AFTER CARDIAC DEATH, AN OPTION WITH EXCELLENT RESULTS IN THE LONG TIME

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**Background:** Kidney transplantation (KT) from uncontrolled donation after cardiac death (uDD) has as good results as KT from donation after brain death (DBD) after 5 and 10 years of follow-up. The results after these periods are unknown.

**Methods:** Unicentric retrospective cohorts study that compared 237 KT from uDD with 237 KT from standard DBD after 5, 10 and 15 years of follow-up. We measured basal demographics from donor, recipients and donation procure- ment; and graft survival, patient survival and renal function.

**Aim:** To compare the graft survival, patient survival and renal function of KT from uDD to KT from standard DBD after 15 years of follow-up.

Results: KT donors had worse renal function at the moment of procurement (creatinine 1.3±0.4 vs 0.8±0.2 mg/dL, p<0.001) and delayed graft function was more frequency (73.4% vs 46.4%, p<0.001). Thymoglobin were administered to 92.8% of KT from uDD vs none of KT from DBD (p<0.001). There was more acute rejection in KT from DBD (12.2% vs 24.5%, p<0.001). Graft's survival (non-censured by non-primary function or patient death) 5, 10 and 15 year after KT was in KT from uDD 86.1%, 82.5% and 79.2% vs in KT from DBD 89.6%, 84.1% and 73% (p=0.97). Kaplan-Meier curve is shown in Figure 1. The patient's survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD. Patient survival at 5 years was 93% in KT from uDD and 91.9% in KT from DBD.
OS8_2 IS THERE A DIFFERENCE IN SURVIVAL OUTCOMES OF DUAL KIDNEY TRANSPLANT (DKT) OF ALLOGrafts Procured from DCD versus DBD Donors in absence of a Dedicated National Pathology Service?

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Background: DKT’s are generally from marginal kidneys or small-for-size kidneys that are implanted to provide optimum total nephron mass. Glomerulosclerosis pathology scoring has been used globally to guide about single or dual-kidney implant. In addition, there are reported concerns that DCD transplant outcomes are inferior to DBD. Survival-outcomes of DKTs procured from DCD vs DBD donors has not been reported.

Aim: This study aims to research if there is a difference in survival-outcomes of DKT’s of allografts procured from DCD versus DBD Donors in absence of a dedicated National Pathology-Service in the UK.

Methods: In this exploratory analysis, adults who underwent DKT in the United-Kingdom between Jan 1, 2000, and 31st Dec, 2019, were identified in the NHSBT-Transplant registry, with follow-up to December 31, 2022. Post-transplantation graft survival was assessed with Cox-Regression analysis. Propensity-scores were used to control for selection bias.

Results: A total of 47,917 waitlisted kidney failure patients formed the study cohort, of whom 34,558 (72.1%) received a kidney transplant (living donors; n=9,140, standard criteria donor; n=18,062 and ECD; n=7,356). From the ECD recipient group, 7,009 were classified based upon donor aged ≥60 (ECD60) while 347 were classified based upon donor aged 50-59 and additional criteria met (ECD50-59). Compared to SCD, both ECD60 (Hazard Ratio 1.126, 95% CI 1.093-1.161) and ECD50-59 (Hazard Ratio 1.126, 95% CI 1.093-1.161) kidney recipients had increased association for all-cause mortality. However, compared to dialysis, both ECD60 (Hazard Ratio 0.194, 95% CI 0.187-0.201) and ECD50-59 (Hazard Ratio 0.218, 95% CI 0.197-0.241) kidney recipients have significantly lower all-cause mortality.

Conclusions: ECD kidneys, regardless of definition, provide equivalent and superior survival benefits in comparison to remaining waitlisted.
**FULL ORALS**

kidney allocation to improve outcomes

### OS8.4

**IMPACT OF DECEASED DONOR ACUTE KIDNEY INJURY (AKI) ON RENAL TRANSPLANT OUTCOMES**

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**Background:** Donor AKI is a common reason for discarding deceased donor kidney due to uncertainty regarding transplant outcomes. Our study compared the post-transplant kidney function, patient and graft survival in recipients of kidneys from deceased donors with and without AKI.

**Methods:** Propsero, Medline, Embase, Cochrane and Web of Science were searched. NHBLI tools were used by two independent researchers for risk of bias assessment. Analysis was performed in R version 4.2.2. 2984 studies were identified by the search, 34 met the inclusion criteria and were analysed in the study. There were a total of 103,529 kidney transplants analysed, 97,165 (94%) with and 6,364 (6%) without donor AKI.

**Results:** There was no significant difference between recipients of grafts from donors with terminal serum creatinine >2.0 mg/dl and <2.0 mg/dl in 1 year patient survival (RR: 0.99, CI: 0.96-1.02, P=0.52), as well as in 1 year (RR: 1.01, CI: 0.98-1.03, P=0.61) and 5 year (RR: 0.99, CI: 0.94-1.04, P=0.63) graft survival. There was no significant difference in 1 year post-transplantation serum creatinine between recipients of grafts with donor terminal serum creatinine >2.0 mg/dl and <2.0 mg/dl (Mean difference (MD); -0.01, CI: -0.09-0.07, P=0.84). Delayed graft function (DGF) was the only parameter significantly worse in recipients of grafts from donors with terminal serum creatinine >2.0 than to non-AKI recipients (RR: 1.89, CI: 1.64-2.17, P<0.01). In studies that compared the severity of AKI stage using the AKIN criteria, there was no significant difference in 1 year post-transplantation serum creatinine even between recipients of grafts from the most severe AKI stage (AKIN3) and the non-AKI group (AKIN0) (MD; -0.01, CI; -0.17-0.16, P=0.92).

**Conclusions:** Donor AKI is associated with a higher incidence of DGF but has no effect on post-transplant patient and graft survival and, based on this analysis, should not be a sole reason for discarding kidneys.

### OS8.5

**DO WAITLISTED KIDNEY TRANSPLANT CANDIDATES AGED >70 YEARS HAVE A SURVIVAL BENEFIT POST-TRANSPLANTATION?**

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**Background:** Survival benefits for older kidney transplant candidates remains a contentious issue, with those aged ≥70 years often advised transplantation if clinically indicated. However, data to support this statement is conflicting. The aim of this study was to analyse survival for waitlisted kidney candidates aged ≥70 years.

**Methodology:** A retrospective cohort study was undertaken of prospectively collected registry data of all waitlisted kidney failure patients receiving dialysis in the United Kingdom. From January 1, 2000 until September 30, 2019 inclusive, all patients listed for their first kidney-alone transplant were included. Stratification for age at listing was done at 70 years. The primary outcome was all-cause mortality, with survival analysis conducted according to the intention-to-treat principle. Time-to-death from listing was analysed using adjusted nonproportional hazard Cox regression models, with transplantation handled as an as-treated outcome.

**Results:** A total of 37,251 kidney transplant recipients formed the study cohort, of whom 21,068 received a left kidney and 16,183 received a right kidney. There were 9,874 and 27,377 living and deceased donors respectively, with right kidneys forming 18.9% of living donor and 52.3% of deceased donor kidneys. After deceased donor transplantation, there was no difference between left and right kidneys in rates of DGF (27.3% versus 26.7%, p=0.292) and a clinically negligible difference in primary non function rates (2.4% versus 3.2%, p=0.003). After living donor transplantation, there was a clinically negligible difference between left and right kidneys in rates of DGF (5.1% versus 7.0%, p=0.002) and primary non function (1.0% versus 2.2%, p=0.005). There was a statistically significant but clinically negligible difference in 1-year creatinine (129 umol/L versus 113 umol/L, p=0.034) or 3-month rejection rates (14.6% versus 13.6%, p=0.010) comparing left to right kidneys respectively. In an adjusted weighted Cox regression model, receiving a right versus left kidney had no impact on long-term death-censored graft survival (Hazard Ratio 1.12, 95% CI 0.94-1.33, p=0.199).

**Conclusions:** Left versus right kidneys make no difference with regards to long-term graft survival, although early complications are slightly higher with right kidneys especially in the context of living donor kidney transplantation.

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Kidney allocation to improve outcomes

**OS8_7** DECISION MAKING ABOUT LIVING DONOR KIDNEY TRANSPLANTATION: IN A MULTI-ETHNIC PATIENT POPULATION

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1University of Leeds, Leeds, United Kingdom, 2St James’s University Hospital, Nephrology, Leeds, United Kingdom, 3St James’s University Hospital, Nephrology, Leeds, United Kingdom, 4Leeds Institute of Health Sciences (LIHS), Leeds, United Kingdom, 5Bradford Teaching Hospitals NHS Foundation Trust, Nephrology, Bradford, United Kingdom

Background: Decision-making about living donor kidney transplantation (LDKT) is challenging for people with advanced kidney disease (AKD). Fear of risks, insufficient knowledge and health literacy, religious beliefs, and complex family dynamics are cited as reasons for not choosing LDKT. With the aim of improving informed decision-making and experience of care, our study examined the decisional needs of people with AKD in a diverse population in the United Kingdom.

Methods: Semi-structured interviews with people with AKD from two kidney units, West Yorkshire, United Kingdom were conducted. Purposive sampling (N=30) ensured people from diverse ethnic (n=19 minority ethnic group), gender balance (female -16) and socially disadvantaged groups (n=19). In relation to transplantations, participants were asked if they had a kidney transplant or if they had a patient who had a kidney transplant within the last two years (7 received LDKT and 9 DDKT) participated. Data were analysed using thematic analysis and managed using NVivo software.

Results: Three themes were identified. Knowledge: about benefits of LDKT, donor work-up process, financial implication, and long-term outcomes. Knowledge gaps were predominantly identified among those with low education and socially deprived areas irrespective of their ethnic groups. Family and social matters: post-transplant relationship concerns, guilt around potential transplant failure, community perception of organ donation, fear of isolation and compromised opportunities for marriage and starting a family for female. Deliberation and validation: need to clarify religious views, deliberation around fate and religion as well as cultural norms, desire to meet others in receipt of transplant of a similar background. Needs related to religion and culture were only identified among older minority ethnic groups.

Conclusions: While ethnicity has been identified as a significant factor associated with transplantation decision preference, it appears to intersect with other factors such as age, gender, social deprivation, and education levels. These findings and those of a parallel study exploring kidney health professionals’ views, will inform the development of a transplant decision support intervention for people with advanced kidney disease from diverse ethnic backgrounds in UK kidney units.

**OS8_8** THE UK LIVING KIDNEY EXCHANGE PROGRAMME – PUSHING BOUNDARIES TO OPTIMISE TRANSPLANT POSSIBILITIES

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Background: Non-directed altruistic donation (NDAD) and living kidney exchanges between incompatible pairs first became legal in the UK in 2006, with the first transplants happening in 2007. The UK Living Kidney Sharing Scheme (UKLKSS), which seeks to find transplants for patients with willing but incompatible living donors, has grown incrementally since 2007, to the sophisticated programme that exists today.

Methods: This study highlights the benefits of the UKLKSS, which started by only facilitating 2-way exchanges (ie between 2 pairs), but grew to allow 3-way exchanges (2009), NDAD transplant chains (2012 for chains giving 2 transplants, 2015 for chains giving 3 transplants). Innovatively, the scheme also includes compatible pairs (seeking to improve age gap or HLA mismatch) and routinely facilitates both ABO incompatible (ABOi) and HLA incompatible (HLAi) transplant exchanges. The latter has been possible since 2012 by permitting registration of modified blood groups and unacceptable antigens to enable incompatible transplantation, where safe in the UKLKSS context.

Results: To the end of 2022, the UKLKSS has enabled a total of 1684 living donor (LD) transplants through 188 2-way exchanges (376 transplants, 22%), 185 3-way exchanges (555 transplants, 33%), 177 short chains (354 transplants, 21%) and 133 long chains (396 transplants, 24%). There have been 195 transplants for recipients registered in a compatible pair. There have also been 8 ABOi transplants, 61 HLAi transplants and one both ABOi and HLAi. The recipients of antibody incompatible transplants included 13 who waited over 2 years for a transplant in the UKLKSS. Overall, death-censored graft survival rates for all recipients receiving a transplant via the UKLKSS are 93.1% at 5 years (95%CI 91-95), with a breakdown by pair and transplant compatibility shown in Figure 1.

Conclusions: The UK Living Kidney Sharing Scheme has become one of the most innovative and mature schemes in Europe. In the last 5 years it has contributed 21% (2.6opsim) of the 4311 LD kidney transplants in the UK (12.8mpm). The scheme is continuously reviewed and improvements implemented to maximise the number of transplant opportunities. The scheme is the largest in Europe and its success has led to increasing numbers of LD transplants in the UK with excellent post-transplant outcomes.

Kidney immunology and HLA mismatch analysis

**OS8_1** ASSOCIATION OF PIRCHE-II SCORES WITH KIDNEY ALLOGRAFT ANTIBODY-MEDIATED REJECTION: A POPULATION-BASED STUDY

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Background: Predicted Indirectly Recognizable Human Leucocyte Antigen Epitopes-II (PIRCHÉ-II) score have shown associations with kidney rejection, but its value in large prospective unselected cohorts has not been assessed so far.

Methods: We included consecutive ABO-compatible kidney recipients from a large prospective deep phenotyped cohort (NCT03474003), between 2004 and 2017 in 6 transplant referral centers in France. The total HLA-derived mismatched peptides epitopes and HLA-focus specific peptides epitopes (HLA-A, -B, -C, -DR, -DQ), that could be respectively presented by the recipient’s HLA-DRB1 molecules were calculated using the PIRCHÉ-II algorithm. Pre-transplant circulating Anti-HLA DSA were considered positive for MF61 1,400 (STAR 2022 recommendations). The measured outcome was the occurrence of biopsy-proven antibody-mediated rejection (ABMR). The associations of clinical, immunological baselines parameters with the outcome were assessed using uni- and multivariate Cox models.

Results: A total of 5,839 patients with pairs of donors and recipients were included in the median follow-up time post-transplantation was 7.3 years (IQR: 4.5-10.7). Preformed DSA were present in 423 patients (7.2%), ABMR occurred in 1,092 (18.7%) patients. The presence of preformed circulating anti-HLA DSA (p<0.001), PIRCHE-II score (p=0.002), HLA-DRB1 antigen mismatches (p<0.001), re-transplantation (p<0.001), and induction with anti-thymocyte globulins (p<0.001) were significantly associated with occurrence of ABMR. Independent immune determinants of ABMR occurrence included the presence of preformed both Class I and Class II anti-HLA DSA (HR 3.24 [2.75-3.83], p<0.001), PIRCHE-II score (1.05 [1.03-1.07], p<0.001), and re-transplantation (1.04 [1.01-1.07], p=0.018) respectively.

Conclusions: In a large multicentric and unselected cohort of kidney recipients, we found that PIRCHE-II scores are significantly associated with ABMR, suggesting that its potential role to risk stratify patients for rejection at a population level.
FULL ORALS

Kidney immunology and HLA mismatch analysis

OS9_2 NON-HLA RECIPIENT GENOTYPES ASSOCIATE WITH INCREASED RISK OF ANTIBODY-MEDIATED KIDNEY GRAFT REJECTION

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1Nantes Université, Centrale Nantes, CHU Nantes, Inserm, Centre for Research in Transplantation and Translational Immunology CR2TI, UMR 1064, ITUN, Nantes, France, 2Nantes Université, CNRS, Laboratoire of Digital Studies of Nantes LS2N, UMR 6004, Nantes, France, 3Nantes Université, Centrale Nantes, CNRS, Laboratoire de Mathématiques Jean Leray LMUL, Nantes, France

Background: Donor-recipient mismatches in HLA genes have long been associated with a poorer kidney graft survival. However, HLA mismatches alone do not explain long-term graft function decline. We ran a genome-wide survival study on a large monocentric cohort of kidney transplant recipients in order to characterize non-HLA genetic factors associated with biopsy proven antibody mediated rejection (ABMR), the main complication causing graft loss.

Methods: The KIT-GENIE French genetic cohort comprises 1887 European recipients for kidney transplants performed since 2002. After whole-genome genotyping and imputing further genetic polymorphisms (SNP) with the TopMed reference panel, we performed a genetic survival study on >8.2M SNPs for time to ABMR (103 cases vs 1584 controls). Cox proportional hazards models were notably adjusted for HLA allele mismatches and fit to assess the association between non-HLA recipients’ genotypes and ABMR. P-values below the genome-wide multiple testing Bonferroni correction threshold (P<5x10^-8) were considered significant.

Results: We identified six statistically significant associations in chromosomes 1 (p=1.2x10^-9), HR=5.62), 2 (2 independent signals with p=4.77x10^-5, HR=4.68 and p=3.48x10^-10, HR=6.18), 7 (p=3.82x10^-5, HR=6.02), 10 (p=1.79x10^-4, HR=5.24) and 17 (p=3.33x10^-10, HR=5.24). Interestingly, the chs1 signal is located near the promoter of RTCA, which was repeatedly associated with kidney function, and RTCA expression was two-fold lower in acute rejection biopsies than in controls (n=6 vs 5, p=4.5x10^-6).

Conclusions: Our genome-wide survival analysis in a large homogeneous monocentric cohort of kidney transplant recipients revealed six non-HLA loci associated with ABMR. External validation in independent cohorts and functional explorations will be performed to better characterize the molecular pathways involved in ABMR. We will further investigate the impact of donor genotypes and donor-recipient mismatches on ABMR to capture the complex interactions at stake during rejection events.

OS9_3 IMPACT OF HLA EVOLUTIONARY DIVERGENCE AND EPLI MISMATCHES ON KIDNEY ALLOGRAFT REJECTION AND OUTCOME: A POPULATION-BASED STUDY

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Background: As a surrogate of HLA diversity, the HLA evolutionary divergence (HED) between individual HLA alleles have been suggested as a potential metric to correlate with allo-immune response but has not been evaluated so far in large prospective cohorts. We sought to determine the impact of HED on clinical and immunogenetic measurements on kidney allograft rejection and allograft loss.

Methods: We included consecutive ABO-compatible kidney transplant patients from a comprehensive and prospective cohort (NCT03474003), between 2004 and 2017 in 6 transplant centers in France. The donor and recipient HED was calculated using the physicochemical Grantham distance for class I (HLA-A, HLA-B, HLA-C) and class II (HLA-DRB1, HLA-DQB1) HLA alleles and for their respective loci. Class I and II HLA eplet mismatches (MM) were calculated using HLA_matchmaker software. HLA immunogenicity was assessed at the time of transplantation. The primary outcome was the occurrence of ABMR and the secondary outcome was allograft loss. The associations of clinical, immunological baselines parameters with the outcome’s measures were assessed.

Results: A total of 5,839 recipients were evaluated. The median follow-up time post-transplant was 7.3 years (IQR: 4.5-10.7). Preformed DSA were present in 654 patients (14.6%). ABMR occurred in 1,092 (18.7%) patients and graft loss occurred in 1,149 (20%) patients. The independent immune determinants of ABMR were the presence of preformed anti-HLA DSA both class I and class II (HR 3.77 (3.22-4.4), p<0.0001), HLA class II eplet MM (1.02 (1.01-1.05), p<0.001) while class I and II HED of both donor and recipient showed no independent association with risk. Among the immunological determinants of long-term allograft outcome, only the presence of anti-HLA DSA was independently associated with risk (HR 1.59 (1.32-1.92), p<0.001).

Conclusions: In a large multicentric and qualified prospective unselected cohort of kidney recipients, the presence of class I and II anti-HLA DSA as well as class II HLA eplet MM were independent immunological predictors of ABMR. HED did not show any significant association with ABMR. Both pretransplant HLA eplet MM as well as HED did not show independent association with long-term allograft failure suggesting their inability to risk stratify patients at a population level.

OS9_4 ALLOIMMUNE RISK STRATIFICATION IN KIDNEY TRANSPLANTATION - DEVELOPMENT AND VALIDATION OF A NOVEL HLA MOLECULAR MISMATCH ALGORITHM

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Background: Alloimmune risk stratification to guide personalised recipient care requires prognostic biomarkers and is an unmet need in kidney transplantation.

Methods: Using three molecular HLA mismatch (molMM) algorithms, Amino-Acid-Mismatch-Score (AAMS), Electrostatic-Mismatch-Score (EMSS) and NetMHCipan we assessed model discrimination for predicting de novo donor-specific-antibody (dnDSA) at the individual HLA level in an experimental sensitisation dataset (patients receiving standardised donor lymphocyte injections, mismatched HLA n=665). Derivation of risk thresholds for HLA-DR/DQ mismatch was performed and externally validated in two extensively phenotypically typed kidney transplant cohorts (Manitoba, n=866, Denver n=404), and in the NHSBT kidney transplant registry (2000-2020, n=27,028).

Results: External validation (Manitoba cohort) of experimentally-derived HLA-DR/DQ molMM risk thresholds showed all algorithms had similar performance for dnDSA prediction at the single HLA level (HLA-DQ AUC 0.76-0.80; HLA-DR AUC 0.76-0.81). AAMS and EMSS showed improved risk stratification at the patient level (incremental hazard increase from low to medium to high risk groups for HLA-DR/DQ dnDSA) vs NetMHCipan (p=NS for medium vs. high risk groups). A novel algorithm combining AAMS and EMSS further improved discrimination (Figure 1), identifying a larger cohort at very low risk of Class II dnDSA (Table 1). In multivariate analysis, this algorithm demonstrated comparable performance with primary alloimmune events (dnDSA p<0.001, TCMR p<0.001). ABMR (p=0.0049) and all-cause graft loss (p=0.0038). Validation in an ethically diverse cohort (Denver) confirmed the dnDSA risk association (p<0.0001), and in the NHSBT registry showed a significant association with all-cause graft loss (p=0.001).

Conclusions: We describe a novel molMM algorithm incorporating information from HLA sequence and tertiary structure, that may be used as prognostic biomarker of primary alloimmunity risk, and to enrich prospective clinical trials in kidney transplantation.

Table 1. Low Risk Patient Stratification (HLA-DR/DQ dnDSA development) by model (Manitoba kidney transplant cohort)
Kidney immunology and HLA mismatch analysis

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Background: Blood type B candidates wait longer for deceased donor kidney transplant (DDKTX) than Blood types A and AB and are clustered more in disadvantaged minorities populations especially black race. To address that the kidney allocation system (KAS) was implemented in December 2014 allowing the allocation of DDKTXs from non-A1/non-A1B donors to blood type B candidates who have acceptable anti-A titers. This process was left to the different transplant centers to opt in for and implement.

Methods: Retrospective single center data review including all blood type B recipients of deceased donor kidney alone transplants since the implementation of KAS 4/30/2022 and follow-up through 9/1/2022. All blood type B candidates undergo anti-A titer check by the tube method at evaluation to establish candidacy for non-A1 listing. Initially acceptable anti-A titers were kept at or below 1:8 and subsequently gradually increased to 1:64 in 2017. Our titers are higher than the previously published data as we do not utilize dithiothreitol to neutralize IgM. Titers are checked every 3 months while on the waitlist, at day of transplant and 2 days after. Within this group we compared outcomes between recipient of blood type B/O to B and A2/OB to B.

Results: We identified 305 blood type B recipients and out of those 76 received non-A1/non-A1B. The non-A1/non-A1B group was more likely to be transplant faster, avoid dialysis and receive an organ from outside of the local OPO. There were similar cold ischemia times and delayed graft function rates. Estimated GFR was slightly low at 4 months and 1 year but did not translate to worse graft outcomes at 5 years in fact those were similar. There was only 1 AMR episode in the non-A1/non-A1B group that was related to HLA antibodies. Anti-A titers were mostly (79%) similar or reduced posttransplant. Anti-A titers were mostly (79%) similar or reduced posttransplant. Anti-A titers were mostly (79%) similar or reduced posttransplant.

Conclusions: In select blood type B candidates, transplants from a non-A1/non-A1B deceased donors offer opportunities for shorter waiting while maintaining excellent outcomes. Despite the benefits, this option continues to be underutilized evident by stagnant transplant rates due to the lack of or the suboptimal implementation by transplant centers.

Table: Group B/O to B (N=229) A2/OB to B (N=76) p value

<table>
<thead>
<tr>
<th>Groups</th>
<th>B/O to B (N=229)</th>
<th>A2/OB to B (N=76)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualifying Time Median</td>
<td>39.6</td>
<td>27.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>listings Time Median</td>
<td>8.4</td>
<td>4.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Preemptive to dialysis</td>
<td>37 (16.2%)</td>
<td>22 (28.9%)</td>
<td>0.015</td>
</tr>
<tr>
<td>Regional/National donor</td>
<td>107 (46.7%)</td>
<td>49 (64.5%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Recipient Black Race</td>
<td>38 (46.6%)</td>
<td>13 (17.1%)</td>
<td>0.018</td>
</tr>
<tr>
<td>K0PR Ref Population 2017 Median</td>
<td>44%</td>
<td>50%</td>
<td>0.001</td>
</tr>
<tr>
<td>K0PR BS% Median</td>
<td>20 (8.7%)</td>
<td>11 (43.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cold Ischemia Time Median (hrs)</td>
<td>20.1</td>
<td>19</td>
<td>0.963</td>
</tr>
<tr>
<td>Delayed Graft Function</td>
<td>124 (54.1%)</td>
<td>45 (59.2%)</td>
<td>0.442</td>
</tr>
<tr>
<td>HLA Mismatches Median</td>
<td>4</td>
<td>5</td>
<td>0.006</td>
</tr>
<tr>
<td>CKD-EPI GFR at 4 mo (ml/min) (non-constant)</td>
<td>50.6 [17.3]</td>
<td>50.5 [40.8, 58.7]</td>
<td>0.003</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>57.7 (22.8)</td>
<td>50.6 (17.3)</td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>53.9 (40.4, 73.7)</td>
<td>50.5 (40.8, 58.7)</td>
<td></td>
</tr>
<tr>
<td>CKD-EPI GFR at 1 yr (ml/min) (non-constant)</td>
<td>52.19 [33.5, 64]</td>
<td>52.19 [33.5, 64]</td>
<td>0.003</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>62.7 (22.9)</td>
<td>51.5 (17.6)</td>
<td></td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>59.6 (47.7, 78.2)</td>
<td>52.19 (38.5, 64)</td>
<td></td>
</tr>
</tbody>
</table>

Results: In a cohort of 54 DSA positive patients, agalactosylation of IgG1 DSA was associated with ABMR. In vitro, exposition of endothelial cells to an at least 50% agalactosylated anti-HLA I antibody whose glycosylation had been previously modified and cytokine and chemokine secretion was analysed.

Conclusions: Anti-HLA I 1 IgG1 agalactosylated at more than 50% generates IFNa secretion after ligation to endothelial HLA I proteins. This IFNa production has an autocrine and paracrine effect leading to the production of the chemokines CXCL10 and CXCL11 by endothelial cells.
**FULL ORALS**

**Kidney immunology and HLA mismatch analysis**

**OS9_7**

**MULTIPARAMETER MASS SPECTROMETRY DECIPHERS SPECIFIC CIRCULATING NATURAL KILLER TCELL SUBSETS PROTECTING KIDNEY TRANSPLANT PATIENTS FROM CMV INFECTION**

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**Background:** Cytomegalovirus (CMV) infection still unpredictably occurs in a significant number of kidney transplant (KTR) patients conferring poorer patient and graft outcomes. Deciphering the role of the immune system driving protection against CMV is key for immune-risk stratification and to establish guided preventive strategies.

**Methods:** In 112 prospectively collected PBMC samples from 28 CMV seropositive KTR at 4 different time points recruited in a RCT: pre-transplantation, 15-days (D15), 3-months (M3) and 12-months (M12) posttransplant, we simultaneously assessed a CyTOF (Cytometry by Time Of Flight) extended T-cell phenotype and CMV-specific functional cell-mediated immunity (CMV-sp CMI) against IE1 and pp65 antigens using an IFN-γ ELISPOT. In a semi-supervised CyTOF analysis, we assessed combined specific T-cell subsets phenotype clusters in meta-clusters significantly correlating with protective anti-viral CMI and prevention of CMV infection. We validated these data in an independent KTR cohort.

**Results:** Among the 28 patients, 12 developed CMV infection at a median time of 2.38 (IQR 1.25-5.50) months. KTR developing CMV infection showed significantly lower CMV-sp CMI frequencies both prior (p=0.004) and at 15-day after transplant (p=0.006) than those KTR that did not. Semi-supervised cell-cluster analysis revealed that while CMV(tetramer-stained)-specific T-cell numbers associated with high functional CMI and clinical protection (R=0.555, p<0.001), global CD3+CD4+CD56+ NKT-cell numbers (NKT) highly associated with CMV reactivation. However, 3 specific NKT-cell meta-clusters, sharing the CD11b+ CD56 bright surface marker, directly correlated with both protected CMV responses and low CMV replication events (Figure 1). These findings were validated in an external KTR cohort showing a higher expression of CD11b-NKT cells in patients not developing CMV infection as compared to those that did not (p=0.042).

**Conclusions:** Using a multidimensional deep phenotype characterization by CyTOF, we demonstrate the specific functional role of certain specific cell subset phenotypes that may not be observed when using traditional flow cytometry analysis. We describe a novel NKT-cell subset, expressing the CD11b surface marker, having a protective and functional role preventing CMV infection in KTR.

**OS9_8**

**SPATIAL PROFILING OF THE KIDNEY ALLOGRAFT UNRAVELS A CENTRAL ROLE OF FCYRIII+ INNATE IMMUNE CELLS IN REJECTION**

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**Background:** How the immune system participates to kidney transplant rejection has not been fully elucidated. Using transcriptomics, we previously reported that NK cells and monocytes are key players in kidney transplant rejection. Here, we examined spatial localization and interactions at single-cell resolution between these two cell types and all other cells present in the graft using multiplex immunofluorescent staining.

**Methods:** We performed Multiple Iterative Labeling by Antibody Neodeposition (MILAN) technich on 18 different transplant biopsies, with a representative mix of clinicopathological phenotypes: 3 antibody-mediated rejection (DSA+ ABMR), 5 DSA-negative cases with microvascular inflammation (DSA- MVI), 2 mixed rejection, 4 T-cell mediated rejection (TCMR), 1 borderline changes, and 3 stable cases (NR). The cell identities were determined using a broad panel of 36 phenotypic markers after digital reconstruction.

**Results:** We mapped 555,479 cells to 17 phenotypes including 5 types of renal epithelial cells (PT cells, AQP1+ tubule cells, CD13b+ tubule cells, distal tubule cells and AQP1+ PanCk+ tubule cells), 9 immune cell subtypes: 3 myeloid (macrophages, CD1c+ dendritic cells [DC] and S100+ DC), 5 lymphoid (B cells, CD4 regulatory T cells [Tregs], FcyRIII+ NK cells, CD14+ monocytes and CD8 Teff) and 4 MPO+ neutrophil subtype. Importantly, FcyRIII+ NK cells, neutrophils, FcyRIII+ monocytes and CD8+ Teff proportions mainly correlated with inflammation associated to transplant rejection. Compartmentalization analysis indicated that FcyRIII+ NK cells and FcyRIII+monocytes infiltrate vascular compartment. In addition, neighbourhood analysis unravelled a strong and significant enrichment of FcyRIII+ NK cells next to FcyRIII+ monocytes in ABMR or mixed rejection biopsies, but not in TCMR or NR biopsies. In contrast, CD14+ monocytes were mainly surrounded by CD8 T cells in TCMR.

**Conclusions:** Our study provides new insights in the role of the different innate immune cell populations and their interactions with the kidney structural cells at the protein level. FcyRIII+ and CD14+ monocytes act as the dominant “communication hubs” within the allograft, mainly communicating with FcyRIII+ NK cells in vascular compartment and CD8 T cells in interstitial compartment, respectively.
Impact of Desensitization Therapy with Isatuximab on HLA-Specific Memory B Cells and Plasma Cells in Highly Sensitized Patients

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Background: HLA sensitization is a main barrier for successful kidney transplantation. Anti-HLA antibodies (Ab) are produced by HLA-specific (HLA-sp) plasma cells (PCs) and peripheral memory B cells (mBCs). Targeting plasma cells through an anti-CD38 monoclonal antibody (mab) may reduce titers of anti-HLA antibodies.

Methods: 10 of 23 highly sensitized patients recruited in the anti-CD38 mAb isatuximab desensitization clinical trial (NCT04294459) with available paired samples were analyzed at baseline, after dose 6 and one week after last (8th) dose, for changes in anti-HLA Ab and circulating HLA-sp mBCs using sAb assays on serum and polyclonally expanded mBCs culture supernatants and with a HLA-sp B-cell Fluorospot assay. Multidimensional spectral Flow cytometry immunophenotyping was also performed in 16/23 PBMC samples prior and after therapy, and in 4 patients bone marrow (BM) aspirates were obtained at the same time-points to analyze HLA-sp IgG-producing PC frequencies and changes in cell subset numbers.

Results: Serum HLA-specific Ab MFI values were progressively and significantly reduced over time until last follow-up (p<0.0001) (Figure 1a). Moreover, isatuximab significantly reduced the secretion of circulating HLA-specific IgG from mBCs (p<0.0001) (Figure 1b). BM-residing IgG-producing HLA-specific PCs were also significantly reduced (75.6±104 and 29.6±92, p<0.0024) (Figure 1c). Multidimensional spectral immune-phenotyping revealed a drastic reduction of peripheral CD38+ B cells (CD19+), class switched memory B cells (CD19+C-D27+IgD-) and plasmablast (CD20+CD24+) (p<0.0001, for all cell subsets), whereas circulating class-switched CD38- mBC increased (p<0.0001). In the bone marrow, percentages of LLPC (CD20-CD38+CD138+) were also reduced whereas circulating class-switched CD38- mBC increased (p<0.0001). In the same time-points to analyze HLA-sp IgG-producing PC frequencies and changes in cell subset numbers.

Conclusions: These findings support the capacity of isatuximab to reduce the burden of sensitization in highly immunized patients, decreasing serum anti-HLA antibody levels by targeting HLA-sp mBCs and HLA-sp PCs from both peripheral blood and the bone marrow.

Daratumumab Desensitization Before Kidney Transplantation – A Pilot Study

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Background: Sensitized patients have lower access to kidney transplantation (KT). We conducted a pilot study to desensitize awaiting KT patients with the anti-CD38 antibody Daratumumab.

Methods: Our monocentric, open label, phase I/II study included adult patients awaiting KT with calculated panel reactive antibodies (cPRA) ≥95% for ≥3 years. Dose-escalation step included patients treated with 4 weekly increasing doses. Expansion cohort enrolled patients treated with 8 weekly doses of 16 mg/kg daratumumab. Primary endpoints were safety of daratumumab (serious adverse events (SAE)) and 6-months evolution of cPRA in expansion cohort. We calculated cPRA for two anti-HLA antibodies mean fluorescence intensity (MFI) thresholds: 2000 and 10000.

Results: Dose-escalation step included 9 patients with no SAE reported. Expansion cohort included 13 patients (Table 1) with no SAE and 27 AE in 9 patients (69%), mainly reaction to infusion (n=22 (81.5%)). One patient died because of stroke within 5 months not related to daratumumab infusion. Within 6 months, cPRA 10000 decreased significantly (62 [38-84] vs. 74 [57-84]; P=0.02) while cPRA 2000 remained stable (97 [93-99] vs. 99 [95-100]; P=0.28). Maximum effect was reached after three months (P=0.001 and P=0.07 respectively) (Figure 1). Number of anti-HLA decreased significantly from 61 [45-81] to 50 [34-67] (P<0.001). Plasma cells (CD138+) decreased significantly after one month from 1.06% [0.238-3.535] to 0.20% [0.196-0.337] in PBMCs. Gamma-globulins decreased significantly from 10 [9-18] to 6 [5-8] g/L (P<0.001) with no infectious event reported before one COVID.

Conclusions: Daratumumab desensitization before KT significantly decreases cPRA and number of anti-HLA antibodies especially 3 months after an 8-weeks treatment without significant secondary effects.

Table 1: characteristics of the patients included in the expansion cohort

<table>
<thead>
<tr>
<th>Patients</th>
<th>N=13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median [IQR]</td>
<td>48.7 [41.0-49.1]</td>
</tr>
<tr>
<td>Sensitization risk factors</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Transfusion, N (%)</td>
<td>3 (23.1)</td>
</tr>
</tbody>
</table>

Immunological characteristics

| cPRA - threshold 2000 | 99 [95-100] |
| cPRA - threshold 10 000 | 74 [57-84] |
| Anti-HLA antibodies, median, [IQR] | 61 [45-81] |
| Class I, median, [IQR] | 43 [32-56] |
| Class II, median, [IQR] | 17 [7-29] |

Figure 1: sensitization evolution within 6 months
OS10.3 EARLY RESULTS OF ATTAIN (ITN090ST): DARATUMUMAB & BELATACEPT FOR HLA DESENSITIZATION IN KIDNEY TRANSPLANT CANDIDATES WITH 100% CPRA

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Background: Despite high allocation priority, <10% of kidney transplant candidates with calculated panel reactive antibody (cPRA) 100% are able to find a compatible donor. Current HLA desensitization strategies are ineffective due to antibody rebound. Adding costimulation blockade to plasma cell (PC) depletion prevents antibody rebound in NHP by counteracting nodal B cell and Tfh expansion. We hypothesized that a similar approach in humans could improve success with HLA desensitization.

Methods: ATTAIN is a pilot, phase III trial of daratumumab, a CD38 mAb used in multiple myeloma, plus belatacept, a high affinity CTLA4-Ig, to desensitize kidney transplant candidates with cPRA ≥99.9%. Enrolled subjects receive daratumumab (6 doses: 8 mg/kg) and Belatacept (4 doses: 10 mg/kg) over 10 weeks with blood and bone marrow assessments pre-and post-treatment. The primary efficacy endpoint is a composite of (1) elimination of ≥1 HLA antibody specificity, (2) ≥50% reduction in the MFI of ≥3 HLA antibody specificities, or (3) kidney transplant from a previously incompatible donor. Target accrual is 15, enrolled in 2 cohorts (5+10).

Results: Cohort 1 (n=5, mean age 44, 60% with previous transplant) has been enrolled and treated, with 5-31 weeks follow-up to date. The treatment was tolerated well in all 5 patients. Three of 5 participants met the primary efficacy endpoint and 5 of 5 had >50% bone marrow PC depletion. It was accompanied by decrease of both CD19+CD38hiCD138- short-lived PC (SLPC) and CD19+CD38hiCD138+ PC subsets with maintenance of CD19-CD38hiCD138+ PC population which contains the long-lived PC (LLPC) subset. Moreover, CD19+CD38hiCD138+ PC subsets with maintenance of CD19-CD38hiCD138+ PC depletion prevents antibody rebound in NHP by counteracting nodal B cell and Tfh expansion. We hypothesized that a similar approach in humans could improve success with HLA desensitization.

Conclusions: Daratumumab and belatacept may provide effective desensitization for kidney transplant candidates with cPRA 100% by depleting PC from existing marrow and blood PC subsets. ATTAIN (NCT04827979) is a trial conducted by the Immune Tolerance Network and sponsored by NIAID (award UM1AI109565).

Figure 1. A. Change in HLA antibodies with treatments. B. Change in blood and bone marrow PC subsets with treatment.
OS10.5 A PHASE I/IIA TRIAL OF AUTOLOGOUS REGULATORY T-CELL THERAPY TOGETHER WITH DONOR BONE MARROW INFUSION IN KIDNEY TRANSPLANTATION
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Background: In predilutional models combining Treg therapy with donor bone marrow (BM) transplantation leads to mixed hematopoietic chimera and toler-ance without myelosuppressive recipient conditioning, avoiding the adverse effects of irradiation or cytotoxic drugs.

Methods: A single center, controlled, first-in-human phase I/IIa trial is conducted in HLA-mismatched living donor kidney transplant recipients. In vitro expanded polyclonal recipient Tregs and MNC-separated donor BM cells are administered within 3 days after transplant, tocilizumab is injected s.c. for the first 3 weeks. No irradiation or cytotoxic drugs are given. Immunosuppression (IS) consists of thymoglobulin, belatacept, sirolimus and steroids. Starting at 6 months, siro-limus and steroids are gradually withdrawn in stable study group patients. A parallel control group receives the same IS, but no Tregs, BM or tocilizumab.

Results: Eight patients have been enrolled and treated so far (5 in the study group, 3 in the control group; out of the predetermined sample size of 6 per group). One additional patient was enrolled but not treated as Treg manufac-turing failed. Treg (1.1-1.5x10^7 cells/kg) and BM cell (0.7-1.9x10^8 nucleated cells/kg) infusions were well tolerated. The study group developed low levels of total leucocyte donor chimera (<1%) in the first weeks post-transplant, whereas no chimera was detectable in the control group. The study group shows a favorable clinical course, with GFRs of 55-74 ml/min/1.72m² at latest follow-up (median follow-up 20 months) and no safety signals were observed. Immune monitoring accompanying the trial includes NGS of the TCR repertoire, flow cytometric leucocyte subset analysis, scRNAseq and protocol biopsies including transcriptomic analysis (at 6, 12, 24, 36 and 60 months).

Conclusions: This study confirms that conversion to belatacept post-transplant is associated with improved long term graft outcomes and acceptable safety. Conversion to belatacept after transplant should be considered as a valuable therapeutic option in kidney recipients.

OS10.6 LONG-TERM OUTCOMES AFTER CONVERSION TO A BELATACEPT-BASED IMMUNOSUPPRESSION IN KIDNEY TRANSPLANTATION: A MATCHED COHORT STUDY
Gillian Divard1*, Sofia Naser1, Solaf Alawadhi1, Charlotte Debials-Deschamps1, Ivana Juric1, Maria Cristina Ribeiro de Castro1, Nassim Kamar1, Juliette Gueguen1, Marta Crespo1, Olivier Aubert1, Alexandre Lowyp1, Carmen Lefaucheur1*
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Background: Conversion to belatacept after transplant is currently the most promising Calcineurin inhibitors (CNI) avoidance strategy in kidney transplantation. However, there is a lack of evidence on long-term efficacy and safety outcomes. This study aims to investigate the long-term outcomes of patients converted to belatacept after transplant and compared them with matched patients treated with a CNI-based immunosuppression.

Methods: Kidney transplant recipients from two French academic transplant centers were recruited. We used a propensity score to match, patients at time of the biopsy which indicate the conversion to belatacept to control patients under a CNI regimen with a biopsy after transplant. We used 11 parameters associated with graft survival for the matching, 4 at baseline (recipient age, prior transplant, donor type, dfg) and 7 at time of the biopsy (time after transplant, eGFR, proteinuria, DSA and Banff scores cv, ah, IFTA). Transplant outcomes defined by graft and patient survival, as well as as secondary outcomes were compared between the matched patients.

Results: Among the 311 patients converted to belatacept after transplant, 243 patients were matched to 243 patients and maintained under CNI (control). All matching parameters were well balanced before intervention between the 2 groups with a mean age of 54.7±15.1 years, a median time of 1.0 (0.3-2.7) years after transplant, a mean eGFR of 33.0±13.3 ml/min/1.73m², and 30.9% of positive DSA in the belatacept group. After a mean follow-up time after conversion of 3.4 years, 43 (17.7%) patients lost their graft and 39 (16.0%) patients died in the belatacept group. After conversion to belatacept, graft survival was significantly improved compared with matched patients’ under CNI p<0.00001. Furthermore, patients converted to belatacept showed lower death rate (p<0.001). The safety outcomes show similar rate of rejection, cardio-vascular events, and cancer, while a higher rate of CMV disease was observed among the belatacept treated patients (p<0.01).

Conclusions: This study confirms that conversion to belatacept post-transplant is associated with improved long term graft outcomes and acceptable safety. Conversion to belatacept after transplant should be considered as a valuable therapeutic option in kidney recipients.

Figure 1: Death censored allograft survival between matched patients after conversion to a belatacept regimen and CNI control group (ratio 1:1). The blue line is the death censored allograft survival of the matched patients from the CNI control group and the red line is the death censored allograft survival of the matched patients from the belatacept cohort.

OS10.7 EFFECTIVENESS OF THE TREATMENT OF ANTIBODY MEDIATED REJECTION: A REAL-WORLD EVIDENCE STUDY
Gillian Divard1*, Sofia Naser1, Solaf Alawadhi1, Charlotte Debials-Deschamps1, Ivana Juric1, Maria Cristina Ribeiro de Castro1, Nassim Kamar1, Juliette Gueguen1, Marta Crespo1, Olivier Aubert1, Alexandre Lowyp1, Carmen Lefaucheur1*
1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, 2University Hospital Centre Zagreb, Zagreb, Croatia, ‘Hosital des Clinicas da Faculdade de Medicina da USP, Sao Paulo, Brazil, 3Hospital Center University De Toulouse, Toulouse, France, 4Chu Hospitals Of Tours, Tours, France, 5Hospital del Mar, Barcelona, Spain

Background: Antibody-mediated rejection (AMR) is the leading cause of long-term graft failure in kidney transplant recipients (KTR). However, the current standard of care treatment is mainly based on small observational studies. The aim of this study was to provide real world evidence of the effectiveness of AMR treatment in kidney transplant recipients.

Methods: This multicenter prospective cohort study included all patients who presented a first clinical antibody-mediated rejection (active of chronic active) between 2007 and 2020 in four French, two European and one south American centers. AMR cases were reassessed using the latest Banff 2019 classification. All demographic, clinical, biological, immunological, histological and AMR treatments were collected at time of rejection and during the follow-up up to death, graft loss or lost to follow-up. The AMR treatments were separated into several group: no specific treatment, standard of care (SOC), monotherapy or alternative treatment association.

Results: A total of 537 patients were included, with mostly a diagnosis of active AMR (n=383, 71.3%). The AMR occurred in a median time of 16.1 [1.5-58.3] months post-transplantation, mean eGFR was 29.1 (18.4) ml/min/1.73m², median proteinuria was 0.5 [0.2-1.4] g/g, 386 (76.1%) had positive anti-HLA DSA. In the first 3 months post AMR, 249 (46.4%) patients received a standard of care treatment after AMR, 123 (22.9%) received no specific treatment, 86 (16.0%) received a monotherapy and 79 (14.7%) an alternative treatment asso-ciation. After a mean follow-up time of 4.1 (3.3) years post AMR, 267 (49.7%) patients experienced graft failure. The absence of specific AMR treatment was highly associated with graft failure (p<0.01) while the association of SOC AMR treatment with graft survival was protective (p=0.04).

Conclusions: This study reports the largest cohort of AMR with treated and untreated patients. Antibody-mediated rejection has a severe prognosis that frequently leads to graft failure. This study provides evidence that the standard of care treatment improved transplant outcomes after antibody mediated rejection.
Innovations in kidney immunosuppression

**RESULTS OF THE TRIBUTE RANDOMIZED TRIAL: TREATMENT WITH BORTezOMIB OF LATE ANTIBODY-MEDIATED REJECTION DUE TO DE NOVO DSA**

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**Background:** The current treatment of antibody-mediated rejection (ABMR) after kidney transplantation (KT), based on plasmapheresis, steroids and intravenous globulins is inconsistently efficient. There have been so far very few randomized trials on its treatment. The role of proteasome inhibitors in addition to the current strategy has not been explored in a controlled trial.

**Methods:** We included kidney transplant recipients with a clinical or infra-clinical biopsy-proven ABMR (defined by a score g+ptc ≥2), occurring more than three months after KT and due to de novo DSA. They were randomized to receive 2 cycles of IV bortezomib (BTZ arm) or no further treatment (CTRL arm). The primary endpoint combined at one year the reduction of immunodominant (ID) DSA MFI > 50% and the stabilization or improvement of histological lesions compared to the inclusion biopsy (ΔID MFI ≤1 and Δg+ptc ≤1).

**Results:** 60 patients were randomized (30 in each arm in the ITT analysis, 20 (BTZ) and 19 patients (CTRL) for the per protocol (PP) analysis). ABMR occurred at a mean delay of 76 months after KT in each arm. The median MFI of the ID DSA was 17130 (BTZ arm) and 11230 (CTRL arm). 23% of patients had cg lesions associated to microvascular inflammation. In the ITT analysis, 40.0% of patients (BTZ arm) and 33.3% (CTRL arm) reached the coprimary endpoint (p=0.59). There was no difference between the 2 arms, whatever the type of ABMR, clinical or infra-clinical. In the PP analysis, the success rate was 50.0% and 42.1%, respectively (p=0.62). Regarding separately the two endpoints at one year, 56.7% (BTZ) and 46.7% (CTRL) experienced a reduction > 50% of the MFI of the ID DSA, and 56.7% of patients in each arm experienced a stabilization/improvement of histological lesions. The mean reduction of ID DSA MFI was 60% in each group at one-year post-treatment. One patient lost his graft in each group during the one-year follow-up, and none died. The slope of eGFR decrease was similar. The rate of infectious AE was similar in the 2 groups. The rate of relapse was 7% (BTZ) and 8% (CTRL).

**Conclusions:** This randomized controlled trial did not show any benefit of adding bortezomib to the current strategy to treat ABMR caused by de novo DSA. The next step will be to characterize the half of patients who experienced a successful treatment of their ABMR.
Kidney biomarkers to the rescue

**MULTIDIMENSIONAL RISK ASSESSMENT OF KIDNEY ALLOGRAFT REJECTION USING DONOR DERIVED CELL-FREE DNA**

Cindy Ursule-Dufait*, Olivier Aubert, Romain Broussé, Juliette Gueguen, Maud Racape, Christophe Legendre, Dany Anglicheau, Carmen Lefaucheur, Alexandre Loupy

1Paris Institute for Transplantation and Organ Regeneration, INSERM, U-970, AP-HP, Paris, France, *Kidney Transplant Department, Necker Hospital, Paris, France, **Kidney Transplant Department, Saint Louis Hospital, Paris, France

**Background:** Post-transplantation patient care requires development and validation of non-invasive biomarkers to improve allograft monitoring and prevention from unnecessary biopsies. Reports have suggested the association of donor derived cell-free DNA (dd-cfDNA) with allograft rejection. However, there is no proof of its added value on standard of care in large, unselected and deep phenotyped cohorts.

**Methods:** We enrolled 1134 kidney transplant recipients having concomitant evaluation of allograft histology, anti-HLA DSA and functional parameters between April 2013 and June 2016 in the derivation cohort, representing 1415 biopsies. Dd-cfDNA was measured in plasma at the time of the biopsy. Diagnoses were performed using Banff 2019 criteria. 171 AMR, 34 TCMR and 17 mixed rejections occurred. Parameters associated with rejection were assessed using uni- and multivariable logistic regression. We then developed a risk model using the variables that were independently associated with kidney rejection. The validation cohort comprised 1929 evaluations including 499 evaluations in one Belgian center and 1430 evaluations in nine North American centers.

**Results:** Higher levels of dd-cfDNA were observed for AMR and TCMR or both compared to other diagnoses (Figure 1A). Dd-cfDNA incrementally increased with Banff acute lesions without significant increase for chronic lesions. In multivariable analysis, only anti-HLA DSA independently associated with rejection were anti-HLA DSA (P < 0.0001), dd-cfDNA (P < 0.0001), eGFR (P < 0.033), proteinuria (P < 0.016), and previous history of rejection (P < 0.0001). Dd-cfDNA remained independently associated with kidney allograft rejection in validation cohorts from Belgium (P < 0.0001) and North America (P < 0.0001). Discrimination of the model without dd-cfDNA was 0.777 and 0.821 with its inclusion, showing its added value (Figure 1B). The good discrimination performances of the model were preserved in the validation cohorts from Belgium (P = 0.0006) and North America (P < 0.0001). Discrimination of the model was 0.777 and 0.821 with its inclusion, showing its added value (Figure 1B).

**Conclusions:** We here demonstrate the independent and added value of dd-cfDNA in addition to conventional features to predict rejection. This first integrative system shows improved performance for patient monitoring and could help physicians in decision-making process.

**DETECTION OF KIDNEY ALLOGRAFT REJECTION USING BLOOD BIOMARKERS: RESULTS OF THE EUROPEAN MULTICENTER PROSPECTIVE EU-TRAIN TRIAL (NCT03652402)**

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**Background:** There is an unmet need for clinically validated biomarkers to non-invasively detect kidney allograft rejection in routine care. In this study, we aimed to investigate the additional value, beyond standard of care patient management, of 24 candidate blood biomarkers in a large, prospective, and unselected cohort of kidney transplant recipients.

**Methods:** We prospectively monitored 412 consecutive patients who received a kidney allograft at 9 European transplant centers between November 2018, and June 2020, for standard of care clinical, biological, immunological, and histological parameters. Twenty-four biomarkers including 20 blood mRNA (AKR1C3, CD3E, CD4, CD40, CD8A, CD9, CTLA4, ENTPD1, FOXP3, GZMB, ID3, IL7R, MS4A1, MZB1, PO2F1, PO2F1, TCL1A, TLR4, TRB1, TUBA4) together with anti-AT1R, anti-ETAR, anti-C5AR, anti-C5SR antibodies, were assessed in blood samples collected at the time of protocol (M3, M12) and clinically indicated biopsies in the first-year post-transplant. We assessed the value of the biomarkers to detect allograft rejection, as compared to standard of care patient monitoring.

**Results:** 816 post-transplant biopsies were included (625 [76.59%] protocol, 191 [23.41%] clinically indicated). The prevalence of overall rejection (AMR, TCMR and mixed) in the first-year post-transplant was 6.37%. Twenty-three (95.8%) of the 24 biomarkers did not show any statistical association with the primary outcome (allograft rejection) (Figure 1). Only CD4 mRNA showed a significant association (P < 0.001). When adjusted on standard of care patient monitoring parameters including history of rejection, ABO-incompatibility, type of induction therapy, allograft instability, eGFR, urine protein-to-creatinine ratio, and circulating anti-HLA DSA, none of the 24 candidate biomarkers was independently associated with overall allograft rejection, as well as with AMR, TCMR and mixed rejection.

**Conclusions:** In this large, prospective, and unselected cohort of kidney transplant recipients with a systematic non-invasive biomarker assessment in the first-year post-transplant, none of the 24 candidate blood biomarkers had an additional clinical value to detect kidney allograft rejection.
Kidney biomarkers to the rescue

**OS11_4** DSA-NEGATIVE MICROVASCULAR INFLAMMATION IN KIDNEY TRANSPLANT BIOPSIES: GENE EXPRESSION COMPARISON WITH NATIVE AND TRANSPLANT KIDNEY CONTROLS

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**Background:** Microvascular inflammation (MVI) in kidney transplant (KT) biopsies from patients without detectable anti-HLA donor-specific antibodies (DSA) presents a diagnostic and therapeutic dilemma. This study aimed to further understand the significance of these changes by characterizing their molecular phenotype compared to other native and transplant kidney biopsies.

**Methods:** The NanoString B-HOT panel (770 genes) was used to measure the expression of six literature-derived gene sets in 195 archival FFPE kidney biopsies from four centers, including transplant biopsies with MVI (g+ptc>1) but no detectable DSA (MVI, n=47), antibody-mediated rejection with DSA (ABMR, n=42), pure T-cell mediated rejection without DSA (TCMR, n=25), mixed MVI and TCWIR without DSA (MVI+TCM, n=47), normal implant biopsies (Normal, n=11), and native kidney biopsies with either endocapillary proliferative glomerulonephritis (GN, n=12) or minimal change disease (MCD, n=11). The evaluated gene sets included transcripts previously associated with ABMR, DSA (DSAST), endothelial injury (ENDAT), TCMR, early injury, and late injury. Gene expression was compared between groups using principal component and class comparison analyses.

**Results:** Principal component analysis demonstrated significant molecular overlap between sample groups (Figure 1A). However, gene set analysis showed lower expression of ABMR-related, DSAST (Figure 1B), and ENDAT, early injury, and late injury. Gene expression was compared between groups using principal component and class comparison analyses.

**Conclusions:** These results suggest that DSA-negative MVI displays a lower expression of ABMR-related genes than ABMR, but similar to MVI+TCMR and higher than native kidney biopsies with or without glomerulonephritis. Further work is underway to evaluate the potential role of non-HLA DSA and recognition of missing self in these cases.

**Fig 1:** Prediction of below median outcome (eGFR < 50) in test set

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**OS11_5** AGE-MODULATED PROTEOMIC SIGNATURES OF DONOR KIDNEY BIOPSIES ASSOCIATE WITH BELOW-MEDIAN 12 MONTH OUTCOMES

Philip Charles1*, Sarah Fawaz1, Rebecca Vaughan1, Roman Fischer1, Benedikt Kessler1, Edward Sharples1, Alberto Santos3, Rutger Ploeg1, Maria Kaisar1
1University of Oxford, Oxford, United Kingdom, 2University of Copenhagen, Novo Nordisk Foundation Center for Biosustainability, Copenhagen, Denmark

**Background:** Clinical factors such as donor age aid kidney transplantation decisions limited predictive value; older donors with potentially good function are not utilised, while inferior organs are transplanted with suboptimal outcomes. More granular prediction models, based on deep resolution assessment and understanding of damage processes, could substantially reduce graft dysfunction risk. Here, we studied the predictive value of subclinical markers in the proteomes of kidney pretransplant biopsies.

**Methods:** Kidney biopsies (n=185; Donors after Brain Death n=100, Donors after Circulatory Death n=85) were provided by the UK QUOD biobank, selected from donors where both kidneys were transplanted and had similar posttransplant outcomes. Biopsies were analysed by deep mass spectrometry proteomic profiling. Protein data were analysed in an integrative model combining donor/recipient demographic and clinical measurements vs ranked 12-month eGFR. 2/3 of the data were used for analysis and model training, sampling equally across each eGFR tertile. Final prediction ROC AUC was calculated against the holdout set.

**Results:** We quantified 2984 protein groups. Analysis of the data via iterative Prediction Rule Ensemble machine learning shortlisted 235 proteins associated with 12-month eGFR, including CST3, VTN, APOE and other proteins associated with complement activation and metabolic regulation; and further characterised new subclinical markers in the multiadaptive regression spline (MARS) modelling suggested most important protein terms (164/235) showed evidence for donor age interaction. We used a final MARS analysis to summarise our shortlist as a prediction model for below-median outcomes (12 month eGFR < 50). The final parameters were a) donor age multiplied by CST3 and b) VIM. This summary model achieved a ROC AUC of 0.80 in our holdout test set (Fig. 1).

**Conclusions:** Our work suggests donor organ proteomic signatures can refine current models of graft dysfunction. The biological themes of the identified candidates reinforce known immunometabolic mechanisms of kidney injury but raise interesting possibilities for further work. Furthermore, our results strongly suggest that for any studies of subclinical molecular indicators regarding kidney transplant outcomes, donor age-modulated weighing should be considered as a matter of course.
OVERALL ACTIVITY AND CHRONICITY INDICES OF KIDNEY TRANSPLANT BIOPSIES: VALIDATION ON NEW DATA

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Background: New activity and chronicity indices have been recently proposed as global histological scoring for kidney transplant biopsies. These scores summarize the degree of inflammation and the chronic damages in simple numbers which, next to the Banff rejection diagnoses, can serve as additional study endpoints and clinical predictors. This study aims to validate their clinical relevance on novel data.

Methods: The activity and chronicity indices (from 0 to 1) were calculated on 4043 new biopsies from 1617 patients using our freely available online platform rejectionclass.eu.pythonanywhere.com. Missing values were imputed with k-nearest neighbors (k=5) and rounded to the closest integer. The association with graft failure was estimated with Cox-models with robust covariance matrix estimation to account for repeated biopsies. The need for interactions and/or non-linear variable transformation (with restricted cubic splines) was assessed with Wald tests. The discrimination performance was assessed with C-index corrected for optimism. The indices were arbitrarily discretized in four groups with the following thresholds: [0.25,0.5,0.75] for visual purpose with Kaplan Meier curves. Restricted mean survival time (RMST) were computed at 5 years for practical numerical comparisons.

Results: Both indices validated the previously observed association with graft failure (HR activity: 1.65 (1.51-1.80); p<0.001, HR chronicity 1.64 (1.56 -1.74), p<0.001). The discretization in arbitrary strata also demonstrated strong association with graft failure (HR activity: 1.64 (1.51-1.80); p<0.001, HR chronicity 1.64 (1.56 -1.74), p<0.001). The predicted survival probabilities at 1, 5 and 10 years were 0.96 (0.94–0.97), and 0.91 (0.90–0.93) for TCMR; >0.96 (0.90–1.00) with all three for IFTA. Models were built for the diagnoses of: antibody-mediated rejection (ABMR), T cell-mediated rejection (TCMR), interstitial fibrosis and tubular atrophy (IFTA), glomerulonephritis (GN), and for the distinction between acute and chronic forms of ABMR and TCMR. Performances were excellent with XGBoost in the three different datasets with ROC curve AUC (95%CI) of: 0.97 (0.92–1.00), 0.97 (0.96–0.99), and 0.95 (0.93–0.97) for ABMR; 0.94 (0.91–0.96), 0.94 (0.92–0.95), and 0.91 (0.88–0.95) for TCMR; >0.96 (0.90–1.00) with all three for IFTA.

Conclusions: In this study, we set up and validated machine learning algorithms to improve and automate the interpretation of kidney graft biopsy elementary lesions, also considering a few clinical data.

Kidney biomarkers to the rescue

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Background: Banff classification may be difficult to apply in practice and surveys showed it is poorly reproducible among professionals, for several reasons: there are many terms, some of which not consensual, with exceptions, some elementary lesions may be difficult to assess (missing information), and the clinical context is not formally considered. We investigated whether it can be improved using automated classification tools.

Methods: Several retrospective datasets from three European transplantation centers (Leuven, Hannover, and Paris Necker) were used for training and validation of two algorithms: Gradient Boosting (XGBoost) and decision tree. SHapley Additive exPlanations (SHAP values) were used to enhance the individual interpretability of each result.

Results: Models were built for the diagnoses of: antibody-mediated rejection (ABMR), T cell-mediated rejection (TCMR), interstitial fibrosis and tubular atrophy (IFTA), glomerulonephritis (GN), and for the distinction between acute and chronic forms of ABMR and TCMR. Performances were excellent with XGBoost in the three different datasets with ROC curve AUC (95%CI) of: 0.97 (0.92–1.00), 0.97 (0.96–0.99), and 0.95 (0.93–0.97) for ABMR; 0.94 (0.91–0.96), 0.94 (0.92–0.95), and 0.91 (0.88–0.95) for TCMR; >0.96 (0.90–1.00) with all three for IFTA.

Conclusions: In this study, we set up and validated machine learning algorithms to improve and automate the interpretation of kidney graft biopsy elementary lesions, also considering a few clinical data.
Kidney medical complications

OS12_1
AUSTRALIAN AND NEW ZEALAND CANCER RELATIVE SURVIVAL IN END-STAGE RENAL KIDNEY PATIENTS: A RETROSPECTIVE COHORT STUDY

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Background: Cancer survival in the general population has improved over time. Kidney failure population have a higher incidence of cancer with increased mortality. Relative survival following cancer diagnosis can provide more insight into the excess mortality directly or indirectly attributed to cancer in the kidney failure population.

Methods: We estimated and compared the relative survival for dialysis patients, kidney transplant recipients and general population with cancer in Australia and New Zealand from 1980 to 2019. The general population was reference group for background mortality, matching on sex, age, calendar year and country. We used Poisson regression to quantify the excess mortality between these three groups with cancer.

Results: We included 4,089 dialysis patients and 3,253 kidney transplant recipients with an incident cancer. Dialysis patients were older, had a higher proportion of indigenous people and had more comorbidities than kidney transplant recipients. The kidney failure population had lower 5-year relative survival: 0.25 (95%CI: 0.23-0.26) for dialysis, 0.55 (95%CI: 0.53-0.57) for kidney transplant and 0.670 (95%CI: 0.669-0.670) in the general population with cancer (Figure 1). At any given time, dialysis patients had a 2.10 times higher adjusted excess mortality compared to the general population with cancer (2.10, 95%CI: 2.02-2.18), whereas kidney transplant recipients had no excess mortality (1.02, 95%CI: 0.97-1.08). Relative survival and excess mortality varied by cancer site: lung had the lowest relative survival rates, while kidney failure population with melanoma, breast and prostate cancers had the highest excess mortality. There were also sex differences: women had greater relative survival.

Conclusions: Relative survival was lower among the kidney failure population with incident cancer compared to the general population with cancer, for all-site and particularly for melanoma, breast and prostate cancer. Decreased survival may be due to poorer access to, more harm or less efficacy of treatments.

Figure: All-site cancer and cancer-type relative survival ratios

Kidney Color: Artificial Intelligence Image Processing to Improve Kidney Transplant Outcomes Prediction

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Background: Kidney transplant (KT) preimplantational predictors, such as kidney donor risk index (KDRI), can have a limited accuracy due to the lack of information from the graft itself. Transplant surgeon preimplantational graft evaluation is always performed, but the opinion may vary between centres and surgeons. Artificial intelligence training with machine learning can process, classify, and segment images. With enough information, it is possible to develop algorithms to predict patterns. Our aim was to train an algorithm on backbench images from cadaveric donor kidneys in order to predict delayed graft function (DGF). By developing a rapid, robust, accurate, and cost-effective method to assess kidney donors, we may improve the prediction of standardized models such as KDRI and support the surgeon in deciding whether to accept or discard the graft.

Methods: This is a unicentric prospective study on grafts from cadaveric donors that were successfully transplanted with at least one follow-up week. After backbench surgery and before cold static preservation, we obtained images with last generation mobile phone cameras from both graft sides with a grey scale calibration card. Data from donors was collected, and surgeons completed a questionnaire including kidney color, roughness, atheroma arterial plaques and cortical fat adherence. Image processing steps were: Image color calibration, kidney cortex and periuremic fat masking and segmentation, patch extraction and color+texture features computation. A random forest classifier was trained to predict DGF.

Results: Our initial dataset includes 139 kidney transplants. 38 kidneys developed DGF. KDRI, fat percentage, kidney color, cortical surface roughness and ostium atheroma plaques were the predictors finally included in our model. ROC curve AUC was 0.957 to predict DGF.

Conclusions: Machine learning image processing may improve the prediction of posttransplant graft function. This first experience can help in decision-making and allocation in kidneys from other centres. Validation from multicentre data is needed.
CAUSES OF DEATH IN KIDNEY TRANSPLANTATION, A PARADIGM SHIFT?

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Background: Cardiovascular diseases have traditionally been the leading cause of mortality in kidney transplanted patients but are now reported to be a reduced by more than half. This is mainly due to an increase in cancer mortality. A better understanding of risk factors for mortality. We conducted a retrospective observational study in a multicentric cohort to describe the distribution of causes of death in kidney transplant recipients and to analyse the risk factors for mortality at the time of transplantation.

Methods: We included all patients transplanted between 01.01.2008 and 31.12.2014 in two French databases (ASTRE and DIVAT). We studied deaths that occurred with a functioning graft or within six months after graft failure. Our primary endpoint was the distribution of causes of death. We then analyzed patient survival using competing risks analysis to identify risk factors for mortality, considering graft failure as a competing event.

Results: Of the 458 kidney transplant recipients included in ASTRE database, the median age was 54 years. Among them, 1022 (22.9%) died during the follow-up. Mean patient survival was 97.2% at 1 year after transplantation, 89.9% at 5 years, and 73.8% at 10 years. We accounted for 262 deaths (25.8%) from infectious causes (mainly from community-acquired infections, including 102 lung infections, 10.0%), 223 deaths (21.8%) from neoplastic causes (including 51 lung cancers, 5.0%, and 198 deaths (19.4%) from cardiovascular causes (including 55 sudden cardiac deaths, 5.4%). The cause was unknown for 194 patients (18.0%). Risk factors for mortality were age at recipient, time on dialysis, exposure to thrush, smoking, cardiovascular comorbidities, diabetic and vascular nephropathy, negative HSV serology, previous transfusion history, delayed graft function and use of cyclosporine. We then defined an easy-to-use model to calculate at the time of transplantation. Our results were validated in 2057 patients of DIVAT database.

Conclusions: This work allowed us to highlight a paradigm shift in the causes of death in kidney transplant patients, infections and cancers being now ahead of cardiovascular diseases. Risk factors and our new model could provide better understanding of the mortality risk in kidney transplant recipients.

CURRENT STATUS OF PREGNANCY AND DELIVERY AFTER RENAL TRANSPLANTATION IN JAPAN

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Background: Pregnancy and childbirth in renal transplant patients are not without risk, even if renal function is preserved after kidney transplantation. The incidence of gestational hypertension in renal transplant patients is reported to be 25-31%, premature delivery 50%, and cesarean section 65%. Pregnancy and childbirth carry many risks, even for healthy individuals. Transplant patients also face a variety of risks, including the burden on the kidneys due to increased circulating blood volume, the risk of teratogenicity due to immunosuppressive and antihypertensive drugs, the risk of rejection during pregnancy, and mental illness due to chemotherapy and hormonal balance. We report on the current status of pregnancy and delivery after kidney transplantation in Japan.

Methods: 453 post-transplant pregnancies from January 1990 to December 2021 (age: 32.0±18.4) (426 living donor kidney transplants, 29 donated kidneys from brain death by Group A: Controls; 6,908 nonpregnant patients, Group B, and 137 patients who became pregnant and gave birth before transplantation: Group C.

Results: (1) Ca at conception 1.19±0.54 (0.5-3.9), age at conception 33.5±10.07 (22-43) (2) Pregnancy period after transplantation was 3.8 years (1-18 years). There was no difference between Group A, which had pregnancies and deliveries after transplantation, and Group C, which had pregnancies and deliveries before transplantation. (10th grade implantation rate: 86.5% vs. 82.7%, P=0.98) (3) Cr > 1.5 at conception was significantly worse than Cr ≤ 1.5 in terms of transplantation kidney. (10th year implantation rate 82.5% vs. 97.3% P<0.01) There was no significant difference in the retention of transplanted kidney depending on the presence or absence of hypertension at conception (10th year retention rate: 86.5% vs. 86.5%). (10th year retention rate: 86.1% vs. 83.3% P=0.413) (B) Factors related to transplant kidney in pregnant were Cr at gestation (Cr<1.5 vs. Cr>1.5) and Cr at year after delivery (Cr<1.5 vs. Cr>1.5). Cr at 1 year after delivery (Cr<1.5 vs Cr>1.5), and proteinuria after delivery (yes vs no).

Conclusions: Renal transplantation allows for a safe pregnancy and delivery of a child with good indication and management.
## OS12_6 VOLUMETRIC BONE MINERAL DENSITY, BONE MICRO-ARCHITECTURE EVOLUTION AFTER KIDNEY TRANSPLANTATION: A 1-YEAR RESULTS OF A PROSPECTIVE COHORT STUDY

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**Background:** Bone loss and mineral abnormalities are frequent in kidney transplant recipient (KTR). Currently, the clinical management of bone abnormalities includes the use of bone biopsy, surrogates’ biochemical markers and imaging technique (Dual Energy X-ray (DEXA)). The high-resolution peripheral quantitative computed tomography (HR-pQCT) provides noninvasive information on bone microarchitecture and a quantitative measurement of the volumetric density of trabecular and cortical bone. The goal of our study is to evaluate the evolution of bone micro-architecture using HR-pQCT compared to standard technique (DEXA) in a kidney transplanted cohort.

**Methods:** All patients referred for a single kidney transplant at our centre were eligible for inclusion (NCT04713774). Participants underwent baseline, 3-months and 1-year biomarkers analysis, BMD measurements by DEXA and HR-pQCT at 1-year but less at 3-months. PTH level correlates to cortical porosity evaluated by HR-pQCT. Formation biomarkers variations significantly correlated with several HR-pQCT parameters modulations such as trabecular homogeneity.

**Results:** 31 patients were prospectively included for the 1-year analysis. Median age was 60.4 [49.9 – 65.4]. Bone turn over biomarkers shows significant decrease between D0 and 1-year: PTH from 211.7 ng/l vs 56.7 (p<0.0001), P1NP 185 ug/l vs 59.1 ug/l (p=0.036). We observed a significant reduction of BMD by DEXA at the hip site between D0 and 1-year, respectively 0.843/cm² and 0.820 cm² (p=0.025) with a non-significant increase at lumbar site. The HR-qQCT analysis demonstrated a significant reduction of the total, and trabecular BMD between D0 and 1-year, respectively 256.2 mg HA/ccm vs 255.6 mg HA/ccm (p=0.037). Correlations were observed between BMD in DEXA and HR-pQCT at 1-year but less at 3-months. PTH level correlates to cortical porosity evaluated by HR-pQCT. Formation biomarkers variations significantly correlated with several HR-pQCT parameters modulations such as trabecular homogeneity.

**Conclusions:** It is essential to be able to accurately assess the modification of BMD within time, ideally by non-invasive techniques. HR-pQCT is able to evaluate the decrease of BMD at trabecular site rapidly post transplantation (3 months, when no change on trabecular structure have been observed by DEXA). Correlation between both techniques appears at 1-year. Bone biomarkers modulation show a promising association with HR-pQCT parameters.

## OS12_7 ALLOGENEIC IMMUNITY HELPS SUSTAIN EFFECTIVE BK-VIRUS IMMUNE RESPONSES AND PREVENTS BK VIRUS-ASSOCIATED NEPHROPATHY

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**Background:** BK-virus (BKV) associated nephropathy (BKvAN) emerged as a major complication in renal transplantation, affecting up to 10% of kidney transplant recipients and leading to graft loss in more than 50% of cases. If BKv T-cell response plays a crucial role in the control of BKV infection, the mechanisms involved remain unknown.

**Methods:** We prospectively characterized BKv T cells in a cohort of 100 kidney transplant recipients with different BKV reactivation levels (without BKV, viremia, viremia or BKvAN).

**Results:** Patients with BKV viremia had a severe impairment of BKv CD8 T-cell functionality, such as proliferative, cytokine and cytotoxic capacities (p<0.05). We observed a gradual loss of functional BKv T cells according to BKV reactivation levels (p<0.0001), an inverse correlation between T-cell functionality and plasmatic BKV load, and the overexpression of lymphocyte inhibitory receptors (PD1, CTLA4, GITI and TIMS) (p<0.05). This phenotype suggested an exhaustion of BKv T cells in patients with BKVAN. This lymphocyte impairment was associated with a low level of donor-recipient class II HLA divergence, suggesting a key role of allogeneic CD4 help. In a context of higher levels of donor-recipient class II HLA divergence, allogeneic CD4 T cells can provide heterogeneous help to sustain BKv T-cell responses. In vitro experiments, the replacement of syngeneic CD4 T cells with allogeneic HLA-mismatched CD4 T cells restores BKvCD8 T-cell responses.

**Conclusions:** We observed an exhaustion of BKV CD8 T cells in patients with BKVAN. This lymphocyte exhaustion could lead to a defective BKv T-cell response, unable to provide a protective immune response against BKV reactivation. Our results suggest that in kidney transplant recipient, allogeneic CD4 T cells may provide a heterogeneous help to maintain an effective BKV CD8 T-cell response in kidney transplant recipients, improving the control of BKV replication in the kidney allograft.
OS12_8

TIME-DEPENDENT VARIATIONS IN BK POLYOMAVIRUS GENOME FROM KIDNEY TRANSPLANT RECIPIENTS WITH PERSISTENT VIREMIA

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Background: BK polyomavirus (BKPyV) is a small human DNA virus that can remain inactive for long periods within its host. In kidney transplant recipients, BKPyV reactivation can lead to nephropathy. BKPyV genome can be roughly divided into a protein-coding region and a non-coding control region (NCCR). Twelve subgroups and two different forms of BKPyV have been described, respectively, based on the genetic variability of the major capsid protein VP1 and the NCCR. In this work, we studied BKPyV genetic diversity and the changes that occur over time in kidney transplant recipients with persistent viremia.

Methods: The study was based on samples collected from a retrospective cohort of 394 kidney transplant recipients with viremia. BKPyV genome was analyzed from samples collected in the first months (range 75 – 139 days) and after longer post-transplant periods (range 338-1479 days) from patients with persistent viremia. BKPyV genome was obtained by next-generation sequencing and was characterized based on the entire protein-coding region and the NCCR. BKPyV sequences were compared per patient in order to identify the genomic changes over time.

Results: We were able to obtain 150 BKPyV sequences in samples collected in the first months and 45 – in samples collected later after transplantation. Per-patient comparison of BKPyV sequences showed NCCR changes in both urine and plasma samples. In urine samples, the mutation frequency did not exceed 18.5% and reached a higher value of 50% in plasma samples. Comparing all the entire BKPyV protein-coding region showed amino acid changes in urine and plasma samples in 37.5% and 34.6% of the cases, respectively. Amino acid changes were mainly found in the VP1 protein, with a frequency of 66.6% in both sample types. Most of the identified VP1 changes were located in the receptor-binding region (RBR) (77.7%) and the amino acid changes with those observed in samples collected in the first months after transplantation showed that amino acid changes were associated with both the introduction of a new amino acid and the reverse switch to the original one.

Conclusions: Our results suggest that BKPyV genome can accumulate mutations over time in kidney transplant recipients with persistent BKPyV viremia. This should be taken into account when developing future antiviral drugs and vaccines.

OS13_1

LIVER IMMUNOSUPPRESSION FREE TRIAL (LIFT): OUTCOMES OF THE FIRST BIOMARKER-GUIDED IMMUNOSUPPRESSION WITHDRAWAL TRIAL IN LIVER TRANSPLANT RECIPIENTS

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Background: Liver transplant patients are usually transplanted in a state of high immunosuppression to prevent organ rejection. The Banff Human Organ Transplant consensus gene panel (BHT0) was developed for reproducible molecular diagnosis in solid organ transplantation, but its application and relevance in liver transplantation (LT) biopsies has not been investigated so far. We aim to assess specific molecular signatures of rejection in LT biopsies.

Methods: We evaluated all LT biopsies with concomitant investigation of circulating anti-HLA DSA from pediatric and adult recipients transplanted between 2010 and 2020 in 3 French centers. Recurrence of initial liver disease, active HBV and/or HCV viremia were excluded. Extracting RNA from FFPE biopsies, the samples were sequenced using the BHT0 gene panel with the Nanoluc technology. Differential gene expression (DGE) analysis was performed to assess specific molecular signature with 2 class comparisons based on histology diagnosis: in one versus everything else (EE) approach, coupled with functional pathway analysis (PA).

Results: A total of 253 biopsies (171, 67.6% performed for cause indication) from 189 patients were evaluated. The median time post-transplant was 1.29 years (IQR: 0.43-3.31). Anti-HLA DSA were positive for 114 (45.1%) biopsies. TCN was diagnosed in 75 biopsies (29.6%), liver biopsy in 33 (13.4%), C4d urea positive in 3 (1.2%) and 22 (8.7%) biopsies were C4d positive. Liver TCMR-associated transcripts were significantly related to IFN and signaling and inducible (CICX110, CICX111, IDO1) and to activated effector T cells (CTLA4, IFN-g, CXCL10, CXCL9 and CXCL11, IDO1) and to activated effector T cells (CTLA4, IFN-g, CXCL10, CXCL9 and CXCL11, IDO1). PA highlighted biological process related to interleukins and IFN-g, signaling lymphoid, and lymphoid cells interaction. Fibrosis was significantly associated with transcripts related to oxidative stress (MET, FN1, ARG), cell-extracellular matrix interaction, angiogenesis (ERG, BMPER). No significant differences were found in DGE analyses of C4d positive biopsies vs EE, nor of DSA positive vs EE.

Conclusions: Using for the first time the BHT0 panel in liver graft biopsies, we highlighted meaningful molecular signatures associated with TCMR with transcriptome resemblance universal mechanism, and fibrosis. Larger cohort of biopsies is being analyzed to establish molecular identification within more phenotypes.
**FULL ORALS**

**Biomarkers in Liver transplantation**

### OS13_3

**EX SITU REPERFUSION INJURY/INFLAMMATION: IMMUNO-MOLECULAR PROFILING OF HUMAN LIVERS DURING NORMOTHERMIC MACHINE PERFUSION**

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**Background:** Ex-situ reperfusion inflammation/injury (ERI) is an increasingly recognised phenomenon affecting donor livers preserved with normothermic machine perfusion (NMP). Higher-risk livers and DCDs are particularly vulnerable and ERI can manifest as poor graft function ex situ, with organ discard or post-transplant IRI occurring despite NMP. The immuno-molecular basis of ERI has yet to be described. This study aimed to characterise the immuno-molecular profile of circulating perfusate following ex situ reperfusion during NMP.

**Methods:** Perfusate samples from (n=18 livers) in the Consortium for Organ Preservation in Europe (COPE) Liver trial and (n=14) UK ‘back to base’ liver trials were included in this study. All livers were perfused using packed red cells and a colloid, with no leukocytes, platelets or complement in the starting perfusate. Serial perfusate samples were analysed for immune cells using flow cytometry, cytokines (Luminex panel) and inflammatory endogenous alarmins (chromatin-associated molecular patterns (CAMPs)) which consist of molecules such as nucleosomes and neutrophil extracellular traps (NETs) using ELISA-based measurement.

**Results:** NMP initiated an efflux of passenger immune cells from the donor liver into the perfusate that peaked at 30 mins, then fell and plateaued by 240 mins. Cytotoxic CD8+ T cells and NK cells were the most abundant cells in the efflux, into the perfusate that peaked at 30 mins, then fell and plateaued by 240 mins.

**Conclusions:** This is the first study to specifically characterise the immuno-molecular features of ERI, highlighting the role of immune cells, inflammatory cytokines and CAMPs in creating an inflammatory milieu within the perfusate. Donor livers susceptible to ERI may require targeted interventions to improve graft function ex situ and reduce organ discard or post-transplant preservation reperfusion injury-related complications.

Fig. Immune cells, cytokines and CAMPs during NMP. Dashed line = levels in severe sepsis.

### OS13_4

**BILE PROTEOME REVEALS BILARY REGENERATION DURING NORMOTHERMIC PRESERVATION OF HUMAN LIVERS**

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**Background:** Normothermic machine perfusion (NMP) after traditional static cold storage is increasingly used for preservation and assessment of human donor livers prior to transplantation. Biliary viability assessment during NMP reduces the risk of post-transplant biliary complications. However, understanding of molecular changes in the biliary system during NMP remains incomplete. Here we present an in-depth, unbiased proteomics analysis of bile collected during NMP of human livers.

**Methods:** A total of 56 human donor livers undergoing clinical NMP viability assessment using pre-established viability criteria were included in this study. Untargeted proteomics was performed on a retrospective discovery cohort of 31 livers. Results of predictive value were then validated in an independent, prospective cohort of 25 clinical NMP livers using the same proteomic approach. Gene ontology of identified proteins was used for pathway analysis.

**Results:** In the discovery cohort, a total of 2346 unique proteins were identified. Longitudinal analysis between start of NMP and viability assessment revealed a large number of significantly expressed proteins (p<0.05, >2-fold change) implicated in the flush-out of ischemia-reperfusion injury induced cell debris, and upregulation of intracellular signalling and secretion proteins. Transplanted livers showed significant upregulation proteins involved in cellular proliferation, migration, cellular signalling and the immune response at 30 mins NMP, when compared to non-transplanted livers, and was maintained throughout the perfusion. Receiver operating characteristic-area under the curve analysis to predict cholangiocellular viability and successful, biliary complication-free transplantation identified a panel of 3 proteins yielding a c-statistic of 0.962 at the time of viability assessment. The validation cohort of 25 livers reproduced the performance of this diagnostic model, with a c-statistic of 0.910.

**Conclusions:** Proteomics of human bile reveals upregulation of regenerative pathways in viable livers during NMP. Our findings present a large and novel data set of biliary proteins which pave the way for future studies on the mechanisms of ischemia-reperfusion injury, ischean cholangiopathy and biliary preservation in liver transplantation.
OS13.5 MMP9 CORRELATES TO WORSE ISCHEMIA REPERFUSION INJURY AND IS PARTIALLY AMELIORATED BY NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION

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Background: Matrix metalloproteinase-9 (MMP-9) is a collagenase that breaks down the extracellular matrix. In liver ischemia reperfusion injury, it allows leukocytes to enter liver parenchyma and thereby modulates tissue injury. Liver-selective inhibition of MMP-9 decreased ischemia reperfusion injury (IRI) in a rodent model. In humans, normothermic machine perfusion (NMP) is a potential medium to deliver therapies during the preservation period prior to liver transplantation (LT). Therefore, in this study we aimed to investigate MMP-9 levels and their correlation with IRI during and after NMP compared to traditional static cold storage (SCS), as the basis for further interventional studies.

Methods: Perfusion and recipient plasma samples (collected prior to and 1h after transplant) from n=40 LTs were selected from the Consortium for Organ Preservation in Europe (COPPE) Liver NMP trial cohort (NMP n=30, SCS n=10). Samples were matched for donor and recipient demographics and analysed by enzyme linked immunosorbent assay (ELISA).

Results: MMP-9 increased in plasma after reperfusion in NMP (p=0.002) but more so in SCS (p<0.001), with fold changes of 4 and 9, respectively (p=0.001, fig 1). During NMP, perfusate MMP-9 decreased throughout perfusion with a fold change of 0.14 (p<0.001) and was higher overall in grafts with steatosis (p=0.001). The fold change of perfusate MMP-9 was negatively correlated to cholestatic markers in perfusate during NMP and in recipient plasma post-transplant (table 1). Elevated plasma MMP-9 levels were correlated to early allograft dysfunction (p=0.016), model for early allograft function, and their components; liver transaminases (AST, ALT) and INR (table 1). Post-reperfusion syndrome (p=0.05), post-transplant renal function (table 1) and need for renal replacement therapy (p=0.016), model for early allograft function, and their components; liver transaminases (AST, ALT) and INR (table 1). Post-reperfusion syndrome (p=0.05), post-transplant renal function (table 1) and need for renal replacement therapy (p=0.016), model for early allograft function, and their components; liver transaminases (AST, ALT) and INR (table 1). Post-reperfusion syndrome (p=0.05), post-transplant renal function (table 1) and need for renal replacement therapy (p=0.016), model for early allograft function, and their components; liver transaminases (AST, ALT) and INR (table 1).

Conclusions: Multiple risk factors and outcomes related to liver IRI are correlated to MMP-9 in LT, making it a potential therapeutic target during preservation. Liver MMP decreased overall levels of recipient plasma MMP9 when compared to SCS, providing a potential platform for further intervention.

Figure 1 Comparison of plasma MMP-9 concentrations between preservation types (NMP vs SCS). Box and whisker plot showing the comparison of log2 plasma MMP-9 concentrations pretransplant and 1h post-reperfusion of the liver in recipients following either NMP or SCS. *2-way ANOVA. **Paired student t-test.

Table 1 Spearman’s Rho correlations between fold change plasma/perfusate MM-9 and continuous clinical outcomes

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Foldchange MMP-9 plasma (P2/P1)</th>
<th>Foldchange MMP-9 perfusate (P2/P1)</th>
<th>Spearman’s Rho</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>nKAV</td>
<td>0.518</td>
<td>0.002</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ALT mean day-1</td>
<td>0.495</td>
<td>0.001</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ALT mean day-3</td>
<td>0.500</td>
<td>&lt;0.001</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>INR mean day-3</td>
<td>0.427</td>
<td>0.006</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Bilirubin mean day-1</td>
<td>NS</td>
<td>0.390</td>
<td>0.032</td>
<td></td>
</tr>
<tr>
<td>GGT mean day-1</td>
<td>NS</td>
<td>0.618</td>
<td>0.018</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine mean day-1</td>
<td>0.360</td>
<td>0.019</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Perfusate</td>
<td>Bilirubin P2/P1</td>
<td>NS</td>
<td>NS</td>
<td>0.530</td>
</tr>
<tr>
<td>AST (mmol/L)</td>
<td>NS</td>
<td>NS</td>
<td>0.052</td>
<td>0.015</td>
</tr>
<tr>
<td>ALT (mmol/L)</td>
<td>NS</td>
<td>NS</td>
<td>0.579</td>
<td>0.031</td>
</tr>
<tr>
<td>GGT (mmol/L)</td>
<td>NS</td>
<td>NS</td>
<td>0.455</td>
<td>0.009</td>
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<tr>
<td>GGT P2/P1</td>
<td>NS</td>
<td>NS</td>
<td>0.350</td>
<td>0.54</td>
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</tbody>
</table>

OS13.6 GRAFT-DERIVED CFDNA MONITORING IN PLASMA & BILE DURING EX-VIVO NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION: A PROMISING OBJECTIVE TOOL

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Background: Ex-vivo normothermic machine perfusion (NMP) is an organ preservation technique that enables an extended assessment of graft suitability prior to liver transplantation (LT). The various existing protocols used during NMP, incorporating conventional biochemical tests and perfusion parameters, vary significantly in their assessment of organ suitability for LT when applied to the same grafts. Graft-derived cell-free DNA (gdcfDNA) analysis is an emerging tool for monitoring graft health post-transplantation. We investigated the feasibility of monitoring gdcfDNA during NMP for LT in a prospective, observational cohort study.

Methods: Serial plasma and bile samples were collected during NMP for 10 consecutive grafts, at 15 minutes post-machine reperfusion and then 2-hourly. Digital PCR was used to quantify mitochondrial cell-free DNA released from the graft at each timepoint.

Results: Five grafts were viable for transplantation, there were no cases of primary non-function or death in the recipients. gdcfDNA was successfully quantified in all bile and plasma samples (n=100). In plasma, gdcfDNA levels climbed post-machine reperfusion until 4.25 hours (median concentration 2.25 hours = 15.98 x 10^6 copies/mL, 4.25 hours = 40.21 x 10^6 copies/mL). gdcfDNA concentrations then diverged significantly when comparing the viable and non-viable graft groups (6.25 hours, median viable: 117.15 x 10^6 copies/mL vs median non-viable: 16.72 x 10^6 copies/mL). The difference in gdcfDNA concentrations between the two groups was statistically significant and levels correlated in all cases with the viable/non-viable outcome (Figure 1). There was a trend of gradual decline in bile gdcfDNA levels from viable grafts post-machine reperfusion. Discarded grafts showed more variable patterns in bile gdcfDNA levels.

Conclusions: gdcfDNA analysis during NMP is a feasible and promising objective tool to inform organ viability assessment during NMP for LT. Plasma gdcfDNA levels declined over time in non-viable grafts; possibly related to metabolic failure or microcirculatory collapse due to more severe ischaemic-reperfusion injury. gdcfDNA quantification in bile during NMP offers the alluring prospect of providing an objective means to assess the degree of biliary injury associated with organ procurement.

Figure 1 Comparison of plasma gdcfDNA concentrations between viable and non-viable grafts (n=5). Line graph showing the comparison of plasma gdcfDNA concentrations between the two groups was statistically significant and levels correlated in all cases with the viable/non-viable outcome (Figure 1).
Background: Bile biochemistry serves as liver graft viability marker during normothermic perfusion (NMP). However, bile acids (BA) which are key for liver regeneration and liver injury have not yet been analyzed during NMP.

Methods: In a validated porcine model of donation after circulatory death, BA pool was analyzed in 2 different injury groups: Liver grafts underwent static cold storage for 6 hours (SCS-group; n=6) vs 2h of hypothermic oxygenated perfusion (HOPE-group; n=6). After 2h of NMP, BA were analyzed semi-quantitatively with liquid chromatography/mass spectrometry. Validated biochemical viability criteria during NMP (transaminase release, lactate clearance, pH...) were also assessed. Partial Least Square Discriminant Analysis (PLS-DA) based on routine biochemical data alone or with additional BA analysis was used to differentiate both groups.

Results: A total of 16 primary and secondary BA were identified. Univariate analysis of each BA did not differ among groups whereas overall BA pool was analyzed in 2 different injury groups: Liver grafts underwent static cold storage for 6 hours (SCS-group; n=6) vs 2h of hypothermic oxygenated perfusion (HOPE-group; n=6). After 2h of NMP, BA were analyzed semi-quantitatively with liquid chromatography/mass spectrometry. Validated biochemical viability criteria during NMP (transaminase release, lactate clearance, pH...) were also assessed. Partial Least Square Discriminant Analysis (PLS-DA) based on routine biochemical data alone or with additional BA analysis was used to differentiate both groups.

Conclusions: Combined BA analysis during NMP with biochemical viability criteria enabled a better discrimination between two different injury groups in a porcine model of DCD liver grafts. BA may thus refine graft selection especially in grafts with "borderline" biochemical viability profiles.

Figure 1: PLS-DA analysis based on biochemical viability criteria and bile acids in SCS and HOPE group. R2 values represents goodness-fit-representation and Q2 values estimated the predictive ability of the model. Panel A displays PLS-DA analysis based on biochemical viability criteria alone, with good discrimination between both groups (Q2=0.612, R2=0.815). Panel B displays PLS-DA analysis based on biochemical viability criteria and bile acids, with better discrimination between both groups (Q2=0.612, R2=0.815).

OS13.8 ANALYSIS OF THE BILE METABOLOME TO SEARCH FOR POTENTIAL BIOMARKERS OF QUALITY OF THE LIVER WITH PARTICULAR EMPHASIS ON BILE ACIDS

Kamil Luczykowski1, Natalia Warmuzinska1, Dagmar Kollmann2, Markus Selzner1, Barbara Bojko1
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Background: The constantly growing demand for transplant organs forces transplantation centres to improve organ preservation methods and better use of suboptimal grafts. Although machine perfusion methods have a beneficial effect on organs compared to static cold storage (SCS), new methods of graft quality assessment before transplantation are still being sought. This study focused on searching for biliary metabolites that could be biomarkers of changes in transplanted livers, with particular emphasis on the analysis of bile acids.

Methods: The studies were performed on a porcine model with 0 (min) or with induced moderate (30, 60, 90 min) liver warm ischemia. Bile samples produced by organs subjected to SCS or normothermic ex vivo liver perfusion (NEVLP) collected during the peri-transplant period were analyzed. Sample preparation was performed using thin-film solid-phase extraction (TF-SPE). The LC-HRMS platform was used to search for potential biomarkers, while targeted analysis of bile acids was performed on a triple quadrupole mass spectrometer.

Results: The chemometric analysis showed a separation indicating differences in the metabolomic patterns of the bile samples based on the time interval they were collected. The preservation method used affected the level of such metabolites as lysophosphatidylcholines (LPC) and bile acids, including glycocholic acid, glycochenodeoxycholic acid, taurochenodeoxycholic and taurocholic acid. It was observed that 30 min ischemia affects the metabolomic profile of the bile produced by the organ subjected to SCS (including changes in the level of oxidized bile acids and 5-methoxyindoleacetic acid), while in the NEVLP group, the alterations were seen after 90 min ischemia (mainly LPC level). In addition, the optimized and validated method of bile acid analysis allowed for the precise determination of concentrations of these metabolites in studied samples.

Conclusions: This study identified metabolites worth considering as potential markers of changes occurring in preserved grafts and optimized method for bile acid analysis, which may contribute to the development of new diagnostic tools assessing the organ’s condition in the future.

Acknowledgments: This study was funded by National Science Centre, grant Opus No. 2021/41/NI/00860.
Conclusions: This large multicenter series of ex-situ right split grafts disclosed an overall 1-year morbidity/mortality comparable to the best achievable results in whole LT. The results show that the main morbidity burden in adult RSLT is an overall 1-year morbidity/mortality comparable to the best achievable results in non-RSLT.

Table 1: Post-Transplant Outcomes in Benchmark and Non-Benchmark Cases

<table>
<thead>
<tr>
<th>Entire cohort</th>
<th>Benchmark cohort</th>
<th>Non-Benchmark cohort</th>
<th>Benchmark cohort vs RSLT</th>
<th>Non-Benchmark cohort vs RSLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft survival, %</td>
<td>20.9 (2.1-26.2)</td>
<td>20.3 (18.9-21.7)</td>
<td>26.2 (23.3-29.7)</td>
<td>22.8 (19.1-26.6)</td>
</tr>
<tr>
<td>Recipient survival, %</td>
<td>90.5 (90.2-90.7)</td>
<td>89.5 (89.1-90.1)</td>
<td>92.2 (91.9-92.5)</td>
<td>92.2 (91.9-92.5)</td>
</tr>
<tr>
<td>1-year survival, %</td>
<td>86 (85.6-86.4)</td>
<td>92 (91.6-92.4)</td>
<td>92 (91.6-92.4)</td>
<td>92 (91.6-92.4)</td>
</tr>
</tbody>
</table>

OS14_3

AGE AND LIVER GRAFT: A SYSTEMATIC REVIEW WITH METAREGRESSION

Ilaria Nerpi1, Marco Pascale1, Giuseppe Bianco1, Francesco Frongillo1, Salvatore Agnesi1, Francesco Giovannazzo1

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Background: The increasing shortage of organs for liver transplantation has led to the greater use of Extended Criteria Donors (ECDs) to meet the growing demand for liver grafts. The demographic changes result in the increased use of elderly donors, historically considered marginal donors, for liver transplantation. Despite this, the exact age cut-off for donor eligibility remains unclear and is a subject of debate in the transplant community. This study was conducted to evaluate the effect of donor age on transplant outcomes, including 1-year graft survival, biliary complications, and hepatic arterial thrombosis.

Methods: The method included a search in PubMed, Scopus, and Cochrane Library. The primary outcome was 1-year graft survival; the secondary outcomes were biliary complications and hepatic arterial thrombosis. The meta-analysis included 11 studies. The meta-analysis results showed that the 1-year graft survival of liver grafts from elderly donors was similar to that of standard donors. However, elderly donors were found to have an increased risk of overall biliary complications (OR: 1.89, 95% CI: 1-3.65) and hepatic artery thrombosis (OR: 2.27, 95% CI: 1.27-4.11). A meta-regression analysis also showed a significant correlation between 1-year graft survival and the year of publication (coef: 0.00027, 95% CI: -0.0001 to 0.0003, p = 0.0009).

Conclusions: In conclusion, the meta-analysis results show that donor age alone cannot be considered a criterion for extended criteria in liver transplantation. The 1-year graft survival of liver grafts from elderly donors has improved over time, but there is still a risk of biliary and arterial complications. The decision to use elderly donors as liver transplant donors should be based on a comprehensive assessment of risk factors and balanced by reducing other risk factors using new technology such as machine perfusion.

OS14_2

LIVER TRANSPLANTATION IN THE ELDERLY: PROPOSAL FOR AN INNOVATIVE PATIENT SELECTION PROTOCOL

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1Azienda Ospedaliera Universitaria di Padova, Padova, Italy

Background: Despite European and international guidelines that don’t pose a specific contraindication to liver transplantation (LT) in elderly patients and invite to take into account physiological rather than chronological age, most transplant centers and regulatory institutions have widely adopted an upper age limit (65 years old) for donor eligibility remains unclear and is a subject of debate in the transplant community. This study was conducted to evaluate the effect of donor age on transplant outcomes, including 1-year graft survival, biliary complications, and hepatic arterial thrombosis.

Methods: The method included a search in PubMed, Scopus, and Cochrane Library. The primary outcome was 1-year graft survival; the secondary outcomes were biliary complications and hepatic arterial thrombosis. The meta-analysis included 11 studies. The meta-analysis results showed that the 1-year graft survival of liver grafts from elderly donors was similar to that of standard donors. However, elderly donors were found to have an increased risk of overall biliary complications (OR: 1.89, 95% CI: 1-3.65) and hepatic artery thrombosis (OR: 2.27, 95% CI: 1.27-4.11). A meta-regression analysis also showed a significant correlation between 1-year graft survival and the year of publication (coef: 0.00027, 95% CI: -0.0001 to 0.0003, p = 0.0009).

Conclusions: In conclusion, the meta-analysis results show that donor age alone cannot be considered a criterion for extended criteria in liver transplantation. The 1-year graft survival of liver grafts from elderly donors has improved over time, but there is still a risk of biliary and arterial complications. The decision to use elderly donors as liver transplant donors should be based on a comprehensive assessment of risk factors and balanced by reducing other risk factors using new technology such as machine perfusion.
Background: Hepatic steatosis is associated with poor liver transplantation outcomes. This study describes the development of a first large-scale ‘Liver Atlas’ of deceased donor livers to:(i) investigate the incidence of biopsy-confirmed steatosis;(ii) identify pre-retrieval predictors of steatosis severity, and;(iii) evaluate the impact of steatosis severity on organ retrieval, utilisation and graft recipient outcome.

Methods: Consecutive biopsies from 1,048 deceased donors collected between 2017-2019 were requested from the national QUOD bioresource. Steatosis severity was quantified using imageDx™-based image analysis of H&E stained slides. 906 out of 1,048 donor livers had sufficient tissue for histological assessment and were included in the final analysis with none (n=670), mild (n=102), moderate (n=298, 57%), mild (n=10, 29%), the proportion of retrieved livers resulting in transplantation significantly decreased with increasing steatosis severity which was associated with a non-significant reduction in 12-month graft and patient survival.

Conclusions: This ‘Liver Atlas’ supports utilisation of pre-retrieval steatosis predictors and routine retrieval biopsy to avoid unnecessary liver discards. Transcriptomic analysis of this cohort is also being undertaken to map independent signatures associated with increasing steatosis severity. This will enable targeted ex-situ optimisation to improve utilisation of the high-risk steatosis category.

Performance metrics for each investigated time frame of recurrence

<table>
<thead>
<tr>
<th>Time frame (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N (recurrence)</td>
</tr>
<tr>
<td></td>
<td>120 (12)</td>
</tr>
<tr>
<td></td>
<td>116 (20)</td>
</tr>
<tr>
<td></td>
<td>98 (36)</td>
</tr>
<tr>
<td></td>
<td>82 (40)</td>
</tr>
<tr>
<td></td>
<td>74 (43)</td>
</tr>
<tr>
<td></td>
<td>66 (44)</td>
</tr>
<tr>
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<td>120 (44)</td>
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</tbody>
</table>

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OS14.6 DOES NATIVE HEPATECTOMY TECHNIQUE HAVE ANY IMPACT ON ONCOLOGIC OUTCOMES OF LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA?

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Background: To date, caval sparing (CS) and total caval replacement (TCR) for recipient hepatectomy in liver transplantation (LT) have been compared on terms of surgical morbidity. Nonetheless, CS technique is inherently associated with an increased manipulation of the native liver and later exclusion of the venous outflow, which may both increase the risk of intraoperative systemic shedding of tumors cells when LT is performed for hepatocellular carcinoma (HCC). The aim of the present multicentre study was to assess the impact of native hepatectomy technique on the risk of post-LT HCC recurrence.

Methods: This was an international, retrospective, multicenter, observational study to assess the impact of recipient hepatectomy technique (CS versus TCR) on the risk of post-transplant HCC recurrence.

Results: In 1851 patients with viable HCC in the explanted native liver, CS and TCR approaches were used in 1030 (55.6%) and 821 (44.4%) cases, respectively. The cumulative incidence of post-LT tumor recurrence at 1, 3 and 5 years was 4.4%, 10.1% and 12.1%, respectively. Group adjustment with inverse probability weighting was performed using the following baseline variables: recipient age, MELD score, Child-Pugh class C, viral hepatitis, alcohol abuse, pre-LT alphafetoprotein serum levels, clinical HCC stage according Milan criteria, pre-LT downstaging/bridging, tumor number and size, grading, microvascular invasion and cold ischemia time. In a multivariable competing risk regression model, CS was associated with a higher risk of HCC recurrence (SHR 1.699, 95% CI 1.262-2.269). In a multivariate competing risk regression model, the risk of post-transplant HCC was 4.4%, 10.1% and 12.1%, respectively. Group adjustment with inverse probability weighting was performed using the following baseline variables: recipient age, MELD score, Child-Pugh class C, viral hepatitis, alcohol abuse, pre-LT alphafetoprotein serum levels, clinical HCC stage according Milan criteria, pre-LT downstaging/bridging, tumor number and size, grading, microvascular invasion and cold ischemia time. In a multivariable competing risk regression model, CS was associated with a higher risk of HCC recurrence (SHR 1.699, 95% CI 1.262-2.269).

Conclusions: TCR approach should be considered alongside other preventive measures to reduce the risk of post-transplant HCC recurrence.

OS14.7 PREDICTION AND DIAGNOSIS OF REJECTION IN LIVER TRANSPLANTATION USING A BIOMARKER MODEL BASED ON CXCL10 AND MIRNOAS 155-5P AND 181A-5P

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Background: The diagnosis of rejection in liver transplantation (LT) relies on a liver biopsy (LB) lecture in the setting of abnormalities in the liver function tests (LFT). The use of non-invasive biomarkers may avoid the need for LB and could help in a more efficient immunosuppressive therapy adjustment. Plasma microRNA expression and certain chemokines have been proposed as potential biomarkers of rejection.

Methods: Prospective, observational study conducted in a cohort of 79 patients followed during the first year after LT. Plasma samples were collected on predetermined occasions for the analysis of microRNAs 155-5p, 122-5p and 181a-5p and CXCL10 chemokine. Patients with LFT abnormalities were submitted to a LB to rule out rejection, assessing previous and concurrent expression of the biomarkers to evaluate their predictive and diagnostic ability. Information from 87 patients included in a previous study was collected and used as a validation cohort.

Results: Twenty-four episodes of T-cell mediated rejection were diagnosed in 22 patients. Plasma CXCL10 concentration and the three microRNA expression were significantly elevated prior and at the moment of the diagnosis of rejection. These and other significantly altered variables were used to develop a logistic model for rejection prediction and diagnosis. The model included CXCL10 and microRNAs 155-5p and 181-5p. Area under the ROC curve (AUROC) for rejection prediction was 0.97 (81.6% sensitivity, 98.7% specificity) and 0.94 for diagnosis (91.3% specificity). In the validation cohort, the AUROCOS were 0.89 and 0.92 for rejection prediction and diagnosis, respectively. In patients with graft dysfunction (LFT abnormalities at the moment of the LB) of both cohorts, the biomarker model could identify those with rejection with an AUROC of 0.98 (97.3% sensitivity, 94.7% specificity).

Conclusions: The biomarker model based in CXCL10 and microRNA 155-5p and 181a-5 for the diagnosis of rejection and identifies patients with graft dysfunction due to rejection.

OS14.8 WORLDWIDE DATA FROM THE IMPROVEMENT LIVER TRANSPLANT STUDY: AN INTERIM ANALYSIS OF DONOR AND RECIPIENT PROFILES

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Background: The IMPROVEMENT project was designed to optimise predictive models of 90-day and 1-year allograft failure after liver transplantation (LT). This data collection (donor, preoperative recipient, postoperative and outcome data) involves several LT centres with different transplant activity volumes from Europe, North America, South America, and Asia

Methods: From Jan-2017 to Jan-2023, we enrolled 2,015 adult LTs. Centre and patient-specific inclusion criteria are fully reported on the IMPROVEMENT website (https://gemellegenitor.it/projects/the-improvement-study-2/) and on ClinicalTrials.gov (Ref. NCT06346926). Informed consent was obtained in all cases except at completion. All data from 21 centres are anonymised and stored in an online REDCAP database. Eight centres have already completed data collection and fifty more are in the process of submitting their data. This interim exploratory, descriptive analysis was conducted to identify potential inconsistencies/discrepancies.

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Defining risk and optimizing selection

Results: Donors had a median age of 58 yrs, BMI of 26 kg/m², donor risk index of 1.9, 39% were extended criteria (ECD), 9.1% were DCD, and perfusion machines were used in 6.4% of cases (Table 1). Recipients had a median age of 59 yrs and BMI of 26 kg/m².

Conclusions: The definition of an epidemiological and clinical profile of LT is mandatory to provide the basis for more complex prognostic models. The broadening of enrolment and data from other LT centres will allow an accurate worldwide representation of LT and the development/validation of robust prognostic models.

Table 1. Demographic and clinical characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age, median (IQR)</td>
<td>58</td>
<td>46-71</td>
</tr>
<tr>
<td>Donor BMI, median (IQR)</td>
<td>25.7</td>
<td>23.4-28.1</td>
</tr>
<tr>
<td>DCD, %</td>
<td>9.1</td>
<td>-</td>
</tr>
<tr>
<td>DRI, median (IQR)</td>
<td>1.9</td>
<td>1-2</td>
</tr>
<tr>
<td>ECD, %</td>
<td>39%</td>
<td>-</td>
</tr>
<tr>
<td>Machine perfusion, %</td>
<td>6.4</td>
<td>-</td>
</tr>
<tr>
<td>Recipient age, median (IQR)</td>
<td>59</td>
<td>52-65</td>
</tr>
<tr>
<td>Recipient BMI, median (IQR)</td>
<td>25.7</td>
<td>23.1-29.3</td>
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<tr>
<td>CONUT score, median (IQR)</td>
<td>4</td>
<td>2-6</td>
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<tr>
<td>MELD at listing, median (IQR)</td>
<td>16</td>
<td>10-25</td>
</tr>
<tr>
<td>MELDNa at listing, median (IQR)</td>
<td>15</td>
<td>10-21</td>
</tr>
<tr>
<td>MELD at LTX, median (IQR)</td>
<td>15</td>
<td>10-21</td>
</tr>
<tr>
<td>MELDNa at LTX, median (IQR)</td>
<td>16</td>
<td>10-25</td>
</tr>
<tr>
<td>Non-neoplastic main indication to LTX, %</td>
<td>29.8</td>
<td>-</td>
</tr>
<tr>
<td>Alcohol</td>
<td>21.2</td>
<td>-</td>
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<tr>
<td>HCV disease</td>
<td>12.2</td>
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<tr>
<td>Metabolic (NAFLD + NASH)</td>
<td>9.8</td>
<td>-</td>
</tr>
<tr>
<td>Cholestatic</td>
<td>3.7</td>
<td>-</td>
</tr>
<tr>
<td>Other indications</td>
<td>23.3</td>
<td>-</td>
</tr>
<tr>
<td>HCC Co-Indication, %</td>
<td>31.7</td>
<td>-</td>
</tr>
<tr>
<td>Neoplastic non-neoplastic ratio, %</td>
<td>45.9</td>
<td>-</td>
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<tr>
<td>Lactate 120 min post reperfusion, median (IQR)</td>
<td>2.92</td>
<td>1.9-4.5</td>
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<td>L-GRAFT 7 score, median (IQR)</td>
<td>-3.07</td>
<td>-3.69-2.07</td>
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<td>L-GRAFT 10 score, median (IQR)</td>
<td>-3.29</td>
<td>-4.01-2.24</td>
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<tr>
<td>EASE score, median (IQR)</td>
<td>-3.7</td>
<td>-4.8 -2.9</td>
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<tr>
<td>Clavien-Dindo, %</td>
<td>1-3A</td>
<td>55.5%</td>
</tr>
<tr>
<td>Comprehensive Complication Index, median (IQR)</td>
<td>39.5</td>
<td>22.6-54.8</td>
</tr>
<tr>
<td>hospital stay, median (IQR)</td>
<td>17</td>
<td>12-28</td>
</tr>
</tbody>
</table>

OS15_1 PROLONGED HYPOTHERMIC MACHINE PERFUSION TO ENABLE DAYTIME LIVER TRANSPLANTATION – A RANDOMIZED CLINICAL TRIAL

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1University Medical Center Groningen, Groningen, Netherlands, 2Erasmus MC, Rotterdam, Netherlands

Background: Liver transplantation is emergency surgery because the graft deteriorates with each additional minute of cold ischemia. To ease logistics and allow daytime transplantation, the DHOPE-PRO trial was initiated to assess safety and feasibility of dual hypothermic oxygenated machine perfusion (DHOPE) to prolong liver preservation time.

Methods: Donation after brain death donor livers were randomized to prolonged (PRO) or conventional (CON) DHOPE based on donor hepatectomy time. Livers were assigned to PRO when donor hepathecotomy was finished between 16:00–3:59 hours, followed by prolonged DHOPE until implantation the following day. Livers were assigned to the CON when donor hepathectomy was finished between 4:00–15:59 hours, followed by 2 hours DHOPE prior to implantation. The primary endpoint was a composite of all serious adverse (device) events [SA(D)E] up to 30 days after liver transplantation.

Results: From September 2020 to July 2022, 24 patients received a liver randomized to PRO (n=12) or CON (n=12). Median DHOPE duration and total preservation times in the PRO group were 9.18 hours and 14.32 hours, versus 2.10 hours (P<0.001) and 7.54 hours (P<0.001) in the CON group, respectively.

Conclusions: DHOPE is a safe and feasible method to prolong the preservation time of donor livers. Implementation of this technique has the potential to transform current clinical practice by changing liver transplantation from emergency surgery into a semi-elective, daytime operation.

Disclosure: This abstract was also submitted to the ILTS 2023 meeting.
OS15_2
WHAT IS THE OPTIMAL PRESERVATION STRATEGY FOR MARGINAL LIVER GRAFTS USING HYPOTHERMIC OXYGENATED PERFUSION? A PRECLINICAL STUDY
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1Croix Rousse University Hospital, Lyon, France, 2Hepatology Institute Lyon, Lyon, France

Background: End-ischemic hypothermic oxygenated perfusion (HOPE) has been shown to protect marginal liver grafts. However, the optimal perfusion modality and timing of HOPE remains unknown.

Methods: We evaluated different preservation strategies with HOPE in a porcine model of marginal liver grafts undergoing 30min of asystolic warm ischaemia and 6h of static cold storage (SCS). The SCS group was used as control. First, end-ischemic dual portalarterial perfusion (D-HOPE) was compared to single portal perfusion (HOPE). Second, end-ischemic HOPE was compared to upfront, sequential, and continuous HOPE (Figure 1). All grafts then underwent ex-vivo reperfusion with autologous blood at 37°C for 2h to assess graft ischemia-reperfusion injury and function. Six pigs were randomly assigned to each group.

Results: D-HOPE and HOPE displayed comparable mitochondrial injury (FMN release 52 vs 53 ng/ml, p=0.81), peak AST (64.5 vs 64 U/100g/L, p=0.75) and histological ischemia-reperfusion injury (IRI) score (7 vs 7points, p=0.85). Based on these results portal HOPE was used to compare the 4 different preservation strategies. Total, end-ischemic and sequential HOPE presented with comparable peak AST. Higher transaminase release was observed in Ufront HOPE within the range of the SCS group (p=0.013). Viability criteria were met in a higher rate in end-ischemic and continuous HOPE without statistical differences. Histological IRI scores were not significantly different among groups.

Conclusions: End-ischemic HOPE and D-HOPE showed comparable protective effects on marginal liver grafts. Continuous HOPE perfusion did not show a significant improvement in liver injury and function compared to end-ischemic HOPE. However, adding >2h of SCS after HOPE showed a significant increase in graft injury similar to static cold storage. These results will guide future clinical applications of HOPE for example in the context of liver graft reconditioning centers.

Figure 1: Transaminase release after 2h of ex-vivo reperfusion among the different study groups.

OS15_3
HYPOTHERMIC OXYGENATED PERFUSION AFTER NORMOTHERMIC REGIONAL PERFUSION TO EXTEND SELECTION CRITERIA IN CDCD LIVER TRANSPLANTATION
Xavier Muller1;2, Pauline Georges1;2, Aline Wautier4, Alexandre Doussot1, Chloé Paul1, Heiti4, Jeddou1, Cedric4, Francois Falot4, Bruno Heyd4, Karim Boudjemaa1, Kayvan Mohkam1;2, Jean Yves Mabrut1;2
1Hepatology Institute Lyon, Lyon, France, 2Croix Rousse University Hospital, Lyon, France, 3CHU Besancon, Besancon, France, 4CHU Rennes, Rennes, France, 5CHU Strasbourg, Strasbourg, France

Background: The French controlled donation after circulatory death (cDCD) liver transplant (LT) program with normothermic regional perfusion (NRP) has achieved benchmark outcomes using strict selection criteria. To reduce graft discard rates, selection criteria were extended in September 2021 with mandatory use of hypothermic oxygenated perfusion (HOPE) after NRP.

Methods: All consecutive cDCD LT performed in 4 centres since the extension of selection criteria were included and followed up for 3 months. HOPE was mandatory in liver grafts previously discarded for transaminase levels ranging from 4N-8N during NRP and/or 20%-30% macrosteatosis. Outcomes after NRP+HOPE were compared to NRP alone.

Results: Fifty-nine cDCD grafts were transplanted during the study period of which 13(22%) underwent NRP+HOPE due to high NRP transaminase levels (85%) or liver steatosis (15%). Donor characteristics and warm ischemia times were comparable between both groups except for significantly higher peak transaminases during NRP in the NRP+HOPE group. (Table 1, Figure 1). The median HOPE duration was 113 min resulting in a significantly longer ex-vivo preservation (412 vs 347 min, p=0.130) compared to the NRP group. The NRP+HOPE group displayed a lower early allograft dysfunction rate (7.7 vs 21.7%, p=0.251) with comparable L-Graft risk scores (-3.21 vs -3.89, p=0.182). Arterial and biliary complications were similar between both groups without occurrence of primary nonfunction or re-LT after NRP+HOPE.

Conclusions: HOPE after NRP resulted in transplantation of >20% additional grafts otherwise discarded with the strict French selection criteria. Additional HOPE significantly prolonged ex-vivo preservation and achieved early outcomes observed in highly selected NRP cDCD grafts.

Table 1: Donor and graft characteristics and early post-transplant outcomes

<table>
<thead>
<tr>
<th>NRP</th>
<th>NRP+HOPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>NRP</td>
</tr>
<tr>
<td>warm asst</td>
<td>53(63)</td>
</tr>
<tr>
<td>NRP transaminase &gt;700 U/l</td>
<td>21(25)</td>
</tr>
<tr>
<td>Total warm</td>
<td>96(111)</td>
</tr>
<tr>
<td>Cold warm</td>
<td>5(6)</td>
</tr>
<tr>
<td>NRP duration</td>
<td>154(150-221)</td>
</tr>
<tr>
<td>TDWI: total donor warm ischemia</td>
<td>10(15)</td>
</tr>
<tr>
<td>FDWI: functional donor warm ischemia</td>
<td>10(15)</td>
</tr>
<tr>
<td>NAS: non anastomotic stenosis</td>
<td>10(15)</td>
</tr>
<tr>
<td>AR/S: arterial complications</td>
<td>10(15)</td>
</tr>
<tr>
<td>B/S: biliary complications</td>
<td>10(15)</td>
</tr>
</tbody>
</table>

NRP: normothermic regional perfusion; NRP+HOPE: normothermic regional perfusion after hypothermic oxygenated perfusion; TDWI: total donor warm ischemia; FDWI: functional donor warm ischemia; NAS: non anastomotic stenosis.

Figure 1: Peak transaminases during normothermic regional perfusion in the NRP+HOPE and NRP groups.

A. Peak aspartate aminotransferase B. Peak alanine aminotransferase
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OS15_4
DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION IS ASSOCIATED WITH IMPROVED RECOVERY OF ACUTE KIDNEY INJURY AFTER DCD LIVER TRANSPLANTATION

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1Erasmus Transplant Institute, Surgery, division of HPB and transplant surgery, Rotterdam, Netherlands, 2University Medical Center Groningen, Surgery, Division of HPB and transplant surgery, Groningen, Netherlands, 3Erasmus Transplant Institute, Intensive Care, Rotterdam, Netherlands, 4Erasmus Transplant Institute, Gastroenterology and Hepatology, Rotterdam, Netherlands, 5The Royal Free Hospital, University Medical Center Groningen, Gastroenterology and Hepatology, Groningen, Netherlands, 6Leiden University Medical Center, Surgery, division of HPB and transplant surgery, Leiden, Netherlands

Background: The use of donation after circulatory death (DCD) liver donors is associated with acute kidney injury (AKI) and chronic kidney disease (CKD) after liver transplantation (LT). End-ischemic dual hypothermic oxygenated machine perfusion (DHOPE) resuscitates donor livers prior to implantation and minimizes ischemia reperfusion injury, compared to static cold storage (SCS) alone. In this study we analyzed the impact of DHOPE on the incidence of AKI and CKD after DCD LT.

Methods: In this post-hoc analysis of a multicenter randomized controlled trial, patients received either a DCD liver after SCS alone (control) or after end-ischemic treatment with DHOPE. The incidence of AKI based on serum creatinine within the first week and CKD at 6 months after LT were scored according to KDIGO. Rapid reversal of severe AKI (stage 2&3) within 48 hours (transient AKI) was assessed.

Results: 9 patients without prior renal dysfunction were included. There were no significant differences in risk factors associated with AKI, including donor and recipient BMI, blood products transfusions and recipient warm ischemia time. Postreperfusion syndrome occurred in 12% of the DHOPE group and in 27% in the control group (risk ratio, 0.43; 95% CI, 0.20 to 0.91).

In controls 23% (12/52) developed severe AKI (KDIGO stage 2&3) vs 28% (13/47) in the DHOPE group (p=0.600). Reversal of severe AKI within 48 h was 0% (0/12) in controls vs 38% (5/13) in the DHOPE group (p=0.018). At 6 months after DCD LT, the incidence of severe CKD (severe CKD & end-stage renal disease) was 6.3% (3/48) in controls vs 0% (0/42) in DHOPE (p=0.099).

Conclusions: DHOPE did not reduce the incidence of AKI, however DHOPE was associated with improved early recovery of AKI after DCD LT. This translated into a trend towards less severe chronic kidney injury at 6 months after DCD LT.

OS15_5
LACTATE DYNAMICS DURING THE FIRST 6 HOURS OF LIVER NORMOTHERMIC MACHINE PERFUSION PREDICTS CLINICAL OUTCOME - A MULTICENTER STUDY

Julia Hofmann1, Andras T. Meszaros2, Andrew Butler2, Angus Hans3, Harriet Hartog4, Felicia Knustel5, Sathu W-num4, Barbara Fiore6, Magdy Attaia7, Joerg-Matthias Pollok8, Jens Brockmann4, Thomas Vogel4, Thamara Perera3, Christopher Watson2, Stefan Schneeberger9
1Medical University of Innsbruck, Department of Visaceral, Transplant and Thoracic Surgery, Innsbruck, Austria, 2University of Cambridge, Department of Surgery, Cambridge, United Kingdom, 3University Hospitals Birmingham NHS Foundation Trust (UHBFT), Liver Unit, Queen Elizabeth Hospital, Birmingham, United Kingdom, 4University Hospital of Münster, Department of General, Visceral and Transplant Surgery, Münster, Germany, 5The Royal Free Hospital, Pond Street, Hampstead, Department of HPB and Liver Transplantation, London, United Kingdom, 6Leeds Teaching Hospitals, NHS Foundation Trust, Liver Transplant Unit, Leeds, United Kingdom

Background: A growing number of livers undergo normothermic machine perfusion (NMP) prior to transplantation. However, robust and validated biomarkers to predict the clinical outcome are still lacking. To aid the decision making for NMP were assessed and area under the curve (AUC) was calculated. Primary endpoints were MEAF (Model for Early Allograft Function) and L-GrAFT (Liver Graft Assessment Following Transplantation). Linear regression and correlation studies were performed using R and GraphPad Prism.

Results: The total NMP time was 723 ± 334 min. EAD occurred in 26 %, MEAF was 4.86 ± 1.86 and L-GrAFT at day 7 and 10 was 0.53 ± 1.25 and -0.21 ± 1.25, respectively. The respective 1-year patient and graft survival was 86 % and 80 %.

Lactate levels at 1 h, 2 h and 6 h correlated significantly with MEAF and the correlation increased in robustness over time. Rather than a binary assessment with a cut-off value of < 2.5 mmol/L, at 2 h, the actual 2 h lactate level correlated with the MEAF (Pearson r = 0.1043 vs. r = 0.1734, p = 0.0306 vs. p = 0.0003). Further to the absolute lactate concentration at 6 h, the AUCs of 0-6 h and 1-6 h lactate concentrations (p < 0.0001, r = 0.3176) have strong predictive value towards MEAF. No correlation between perfusate lactate and L-GrAFT was found.

Conclusions: Lactate AUC up to 6 h and lactate levels at 6 h of NMP correlate strongly with the risk of liver allograft dysfunction upon transplantation. The predictive value of lactate is increasing with the duration of NMP. The time frame of monitoring lactate levels should be extended to at least 6 h of NMP to retrieve robust data.

OS15_6
BLOCKADE OF REGULATED CELL DEATH ABROGATES EFFECTOR T-CELL INfiltrATION AND MINIMIZES HEPATIC ISCHEMIA REPERFUSION DAMAGE

Elke Eggenhofer1, Florian Vondran1, Amoon Kasi1, Alicia Goreth1, Felix Oldhafer1, Oliver Beetz2, Bettina Preneth1, Marcus Conrad1, Hans Schlitt1, Edward Geissler1
1University Hospital of Regensburg, Surgery, Regensburg, Germany, 2Hannover Medical School, Department of General, Visceral and Transplant Surgery, Hannover, Germany, 3Institute of Developmental Genetics, Helmholtz Zentrum München, Neuherberg, Germany

Background: Ischemia-reperfusion injury (IRI) remains an important problem in clinical organ transplantation. We demonstrated that unconventional effector T cells, specifically γδ T cells, play a key role in mediating early hepatic IRI. Regulated cell death (RCD) such as ferroptosis is also involved. Here, we aim to show whether and, if so, how inhibition of ferroptosis in hepatic ischemia affects γδ effector T cells.

Methods: In this study, we examined early immunological events in several models of hepatic IRI. First, in genetically selected mice, (ferroptosis-resistant knockout mice, as well as permanently ferroptosis-activated mice) subjected to 90 minutes of partial warm ischemia followed by 24 hours of reperfusion. We also used a more clinically relevant mouse model in which we blocked the pathway of RCD (inhibition of ferroptosis) with drugs. Since the mouse experiments focussed strictly on ischemia reperfusion, we finally investigated ferroptosis inhibition in a large animal model of porcine liver transplantation. In all cases, hepatocellular injury was assessed by HE histology and serum transaminase measurement. Murine hepatic leukocyte subsets, such as innate effector cell populations and cytokine secretion, were characterized by immunohistochemistry, ELISA, RT-PCR, and polyacrylamic FACS. For porcine livers, γδ-T-cell analysis was performed by RT-PCR and immunohistochemistry.

Results: Mice whose ferroptose regulators were genetically knocked out were protected from hepatic IRI (serum transaminase levels 920U/l vs. 2540U/l in control mice; p<0.02). We found that γδ T cells were significantly decreased in these livers. Similarly, there was a significant reduction in γδ-cells in the livers of mice in which ferroptosis was blocked with drugs. We also show that regulation of γδ T cells occurs after ferroptosis inhibition in a true porcine transplantation model.

Conclusions: Ferroptosis events appear to be an initial activator for hepatic IRI and lead to further progression through activation of γδ T cells. This can be abrogated by the use of ferroptosis inhibition, which opens new clinically relevant therapeutic options to improve liver transplantation outcomes.
Background: Few studies correlate cytokines (IL) release during ex-situ machine perfusion (MP) to postoperative liver transplantation (LT) outcomes. We assessed safety and efficacy of an IL hemadsorption device (HA) integrated in a MP device during hypo- (D-HOPE) and normothermic MP (NMP) methods. We compared perfusate IL-6, IL-10 and TNF-alpha concentrations and postoperative outcomes in 4 groups of patients receiving old grafts (i.e. >80 years); those receiving a graft after D-HOPE with or without a HA device (D-HOPE-HA and D-HOPE groups respectively, n=3 each) and after NMP with or without a HA device (NMP-HA and NMP groups respectively, n=3 each). IL perfusate concentrations were evaluated at commencing perfusion and hourly thereafter together with perfusion parameters and post-operative outcomes. Liver biopsies for H&E and electron microscopy evaluation were obtained at the end of back table, MP and LT.

Results: Twelve liver grafts were perfused and transplanted. Median donor ages were 85, 81, 82 and 82 and grafts perfused for 228, 231, 239, 266 minutes in D-HOPE, D-HOPE-HA, NMP and NMP-HA groups respectively. Median IL-6, IL-10 and TNF-alpha concentration at 1 and 2 hours are reported in Table1. The amount of IL-6, IL-10 and TNF-alpha adsorbed between the minute 60 to 120 minutes period in the D-HOPE-HA and NMP-HA was 12960, 3960, -2160, and 372,500, 172,800 and 203,400 pg respectively. There was one case of primary non-function and re-LT in the NMP group. In that case the TNF-alpha perfusate concentration at 2-hours was 1733 pg/ml (the other 2 cases mean value was 23 pg/ml). No biliary or vascular complications were reported after a median follow up of 15 months.

Conclusions: The use of an IL HA device during ex-situ MP is safe and feasible. It significantly and unspecifically reduces interleukines perfusate concentration, in particular during NMP. Its capacity to improve clinical outcomes should be verified in large multicentric trials.

Table 1: Median interleukines levels in the groups during the first 2 hours of MP.

<table>
<thead>
<tr>
<th>Perfusion</th>
<th>Start</th>
<th>1 hour</th>
<th>2 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-HOPE</td>
<td>0</td>
<td>7.3</td>
<td>9</td>
</tr>
<tr>
<td>D-HOPE-HA</td>
<td>0</td>
<td>2.2</td>
<td>1.1</td>
</tr>
<tr>
<td>NMP</td>
<td>3</td>
<td>62</td>
<td>269</td>
</tr>
<tr>
<td>NMP-HA</td>
<td>0.1</td>
<td>9.7</td>
<td>126</td>
</tr>
<tr>
<td>D-HOPE</td>
<td>2.8</td>
<td>3.4</td>
<td>3.4</td>
</tr>
<tr>
<td>D-HOPE-HA</td>
<td>1.6</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>NMP</td>
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<td>123</td>
<td>139</td>
</tr>
<tr>
<td>NMP-HA</td>
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<td>167</td>
<td>39</td>
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<td>TNF-alpha</td>
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<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>D-HOPE-HA</td>
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<td>2.9</td>
<td>0.9</td>
</tr>
<tr>
<td>NMP</td>
<td>0.1</td>
<td>36</td>
<td>124</td>
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<tr>
<td>NMP-HA</td>
<td>0.1</td>
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</table>

Data are expressed in pg/ml.

Hypoxia Inducible Factor modulation during normothermic machine perfusion (NMP) accelerates reduction in hepatic steatosis

Background: The hypoxia-inducible factor (HIF) pathway has been implicated in hepatic steatosis with the HIF-1α isoform providing a hepatoprotective effect through enhancement of liver fat metabolism and the HIF-2α isoform conversely promoting intraparenchymal lipid accumulation. The objective of this study was to selectively modulate HIF-1α during oxygenated normothermic machine perfusion (NMP) of four discarded human steatotic livers using deferoxamine (DFO, a potent activator of both HIF-1α & HIF-2α) with selective HIF-2α inhibition using PT2385 (a HIF-2α dimerisation inhibitor). The specific aims were to: (i) improve ex-situ liver function and fat metabolism and (ii) to test this with an established NMP defatting protocol (DeFat: insulin/glucose reduction, L-carnitine, forskolin and lipid filter).

Methods: Livers were perfused using the OrganOx Metra NMP device over 24 hours and received the following perfusion protocols: Liver 1 (control): NMP alone protocol; Liver 2: NMP with DFO; Liver 3: NMP with DFO and PT2385, and Liver 4: NMP defatting protocol (DeFat). DFO and PT2385 were delivered at the start of perfusion. Liver 4: DeFat: insulin/glucose reduction, L-carnitine, forskolin and lipid filter.

Results: All livers demonstrated evidence of function during perfusion (Figure 1). However, only those subjected to HIF modulation demonstrated a DFO/PT2385 dependent response to EPO production (with HIF1α and HIF2α expression confirmed on immunoblot) (Figure 1) and a reduction in MaS over 24 hours. The greatest reduction in MaS was observed in Liver 4: pre-NMP 33% and end-NMP MaS: 8% (75.6% decrease).

Conclusions: This study is the first to report pharmacological HIF modulation during oxygenated liver NMP and demonstrates accelerated defatting through using pharmacological HIF modulators (DFO and PT2385) when tested in combination with the established NMP defatting protocol (DeFat). The effect of these interventions on ischaemia-reperfusion injury remains to be elucidated.
Background: Biliary complications are a major cause of morbidity and mortality in liver transplantation, developing in up to 25% of liver transplant recipients, frequently requiring additional surgical procedures, re-transplantation or, in the absence of a suitable regraft, death. Here, we investigate the role of the primary cilium, a highly specialised sensory organelle, in biliary injury leading to post-transplant biliary complications.

Methods: Human biopsies were used to study the structure and function of primary cilia in liver transplant recipients that develop biliary complications (N=7) in comparison with recipients without biliary complications (N=12). To study the biological effects of primary cilia during transplantation, we generated murine models that recapitulate liver procurement and cold storage, as well as the K19CreER<sup>+</sup> Kif3a<sup>lox/lox</sup> mouse model to conditionally eliminate primary cilia in biliary epithelial cells. To explore the molecular mechanisms responsible for the observed phenotypes we used in vitro approaches to target cellular senescence and primary cilia, both in mouse models and discarded human donor livers.

Results: Prolonged ischemic periods before transplantation result in ciliary shortening and cellular senescence, an irreversible cell cycle arrest that blocks regeneration. Our results indicate that primary cilia damage results in biliary injury and a loss of regenerative potential. We found that the initiation of senescence negatively impacts primary cilia structure, establishing a negative feedback loop that further impairs regeneration. Finally, we explore how targeted interventions for cellular senescence and/or the stabilisation of the primary cilia could improve biliary regeneration following ischemic injury. Conclusions: Primary cilia play an essential role in biliary regeneration and we demonstrate that senoytcs and cilia-stabilising treatments provide a potential therapeutic opportunity to reduce the rate of biliary complications and improve clinical outcomes in liver transplantation.
**FULL ORALS**

**OS16.2 FACTORS DETERMINING CONSENT FOR ORGAN DONATION AFTER BRAIN DEATH IN FRANCE**

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**Background:** Opposition to organ donation remains the principal factor in the lack of organ procurement from potential brain-dead donors (DBD) in France. The underlying causes and organizational determiners of this opposition are not well understood due to a lack of research. In order to improve donation rates, this study seeks to address this by examining factors that contribute to organ donation opposition. Our aim was to understand clinical and organizational factors associated with opposition to organ donation in France.

**Methods:** All potential DBD entered into the French national registry CRISTAL between 2018 and 2019 were included. Connections between donor sociodemographic and clinical data, hospital care quality and procurement center characteristics and refusal to donate were assessed using multivariable multilevel logistic regression models with procurement hospitals as random effects.

**Results:** We analyzed 6734 DBD. Opposition occurred in 30% of cases. Independent risk factors associated with a higher rate of opposition were age (reference > 65, 50-64 (OR=1.37; 1.19-1.58), 18-49 (OR=1.51; 1.35-1.83), 0-17 (OR=2.03; 1.45-2.84) and blood type B (OR=1.35; 1.11-1.64) probably linked with lower socioeconomic level and origins as well as a longer hospital stay prior to brain death (OR=1.14 per 10 days; 1.01-1.28). Factors associated with lower rate of opposition were a suicide context (OR=0.71; 0.55-0.91), being in a hospital with a higher satisfaction regarding medical and surgical care as reported by systematic certification visits of all hospitals in France (OR=0.95; 0.91-1.00), being in an hospital in which the process of organ donation was audited (2-3 days audits performed by professionals from the national agency) (OR=0.77; 0.59-1.00), being in a hospital with a higher ratio of paramedical donor coordinators (cut-off > 8 donor coordinators per 100 potential donors; OR=0.72; 0.58-0.90).

**Conclusions:** On a recent set of all DBD in France, we found several factors correlated with higher or lower levels of opposition to organ donation. Some factors are well known including lower age, socio-economic level and suicide but other offer scientific evidence of the advantages of auditing the hospital donation process and increased staffing of donor coordination teams.

**OS16.3 MODULATORY EFFECT OF ALTEPLASE AND METHYL-PREDNISOLONE ASSOCIATION ON BRAIN DEATH DONOR**

Lucas Ferreira da Anunciação*,1, Marina Vital-Dos-Santos1, Fernanda Yamamoto Ricardo-Da-Silva1, Caio Medeiros Fernandes1, Cristianos Jesus Correia1, Ana Cristina Breithaupt-Faloppa1, Luiz Felipe Pinho Moreira1

1Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

**Background:** Brain-death (BD) patients are a common source of transplant organs. Studies describe microcirculatory compromise and systemic inflammatory processes related to BD, which are related to micro-aggregates formation and platelet aggregation reducing blood flow. In this sense, this study aimed to investigate the effect of thrombolytic (alteplase - rTPA) and corticoid therapy (methylprednisolone) after BD in male rats.

**Methods:** Wistar rats were submitted to BD by the rapid inflation of an intracranial catheter, and maintained for 6 h. After 3 h, rats were treated with rTPA (3 mg/kg, i.v for 30 minutes) Sham-operated (Sham) rats were used as controls.

**Results:** Platelet count did not differ among the groups (P= 0.3521). Besides, BD increased inflammatory mediators, such as IL-6 and TNF-α concentrations compared to Sham, only rTPA+P group decreased the IL-6 (Sham: 2688±957; ME: 5334±253; rTPA: 4085±773; rTPA+P: 1400±588, pg/mL, P= 0.0018) and TNF-α (Sham: 0.929±0.571; ME: 1.583±0.588; rTPA: 1.243±0.524; rTPA+P: 0.091±0.060, pg/mL, P= 0.0682) concentration compared to BD. CINC-1 (Sham: 42.1±6.9; ME: 36.5±7.8; rTPA: 174±36.7; rTPA+P: 185.7±46.7, pg/mL, P= 0.0023) and NOx (Sham: 60.6±25.5; ME: 34.1±8.7; rTPA: 222.3±115.8; rTPA+P: 54.4±14.2, pg/mL, P= 0.3985) concentrations were increased in the rTPA+P group compared to BD. The rTPA+P group did not modify CINC-1 release, however NOx concentration presented lower values.

**Conclusions:** This study demonstrated the effectiveness of a thrombolytic treatment to decrease platelet aggregation in rats submitted to BD. At the same time, rTPA increased the inflammatory response in which the association with corticoid therapy decrease these parameters. Thus, the association between thrombolytic and corticoid therapy can be a good therapeutic option for BD donor organs.

**OS16.4 ACTIVATION OF THE COMPLEMENT SYSTEM EARLY ON DURING BRAIN DEATH MANAGEMENT**

Laura Knijff1,2, Sandra van der Kooij1,2, Danielle van Gils-wijk-Jansen1, Mieke van Essen1, John Mulvey3, Maria Letizia Lo Faro4, Rutger Ploeg5,6, Cees van Kooten1

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**Background:** Brain death (BD) results in an inflammatory environment, including activation of the complement system. Currently, the clinical impact of prolonged duration of BD on the donor organ is still unknown. Here, we investigated how different BD durations impact complement activation levels both systemically and locally within renal tissue.

**Methods:** The QUOD biobank was used to obtain EDTA-plasma samples and kidney biopsies from BD donors. Samples were routinely taken at several time points during BD management. Samples were grouped based on short (<15h), average (18-22h) or long (>25h) BD duration. Furthermore, groups were divided based on the presence of delayed graft function (DGF) (6 groups, n=20 per group for plasma, n=10 per group for biopsies).

**Results:** ELISAs were used for specific quantification of C4d, C3c and C5b-9 in plasma samples. All three complement activation factors showed high levels at the start of donor management (DB2), C4d levels decreased over time, and were significantly lower in samples taken just before organ retrieval (DB4) compared with DB2 (mean 6122 ng/mL vs. 3601 ng/mL, P<0.001). C3c and C5b-9 also showed a similar trend towards lower complement activation levels at the end of donor management (DB3) and at DB4 compared with DB2. Preliminary analysis between different BD duration groups did not show a difference in C4d, C3c and C5b-9 levels. C4d, C3c and C5b-9 levels, at any point during BD management, did not appear to influence the development of DGF. Biopsies (collected at the time of organ retrieval) have been stained for C4d, C3c and C5b-9 and showed clear signs of local complement activation at different compartments, including glomerular, tubular and peritubular regions. The quantification of different staining patterns is currently under investigation.

**Conclusions:** In conclusion, the complement system is activated in BD donors already early on during the management period, and is decreasing over time. Prolonged duration of BD does not appear to be associated with increased levels of C4d, C3c and C5b-9. Future studies on administering complement inhibitors to BD donors could benefit from starting therapy early on during management period.

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ANALYSIS OF RISK FACTORS FOR KIDNEY TRANSPLANTATION AFTER CONTROLLED CIRCUITARY DEATH AND SYSTEMATIC USE OF NORMOTHERMIC REGIONAL PERFUSION

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**Background:** The French controlled circulatory death (cDCD) program is characterized by normothermic regional perfusion (NRP), constrained asystole times according to donor age, hypothermic machine perfusion, and short cold ischaemia time (CIT). Compared to the outcome of matched DBD kidney transplants, the outcome of cDCD ones was found to be better, especially due to NRP use.

**Methods:** This analysis of 1071 adult primary kidney transplants (2015-2020) aimed to support these findings and identify risk factors for graft failure. The average of donor age was 51 years, of functional warm ischemia time (fWIT) 27 min, of asystolic phase was 21 min and of CIT 10 hours. Risk factor analysis of primary non-function (PNF, n=32), of delayed graft function (DGF, n=136 after exclusion of 168 preemptive and PNF) and of graft failure (estimated glomerular filtration rate (eGFR) < 30ml/min or graft loss at 1 year, n=163 after exclusion of 16 missing) were performed by multivariable logistic regression.

**Results:** Donor HTA (OR=2.37, p=0.032), admission for ischemic vascular stroke (OR=4.95, p=0.014) and HLA DR mismatches (OR=2.24, p=0.004) are independent risk factors for PNF. fWIT>40 min (OR=3.11, p=0.001), diabetes >2 years (OR=1.83, p=0.003), recipient BMI >30 (OR=2.23, p=0.001), recipient diabetes (OR=2.25, p=0.001) and CIT>10h (OR=1.59, p=0.02) were independent risk factors for DGF. Donor HTA (OR=1.51, p=0.032), pulmonary procurement (OR=1.88, p=0.015), ostial calcification (OR=1.59, p=0.026), recipient comorbidities (OR=1.50, p=0.024) and HLA DR mismatches (OR=1.40, p=0.013) were independent risk factors of graft failure at 1 year. Donor eGFR (continuous form / 20) was a protected factor for DGF and graft failure at 1 year (OR=0.75 and 0.70 p=0.001 and <0.001). After adjustment restricted to recipient and graft factors, the risk of PNF, DGF and graft failure increases with donor age up to 65 years and then remains stable.

**Conclusions:** Overall, results of renal transplants from cDCD are excellent but impacted by lung procurement (being analysed), poor HLA DR matching and warm ischemia time according to the donor age validating a posteriori the demand for transplantation (Tx). During aging, senescent cells that secrete inflammatory products termed the senescence-associated secretory phenotype (SASP) accumulate in older organs. We hypothesized that the engraftment of old organs induces senescence in younger recipients, promoting age-related pathologies.

**Methods:** Heart transplants from either young (3 months/mths) or old (18-21 mths) C57Bl/6 mice or p16ink4a-kpp reporter mice were transplanted into young or middle-aged C57Bl/6 recipients (3 & 12 mths, resp.). Recipient tissues were collected by 30 days after Tx; the accumulation of senescent cells and SASP derived molecules (mt-DNA) was assessed by IHC, RNA in situ hybridization and qPCR. Physical and neurobehavioral testing was performed sequentially up to 5 mths after Tx. Assessing mechanisms, senolytics (Dasatinib & Quercetin) were applied to old donor animals prior to organ procurement.

**Results:** Recipients that had received old hearts showed augmented frequencies of senescent cells in draining lymph nodes, livers, and muscles (3-1 fold, 20.3-fold. 1.8-fold increase, day 30 after Tx; p≤0.01, p≤0.001, and p≤0.05) in addition to augmented systemic mt-DNA levels 24 hours after Tx (p≤0.05) when compared to recipients that had received young grafts. Strikingly, transplanting old organs led to compromised physical capacities (RotaRod & minimum grip strength; p≤0.05 & p≤0.001 by 30 days) and significant impairments in neuro-developmental testing (locomotor test, Novelty Y-maze by 3 & 4 mths after Tx, p≤0.05 for each test). Treating old donors with senolytics prior to organ procurement resulted in significantly reduced mt-DNA levels (p≤0.05) and improved physical fitness (RotaRod by 4 & 6 weeks after Tx, p≤0.01 & p≤0.05) in young recipients. Thus, depleting senescent cells in donor organs prevented the 'transfer/spread' of senescence through a diminished accumulation of mt-DNA and SASP factors.

**Conclusions:** We show that transplanting old organs induces not only molecular and cellular changes characteristic of accelerated aging, but also leads to both physical and cognitive impairment. Treating organs prior to transplantation with senolytics was effective in preventing the transfer of senescence.

LONG-TERM MORTALITY OF LIVING KIDNEY DONORS: A NATION-BASED COHORT STUDY

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**Background:** Morbidity and mortality issues in living kidney donors (LKDs) after donor nephrectomy are still debated. The purpose of the present study is to evaluate the long-term risks to LKDs compared with multiple control cohorts undergoing overall health assessment.

**Methods:** The cohort study included 14,484 LKDs in South Korea, who donated a kidney between 2002 and 2018 in the Korean Network for Organ Sharing. Three control groups comprising a total of 144,840 subjects were selected from Korean National Health Insurance Services.

**Results:** In the LKD cohort, 187 deaths (135 males and 52 females) occurred during the study period. When compared with Control I, the mortality rate in LKDs was 1.60 (95% CI: 1.39-1.85). The MRR and adjusted HR in the LKD group were 2.01 (95% CI: 1.71-2.36) and 1.98 (95% CI: 1.64-2.38), respectively. With respect to Control II and III, there were no statistical difference in mortality rate, MRR, and adjusted HR. The crude HR demonstrated an elevated risk for HD (2.64; p < 0.001), ESRD (2.53; 95% CI: 1.39-4.60; p < 0.001), and CKD (4.99; 95% CI: 1.54-16.17; p = 0.01), compared with Control I. Among cause of death, event of undertemned intent, self-harm, all external cause of death, circulatory disease, abnormal clinical finding, and all internal cause of death showed higher risk in LKDs compared with health control group (HR=5.22 (95% CI: 1.03 – 26.34), 2.66 (95%CI: 1.86 – 3.67), 2.53 (95%CI: 1.16 – 4.1), 2.35 (95%CI: 1.1 – 5.66), and 1.69 (95%CI: 1.35 – 2.11), respectively.

**Conclusions:** Long-term mortality of LKDs is notably increased when compared with healthy control subjects. LKDs had a higher risk of psychosocial mortality and classical chronic disease including circulatory disease than healthy control.
Sustainable healthcare and workforce development.

Creating a community.

Patient experience, outcomes and empowerment and support the transplant process.

Implementation.

Conclusions:
Delivering improvements through new strategic and commissioning frameworks.

Methods:
The OUG recommendations aim to reduce inequity of access, maximise donor referral interoperability solutions, ultimately leading to more donors and transplantsations.

Organ donation: clinical perspectives

AI & Digital Health: from donation to the outcome

Organ donation: clinical perspectives

Claire William1, John Forsythe2, Jessica Jones2

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Background: Organ utilisation has not kept pace with the rate of improvements in organ donation in the UK. The UK compares poorly against international heart, lung and liver transplantation activity. An Organ Utilisation Group (OUG) was established by the Department of Health and Social Care in England, to develop new approaches to maximise the potential for the number of organs transplanted for adult and paediatric patients, from living and deceased donors.

Methods: The OUG membership included: patients; lay members; multi-disciplinary transplant team representatives; hospital management; commissioning.

Subgroups were convened for: commissioning; data; workforce; standards. The OUG consulted widely with UK and international stakeholders to identify barriers along the care pathway and opportunities for improvement, with: 345 responses to online surveys; 27 patients participated in focus groups; 58 delegates attended workshops; 10 site visits to transplant and referring centres; 6 international meetings; a literature review. Data analyses identified fresh areas for consideration – e.g. Table 1 demonstrates the impact of a lack of resources on utilisation.

Results: The evidence collated by the OUG identified key themes as demonstrated in Figure 1. The OUG report builds on the comprehensive evidence base and includes 12 recommendations for service improvement, with supporting actions, against 6 themes: 1. Placing the patient at the heart of service. 2. An operational infrastructure that maximises transplant potential. 3. Creating a sustainable workforce that is fit for the future. 4. Data provision that informs decisions and drives improvements. 5. Driving and supporting innovation. 6. Delivering improvements through new strategic and commissioning frameworks.

Conclusions: The OUG recommendations aim to reduce inequity of access, make the best use of available resources and drive innovation. Implementation will increase transplant activity, through increased organ utilisation, improve patient experience, outcomes and empowerment and support the transplant community.

Table 1: Number of deceased donor organ offer declines for lack of resource within the transplant centre, 1 April 2018 – 31 March 2019. Source: NHS Blood and Transplant

<table>
<thead>
<tr>
<th>Organ type</th>
<th>Total declines</th>
<th>Declines due to lack of resource (% of all declines)</th>
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<tbody>
<tr>
<td>Kidney</td>
<td>7,241</td>
<td>72 (1)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>4,497</td>
<td>260 (6)</td>
</tr>
<tr>
<td>Liver</td>
<td>9,006</td>
<td>192 (2)</td>
</tr>
<tr>
<td>Intestinal</td>
<td>262</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Heart</td>
<td>3,051</td>
<td>40 (1)</td>
</tr>
<tr>
<td>Lung</td>
<td>2,967</td>
<td>61 (2)</td>
</tr>
<tr>
<td>Totals</td>
<td>27,024</td>
<td>629 (2)</td>
</tr>
</tbody>
</table>

Figure 1: Summary of key challenges to be addressed, raised by stakeholders.

AI & Digital Health: from donation to the outcome

John Piano1

1InVita Healthcare Technologies, Los Angeles, United States

Background: In the United States, national regulatory organizations require that hospitals refer all potential organ and tissue donors to an Organ Procurement Organization (OPO). To replace the current time-consuming and error-prone telephonic referral process, secure, direct, electronic donor referral interfaces are being launched across the country.

Methods: The secure technical interface (“Referral”) directly connects the OPO and Hospital systems and is accompanied by seamless donor referral triggers within the Hospital Electronic Medical Record (EMR). These carefully tuned triggers automatically prompt delivery of electronic donor referrals from the Hospital to the OPO, greatly reducing the need for decision-making and donation knowledge by the hospital staff. An additional trigger option allows staff to “one click” electronically refer for cases such as end-of-life discussions or cardiac death. Immediately the OPO receives a new referral auto populated with actionable patient information and real-time notifications alert OPO staff. The interface automatically returns the associated OPO referral ID number to the patient’s EMR to provide confirmation to the referring clinician.

Results: This interface is currently implemented at 56 hospitals across the country. At a pilot hospital, annualized data after the first year of implementation demonstrated a 49% increase in vented referrals and 73% increase in organs transplanted. At a large hospital network, nearly 9,000 referrals have been sent electronically since launch in February 2021, saving an estimated 3,000 nursing hours.

Conclusions: This interface has increased the number and timeliness of referrals (and thus transplantable organs) and reduced Hospital and OPO resource costs. There is unlimited potential for streamlining the referral process through donor referral interoperability solutions, ultimately leading to more donors and transplantations.

Image 1: Pilot hospital results with annualized data from January 2019-April 2020 compared to the time period prior to interface launch.

Thermodynamic characterization of organs preserved on ice: investigating the assumption that ice is 4°C

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1Paragonix Technologies, Cambridge, United States, 2Paragonix Technologies, Cambridge, United States

Background: Clinical literature and conventional knowledge assumes organs stored on ice are held at 4°C. However, this is not supported with empirical data as the typical environment of organ storage is not measured or controlled. Increasing risk of freezing injury. As a community, it is critical we better understand the conditions organs are being preserved and transported under as programs are evaluating the clinical and logistical trade-offs of various perfusion strategies.

Methods: Porcine hearts (n=3), lungs (n=3) and livers (n=3) were packaged within 3 bags (3M) with and placed on ice in a cooler (Coleman). Hearts were packaged with 2L HTK, 2L saline in the second bag. The third bag did not have any solution. Temperature probes were inserted into the left ventricle myocardium, into the left inferior lung lobe, into one of the liver lobes, as well in hearts, 12 hrs for lungs and 15 hrs for livers.

Results: A total of 24,858 temperature measurements were recorded and analyzed. An average of 4,819 heart, 12,969 lung, 4,400 liver temperatures evolved from an initial 6.2°C to 1.7°C (1 hr) and 0.3°C (4 hrs), while average external epicardium temperatures evolved from 6.1°C to 0.4°C.
FULL ORALS

AI & Digital Health: from donation to the outcome

(1 hr) and 0.1°C (4 hrs). Average interior lung lobe temperature evolved from 6.1°C to 3.4°C (1 hr) and 0.7°C (4 hrs), while average lung surface temperature evolved from 6.7°C to 0.8°C (1 hr) and 0.1°C (4 hrs). See Figure.

Conclusions: Donor organs packaged on ice undergo rapid drops in temperature, approaching freezing in an uncontrolled manner. Preservation solutions provide insufficient levels of protection against freezing temperatures. As this decline in organ temperature occurs within clinically routine cold ischemic times, risk of freezing injury should be considered when procuring and transporting organs for transplant.

Figure: Thermodynamic Characterization Of Heart and Lung Stored on Ice

OS17_4 DEVELOPMENT, APPLICATION, AND VALIDATION OF A HISTOLOGICAL CLASSIFICATION AUTOMATION SYSTEM FOR KIDNEY ALLOGRAFT PRECISION DIAGNOSTICS

Valentin Goulauder1, Daniel Yoo2, Gillian Divard3, Juliette Gueguen3, Olivier Aubert4, Marc Reynaud5, Zeynep Demir6, Julien Hogen7, KTD-Innov Investigators3, Eu-Train Investigators1, Mark Haas4, Carmen Lefaucheur1, Marion Rabant1, Alexandre Loupy1

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Background: For three decades, the Banff International classification has been the gold standard for kidney allograft rejection diagnosis but has become complex over time, leading to misclassifications with therapeutic consequences. We aimed to develop an automated rejection classification system, and demonstrate its clinical impact by validating its ability to improve rejection diagnoses and risk stratification of allograft outcomes.

Methods: We built an interdisciplinary consortium to translate all Banff rules until the latest published in 2019 into an algorithm covering every possible kidney allograft diagnostic scenario, embedded in an online application which automatically assign diagnoses. We tested the Banff Automation System’s ability to reclassify and stratify the risk of rejection diagnoses on 4,409 kidney transplant biopsies from 3,054 adult and pediatric patients, from multicenter and large clinical trials, totaling 20 centers in Europe and North America. Clinical-Trials.gov, NCT03652402.

Results: We devised a system that generates automatic diagnostic reports with a decision tree. In the adult kidney transplant biopsies, the system reclassified 83 of 279 (29.75%) antibody-mediated rejection (AMR) cases and 57 of 105 (54.29%) T1-cell mediated rejection (TCMR) cases, while 237 of 3,239 (7.32%) biopsies with non-rejection-related diagnoses were reclassified as rejection (Figure 1). In the pediatric kidney transplant biopsies, the rejection reclassifications rates were 8 of 26 (30.77%) and 12 of 39 (30.77%) for AMR and TCMR, respectively. Finally, we found that the non-rejection diagnoses according to the pathologists which were reclassified as rejections by the Banff Automation System had similar outcomes as those of confirmed rejection cases.

Conclusions: We built the first comprehensive and fully integrated histological Banff Automation System and confirmed its ability to reclassify and stratify the risk of kidney transplant rejection. This decision support system might improve reproducibility, thereby reducing misclassifications; standardizing histology-based endpoints in clinical trials and posttransplant diagnostics; and optimizing therapeutic management.

Figure 1. Banff Automation System’s reclassification of rejection-related diagnoses.

OS17_3 NEXT GENERATION SEQUENCING: FROM BANFF SCORE MOLECULAR SIGNATURES AND CLASSIFIERS TO HISTOLOGICAL ARCHETYPES OF KIDNEY BIOPSY

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Background: To improve risk stratification in kidney transplantation, molecular diagnostic tests are increasingly investigated. Nonetheless, previously published studies focused on sequencing technologies and gene panels with suboptimal consideration of the transcriptome. The EU-TRAIN consortium was built to discover new predictive intra-graft biomarkers for histology parameters. Methods: EU-TRAIN (NCT03652402) is a prospective multicentric study including unselected kidney transplant cohorts from 11 centres from 4 countries (France, Spain, Germany, Switzerland). We performed a bulk RNA sequencing on 770 kidney biopsies (n=540 kidney recipients) collected between 2018 and 2021. For all Banff scores, differentially-expressed genes (DEGs) were derived, then reduced using an ElasticNet feature selection and we trained four machine learning classifiers (Naïve Bayes, Extreme Gradient Boosting, Linear Support Vector Machine (LSVM) and K-Nearest Neighbours) using cross-validation. Models’ performances were compared on a test set (30% of the total samples).

Finally, we trained an archetypal analysis based on the samples’ predicted Banff scores. Results: The ElasticNet feature selection lowered the number of DEGs to be included from a range of [859,10,839] to [52,867]. The best discrimination were obtained with the LSVM with a precision-recall area under the curve in the interval [0.708;0.980] (Tptc). Excluding cv and ah, all models calibrated properly (Hosmer and Lemeshow goodness of fit p-value > 0.05). The gene expression-based predicted Banff score probabilities were used for an archetypal analysis which resulted in 8 profiles: acute and chronic antibody-mediated rejection (DSA, C4d, g, ptc and cg lesions), acute T-cell mediated rejection (l, t and t lesions), chronic TCMR (l, i, t, ci, ct and i-IFTA lesions), mixed rejection (g, ptc, l and t lesions), vascular injuries (cv and ah), fibrosis (ci and ct lesions, older donors with history of hypertension), minimal fibrotic change (ci and ct) and minor changes (no lesions).

Conclusions: From new transcripts, we managed to develop gene expression-based models that predict accurately the Banff score lesions and 8 clinically-meaningful histological profiles were identified among these predictions.
Purpose: Gene expression profiling of allograft biopsies is an unmet need in kidney transplant patient care with demonstrated potential to improve rejection diagnosis and guide therapeutic decision making. Despite several gene sets being described and validated over the past few decades, molecular assessment of biopsies has yet to be integrated into clinical practice.

Methods: The Banff Human Organ Transplant (B-HOT) gene panel has the advantage of being performed on the same tissue sample as used for histology, allowing histo-molecular data integration. We sequenced 664 biopsies from a well-phenotyped multicenter renal transplant cohort consisting of more than 180 variables, including recipient and donor baseline characteristics, histology, clinical data, infection status, treatments, and graft characteristics. Predictive models were developed based on B-HOT expression data for AMR (antibody-mediated rejection) and TCMR (T-cell mediated rejection). Gene selection was performed for each outcome using regularized logistic regression. Models were developed using an ensemble approach, with the median probability of the base models assigned to each biopsy.

Results: Model performance was assessed in one internal and two external validation cohorts (respective PR-AUC for AMR=0.82, 0.86, 0.9 and TCMR=0.78, 0.80, 0.82). Discrepancies between histology and expression-based probabilistic scores were confirmed as follows: 1) iBox + different eGFR formulas (MDRD_Scr, MDRD_Scr.OKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data; 4) iBox functional without histological data (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. We stratified the recipients according to several real-life scenarios: 1) iBox + different eGFR formulas (MDRD_Scr, MDRD_Scr.OKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data; 4) iBox functional without histological data (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. The performances transportability and surrogacy of the iBox system, further reinforcing its use as a surrogate endpoint for clinical trials including the validation cohort, there is a need for proof of validity in geographically distinct and diverse medico-economic cohorts and transplant allocation systems.

Methods: 10,851 transplant recipient were included from 17 academic medical centers. We applied the iBox algorithm that integrates eight independent prognostic factors: time from transplantation to risk evaluation, functional parameters (eGFR, proteinuria), allograft histological lesions (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. We stratified the recipients according to several real-life scenarios: 1) iBox + different eGFR formulas (MDRD_Scr, MDRD_Scr.OKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data; 4) iBox functional without histological data (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. The performances transportability and surrogacy of the iBox system, further reinforcing its use as a surrogate endpoint for clinical trials including the validation cohort, there is a need for proof of validity in geographically distinct and diverse medico-economic cohorts and transplant allocation systems.

Results: The derivation cohort included 4,000 recipients from France and the external validation cohort included 6,851 recipients from Europe (n=4,643), the United States (n=1,537) and South America (n=671). The mean recipient age was 50.3 years, with a median follow-up after evaluations of 5.4 years (IQR: 3.3 to 7). 12.3% of patients lost their graft during the follow-up period. The performances were confirmed as follows: 1) iBox + different eGFR formulas (0.81; 2) iBox + urinary dipstick (0.80); 3) iBox Functional without immunological data (0.80 (derivation) and 0.84 (validation)); 4) iBox functional without histological data (0.80 (derivation) and 0.83 (validation)); 5) iBox in response to treatment in TCMR: 0.81; 6) iBox in response to treatment antibody mediated rejection (ABMR) clinical trials. The performances of the iBox were assessed with the discrimination and the calibration.

Conclusions: The iBox has the advantage of being performed on the same tissue sample as used for histology, allowing histo-molecular data integration. We sequenced 664 biopsies from a well-phenotyped multicenter renal transplant cohort consisting of more than 180 variables, including recipient and donor baseline characteristics, histology, clinical data, infection status, treatments, and graft characteristics. Predictive models were developed based on B-HOT expression data for AMR (antibody-mediated rejection) and TCMR (T-cell mediated rejection). Gene selection was performed for each outcome using regularized logistic regression. Models were developed using an ensemble approach, with the median probability of the base models assigned to each biopsy.

Results: Model performance was assessed in one internal and two external validation cohorts (respective PR-AUC for AMR=0.82, 0.86, 0.9 and TCMR=0.78, 0.80, 0.82). Discrepancies between histology and expression-based probabilistic scores were confirmed as follows: 1) iBox + different eGFR formulas (MDRD_Scr, MDRD_Scr.OKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data; 4) iBox functional without histological data (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. We stratified the recipients according to several real-life scenarios: 1) iBox + different eGFR formulas (MDRD_Scr, MDRD_Scr.OKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional without immunological data; 4) iBox functional without histological data (IFTA, c+ptc, i+t, cg Banff scores) and circulating anti-HLA DSA. The performances transportability and surrogacy of the iBox system, further reinforcing its use as a surrogate endpoint for clinical trials including the validation cohort, there is a need for proof of validity in geographically distinct and diverse medico-economic cohorts and transplant allocation systems.

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Conclusions: The iBox has the advantage of being performed on the same tissue sample as used for histology, allowing histo-molecular data integration. We sequenced 664 biopsies from a well-phenotyped multicenter renal transplant cohort consisting of more than 180 variables, including recipient and donor baseline characteristics, histology, clinical data, infection status, treatments, and graft characteristics. Predictive models were developed based on B-HOT expression data for AMR (antibody-mediated rejection) and TCMR (T-cell mediated rejection). Gene selection was performed for each outcome using regularized logistic regression. Models were developed using an ensemble approach, with the median probability of the base models assigned to each biopsy.

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Background: The iBox is a validated prognostication system predicting long-term kidney allograft failure. It received regulatory endorsement by EMA for surrogate endpoint for clinical trials. As it was primarily built using a deep phenotyped cohort, there is an ongoing program to evaluate its performance in other populations and transplant centers.

Methods: This was an open label, 1:1 randomized study in which 155 patients with 1 year of transplantation were allocated either in the eHealth program or in the SOC during 2 years. The primary outcome was defined by the absence of major complications (death, graft failure, acute rejection, decrease in the eGFR >25% or cancer). We aimed to show the non-inferiority of the eHealth program based on a lower limit of the 90%CI of the difference in the primary outcome higher than 3%. The secondary outcomes were the incremental cost-effectiveness ratio (ICER) expressed as the cost per Quality-Adjusted Life-Year (QALY) gained, and the evolution of the several patient-reported outcomes. Despite the randomization, we considered possible confounders by weighting on propensity scores.

Results: 135 patients respecting the intention-to-treat principle and without missing data were analyzed in whom 31 patients presented at least one major complication (2 deaths, 3 graft failures, 5 rejection episodes, 9 decreases in eGFR and 21 cancers). The confounder-adjusted difference of proportions of

Flow diagrams of histology based diagnosis and gene expression based predicted probability for AMR and TCMR for each biopsy in validation cohorts (n=397).
AI & Digital Health: from donation to the world outcomes

OS18_1 BELATACEPT OUTCOMES IN PEDIATRIC KIDNEY TRANSPLANTATION: AN INTERNATIONAL MULTI-CENTER STUDY

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1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, U-970, AP-HP, Paris, France, 2Robert Debri Hospital, APHP, Pediatric Nephrology department, Paris, France, 3Emory University School of Medicine, Surgery Department, Atlanta, France, 4Emory University School of Medicine, Pediatric Nephrology department, Atlanta, France, 5Mother and Child Lyon University hospital, Pediatric Nephrology department, Bron, France, 6Félix Guyon University Hospital, Pediatric Nephrology department, La Réunion, France

Background: Belatacept is associated with better long-term outcomes in adult patients compared to CNI based regimens. Data on its use in older children and young adults are lacking. We are the 1st to report outcomes for 45 pediatric kidney transplant recipients converted to belatacept.

Methods: Patients were included from 4 centers (USA and France) from 2018 to 2021. Patients received an induction with basiliximab (n=39) or ATG (n=6). Maintenance immunosuppression included CNI, MMF +/- steroids. Patients’ viral status (EBV, CMV) were monitored monthly and allograft biopsies were performed prior and ~6 months after starting belatacept. The first 5 belatacept injections were administered at 5mg/kg/dose (10mg/kg/dose if early conversion) every 2 weeks, then monthly. CNI were progressively reduced and stopped. MMF doses were also increased at CNI withdrawal.

Results: Median age at conversion was 17.7y (range 10.3-20.6). 7/45 patients received an early conversion (median: 1 month post-transplant, IQR 0.5-1.2): 6 patients for delayed graft function and 1 for post-transplant diabetes. 38/45 patients were converted after a median of 4.1 years post-transplant (IQR 1.7-6.0). Conversion indication was CNI avoidance: either because of toxicity (histology, post-transplant diabetes, tremors; n=13) or sub-optimal creatinine (n=12) or to improve adherence (n=13). CNI were withdrawn in 42/45 patients by a median of 2.4 months (IQR 1.4-6.0). GFR was stable or improved over a median follow-up time of 1.6 years (IQR 1.1-2.4), Fig A. Ten rejections (22%) after a median of 10.2 months (IQR 6.1-15.8) and included 7 TCMR, 2 ABMR and 1 mixed rejection. None of these patients were converted early (<3m), 5 had been converted for non-adherence, 4 had pre-existing DSA and 4 had prior history of rejection. Evolution of GFR in rejectors is shown in Fig B. CNI were reintroduced for 6/10 and belatacept stopped for 3/10. Regarding viral complications, 1 severe BKv nephropathy required the discontinuation of belatacept. All patients were EBV+ at conversion (4 were EBV- at the time of transplant). No EBV relapse was observed.

Conclusions: Selected pediatric kidney recipients benefit from long-term CNI toxicity avoidance, but selection criteria need to be refined to avoid rejection under costimulation blockade.
OS18_2 LONGITUDINAL DYNAMICS OF SOLUBLE IMMUNE MEDIATORS IN PAEDIATRIC LIVER TRANSPLANTATION IDENTIFIED SIGNATURES ASSOCIATED WITH A FREEDOM OF REJECTION

Eugeny Chichelnitskiy1, Imeke Goldschmidt2, Louise Ruhl1, Nicole Rubaen3, Veronika Jäger1, André Karch1, Lorenz D’antiga1, Dominique Debray1, Loreto Hierro1, Deirdre Kelly1, Valérie MC Lin2, Emanuele Nicastro3, Joanna Pawłowska4, Piotr Czubkowski9, Ulrich Baumann1, Christiane S. Leber1
1Institute of Transplant Immunology, Hannover Medical School, Hannover, Germany, 2Division of Pediatric Gastroenterology and Hepatology, Hannover Medical School, Hannover, Germany, 3Institute for Epidemiology and Social Medicine, University of Munich-Künzler, Munich, Germany, 4Ospedale Riunito di Bergamo, Bergamo, Italy, 5Hospital Necker-Enfants Malades, Paris, France, 6Hospital Infantil Universitario La Paz, Madrid, Spain, 7Birmingham Children’s Hospital, Birmingham, United Kingdom, 8Service Spécialités Pédiatiques, Genève, Switzerland, 9Department of Gastroenterology, Hepatology, Nutritional Disorders and Pediatrics, The Children’s Memorial Health Institute, Warsaw, Poland

Background: In the European multicentre ‘ChilSFree’ study, we aimed to characterize longitudinal dynamics of soluble and cellular immune mediators during the first year after pLT and identify early biomarkers associated with outcome.

Methods: Using Luminex-based multiplex technique, we measured 50 cytokines/chemokines, growth and adhesion factors in recipient plasma at eight visits: before (V0), 7/14/21/28, 3/6/12 months (3/6/12Mo) after pLT (n=244). Absolute cell counts and relative proportions of immune cell populations in patient blood were analyzed after flow cytometry. For each immune cell type, the most frequent pattern was characterized by the absence of pro-inflammatory markers CXCL8/9/10/12, CCL7, reduced liver enzymes (AST, GGT), rejection score and, hence, might be predictive for improved outcome after pLT. In addition, we found higher frequencies of CD56bright NK cells in the blood of the same patients, a cellular hallmark described in operationally tolerant patients. Of note, this special SIM pattern was observed few weeks after pLT and could predict superior outcome of the underlying patients over entire year. The longitudinal dynamics of immune cell counts revealed that absolute cell counts and proportions of myeloid cells peaked at D7, followed by gradual decrease at later visits. Simultaneously, CD4+ and CD8+ T cells and CD56 NK cell counts were reduced at D7 but recovered at D21 with a further increase at 12Mo. The dynamics of T and NK cells but not B cells, granulocytes and monocytes after pLT was affected substantially by the age of patients.

Conclusions: SIM blood signatures may act as biomarkers for improved outcome after pLT, hence, paving the way to early adjustment of immunosuppression and improved therapeutic options.

OS18_3 MOLECULAR HLA MISMATCHING FOR PREDICTION OF PRIMARY HUMORAL ALLOIMMUNITY AND GRAFT FUNCTION DETERIORATION IN PAEDIATRIC KIDNEY TRANSPLANTATION

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1University of Cambridge, Department of Surgery, Cambridge, United Kingdom, 2University Children’s Hospital Heidelberg, Department of Pediatric Nephrology I, Heidelberg, Germany, 3University of Turin, School of Medicine, New Orleans, United States, 4Koc University, School of Medicine, Istanbul, Turkey, 5Ospedale Pediatrico Bambino Gesu, Divisione di Nefrologia e Dialisi, Rome, Italy, 6University Hospital Hamburg, Pediatric Nephrology, Hamburg, Germany, 7Institute of Transplant Immunology, Hannover Medical School, Einshoven, Germany, 8University Hospital Cologne, Pediatric Nephrology, Cologne, Germany, 9University Hospital Tübingen, Pediatric Nephrology, Tubingen, Germany, 10University Children’s Hospital Heidelberg, Pediatric Nephrology, Mannster, Germany, 11University Children’s Hospital Heidelberg, Department of Pediatric Nephrology I, Heidelberg, Germany

Background: Rejection remains the main cause of allograft failure in paediatric kidney transplantation and is driven by donor-recipient HLA mismatching.

Modern computational algorithms enable assessment of HLA mismatch immunogenicity at the molecular level (molecular-mismatch, molMM). Whilst molMM has been shown to correlate with alloimmune outcomes, evidence demonstrating improved prediction performance against traditional antigen mismatching (antMM) is lacking.

Methods: We analysed 177 patients from the CERTAIN registry (median follow-up 4.5 years). molMM scores included Amino-Acid-Mismatch-Score (AAMS), Electrostatic-Mismatch-Score (EMSM) and netHHCilpan (netHHC1k: peptide binding affinity ≤1000 nM; netHHC ≤500 nM; netHHC1k ≤500 nM plus rank ≤2%). We stratified patients into high/low-risk groups based on risk models ofDSA development.

Results: Donor-specific HLA antibodies (DSA) predominantly targeted the highest scoring molMM donor antigen within each HLA locus. MolMM scores offered superior discrimination versus antMM in predicting de novo DSA for all HLA loci; the EMS3D algorithm had particularly consistent performance (area under the receiver operating characteristic curve (AUC) >0.7 for all HLA loci vs. 0.52-0.70 for antMM). ABMR (but not TCMR) was associated with HLA-DQ molMM scores. Patients with high-risk HLA-DQ molMM had increased risk of graft function deterioration (50% reduction in baseline eGFR eGFR50, adjusted HR: 3.5, 95% CI 1.6-8.2 high vs. low EMS3D). Multivariable modelling of the eGFR50 outcome using EMS3D HLA-DQ stratification showed better discrimination (AUC EMS3D vs. antMM at 2 years: 0.81 vs. 0.77, at 4.5 years: 0.72 vs. 0.64) and stratified more patients into the low-risk group, compared to traditional antMM.

Conclusions: Molecular mismatching was superior to antigen mismatching in predicting humoral aloimmunity. Molecular HLA-DQ mismatching appears to be a significant prognostic factor for graft function deterioration in paediatric kidney transplantation.

Figure: Survival analysis for eGFR50 outcome, adjusted for baseline eGFR, recipient age, donor age and transplant number based on HLA-DQ mismatching. A) molMM stratification using EMS3D, B) antigen mismatching.

Guillaume Rossignol1,2, Xavier Muller2, Mathias Ruiz1, Sophie Collardeau-Frachon1, Remi Dubois1, Celia Depaulis1, Teresa Antonini1, Kayvan Mohkan1,2, Jean Yves Mabrut1,3
1Femme Mere Enfant University Hospital, Department of Pediatric Surgery and Liver Transplantation, Lyon, France, 2Croix Rousse University Hospital, Department of General Surgery and Liver Transplantation, Lyon, France, 3The Cancer Research Center of Lyon, Inserm 1092, Lyon, France, 4Femme Mere Enfant University Hospital, Department of Anesthesiology, Lyon, France, 5Croix Rousse University Hospital, Department of Hepatology, Lyon, France

Background: The gold standard in pediatric split liver transplantation (SLT) is living donation (LD) providing high-quality grafts with short static cold storage (SCS). This study investigates the protective effect of hypothermic oxygenated perfusion (HOPE) on ex-situ partial grafts from deceased donors in comparison to standard ex-situ Static-Split and LD SLT.

Methods: We included all consecutive HOPE Split, Static-Split and LD SLT performed from 2018-2022. The primary endpoint was early ischemia-reperfusion injury (IRI) based on reperfusion biopsy (graded from none/0 to severe/4), occurrence of post reperfusion syndrome (PRS, drop≥30% of systolic arterial pressure) and post-LT transaminase release.
Results: A total of 46 SLT (14 HOPE-Split, 17 Static-Split, and 15 LD) were included. With a median perfusion duration of 100min, HOPE-Split had a significant decrease of SCS compared to Static-Split (473 min vs 538 min; p=0.02) with similar total preservation time (p=0.13). This translated into lower rates of mild to severe IRI (grade2; p=0.03) and significantly reduced neutrophilic infiltrate than Static-Split (p=0.04; Fig.1). The PRS was also reduced in HOPE-Split (0% vs 35%; p=0.02) with less transaminase release. Despite prolonged SCS (473 vs 171min; p<0.001), HOPE-Split was comparable to LD regarding grade2 IRI (64 vs 40%; p=0.17) and PRS (0 vs 6.7%; p=0.04), with however higher transaminase release (571 vs 244 UI/L/100g; p=0.004). Overall, 3 months surgical complications, graft and recipient survival did not differ among groups.

Conclusions: HOPE allowed improved preservation of split grafts compared to Static-Split, resulting in similar early IRI profiles to LD.

Table 1. Demographic and post-operative data

<table>
<thead>
<tr>
<th>Data are expressed as n (%) or median (interquartile range).</th>
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<tbody>
<tr>
<td><strong>Recipient characteristics</strong></td>
</tr>
<tr>
<td>Recipient Age, months</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>PELD, weeks</td>
</tr>
<tr>
<td><strong>OAQOL scores</strong></td>
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<td>AST peak, UI/L (1st)</td>
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<tr>
<td>Graft arterial complications Grade 2-3 Cloven-Dindo</td>
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<tr>
<td>Graft Biliary complications Grade 2-3 Cloven-Dindo</td>
</tr>
<tr>
<td>3 month graft survival</td>
</tr>
<tr>
<td>3 month recipient survival</td>
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</tbody>
</table>

Conclusions: This is the first study to look at QoL in paediatric MSOT recipients and results show excellent long-term clinical and QoL outcomes.

FULL ORALS

### OS18_6 MONITORING OF TORQUE-TENO VIRUS LOADS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS MAY PREDICT OPPORTUNISTIC VIRAL INFECTIONS DURING FOLLOW-UP

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Background: The risk for infectious complications and graft rejection by alloimmunity, still remaining as the major cause of late graft failure after kidney transplantation (KTx), is subject of careful balance of immunosuppression during post transplant follow-up. Torque Teno virus (TTV) plasma load was identified as a biomarker reflecting patients individual immune status after solid-organ transplantation (i.e., was also shown to correlate with immunosuppressant dosage in pediatric KTx patients). The aim of this study was to investigate associations and the predictive capability of TTV loads with major opportunistic viral infections (e.g., cytomegaly virus (CMV)) during follow-up of pediatric KTx patients.

Methods: All pediatric patients at the Medical University of Vienna with a post KTx time of >3 months were included. Viral loads (TTV, CMV, Epstein-Barr virus (EBV), Polyomavirus (BKV)) were routinely measured every four to eight weeks by quantitative PCR. Generalized poison mixed models and mixed effects logistic regression for log10 TTV loads with log10 EBV, CMV, and BKV loads were calculated with fixed effects accounting for potential confounders (age, time after KTX), alongside Receiver Operating Characteristics (ROC).

Results: In total 72 pediatric KTx recipients were included. Baseline characteristics and primary kidney disorders are displayed in Table 1. TTV loads were able to predict significant CMVemia above predefined plasma loads of 10^3 c/mL 4 to 8 weeks before occurrence (OR 2.56; p=0.002) after adjustment for potential confounders. Prediction of the first significantly positive CMVemia with plasma TTV achieved a sensitivity of 88% and a specificity of 79%. Furthermore, TTV loads were able to significantly predict significant BKVuria (p=0.02) above predefined urine loads of 1.7 x 10^9 c/mL for the next visit and BKVemia above predefined plasma loads of 10^4 c/mL on the same visit (p=0.005). Associations with EBV were not significant.

Conclusions: This is the first study to demonstrate significant predictive capability of plasma loads of TTV for occurrence of clinically relevant viral infections (CMV, BKV) above relevant cut-offs on the same or for the next visit, 4 to 8 weeks later, in pediatric KTx patients during follow-up.

Table 1. Primary kidney disorders

<table>
<thead>
<tr>
<th>N</th>
<th>%</th>
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<tr>
<td><strong>Primary kidney disorders</strong></td>
<td>25</td>
</tr>
<tr>
<td>Glomerular disorders</td>
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<tr>
<td>Polycystic kidney disease</td>
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<tr>
<td>Congenital nephrotic syndrome</td>
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</tr>
<tr>
<td>Metabolic disorders</td>
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<tr>
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Baseline TTV characteristics

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<td>Calcineurin- or mTOR-inhibitor</td>
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<td>Azathioprine</td>
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<tr>
<td>Sildenaflu</td>
<td>1</td>
</tr>
<tr>
<td>Steroids</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusions: This is the first study to demonstrate significant predictive capability of plasma loads of TTV for occurrence of clinically relevant viral infections (CMV, BKV) above relevant cut-offs on the same or for the next visit, 4 to 8 weeks later, in pediatric KTx patients during follow-up.

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<tbody>
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Baseline TTV characteristics

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**FULL ORALS**

**Paediatric Transplantation around the world**

**OS18_7**

**NATIONAL LIVER ALLOCATION POLICIES FOR PEDIATRIC LIVER TRANSPLANTATION ACHIEVE OPTIMAL OUTCOMES: INTENTION-TO-TREAT ANALYSIS OF ITALIAN WAITING LIST**

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**Background:** Despite pediatric liver transplantation (pLT) achieved excellent outcomes, the waiting list (WL) mortality is still an issue. We analyzed the Italian pLT WL to evaluate the intention-to-treat (ITT) success rate and identifying factors influencing success rate and WL mortality.

**Methods:** All children (<18 years) listed for pLT in Italy during 2002-2018 were included (Era 1(2002-2007); center-based pediatric organ allocation; Era 2(2008-2014): start of pediatric national allocation; Era 3(2015-2018): start of national mandatory-split policy).

**Results:** 1,424 patients [age: 2.0 years (IQR=1.0-9.0); weight: 12.0kg (IQR=7-27)] were listed for pLT. Indications included chronic (70.1%) and acute liver failure (13.3%), metabolic disease (7.4%), tumor (7.2%) and undetermined (2%). Median WL time was 2 days (IQR=1-5) for Status 1, while 44 days (IQR=15-120) for non-Status 1. 1,302 (91.4%) were transplanted (64.4% with split liver grafts), while 50 children (3.5%) dropped from WL due to WL mortality without compromising ITT patient survival rates were 90.5% at 1 year and 87.5% at 5 years and didn't change across Eras. Risk factors for ITT failure (13.3%) were related donors.

**Conclusions:** In Italy, the continuous adaptation of the pediatric organ allocation policies permitted to constitute a unique national allocation model. The presence of a national organ exchange organization, pediatric prioritization rules, and mandatory-split liver policy are key factors to maximize the use of donors for pediatric candidates and to minimize the WL mortality without compromising outcomes.

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Access to transplantation & donation: is luck involved?

**FG1_1**

THE KIDNEY DISTRIBUTION SYSTEM FOR TRANSPLANTATION IN CHILE EXPLAINED ACCORDING TO GAME THEORY: HOW THEORETICAL GENEROSITY TRANSFORMS INTO SELFISHNESS

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**Background:** There is a huge mismatch between demand and supply of kidneys for transplantation. While allocation systems try to assign a scarce resource equitably to the best recipient, using different graft survival maximization; allocation systems can also incentivize the procurement activity. The Chilean allocation system delivers one kidney to the procuring institution and the second nationality policy designed seeking to stimulate procurements (FR) transplant institutions, which should receive a kidney every time they procure a donor. Has this policy been effective in achieving its intent?

**Methods:** We obtained all records of organ donors by private and public institutions, and matched those organs with the centers that implanted them between 2010-2020. We used descriptive statistics and game theory modeling to analyze healthcare institution’s behavior. We obtained public and private prices of kidney procurement and compared them to the price an institution must transfer to the system in exchange for a pool kidney.

**Results:** We found no significant increase in the number of donors in the country during that period. We observed that private institutions are increasing their participation in the transplant market (p = 0.003), and they do so at the expense of public institutions (p = 0.702) and without increasing their contribution of organs (8.2 ± 1.7 vs 5.8 ± 1.6 donors pmp for public vs private, p = 0.002).

Private centers have higher transplant / procurement ratios (4.40 ± 1.59 vs 2.56 ± 0.54; p = 0.0017), which means that these institutions benefit over public ones from the organ allocation system that delivers one of the two kidneys to a national waiting list over a local one. In terms of price, we found it is 2.7% more expensive to procure a kidney in private centers, and both costs are 5 times higher than the transfer price set by law.

**Conclusions:** This behavior can be framed within Game Theory, specifically the Tragedy of the Commons, describing that the players maximize their benefit at the expense of the rest, leading to an imbalance between demand and supply of organs that worsen over time and lengthens waiting lists, especially those listed in a public institution. Chile must change its allocation model to achieve equity and increase transplants. We propose shifting to a local model as most countries in the world.

**FG1_3**

APOL1 GENETIC RISK FACTORS ELIMINATES POTENTIAL LIVING KIDNEY DONORS

Nicole All1, Maya Cumento1, Tamar Schiff1, Brendan Parent2, Lisa Kienan1, Anangely Bello1, Patricia Canda1, Carly McNulty1, Bruce Gelb1; Anthony Watkins1

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**Background:** Apolipoprotein L1 (APOL1) genetic testing is used in living kidney donor (LD) evaluation to assess risk of CKD in those with African heritage. The presence of 2 kidney risk variants (KRVs) is an absolute contraindication. To increase equity in transplant access for patients with African heritage, we changed our practice allowing for more thorough assessment and shared decision making.

**Methods:** We received requests from potential donors who were declined by other centers due to the presence of two APOL1 KRVs. Some were healthy with no additional CKD risk factors. Patients wished to be included in decision making when informed about their testing. To examine options to reduce barriers to living donation in disadvantaged groups, our team established a workgroup to reassess the application of APOL1 genetic testing in LD evaluation.

**Results:** A workgroup of nephrologists, surgeons, nurses, a research associate, and medical ethicists discussed the practice of APOL1 screening and its impact on LD. Extensive literature review was conducted. A team survey reflected willingness to change historical practice which prohibited any donor with 2 KRVs from donation. We established a new guideline focused on patient education regarding APOL1 KRV and risk factor assessment for kidney disease which supported shared decision making. A donor with 2 KRVs also completes a 24-hour ABPM and echocardiogram. A transplant nephrologist reviews the results with donor, discusses available data on LD with APOL1 KRVs and the impact of social determinants of health in long-term outcomes. Donors with a normal 24-hour ABPM, ECHO, excellent creatinine clearance, no proteinuria or other metabolic risk factors can be considered for donation.

5 donors completed further testing since Fall 2021. 1 declined due to abnormal ABPM results and 1 due to unrelated findings. 3 donors successfully donated and have will have longer follow up than lower-risk donors (5 years vs. 2 years).

**Conclusions:** Transplant centers should consider examining historical practices that may potentiate the disparities that exist in access to transplantation and LD. By implementing a practice of careful testing and supporting engagement in shared decision making, we are able to eliminate one of the potential barriers to donation in patients who identify with African ancestry.

**FG1_2**

IMPROVING THE ACCESS TO HEART TRANSPLANTATION FOR FOREIGN PATIENTS OVER 10 YEAR PERIOD

Giada Giovannelli1, Annamaria Minervini1, Laura Borgese1, Marco Valente1, Letizia Marcantoni1, Francesca Aversano1, Laura Giovannini1, Sofia Martin-Suarez1, Antonio Russo1, Marco Masetti1, Paola Prestianni1, Mario Sabatino1, Lucia Goffeni1, Luciano Potena1
1IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

**Background:** While disparities in access to transplantation related to ethnicity and socioeconomic status have often been reported in private-based health-care systems, reports in the setting of public healthcare system are sparse. We reviewed waitlist and heart transplant outcomes of adult foreign residents (FR) referred in the 2012-22 period aiming to assess potential disparities related to descent nationality, and the impact of the change in the procedures for referral and psychosocial management developed in our center in 2019.

**Methods:** We reviewed waitlist registry and clinical charts for demography, clinical features, and outcomes of patients listed in the period 2012-2022. We compared outcomes of FR to patients of Italian descent (ID), over the entire study time frame and between 2012-18 vs. 2019-22.

**Results:** 337 patients were listed (82(24%) females, 50±12y; 37%(10%) FR), and 200(59%) were transplanted in the 2012-22 period. Most of FR were from Eastern Europe (56%) or Africa (24%), with overall 18 countries represented. The proportion of FR listed significantly raised in the 2019-22 period vs. 2012-18 (6.5 vs 15.3%; P<0.01), achieving a rate similar to that of age matched FR living in Northern Italy. Rate of waitlist death/deterioration was similar between FR and ID (70±3% vs. 65±10%; P=0.5). However, time to transplant was shorter in FR only in the 2012-18 period, but not in 2019-22. In the 2012-18 period ICD/CRT implants were less common in FR than ID (46% vs. 85%; P<0.01), but not in those listed in the 2019-22 period (70% vs. 82%; P=0.4). The differences between time periods suggest that before 2019 FR referred for transplant were undertreated or referred late with a more severe phenotype needing a short waitlist period. Post-transplant estimated 10-y survival was similar between FR and ID (70±3% vs. 65±10%; P=0.5).

**Conclusions:** Despite universal healthcare coverage, disparities in access to transplantation are possible between FR and ID. This analysis suggests that the current referral and psychosocial framework implemented at our Center eased access to care for FR by improving the number of patients with timely access to our transplant waitlist. Of note, descent nationality did not impact post-transplant survival.
FG1.4 GENDER DISPARITY TO ACCESS TO KIDNEY TRANSPLANTATION IN TURKEY: 10-YEARS EVALUATION

Yaprak Sarıgöl Ordin,1, Buket Çelik,1, Eda Ayten Kankaya1
1Dokuz Eylül University, Nurisng Faculty, Izmir, Turkey

Background: Kidney transplantations in Turkey have increased since the first transplantation in 1975. Most of them are from live donors. It is known that there is gender disparity to access to transplantation, especially those from live donors. This study aimed to examine the effect of gender on access to kidney transplantation in Turkey in the past ten years.

Methods: In this descriptive, retrospective study, data were obtained from the reports issued by The Turkish Society of Nephrology Registry of The Nephrology, Dialysis and Transplantation in Turkey.

Results: Official electronic records of data about all transplantations in Turkey started in 2013. Data about transplantations in 2022 have not been revealed yet. Therefore, data issued between 2013 and 2021 were evaluated. The males and the age group of 45-64 years had the highest rates of hemodialysis and peritoneal dialysis. The males and the age group of 20-44 years had the highest rate of kidney transplantations and the females and the age group of >75 years had the lowest rate of transplantations. The highest rate of kidney transplantations was from live donors and in the age group of 20-44 years. The highest rate of the live donors was first-degree relatives. The rate of hemodialysis was high initially (66.58%), but it decreased later and preemptive transplantations increased and reached the highest rate over the years (55%).

Conclusions: A higher rate of the males has accessed hemodialysis, peritoneal dialysis and transplantation for end-stage renal disease in Turkey recently. It is seen that being a woman is a disadvantage in accessing renal replacement therapy. Women are seen to be disadvantaged in accessing renal replacement therapy in Turkey, and this inequality is more common in older women. This suggests gender disparity in access to kidney transplantation, which can be attributed to cultural features, gender inequalities and economic factors.

FG1.6 EXCELLENCE IN ORGAN TRANSPLANTATION – A QUALITATIVE STUDY OF GENDER SPECIFIC CARE NEEDS IN TRANSPLANTATION

Claire Williment1, Jessica Jones2, John Forsythe1, Deirdre A Kelly2, Hilaria Asumu3, Lisa Burnapp1
1NHS Blood and Transplant, London, United Kingdom, 2NHS Blood and Transplant, Birmingham, United Kingdom, 3Patient led care, Manchester, United Kingdom

Background: Current National Health Service care models are often based on male prototypes. An Organ Utilisation Group (OUG) was established in the UK, to identify ways to improve transplant patient experience and outcomes, including a focus on the ‘less heard’ female patient voice.

Methods: Four online focus groups were held in 2021, Chaired by patient representatives. Delegates were invited via patient representative groups and were self-selected. Delegates were not identifiable by the focus group organisers and responses were completely anonymised.

Results: Figure 1 demonstrates the key points raised by patients. Effective psychological and social support pre- and post-transplantation was important for all patients. Female patients highlighted the impact and importance on the wider family (children; partners/spouses; parents; siblings). A lack of social care adversely impacted on families being able to stay together and therefore the family bond. A lack of effective psychological support led to a deterioration in relationships and in some cases a complete breakdown. Some female patients also expressed concerns: that they did not feel listened to; poor pain management; limited information about the impact of/ care through the menopause; a lack of advice regarding contraception, which adversely impacted on their experiences with partners and on psychological well-being.

Conclusions: Whilst there are similarities between male and female needs, female transplant patients have specific needs that may be unmet. The focus group participants explained how a lack of tailored care and support is adversely impacting on outcomes and experiences. The focus group had limitations: small sample size; self-selected participants. Further qualitative and quantitative research is needed, with increased segmentation (ethnicity; geography; socio-demographic) to identify how needs vary between female patients.

Not misogynistic but myopic: the new women’s health strategy in England - The Lancet

Table 1: Diversity of Focus Group Delegate

<table>
<thead>
<tr>
<th>Focus Group 1:</th>
<th>Focus Group 2:</th>
<th>Focus Group 3:</th>
<th>Focus Group 3:</th>
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<td>Lung</td>
<td>Kidney</td>
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<td>5 White</td>
<td>6 Black</td>
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<tr>
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<td>1 male; 4 female</td>
<td>2 males; 4 female</td>
</tr>
<tr>
<td>Age</td>
<td>1 parent of paediatric patient</td>
<td>1 patient who had been a child at the time of listing</td>
<td>6 adult patients</td>
</tr>
<tr>
<td>Pre- or Post-transplant</td>
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<td>2 pre-transplant; 3 post-transplant</td>
<td>2 pre-transplant; 4 post-transplant</td>
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<tr>
<td>Patient/carer</td>
<td>6 patients; 1 parent of paediatric patient with special needs; 1 representative of adult special needs patient</td>
<td>5 patients</td>
<td>6 patients</td>
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Figure 1: Summary of feedback from Focus Group delegates, segmented by gender and ethnicity.
THE GRAPHIC NOVEL "THE NEW US" TO SUPPORT DOCTOR-PATIENT RELATIONSHIP IN TRANSPLANT PATIENT CARE-PATHWAY

Enrica Baraldi*, Cristina Anfossi1, Andrea Voglino1, Paola Kruger1, Patrizia Burra2

1Chiesi Italia SpA, Medical Department, Parma, Italy, 2Elma Academy, Milano, Italy, 3Graphic Medicine Italia, Milano, Italy, 4EUPATI, Roma, Italy, 5Padua University Hospital, Multivisceral Transplant Unit, Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua, Italy

Background: Transplant recipients will need to learn to live with a new condition that has implications for day-to-day life. Many communication tools for improving lifestyle and adherence to immunosuppressive therapy are often developed based on the assumptions of health care providers (HCPs) on the needs of the patients without prior consultation of them. This project aims to creatively bridge this gap—incorporating transplant patients and HCPs in the development of a graphic novel to improve the doctor-patient relationship and dialogue and to become leader of their long-term health.

Methods: Insight from previous ethnographic research on twelve transplant patients were the input guiding the style and substance of the graphic novel. The interviews focused on what were the most bothersome aspects of life post-transplant: adherence to lifestyle and immunosuppressive therapy, what patients may be worried about in the future, and difficulties in communication with HCPs. A team composed by HCPs, a Patient Expert, illustrator, communication expert and writer has developed a graphic novel that has the potential for empowering patients through customized patient-relevant information, thus equipping them with the skills to make fully informed decisions.

Results: Two main characters were identified: Luca, a kidney transplant recipient with a story of illness that shaped his identity and Gabriella, transplant liver recipient who finds herself unprepared for the new life. The story has two parallel tracks: the evolution of their relationship, and the evolution of their role as patients that become in charge of their care-pathway. In between a funny animated kidney, Renny, that helps Luca to manage the ‘rules’ of his daily life. The story script, as well as the models for characters during the drawing process, were defined, reviewed, and revised with input and clarifications from the whole team to enhance trustworthiness of ethnographic research analysis/transposition into narrative and graphic form, and to ensure that the content was appropriate and accurate. “The new us” was distributed to Transplant Centers.

Conclusions: “The new us”, realized through patients and HCPs co-creation, can offer multi-faceted communication opportunities and support doctor-patients relationship in the transplant patient care-pathway.
**FOCUS GROUPS**

**Insights on IRI and PGD in cardiothoracic transplantation**

**FG2_1**

**POSITIVE LONG-TERM EFFECTS OF 17ß-ESTRADIOL AND METHYL-PREDNISOLONE ASSOCIATION ON LUNG INFLAMMATION Triggered by Brain Death in Female Rats**

Marina Vidal-dos-Santos1,2, Lucas Ferreira Da Anunciação1, Roberto Armstrong Junior1, Fernando Yamamoto Ricardo-da-Silva1, Cristiano de Jesus Correia1, Luiz Felipe Pinho Moreira1, Henri Leuvenink1, Ana Cristina Breithaupt-Faloppa1

1Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 2Surgery Department, University Medical Center Groningen, Groningen, Netherlands

**Background:** After brain death (BD), females tend to present higher lung inflammation in comparison to males. It is believed that the acute reduction of estradiol (E2) after BD compromises the female immune response and evidence points to a connected action of E2 and corticoids in this sex. Impairment of the donor response to BD could compromise the recipient prognostic in the long-term. Thus, we aimed to investigate the prolonged effects of E2 and methylprednisolone (MP) treatment on lung inflammation in female BD rats using tissue culture method.

**Methods:** Female Wistar rats were submitted to BD by rapid insufflation of a balloon catheter in the intracranial space and maintained for 6h. Rats received MP (4 mg/ml i.v–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml i.v–2 ml/h) after 3h of BD until the end of experiment. Sham-operated (S) were used as control. Bronchoalveolar lavage (BAL) and lung tissue were collected. Lung fragments were kept in culture for 24h (explant) and inflammatory mediators were measured.

**Results:** Compared to sham, BD animals presented higher total leukocyte infiltration in BAL, which was prevented by both treatments (S: 10.75±1.3; BD: 23.63±3.6; MP/E2:11.50±2.97; MP: 15.5±2.75 cells (x10^5)/ml-

**Conclusions:** These results point to lasting positive effects of the association between MP and E2 in lung inflammation triggered by BD in females. This is highlighted by the decrease of infiltrate cells, followed by the reduction of cytokines and chemokine release after 24h in the MP/E2 group, as well an overall lower level of VEGF in the same group, suggesting modulation of vascular permeability.

This study was financed by 2020/11211-6, Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP.

**FG2_2**

**MITOCHONDRIAL DAMAGE COMPARISON BETWEEN BRAIN DEATH DONORS AND DONORS AFTER CIRCULATORY DEATH IN LUNG TRANSPLANTATION: PROSPECTIVE MULTICENTER STUDY**

Irene Bello1,2, Alberto Sandiumenge1,2, Ramon Martí1, Elisabeth Coll1, Marina Pérez Redondo1, Silvana Crowley1, María Ángeles Ballesteros1, Sara Narango1, Fernando Mosteiro2, Eva Fleira1, Aroa Gomez Brey1, Teresa Pont Castellana1

1Hospital Clinic, Barcelona, Spain, 2IDIBAPS, Barcelona, Spain, 3Hospital Vall d’Hebron, Barcelona, Spain, 4Vall d’Hebron Institut of Research, Barcelona, Spain, 5ONT, Madrid, Spain, 6Hospital Puerta de Hierro, Madrid, Spain, 7Hospital Marqués de Valdecilla, Santander, Spain, 8Complejo Hospitalario Universitario A Coruña, A Coruña, Spain

**Background:** The warm ischemia time associated to donation after circulatory death (cDCD) may enhance the apoptosis process in lung tissue leading to post-mortem degradation of mitochondrial-DNA (mtDNA) into damage associated molecular patterns (DAMPs). Multiple observations suggest that the DAMPs could serve as sentinel marker to primary graft dysfunction (PGD). Our objective is to compare the DAMPs observed in lung recipients from donors after brain death (BD) and cDCD.

**Methods:** Eighty adult lung recipients, 40 from BD and 40 from cDCD donors (paired by lung transplantation indication and age) were prospectively enrolled in 4 Spanish transplant centres from Jul-18 to Jul-19. Blood samples were collected from the donor before (E0) and during the retrieval process (E1), and from the recipient before implant (R-1), after graft reperfusion (R0) and R72 (R72) hours after lung transplantation. Mitochondrial damage (DAMPs) was analysed and compared between groups.

**Results:** Demographics of donors and recipients as well as transplant surgical procedure characteristics were similar between groups except for a higher rate of corticoid treatment and vaso-active support in BD group and higher blood transfusion requirements in cDCD group. No differences were found in mitochondrial damage between groups in E0, E1, R-1, R0 and R72 (Figure 1). Primary graft dysfunction (PGD) incidence did not have statistically differences between both groups. Table 1.

**Table 1. Outcomes**

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<th>DCD (n=40)</th>
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<td>26 (65)</td>
<td>0.100</td>
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<tr>
<td>Of any grade</td>
<td>27 (67.5)</td>
<td>26 (65)</td>
<td>0.469</td>
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<tr>
<td>primary graft dysfunction, n (%)</td>
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<tr>
<td>Post-operative mortality</td>
<td>2 (5)</td>
<td>0 (0)</td>
<td>0.494</td>
</tr>
<tr>
<td>Three-month mortality</td>
<td>2 (5)</td>
<td>0 (0)</td>
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**Fig.1. mtDNA number of copies/plasma**
**INSIGHTS ON IRI AND PGD IN CARDIOTHORACIC TRANSPLANTATION**

**FOCUS GROUPS**

**FG2.3 A NOVEL WHOLE-BODY COOLING SYSTEM PROTECTS DONOR LUNGS FROM IRI AND PGD DURING DCD: TARGETING UNCONTROLLED DONATION AFTER CIRCULATORY DEATH DONORS**

**Hiromichi Niikawa**, Daaike Sakota, Ryo Kosaka, Katsuhiro Ohuchi, Hirokuni Arai, Kenneth Mccurry, Yoshinori Okada, Toshitomo Okamoto

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**Background**: Lung transplantation using lungs from uncontrolled donation after circulatory death (uDCD) may increase lung donor pool. We developed a novel chest cooling system for uDCD donors without surgical intervention. We hypothesized that the system described as involving whole-body cooling using a proprietary material could improve pulmonary function of uDCD donors. The aim of this study was to verify whether the cooling system ameliorates the physiological parameters, compared to control using ex vivo lung perfusion (EVLPE).

**Methods**: Ten pigs were divided into two groups (DCD or cooling group). In the DCD group, lungs were subjected to 90 min of warm ischemia time (WIT) at room temperature, whereas lungs were cooled with the cooling system during WIT in the cooling group. Tracheal temperature was continuously measured during WIT. Subsequently, lungs were procured in a standard fashion and then perfused in 2 hours of Lund-type EVLP following 5 hours of cold preservation. Transplant suitability was decided based on physiological parameters and visual findings. Lung tissue samples were collected for measurement of wet to dry ratio.

**Results**: The tracheal temperature in the cooling group gradually decreased during WIT and finally reached 28.5°C, while there was no decrease in the temperature of the DCD group (Figure A). In EVLP evaluation, the cooling group was significantly associated with higher PaO2/FiO2 ratio (412 ± 82 vs. 261 ± 71, p < 0.05) than control.

**Conclusions**: These results demonstrated that the novel chest cooling system resulted in better pulmonary function in a pig lung uDCD model, suggesting that the new cooling system without surgical intervention may protect uDCD donor lungs from ischemia reperfusion injury and expand the lung donor pool.

**FG2.4 NOT TOO WARM, NOT TOO COLD: REAL-WORLD MULTI-CENTER OUTCOMES WITH ELEVATED HYPO- THERMIC PRESERVATION OF DONOR LUNGS**

**John Haney**, Matthew Hartwig, Natalie Langer, Pablo G. Sanchez, Jasleen Kukreja, Errol Bush

1 Duke University Medical Center, Durham, United States, 2 Massachusetts General Hospital, Boston, United States, 3 University of Pittsburgh Medical Center, Pittsburgh, United States, 4 UCSF Medical Center, San Francisco, United States, 5 Johns Hopkins University, Baltimore, United States

**Background**: Recent reports highlight the potential clinical improvements from hypothermic preservation at elevated temperatures of donor lungs, avoiding risk of mitochondrial injury with standard ice storage (ICE) where lungs reach temperatures near or below 0°C. The LUNGuard Donor Lung Preservation System (LG) is the only FDA and CE cleared preservation technology that maintains donor lungs at controlled elevated hypothermic temperatures, potentially mitigating temperature-related tissue injury. Real-world experience of this preservation strategy on recipient outcomes as studied in the GUARDIAN-Lung Registry is presented.

**Methods**: The GUARDIAN Lung Registry is a multicenter registry assessing outcomes following lung transplants comparing LG and ICE. Retrospective review of clinical outcomes was examined using summary statistics and Kaplan-Meier survival analysis. Continued enrollment will allow updated data to be presented.

**Results**: Transplants in patients using LG (n=86) vs ICE (n=90) had similar baseline characteristics, except significantly more LG-preserved lungs were retrieved from donors after circulatory death (DCD) donors, 17.6% LG vs 6.7% ICE, p = 0.025, see Table. The LG cohort had a clinically meaningful 54% reduction in primary graft dysfunction at 72 hours (p=0.058). LG was also associated with significantly improved one year Kaplan-Meier estimated survival, 95.0% vs 90.0%, p = 0.02, LG vs ICE, respectively (see Figure).

**Conclusions**: Use of LUNGuard is associated with a reduction in PGD3 and enhanced 1-year survival compared to ICE. These data suggest growing evidence that avoiding donor lung near-freezing injury through controlled, elevated hypothermic preservation has a meaningful impact on post-transplant outcomes.

**Table:** Demographic Characteristics and Post-Transplant Outcomes in GUARDIAN-Lung

- **ICE**
  - Donor Age (years) 34.3 ± 11.9
  - Donor Sex (%) Male 61.3 ± 26.4
  - Donor Weight (kg) 179 ± 50
  - Donor BMI (kg/m²) 26.7 ± 4.8
  - Donor PGD 3 hour (min) 374 ± 56.4
  - Peak PaO2/FiO2 312 ± 45.2
  - Lung temperature (°C) 34.7 ± 2.0
  - Intubation time (min) 34.0 ± 1.6
  - Mortality 30%
  - 1-year Lung Graft Survival (%) 95.0

- **LG**
  - Donor Age (years) 36.7 ± 13.4
  - Donor Sex (%) Male 48.8 ± 25.0
  - Donor Weight (kg) 171.9 ± 40.7
  - Donor BMI (kg/m²) 24.5 ± 6.4
  - Donor PGD 3 hour (min) 309 ± 51.4
  - Peak PaO2/FiO2 412 ± 82
  - Lung temperature (°C) 34.7 ± 2.5
  - Intubation time (min) 34.0 ± 2.5
  - Mortality 30%
  - 1-year Lung Graft Survival (%) 90.0

**Figure A**

![Diagram](image)

**Figure B**

![Graph](image)

**Table:** Demographic Characteristics and Post-Transplant Outcomes in GUARDIAN-Lung
Background: The Perioperative Mortality Study (POMS) is a multinational, prospective, observational study that assesses the incidence and predictors of 30-day mortality among patients undergoing cardiac surgery.

Methods: Data from the POMS registry were used to identify patients who underwent cardiac surgery with CPB. The primary endpoint was 30-day mortality. Univariable and multivariable logistic regression analyses were performed to identify predictors of 30-day mortality.

Results: A total of 173,214 patients from 504 hospitals were included in the analysis. The overall 30-day mortality rate was 2.3%. Independent predictors of 30-day mortality included age, gender, and comorbidities such as hypertension, diabetes, and chronic obstructive pulmonary disease.

Conclusions: The POMS registry provides valuable insights into the incidence and predictors of 30-day mortality among patients undergoing cardiac surgery with CPB. These findings can be used to improve perioperative care and reduce mortality.
FOCUS GROUPS

1 Insights on IRI and PGD in cardiothoracic transplantation

**FG2_8 EARLY ECMO OVERCOMES PRIMARY GRAFT DYSFUNCTION AFTER HEART TRANSPLANT**

Angeliki Gkouzioutsa1, Demetrios Miliosopoulos1, Iakovos Armenis1, Michael Bonios1, Antigoni Koliopoulou1, Androniki Tassouli1, Stavros Dimopoulos1, Konstantinos Ieromonachos1, Nektarios Kogerakis1, Themis Champa-Gorgoulia1, Stamatia Adamopoulos1

**Background:** Primary graft dysfunction (PGD) is the main cause of early mortality after heart transplantation. Despite affecting approximately 7-8% of all recipients, the etiology and optimal treatment of this condition remains unknown. Extracorporeal membrane oxygenation (ECMO) is a key treatment modality, however optimal timing of initiation has not been established.

**Methods:** A single-institution retrospective study was conducted. Between January 2003 and December 2022 a total of 25 recipients experienced PGD treated with ECMO. At the beginning of 2016, our institution adopted an early ECMO policy, with PGD patients placed on ECMO prior to leaving the OR at the time of transplant. Patients were stratified into pre-2016 (n=5) and post-2016 (n=20) cohorts. Outcomes including duration of support, ICU and total hospital stay, Ejection Fraction (EF), need for vasoactive or inotropic medication, in-hospital survival, 1-year survival, and complications were analyzed.

**Results:** Among the pre-2016 and post-2016 cohorts there was no difference in duration of ECMO, ICU stay, and total hospital stay. The average time from release of cross-clamp to initiation of ECMO was 8.04 vs 3.05 hrs in each cohort, respectively (p=0.02). In all patients, ECMO resulted in a reduction in the need for vasopressors and inotropes as assessed by the vasoactive inotropic score. LVEF normalized within the first 5 days of therapy for all patients and subsequently was sustained after decannulation. Complication rates among cohorts were similar with respect to bleeding, stroke, infection, and need for temporary dialysis. When compared to the post-2016 cohort, the pre-2016 cohort demonstrated significantly worse in-hospital (75% vs 100%, p=0.04) and 1-year (89% vs 100%, p=0.02) survival.

**Conclusions:** Early initiation of ECMO results in decreased mortality for PGD after heart transplant without an increased risk of complications.

2 Biomarkers and monitoring kidney health

**FG3_1 EVOLUTION OF DDCF DNA DURING THE FIRST WEEK AFTER SURGERY PREDICTS MEDIUM TO LONG-TERM RENAL OUTCOMES**

David Cucchiari1,2*, Elena Cuadrado1, Eva Gonzalez2, Pedro Ventura-Aguilar1, Maria Ramirez-Bajo1, Ignacio Revueltas1, Joan Anton Puig1, Fritz Dickmann1,2

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**Background:** Donor-derived cell-free DNA (ddcfDNA) is usually employed starting from the second week after kidney transplantation (KT), as its earlier increase can be due to the ischemia-reperfusion injury (IRI) and would not reflect the presence of rejection. We hypothesized that ddcfDNA released soon after IRI during the first week after surgery is associated with renal function decline and eGFR, and would be a critical predictor of kidney allograft outcomes. In clinical practice, the extent of IFTA in renal cortical tissue is estimated through analysis of graft biopsy, which is an invasive procedure. A non-invasive test accurately reproducing the degree of IFTA would be beneficial for patients. We aimed at evaluating the accuracy of an MRI radiomic-based machine learning (ML) algorithm in estimating the degree of IFTA in a cohort of patients who received graft biopsy and MRI for clinical practice.

**Methods:** Patients who underwent MRI and renal biopsy within a 6-month interval from 1/1/2012 to 1/3/2021 were included. Stable MRI sequences were selected, and renal parenchyma, renal cortex and medulla were segmented using the 3DSlicer software. After image pre-processing and wavelet filtering, images were elaborated through an in-house version of py-radiomics extracting radiomic features. These were subsequently selected through a LASSO algorithm for their highest correlation with the reference standard and lowest inter-correlation. Selected features and relevant patients’ clinical data were used to produce a-ML-algorithms of chronic kidney disease (CKD) cases for training and validation with a 10-fold cross-validation, and 30% for model testing. Diagnostic performances were evaluated using AUC with a 95% confidence interval (CI).

**Results:** 70 coupled tests (63 patients, 35.4% females, mean age 52.2 years) have been included and subdivided into a wider cohort of 50 for training and a smaller cohort of 20 for testing (table 1). For IFTA ≥ 25%, AUCs in test cohort were 0.60, 0.59, and 0.54 for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively. For IFTA ≥ 50%, AUCs in test cohort were 0.60, 0.59, and 0.54 for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively.

**Conclusions:** An ML-based MRI radiomic algorithm showed promising discrimination capacity for patients with IFTA≥50%, especially when included clinical variables.

**FG3_2 MAGNETIC RESONANCE IMAGING TEXTURE ANALYSIS TO ASSESS GRAFT INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY IN PATIENTS WITH TRANSPLANTED KIDNEYS**

Francesco Fontana1, Gaetano Alfano1, Filippo Monelli2, Giulia Besutti2, Valeria Trojani1, Mattia Fantoni1, Gabriele Di Micco1

1Azienda Ospedaliero Universitaria di Modena, Nephrology, Dialysis and Kidney Transplant Unit, Modena, Italy, 2Azienda Unità Sanitaria Locale - IRCCS Reggio Emilia, Radiology Unit, Reggio Emilia, Italy, 3Azienda Unità Sanitaria Locale - IRCCS Reggio Emilia, Medical Statistics Unit, Reggio Emilia, Italy

**Background:**Interstitial fibrosis / tubular atrophy (IFTA) is a common, irreversible, and progressive form of chronic kidney allograft injury, and it is considered a critical predictor of kidney allograft outcomes. In clinical practice, the extent of IFTA in renal cortical tissue is estimated through analysis of graft biopsy, which is an invasive procedure. A non-invasive test accurately reproducing the degree of IFTA would be beneficial for patients. We aimed at evaluating the accuracy of an MRI radiomic-based machine learning (ML) algorithm in estimating the degree of IFTA in a cohort of patients who received graft biopsy and MRI for clinical practice.

**Methods:** Patients who underwent MRI and renal biopsy within a 6-month interval from 1/1/2012 to 1/3/2021 were included. Stable MRI sequences were selected, and renal parenchyma, renal cortex and medulla were segmented using the 3DSlicer software. After image pre-processing and wavelet filtering, images were elaborated through an in-house version of py-radiomics extracting radiomic features. These were subsequently selected through a LASSO algorithm for their highest correlation with the reference standard and lowest inter-correlation. Selected features and relevant patients’ clinical data were used to produce a-ML-algorithms of chronic kidney disease (CKD) cases for training and validation with a 10-fold cross-validation, and 30% for model testing. Diagnostic performances were evaluated using AUC with a 95% confidence interval (CI).

**Results:** 70 coupled tests (63 patients, 35.4% females, mean age 52.2 years) have been included and subdivided into a wider cohort of 50 for training and a smaller cohort of 20 for testing (table 1). For IFTA ≥ 25%, AUCs in test cohort were 0.60, 0.59, and 0.54 for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively. For IFTA ≥ 50%, AUCs in test cohort were 0.60, 0.59, and 0.54 for radiomic features only, clinical variables only, and combined radiomic-clinical model, respectively.

**Conclusions:** An ML-based MRI radiomic algorithm showed promising discrimination capacity for patients with IFTA≥50%, especially when included clinical variables.

---

**Table 1:** Clinical variables

<table>
<thead>
<tr>
<th>Total (n=70)</th>
<th>Training set (n=50)</th>
<th>Test set (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M:F)</td>
<td>45:25</td>
<td>30:15</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian:Sub-Saharan</td>
<td>62:8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58±13,7</td>
<td>54±13,32</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0±5.5</td>
<td>26.0±5.3</td>
</tr>
<tr>
<td>DCF DNA (median, IQR)</td>
<td>16.4±8.2</td>
<td>16.4±8.2</td>
</tr>
<tr>
<td>eGFR (median, IQR)</td>
<td>40.8±18.3</td>
<td>40.8±18.3</td>
</tr>
<tr>
<td>Post-transplant renal function (n=70)</td>
<td>0.79±0.35,0.10</td>
<td>0.74±0.33,0.20</td>
</tr>
</tbody>
</table>

**Transplant type (n=70)**

| DCD | 50 (70.29%) | 42 (84.00%) | 37 (75.00%) |
| DCD | 2 (2.86%)  | 4 (8.00%)  | 0 (0.00%)  |

**ID**

10 (14.29%)  10 (14.29%)  10 (14.29%)

**Transplant age (median, IQR)**

57.67 (17-77)  57.67 (17-77)  57.67 (17-77)

**IFTA ≥ 25% (n=70)**

24 (34.29%)  24 (34.29%)  24 (34.29%)

**IFTA ≥ 50% (n=70)**

20 (28.57%)  20 (28.57%)  20 (28.57%)

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**Table 2:** Clinical characteristics of the included patients / paired tests, CCB donation after brain death; DCD donation after cardiac death; SD living donor

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**FOCUS GROUPS**

### VALIDATION OF THE INTERNATIONAL IGA NEPHROPATHY PREDICTION TOOL IN KIDNEY TRANSPLANT RECIPIENTS WITH IGA NEPHROPATHY RECURRENCE

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**Background**: The recurrence of IgA nephropathy (IgAN) worsens the prognosis of renal transplantation, representing the third cause of graft loss in these patients. Several variables at the time of recurrence, such as renal function, proteinuria, steroid withdrawal, and MEST-C findings relate to a higher risk of graft loss after recurrence. The International IgAN Prediction Tool (IIgAN-PT) uses clinical and histological predictor variables at the time of native kidney biopsy to predict the risk of end-stage kidney disease (ESKD) or a 50% decline in estimated glomerular filtration rate, allowing a proper patient-specific risk stratification. Our aim was to analyze the performance of this tool in a population of kidney transplant recipients with rIgAN.

**Methods**: A multicenter retrospective study was carried out including renal transplant recipients with biopsy-proven IgA nephropathy as the underlying disease in which the recurrence of the primary disease had been verified by means of graft biopsy. IIgAN-PT was used to calculate the risk of ESKD or a 50% decline in eGFR at 3-years in an app calculator ([xqmd.com/calculate-by-qxmd](https://xqmd.com/calculate-by-qxmd)).

**Results**: 118 kidney transplant recipients were included with an age of 46 ± 14 years at recurrence. 79% male, with a mean time to biopsy of 63 ± 67 months and a post-transplant follow-up of 120 ± 72 months. After recurrence, 32 (27%) transplants were lost after 37 ± 27 months, excluding death. Mean IIgAN-PT was 16 ± 13%. By Cox regression analysis, IIgAN-PT related to death censored graft loss (DCGL) (HR 1.115, 95%CI 1.080-1.151, p < 0.001). By logistic regression analysis IIgAN-PT related to DCGL at 3 years (OR 1.279, 95%CI 1.145-1.428, p=0.0012). By logistic regression analysis, IIgAN-PT related to death censored graft loss. The International IgAN Prediction Tool (IIgAN-PT) performed well in a kidney transplant population with rIgAN with good discrimination ability and good calibration to predict DCGL.

**Conclusions**: IIgAN-PT performed well in a kidney transplant population with rIgAN with good discrimination ability and good calibration to predict DCGL. Using an app calculator, we can stratify patients with the highest risk of graft loss due to IgAN recurrence and carry out the most appropriate therapy to improve their prognosis.

### CORTICAL IRON DEPOSITION ASSESSED BY MAGNETIC RESONANCE IMAGE IS ASSOCIATED WITH FIBROSIS

Carlos Couceiro*, Diego Sandoval, Eugenia De Lama, Isabel Puig, Sergi Codina, Laia Oliveras, Alexandre Favà, Ana Coloma, Nuria Montero, Edoardo Melilli, Anna Manonelles, Mate Mauß, Manuel Serrano, Josep Maria Cruzado

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**Background**: Fibrosis is responsible for the loss of kidney function as a result of several insults, such as ischemia-reperfusion injury (IRI) or hyperfiltration. This process can continue even after cessation of the primary insult, as documented in acute kidney injury to chronic kidney disease. Recently, we discovered that iron accumulation is a hallmark of fibrotic diseases. We found that in mouse models, iron deposition in the kidney accompanies the progression of the disease. Based on these results, we propose that chronic-low grade hemolysis produced in situation like IRI may be one of the drivers of fibrosis through the damage that the filtrated hemolytic iron cause to the kidneys. Early detection of this iron could help the detection of ongoing fibrogenesis and improve the outcomes by prompt intervention. The challenge of this approach is the lack of non-invasive markers of fibrosis. We evaluated if magnetic resonance image (MRI)-based detection of iron levels in the kidney are correlated to fibrosis in biopsies from kidney transplant (KT) recipients.

**Methods**: After approval from the Institutional Revision Board, we carried out a transversal study in our center between 2020 and 2021. We evaluated iron deposits through MRI in patients who underwent a kidney biopsy (per protocol or by clinical indication) and its association with histological parameters. MRI was performed at the same period the biopsy was done. Iron deposits were estimated by using the R2* sequence considering the Grassedonio protocol.

**Results**: We collected data from 15 kidney transplant recipients. Mean age, time from KT to biopsy and eGFR were respectively 58.3 years old, 4.3 years and 44.4 ml/min/1.73m². We analyzed by MRI the R2* signal in the kidney cortex, and their level of fibrosis measured on the biopsies (IFTA score, interstitial fibrosis and tubular atrophy). We found that patients with high IFTA score (2 and 3) presented with significantly higher R2* signal (p=0.005), than patients with low IFTA score (0 and 1). We also found positive and significant correlation between IFTA (0-3) and iron deposits (Spearman correlation index: r=0.757, p=0.0012).

**Conclusions**: Iron deposits in the kidney are higher in patients with more fibrosis, and its detection through MRI could be considered a non-invasive marker.
**Thibaut Vaulet**, Jasper Calleymen, Baptiste Lamarthé, Tim Debyser, Priyanka Koshy, Dany Angelcheau, Wilfried Gwinner, Pierre Marqueul, Maarten Naesens

1UZ KU Leuven, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium, 2UZ Leuven, Department of Nephrology and Kidney Transplantation, Leuven, Belgium, 3University of Bourgogne Franche-Comté, Dijon, France, 4KU Leuven, Department of Imaging and Pathology, Leuven, Belgium, 5Necker-Enfants Malades Hospital, Assistance Publique-Hôpitaux de Paris, Department of Nephrology and Kidney Transplantation, Paris, France, 6Hôpital Saint-Pierre, Inserm U1151, Necker Enfants Malades Institute, Paris, France, 7Hannover Medical School, Department of Nephrology, Hannover, Germany, 8University of Limoges, Department of Pharmacology and Transplantation, Limoges, France

**Background:** The terminally differentiated effector memory CD+ (TEMRA CD8+) T cells, which re-express the native CD45RA in absence of CCR7, have been hypothesized to be a potential key player in humoral allograft rejection. This study aims to better characterize the association of intra-graft TEMRA CD8+ T cells with both the main Banff rejection categories and graft outcome.

**Methods:** The proportion of TEMRA CD8+ T cells was estimated via the deconvolution of three transcriptomic datasets (N=224, N=403 and N=282) of kidney transplant biopsies using a novel signature matrix derived from single cell transcriptomics. Difference in TEMRA CD8+ T cell proportion was assessed with Student t-test for each pair of Banff diagnoses (No rejection, AMR, TCNMR and Mixed rejection). The discrimination performance was assessed with pairwise AUC and the polytomous discriminant index (PDI) for multi-class discrimination. Association with graft failure was performed with a Cox model, adjusted for time post-transplantation and reported as hazard ratio (HR).

**Results:** No significant differences in TEMRA CD8+ T cell proportion were observed between the Banff categories (Fig. 1A), excepted for AMR vs No rejection (Student t-test p<0.033, although the magnitude of the difference was low (0.29% [0.03% - 0.58%]). TEMRA CD8+ T cells demonstrated limited discrimination performance between the major Banff rejection categories: AUC for rejection vs no rejection: 0.59 [0.54 - 0.64]; the best AUC for No rejection vs Mixed rejection: 0.60 [0.51 - 0.69]; DDI: 0.29 [0.22 - 0.36] (a random classifier has a PDI of 0.25). Despite the lack of relation to specific inflammatory patterns/rejection subtypes, TEMRA CD8+ T cells demonstrated a strong association with graft failure (HR 1.75 [1.48 - 2.01], p<0.0001) (Fig. 1B) which remained consistent across the independent subsets with survival data available (HR 2.00 [1.45 - 2.67], p<0.0001 and HR 1.75 [1.48 - 2.11], p<0.0001).

**Conclusions:** We demonstrated a strong association between the intra-graft proportion of TEMRA CD8+ T cell and graft failure, independent of the Banff rejection subtypes. TEMRA CD8+ T cell constitute a promising and specific therapeutic target for improvement of transplant outcome.

**FG3.5 INTRA-GRAFT TEMRA CD8+ T CELLS: AN INDEPENDENT PREDICTOR OF KIDNEY ALLOGRAFT FAILURE INDEPENDENT OF REJECTION CATEGORIES**

**FG3.6 LONGITUDINAL MONITORING OF TORQUE TENO VIRUS DNAEMIA IN RENAL TRANSPLANT RECIPIENTS Predicts LONG-TERM COMPLICATIONS OF INADEQUATE IMMUNOSPRESSION**

Luc Chavquel, Thomas Barba, Carole Saison, Alice Koening, Valerie Dubois, Maud Babey, Carole Janis, Emmanuel Morelon, Stephan Bakker, Olivier Thaunat

1Lyon University Hospital-INSERM U11111, Lyon, France, 2Lyon University Hospital-INSERM U1111, Lyon, France, 3University Claude Bernard Lyon 1, Lyon, France, 4Lyon University Hospital, Lyon, France, 5Biomerieux, verniolle, France, 6University of Groningen, Department of Internal Medicine, groningen, Netherlands

**Background:** Recent studies have suggested that Torque Teno Virus (TTV) load reflects the “depth” of therapeutic immunosuppression during the first 12 months post-transplantation but whether this non-invasive biomarker can predict long-term complications of inadequate immunosuppression is not yet established.

**Methods:** A discovery cohort of 124 healthy controls and 34 stable kidney transplant recipients enrolled 23±17 months after transplantation was used to define thresholds of TTV DNAemia. These results were validated in an independent validation cohort of 92 kidney transplant recipients, enrolled 1-year post-transplantation and prospectively followed for 3 years.

**Results:** With the discovery cohort, we defined the lower (3.75 log10 cp/mL) and upper (5.1 log10 cp/mL) threshold of TTV DNAemia associated respectively with: i) an increased T cell residual activativity in vitro as well as the magnitude of antibody response against a model protein antigen (Flu vaccine), ii) and a higher risk for serious infection or cancer during the next 50 months in stability kidney transplant recipients. In the validation cohort, patients in whom the yearly TTV DNAemia was within target at ≥ 2/3 time points were less prone to experience long-term complications due to inadequate immunosuppression (defined as de novo CSA, biopsy proven rejection, serious infection or cancer). Multivariate analysis confirmed that in contrast with all other variables (including T0 of CNI), in target TTV DNAemia was the only variable independently associated with a reduced risk for long-term complications due to inadequate immunosuppression (HR:0.29 [0.09-0.82]; p=0.025).

**Conclusions:** Longitudinal monitoring of TTV DNAemia in kidney transplant recipients predicts long-term complications due to inadequate immunosuppression and might serve for individual optimization of therapeutic immunosuppresion.

**FG3.7 TORQUE TENO VIRUS PLASMA CONCENTRATION TRENDS IN KIDNEY TRANSPLANT RECIPIENTS BEFORE PATHOGENIC INFECTIONS AND ALLOGRAFT REJECTION**

Rohita Singh, Zixuan Zhu, John Friedewald, Steve Kleiboeker

1Eurofins Viracor, Lenexa, United States, 2Northwestern University Feinberg School of Medicine, Chicago, United States

**Background:** In kidney transplant recipients (KTRs) under or over immunosuppression may lead to allograft rejection and opportunistic infections, respectively. The presence and/or concentration of Torque Teno Virus (TTV), a ubiquitous viral species, may act indicate the net state of immunosuppression, thus informing infection and rejection probabilities.

**Methods:** 1980 plasma samples from 255 CTOT–08 subjects were analysed by gene expression profiles (GEP) for rejection (AJT 19:98-109,2019) and by NGS for dd cfDNA (CJASN 16: 1539–1551, 2021), as previously described. The NGS data was further analysed to detect DNA viruses, with presence was ascertained by a combination of Reference Assisted Assembly and Kmer-frequency based methods. Viral concentration was calculated as the number of associated NGS reads normalized to viral genome length.

**Results:** To assess correlation between TTV and infection, TTV concentration was assessed from 150 days before to 49 days after reported clinical infections of BKV, CMV, EBV, hepatitis B or influenza (Fig. 1). Concentrations of TTV increased from 150 to 0 days before the onset of infection, with a Pearson correlation of 0.99 between median values and days pre-infection (p=0.0242). Before and after clinically reported rejection events, TTV concentration variations were not significantly different based on the Fisher-test before and after rejection (Fig. 1). The TTV positivity rates did not vary significantly for either infection or rejection events. The probability of allograft rejection (subclinical acute rejection (subAR) or acute rejection (AR)) given a positive GEP was 0.491. For subAR or AR, the rejection probability increased when either TTV or TTV and viral pathogens were absent. Conversely, subAR and AR rejection probabilities decreased when TTV or TTV and viral pathogens were present. Similar patterns were observed for subAR but not AR analysed separately (Table 1).

**Conclusions:** In this retrospective study of TTV dynamics in the context of clinical rejection and infection events, we found that TTV concentration correlates with infections such as pathogenic viral infections and allograft rejection. Our results suggest that profiling of viral DNA including TTV in KTRs may serve as a useful biomarker of net state of immunosuppression.
Figure 1: FG3_8

**TORQUE TENO VIRUS VIRAL LOAD PREDICTS SARS-COV-2 VACCINE RESPONSE IN KIDNEY TRANSPLANT RECIPIENTS**

Morgane Solis1,2, Ilies Benotmane1,2, Floriane Gallais1,2, Sophie Gaillard1,2, Samira Fafi-Kremer1,2

1Hôpitaux Universitaires de Strasbourg, Laboratoire de Virologie, Strasbourg, France, 2Université de Strasbourg, INSERM, UMR_S1109, LabEx TRANSPLANTEX, Centre de Recherche d’Immunologie et d’Hématologie, Faculté de Médecine, Fédération Hospitalo-Universitaire (FHU) CMICARE, Fédération de Médecine Translationnelle de Strasbourg (FMTS), Strasbourg, France

**Background:** Transplant recipients display poor responses to SARS-CoV-2 mRNA vaccines. In this retrospective study, we investigate Torque teno virus (TTV) viral load (VL), a ubiquitous virus reflecting global immune response levels, as a predictive factor of vaccine response in kidney transplant recipients (KTR).

**Methods:** 459 KTR having received two SARS-CoV-2 mRNA vaccine doses were enrolled, and 241 of them subsequently received a third vaccine dose. Anti-receptor-binding domain (RBD) IgG response was assessed after each vaccine dose and TTV VL was measured in pre-vaccine samples.

**Results:** Pre-vaccine TTV VL >6.2 log10 copies (cp)/mL was independently associated with non-response to two doses (Odds Ratio (OR)=6.17, 95% confidence interval (CI95)=2.42–15.78) as well as to three doses (OR=3.62, 95% CI95=1.55–8.49). In non-responders to the second dose, high TTV VL in pre-vaccine samples or measured before the third dose were equally predictive of lower seroconversion rates and antibody titers.

**Conclusions:** High TTV VL before and during SARS-CoV-2 vaccination schedules are predictive of poor vaccine response in KTR. This biomarker should be further evaluated regarding other vaccine responses.
FOCUS GROUPS

We do need incompatible kidney transplant

F4G2 THE IMPACT OF NON-DIRECTED ALTRUISTIC DONORS (NDAD) IN LIVING KIDNEY EXCHANGE IN THE UK

Rachel Johnson1, Matthew Robb1, Lisa Mumford1, Lisa Burnapp1

1NHS Blood and Transplant, Bristol, United Kingdom, 2NHS Blood and Transplant, London, United Kingdom

Background: The first kidney transplants from NDADs happened in the UK in 2007, following a change in legislation. Until 2012, NDADs donated directly to the deceased donor waiting list (DDWL), following the deceased donor offering scheme to identify the recipient. In 2012, NDADs could choose to donate to DDWL or into the UK Living Kidney Sharing Scheme (UKLKSS), whereby they would donate into a chain of incompatible (and some compatible) pairs, enabling a chain of 2 or 3 transplants, completing with a recipient on the DDWL. Since 2018, NDADs have been included in the UKLKSS by default, to maximise transplants. This is subject to not matching with a high priority recipient on the DDWL. If they are not matched in a chain, then they have the choice of donating direct to DDWL.

Methods: This study examines the benefit that NDADs have made to the kidney exchange programme in the UK (ie UKLKSS), by looking at donor and transplant activity.

Results: In 2012, the first year in which donors could choose to donate into the UKLKSS to create chains of transplants, there were 60 donors, only 3 (5%) of whom donated into the pool. These 3 donors each generated 2 transplants, involving one pair in the UKLKSS and one recipient on the DDWL. In 2013, 21% of 107 NDADs donated to create a chain, rising to 57% of 70 NDADs in 2022 resulting in 130 transplants. In total, between 2012 and 2022, there were 887 NDADs in the UK donating either direct to the DDWL (n=577, 65% of donors) or into the UKLKSS and creating a chain of transplants (n=310, 35% of donors). Taking into account the additional 443 transplants generated by these, this resulted in a total of 1330 transplants. This included 176 recipients with more than 5 years waiting time on the DDWL and 30 paediatric recipients.

Conclusions: NDADs are an important contributor to living donor kidney transplantation in the UK and in the last 5 years, 55% of 344 NDADs have created a chain of 2 or 3 transplants rather than a single transplant through donation direct to the DDWL. The 631 transplants resulting from the 344 NDADs in the last 5 years, represent 15% of all living donor transplants in the UK in that time.

F4G3 COMPARING OUTCOMES OF KIDNEY EXCHANGE PROGRAMMES WITH DIRECT LIVING DONOR KIDNEY TRANSPLANTATION IN A COUNTRY WITH HIGH LIVING DONATION RATES

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Background: Kidney exchange programmes (KEP) provide an option for transplantation for patients who cannot find a compatible or suitable living donor. Compared to non-KEP, these patients are often higher risk patients on baseline due to higher sensitization, longer dialysis vintage and other risk factors resulting in challenges among their transplants. In KEPs, either the donor’s kidney is transported to the recipient centre, or the donor travels to the recipient centre for the nephrectomy. Importantly, the cold ischaemia time (CIT) is prolonged when the graft is transported to another hospital, and it is unknown if any mode of transportation is favoured above the other. In our national KEP, the donor travels to the recipient center. In this study, we assessed the differences in graft outcomes between KEP and non-KEP living donor kidney transplants (LDKT).

Methods: All LDKTs performed nationally from 2004 - 2021 were included. The primary outcome measures were 5- and 10-year death censored graft survival (DCGS). The secondary outcome measures were delayed graft function (DGF), rejection rates and patient survival. We used propensity score-matching to account for differences in pre-transplant covariates.

Results: 7536 LDKTs were included of which 694 (9.21%) transplanted via KEP. There was no difference in DCGS at 5 year (survival probability 0.916 (95% CI: 0.894 - 0.939) for KEP versus 0.915 (0.912 - 0.926, p = 0.82) for non-KEP) and 10 year DCGS (survival probability 0.883 (95% CI: 0.857 - 0.910) for KEP and 0.882 (95% CI: 0.874 - 0.890, p < 0.01) in non-KEP, figure 1). We found significant differences in DGF (11.85% versus 5.17%, p < 0.01), 5 year rejection (11.76% versus 7.09%, p < 0.001) and 5 year patient survival: 0.839 (95% CI: 0.812 - 0.868) in KEP and 0.895 (95% CI: 0.887 - 0.902, p = 0.001) in non-KEP. The significant difference in patient survival turned not significant after propensity score-matching.

Conclusions: The excellent results of patients transplanted through KEP highlights the unique option for patients without a compatible or suitable living donor that would otherwise not have been possible without specific and more invasive pre- and post-transplant treatments. The long-term transplant outcomes of KEP are comparable to non-KEP LDKTs and this takes away another level of reluctance to further develop KEPs.

Figure 1. Kaplan-Meier survival estimates for 10-year death censored graft survival.
**FOCUS GROUPS**

**DESENSITIZATION AND IMMUNOMODULATION IN SENSITIZED KIDNEY TRANSPLANT RECIPIENTS: A DELPHI METHOD CONSENSUS FROM THE ENGAGE WORKING GROUP OF ESOT**

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**Background:** The objective of the European Guidelines for the management of ABO-compatible and ABO-incompatible kidney transplantation (ABOi KT) has been considered to overcome donor shortage. We investigated the long-term clinical outcomes in ABOi KT in patients with high baseline anti-A/B antibody titer.

**Methods:** We retrospectively included 271 patients who had undergone ABOi KT from May, 2009 to November, 2020. One hundred and ninety-one patients with a baseline immunoglobulin G (IgG) titer of ≥1:128 were assigned to the high-titer group and 80 patients with a baseline titer of ≤1:64 were assigned to the low-titer group. We used a protocol composed of rituximab, plasmapheresis, and intravenous immunoglobulin (RTX/PP/IVIG). We compared the clinical outcomes of the two groups.

**Results:** The median follow-up periods were 59.12 months (high titer group) and 41.53 months (low-titer group) (p = 0.003). The high titer group required more sessions of PP/IVIG than the low titer group (7.50±2.47, 3.39±1.30, p < 0.001, respectively). Patient survival at 5 years was 93.80% in high titer and 92.60% in low-titer group (p = 0.563). During the follow-up period to five years, antibody titer remained higher in the high titer group. And serum creatinine showed no difference between two groups up to 9 years (p for interaction = 0.171). No significant differences were detected in the graft survival rate, patient survival rate and rejection free survival rate between two groups. However, the infection free survival rate was significantly lower in the high-titer group (p = 0.049). The incidence of bacterial infection was higher in high-titer group (45.00% vs. 28.27%, p = 0.008).

**Conclusions:** Patients with high baseline anti-A/B IgG isoagglutinin titers had equally successful long-term outcomes as those with low titers. However, ABOi KT in the high-titer group may require greater caution compared to the low-titer group because of the higher tendency of infection.

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**CLINICAL OUTCOMES IN ABO- AND HLA-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION: A NATIONALWIDE STUDY**

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**Background:** ABO-incompatible (ABOi) or Human leukocyte antigen-incompatible (HLAi) living donor kidney transplantation (LDKT) is increasing, however, still inferior to immune-compatible transplantation. We aimed to analyze clinical outcomes of ABOi or HLAI LDKT using nationwide cohort data.

**Methods:** We utilized the nationwide data repository from the Korean Organ Transplantation Registry (KOTRY) with the cases of LDKT between 2009 and 2018. The kidney transplants were classified according to the presence of anti-A/B or donor-specific anti-HLA (HLA-DSA) antibodies. We compared the incidence of biopsy-proven acute rejection (BPAR), graft survival, and patient survival.

**Results:** A total of 5046 patients were classified into three groups: transplants in recipients with HLAI-LDSA (DSA+, n=512), transplants in recipients without HLAI-LDSA and ABOi donors (DSA- & ABOi, n=1168), and transplants without HLAI-LDSA and ABO compatible donors (CONTROL, n=3346). The incidence of acute antibody-mediated rejection (AABMR) was the highest in the DSA+ group, followed by DSA- & ABOi group, both higher than the CONTROL group (p<0.001, DSA+ vs. CONTROL, p=0.017 DSA- & ABOi vs. CONTROL). The overall graft survival was superior in the CONTROL group compared to other groups (p=0.005, DSA- vs. CONTROL, p=0.039, DSA- & ABOi vs. CONTROL). The overall patient survival was superior in the CONTROL group compared to DSA- & ABOi group (p=0.020). For subgroup analysis of the DSA+ group, no statistical difference in BPAR, graft survival, and patient survival was revealed between ABO-incompatible and compatible groups. For DSA- group, the incidence of AABMR and graft loss was higher in ABOi than ABO-compatible group. The multivariable analysis resulted that positive T cell crossmatch (HR 1.962, 95% CI 1.036-3.715, p = 0.039), ABOi (HR 1.496, 95% CI 1.041-2.151, p = 0.030), ABBMR (HR 2.901, 95% CI 1.751-4.807, p<0.001), and ATCMR (HR 3.987, 95% CI 2.634-6.036, p<0.001) were risk factors of graft loss.

**Conclusions:** AABMR and graft loss was higher in ABOi than ABO-compatible group. The presence of anti-A/B or donor-specific anti-HLA (HLA-DSA) antibodies had unfavorable impacts on clinical outcomes in living donor kidney transplantation. The suspicion of hostile events and appropriate management for AABMR should be undertaken to improve graft and patient survival.
Methods: Six pairs of human kidneys rejected for transplantation and offered for research were used in this study with approval from the National Research Ethics committee and Research and Development office (NRES: 15/NE/0408). Three pairs were perfused for 6hrs using normothermic machine perfusion (NMP), and three pairs were perfused for 24hrs using hypothermic machine perfusion (HMP), with one kidney per pair randomised to enzyme treatment. Cortical biopsies collected throughout perfusion were examined for antigen loss using immunofluorescence microscopy.

Results: After 2hrs of NMP, a significant loss of 83.4±10.2% blood group A antigen expression was observed compared to pre-treatment levels (p=0.012), while no significant changes were observed in control kidneys (p=0.999). For HMP, a maximal loss of 71.2±21.9% was observed after 6hrs (p=0.066), with no significant change in control kidneys (p=0.999). For all groups, significant loss of blood group A antigens was observed as little as 2hrs of NMP, and 6hrs of HMP. These approaches pave the way for future clinical use of enzyme treatment.

Conclusions: Our results show a loss of 70-80% of blood group A antigens in as little as 2hrs of NMP, and 6hrs of HMP. These approaches pave the way for future clinical use of enzyme treatment.
Background: De novo donor-specific antibodies (DSAs) are associated with antibody-mediated rejection (AMR) and allograft loss. Whether monitoring of subclinical de novo DSA (dnDSA) paired with systematic kidney biopsy should become routine remains to be established and long-term graft survival according to the results of this biopsy is not, so far well reported.

Methods: Retrospective multicentric study: 123 patients without graft dysfunction were biopsied because of the presence of dnDSA (One Lambda, mean fluorescence intensity [MFI], >1000). Fifty-one subclinical ABMR (sABMR) (41.4%) were diagnosed, of which 32 (62.5%) active AMR (group 1), 19 (37.5%) chronic AMR (group 2) and 4 (7.8%) active sABMR (group 3). In 72 patients (group 3), biopsy did not show any lesion of ABMR. We report here the long-term follow-up of the three groups.

Results: In group 1, after a median follow up of 7.8 years (IQR: 4.8-9.7), we reported 12 graft losses (12/32: 37.5%). In group 2, after a median follow-up of 6.1 years (IQR: 3.5-7.6), we noticed 10 graft losses (10/19: 52.6%). In group 3, during a median follow up of 9.2 years (IQR: 6.8-10.3), 15 patients (15/72: 20.8%) presented an episode of clinical ABMR (group 3a) confirmed by a graft rejection (6/15: 40%) and 7 (57.9%) chronic rejection (group 3b). In 72 patients (group 3), biopsy did not show any lesions of AMR. We reported here the long-term follow-up of the three groups.

Conclusions: The results of a biopsy performed for a subclinical dnDSA has an impact on the long-term death censored graft survival. Clinicians have to be cautious with patients with initial normal biopsy, because up to 20% of them could present an episode of clinical AMR.

Figure 1: Death censored graft survival according to the results of the first protocolar biopsy in subclinical de novo DSA.
The clinical spectrum of kidney transplant rejection

Figure 1: Rate of detection of dDSA during the follow-up.

Methods: In a cohort of 76 kidney transplant recipients (stable, N=41; ABMR, N=23; TCMR, N=12) and 16 healthy controls, we used high dimensional flow cytometry and single-cell RNA seq to deeply profile peripheral blood CD8 T cells at the time of allograft biopsy. Concomitantly, we assessed CD8 T cell gene expression profiles in allograft biopsies using bulk RNAseq.

Results: Compared to stable and TCMR subjects, ABMR patients displayed significantly expanded cell populations of resting naïve and proliferating effector memory CD45RO-CD28 CD8 T cells. TCMR patients showed specific expansion of CD45RO-CD28 terminally differentiated effector memory (TEMRA) CD8 T cells expressing IL-2R and CXCR5. At the single-cell transcriptional level, ABMR was characterized by elevated transcripts related to T-cell receptor activation and FcγRIIA pathways, while TCMR was associated with enhanced cell cytotoxicity transcripts, and IL-21 and Th1 signaling pathways in CD28 CD8 T cells. Consistently, ABMR biopsies were enriched for antibody-dependent cytotoxicity related transcripts and TCMR biopsies for TBX21 gene expression and cell-dependent cytotoxicity related transcripts.

Conclusions: We identified predominant effector memory differentiation with antibody-dependent cytotoxicity potential in CD28 CD8 T cells during ABMR, while TCMR was characterized by type-1 and IL-21 driven CD28 CD8 T cell changes. Thus, our study identifies novel CD28-CD8 T cell populations with potential for allograft injury which may be therapeutically targeted for treatment of kidney allograft rejection.

FSG 8

SUBCLINICAL REJECTION-FREE DIAGNOSTIC AFTER KIDNEY TRANSPLANTATION USING BLOOD GENE EXPRESSION

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Background: Spontaneous and rare cases of patients undergoing a functional renal transplant in the absence of immunosuppression represent a particular situation of immune tolerance. We previously established a blood score of operational tolerance (cSoT) which was reversed in patients developing anti-HLA and donor-specific antibodies (DSAs), suggesting that this biomarker could be associated with immunological events and risk of rejection.

Methods: We measured the 6 genes composing the cSoT using quantitative PCR (qPCR) and NanString enzyme-free methods in an independent multicenter cohort of 588 renal transplanted patients with paired blood samples and biopsies at 1 year after transplantation.

Results: We validated its association with pre-existing and de novo DSA. In addition, from the 441 patients with protocol biopsies, we evidenced a significant decrease of the cSoT in the 45 patients with biopsy-proven subclinical rejection (SCR), a major threat associated with pejorative kidney allograft outcomes that prompted us to refine a SCR score (SCR-S), with only two genes, AKR1C3 and TCL1A, and 4 clinical parameters. The SCR-S was able to identify patients unlikely to develop SCR with an AUC of 0.864 and a negative predictive value of 98.3% and also reclassifying patients with discrepancies between the presence of DSA and the histological diagnosis of antibody mediated rejection. The SCR-S was technically validated with qPCR and NanString, externally validated on 447 patients from the independent and multicenter cohort of the KTD-Innov consortium and reproduced in an independent and external laboratory.

Conclusions: The presentation will describe a composite score that could improve detection of subclinical rejection to allow a closer and noninvasive patient monitoring, allowing early medical management of these kidney transplant patients.
**FG6_1**

**FIVE-YEAR OUTCOMES OF KIDNEY TRANSPLANTATION FROM DONORS AFTER CIRCULATORY DEATH OLDER THAN 65 YEARS OLD**

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**Background:** The age of donors after circulatory death has increased in our country allowing an expansion in the number of kidney transplants performed. The aim of our study is to compare the short- and medium-term results of transplants performed with donors after circulatory death older than 65 years vs. younger ones.

**Methods:** Retrospective, single-center study including all kidney transplantation recipients of donors after circulatory death performed in our center between April 2015 and December 31, 2021. Data was analyzed using logistic and Cox regression for multivariable analysis and survival was analyzed using Kaplan-Meier curves and long rank. The mean follow-up time was 33 months.

**Results:** 96 renal transplants were performed with donors after circulatory death, 20 of which with donors ≥ 65 years old. Recipient age was significantly higher in the group of patients with donors ≥ 65 years (67.7 vs. 52.4 p<0.05), as well as pre-transplant comorbidity. Renal function at 1 year was significantly lower in recipients with donors ≥ 65 years (cr 1.9 vs. 1.6 mg/dl, p<0.05) presenting no differences at 3 (cr 1.8 vs. 1.7 mg/dl, p=0.4) and 5 years (cr 1.2 vs. 1.6 mg/dl, p=0.15). There were no differences in patient survival (89% vs. 85% p=0.09) or graft survival, death-censured (100% vs. 83% p=0.11) or not death-censured (69% vs. 70%) at 5 years. They presented more delayed graft function (70% vs. 48.7%, p=0.005), but less acute rejection (0% vs. 7.9%, p<0.05). In the multivariate analysis, donor age was not related to worse graft survival or worse renal function at one year.

**Conclusions:** The use of donors after circulatory death older than 65 years is an adequate source of kidneys for patients awaiting renal transplantation.

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**FG6_2**

**KIDNEY OUTCOMES FROM UNCONTROLLED DONATION AFTER CIRCULATORY DEATH: A LONGITUDINAL COHORT**

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**Background:** In January 2016, our hospital started a program of uncontrolled donation after circulatory death (uDCD) to increase organ availability for kidney transplantation.

**Methods:** We longitudinally analysed the results of 294 consecutive recipient’s kidney transplant (KT) performed from January 2016 to December 2020 in our centre and compared the outcomes of 84 KT from uDCD donors maintained by normothermic extracorporeal membrane oxygenation (nECMO) with those from 117 KT from standard-criteria brain-death donors (SCD) and 93 KT from expanded-criteria brain-death donors (ECD).

**Results:** Primary non-function (PNF) was more common in both uDCD (14.3%) and ECD (16.1%, p=0.895) groups than in SCD (6.0%) group (p=0.081 and p=0.03). In addition, delayed graft function (DGF) was more frequent in uDCD group (79.2%) than in ECD (59.0%) and SCD (31.8%) groups (p=0.008 and p<0.001). However, estimated glomerular filtration rate (eGFR) at 5 years was higher in uDCD (62.27±18.38 mL/min/1.73m2) than in ECD (47.67±23.05 mL/min/1.73m2, p<0.01) and similar to SCD (65.48±19.24 mL/min/1.73m2, p=1). When excluding PNF, uDCD and SCD groups had similar 5-year death-censored graft survival (97.1% vs 96.4%, p=0.977).

**Conclusions:** Despite the increased risk of PNF and DGF, functional and survival outcomes of uDCD KT at 5 years were comparable to those of SCD, thus supporting the use of uDCD kidneys maintained under nECMO support as a successful resource to address organ scarcity.
Deceased donor kidney transplantation issues

**FOCUS GROUPS**

**FG6_3** BIOLOGICAL INJURY ASSOCIATED WITH DECEASED DONOR PATHWAYS REFLECT DIFFERENCES IN THE DONOR KIDNEY PROTEOME AND CELLULAR STRESS RESPONSES

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Background: Deceased donation remains the primary source of organs for transplantation, yet short- and long-term outcomes remain difficult to predict. Brain stem death characteristic of the deceased after brain death (DBD) pathway induces haemodynamic and metabolic dysregulation and systemic inflammation in the donor, inducing injury. Whilst lengthy ischaemia inherent to the deceased after circulatory death (DCD) pathway correlates with increased incidences of delayed graft function and early graft loss. Organ specific injury in deceased donors remains under explored and may provide tangible targets for intervention pre or posttransplant. Here, we analysed the proteome of DBD and DCD kidneys to identify differences in pathophysiological processes associated with donor type.

Methods: Kidney biopsies from DBD (n=100) and DCD (n=85) donors were provided by the Quality in Organ Donation biobank. Biopsies were selected based on paired recipient eGFR outcomes at 12mths posttransplant and their proteomes analysed using mass spectrometry. We explored protein expression differences that separated donor type using partial least square discriminant analysis (PLS-DA).

Results: We quantified n=2984 protein groups (5% FDR). Supervised analysis comparing the DBD and DCD proteome using PLS-DA showed incomplete separation of the samples by donor type (Figure 1a); the first latent variable (LV) separated a subset of DCD donors, and the second LV separated a subset of DBD donors. Notably, the first LV that separated DCD donors had a weakly significant positive correlation with the length of functional warm ischaemia (rho=0.26, p=0.051).

Conclusions: Proteomes of deceased donor kidneys partially separate based on donor type by a linear combination of protein abundances. Our analysis highlights changes in cellular and metabolic stress responses, indicating that injury and repair mechanisms may differ between donor types.

**FG6_4** RISK FACTORS OF ACUTE KIDNEY INJURY IN DECEASED KIDNEY DONORS

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Background: Acute kidney injury (AKI) in deceased donors affects kidney graft outcome. Little is known about risk factors associated with AKI in deceased donors.

Methods: In this prospective single center study, procurement biopsies of each kidney were performed in all deceased donors referred to our center in May 2021 - December 2022. AKI was defined by AKIN criteria. Clinical data were collected and AKI markers in urine were measured.

Results: 196 deceased (DBD 188, DCD 8) kidney donors were included in the analysis. 9 donors were excluded for insufficient data to determine AKI. AKI occurred in 89 donors (AKI+, 45.5%). AKIN stage 1 was observed in 69 donors (77.5%), AKIN stage 2 in 16 (17.9%) and stage 3 in 4 (4.4%) donors, respectively. AKI+ donors had higher BMI (27.3 (IQR 24.28–31.75) vs. 25.4 (22.35–29.80), p = 0.016) as compared to AKI-. There were no significant differences in age, gender, diabetes and hypertension. The procurement biopsies in AKI+ donors displayed higher cv (p = 0.002), ah (p = 0.02) and IF/TA scores (p = 0.019), and higher ATN rate (p = 0.002). We found higher urinary NGAL/creatinine (20.03 μg/mmol (IQR 6.37–48.66) vs. 8.47 (3.35–27.27) p=0.003) and higher urinary NGAL/creatinine ratio (22.35 (6.36–22.87) vs. 8.47 (3.35–27.27) p=0.003) in AKI+ compared to AKI- donors respectively. There were no significant differences in other urinary AKI markers such as NAG, beta-2-mikroglobulin and albumin. AKI was associated with ATN (OR 1.55, 95% CI 1.03 – 2.45, p=0.044), cv score (OR 1.29, 95% CI 1.09 – 1.53, p=0.003) IF/TA score (OR 1.37, 95% CI 1.05 – 1.80, p=0.020), and highest NGAL/creatinine ratio tertile (>22.3 μg/mmol, OR 2.86, 95% CI 1.41 – 5.93, p=0.004) in logistic regression. Body mass index and diabetes status were not significantly associated with AKI.

Conclusions: Deceased donors with AKI were more likely to have kidney structural abnormalities and AKI was independent on BMI, hypertension, diabetes status and other donor categories. Procurement biopsies and urinary NGAL assessment allows the identification of deceased donors at risk of AKI which might have implications for kidney transplantation outcomes.
Background: Thrombotic microangiopathy (TMA) is a serious complication that significantly affects allograft survival. Endothelial injury is one of the pathogeneses of TMA. Donor factors with the consequence of ischemic reperfusion injury might be the risk of early TMA after transplantation.

Methods: A retrospective cohort study of patients who underwent deceased donor kidney transplantation at Siriraj hospital between 2006 and 2020 was conducted. The definition of early TMA was biopsy-proven TMA within one month after transplantation. We determined incidence, risk factors of early TMA and its effect on graft outcomes.

Results: Of all 412 patients, the incidence of early TMA after kidney transplantation was 12.4% (51 patients). The median time to diagnosis was 7 days after transplantation. Only 20 patients (39.2%) developed TMA with evidence of antibodies-mediated rejection in graft biopsy. Donor profiles in TMA patients showed higher KDPI scores, including an increased number of hypertension and cerebrovascular accidents. The cold ischemic time over 20 hours [OR, 2.51 (95%CI 1.44, 4.39); p=0.001] and donor with hypertension [OR, 2.80 (95%CI 1.06, 7.43); p=0.038] were significant independent risk factors for developing early TMA. Patients with TMA had significantly lower 5-year graft survival than patients without TMA (57.2% and 93.4%, p<0.001).

Conclusions: Early TMA post-transplantation is associated with limited donor characteristics including hypertension and cerebrovascular accident. This condition is aggravated by longer cold ischemic time and anastomosis time, leading to premature graft failure.

Table 1. Factors associated with early TMA post-transplantation

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate (OR and 95%CI)</th>
<th>p-value</th>
<th>Multivariate (OR and 95%CI)</th>
<th>p-value</th>
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<tr>
<td>Recipient age (years)</td>
<td>1.02 (0.99, 1.05)</td>
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<td>Donor age; ≥39 years</td>
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<td>Donor hypertension</td>
<td>2.36 (1.34, 4.16)</td>
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<td>2.80 (1.06, 7.43)</td>
<td>0.038</td>
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<td>Donor with cerebrovascular accident</td>
<td>1.74 (0.99, 3.03)</td>
<td>0.05</td>
<td></td>
<td></td>
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<tr>
<td>Thai kidney donor profile index; ≥80</td>
<td>1.96 (1.13, 3.39)</td>
<td>0.016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold ischemic time; ≥90 hours</td>
<td>2.32 (1.34, 4.02)</td>
<td>0.003</td>
<td>2.51 (1.44, 4.39)</td>
<td>0.001</td>
</tr>
<tr>
<td>Anastomosis time; ≥60 minute</td>
<td>1.86 (1.06, 3.24)</td>
<td>0.03</td>
<td>2.11 (1.17, 3.79)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

NON-IMMUNOLOGICAL RISK FACTORS AND CLINICAL OUTCOME OF SLOW GRAFT FUNCTION AFTER DECEASED DONOR KIDNEY TRANSPLANTATION

Jun Bae Bang¹, Chang-Kwon Oh²
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Background: The slow graft function (SGF) is associated with an increased risk of acute rejection and inferior long-term outcome after kidney transplantation. The exact mechanism whether the SGF might influence long-term outcome immunologically or non-immunologically, is still unclear. In order to find the non-immunological risk factors of the SGF, we selected the study population with the kidney recipients from deceased donors with immunological low risks.

Methods: Total 363 recipients underwent deceased donor kidney transplantation at Ajou university hospital between March 2010 and December 2020. Among these recipients, 137 recipients with extended criteria donor transplantation, re-transplantation, positive donor-specific antibody, delayed graft function were excluded. Two hundred twenty-six recipients were finally included in this study. Study population was divided into immediate recovery of graft function (IGF, n=120) and slow graft function (SGF, n=38) according to serum creatinine (3mg/dl) at post-operative day 5. Clinical parameters were analyzed and compared between the two groups, and we attempted to identify the risk factor of developing SGF in immunological low risk deceased donor kidney transplantation.

Results: There were significant differences in recipient’s body mass index (BMI), total ischemic time. Other factors were not associated with developing SGF. A multivariate analysis of risk factors for SGF showed recipient’s BMI >25 kg/m² (odds ratio=2.23; p=0.044) and total ischemic time (odds ratio=1.004, p=0.032) to be the independent risk factors. The estimated glomerular filtration rates (eGFRs) at 1-year post-transplantation were significantly higher in IGF group. There was one graft failure in IGF group and no graft failure in SGF group with the 1-year post-transplantation. The 1-year acute rejection rates were not statistically different between the groups.

Conclusions: The recipients with SGF showed significantly low eGFR at 1-year post-transplantation. The factors of recipient’s high BMI and prolonged ischemic time were independent risk factors of developing SGF in deceased donor kidney transplantation with low immunological risk. To improve long-term graft function, donor selection is important in terms of high BMI and prolonged ischemic time.
**FOCUS GROUPS**

**Deceased donor kidney transplantation issues**

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1University of Padova, Kidney and Pancreas Transplantation Unit, Padova, Italy

**Background:** Kidney transplantation (KT) is the treatment of choice for end-stage renal disease (ESRD). New strategies have been adopted for increasing donor pool, including the use of kidneys from extended criteria donors (ECD). An increasing number of studies are evaluating the outcome of KT from donors > 80 years, but only few of them considered donors older than 80 years. The aim of this study was to assess the outcome of Single Kidney Transplantation (SKT) and Dual Kidney Transplantation (DKT) performed from donors > 80 years.

**Methods:** Data about all patients who underwent a KT form donor more than 80 years old in a single-centre between 2011 and 2022 were collected. Patients were divided in two groups according to the type of KT: SKT group and DKT group. Decision to perform SKT or DKT was based on the histological evaluation of graft (Kapinskii score) and clinical donor evaluation (past medical history, kidney function and cause of death). Table 1 depicts recipient characteristics, serum creatinine at discharge, delayed graft function, acute rejection and graft failure. Comparison in terms of transplant outcome and graft function between the two groups was carried out.

**Results:** Between January 2011 and December 2022, 100 kidney transplants using grafts from octogenarian donors were performed. Thirty-one of them were SKT and 69 were DKT. Median donor age was significantly higher for DKT (83.8 ± 2.5 years) compared to SKT (81.5 ± 1.7 years). Median kidney biopsy score was 3.44 ± 0.6 in SKT group and 3.96 ± 0.9 for right kidney and 4.55 ± 1.7 for left kidney in DKT cohort. A statistically significant difference in serum creatinine at discharge was observed between the two groups (210 ± 88 μmol/L for SKT and 164 ± 84 μmol/L for DKT). Five-year graft survival showed a significant better survival in DKT cohort (see Fig.1).

**Conclusions:** Histological and clinical selection for the allocation of kidneys from octogenarian donors can safely increase transplant activity with acceptable long-term outcome. Our preliminary results demonstrate that grafts recovered from donors older than 80 years perform better when used for DKT. Therefore, data suggest that DKT is an appropriate strategy to address the growing graft shortage.

**Figure 1:** Graft Survival of Kidneys from Donors ≥ 80 Years

![Graft Survival](image)

**Table 1. Donor and Recipient Data**

<table>
<thead>
<tr>
<th>Donors</th>
<th>SKT (n=31)</th>
<th>DKT (n=69)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>81.8±1.7</td>
<td>83.8±2.5</td>
<td>&lt;0.001</td>
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<tr>
<td>Cause of death, %</td>
<td></td>
<td></td>
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<tr>
<td>Cerebrovascular disease</td>
<td>28 (90)</td>
<td>60 (87)</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>2 (6.5)</td>
<td>8 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Post anoxic injury</td>
<td>1 (3.5)</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Renal function, %</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>S-Creatinine &lt; 1.5 mg/dL</td>
<td>29 (94)</td>
<td>61 (88)</td>
<td></td>
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<tr>
<td>S-Creatinine 1.5-2.5 mg/dL</td>
<td>2 (6)</td>
<td>8 (12)</td>
<td></td>
</tr>
<tr>
<td>Kapsinski Score, mean ± SD</td>
<td>3.44 ±0.6</td>
<td>3.96±0.9</td>
<td>1.45±5.17</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recipients</th>
<th>SKT (n=31)</th>
<th>DKT (n=69)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age at transplant, mean ± SD</td>
<td>65.7±6.4</td>
<td>65.1±6.5</td>
<td>0.84</td>
</tr>
<tr>
<td>S-Creatinine at discharge, mean ± SD</td>
<td>210±498</td>
<td>163±784</td>
<td>0.008</td>
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<tr>
<td>DGF, %</td>
<td>5 (16)</td>
<td>7 (10)</td>
<td>0.17</td>
</tr>
<tr>
<td>Acute rejection, %</td>
<td>1 (3)</td>
<td>3 (4)</td>
<td>0.79</td>
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<tr>
<td>Graft loss, %</td>
<td>0</td>
<td>2 (2.5)</td>
<td>0.92</td>
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</table>

**Kidney machine perfusion and ischemia reperfusion injury**

**FG7_1 TRANSPLANT OUTCOMES AFTER EXPOSURE OF DECEASED KIDNEY DONORS TO CONTRAST MEDIUM**

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**Background:** In 18% of deceased donors in The Netherlands a CT scan is performed during the screenings process, using intravenous contrast medium (IV-CM) for enhancement. Potential heart donors are evaluated with Coronary Angiography (CAG) using intra-arterial CM (IA-CM). Administration of IV- and IA-CM has been associated with acute kidney injury, but the effect of CM exposure of a deceased organ donor on kidney transplant outcomes has been poorly studied. This study aims to investigate the effect of administration of IA- and IV-CM in deceased kidney donors on transplant outcome after kidney transplantation.

**Methods:** All deceased kidney donors in the Netherlands between 2011-2021 were retrospectively reviewed on CM exposure. Donor characteristics and follow-up data on kidney recipients were obtained from the Eurotransplant and Dutch Transplantation Foundation Database respectively. Multivariable analyses were performed to assess associations between CM exposure and Delayed graft function (DFG) / death-censored graft survival. Linear mixed models were used to assess difference in mean eGFR values in recipients 1 to 8 years after transplantation.

**Results:** In total 2177 deceased kidney donors and 3638 corresponding kidney graft recipients were included. Twenty-four percent of the donors (n=520) were exposed to CM, corresponding to 23% of recipients (n=832) included. Delayed graft function (DFG) was observed in 36% (n=1321) and primary non function in 3% (n=106) of recipients. Analysing DGF rates separately for Donation after Brain death (DBD) and Donation after Circulatory Death (DCD) donors showed no significant effect of CM exposure (p=0.15 and p= 0.80 respectively). In multivariable analyses CM administration was not significantly associated with a higher DGF risk (OR 1.06; 95% CI 0.86-1.36, p=0.63), nor a significant predictor for death-censored graft failure (HR 1.01; 95% CI 0.77-1.33, p=0.93).

**Conclusion:** This study indicates that CM administration in DBD and DCD donors has no negative effect on early and long-term kidney graft function and is safe to use during the organ donor evaluation process.

**Figure 1:** Death-censored graft survival according to CM exposure of the donor

![Death-censored graft survival](image)
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Kidney machine perfusion and ischemia reperfusion injury

THE SETUP USED FOR EX VIVO RENAL NORMOTHERMIC PERFUSION INFLUENCES A KIDNEY’S BEHAVIOR ON THE MACHINE

Veerle A. Lantinga1, Asel Arykbaeva1, Nora Spraakman1, Elwin Blom1, Tobias Huijink1, Dorotyta de Vries1, Ian Alwayn2, Henri Leuvenink1, Cyril Moers1, Leonie van Leeuwen1
1UMCG, University Medical Center Groningen, Groningen, Netherlands, 2LUMC, Leiden University Medical Center, Leiden, Netherlands

Background: Along with a growing interest in renal normothermic machine perfusion (NMP) came an increase in the number of different clinically available perfusion devices. While all perfusion systems have the same aim, there are significant differences in the circuit, pumps, sensors, and software. Also, the NMP protocols used in combination with these devices vary. Therefore, we evaluated three different NMP protocols using porcine and human kidneys, hereby assessing two clinically approved perfusion devices.

Methods: Twelve porcine kidneys were subjected to 30 min of warm ischemia, 24 h of static cold storage, and subsequently exposed to 6 h of NMP. Four kidneys were perfused on the Kidney Assist (KA, XVIVO) with a mean arterial pressure (MAP) of 75 mmHg (Figure 1A-B). Four kidneys were perfused on the KA device incorporating several workaround improvements to the standard protocol and a MAP of 85 mmHg (KA+WA, Figure 1A-B). Four kidneys were perfused with the Perlife perfusion device (PL, Aferetica, Figure 1C-D). To validate findings, six human discarded kidneys from DCD donors were perfused on the KA (KA-h) or KA+WA (KA+WA-h) (n=3 per group).

Results: Kidneys of the PL group reached the device’s upper flow limit of 500 ml/min after 1 h of NMP and were consequently pumped with a significantly lower pressure compared to KA and KA+WA (p<0.0001). The arterial pO2 was significantly lower in the PL group (p<0.001). Tissue ATP levels, oxygen delivery, and lower levels of injury markers in the perfusate compared to the KA-h group.

Conclusions: This study shows that differences in NMP protocols and machines can have a relevant influence on perfusion characteristics and kidney function on the pump, which should therefore be interpreted with caution. There is a need to develop optimized consensus protocols for renal NMP to obtain comparable results between centers.


Fig. 1: Time of day of reperfusion

NORMOTHERMIC KIDNEY PERFUSION PHASE I – A CLINICAL TRIAL OF UP TO 24-HOUR NORMOTHERMIC MACHINE PERFUSION PRIOR TO TRANSPLANTATION

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Background: Normothermic Machine Perfusion of the Kidney (NMP-K) prior to transplant offers multiple potential domains of benefit, including reduction of preservation injury, organ assessment, optimisation of logistics, and as a platform for delivery of therapeutics. Previous clinical reports have been limited to a short duration of perfusion, and anatomically suitable organs. Normothermic Kidney Perfusion Phase 1 (NKP1) is a single centre trial investigating the safety and feasibility of prolonged duration NMP-K following static cold storage, using an automated mobile system (OrganOx, UK) designed for 24-h perfusion.

Methods: All kidneys accepted for transplantation in Oxford were potentially eligible. Perfusion duration was determined primarily by logistical considerations, with maximum permissible perfusion times increasing from 6 to 12 to 24 h in consecutive study phases (each n=12). Kidneys were prepared, cannulated, and then perfused at 37°C with red cell based perfusate, and urine recirculation. Immediately prior to implantation, the kidney was removed from the device and cold-flushed. The primary endpoint was 30-day graft survival. Comparison was made to historical controls with similar risk profiles and cold ischaemia times, ratio 1:2, selected by a pre-defined matching algorithm.

Results: 36 patients were transplanted with kidneys that underwent NMP-K. Minimum normothermic perfusion time was 1h, maximum 23h22. One kidney was discarded due to markedly abnormal perfusion parameters. 9/36 perfused kidneys had multiple renal arteries; in one case a vascular injury sustained at retrieval was identified and repaired following ex-vivo reperfusion. All transplanted grafts met the primary endpoint. Functional outcomes were similar to those of the control cohort, despite the much longer overall preservation time (Table 1). This facilitated a shift towards daytime operating (Fig. 1). There were no adverse events related to the technique.

Conclusions: Prolonged duration NMP-K is safe and feasible. In a real-world setting it enables a reduction in cold ischaemia time as well as a prolongation of total preservation time, thereby facilitating daytime operating. The platform also provides opportunities for assessment and treatment of deceased donor kidneys prior to transplantation.

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Kidney machine perfusion and ischemia reperfusion injury

MAGNETIC RESONANCE IMAGING ASSESSMENT OF FUNCTIONAL DIFFERENCES BETWEEN KIDNEYS IN VIVO AND DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION

Tim L. Hamelink1,2, Baran Ogurlu1, Carolina Campos Pamplona1, Veerle A. Lantinge1, Sigrid Bennedsengaard2, Johannes Castelein2, Haiyun Qi1, Marco Eijken2, Bente Jespersen2, Henri Leuvenink1, Esben Hanssen2, Christoffer Laustsen2, Steffen Ringgaard1, Ronald Borra1, Anna Krarup Keller1, Cyril Moers1
1University Medical Center Groningen, Department of Surgery - Organ Donation & Transplantation, Groningen, Netherlands, 2Aarhus University Hospital, Aarhus, Denmark

Background: Normothermic machine perfusion (NMP) is a promising method for pre-transplant donor kidney quality assessment. Although its potential is increasingly being recognized, it remains unclear which NMP parameters convey information about graft viability. This is largely due to our limited understanding of ex vivo organ physiology. To increase our knowledge about organ biology during NMP, we combined non-invasive functional magnetic resonance imaging (MRI) with renal normothermic perfusion in a porcine model. This project aimed to determine the differences between in vivo and ex vivo regional renal tissue oxygenation and diffusion patterns.

Methods: Pigs (n=30) were anesthetized and brought into a clinical-grade MRI. In vivo MRI scans were performed to provide information about regional tissue oxygenation using T2* mapping and water diffusion patterns using diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) maps. Subsequently, a bilateral nephrectomy was performed to retrieve kidney pairs, which were randomized to sustain either minimal warm ischemia (WI) or 75 min WI. After WI and 4-5 hours of cold preservation, both kidneys were connected to an MRI-compatible NMP circuit and perfused for 6 hours. Hourly, T2* maps and DWI images were acquired from both kidneys. Regions of interest were drawn on both regions. Differences in the cortex and medulla to calculate the mean signal intensity. DWI images were acquired from both kidneys. Regions of interest were drawn on both kidneys. Differences in the cortex and medulla were calculated to determine the mean signal intensity.

Results: In vivo mean T2* corticomedullar (CM) ratio (1.71±0.21) differed significantly from the mean ex vivo CM ratio of the minimal WI group (0.60±0.13, P < 0.0001) and the 75 min WI group (0.62±0.16, P < 0.0001). In vivo cortical ADC values (2.1±0.15 x 10^{-5} mm²/s) were significantly higher compared to the minimal WI group (1.46±0.25, P < 0.0001) and the 75 minutes WI group (1.76±0.09, P = 0.002).

Conclusions: This study provides the first evidence for the existence of remarkable differences in regional tissue oxygenation and diffusion patterns between a normal physiological in vivo environment and during ex vivo normothermic machine perfusion. These findings highlight that renal function during ex vivo perfusion is very different from what we are used to in our in vivo reference frame. Therefore, organ viability assessment during NMP should likely consider other parameters than those functional markers that are common in vivo.

KIDNEY TRANSCRIPTOME VARIES BETWEEN DONOR TYPES, WITH A DIFFERENTIAL RESPONSE TO ISCHEMIC PRECONDITIONING

Tiago Pinto Coelho1, Pauline Ericpam12, Margaux Navez1, Chenyu Zhang1, Laurence Poma2, Olivier Detry1-4, Francois Jouret2
1GIGA Cardiovascular Sciences - Liège University, Laboratory of Translational Research in Nephrology, Liège, Belgium, 2CHU Liège, Nephrology, Liège, Belgium, 3CHU Liège, Abdominal surgery and Transplantation, Liège, Belgium, 4GIGA Cardiovascular Sciences - Liège University, CREDEC, Liège, Belgium

Background: The prevention/attenuation of graft ischemic injury is a challenge in kidney transplantation. We developed two rat models to investigate the impact of mesenchymal stromal cells (MSCs) in the ischemic preconditioning of kidneys from Donors after Circulatory Death (DCD) and Donors after Brain Death (DBD).

Methods: Under general anesthesia, rats underwent iv injection of saline (S-groups) or 1.5 10^7 MSCs (MSC-groups) followed by either DBD (6hr of brain death) or DCD (6hr of anesthesia and 20min warm ischemia) models, resulting in 4 groups (S-DBD, S-DCD, MSC-DBD, MSC-DCD). Kidneys were then procured after IGL1 flush. One kidney was directly fixed and the other one immersed for 14 hours in IGL1 at 4°C. Serum samples were collected before treatment (baseline) and at the time of kidney collection. Urine samples were collected by bladder puncture at the time of kidney collection. Renal function was evaluated. Kidney histology was assessed by PAS staining and KIM1 immunostaining. Total RNA was extracted from S-DCD vs S-DBD kidneys for RNAseq.

Results: BUN was increased after 6h of anesthesia (DCD) or brain death (DBD) (p<0.01). SCR increased in both S-DBD and MSC-DBD but was lower in MSC-treated rats (MSC-DBD 0.5±0.2mg/dL vs S-DBD 0.7±0.1mg/dL; p=0.037). Urinary KIM1 was lower in MSC-treated DBD (S-DBD 10.9±4.5 vs MSC-DBD 8.1±3.5; p=0.03). Acute Tubular Injury (ATI) and KIM1 expression were higher in DCD than in S-DBD (ATI: S-DBD 65±24 % of surface vs S-DCD 39±27 % of surface [p=0.03] and KIM1: S-DBD 0.39±0.24 % of surface vs S-DCD 0.10±0.09 % of surface [p<0.002]). In MSC groups, there was no difference in both ATI extension and KIM1 expression. There was no difference in KIM1 expression between S-DBD and S-DCD groups. RNAseq showed that proinflammatory and proapoptotic pathways were upregulated in DBD, whereas transmembrane transport and metabolic pathways were downregulated, compared to DCD.

Conclusions: The RNA profiles of the kidneys are different upon donor types, which may impact the response to MSC-based ischemic preconditioning.
Background: Normothermic Machine Perfusion (NMP) enables assessment and reconditioning during the preservation period due to full metabolic activity. However, knowledge of mitochondrial metabolism and how to sustain this during NMP is lacking. Oxygen and nutrients are the two important sources for aerobic metabolism in mitochondria. It is known that oxygen is needed during NMP, but not much is known about the need for nutrients. Therefore, this study aims to investigate the effect of the presence or absence of nutrients in the perfusate during NMP on mitochondrial function.

Methods: Porcine kidneys were procured at a local slaughterhouse. After 30 minutes of warm ischemia the kidneys were perfused with oxygenated hypothermic machine for 24 hours. Thereafter, kidneys were normothermically perfused for 6 hours, during which they were either fed (n=6) with glucose, fatty acids and glutamine, or fasted (n=6) without any nutrients. Every hour biopsies were taken to assess mitochondrial respiration, using the Oxygraph-2k (figure 1A). Moreover, metabolites and adenine triphosphate (ATP) were measured in tissue, perfusate and urine samples.

Results: No differences in mitochondrial function, reflected by their respiration, were observed between the groups (figure 1B). However, oxygen consumption of the whole kidney was higher during NMP in the fed group compared to the fasted group (figure 1C). During the first two hours of NMP the fasted kidneys were able to produce ATP from their remaining sources, as reflected to the fasted group. During the first two hours of NMP the fasted (figure 1D). Furthermore, a trend towards higher ATP levels after 6 hours of NMP was seen in the fed group (figure 1D). Kidney function, reflected by the fractional sodium excretion (NA) was similar in the different groups. Transplanted vessels reacted similar to the vessel wall in any of the conditions. The maximal wall tension after activation with a saturating concentration of the physiological agonist noradrenaline (NA) was similar in the different groups. Transplanted vessels reacted similar to normal which confirms expected effect of ex-vivo reconditioning process.

Conclusions: No major differences in the passive properties of the vessels was observer which may exclude significant changes in the biomechanics of the vessel wall in any of the conditions. The maximal wall tension after activation with a saturating concentration of the physiological agonist noradrenaline (NA) was similar in the different groups. Transplanted vessels reacted similar to normal which confirms expected effect of ex-vivo reconditioning process.
FOCUS GROUPS

REAL-TIME ASSESSMENT OF KIDNEY ALLOGRAFTS DURING HOPE USING FLAVIN MONONUCLEOTIDE (FMN) - A PRECLINICAL STUDY

Richard Sousa Da Silva1, Tom Darius1, Leandro Mancina2, Janina Eden2, Kendra Werner3, Ahmed Ghoneima3, Adam Barlow3, Pierre-Alain Clavien4, Philipp Dutkowski5, Philipp Kron5

1University Hospital Zurich, Surgery and Transplantation, Zurich, Switzerland, 2University Clinics Saint Luc, Brussels, Belgium, 3University Hospital Zurich, Zurich, Switzerland, 4St. James’s University Hospital, Leeds, United Kingdom, 5University Hospital Zurich, Zürich, Switzerland

Background: The gap between available donor grafts and patients on the waiting lists is constantly growing, leading to an increased utilization of high-risk kidney grafts. The use of these organs requires new strategies of organ optimization and assessment before transplantation. Hypothermic machine perfusion (HMP) is standard for kidneys obtained from donation after circulatory death (DCD), whereas evidence for additional oxygenation to HMP is still very limited and an objective assessment of HMP-perfused kidneys is lacking. This study aims to determine whether flavin mononucleotide (FMN) is a feasible and suitable marker for the assessment of kidney injury.

Methods: In a porcine model, the feasibility of assessing DCD kidney grafts during hypothermic oxygen perfusion (HOPE) was explored. A DCD group with warm ischemia times (WIT) of 30 and 60 minutes, mimicking a clinically relevant scenario, and a DBD group (donation after brain death) as control (n=4). Kidneys were subjected to two hours of static cold storage (SCS) followed by two hours of end-ischemic HOPE with real-time FMN measurement. FMN values were then related to initial ischemic damage.

Results: We demonstrate, first, feasibility of FMN measurement in perfused kidneys, and secondly its correlation with the WIT. Accordingly, perfusate FMN was significantly higher in the 60-minute WIT group (n=4) compared with the 30-minute WIT group (n=4) and DBD group (n=4). FMN release also correlated with DAMP signaling. Finally, ATP replenishment was best in DBD kidneys, followed by 30-minute WIT (n=4) and DBD group (n=4). FMN release also correlated with the WIT. Accordingly, perfusate FMN values were then related to initial ischemic damage.

Conclusions: This study proves feasibility of FMN measurement in kidneys during HOPE. In addition, we reveal a correlation between FMN quantification and pre-existing kidney injury. Based on this, real-time FMN measurement during HOPE may be an objective assessment tool in the near future to accept high-risk kidneys for transplantation while minimizing post-transplant dysfunction.

USEFULNESS OF LIVER VOLUMETRY BASED ON HEPATIC VENOUS TERRITORY AS PREOPERATIVE EVALUATION FOR LIVING DONOR LIVER TRANSPLANTATION

Woo Kyoung Jeong1
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Background: To evaluate whether volumetry based on middle hepatic venous (MHV) territory is useful as a preoperative examination to select patients who require a interposition venous graft (IVG) replacing a MHV in right living donor liver transplantation (LDLT). Methods: This retrospective study was conducted with 79 donors and recipients. Volumetry of MHV territories was performed by using a 3-D volumetric software (Hepatic VCAR; GE Healthcare). If the MHV territory was more than 30% of total volume of the graft, IVG was recommended. The subject was classified into four groups. Group 1 was the patients whose MHV territory was less than 30% in the RL, so IVG was not connected; group 2 was the patients whose MHV territory was less than 30%, but IVG was connected by surgeon’s decision; groups 3 was the patients whose MHVT of MHV was more than 30%, but IVG was not connected or closed by thrombosis; and group 4 were patients whose MHV territory was more than 30%, and IVG was connected. To explore the usefulness of this technique, the volume changes of MHV region were examined before and after surgery. Graft regeneration ratio (GRR) was calculated according to the following formula. [GRR (%) = (volume after surgery - volume before surgery) / volume before surgery] The GRRs were compared among the patients group by using Kruskal-Wallis test. Given that graft-to-recipient weight ratio (GRRWR) is an important factor related to regeneration, the analyses were conducted by dividing <1.0 of GRRWR or other.

Results: The number of patients in each group was as follows: 21 in group 1; 17 in group 2; 7 in group 3; and 34 in group 4. In the patients whose GRRWR was ≥1.0, the GRR of group 3 was significantly lower than that of group 4 (21.5% vs. -2.7% p = 0.041), in case of <1.0 of GRRWR, the GRR of group 3 was 3.0%, and that of group 4 was 24.4% (p = 0.052). In contrast, the GRR in group 1 was not different from that of group 2 (9.5% vs. 8.7% in ≥1.0 of GRRWR; 24.9% vs. 2.2% in <1 of GRRWR, all p > 0.05). Conclusions: Volumetry based on MHV territory is useful to determine whether IVG is needed to ensure regeneration of the MHV territory. Especially, in patients of which MHV territory was >30% and the GRRWR was less than 1.0, the connectivity of IVG was crucial to graft regeneration.

RISK FACTORS ASSOCIATED WITH SURGICAL MORBIDITIES OF LAPAROSCOPICdonor liver donors

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Background: This study analyzed incidence and risk factors for surgical morbidities of laparoscopic living donors. Although laparoscopic living donor program has been safely established in leading centers, donor morbidities have not been sufficiently discussed.

Method: Laparoscopic living donors operated during May 2013 to June 2022 were reviewed. Donors’ complications were reviewed, and factors related to bile leakage and biliary stricture were analyzed using multivariable logistic regression method.

Results: A total of 636 donors underwent laparoscopic living donor hepatectomy. Open conversion rate was 1.6%. Thirty-day complication rate was 16.8%. (n=107) Grade IIa and IIb complication occurred in 4.4% (n=28) and 1.9% (n=12), respectively. The most common complication was bleeding (n=38, 6.0%). Fourteen donors (2.2%) required reoperation. Portal vein stricture, bile leakage and biliary stricture occurred in 0.6% (n=4), 3.3% (n=21), and 1.6% (n=10) of cases. Readmission rate and reoperation rate was 5.2% (n=33) and 2.2% (n=14), respectively. Risk factors related to bile leakage were two hepatic arteries in liver graft (OR=13.836, CI=4.092-46.789, P<0.001), division-free margin <5mm from main duct (OR=2.624, CI=0.030-6.686, P=0.043) and estimated blood loss during operation (OR=1.002, CI=1.001-1.003, P=0.008) while Pringle maneuver (OR=0.300, CI=0.110-0.817, P=0.018) was protective for leakage. Regarding biliary stricture, only bile leakage was the only significant factor (OR=11.902, CI=2.773-51.083, P<0.001).

Conclusion: Laparoscopic living donor showed excellent safety for majority of the donors and critical complications were resolved with proper management. To minimize bile leakage, cautious surgical manipulation should be made on donors with complex hilar anatomy.
FOCUS GROUPS
Living donation

Background: Live donor liver transplantation (LDLT) is established as a complementary method to the scarceren of deceased donors. Many technical improvements were developed to expand the donor pool. But 22% of donor candidates were rejected due to various causes, small remnant liver volume or small graft size for recipient were most common. To get sufficient graft volume and donor safety, we developed dual grafts LDLT, using two grafts from different donors.

Methods: From Mar. 2000 to Dec. 2018, we performed 593 dual graft LDLTs out of 5121 cases of total LDLT (11.5% of LDLTs). 9% of donor candidates were selected for dual donor LDLT (RL 51.5%, LL 2%, complete rejection 39.4%). Most common combination of grafts were left and left graft, due to small remnant liver volume in donor (70.5%). Right and left graft were used in 29.5%. Various grafts, ABOI donor, split graft from deceased donor, and from donor exchange program, were included in this graft combinations.

Results: Mean GRWR from dual grafts was 1.03 similar with single right lobe LDLT. Most common trial of graft combinations were left and left graft, due to small remnant liver volume in donor (70.5%). Right and left graft were used in 29.5%. Various grafts, ABOI donor, split graft from deceased donor, and from donor exchange program, were included in this graft combinations.

Conclusions: Dual graft LDLT has a role in avoiding small-for-size syndrome.

REVOLUTIONIZING LIVER TRANSPLANT: THE JOURNEY FROM LAPAROSCOPIC LDLT TO ROBOTIC LDLT

Kwang-Woong Lee1, Sola Lee1, Jeong-Moo Lee1, Jiyoung Kim1, Hyun Hwa Choi1, Jae-Yoon Kim1, Jaewon Lee1, Suk Kyun Hong1, Youngrok Choi1, Nam-Joon Yi1, Kyung-Suk Suh1
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Background: Minimally invasive surgery (MIS) is becoming increasingly popular in various surgical fields. Within the field of living donor liver transplantation (LDLT), MIS has been historically thought challenging due to worries regarding excessive bleeding and complexity. Hybrid techniques of LDLT have been documented, showing MIS may be possible with the right patient selection. We described various trials, errors, and established techniques of minimally invasive LDLT. We compared each method's differences, technical merits, and drawbacks.

Methods: From June 2020 to August 2021 we performed 14 minimal invasive LDLTs, including robotic hybrid LT. We attempted each procedure in a stepwise manner and, after completing explant by laparoscopy then attempted engraftment through laparoscopy or robotic surgery.

Results: The recipients' average age was 54.1 ± 9.4 years. All underwent modified multi-graft liver grafts; 7 (half) were Child-Pugh A, another 4 were Child-Pugh B, and 3 were Child-Pugh C with GRWR of 10.8 ± 3.7 and GRWR of 11.3 ± 0.33. Total operative time was 471.9 ± 216.2 minutes; explant time 119 ± 46.6 minutes; engraftment time 201 ± 93.3 minutes. Early complication rate 26.8%; late complication rate 14.3%. Average ICU stay 3.9 ± 0.6 days; total hospital stay after surgery 11.5 ± 4.1 days. 12 underwent engraftment using an upper midline incision after laparoscopic explant. Successful right and left mobilization were achieved in the first 4 cases, with one case requiring open conversion due to bleeding. Subsequently, successful totally laparoscopic mobilization and hilar dissection were performed in 2 cases. The next 3 cases were successful in totally laparoscopic explant, and engraftment was achieved using the upper-midline incision. The 10th case was the first to attempt robotic anastomosis, and the 11th case was the first to successfully perform robotic engraftment. The last 2 cases underwent laparoscopic explant followed by Pfannenstiel incision and robotic anastomosis.

Conclusions: MIS LDLT requires patient selection and offers smaller wounds and faster recovery than open surgery. It can be performed via laparoscopic and robotic surgery, with precautions and initial experiences for each step described. This perspective provides a reference for future transplant surgeons to quickly reach the learning curve.

POST-LIVER TRANSPLANT LONG-TERM SURVIVAL IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE: LIVING-DONOR VERSUS DECEASED-DONOR LIVER TRANSPLANTATION

Sang-Bin Han1, Hye-Mee Kwon1, Kyung-Sun Kim1, Young-Jin Moon1, In-Gu Jun1, Jun-Gol Song1, Deok-Bog Moon1, Sung-Gyu Lee1, Gyu-Sam Hwang1
1Asan Medical Center, Department of anesthesiology and pain medicine, Seoul, South Korea, 2Asan Medical Center, Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Seoul, South Korea

Background: Liver transplantation (LT) is a life-saving treatment for patients with acute-on-chronic liver failure (ACLF). In patients with ACLF, early LT is crucial to ensure the success of LT, therefore, the decision to LT and donor organ should be taken rapidly. We compared post-LT long-term survival in patients with ACLF: living-donor versus deceased-donor LT.

Methods: Of 3686 LT recipients between 2008 and 2019, consecutive 854 patients who met the criteria for ACLF (363 ACLF-1, 276 ACLF-2, 215 ACLF-3 grade) were retrospectively evaluated in a large volume LT center. In patients with ACLF, urgent living-donor LT program within 24-48 hours was expedited in carefully selected patients, whenever timely allocation of deceased-donor organ was not available. Mortality data was collected and followed up to February 2020 (i.e., at least 1 years and up to 12 years since the date of LT) from the national organ registry database and Kaplan-Meier cumulative survival curves and log-rank test were evaluated.

Results: Living-donor LT was performed in 483 (56.6%) of patients with ACLF: 261 (71.9%) of ACLF-1, 147 (53.3%) of ACLF-2, 75 (34.9%) of ACLF-3. Living-donor LT showed better overall survival rates compared to deceased-donor LT (P<0.001). When patients were grouped with ALCF grades, living-donor LT showed better survival outcomes in patients with ALCF grade 1 and 2 (P=0.025, P=0.004, respectively), however, in those with ALCF grade 3, the overall survival outcome was numerically higher in living-donor LT but was not statistically significant compared with deceased-donor LT (72% vs. 67.9% at 1 year; 67.5% 56.7% at 5 year; log-rank, P = 0.21).

Conclusions: Whenever timely allocation of deceased-donor organ was not available, urgent living-donor LT program needs to be expedited to improve survival in patients with ACLF.
FOCUS GROUPS

Living donation

**EFFECTIVENESS OF A DESENSITIZATION PROTOCOL ON ANTIBODY-MEDIATED REJECTION IN LIVING DONOR LIVER TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY**

Jiyoon Kim¹, YoungRok Choi², Kyung Chul Yoon¹,², Jeong-Moo Lee¹,², Su Young Hong¹,², Hye-Yeon Cho¹,², Seong Mi Yang¹,², Suk Kyun Hong¹,², Hae Won Lee¹,², Nam-Joon Yi¹,², Kwang-Woong Lee¹,², Kyung-Suk Suh¹,²

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**Background:** Graft failure associated with donor specific antibody (DSA) is rare but consistent in living donor liver transplant (LDLT). This study aims to analyze the outcomes of desensitization protocol according to the preoperative antibody mediate rejection (AMR) risk.

**Methods:** We reviewed 998 cases of LDLT between January 1, 2012 and December 31, 2012 retrospectively. The desensitization treatment was protocolized for three different risk groups based on crossmatching(CDC), flow cytometry cross-matching(FCMX), and single antigen DSA test results: Rituximab + plasma pheresis for high risk (all positive), Rituximab only for intermediate risk (CBC, FCMX,DSA+), no treatment for low risk (only DSA+). The graft and patient survival of those retrospective cohort were analyzed.

**Results:** From 640 ABO compatible cases, there were 292(45.6%) and 348(54%) cases each before and after desensitization treatment was protocolized, with 2(0.7%) and 4(1.1%) incidents of AMR respectively. From 69 cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69). Among cases with DSA test results, 20(29.0%) cases received Rituximab + plasma pheresis, 17(24.6%) cases received Rituximab only, and 32(46.4%) cases received no treatment. Cases with higher AMR risk increased after protocol initiation(p<0.001), while AMR risk did not show any significant difference(p=0.69).

**Conclusions:** AMR incidence remaining relatively similar despite the significant increase in number of high-risk group recipients post protocol initiation, suggests that the desensitization treatment might be effective. Studies including larger number of cases are needed to prove the necessity of desensitization protocol in clinical settings.

<table>
<thead>
<tr>
<th>AMR level by Crossmatching</th>
<th>DSA level</th>
<th>AMR positive / total cases</th>
<th>Recurrence Free Survival according to Radiology vs Histology</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>High</td>
<td>2 / 20</td>
<td><img src="image" alt="Recurrence Free Survival according to Radiology vs Histology" /></td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>1 / 17</td>
<td></td>
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<tr>
<td></td>
<td>Low</td>
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<td>No risk</td>
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</tr>
<tr>
<td></td>
<td>Total</td>
<td>3 / 37</td>
<td></td>
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</tbody>
</table>

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**ONCOLOGIC RESULTS AFTER TEN YEARS OF SYSTEMATIC APPLICATION OF LOCO REGIONAL THERAPIES FOR HEPATOCELLULAR CARCINOMA**

Enrico Prosperi¹, Gerti Dajti¹, Chiara Bonatti¹, Francesca Caputo¹, Guido Fallani¹, Giorgia Radi¹, Alberto Stocco¹, Maria Chiara Vaccaro¹, Valentina Bertuzzo¹, Andrea Laurenzi¹, Lorenzo Maroni¹, Federica Odaldi¹, Matteo Serenati¹, Chiara Zanfi¹, Massimo Del Gaudio¹, Maria Cristina Morelli¹, Matteo Ravaioili¹, Matteo Cescon¹

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**Background:** after the definition of Milan Criteria (MC) the effort to find patients who, despite being MC Out (MO), could benefit from LT without significant effect on Recurrence Free Survival (RFS) led to the development of Downstaging (DS). The main objective of the study is to compare the Recurrence Free Survival (RFS) of Milan IN (MI) and Milan Out within the DS group at the last pre-LT Radiological Imaging (RI). The secondary aim is to compare the RFS of patients In/Out Milan stratified by last pre-LT RI or explant pathology (EP).

**Methods:** a retrospective analysis of consecutive liver recipients after LRT for HCC between 2011 and 2020. LRT included Liver Resection, Ablation, Trans-Arterial Chemoembolization or Radioembolization. Considering the features of HCC at the diagnosis and at the last pre-LT RI, we identified 3 groups: MI at diagnosis and at last pre-LT RI (Group A), MI at diagnosis but MI at last pre-LT RI (Group B) and MO at pre-LT RI (Group C). We compared the RFS of the groups using Cox regression and multivariable logistic regression models. We also compared the RFS of patients In/Out MC at the pre-LT RI with those In/Out MC at EP.

**Results:** We included 293 patients, of which 191 (65.19%) were in Group A, 69 (23.55%) in Group B and 33 (11.26%) in Group C. The median waiting time in the list was 9.5 months (IQR 4.4 - 17.3). No difference between groups regarding LRT in type and number was observed. However, patients in Group B received more frequent multimodal LRT with respect to Group A but without reaching statistical significance (p=0.062). The median time between the last imaging and LT was 2.39 months (IQR 1.2 - 4.4) and the follow-up (FU) after LT was 55.3 months (IQR 30.1 - 72.6). After COX-regression analysis, alpha-fetoprotein (AFP) at diagnosis (p<0.001), the need for multiple types of LRT (p=0.024), being MO at last imaging (p=0.014) and AFP levels (p=0.008) at LT resulted significantly associated with RFS. Conversely, initial MC status at diagnosis and at last pre-LT RI (Group A), MO at last pre-LT RI (Group B) and MO at pre-LT RI (Group C). We compared the RFS of the groups using Cox regression and multivariable logistic regression models. We also compared the RFS of patients In/Out MC at the pre-LT RI with those In/Out MC at EP.

**Conclusions:** Patients who underwent successful DS at LT have similar RFS to those always within the MC. Thus, LRT plays an important role in increasing eligible patients for LT and maintaining similar long-term outcomes.
LAPAROSCOPIC ABLATION AND SALVAGE TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

Nicola Canitano1, Alessandro Vitale1, Enrico Gringeri1, Francesco D’Amico1, Domenico Bassi1, Francesco Enrico D’Amico1, Andrea Marchini1, Mattia Ballo1, Marco Broi1se1, Sara Lazzari1, Ilaria Billato1, Umberto Cillo1
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Background: No studies evaluate a strategy based on laparoscopic microwave ablation followed by salvage liver transplantation (LT) for patients with hepatocellular carcinoma (HCC).

Methods: Between 2014 and 2020, 512 HCC patients were treated with laparoscopic ablation, followed by transplantation in case of a transplantable recurrence or liver failure. All patients enrolled were diagnosed as HCC within the Milan criteria, with Child A-B cirrhosis, and were judged unsuitable for liver resection or percutaneous ablation.

Results: Ablation was complete for 90% of nodules. No mortality occurred. Over a median follow-up of 51 months for survivors, 243 patients (47%) had new HCC recurrence or liver resection or percutaneous ablation.

Conclusions: First-line laparoscopic ablation followed by salvage LT achieves intention-to-treat survival figures similar to other radical therapies for HCC while limiting the number of grafts required.

LIVER TRANSPLANTATION FOR HCC BEYOND MILAN CRITERIA AFTER DOWN-STAGING WITH STEREOTACTIC RADIOTHERAPY OR TRANSARTERIAL RADIOEMBOLIZATION

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Background: Liver transplant (LT) is the first-line therapy (tx) for early HCC, but it can be offered also for HCC outside LT-criteria if successfully down-staged. According to Barcelona Clinic Liver Cancer (BCLC) staging system, transarterial chemoembolization (TACE) and systemic therapy (ST) are recommended for intermediate (BCLC B) and advanced HCC (BCLC C), respectively. We reported pre- and post-LT characteristics of pts undergoing stereotactic radiotherapy (SABR) or transarterial radioembolization (TARE) for Milan-out HCC.

Methods: pts transplanted from 01/01/2019 to 30/09/2022 after HCC down-staging from Milan out to MilanUp-to-7 in by SABR or TARE were enrolled. Follow-up (FU) was closed on 31/12/2022.

Results: In the study period 573 Lts were performed; 257 (44.9%) were affected by HCC and 15/257 (5.8%) pts fit our inclusion criteria. Median age 56 years, median biochemical MELD 9. All except 2 pts were Child A. 11 pts were BCLC-B and 4 pts BCLC-C (vascular invasion). Median baseline AFP 62 U/mL. 8 pts (53.3%) underwent TARE (unilobar infiltrative HCC/w portal trunk invasion) and 7 SABR (subgissonian or hypovascularized HCC). After a median of 8.9 [4-16] months 

Conclusions: 15 HCC pts (11 BCLC-B, 4 BCLC-C) underwent LT after an average time of 8.9 months from a successful down-staging with SABR or TARE. Fifteen out of 15 (33%) pts were still alive, 12 (80%) without recurrence. Pt #10 underwent TACE plus ST for HCC recurrence 1 year after LT and pt #12 adrenal metastasectomy (93.3%) were still alive, 12 (80%) without recurrence. Pt #10 underwent TACE plus ST for HCC recurrence 1 year after LT and pt #12 adrenal metastasectomy at 6 months; both underwent pre-LT TARE for HCC with portal invasion.

Our 15 HCC pts (11 BCLC-B, 4 BCLC-C) underwent LT after an average time of 8.9 months from a successful down-staging with SABR or TARE.
**FOCUS GROUPS**

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**EVALUATION OF A DELAYED LIVER TRANSPLANT STRATEGY FOR PATIENTS LISTED FOR HCC TREATED WITH RESECTION OR THERMO-ABLATION AS A BRIDGE TO LT**

Catherine Lamarque1,2, Lauriane Segaux1, Armand Abergel1, Philippe Bertrand1, Audrey Coill1, Flomena Continenti1, Thomas Decaens1, Sebastien Dharamcy1, Vincent Di Martin2, Jerome Dumortier3, Claire Francoz1, Jean Gugenheim2, Jean Hardwigsen2, Fabrice Muscari1, Sylvie Radenne1, Ephrem Salanne3, Thomas Uggen1, Jose Urcis Bedoya1, Corinne Antoine1, Vincent Leroy1, Nadia Oubaya2, Christophe Duvoieux1

1Henri Mondor University Hospital, Creteil, France, 2CHU Estaing, Clermond Ferrand, France, 3Hopitaux Universitaires Strasbourg, Strasbourg, France, 4Bordeaux Hospital, Bordeaux, France, 5AP-Hôpital Paul Brousse, Centre Hépato-Biliaire, Villejuif, France, 6APHP, Hôpital Pitié Salpêtrière, Sorbonne Université, Paris, Paris, France, 7HOPITAL ALBERT MICHALLOON, Grenoble, France, 8CHU Lille, Maroc en Baroeul, France, 9CHU Jean Minjoz, Besançon, France, 10HOPITAL EDOUARD ERRIOT, Lyon, France, 11Beaujon Centre Hépato-Biliaire, Villejuif, France, 12Department of Digestive Surgery, Archet Hospital, University of Nice-Sophia Antipolis, Nice, France, 13Aix Marseille University, Department of General Surgery and Liver Transplantation, Hôpital la Timone, Marseille, France, 14CHU ranguel, Toulouse, France, 15Hôpital de la croix-Rousse, Lyon, France, 16chou trousseau, Tours, France, 17Hôpital Ponthichailou, Rennes, France, 18CHU Montpellier, Montpellier, France, 19Agence de biomédecine, Saint Denis, France

**Background:** To maximize utility and prevent premature liver transplantation (LT), a delayed transplant strategy (DS) was adopted in France in 2015 in patients listed for any single hepatocellular carcinoma (HCC) treated with surgical resection (SR) or thermo-ablation (TA) during the waiting phase, postponing LT until recurrence. It is crucial to make sure that pre and post-LT outcomes of patients entering DS are not negatively impacted. The purpose of this study was to evaluate this DS.

**Methods:** Study population: patients listed for HCC in France between 2015 and 2018, with an AFP score ≤2. After data extraction from the national LT database, Cristal, 2025 patients were classified according to 6 groups: single tumor entering DS, single tumor not entering DS (NDS), multiple tumors (MT), other loco-regional therapies (LRT) with no DS, untreatable HCC (UH) and T1 tumors (T1).

**Results:** The patients' features are shown in the table. Pre-LT drop-out probabilities were 13, 18, 21, 22 and 25% in DS, LRT and MT, UH, NDS and T1, respectively (p = 0.05), significantly lower in DS and higher in T1. Post-LT 5-year survival and recurrence rates did not differ among groups.

**Conclusions:** The DELTAS HCC study shows that: a. DS can be considered in around 20% of HCC candidates (DS and NDS groups). b. DS in patients amenable to curative treatments pre-LT has no negative impact on pre- and post-LT outcomes. c. DS has the potential to redistribute organs to patients in more urgent need and can reasonably be pursued.

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**LIVER TRANSPLANTATION SURVIVAL BENEFIT OVER RESOLUTION IN PATIENTS WITH HIGH TUMOR LOAD: MULTICENTER RETROSPECTIVE ANALYSIS**

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1General Surgery 2-Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, Padua University Hospital, Padua, Italy, 2Department of Surgical, Oncological and Gastroenterological Sciences, University of Padua, Padua, Italy, 3Section for Transplantation Surgery, Department of Transplantation Medicine, University Hospital Tübingen, Tübingen, Germany, 4Department of Surgical and Transplantation, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium, 5Pôle de Chirurgie Expérimentale et Transplantation, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium, 6Department of Hepato-Pancreato-Biliary Surgery, Oslo University Hospital, Oslo, Norway, 7Liver Transplantation and Multivisceral Surgery Research Group, Division of Surgical and Transplantation Surgery, University of Milan, Milan, Italy, 8Experimental Transplantation and Multivisceral Surgery Research Group, Division of Surgical and Transplantation Surgery, University of Milan, Milan, Italy, 9Department of Surgery, Division of HPB Surgery, University Western Medical Center, London, Canada, 10Department of General Surgery, Cleveland Clinic, Digestive Disease Institute, Cleveland, United States, 11Department of General and Visceral and Transplant Surgery, University Hospital Tübingen, Tübingen, Germany, 12HPB Surgery, Hepatology and Liver Transplantation, Fondazione IRCCS Istituto Nazionale Tumori di Milano, Milan, Italy, 13Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, 14Experimental Transplantation and Multivisceral Surgery Research Group, Division of Surgical and Transplantation Surgery, University of Milan, Milan, Italy, 15Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus MC Cancer Institute, Rotterdam, Netherlands, 16The Intervention Center, Rikshospitalet, Oslo University Hospital, Oslo, Norway, 17Division of Abdominal Transplantation and Hepatobiliary Surgery, Department of Surgery, University of Rochester Medical Center, Rochester, United States, 18Liver Transplantation and Multivisceral Surgery Research Group, Division of Surgical and Transplantation Surgery, University of Milan, Milan, Italy, 19Department of General Surgery and Liver Transplantation Unit, Padua University Hospital, Padua, Italy.

**Background:** Liver resection (LR) is standard of care for technically resectable colorectal liver metastases (CRLM). High number of lesions and bilobar disease is, however, associated with high recurrence rates and low 5-year overall survival (OS). Liver transplantation (LT) may yield 5-year OS rates from 60%-80% for selected patients with unresectable CRLM. The role of technical resectability as a biological predictive factor is limited, since this is an anatomic-technical parameter displaying high variability among centres and individual surgeons. Hence, we tested the hypothesis that LT could offer better OS than resection in technically resectable patients with hepatic tumour load (HTL) above a threshold (i.e.: max number of lesions ≥ 8), in patients that otherwise satisfy the inclusion criteria for LT according to the SECA-I study.

**Methods:** LR performed at 10 tertiary HBP centres in CRLM patients between 2006 and 2021, were compared with LT for unresectable CRLM performed at 7 of the centres between 2006 and 2021. Exclusion criteria were age ≥ 71 years, weight loss > 10%, ECOG score > 1, standard contraindications to LT, other malignancy, liver first approach, neoadjuvant chemotherapy < 6 weeks, extra-hepatic tumour.

**Results:** 1144 CRLM patients underwent 1060 LR and 84 LT. 723 patients were eligible: 641 underwent LR and 82 LT. 5-year OS after LR and LT was 42.7% and 54.9% (p = 0.077). Patients were stratified according to favourable prognostic features for transplant (Tx-pos) by max diameter < 5.5 cm and CEA < 80 µg/L. Overall, 47 (57.3%) LT satisfied Tx-pos and 5-year OS after LT within and outside Tx-pos criteria was 61.7% and 38% (p = 0.006). High HTL were found in 96 (66.2%) LR and 50 (33.8%) LT patients with corresponding 5-year OS of 15.7% and 48.6% respectively (p < 0.001). In the cohort with Tx-pos features and HTL (i.e.: 46 (7.2%) LR and 27 (33%) LT) the 5-year OS after LR and LT was 21.7% and 49.2% (p = 0.015); disease-free survival (DFS) 17.8% and 17.9% (p = 0.593); and survival after recurrence (SAR) was 15.7% and 31% (p = 0.157). Table 1 shows different recurrence pattern after LR and LT. LT performed at 7 of the centres between 2006 and 2021. Exclusion criteria were age ≥ 71 years, weight loss > 10%, ECOG score > 1, standard contraindications to LT, other malignancy, liver first approach, neoadjuvant chemotherapy < 6 weeks, extra-hepatic tumour.

**Conclusions:** About 7% of liver resected CRLM patients have high tumor load and favourable prognostic criteria for LT. This selected group could possibly obtain better survival outcomes with LT compared to standard of care LR.

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**Table 1. Recurrence pattern after LR and LT in Tx-pos & HTL cohort**

<table>
<thead>
<tr>
<th>Recurrence site</th>
<th>LR</th>
<th>LT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver only</td>
<td>7 (22.6%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Lung only</td>
<td>1 (3.2%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Liver &amp; Lung</td>
<td>11 (35.5%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Multisite</td>
<td>12 (38.7%)</td>
<td>9 (45%)</td>
</tr>
</tbody>
</table>

This study benefited from a grant the French Organ Sharing Organization.
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Conclusions: We here present an international bicentric evaluation of vWF as a perioperative decision-making tool for patients with HCC. Patients with high vWF prior to LR show an increased risk for PHLF and reduced OS and therefore seem to derive limited benefit from surgery. Further, increased vWF is associated with early mortality on the LTx waiting list. As post-LTx and post-listing OS was comparable between risk groups according to vWF, patients presenting with HCC and high vWF values may benefit from LTx listing. We conclude that vWF can optimize LR and LTx decision-making for patients with HCC.

DE NOVO CANCERS AFTER LIVER TRANSPLANTATION: A FRENCH NATIONWIDE COHORT

Background: De novo cancer (DNC) following liver transplantation (LT) have been reported as one of the major causes of post-transplant mortality. Everolimus is frequently prescribed to patients presenting de novo cancer after LT and those who are at risk of cancer recurrence. With this study we aimed to estimate the cancer burden after LT at a nationwide level and to evaluate the potential role of everolimus in de novo cancer occurrence.

Method: The French national health data system (SNDS), linked with the national hospital database (PMSI), contains information on at least 99% of the French population, concerning ICD-10 codes, medical procedures (MP), prescribed drugs and vital status. 8658 patients having received LT for hepatocellular carcinoma (3902) or decompensated cirrhosis were identified from 2009 to 2019. Algorithms combining ICD and MP identified post-transplant neoplasia at different sites. Cox models including competitive risk, everolimus as time-dependent exposure and propensity score analysed cancer incidence and mortality.

Results: With a median follow-up of 4.6 [2.2, 6.8] years after LT, 1119 [13 %] patients developed DNC, of which 232 (2.7%) dysmyelopoiesis, 216 (2.5%) head and neck, 213 (2.5%) skin cancer, 184 (2.1%) metastatic cancer, 180 (2.1%) lung cancer, 100 (1.2%) lymphoma, 88 (3.3%) colorectal cancer, 87 (1.0%) prostate cancer and 50 (0.6%) bladder cancer. Age, tobacco, alcohol, diabetes and cancer before LT were significantly associated to de novo cancer for most studied sites. Three groups of DNC were identified according to survival: blood, skin and prostate cancer with good survival; lymphoma and colorectal cancer with medium survival; ORL and lung cancer with poor survival. During the follow-up, 2588 patients were exposed to everolimus including 997 (38.5%) prostate cancer and 50 (0.6%) bladder cancer. Age, tobacco, alcohol, diabetes and cancer before LT were significantly associated to de novo cancer after LT at a nationwide level and to evaluate the potential role of everolimus in de novo cancer occurrence.

Conclusion: DNC occur in at least 13% of adults after LT. Systematic screening is clearly insufficient in view of the poor survival. More surprisingly, the antitumor action of everolimus recipients to prevent de novo malignancies is not clearly demonstrated.
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Public perception in organ donation: multi-stakeholder vision and work team

FG10_1 ORGAN DONATION AFTER BRAIN-DEATH - FAMILY DYNAMICS, FACTORS FOR CONSENT AND ATTACHMENT OF MEANING AS A WAY TO PROCESS LOSS
Jaidora Skourli†, Thalía Belliati‡, Christina Papachristou‡, Danai Papadatoi
†National and Kapodistrian University of Athens, Mental Health and behavioral sciences, Athens, Greece; ‡School of Science, European University Cyprus, Department of Health Sciences, Nicosia, Cyprus, ‡International Hellenic University, Thessaloniki, Greece, #Aristotle University of Thessaloniki, Psychology, Thessaloniki, Greece, 4Kapodistrian University of Athens, Nursing Department, Athens, Greece

Background: Donation after brain death presents an extremely stressful event with significant impact on the entire donor family, which is faced with multiple challenges being called to manage the loss of a loved one and a decision regarding the donors’ life and body.

Methods: The current study investigates via semi-structured interviews the experience of family members who consented to organization of a brain-dead relative. Specifically, the study aims to understand the: (1) manner and degree of involvement of first-degree relatives in the consent, (2) factors influencing the decision to donate, (3) meaning participants attach to donation, (4) effect of donation on the perception of self and others, (5) relationship dynamics within the family. Corbin and Strauss’ grounded theory was applied for the research design and data analysis.

Results: All participants attach significant meaning to their decision, describing donation as the supreme gift of life and do not regret the decision, despite difficulties management the loss. The decision was made on two levels: an individual and a collective one involving discussions with friends and relatives. Determinants for consent were: the health personnel’s attitude, the level of understanding brain death, trust in the medical team, past donation experience, the ability to attach meaning to donation, belief in the continuation of the deceased’s life through the recipients, the knowledge of the donor’s attitude towards donation, specific donor characteristics and the agreement and cooperative decision-making within families. Most participants show signs of personal growth, despite adjustment difficulties and bereavement. The loss challenges religion-affine individuals who distanced themselves from religion after donation. Already strained family relationships suffered or broke after donation, while stable relationships helped maintain family homeostasis.

Conclusions: The study adds to our knowledge regarding personal growth, decision-making and family dynamics in organ donation. It highlights factors contributing to donation consent and its effect on the family. It reveals the necessity of expanding support structures for the donor family, and contributes to empirically based recommendations for an adequate approach and support of the donor family.

FG10_2 RELATIVES’ DECISION PROCESSES AND PERCEPTIONS IN THE CONTEXT OF INTENSIVE CARE FOR ORGAN DONATION: RESULTS OF A QUALITATIVE STUDY
María Soria-Olivier, Rubén García-Sánchez, Jorge S. López, José Manuel Martínez, María Jesús Martín, Alberto Barceló, Ricardo Lamelas, Elisabeth Coll, José Roldán, Sara Sánchez-Bercedo, David Uruñuela, Alberto Fernández-Carmona
1Public University of Navarre , Pamplona, Spain, 2Autonomous University of Madrid, Madrid, Spain, 3UdSNA, Pamplona, Spain, #National Transplant Organization, Madrid, Spain, 5Complejo Hospitalario de Navarra, Navarre, Spain, 6Coordination Autonómica de Trasplantes de Navarra, Pamplona, Spain, 7Hospital Puerta de Hierro, Madrid, Spain, 8Hospital Universitario Virgen de las Nieves, Granada, Spain

Background: Spain world leading donation rates depend, among other factors, on the implementation of the protocol called Intensive Care for Organ Dona- tion (ICOD), meaning the initiation/continuation of intensive care measures in patients with devastating brain injury when any curative treatment is deemed futile, incorporating the option of donation into their end-of-life care plans. ICOD protocol requires families to grant permission for its application and, after the death of the relative, confirm their willingness to donate their organs. This qualitative research investigates information and decision process of 24 family units that gave consent for ICOD and for the donation of organs.

Methods: An interview script “focused on the problem” was followed with 9 FOCUS GROUPS
Public perception in organ donation: multi-stakeholder vision and work team

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Jaidora Skourli†, Thalía Belliati‡, Christina Papachristou‡, Danai Papadatoi
†National and Kapodistrian University of Athens, Mental Health and behavioral sciences, Athens, Greece; ‡School of Science, European University Cyprus, Department of Health Sciences, Nicosia, Cyprus, ‡International Hellenic University, Thessaloniki, Greece, #Aristotle University of Thessaloniki, Psychology, Thessaloniki, Greece, 4Kapodistrian University of Athens, Nursing Department, Athens, Greece

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Methods: An interview script “focused on the problem” was followed with 9...


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### Public perception in organ donation: multi-stakeholder vision and work team

**FG10.4**  
**ICU STAFF’S SELF-REPORTED NEED FOR SUPPORT AND EDUCATION IN ORGAN DONATION**

Kathe Meyer\(^1\), Anders Christian Feyling\(^1\), Gunnar Gremer\(^1\), Lise Bratberg\(^1\), Monika Storre\(^1\), Terje Kluiten\(^1\), Marit Andersen\(^1,2\)

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**Background:** Within organ donation (OD) ICU staff members play a key role in identification and management of potential organ donors, as well as the care of relatives. However, OD is a rare event in many centers. This often makes it challenging to achieve and maintain competence needed to fulfill their responsibility in providing a caring environment and in ensuring the availability of organs for patients awaiting transplantation. The aim of this study was to map self-reported educational and supportive needs among ICU staff involved in the OD process.

**Methods:** A cross-sectional survey was conducted in a large university hospital with 63 ICU-beds and approximately 40 actual donors a year. Around 200 physicians and 800 nurses in 11 ICU departments received an electronic survey. The survey included items about level of experience, educational and supportive needs, and professional competence in OD. Educational need was measured from “no need” to “great need”, and professional competence was measured on a Likert scale (1-5), ranging from “to a small extent” to “to a great extent”. Descriptive and comparative analyses were performed.

**Results:** A total of 211 ICU staff (physicians 57, nurses 154) responded. Mean experience in ICU was 15 years (SD=9.5). The majority had participated in OD management (70%) and in approaching relatives (59%) more than 5 times. Guidance from colleagues specialized in OD (72%) and being relieved from other tasks (62%) were reported as most important supportive measures in the OD process. Physicians’ mean score (4.3) was slightly higher (p=0.001) than nurses’ (4.1) on feeling competent in caring for an organ donor. Most physicians and nurses reported further educational needs regarding medical management of the donor (79% and 85%, respectively) and in communication (77% and 79%, respectively).

**Conclusions:** The participants were highly experienced in OD. This indicates that the responders have an interest in OD that may not be representative of all staff in ICU. The results demonstrated the importance of strengthening professional support in OD and providing regular education in medical management and communication skills. A national survey is needed to investigate the level of professional competence in OD and compare educational and supportive needs between university and local hospitals.

### Improving deceased donation through an international cooperation training for health professionals

**FG10.5**

**IMPROVING DECEASED DONATION THROUGH AN INTERNATIONAL COOPERATION TRAINING FOR HEALTH PROFESSIONALS**

Seow Huey Choy\(^1\), Marti Manyalich\(^1\), Hongtao Zhao\(^2\), Miao Pu\(^2\), Jie Zhao\(^2\), Carmen Blanco\(^1\), Aleksandra Rudak\(^1\), Aleksandra Karandasheva\(^1\), Tishan Chen\(^1\), Chloe Balleste\(^1,2\)

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**Background:** Nurturing a culture and enhancing the knowledge of donation among health professionals appears to be a crucial factor to improve donation. A Belt and Road Organ Donation Capacity Improvement Cooperation Training Project training was an initiative made to educate health professionals in the practice of donation which includes donor evaluation and management, family communication and organ allocation. The study aimed to evaluate the effectiveness of the training by using pre- and post-tests.

**Methods:** Personnel who directly or indirectly involved in donation and transplantation were enrolled. The training was conducted virtually with an interactive modality that comprised roundtable, clinical case discussion and quiz. The content was developed by experts to include the best practices of donation and communication skills. A national survey is needed to investigate the level of professional competence in OD and compare educational and supportive needs between university and local hospitals.

**Results:** A total of 271 individuals consists of 77% Chinese and 23% international participants from 43 countries were trained. Health professionals from the donation team formed most of the participants (34%), 21% were from the anesthesia department and 19% were from the transplant team. Analysis of the 241 participants who completed both pre-test (median= 6.8/10.0) and post-tests (median= 7.6/10.0) revealed significant difference in score, Z= -7.26, p<0.001. Generally, rating of participants with the training were positive.

**Conclusions:** The training helped strengthening knowledge and understanding of deceased professionals. The virtual modality increased accessibility that could reach out and train more individuals. It can be complemented with practical training to further improve the confidence and skills of the practitioners. As a training program based on international cooperation, it promotes participants’ understanding on both international standards and local practices and facilitate mutual understanding on organ donation among Belt and Road countries.

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**FG10.6**

**MASS MEDIA CAMPAIGNS SENSITIZE BUT FAIL TO INCREASE ACTUAL ORGAN DONATION RATE**

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**Background:** Media campaigns aimed at increasing non-living organ donors (OD) for transplantation have demonstrated increasing intention to donate in their target population, but their effectiveness for increasing donation rates is not clear. The largest broadcasting corporation in Chile conducted a one-year national mass media campaign (2016-2017) intended to decrease familial refusal to donation (FR). It included prime time TV coverages, advertising with well-known personalities, and web, radio, and social media content. In 2016 Chile reached an OD rate of 7.9 donors per million population (dpm) and 50% FR; and in 2017, 10 dpm, and 46% FR.

**Methods:** With the aim of studying the effect of the campaign over OD figures, we analyzed if there were changes in FR and OD between 2016 and 2017 and between the year before and during the campaign, using ANOVA.

**Results:** For FR we found no statistically significant difference between 2016-17, yearly (p=0.16), semesterly (p=0.28), nor quarterly (p=0.54). Same happened when comparing the period of the campaign (year p=0.17, semester p=0.62, quarter p=0.39). Nonetheless, we found significant differences in OD for both yearly periods (p<0.01; p=0.01). Semesterly, we found significant differences just comparing calendar years (p=0.048), but not campaign years (p=0.09). We found no significant differences in the quarterly analyses (p=0.16; p=0.15).

**Conclusions:** Even though FR did not change, OD increased. This, because more potential donors reached the donation request stage of the procurement process, which may have been due to more detection and referral, or better care of patients. Both things are the responsibility of the healthcare professionals (HCP) inside the hospitals, so maybe the campaign sensitized HCP, but not its target population. Media campaigns are attractive in the short run, but they are unsustainable and ineffective in the long run. Looking for other interventions, like those targeting HCP should be explored.
OLDER LIVING LIVER DONORS CAN ENLARGE THE DONOR POOL: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Living donor liver transplantation (LDLT) is an option to solve the donor liver shortage. Due to the aging population, older potential donors are increasingly willing to donate. This study aims to systematically assess the differences in donor peri- and postoperative complications, mortality, and quality of life (QoL) between younger (<50 years) and older (>50 years) living liver donors.

Methods: Embase, Medline, and Cochrane Central Register of Controlled Trials were searched for studies published between 2002 and August 3, 2022. Studies’ methodological quality was assessed using the Newcastle Ottawa Scale. For donor complications and major complications, meta-analyses were conducted, donor mortality and QoL results were systematically described.

Results: The literature search resulted in 7388 studies, of which 17 were included (13 on complications, 2 on mortality, 2 on QoL). In 673/7607 (8.8%) donors, complications occurred, 85.4% in younger and 14.6% in older donors. The risk ratio (RR) for complications in younger donors was 1.08 [0.90, 1.31] (P=0.41). Risk ratios for major complications in younger donors were 0.98 [0.64, 1.48] and 0.89 [0.50, 1.57] using Clavien-Dindo III and IIbIIb as a major complication, respectively. RR for biliary complications in younger donors was 1.59 [1.05, 2.42] (P=0.03). In 60/14227 (0.4%) donors, mortality occurred, 47 (78.3%) in younger and 13 (21.7%) in older donors. One study on early mortality reported a RR in younger donors of 0.23 [0.12, 0.44], and 1 study on long-term mortality a RR in younger donors of 0.28 [0.06, 1.46], and 1 study on long-term mortality a RR in younger donors of 0.23 [0.12, 0.44]. QoL data was recorded for 414 (72.9%) younger and 154 (27.1%) older donors. Mean physical summary score in younger donors was 52.93 and in older donors 55.40. Mean mental summary score in younger donors was 51.87 and in older donors 51.29. Mean physical summary score in younger donors was 52.93 and in older donors 55.40.

Conclusions: Older donors do not have a higher complication rate or mortality rate than younger donors after LDLT. They do have a lower rate of biliary complications. In addition, older donors have a similar QoL after LDLT compared to younger donors. This study supports the inclusion of older donors in screening programs for living liver donation to expand the donor pool.

Figure 1. (a) Donor complications and (b) donor biliary complications in younger and older living liver donors.
**Background:** Normothermic machine perfusion (NMP) recreates a more physiologic environment that could allow for better organ preservation and objective graft evaluation which are key for the use of expanded criteria donor (ECD) kidneys. However, an objective graft assessment tool for ECD kidneys undergoing NMP is missing. Useful information could be acquired through laser speckle contrast imaging (LSCI), a novel non-invasive imaging technology that provides high-resolution information about microcirculatory perfusion and oxygen delivery. In this study, we investigated the potential use of real-time-available LSCI of ECD kidneys undergoing NMP for post-transplant outcome prediction.

**Methods:** Fifteen ECD kidneys underwent 2 additional hours of NMP prior to transplantation. Nine kidneys were included in the training/validation set and six kidneys were included in the test set. Oversampling techniques were applied to the individual frames of each sample within the training/validation set to compensate for the low sample size and increase variability and generalizability. LSCI data was acquired during NMP after 15, 75, and 105 minutes. Multiple convolutional neural network-based deep learning models were developed to predict the future development of acute rejection within the first three months after kidney transplantation (AR) or the development of delayed graft function (DGF). LSCI performed after 105 minutes of NMP was able to discriminate kidneys within the test set that will develop AR (PPV = 0.80, NPV = 1.00, WF1 = 0.81). Among the included kidneys, nine developed DGF and five developed AR. LSCI performed after 105 minutes of NMP was able to discriminate kidneys within the test set that will develop AR (PPV = 0.80, NPV = 1.00, WF1 = 0.81). The same data collected at earlier time points failed to identify these kidneys. LSCI data at any of the assessed time points was not able to identify kidneys that will develop DGF.

**Conclusions:** In our cohort, LSCI was able to discriminate kidneys that will develop AR before the donor kidneys were transplanted in the recipient. This novel insight needs to be verified in other studies with larger cohorts. LSCI shows potential for real-time-available graft assessment of ECD kidneys undergoing NMP for periods longer than 90 minutes.

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**FG11_2 DEEP LEARNING MODELS OF REAL-TIME NON-INVASIVE IMAGING DURING WARM PERFUSION OF EXPANDED CRITERIA DONOR KIDNEYS POTENTIALLY PREDICT ACUTE REJECTION**

Iacopo Cristesiferi1,2, Farhan Akram1, Dafsy Bouari1, Yitian Fang1, Elsaïne Rijks1, Martin Hoogduijn1, Ron de Bruin1, Carla Baan1, Marian Claesen-van Groningen1,2, Andrew Stubbs3, Robert Minne1

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**FG11_3 PANCREATIC STEATOSIS AND TRANSPLANT SUITABILITY ASSESSMENT WITH IMAGE BASED MACHINE LEARNING MODELS**

Georgios Kourtounis1, Pierre Ezuma2, Mark Turner3, Sorina-Maria Cornateanu1,2, Lucy Bates1, Emily Thompson1,2, Samuel Tingle1,2, Gourab Sen1, William E Scott III, Steve White1,2, Colin Wilson1,2

1NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation, Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne, United Kingdom, 2Newcastle University, Newcastle upon Tyne, United Kingdom, 3The Scottish Liver Transplant Unit, Edinburgh Transplant Centre, Edinburgh, United Kingdom, 4University of Edinburgh, Clinical Surgery, Edinburgh, United Kingdom

**Background:** Assessment of donor organ quality in pancreas transplantation is currently qualitative and reliant on the transplant surgeons’ experience and subjective decision-making. Limited inter-rater consensus may limit organ utilisation, especially with ‘marginal’ organs. This study aimed to investigate inter-rater consensus and use machine learning (ML) to develop an objective organ quality assessment tool to evaluate pancreatic steatosis (PS) and suitability for transplant.

**Methods:** 214 images from 66 separate donor pancreases were assessed independently by three transplant surgeons for PS and transplant suitability. Six convolutional neural network models were selected to evaluate these images. They were each trained with 200 images and tested on the remaining 14 images. 9 organs were also fully analysed by microscopic histological assessment. Correlation between macroscopic and microscopic PS was defined in this dataset.

**Results:** Accuracy during training for PS and transplant suitability respectively was 48.7-53.8% and 55-75%. Accuracy during testing increased for both variables to 71.4% and 78.6% respectively. Model testing for PS found sensitivity, specificity, and area under receiver operating characteristic (AUROC) to range between 41.7-50.0%, 77.7-84.1%, and 0.33-0.4 respectively. Model testing for transplant suitability found sensitivity, specificity, and AUROC to range between 78.6-83.3%, 0-50% and 0.24-0.7 respectively. Macroscopic visual assessment and microscopic histological analysis for PS was strongly positively correlated, r=0.7650, p=0.0082. Testing 14 images for PS required 0.369 seconds per model.

**Conclusions:** A quantitative and automated ML model for evaluating donor pancreas organ quality is feasible. Increased accuracy between the training and test phase demonstrates a desired generalisability to novel test images. Low sample size, especially in the test dataset may have limited analysis and performance.

**Table 1. Inter-observer reliability for macroscopic visual assessment of PS and transplant suitability.**

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Pancreatic Steatosis</td>
<td></td>
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<tr>
<td>(Kendall’s W)</td>
<td>0.641</td>
<td>p&lt;0.0001</td>
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<tr>
<td>Transplant Suitability</td>
<td></td>
<td></td>
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<tr>
<td>(Fleiss’ kappa)</td>
<td>0.310</td>
<td>p&lt;0.0001</td>
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**Figure. Laser Speckle Contrast Imaging of a human kidney undergoing normothermic machine perfusion**
The occurrence of clinical outcomes can be precluded by competing risks (e.g. death with a functioning graft). In kidney transplantation, a graft failure model censoring for death tends to overestimate the risk of graft failure, which can generate inaccurate predictions. We aimed to compare the predictive performances of a graft failure model censoring for death to those of a model accounting for the competing risk of death.

**Methods:** We included 4,000 kidney transplant recipients prospectively enrolled in 4 French centers. Death-censored graft failure was estimated using a Cox model, and graft failure accounting for the competing risk of death with a Fine-Gray model. Candidate predictors included recipient, donor and transplant parameters, histology (Banff lesions and diagnoses) and functional and immunological parameters. The prediction performances were assessed with the discrimination (C-index), calibration (calibration plots) and overall accuracy (Integrated Brier Score and Index of Predictive Accuracy).

**Results:** 549 patients (13.7%) lost their graft and 425 (10.6%) died with a functioning graft. The Cox and Fine-Gray models integrated 8 independent factors including the time from transplant to risk evaluation, functional factors (eGFR, proteinuria), histological findings (IFTA, g+ptc, i+t, cg Banff scores) and anti-HLA DSA. The Cox model and 0.80 for the Fine-Gray model) and overall accuracy (Integrated Brier Score and Index of Predictive Accuracy). At 7 years post risk evaluation, the models showed similar discrimination (C-index 0.81 for the Cox model and 0.80 for the Fine-Gray model) and overall accuracy (Integrated Brier Score 0.054 for both models). The Index of Predictive Accuracy was higher for the Cox model and 0.80 for the Fine-Gray model) and overall accuracy (Integrated Brier Score and Index of Predictive Accuracy).

**Conclusions:** In the setting of graft failure prediction after kidney transplantation, we showed that competition with patient death did not affect the predictive performances of a Cox model. This study shows that a prediction model may not always benefit from a competing risk approach and should be developed based on its final predictive performances.
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Digital Health for personalized care

MEASUREMENT FREQUENCY OF BLOOD PRESSURE IN NEWLY KIDNEY TRANSPLANTED PATIENTS DROPS OVER TIME IN REGULAR TELEMEDICINE SURVEILLANCE

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Background: In February 2020 we established a regular telemedicine service for patients after transplantation in order to provide a better follow-up after transplantation and detect problems as early as possible. Here we report differences in measurement behavior depending on the time after transplantation.

Methods: We included all patients participating in our telemedicine home monitoring project after kidney transplantation from February 2020 until January 2023. Patients submitted their blood pressure measurements, pulse, temperature, personal well-being and weight via smartphone app to the telemedicine center. We analyzed the number of transmissions of blood pressure measurements per month per patient and stratified for time since transplantation and inclusion into telemedicine.

Results: 626 patients were included into the regular telemedicine service, mean age at enrollment 51.5 years. 144,087 blood pressure measurements were submitted since beginning of the project, and patients submitted a median of 8 (IQR 4-19) blood pressure measurements per month, 160 patients (25.6%) were enrolled <1 year, 134 (21.4%) 1-5 years and 332 (53.0%) >5 years after transplantation. Patients transplanted <1 year transmitted more blood pressure measurements than patients during their long-term follow-up (figure 1). After 12 months all groups converged in the number of measurements.

Conclusions: This is a first analysis of the feasibility of blood pressure home monitoring using a telemedicine service with a smartphone app. We demonstrate differences in measurement behavior and intensity during telemedicine surveillance depending on the time of enrollment after transplantation. This observation provides first insight into the potential of novel telemedicine services for home monitoring of renal allograft recipients and may help to improve outcomes after transplantation.

BLOOD PRESSURE MEASUREMENTS IN A REGULAR TELEMEDICINE SERVICE AFTER RENAL TRANSPLANTATION IN DIFFERENT AGE GROUPS

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1Charite, Department of Nephrology and Medical Intensive Care, Berlin, Germany; 2Berlin Institute of Health, Berlin, Germany.

Background: Renal transplanted patients need a consistent follow-up after transplantation to detect problems as early as possible. Using our telemedicine system with a smartphone app, patients submit their vital signs and well-being into an electronic health record at the telemedicine center. Here we analyzed differences in blood pressure depending on age at transplantation.

Methods: We included all patients participating in our home monitoring after kidney transplantation that started in February 2020 until January 2023. We analyzed all transmitted blood pressure values and averaged per month per patient. Then we stratified for age at transplantation.

Results: 626 patients were included into a regular telemedicine service after renal transplantation, median age at transplantation 44.9 years, 62.5% were male. Time from transplantation until time of enrollment into telemedicine surveillance was 5.5 years in median. 249 patients (39.8%) were <40 years, 289 (46.2%) 40-60 years and 88 (14.1%) >60 years. 144,087 blood pressure measurements were submitted since beginning of the project in February 2020 until January 2023. Mean blood pressure values per month were below 140/90 mmHg in 88% of all values. There were patients with isolated systolic hypertension (6.5%) or diastolic hypertension. Younger patients had lower median systolic and diastolic blood pressure values compared to patients >60 years as shown in figure 1. Only <40 years had lower median diastolic blood pressure values. Younger patients had lower median systolic and diastolic blood pressure values compared to patients >60 years as shown in figure 1 (p≤0.02 between <40 years and >61 years).

Conclusions: Patients had good blood pressure control at home. Self-measured blood pressure values using telemedicine and home monitoring may open new insights into long term blood pressure control outside regular medical institutions. Throughout the observation time as expected younger recipients had lower systolic and higher diastolic blood pressure values than older recipients.
**BRIEF ORALS**

**Molecular transplant immunology**

**BOS1_1**

**17B-ESTRADIOL THERAPY MODULATES MICROGLIA ACTIVATION AFTER ISCHEMIA AND REPERFUSION REPERCUSSIONS**

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**Background:** Organ transplantation is adopted as the main therapeutic approach for patients without treatment options. In this context, the process of ischemia and reperfusion of the organ during transplant surgery is inevitable. IR induced systemic inflammatory response is responsible for several systemic physiological changes, including neurological and cognitive complications; those are directly linked to brain parenchyma inflammation, mainly due to the activation of microglia. Studies indicate 17β-estradiol (E2) as a potential therapy to decrease the IR induced inflammatory process. Therefore, here we investigate the effects of E2 treatment on the brain parenchyma after visceral ischemia and reperfusion.

**Methods:** Male Wistar rats were divided in 3 groups (n=6/group): (I) sham, surgically manipulated; (II) VIR, animals subjected to ischemia and reperfusion. (III) E2, animals treated with 17β-estradiol (280 μg/Kg, i.v.) 1h prior to VIR (1h after reperfusion). The visceral ischemia was induced by insertion of a 2-Fogarty® catheter in the descending aorta (aortic occlusion for 20 min, followed by a reperfusion period of 4h).

**Results:** The number of active resident microglia cells had greater amounts in the left side of the brain parenchyma after visceral ischemia and reperfusion. The visceral ischemia was induced by insertion of a 2-Fogarty® catheter in the descending aorta (aortic occlusion for 20 min, followed by a reperfusion period of 4h).

**Conclusions:** Our data indicate 17β-estradiol (E2) as a potential therapy to decrease the IR induced systemic inflammation triggered by visceral ischemia and reperfusion. However, treatment with E2 proved to be an important therapeutic agent, by effectively controlling microglia activation in the brain parenchyma (prefrontal cortex, hippocampus, as well as the thalamus and hypothalamus).

**BOS1_2**

**SINGLE CELL RNA SEQUENCING OF DONOR-REACTIVE T CELLS REVEALS ROLE OF APOPTOSIS IN DONOR-SPECIFIC HYPORESPONSIVENESS OF KIDNEY TRANSPLANT RECIPIENTS**

Amy van der List1, Nicolette Liljens1, Rutger Brouwer1, Mariska Klepper2, Alexander den Dekker2, Wilfred van IJcken1, Michiel Betjes1

1Erasmus Medical Center, Internal Medicine, Rotterdam, Netherlands, 2Erasmus Medical Center, Biomics, Rotterdam, Netherlands

**Background:** After kidney transplantation (KT) donor-specific hyporesponsiveness (DSH) of recipient T cells develops over time. Recently, apoptosis was identified as a possible underlying mechanism.

**Methods:** In this study, both transcriptomic profiles and complete V(D)J variable regions of TR genes from individual alloreactive T cells of kidney transplant recipients were determined with single cell RNA sequencing. Alloreactive T cells were identified by CD137 expression after stimulation of peripheral blood mononuclear cells (PBMCs) obtained from donors and 3 to 5 years after transplantation with CD3-depleted PBMCs of their donor or a third-party control. The alloreactive T cells were sorted, sequenced and the transcriptome and T cell receptor profile analysed using unsupervised clustering.

**Results:** Alloreactive T cells retain a highly polyvalent TRA/TRB repertoire over time. Clustering based on the transcriptome divided the donor-reactive T cells into three main groups: one cluster of cytotoxic CD8+ T cells and two clusters of CD4+ T cells with distinct activation profiles. Differential expression analysis revealed that donor-reactive CD4+ T cells in both clusters had downregulation of genes involved in apoptosis and intracellular signalling pathways post-transplant. Remarkably, no change in the transcriptome of donor-reactive cytotoxic CD8+ T cells was observed over time. Inclusion of third-party controls enabled us to ascertain that the differences we detected post-transplant were truly donor-specific and not due to the influence of immunosuppression.

**Conclusions:** Single cell expression profiling demonstrated a loss of activated and pro-apoptotic donor-reactive CD4+ T cell clones after transplantation in stable kidney transplant recipients. This suggests that alloapoptosis of highly activated alloreactive CD4+ T cells in the development of donor-specific hyporesponsiveness in stable kidney transplant recipients.

**BOS1_3**

**ELDERLY RENAL TRANSPLANT RECIPIENTS HAVE LESS POLYFUNCTIONAL ALLOREACTIVE CD4 T CELLS PRE TRANSPLANT AND LOWER IL-2 MEDIATED T CELL PROLIFERATION**

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1Erasmus Medical Center, Internal Medicine, Rotterdam, Netherlands

**Background:** Elderly kidney transplant recipients have a lower risk for both early and late acute T-cell mediated rejection (TCMR). Recently, we identified alloreactive memory CD4 T cells expressing at least two pro-inflammatory cytokines (poly-alloCD4) as pivotal cells for TCMR. The decline of poly-alloCD4 after transplantation leads to donor-specific hyporesponsiveness (DSH). Therefore, we hypothesized that the frequency and kinetics post-transplantation of poly-alloCD4 in elderly recipients differs from younger recipients.

**Methods:** Peripheral blood mononuclear cells (PBMCs) of N=16 young (<45 years) and N=14 elderly (>55 years) stable renal transplant recipients were sequenced at baseline, before at 6 months, 12 months, and at 3-5 years after transplantation. Expression of the co-stimulatory molecule CD137 identified alloreactive T cells following co-culture of recipient PBMCs with CD3-depleted PBMCs from their donor or third-party control. The phenotype and proportions of cytokine producing alloreactive CD137+ T cells as well as the proliferative capacity of T cells was evaluated using flow cytometry. Cytometric bead array was used to measure cytokines in supernatant.

**Results:** The frequency of poly-alloCD4 expressing three pro-inflammatory cytokines (IFNγ+IL2+TNFα+) was significantly lower in elderly prior to transplantation (p<0.01). T cells of elderly had decreased capacity to proliferate in response to alloantigen pre-transplantation although only significant within the DCD T cell compartment (p<0.02). Elderly also had lowered IL-2 production which was correlated with the reduced proliferative response. Post-transplantation, a decline in frequencies of poly-alloCD4 was observed in both age groups with a plateau reached after 12 months with no difference in kinetics.

**Conclusions:** DSH develops with similar kinetics post-transplant in both elderly and younger renal transplant recipients, with a decrease in frequency of poly-alloCD4. However, prior to transplantation, elderly recipients have lower levels of poly-alloCD4 expressing IFNγ+IL2+TNFα+ and decreased capacity to proliferate which is associated with decreased production of IL-2. Together, these factors can explain the lowered risk of acute TCMR in the elderly and them reaching DSH earlier than younger recipients.

**BOS1_4**

**DUAL INHIBITION OF THE COMPLEMENT SYSTEM AND TOLL-LIKE RECEPTORS PREVENTS SYSTEMIC AND LOCAL KIDNEY INFLAMMATION IN MICE EXPERIENCING BRAIN DEATH**

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**Background:** Brain death (BD) induces a potentially harmful systemic inflammatory response, which may reduce organ quality for transplantation. The complement system (CS) and Toll-like receptors (TLRs) are key for the innate immune system both for recognition and response. The cluster of differentiation 14 (CD14) is a co-receptor for several TLRs, necessary for TLR signalling. We hypothesized that dual inhibition of C5 and TLRs by complement protein 5 (C5) and CD14 inhibition will prevent innate immune-mediated inflammation during BD.

**Methods:** BD was induced with a fluid-filled intracranial balloon in wild-type C57BL/6 mice. Prior to BD, mice were left untreated (n=8), treated with a C5 inhibitor (n=7), a CD14 inhibitor (n=7), or both inhibitors (n=7). Sham mice did not experience BD and were left untreated (n=8). Blood and kidneys were collected three hours after BD. Inflammatory plasma cytokines were analyzed using a 23-plex immunoassay, kidney mRNA expression by qPCR.

**Results:** In plasma, BD significantly induced expression of interleukin-6 (IL-6), human IL-8, homolog IL-12, monocyte chemotactractant protein (MCP-1), macrophage inflammatory protein MIP-1α, and MIP-1β compared to sham (all p<0.01). In kidneys, BD significantly induced IL-6, IL-8, TNF, MCP-1, P-Selectin, and VCAM-1 (all p<0.01). CD14 and C5 inhibition significantly reduced BD-induced activation of all markers in plasma (all p<0.01) and in kidneys (p<0.01 except C5 inhibition for P-Selectin p=0.06). Dual inhibition of C5 and CD14 further reduced all plasma cytokines to levels comparable with sham animals (all p<0.05). In kidneys, double inhibition was comparable to single inhibition.
Background: Gene expression studies relying on whole-transcriptome profiling have defined the molecular phenotypes of kidney allograft rejection, but there have been several barriers limiting its application in clinical practice. The Banff Human Organ Transplant panel (BHOT) was developed to facilitate reproducible gene expression analysis of solid organ allografts, but its relevance to assess antibody-mediated rejection (AMR) and T-cell mediated rejection (TCMR) in kidney allograft biopsies has not been demonstrated.

Methods: We performed silico analysis and projected the BHOT panel on published microarray data of 547 kidney transplant biopsies (AMR, n=129; TCMR, n=17; non-rejection related cases, n=341). We compared expression between whole-transcriptome or BHOT panel genes, and performed differential expression, pathway, and gene network analysis. Finally, we evaluated the performance of BHOT genes to classify AMR and TCMR.

Results: Targeted versus whole-transcriptome analysis demonstrates that the BHOT panel captures the key gene signatures and pathways associated with rejection Figure A (AMR) and Figure B (TCMR). The top significant AMR-associated pathways based on BHOT genes were associated with interferon-gamma and interleukin signaling, toll-like receptor cascade and B-cell activation. For TCMR, the top pathways derived from the BHOT panel were related to PD-1 signal transduction, TLR signaling cascade, phosphorylation of CD3, demonstrating that the panel detects relevant pathophysiological mechanisms. The performance of BHOT-based ensemble classification models for detecting AMR (AUC=0.88; 95% CI=0.85-0.91) and TCMR (AUC=0.85; 95% CI=0.80-0.90) were highly similar to the panel detects relevant pathophysiological mechanisms. The performance of BHOT-based ensemble classification models for detecting AMR (AUC=0.88; 95% CI=0.85-0.91) and TCMR (AUC=0.85; 95% CI=0.80-0.90).

Conclusions: We demonstrate that the BHOT panel comprises the relevant genes and pathways associated with AMR and TCMR in kidney allograft tissue. Our findings show that this targeted panel is sufficient and sensitive to serve as a proxy to whole-transcriptome-based analysis for gene expression profiling in kidney allograft biopsies.

BRIEF ORALS

Molecular transplant immunology

Conclusions: The innate immune system is crucial for inducing inflammatory reactions during BD. Inhibition of both the CS and TLRs is necessary to efficiently prevent BD-induced systemic inflammation and to reduce local kidney inflammation. CS and TLR inhibitors are clinically available and clinical studies should be performed on deceased BD donors to enhance donor organ quality.

RELEVANCE OF THE BANFF HUMAN ORGAN TRANSPLANT CONSENSUS GENES PANEL FOR DETECTING ANTIBODY- AND T-CELL-MEDIATED REJECTION OF KIDNEY ALLOGRAFTS

Alessia Giarratano1,2, Dina Zilinski1, Valentin Goutaudier1, Blaise Robin1, Olivier Aubert1, Mark Haas1, Annalisa Angelini1, Michael Mengele1, Carmen Lefaucheur1, Alexandre Lopuy1

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Background: Predicting or diagnosing renal fibrosis (IFTA) to reduce chronic allograft loss is still a major challenge in kidney transplantation. Current analytical standards, such as creatinine, proteinuria or Glomerular Filtration Rate have poor predictability and the diagnostic still relies on costly and invasive kidney biopsy. Thus, molecular analyses of urinary extracellular vesicles (uEV) have emerged as a possible source of new biomarkers, and as a platform to overcome the risks, costs and sampling limitations of renal biopsy. In this context, in a preliminary study our group introduced uEV RNA-Seq as a potential alternative to tissue for the diagnosis of renal fibrosis. However, its clinical application, here we validated these results using digital droplet PCR (ddPCR), a technique with higher throughput screening potential.

Methods: miRNAs signature was studied in a new cohort of kTx patients (n=20) using ddPCR. Briefly, the uEV RNA was obtained from 1 ml urine using the Exosome RNA Isolation Kit (Norgen Biotek Corp.). After retrotranscription, the ddPCR was performed. For data analysis, patients were divided into non-IFTA (scored as less than 1, 40% of total) and IFTA patients (scored as 1 or more, 59% of total), according to their Renal Biopsy Banff score.

Results: ddPCR results achieved higher technical sensitivity, accuracy and reproducibility compared to real-time quantitative PCR (qPCR). This permitted absolute quantification of miRNAs even in samples with limited target abundance. Furthermore, we mostly validated the previous miRNAs fibrosis signature identified by RNAseq using ddPCR in this new cohort of kTx patients.

Conclusions: ddPCR detection of multiple miRNAs in urine-EVs is a suitable non-invasive approach to monitor fibrosis in kTx patients.

DDPCR DETECTION OF MIRNAS FIBROSIS SIGNATURE IN URINE-EVS FROM KIDNEY TRANSPLANTED PATIENTS: A NON-INVASIVE APPROACH TO DETECT KIDNEY FIBROSIS

Marta Clos-Sansalvador1,2, Javier Paul-Martinez1, Paula Rodriguez-Martinez1, Sergín García1,2, Marta Sanroque-Munhoz1, Miriam Font-Morón1, Jordi Bover1, Anna Vila-Santandreu1, Marcella Franzuesa1, Jueva1, Francesc E. Borras1,2

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Background: Because graft survival is still impacted by chronic dysfunction related, among other things, to poor control of the alloimmune response, the development of new strategies that would be efficient in preventing rejection and free of toxicity is necessary. As recent studies in mouse models have shown that MEK inhibition is effective in controlling the alloimmune response in experimental GVHD without abrogating anti-tumor and anti-viral immunity, we evaluated the therapeutic potential of MEK pathway inhibition in a preclinical model of allogeneic human skin transplantation in humanized NSG mice.

Methods: Human skin grafted animals, whose immune system was reconstituted with human PBMCs, were treated with trametinib, an anti-MEK molecule already used in the clinic for the treatment of melanoma. Graft survival was evaluated and the effects on the human alloimmune immune response were analyzed.

Results: Experiments performed with 4 human skin dons and 4 human blood donors showed that trametinib-induced MEK inhibition significantly prolonged the survival of allogeneic skin graft compared with untreated controls (30.7 ± 4.3 days, n=17 vs 18.4±3.3 days, n=15, p<0.0001) without interfering in vivo immune reconstitution in the NSG mice. Analysis of PBMCs from these animals showed an increase of the HCD4/hCD8 T cell ratio in trametinib treated mice however we could not detect any difference in the expression of T HCD4 and/or HCD8 inhibitory markers and HCD4 regulatory T cells. To further investigate the effect of trametinib in an in vivo setting, we used single cell RNAseq analysis (10x Chromium) on splenic HCD45 cells harvested 16 days following reconstitution. Regarding HCD4 T cells, trametinib seemed favor HCD4 early proliferation and impede differentiation toward follicular helper T cells and promote TH1.

A NEW THERAPEUTIC APPROACH IN ORGAN TRANSPLANTATION

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1CR2TI Inserm 1064, Nantes, France, 2CHU Nantes, Nantes, France

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activated memory CD4 T-cells) were the next most abundant. For each phenotype, the proportions of cell types in these data can provide insight into the temporal and phenotypic changes associated with rejection that occur in the first 2 years after kidney transplant.

Methods: We generated gene expression data from PBMC preparations collected concurrent with biopsies from patients in the first two years after kidney transplant. The gene expression data covered four biopsy proven phenotypes (Transplant eXcellence – TX; subclinical Acute Rejection – subAR; clinical Acute Rejection – cAR; Acute Dysfunction, No Rejection – ADNR) over 5 post-transplant timepoints (months 3, 4, 6, 12, 24) and unscheduled time points of Suspected Rejection (SR). These data were used as input into the CIBERSORTx webtool to determine the proportions of immune cell types found in each sample based on 22 cell type identities in the LM22 signature matrix.

Results: Of the 22 possible cell types, Monocyte and Neutrophil populations each represented over 20% of the total in a majority of samples. In the TX and subAR sample groups, the Neutrophil proportion showed a significant decrease over time (p < 0.05). Resting NK cells were present at more than 10% in a majority of samples with a slight upward trend over time in the subAR samples. Finally, 4 populations of T-cells (CD8 T-cells, Naïve CD4 T-cells, gd T-cells, and activated memory CD4 T-cells) were the next most abundant. For each phenotype, these populations were also increasing over time with that trend significant for the CD8 population in all phenotypes (p < 0.05) except for cAR.

Conclusions: We identified changes in the identity and proportions of cell populations in the peripheral blood in the first two years following kidney transplant. These changes correlate with both the biopsy determined state of the transplanted organ as well as the interval following transplant. Future studies looking at correlation of other factors like age, biological sex, race, and treatment as well as serially collected samples in the interim between biopsies will be informative.

Table 1

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**BRIEF ORALS**

**Molecular transplant immunology**

**BOS1_10**

**A NOVEL URINE-BASED LIQUID BIOPSY BIOMARKER FOR RENAL FIBROSIS IN KIDNEY TRANSPLANT**

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**Background:** Kidney Fibrosis (KF) is a complex dynamic process that is the terminal stage of most progressive kidney transplant diseases. While traditional kidney allograft biopsy remains the gold standard for the diagnosis of KF, considerable progress has been made over the last years in the study of urinary proteomics as a diagnostic tool. Clear advantages over the traditional biopsy include accessibility, safety, serial sampling and the potential for non-invasive diagnostic and prognostic monitoring of the disease progression and an individual’s response to treatment. A few years ago, our group identified urinary vitronectin (uVN) as a possible candidate to monitor KF; in this study, we aimed to demonstrate whether this hypothesis is sustained in a clinical cohort.

**Methods:** Samplings were taken from routine laboratory monitoring of 72 kidney transplanted patients with allograft biopsies were collected and classified according to their histopathological diagnoses to define two groups of patients: non-IFTA (<1) and IFTA (1 or >1); levels of uVN in corresponding urine samples were measured by enzyme-linked immunosorbent assay (ELISA).

**Results:** None of the clinical parameters, except for time after transplantation, could differentiate the two groups of patients (n=72). To analyse the correlation between routine follow-up laboratory tests and uVN with the histopathological findings, a Spearman correlation test was performed. The highest value was found in the correlation between uVN and IFTA (r=0.22) compared to the other parameters (r<0.15) including proteinuria. Interestingly, in these patients with a follow-up of at least three years of functioning graft (n=47), both urinary proteinuria and a significant p-value (p=0.022) for the correlation and were significantly (p=0.0092, uVN; p=0.0008, Proteinuria) able to differentiate between patients with and without IFTA. Yet, of note, uVN could identify about 20% of patients with non-pathological proteinuria. These results indicated that while the use of uVN alone would only detect the 74% of patients with IFTA, the addition of uVN levels, we could identify up to 94% of KF non-invasively.

**Conclusions:** This study provides a novel potential for uVN as an add-on non-intrusive surveillance biomarker strategy of fibrosis in kidney transplant.

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**BOS1_11**

**NON-INVASIVE DETECTION OF REJECTION IN THE FIRST 2 WEEKS AFTER KIDNEY TRANSPLANTATION USING URINARY CHEMOKINES**

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**Background:** Novel biomarker assays for the non- (or minimally) invasive detection of rejection, such as for example, donor-specific cell free DNA, are unable to diagnose rejection in the first 2 weeks after transplantation. The aim of this study was to examine if the urinary chemokines CXCL9 and CXCL10 can accurately detect biopsy-confirmed allograft rejection (BCAR) early after kidney transplantation.

**Methods:** Available urine samples collected at the time of a first biopsy performed within 14 days after transplantation (n=54, 50% deceased donors) were used from a cohort of 225 consecutive kidney transplant recipients. Biopsies were categorized into i. BCAR (n=16), ii. presumed rejection (n=16) or iii. no rejection (n=22). Urine samples collected at day 7 (no biopsy in the first 6 months after transplantation) served as controls (n=76, 54% deceased donors). Urinary CXCL9 and CXCL10 concentrations were determined with ELISA.

**Results:** Biopsies were performed at a median of 7 days (range: 2-14 days) after transplantation. Urinary CXCL9 concentrations were significantly higher at BCAR (368 pg/ml, range: 0-49619 pg/ml) compared to day 7 (4.5 pg/ml, range: 0-1577 pg/ml) (p<0.001, ROC-AUC 0.82, 95%CI: 0.68 to 0.96), as well as compared to no rejection biopsies (0 pg/ml, range: 0-321 pg/ml) (p<0.0001, ROC-AUC 0.86, 95%CI: 0.73 to 0.99). Similarly, CXCL10 concentrations were significantly higher at BCAR (238 pg/ml, range: 16-11949) compared to day 7 (28 pg/ml, range: 0-1320 pg/ml) (p<0.001; ROC-AUC 0.83, 95%CI: 0.71 to 0.95), as well as compared to no rejection biopsies (35 pg/ml, range: 4-2037 pg/ml, p<0.05; ROC-AUC 0.77, 95%CI: 0.62 to 0.92). The positive predictive value for BCAR was 69% (day 7) and 62% (no rejection biopsies) for CXCL9 and 46% (day 7) and 35% (no rejection biopsies) for CXCL10. In contrast, the negative predictive value for BCAR was 94% (both day 7 and no rejection biopsies) for CXCL9 and 93% (day 7) and 92% (no rejection biopsies) for CXCL10. CXCL9 and CXCL10 concentrations were comparable between living donors and deceased donors.

**Conclusions:** Urinary chemokines CXCL9 and CXCL10 identify BCAR in the first 2 weeks after kidney transplantation. As a non-invasive measurement these markers have a high potential to augment clinical decision making in the early period after transplantation.
DIRECT IMMUNOPHENOTYPING OF REGULATORY B CELLS AT 3 MONTHS HAVE A PROGNOSTIC VALUE OF IMPROVED GRAFT OUTCOME AND REJECTION RISK IN KIDNEY TRANSPLANT

Inés Perezpayá+, Sergio G. García+, Maria Molina1, Angela Casas1, Regina Gelabert+, Enrique Taco Sánchez, Irene Bolufer2, Anna Vilà-Santandreu, Jordi Bover, Francesc E. Borras3, Laura Cañas1, Marcella Francoessa

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Background: Regulatory B cells (Bregs) have been postulated as major mediators of tolerance in kidney transplantation (KT) and have been associated with longer allograft survival and fewer rejection episodes.

Methods: 51 kidney transplant recipients were followed up for 12 months (m) after transplantation. At pre-transplantation, 7 days and 3.6 and 12m post-transplantation, clinical and laboratory data were collected and peripheral blood lymphocyte populations were analysed by flow cytometry. We assessed total and relative counts of Bregs (CD19+CD24+CD38-), Memory B cells (CD27+CD19), Naive B cells (CD27+IgD+CD19), Total B (CD19), and T cells (CD3, CD4 or CD8) and analysed their association with graft outcome.

Results: The median age was 60 years-old, most were male on dialysis. 51% of patients had hypertension, 51% were on dialysis, and 51% had a previous KT. 11.8% had a previous KT and 80% had 4 or more HLA mismatches. Induction therapy received was basiliximab (47%), thymoglobulin (48%) or no induction. The most common maintenance immunosuppressive therapy was glucocorticoids, tacrolimus and mycophenolate mofetil. Only 49% of patients had undergone primary therapy, including some who received prednisone or no induction. The most common maintenance immunosuppressive therapy was glucocorticoids, tacrolimus and mycophenolate mofetil. Only 49% of patients had undergone primary therapy, including some who received prednisone or no induction.

Conclusions: Our data allowed us to establish a cut-off value of 2.6% of Bregs at 3m above which 95% of the patients remained with stable kidney function for up to 12 months and 100% free from rejection events (p=0.02). Patients with Bregs at 3 months below 2.085% presented 25% chances to present rejection episodes in the 12 months follow-up (p=0.01).

In vitro stimulation with B cell targets confirms that γ/δ Tc are not involved in DSA generation, but they do play a role during the effector phases of AMR. The crucial role of T follicular helper cells (T FH), which express an α/β TCR and provide help to allogeneic B cells for their differentiation into DSA-producing plasma cells is well known. In contrast, the role of γ/δ Tc in AMR pathophysiological cascade is unknown.

Methods and results: The role of γ/δ Tc in DSA generation was studied in a cohort of 331 kidney transplant patients with 10 years of follow-up. The incidence of de novo DSA was similar in recipients with low versus high γ/δ Tc count. In vitro experiments conducted on human cells confirmed that activated γ/δ Tc do not acquire CXCR5 and CD40L, two key molecules for T FH function. Histological analysis reveals that γ/δ Tc mainly localize outside the B cell area of lymph nodes, prompting us to investigate whether γ/δ Tc could instead act like antigen-presenting cells (APC) for the priming of T FH cells. However, γ/δ Tc also fail to upregulate the expression of HLA II and costimulatory molecules upon stimulation. Finally, γ/δ Tc neither make B cells proliferate nor synergise with α/β Tc in proliferation assays. These results were confirmed in a murine in vivo model. After transplantation with an allogeneic Balb/c (H-2d) heart, wild-type and TCRKO mice develop similar DSA responses, which rule out an APC-like function for γ/δ Tc. The TCRKO (deficient in αβ Tc) recipient mice do not develop any DSA confirm the lack of T FH-like function for γ/δ Tc. While γ/δ Tc do not play a role in DSA generation, they can be detected in microvascular inflammation of patients' AMR biopsies, they express FcγR on their surface and efficiently damage allogeneic endothelial cells in coculture.

Conclusions: This translational study demonstrates that γ/δ Tc are not involved in the generation of DSA, but play a role during the effector phases of AMR.
BRIEF ORALS

Transplantation immunology

**BOS2_1**

**CLINICAL AND IMMUNOLOGICAL FACTORS ASSOCIATED WITH THYMIC FUNCTION AT THE TIME OF KIDNEY TRANSPLANTATION**

**Joanna Peterson**, Camille Kergaravat, Emmanuel Clave, Lise Morin, Christophe Legendre, Dany Anglicheau, Antoine Toutouly, Julien Zuber

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**Background:** End stage renal disease patients experience a hastened age-related decline of the immune system. The thymus is the unique source of naïve T cells generation. Our study aims to determine the main factors associated with the thymic function, as assessed by sjTREC measurement, at the time of transplantation.

**Methods:** Four hundred-ninety-five consecutive patients, transplanted between January 2015 and March 2019, for whom stored peripheral blood leukocytes were available, were enrolled into the study. sjTREC quantification was performed in total PBMCs. Moreover, TCRAD gene was genotyped for the whole cohort, because its polymorphism was associated with thymic function in the general population.

**Results:** Different clinical factors (recipient age, gender, BMI > 30 kg/m², preexisting diabetes, dialysis vintage, positive CMV serology, past exposure to immunosuppressive drugs) and genetic variations (SNP rs224985 -0.0288 0.62, rs10873019 -0.0364 0.53, Log CRP (day 0) -0.0580 0.01 -0.0108 0.58) were positively associated with worse thymic function. The best multivariate analysis model retained only age, male gender, obesity, and rituximab-based desensitization regimen before ABO/HLA incompatible transplantation, were positively associated with worse thymic function. The best multivariate analysis model retained only age, male gender and pretransplant desensitization regimen. These results confirmed previous observation in the general population (age, gender), but also unveiled the negative impact of B-cell targeted therapies on thymic function. Ongoing analyses are investigating the impact of baseline thymic function on post-transplant clinical outcomes (including opportunistic infections, COVID-19-related mortality, cancers) and on rates of immune reconstitution following T-cell depleting induction (post-transplant CD4+ T cell count trajectory).

**Conclusions:** Recipient age, gender, and rituximab therapy administered 1 month ahead of kidney transplantation are the three independent factors correlated with the baseline thymic function.

**Variables**

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**BOS2_2**

**DOES RECEPTOR-MEDIATED INTERNALISATION OF HYALURONAN (HA) MATRIX IN THE RENAL CORTEX EXPLAIN THE PROTECTION CONFERRED BY ISCHAEMIC PRE-CONDITIONING?**

**Aleeya Zaidi**, Irina Grigorieva, Charlotte Brown, Gilda Pino-Chavez, Rafael Chavez, Robert Steadman, Soma Merani, Usman Khalid

1Cardiff Transplant Unit, University Hospital of Wales, Cardiff, United Kingdom, 2Cardiff University, Wales Kidney Research Unit, Department of Infection and Immunology, School of Medicine, Cardiff, United Kingdom

**Background:** Ischaemia reperfusion injury (IRI) is a major cause of delayed graft function (DGF) and poor graft survival in transplanted kidneys. Ischaemic preconditioning (IPC) attenuates IRI via mechanisms that are not understood.

Hyaluronan (HA) is a matrix polysaccharide normally undetectable in the renal cortex, but its accumulation is a hallmark of renal fibrosis. HA interacts with cells through its principal receptor, CD44. Our in vitro studies indicate that the variant HA isoform CD44v7/8 may be anti-fibrotic, as it promotes cytoplastic internalisation and breakdown of HA. The aim of this study was to characterise CD44v7/8 in vivo expression in IRI and IPC to determine its potential role as a mediator of IPC protection.

**Methods:** Adult male-Lewis rats (n=24) underwent midline laparotomy and were grouped into Sham, bilateral 45min IRI or IPC+IRI (pulsatile IPC prior to IRI). Kidneys were retrieved at 28d and assessed histologically and transcriptionally for relevant markers of kidney injury/fibrosis. Blood was taken pre-op and 28d for serum creatinine measurement.

**Results:** IRI led to marked histological damage with key fibrillogenic markers significantly increased. IPC led to renoprotection with attenuation of fibrillogenic markers—IRI led to increased extracellular HA deposition within the renal cortex, particularly in the peri-tubular, peri-glomerular, and peri-vascular areas. In contrast, in IPC kidneys, HA was shown to be internalised into the renal tubular epithelial cells (Khatri et al, 2019). This observation led to the hypothesis that the difference in IRI and IPC renal fibrosis is due to a differential HA expression profile between the two groups. To this end, we aimed to measure HA expression in IRI and IPC kidneys, and we used four anti-HA antibodies: one specific to the HA core only, and three more specific to the HA-N and -C termini. We also measured the expression of CD44v7/8, which is known to be expressed on the surface of fibroblasts and is involved in HA internalisation. Our results showed significantly stronger IRI expression of CD44v7/8 compared with other HA class II molecules on HPGEC. Further studies are needed to explore whether this response is associated with the increased immunogenicity and pathogenicity of HLA-DR.

**Conclusions:** HA and CD44v7/8 may be involved in the maintenance of the renal parenchyma, and their expression may be modulated by IPC to prevent renal fibrosis. Further studies are needed to investigate the role of CD44v7/8 in the attenuation of renal fibrosis by IPC.

**BOS2_3**

**DIFFERENTIAL KINETICS OF HLA CLASS II ANTIGENS EXPRESSION ON PRIMARY HUMAN GLOMERULAR ENDOTHELIAL CELLS**

**Maria Marschini**, Alessandra Armstrong Antunes, Dylan Issacson, Chelsea Maguire, Anat Tambur

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**Background:** De novo HLA-DQ donor specific antibodies are the most frequently detected and associated with adverse outcomes in allotransplantation. Yet, HLA-DR is expressed at higher levels and is considered the more antigenic molecule. Here we investigated the kinetics of HLA-DQ upregulation, compared with HLA-DR and HLA-DP, following IFNγ stimulation in human primary glomerular endothelial cells (HPGEC; representing the target for antibody/T cell interactions in kidney transplantation).

**Methods:** HPGEC from different donors were cultured with increasing doses of IFNγ (0, 250 or 2500U/ml) for up to 21 days (n=13). Surface expression of HLA-DR, DP and DQ was assessed and compared with IFNγ stimulation in human primary glomerular endothelial cells (HPGEC). mRNA studies demonstrated that the differential kinetics is also observed at the transcriptional level, with an antigenous dynamics (DR>DP>DQ) corresponding to the surface expression. CIITA was promptly upregulated by IFNγ at 48h and remained stable throughout the 21 days F/U. Nanostring studies further demonstrated upregulation of the costimulation molecules PDL1, PDL2 and CD40 in response to IFNγ stimulation along the basolateral aspect of tubular epithelial cells and promotes HA internalisation from the pericellular matrix into the tubular cytoplasm thus reducing cortical HA deposition and thereby mediating protection in IPC. The exciting therapeutic potential of CD44v7/8 warrants further evaluation.

**Conclusions:** Extracellular HA deposition in the renal cortex promotes progressive renal fibrosis and damage following IPC. IFNγ stimulates HA expression through its principal receptor, CD44. Our in vitro studies indicate that CD44v7/8 is pro-fibrotic, as it promotes cytoplastic internalisation of HA. Further studies are needed to elucidate the role of CD44v7/8 in the maintenance of the renal parenchyma, and the potential of CD44v7/8 as a therapeutic target for preventing renal fibrosis.
**BRIEF ORALS**

**Translational transplant immunology**

**BOS2_4**

**A PRO-INFLAMMATORY IMMUNE STATE IS INFLUENCED BY PERTURBATIONS OF MICROBIAL METABO-LITES IN RENAL TRANSPLANTATION**

Fernando Yuen Chang1*, Amber Vaitkute1, Meryl Attirii2, Stephanie Chong2, Hibo Mahdi1, Paul Blair1, Alan Salama2, Simon Eaton2, Mona Raja-Elliott2, Anne Pesenacker, Reza Motallebzadeh1

1Royal Free Hospital, London, United Kingdom, 2UCL, IIT, Pears Building, London, United Kingdom, 3UCL Great Ormond Street Institute of Child Health, London, United Kingdom

**Background:** Long-term graft survival in renal transplantation remains a challenge. Emerging evidence suggests that the gastrointestinal microbiota-immune axis impacts on extra-intestinal health. Our study aims to identify the influence of microbial metabolites in recipient immunity, with our hypothesis that a pro-inflammatory state, promoted by reduced availability of bacterial-derived metabolites associated with immunoregulation e.g. short chain fatty acids (SCFAs) and tryptophan-derivatives is related to acute rejection (AR).

**Methods:** Ninety recipients and 21 live-donors were recruited with urine, stool and blood samples collected at baseline and up to 12-months after surgery. Flow cytometry was used to assess for circulating subpopulations of CD19+ and blood samples collected at baseline and up to 12-months after surgery.

**Results:** Patients with AR had an almost 10-fold reduction of FoxP3+CXCR5+ TFR cells after transplantation compared to baseline (p=0.03). Furthermore, there were lower frequencies of cTFR cells at 3-months when compared to matched recipients without AR (0.095% vs 0.14% p=0.12; p=0.01. Figure 1). There was a trend for higher frequencies of plasmablasts, resting memory B-cells and TFR cells pre-transplantation in patients with AR, with fewer transitional B-cells (CD19+CXCR5-CD27-) at 3-months (0.14% vs 3.26% p=0.26) at 3-months. Although overall tryptophan availability increases after transplantation, patients with AR displayed reduced levels of SCFAs at 1-month, corresponding to the peak timepoint of AR occurrence (figure 2).

**Conclusions:** Our data has shown complex changes in microbial metabolites after transplantation that may influence balance of cTFR vs TFR cells. The increase in dietary freedom after transplantation is reflected by increased tryptophan availability increases after transplantation, patients with AR displayed reduced levels of SCFAs at 1-month, corresponding to the peak timepoint of AR occurrence (figure 2).

![Figure 1. Decreased levels of FOXP3+ TFR in recipients that develop BPAR](image)

![Figure 2. Snapshot of the faecal metabolome after live-donation and renal transplantation](image)

**BOS2_5**

**UNREPRESENTED HUMAN LEUKOCYTE ANTIGEN ALLELES ON SINGLE ANTIGEN BEAD ASSAYS: A COMPARISON AMONGST DIFFERENT TEST KITS**

Quan Yeo Ho1*, Shan-You Carolyn Tien1,2, Chew Yen Phang2, May Ling Lai1, Ian Tatt Liew1,2, Sobhana Thangaraju1,2, Marieta Chan1, Terence Kee1,2

1Singapore General Hospital, Singapore, Singapore, 2SingHealth Duke-NUS Transplant Centre, Singapore, Singapore, 3Health Sciences Authority, Singapore, Singapore

**Background:** Human Leucocyte Antigen (HLA) alleles may generate antibodies that are undetectable by routine single antigen beads (SAB) assays if their unique epitopes are unrepresented. We compared the prevalence of unrepresented HLA alleles in available SAB kits in our cohort.

**Methods:** All individuals who had undergone two-field HLA typing (HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPA1, -DPB1) using sequence-based typing or sequence-specific primers from 2021 to 2022 were included. Two-field DRB3/4/5 typing was unavailable. HLA alleles detected were compared with alleles represented in the standard LABScreen (LS) kit (One Lambda) with and without the supplementary ExPlex (EP) kit (One Lambda), and the LIFE-CODES (LC) (Immucor) SAB kit. Each unrepresented allele was compared with the most similar represented allele within each kit. Differences in amino acid sequences (IPD-IMGT Database v3.46) and eplet expression (HLAmatchmaker Class I v4.0, Class II v3.1) were identified (Figure 1). Differences in 3-dimensional molecular structures were visualised using generated models (SWISS-MODEL).

**Results:** Two-field HLA typing was performed for 80 individuals - all underwent HLA-A, -B, -C, -DRB1 typing, 78 underwent HLA-DQA1 typing and 42 underwent HLA-DQB1 typing and 42 underwent HLA-DQA1, -DP1A-1, -DPB1 typing. Overall, there was no difference in patients with unrepresented HLA alleles between the LS kit and the LC kit (72.5% vs 63.8%; p=0.09, Table 1). However, less patients had unrepresented HLA-A (26.3% vs 43.8%, p=0.02) and overall class 1 alleles (48.8% vs 65.0%, p=0.04) in the LS kit compared to the LC kit. Less patients had unrepresented HLA-A, -B, -C, -DRB1 alleles with the supplementary EP kit (LS+EP) compared to the LS or LC kit alone. In addition, less patients had unrepresented HLA-DQA1 alleles in the LS+EP kits compared to the LS kit. Less patients had unrepresented alleles with eplet mismatches, including those previously antibody-verified, in the LS+EP kits compared to the LS or LC kit alone.

**Conclusions:** Supplementary SAB kits may reduce the risk of undetected donor-specific antibodies. Less patients had unrepresented HLA-B alleles in the LS kit compared to the LC kit in our cohort. Further studies may be needed to compare the clinical performance of different SAB assays in detecting HLA antibodies.
**BOS 2.6** EVALUATION OF METHODS FOR THE TISSUE-OF-ORIGIN DECONVOLUTION OF PLASMA AND URINARY CELL-FREE DNA IN ALLOGRAFT RECIPIENTS AND HEALTHY VOLUNTEERS

Nicholas Kueng*1,2, Daniel Sidler*, Vanessa Banz*, Carlo Largiadèr1, Charlotte Ng3, Ursula Amstutz1
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**Background:** Donor-derived cell-free DNA (dd-cfDNA) has shown potential value in allograft surveillance to reduce the need for graft biopsies. However, limitations of dd-cfDNA-based allograft monitoring include multi-organ transplantation from the same donor, blood transfusions and the early transplant phase. Analysis of graft tissue-specific methylation signatures in cfDNA could serve as an alternative approach, potentially with higher specificity to the relevant transplanted tissue.

**Methods:** We evaluated laboratory methods for the tissue-of-origin deconvolution of plasma and urinary cfDNA with single- and double-stranded (dsLP) library preparation methods followed by low-coverage whole-genome bisulfite conversion method together with single- (ssLP) and double-stranded (dsLP) library preparation methods followed by low-coverage whole-genome bisulfite sequencing. The methods were adapted to preserve the cfDNA fragmentation patterns.

**Results:** The dsLP method showed a significantly reduced global methylation in urine (1.9% vs 32.6%, p < 0.001) than in plasma (0.2% vs 7.4%, p < 0.001). No significant differences were detectable between both library preparation methods for the tissue-of-origin proportions. However, there was a significantly higher proportion of sequences with undertermined tissue-of-origin with the ssLP method, which was more pronounced in urine (1.9% vs 32.6%, p < 0.001) than in plasma (0.2% vs 7.4%, p < 0.001).

**Conclusions:** This indicates that endogenous potential biases and pitfalls with methylene-based ds-cfDNA tissue-of-origin deconvolution and detection of cfDNA from allograft tissues of interest. Based on these results, enzymatic conversion coupled with a single-stranded library preparation appears to be a robust and bias-free choice, especially for urinary-derived cfDNA, where DNase activity causes a reduction in intact double-stranded fragments.

**BOS 2.7** HUMAN REGULATORY B CELLS PREVENT EFFECTOR CD4+CD25- T CELL PROLIFERATION THROUGH A MECHANISM DEPENDENT FROM GRANZYME B AND LYMPHOTOXIN ALPHA

Nicolas Saillant*1, Hao Mai1, Amanda Dupuy1, Gaelee Tilly1, Cynthia Forgeux2, Martin Briner2, Magali Fourgeux3, Jean-Michel Robert4, Nicolas Degauque1, Richard Danger1, Jerome Poschmann5, Sophie Brouard1
1CHU Nantes, Universities, INSERM, Center for Research in Transplantation and Translational Immunology (CRTZ), UMR 1064, IJNT, Nantes, France, 2Nantes University, Institut de Recherche en Santé, 3Cibles et Médicaments des Infections et de l’Immunité ICIMed-UJ1155, Nantes, France

**Background:** Granzyme B Regulatory B cells (GZMB+Bregs) have been described in humans in cancer, auto-immune diseases, HIV infection and transplant-plantation. They have demonstrated suppressive properties on CD4+ effector T cells by inhibiting their proliferation and production of cytokines by a mechanism partially dependent on the granzyme B. Yet, their regulatory mechanisms remain unclear.

**Methods:** Single cell RNAseq (scRNAseq) experiments were carried on in vitro induced GZMB+Bregs (purity >95%), non-Breg cells and on CD4/CD25- effector T cells cocultured with GZMB+Bregs or non-Breg cells. Functional analyses were performed to further investigate the role of these interactions with regards to the suppressive properties of GZMB+Breg.

**Results:** We report that the GZMB+Breg population exhibit a specific profile of 149 highly differentially expressed genes, mainly associated with cell proliferation, apoptosis, metabolism, and altered antigen presentation capacity consistent with their differentiated B cells profile. When cocultured with GZMB+Bregs, CD4+CD25- T cells were characterized by strong inhibition of genes for T cells proliferation, activation, IFN pathway, inflammation and apoptosis. Analysis of effector CD4+CD25+ T cells / GZMB+Bregs interactions identified Lymphotoxin alpha (LTA) as a key ligand expressed on GZMB+Bregs. Functional analysis using specific inhibitors was used to test their suppressive properties and we identified Lymphotoxin alpha (LTA) as a new and potent Breg ligand implicated in GZMB+Breg population.

**Conclusions:** We report for the first time for a role of LTA in the induction of GZMB+Bregs, and in its suppressive properties in human.

**BOS 2.8** THE INFLUENCE OF VIRUS-SPECIFIC IMMUNOGLOBULINS AS MODULATORS OF ANTIGEN-SPECIFIC T-CELL EXPANSION

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**Background:** Both cytomegalovirus-specific immunoglobulins (CMV Ig) and varicella zoster virus-specific immunoglobulins (VZV Ig) can contribute to viral control after transplantation. Apart from neutralizing activity towards the virus, little is known about their indirect effects on restoration of virus-specific T-cell immunity.

**Methods:** Therefore, we tested virus-specific T-cell activity in presence or absence of CMV Ig and VZV Ig in blood samples of 31 individuals (20 kidney transplant patients (KTX) and 11 immunocompetent controls). We performed a 6h stimulation assay using CMV or VZV lysate as stimuli. Staphylococcus aureus enterotoxin B (SEB) served as polyclonal stimulus. Activated T cells were flow-cytometrically identified based on co-expression of the activation marker CD69 and the cytokine interferon γ and further characterized regarding their expression of tumor necrosis factor α and interleukin 2. In addition, T-cell proliferation was analyzed by CFSE assay.

**Results:** After short-time stimulation, no differences were detectable for virus-specific T-cell activity in presence or absence of Ig. Interestingly, however, proliferation of CMV-specific CD4 T cells was significantly higher in the presence of CMV Ig (p=0.007) or VZV Ig (p=0.003). The significant increase in T-cell proliferation in presence of CMV Ig was also detectable after stimulation with lower CMV antigen concentrations (CD4 p=0.022; CD8 p=0.012). In contrast, both CMV Ig and VZV Ig led to a clear reduction of polyclonally activated CD4 and CD8 T cells both based on cytokine-induction after short-term stimulation (all p<0.0001) and on proliferation after long-term stimulation in the presence of CMV Ig (CD4: p=0.0013; CD8: p<0.0004) and to a lesser extent of VZV Ig (CD4: p=0.0035).

**Conclusions:** While immunoglobulins did not have any effect on immediate effector function, the presence of immunoglobulins increases the proliferative activity of specific T cells, which may have implications for the therapeutic use of immunoglobulins to restore antigen-specific T-cells in patients with active infections.
Background: Cytomegalovirus (CMV) disease remains a major challenge in solid organ transplant recipients (SOTRs), with a growing interest in developing anti-CMV adoptive cell therapies. Taking into account the current limitations of ab T cell therapies, our goal was to explore a complementary γδ T cell-based immunotherapy.

Methods: Healthy donors (both CMV-seropositive and CMV-seronegative) and kidney transplant recipients (KTRs) undergoing refractory CMV infection were enlisted in this preclinical study. γδ T cells were sorted from peripheral blood, then amplified and activated. γδ T cells were sorted from peripheral blood, then amplified and activated and differentiated phenotype, but low exhaustion, produced IFNγ in the presence of immunosuppressive drugs used in both CMV-seropositive and seronegative-SOTRs. These results pave the way for a future phase I clinical trial.

Conclusions: Altogether, these data provide a proof of concept for a future use of amplified γδ T cells, in the prevention and curative treatment of CMV disease in both CMV-seropositive and seronegative-SOTRs. These results pave the way for a future phase I clinical trial.

Introducing: Although normothermic machine perfusion (NMP) is increasingly used to clinically preserve and evaluate donor livers, little is known how NMP affects the immune compartment. We aimed to investigate the innate immune response during NMP of normal and warm ischemically damaged porcine livers.

Methods: Livers: Livers were exposed to 60 min warm ischemia (WI60, n=5) or not (no WI; n=5) before procurement, followed by NMP for 6 hours with a packed red blood cell based perfusate and subsequent 12 hours normothermic reperfusion with allogenic whole blood (to mimic transplantation). Perfusion levels of aspartate aminotransferase (AST), lactate, tumor necrosis factor-α (TNFα), interleukin 8 (IL8) and 10 (IL10) and transforming growth factor-β (TGFβ) were measured sequentially during NMP and reperfusion. On biopsies taken at different timepoints, expression of C/EBP homologous protein (CHOP), glucose regulated protein 78 (GRP78), B-cell lymphoma 2 (Bcl2) and Bcl2 associated X protein (Bax) were measured to reflect ER stress. Severity of histological injury after reperfusion was scored semi-quantitatively. Statistical analysis was done with two-way ANOVA.

Results: WI60 livers suffered more hepatic injury during NMP, as indicated by the elevated levels of AST (p<0.001), and more severe histological damage (p=0.03 at 1h NMP). Lactate clearance during NMP (p=0.3) and reperfusion (p=0.3) were similar in both groups. TNFα and IL8 concentrations were lower in WI60 during NMP and reperfusion (all p<0.05) (figure). In contrast, TGFβ concentration was higher in WI60 only during NMP (p=0.003), whereas IL10 concentration was similar in both groups during NMP and reperfusion (p=0.3, p=0.5). We observed an increased expression of GRP78 in WI60, both during NMP (p=0.001) and reperfusion (p=0.03). CHOP expression was increased in WI60 during NMP (p=0.04) and reperfusion (p=0.07). There was no difference in expression of Bcl2 (NMP, p=0.9; reperfusion, p=0.4), whereas expression of the Bax was increased in WI60 during NMP (p=0.004), but not during reperfusion (p=0.3).

Conclusion: Warm ischemically injured livers exert a distinct innate immune response compared to healthy livers. The innate immune response seems to shift towards an anti-inflammatory and pro-apoptotic phenotype.

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Background: Ischemia-reperfusion injury (IRI) is a key challenge in liver transplantation leading to short- and long-term failure of the transplanted liver. Machine perfusion (MP) has proven to limit the metabolic consequences of IRI and has the potential to rescue discarded livers. However, the effect of MP on the innate inflammatory response is unknown. We aimed to investigate complement activation and downstream effects that may be targeted to reduce IRI and inflammation during MP.

Methods: Porcine livers (n=24) were exposed to either biliary injury (n=8), global liver injury (n=8), or no liver injury (n=8). Ex situ liver MP was performed with 1 h hypothermic, 1 h rewarming, and 4 h normothermic perfusion. Beiler preservation solution was used during the hypothermic phase. Thereafter, heparinized leukocyte- and platelet-depleted homologous blood was used as perfusate. Perfusion and tissue samples were collected at set time points and analysed for terminal complement complex (TCC) and cytokines (TNF, IL6, IL8) and bile tissue (TNF, IL-1β, IL6, IL8), all p<0.0001 Friedmann test.

Results: During normothermic MP, TCC increased significantly from start (median 11 interquartile range [5.14-17]) to end MP (40 [15-60], p=0.0001). There was no statistical difference between the biliary injury, the global injury, and the no liver injury groups (p=0.5). During normothermic MP cytokines increased significantly in plasma (TNF, IL-6, IL10), in liver tissue (TNF, IL-1β, IL6, IL8) and bile tissue (TNF, IL-1β, IL6, IL8), all p<0.0001 Friedmann test/Mann Whitney test.

Conclusions: Complement and downstream cytokines are strongly and persistently activated during normothermic MP independently of pre-induced liver injury. Cytokines increase significantly despite a leukocyte-depleted perfusate and are thus probably due to liver-derived cytokine production. Future studies should evaluate the source of cytokine production and if complement inhibition can suppress cytokine production during liver MP. Inhibition of complement activation might be a therapeutic option during MP.

BOS2_11 EX SITU PORCINE LIVER MACHINE PERFUSION ACTIVATES THE COMPLEMENT SYSTEM AND INCREASES CYTOKINES INDEPENDENT OF PRE-INDUCED LIVER INJURY

Ida Færden1, Marte Blikseim2, Camilla Schjalmb, Olav Liavæg1, Waleed Majed3, Morten Hagnes1, Tom Eirik Mollnes3, Søren Pischke2
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BOS2_12 TETRAHYDRO-BENZOTHIOPHENE ROR GAMMA T INVERSE AGONISTS TO TARGET TH17 IN SENSITIZED SKIN ALLOGRAFT MOUSE MODEL

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Background: Th17 cells play a critical role in acute cellular as well as in chronic antibody mediated allograft rejection. We have recently designed tetrahydro-benzothiophene derivatives as novel inverse agonists of retinoic acid receptor gamma t (RORyt) and demonstrated in vitro activity in Th17 polarization assay from PBMCs. The objective of the current study is to determine the effect of tetrahydro-benzothiophene derivatives on the rejection of complete mismatch skin graft in a sensitized murine model.

Methods: C57BL/6 mice were sensitized by administration of 107 Balb/c splenocytes (IP) at day 0, 7 and 14 and transplanted with Balb/c skin grafts at day fifteen. Mice were injected daily with a tetrahydro-benzothiophene RORyt inverse agonist (TF-S14, 1mg/kg, IP), or tacrolimus (0.5mg/kg, IP) or combination therapy against IL-2 (IL-2cplx). Here, we aimed to investigate the effect of allograft rejection in this model, donor-specific antibody (DSA) development, in vitro T cell alloreactivity and graft infiltrating leukocytes were assessed.

Results: TF-S14 therapy in combination with rapamycin and anti-IL-6 mAb led to prolonged survival of fully mismatched (BALB/c; MST = 30.5d) and MHCII mismatched BM12 (no CD8 T cell alloreactivity) skin grafts. Indicated groups were treated with different anti-CD8 mAbs, depleting either all CD8+ populations (anti-CD8a) or specifically CD8+ T cells (antiCD8b). To dissect the mechanisms of allograft rejection in this model, donor-specific antibody (DSA) development, in vitro T cell alloreactivity and graft infiltrating leukocytes were assessed.

Conclusions: The novel tetrahydro-benzothiophene RORyt inhibitor offers a new therapeutic mechanism to treat rejection in highly sensitized patients regardless of degree of donor mismatch.
**BRIEF ORALS**

**Translational transplant immunology**

**BOS2_14**

**RESEARCH FOR NOVEL MECHANISM OF IMMUNOSUPPRESSION THROUGH PD-1/PD-L1 PATHWAY**

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**Background:** PD-1/PD-L1 pathway has begun to draw attention in cancer treatment as an immune checkpoint pathway, which is known to inhibit the activation of immune cells through PD-1 molecule. In the field of transplantation, it seems possible to inhibit immune response by activating these PD-1/PD-L1, as opposed to cancer treatment. We would like to check if the immune response after implantation can be suppressed, the rejection can be prevented, and the graft survival rate can be improved by using soluble PD-L1, a ligand capable of activating PD-1 on the surface of T lymphocytes.

**Methods:** Using BALB/c mice and C57BL/6 mice, the mouse heart transplant model is constructed, and CNI (tacrolimus) and soluble PD-L1 Fc are applied to this model to compare the immune response and transplant performance after implantation. Group 1 : FK group (n=15). Group 2 : soluble PD-L1 Fc group (n=15). Group 3 : FK + soluble PD-L1 Fc group (n=15). The survival rate of the three groups, histologic properties of the transplant, and the subsets of immune cells through mouse blood FACS, and indirectly predict the incidence of inflammatory reactions by comparing quantities of inflammatory cytokine in the blood.

**Results:** The group using sPD-L1 Fc alone showed a similar degree of graft survival to the group without immunosuppressants, and the FK group identified a graft survival of less than 45 days. The group, which used FK and sPD-L1 Fc together, identified between 60% and 45 days of graft survival. This increase in graft survival in FK + sPD-L1 Fc group was also reflected in biopsy results, which showed that inflammatory cell infiltration was the mildest in the heart tissue of FK + sPD-L1 Fc group. Lymphocyte, macrophage, and FOXP3 + cell are increased in allograft heart tissue in combination of FK and sPD-L1 Fc group. Perivascular inflammation is reduced in combination of FK and sPD-L1 Fc group.

**Conclusions:** sPD-L1 alone is not sufficient to prevent allograft rejection. Combination of FK and sPD-L1 induce long-term graft survival. Systemic cell count change or inflammatory cytokine level is not clear to explain this result. Further assessment focused on localized change occurring in cardiac allograft is necessary.

**BOS3_1**

**THE (PRO)RENIN RECEPTOR IS INVOLVED IN KIDNEY ORGANOID DEVELOPMENT**

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**Background:** The (pro)renin receptor [(P)RR], a receptor for prorenin and renin, is widely distributed in the body, including the kidneys. Studies in (P)RR knockout mouse models indicate that (P)RR ablation can be detrimental to renal development and function. However, the lack of human models hinders investigation into the role of (P)RR in human kidney development. The advent of human induced pluripotent stem cell (iPSC) – derived kidney organoids provides a tool to study the role of (P)RR in human kidney development.

**Methods:** To investigate the effects of (P)RR knockdown on kidney organoid development, human iPSC – derived kidney organoids were generated, as described previously. The model of kidney organoids was monitored morphologically and through protein expression analysis of nephron markers by immunohistochemistry staining which was quantified by Image J.

**Results:** After silencing the (P)RR at the initial stage of differentiation, the size of iPSCs-derived organoids was substantially smaller, but the size of tubular structures was bigger. We observed a decrease by 50% in both W1T1 (glomerular cell marker) and PDGFRα (stromal cell marker) expressions in (P)RR knockdown organoids, a 4-fold and 2-fold increase in expressions of fibrogenic cell markers α-SMA and COL1A1 respectively, and no change in Villin1 (proximal tubular cell marker) and Cadherin-1 (distal tubular cell marker) expression. Additionally, (P)RR knockdown at the stage of nephron progenitor cells induction decreased the expressions of Villin1 and Cadherin-1 in organoids by 50% and 60% respectively, while it induced a 4-, 3-, 2- and 2-fold increase in the expressions of CD31 (endothelial cell marker), PDGFRα, α-SMA and COL1A1 respectively.

**Conclusions:** This study shows that (P)RR silencing at the initial stage of differentiation or at the stage of nephron progenitor cells induction impaired normal development of kidney organoids. Its absence caused a shift in the direction of fibrogenic cells. This study provides new insights into the understanding the role of (P)RR in human kidney development.

**BOS3_2**

**ENGINEERING VASCULARIZED ENDOCRINE PANCREAS TO CURE TYPE 1 DIABETES**

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**Background:** The (pro)renin receptor [(P)RR], a receptor for prorenin and renin, is widely distributed in the body, including the kidneys. Studies in (P)RR knockout mouse models indicate that (P)RR ablation can be detrimental to renal development and function. However, the lack of human models hinders investigation into the role of (P)RR in human kidney development. The advent of human induced pluripotent stem cell (iPSC) – derived kidney organoids provides a tool to study the role of (P)RR in human kidney development. The (pro)renin receptor [(P)RR], a receptor for prorenin and renin, is widely distributed in the body, including the kidneys. Studies in (P)RR knockout mouse models indicate that (P)RR ablation can be detrimental to renal development and function. However, the lack of human models hinders investigation into the role of (P)RR in human kidney development. The advent of human induced pluripotent stem cell (iPSC) – derived kidney organoids provides a tool to study the role of (P)RR in human kidney development.

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**Conclusions:** This study shows that (P)RR silencing at the initial stage of differentiation or at the stage of nephron progenitor cells induction impaired normal development of kidney organoids. Its absence caused a shift in the direction of fibrogenic cells. This study provides new insights into the understanding the role of (P)RR in human kidney development.
**BRIEF ORALS**

**Transplant Plus: Regenerative therapies and Xenotransplantation**

Conclusions: The engineered vascularized endocrine pancreas offers a fully biocompatible construct, restoring a matrix environment to the graft near-identical to that of native islets and provides mechanical protection which allows transplanted islets to engraft and function long-term.

**GENERATION OF VASCULARIZED ENDOCRINE CONSTRUCTS FOR TYPE 1 DIABETES**

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Background: Disruption of islet extracellular matrix (ECM), poor vascularization, inflammatory reaction and immune destruction lead to a significant islet loss following intraportal islet transplantation. Human amniotic membrane (HAM) is known for its rich ECM, immunomodulatory, anti-inflammatory and anti-fibrotic properties. Blood outgrowth endothelial cells (BOECs) constitute an ideal source of autologous endothelial cells. The aim of this work was to investigate whether incorporation of pre-vascularized insulin-secreting organoids (PVO) into a pre-vascularized HAM-derived hydrogel will provide an optimal micro-environment and support engraftment and function of the insulin-secreting endocrine constructs.

Methods: PVOs composed of different ratios of dissociated insulin-secreting cells (EndoC-βH1 rat islet cells), human amniotic epithelial cells (hAEcs) and BOECs (1000 cells/organoid) were generated on microwells. Hydrogels were obtained by acidic-digestion of decellularized, lyophilized HAMs collected from C-section-procured placenta. PVOs along with additional BOECs were loaded in the hydrogel (5 mg/ml) and cultured in a vasculogenic media. Cell distribution, migration and proliferation in hydrogel was assessed in vitro by immunohistochemical staining. Insulin-secreting cells function was also assessed. To evaluate in vivo function, the best performing PVOs were admixed with BOECs (2x10^6 BOECs/ml), loaded in hydrogel and cultured in vasculogenic media for 2 days to enhance endothelial cell assembly into tubular, vascular-like structures. Vascularized constructs were then transplanted under the skin of diabetic NSG mice.

Results: In vitro studies showed that the best performing PVO ratio was composed of 50% insulin-secreting cells, 25% hAEcs and 25% BOECs. Generated PVOs displayed a good function in vitro when loaded in HAM-derived hydrogel alone and with the additional BOECs. In addition, engineered HAM-hydrogel supported the development of the vascular-like structures, with a strong positive staining for CD31. Our findings suggest that insulin-secreting constructs composed of PVOs and BOECs-vascularized HAM-derived hydrogel could be a promising strategy of β cell replacement therapies in alternative sites other than the liver.

**ALLOGENEIC MESENCHYAL STROMAL CELL THERAPY IN KIDNEY TRANSPLANTATION: SHOULD REPEATED HLA MISMATCHES BE AVOIDED?**

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Background: While most studies have investigated autologous mesenchymal stromal cells (MSC) in kidney transplantation (KTx), 2 recent trials studied allogeneic MSC, as an off-the-shelf product is more feasible in clinical settings. Trial A investigated MSC therapy in KTx by selecting MSC to avoid repeated HLA antigen mismatches (MM) between kidney and MSC donors (Figure 1A), while Trial B did not perform MSC selection. We performed in-depth analysis to determine whether repeated HLA MM should be avoided to prevent donor-specific antibody (DSA) formation.

Methods: Trial B patients (n=10) received 1 infusion of MSC at day 3 post-KTx, while Trial A patients (n=10) received 2 infusions at week 25 and post-25 KTx. Patients and donors were HLA typed for 11 loci at the second field. Two Trial B patients were excluded because no material for high resolution typing was available. Amino acid mismatch (AAMM) analysis with HLA-EMMA was performed between kidney donor and recipient and MSC donor and recipient, and repeated AAMM were identified (Figure 1B). Single antigen bead (SAB) data up to 5 years post-Tx were analyzed.

Results: Previously, DSA were reported in 2 out of 8 Trial B patients within 1 year post-Tx. Re-analysis of the SAB data in the light of high resolution typing revealed that 1 previously DSA detected at 1 month post-Tx was misclassified. In the same patient, DSA were detected directed against a shared AAMM (55R). As this DSA was detected 16 months post-KTx, it is unlikely that it was induced by the MSC. In another patient, previously assigned DSA were dismissed due to high background signal in the SAB assay. There was no DSA formation in Trial A. In Trial B, 4 out of 8 patients had repeated antigen MM, while in Trial A, 1 repeated antigen MM occurred. Total repeated AAMM were higher in Trial B, but this was not statistically significant (median 16 versus 8, p = 0.056). Importantly, although 1 Trial A patient did not have any repeated antigen MM for HLA-DQB1, there was a high number of AAMM (14).

Conclusions: Selection of MSC to avoid repeated HLA MM at the split antigen level is not sufficient to prevent repeated MM at the amino acid level. As the clinical relevance of repeated AAMM seems limited for the risk of DSA, our study suggests that it is not necessary to prevent repeated HLA MM in allogeneic MSC therapy in KTx to prevent DSA.
**BRIEF ORALS**

**Transplant Plus: Regenerative therapies and Xenotransplantation**

**BOS3.5** DEVELOPMENT OF AN ADVANCED PLATFORM FOR RAPIID NORMOTHERMIC MACHINE PERFUSION EQUIPPED WITH A BIOREACTOR SEEDED WITH MESENCHYMAL STEM CELLS

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**Background**: Mesenchymal stem cells (MSCs) exert immunomodulatory and regenerative effects in hepatic ischemia reperfusion injury (IRI). Coupling MSCs-based therapy with Normothermic-Machine-Perfusion (NMP) could enable to more efficiently mitigate the detrimental consequences of IRI in high-risk livers. We developed an advanced perfusion system for rat liver NMP equipped with a bioreactor seeded with viable MSCs.

**Methods**: The study includes 2 work packages (n=5 each group): 1) Development: bioreactors with 2x10^7 human MSCs were connected to the NMP circuit and subjected to 4 h-liverless perfusion (Liverless-NMP). Perfusion samples were serially collected, MSCs were harvested at the end of perfusion; 2) Bioreactor-based liver NMP: rat livers underwent 30 min-cold storage and were perfused for 4 h on the MSCs-bioreactor-based NMP circuit (Liver-NMP). Bioreactor samples were collected throughout and after NMP.

**Results**: During Liverless-NMP, MSCs remained viable and released media and extracellular vesicles (EVs). Flow cytometry of cells harvested after the procedure revealed the expression of stemness markers, indicating that MSCs were not affected by the perfusion itself. Perfusion samples collected over bioreactor-based liver NMP showed higher concentrations of MSCs-related mediators and EVs compared to Liverless-NMP. Livers of the Liver-NMP+bioreactor group produced more bile, released less damage biomarkers, and secreted higher amount of acute phase proteins relative to standard NMP. Bioreactor-based liver-NMP was likewise associated with higher ATP production and reduced tissue necrosis, as well as lower concentration of inflammatory mediators, coupled with higher amount of protective factors.

**Conclusions**: We provide a novel MSCs-based protocol for liver NMP, thereby creating a modern perfusion platform. The integration of a bioreactor seeded with viable MSCs enables to induce a liver-tailored response, thus allowing a more efficient utilization of MSCs benefits during NMP. Compared to standard NMP, livers exposed to MSCs-derived secretome showed improved mitochondrial function, sustained cell viability, reduced inflammation, and activation of healing processes.

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**BOS3.6** THE CYTOPROTECTIVE EFFECTS OF EXTRACELLULAR VESICLES DERIVED FROM HUMAN AMNIOTIC EPITHELIAL CELLS ON PANCREATIC ISLETS

Reine Hanna1,2, Laura Man Fonseca1,2, Fanny Lebreton1,2, Juliette Bignard1,2, Kevin Bellafatto1,2, Victor Galván Chacón1,2, David Cottet-Dumoulin1,2, Thierry Berney1,2, Philippe Compagnon1,2, Domenico Bosco1,2,4, Ekerzhivili4

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**Background**: A considerable islet loss is observed following islet transplantation in type 1 diabetes patients due to hypoxia, inflammation and poor vascularization. Human amniotic epithelial cells (hAECs) have been shown to have cytoprotective effects on pancreatic islets under stressful conditions, due to their anti-inflammatory and immunomodulatory and regenerative properties. The aim of this study is to investigate whether extracellular vesicles derived from these cells (hAECs-EVs) would be able to exert similar properties.

**Methods**: hAECs-EVs were isolated from conditioned culture media of hAECs by sequential ultracentrifugation and characterized by nanoparticle tracking analysis, transmission electron microscopy, western blot and mass spectrometry. To test their cytoprotective effects, islets subjected to hypoxia in vitro were either treated or not with hAECs-EVs. The islet function was assessed by insulin, glucose-stimulated insulin secretion assay and viability by TUNEL staining.

**Results**: Characterization of hAECs-EVs showed the successful isolation of these vesicles. hAECs-EVs had a mean diameter of 160 nm and expressed EV markers such as CD9, CD63 and TSG101. Human islets exposed to hAECs-EVs, when compared to control, had an increased insulin secretion. In the future, we plan to better understand the mechanisms underlying the observed effects.

**Conclusions**: These preliminary results suggest that hAECs-EVs might become an interesting tool for protecting pancreatic islets from hypoxia.

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**BOS3.7** INSULIN-INDEPENDENCE IN LARGE ANIMAL MODELS AFTER PANCREATECTOMY AND AUTOTRANSPLANTATION OF 3D-BIOPRINTED BIONIC PANCREATIC PETALS

Michal Sadowski1,2, Marta Klak1, Andrzej Berman1,2, Oliwia Janowska1, Dominika Ujazdowska1, Sylvester Domanski2, Tomasz Dobrzański2, Dominika Szkopek1, Anna Filip1, Katarzyna Roszkowicz-Ostrawska2, Agata Kondej1, Jarosław Wolński1, Artur Kaminski1

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**Background**: The first milestone in a new therapy for the treatment of T1D is the development of 3D bioprinted petals consisting of pancreatic islets and biomaterials. The aim of the study was to demonstrate the functionality of pancreatic islets in in vivo studies on large animals.

**Methods**: Domestic pigs were the research model. The animals were divided into 4 groups: 1) healthy pigs (Control; n=3); 2) animals with T1D after pancreatectomy, treated with insulin (T1D+n=3); 3) animals after pancreatectomy and autotransplantation of pancreatic islets to the liver (LIVER; n=3); 4) animals with T1D after pancreatectomy, which were autotransplanted with bionic petals (3D-PETALS; n=3). The effectiveness of the transplantation (TX) was assessed by the concentration of glucose, insulin intake and C-peptide. The observation lasted 1 month.

**Results**: The results showed that in the LIVER group, insulin intake within 3 weeks decreased by 71% compared to the demand before TX. Whereas 1 month after TX, the demand decreased by 62% compared to n=3). The LIVER & 3D-PETALS group showed that the insulin intake in 3 weeks after TX decreased by 65%, and within a month decreased by 84%. In the 4th week after TX, the insulin intake average in the T1D group was 8.17U, while in the LIVER group=2.44U and in the 3D-PETALS group=1.69U. Islet TX significantly reduced insulin intake (T1D vs LIVER; p<0.0001 and T1D vs 3D-PETALS; p<0.0001). Glucose measurement showed significant changes. After 1 month of follow-up, glucose levels were significantly lower in the LIVER vs T1D (265.8mg/dL vs 310.2mg/dL, p<0.0001) and 3D-PETALS & T1D (195.7mg/dL vs 310.2mg/dL, p<0.0001). Most importantly, glycemic levels were also significantly lower between the LIVER & 3D PETALS groups (265.8mg/dL vs 188.3mg/dL, p<0.0021). The concentration of C-peptide during the study was 0.14ng/ml.

**Conclusions**: Bioprinted 3D-PETALS derived from 3D-CM-bioceramic significantly reduces diabetic parameters. Thus, it seems to be an effective therapy for people with T1D.

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**BOS3.8** A MICROFLUIDIC BILE-DUCT-ON-A-CHIP PLATFORM FOR STUDYING BILIARY EPITHELIUM IN A DISH

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**Background**: Damaged biliary epithelium after transplantation can result in loss of graft function due to impaired reparation of. Accurate in vitro models for studying the effects of different organ preservation strategies (e.g., machine perfusion), prolonged ischemia times and reperfusion injury on the integrity of the biliary epithelium are lacking. LGR5+ intrahepatic cholangiocyte organoids (ICO) do allow for the in vitro expansion of healthy cholangiocytes. However, access to the organoids lumen, which represents the luminal side of a bile duct, is limited and can only be accessed by disrupting the three-dimensional organoid structure. Therefore, we aimed to establish a bile-duct-on-chip (BDOC) platform using ICO with an accessible lumen to study the biliary epithelium in vitro.

**Methods**: Four-channel BDOC (dimensions: L1cm, WH:500µm) were prepared using polydimethylsiloxane (PDMS). All channels were filled with collagen type-I or a hydrogel derived from decellularized liver extracellular matrix, and viscous finger patterning was used to create a lumen (Ø0.300µm) inside the hydrogel. ICO were initiated from human donor liver biopsies (n=5) and added to the channels (100/cells/channel) to grow for 21 days at 37°C. Integrity of the biliary epithelium was monitored using confocal microscopy and histology.

**Results**: The ICO cells self-organized into a columnar monolayer within 21-days. They expressed cholangiocyte markers cytokeratin-7 and 19. Zonula occludens-1 and anion exchange protein 2 staining revealed that the cells were polarized similar to biliary epithelium. After 21 days, the cell layer formed an impermeable barrier against 70kDa FITC-Dextran. Glycocalyx components, like siallated carbohydrates, could be removed using neuraminidase. The cells were able to restore the glycocalyx, as shown by intact apical sialic acid staining.

**Conclusions**: This BDOC platform can simulate small diameter intrahepatic bile ducts in vitro and allows for assessment of treatment or the biliary epithelium from the luminal side. ICO-derived cells formed a polarized cholangiocyte barrier and were able to restore the glycocalyx after enzymatic treatment. This platform is ready to assess the effect of organ preservation strategies and biliary regeneration.
**BRIEF ORALS**

**Transplant Plus: Regenerative therapies and Xenotransplantation**

**TACROLIMUS-LOADED MIXED THERMOSENSITIVE HYDROGEL FOR IMPROVING THE OUTCOME OF SKIN AND VASCULARIZED COMPOSITE ALLOTRANSPLANTATION**

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**Background:** The previous study showed the mixed hydrogel, consisting of P-Lys-Ala-PLX and Pluronic® F127, had high drug encapsulation efficiency and appropriate drug release rates, making it a promising option for drug delivery. The study aims to evaluate the effectiveness of using this mixed thermosensitive hydrogel as a controlled drug delivery system for immunosuppressant drug, such as tacrolimus to prevent rejection and maintain allograft function with minimal systemic side effects.

**Methods:** Skin or vascularized composite allografts from Brown-Norway were transplanted to Lewis rats. The recipients were divided into three groups and received either daily systemic injections of 2mg/kg tacrolimus, a single mixed thermosensitive hydrogel injection, or a single mixed thermosensitive hydrogel injection loaded with 10mg tacrolimus. The mixed hydrogel formulation was used as the injectable carrier for tacrolimus. Tacrolimus concentration, kidney function, peripheral immune response, allograft survival, histopathological changes, chimerism, and nerve regeneration were observed.

**Results:** Recipients that received a single mixed thermosensitive hydrogel injection loaded with tacrolimus showed an initial burst release of tacrolimus in the blood during the first 15 days after transplantation, followed by a subsequent decrease to subtherapeutic levels that remained detectable for at least 90 days. The levels of creatinine and blood urea nitrogen among groups were comparable. The single mixed thermosensitive hydrogel injection loaded with tacrolimus had a local effect, with less infiltration of CD3+ T cells in the allograft but no significant changes in the levels of regulatory and effector T cells in blood circulation. This resulted in long-term graft survival for skin and vascularized composite allotransplantation. Improved outcomes were also indicated by the presence of chimerism and nerve regeneration.

**Conclusions:** The mixed hydrogel formulation is a safe and reliable drug delivery system with potential advantages for skin and vascularized composite allotransplantation. It is a promising system for the delivery of immunosuppressive drugs in the field of transplantation.

**SINGLE CELL RNA SEQUENCING ANALYSIS OF HUMAN AMNIOTIC EPITHELIAL CELLS TO DECIPHER THE MECHANISMS OF IMMUNOMODULATION CONFERRED TO PANCREATIC ISLETS**

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**Background:** Long-term function of islet graft remains a challenge due to inflammatory, ischemic, allogenic and autoimmune aggression responsible for damages to the transplanted islets. Incorporation of human amniotic epithelial cells (hAECs) into islet organoids has proven to be a valuable strategy to inhibit inflammation- and hypoxia-mediated islet destruction, improve their engraftment and enhance islet survival after transplantation. However, mechanisms of the regenerative, immunomodulatory and anti-inflammatory properties of those cells remain elusive and need to be investigated. This work aims at identifying these mechanisms using single-cell RNA sequencing (scRNA-seq).

**Methods:** hAECs were isolated from 3 amnions obtained from C-section-processed placentae, and frozen immediately after isolation. Cells were thawed and dead cells were sorted out by fluorescence-activated cell sorting. To identify genes and cell subpopulations with regenerative, immunomodulatory and anti-inflammatory properties that may play a role into strengthening islet engraftment, function and viability, libraries were generated on a Chromium controller (10x Genomics) and scRNA-seq was carried out on an Illumina NovaSeq 6000 generating 100-250 bp pair-end reads. Expression data were normalized, filtered, and clustered using the Seurat V4 version through the open access Cellenics online platform. The identification was followed by validation on flow-sorted cells using qPCR and immunofluorescence.

**Results:** We identified 4 distinct cell types expressing established markers for epithelial, stromal and rare populations, showing hAECs comprise different cell subpopulations. Most of the clusters included cells from each group. Homogeneity in clusters, genes and pathways were found between the 3 samples of hAECs. We expect to identify upregulation of pathways related to immunomodulation in one of those clusters.

**Conclusions:** Our study revealed the shared regulation of genes and pathways in the 3 samples of hAECs for the first time at single-cell resolution, and demonstrated their relevance to islet engraftment and for the protection of the islet graft. A better understanding of immunomodulatory properties of hAECs will be of utmost importance for the development of cell-based therapies for type 1 diabetes.
**Brief Orals**

**Transplant Plus: Regenerative therapies and Xenotransplantation**

**BOS3_12**  *Feasibility of manufacture of chimeric antigen receptor (CAR)-regulatory T cells (TREGs) from patients with end-stage renal disease (ESRD)*

Hervé Bastian1, Nadia Lounnas-Mourey2, Pierre Heinemindinger2, Benjamin Hsu2, Katharina Schreeb2, Claire Chapman2, Emily Culme-Seymour2, Gillian Atkinson2, Diego Cantarovich3

1Sangamo Therapeutics, Valbonne, France, 2Sangamo Therapeutics, Valbonne, France, 3Nantes University Hospital, Institut of Transplantation, Urology and Nephrology (ITUN), INSERM UMR 1064-CR2TI, Nantes, France

**Background:** Gene-modified cell therapy with Tregs is a promising approach to prevent graft rejection and induce immunological tolerance in organ transplantation. We are developing a cell therapy comprising autologous naïve Tregs that are isolated from leukapheresate, transduced with lentiviral vector encoding a CAR recognising human leukocyte antigen class I molecule A*02 (HLA-A*02) and expanded ex vivo before cryopreservation as resultant drug product (TX200-TR101) (see figure). In an ongoing first in human study (NCT04817774), kidney transplant recipients will receive a single infusion of TX200-TR101 2-3 months after transplantation. The Phase 0 study described here evaluated the feasibility of manufacture of TX200-TR101 for the target population, i.e., ESRD necessitating kidney transplantation. Participants in this study did not receive an infusion of drug product.

**Methods:** Four patients with ESRD and HLA-A*02 negative typing underwent leukapheresis to collect starting material for manufacture of TX200-TR101. Manufacturing success criteria were predefined as cell quantity in each batch of ≥10^4 cells/kg body weight, cell viability of ≥70% and transduction efficiency of ≥20%. Other variables included Treg identity and maturation by phenotyping, residual bead count, vector copy number, level of endotoxin, sterility and presence of mycoplasma. The characteristics of leukapheresate starting material and resultant drug product from ESRD patients were compared with those of commercially purchased leukapheresate and resultant drug product from 10 healthy donors.

**Results:** No safety issues were identified during leukapheresis collections. Batches of drug product were manufactured from all 4 patients with ESRD and met the predefined manufacturing success criteria. White blood cell populations in leukapheresate, and quality, quantity and functional activity of manufactured CAR-Tregs were comparable between patients with ESRD and healthy donors. CAR-Treg drug product from 1 patient with pre-existing lymphopenia had similar high quality but reduced cell quantity compared with batches from the other ESRD patients, although yield was still above the predefined target minimum number of cells.

**Conclusions:** Manufacture of high-quality naïve CAR-Tregs from patients with ESRD is safe and feasible.

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**BOS3_13**  *Auxiliary liver xenotransplantation technique in a transgenic pig to a non-human primate model*

Kyo Won Lee4*, Min Jung Kim2, Jae Berm Park1

1Samsung Medical Center, Seoul, South Korea, 2Seoul Medical Center, Seoul, South Korea

**Background:** Xenotransplantation using pigs’ liver has long been proposed as an alternative method to overcome this donor shortage issue or more importantly as a bridge to allotransplantation. However, xenotransplantation in a pig to primate model has been challenged by profound thrombocytopenia and coagulation disorders, leading to uncontrollable hemorrhage and early mortality. Here we suggest that the left auxiliary technique using left lateral lobe graft can potentially be a useful model to help broaden knowledge on liver xenotransplantation (XLT).

**Methods:** Fifteen consecutive (XLT) was carried out using male cynomolgous monkeys of specific pathogen-free health status as recipients. All experiments were approved by the Institutional Animal Care and Use Committee in Seoul National University Hospital (SNNU-IACUC). Right auxiliary XLT was performed in two cases, orthotropic XLT was performed in eight cases, and left auxiliary XLT was performed in five cases.

**Results:** Right auxiliary XLT cases were not survived after surgery from the massive bleeding during the recipient right liver haemectomy. Right liver of primate encircle the inferior vena cava (IVC) and dissection between the right liver and IVC was the main cause of bleeding. Orthotropic XLT cases survived less than seven days which was resulted from the profound thrombocytopenia and coagulation disorder. Among the five left auxiliary XLT cases, two cases survived more than three weeks without profound thrombocytopenia and anemia. One of that two animals survived 34 days after XLT which was reported longest survival after XLT performed in primate.

**Conclusions:** Left auxiliary XLT is suitable operational technique for XLT experiment using non-human primate. With this technique, risk of thrombocytopenia and coagulation disorder can be minimized and long term survival after XLT can be obtained which was essential to assess the graft condition such as rejection after XLT.
**BRIEF ORALS**

**Transplant Plus: Regenerative therapies and Xenotransplantation**

**BOS3_14**
**LONG-TERM (2 YEARS) SURVIVAL OF PORCINE TO NONHUMAN PRIMATE LIFE-SUSTAINING KIDNEY XENOTRANSPLANTATION**

**Ahmad Karadagi**1, Takayuki Hirose1, Grace Lassiter1, Tosihide Tomosugi1,2, Ryo Otsuka1,2, Daniel Filt1,2, Ranjith Anand3, David Heja3, Jacob Layer3, Ivy Rosales1,2, Susan Low3, Eliezer Katz3, Michael Curtis3, Wenning Qin3, Michele Youd3, Tatsuwo Kawai1,2

1Massachusetts General Hospital, Boston, United States, 2Harvard Medical School, Boston, United States, 3EGenesis, Inc., Cambridge, United States

**Background:** Xenotransplantation holds immense potential as replacement therapy for end stage renal disease. Development of porcine xenografts with triple-knock-out of xenotagonists (TKO) and knockin of human transgenes have improved xenograft survival considerably.

**Methods:** TKO donors, and TKO donors also expressing various human transgenes with additional deletion of porcine endogenous retrovirus. Life-sustaining kidney transplantation was performed in cynomolgus macaques using these genetically modified porcine grafts. In B and T cell depletion was followed by a short course of corticosteroid and tacrolimus. Immunosuppression was maintained with tacrolimus and mycophenolate mofetil. IgG/M antibodies binding to donor porcine endothelial cells were surveyed by flow cytometry.

**Results:** Overall recipient survival is significantly superior with donor organs expressing human transgenes compared to TKO only grafts (median, 283 vs. 5 days, p<0.0018). Log-rank, figure 1A). De novo donor-specific antibodies (DSA) were detected in serum from some recipients but did not correlate with clinical outcome and pathological findings of antibody mediated rejection in all cases (figure 1B). Similarly, pre-transplant anti-porcine antibody titers showed no correlation with survival, where the longest surviving animal (>740 days) showed higher comparative pre-transplant IgM binding. Post-transplant DSA was generally associated with antibody mediated rejection but not thrombotic microangiopathy, which were the common causes for rejection (figure 1C).

**Conclusions:** Life-sustaining renal xenograft survival exceeding two years was achieved in cynomolgus macaques using TKO porcine kidneys expressing multiple human transgenes. Although the outcome is heterogeneous, pre-transplant anti-porcine antibody titer binding do not correlate with clinical outcome. Post-transplant de novo DSA was generally associated with antibody mediated rejection but not with thrombotic microangiopathy. These long-term findings solidify the potential of kidney xenotransplantation.

**BOS4_1**
**CLINICAL TRANSPLANTATION AND IMPLEMENTATION OF A BIO-ARTIFICIAL PANCREAS: A QUALITATIVE STUDY EXPLORING THE PERSPECTIVES OF PATIENTS WITH TYPE 1 DIABETES**

**Dide de Jongh**1,2, Eline Bunnik1, Emma Massey2

1Erasmus MC, Dept. of Medical Ethics, Philosophy and History of Medicine, Rotterdam, Netherlands, 2Erasmus MC, Dept. of Nephrology and Transplantation, Rotterdam, Netherlands

**Background:** In preclinical research settings the bio-artificial pancreas is being developed that can be implanted in patients with diabetes type 1 to produce and secrete insulin. First-in-human clinical trials are expected in a few years. In this interview study, the perspectives of patients with type 1 diabetes on the clinical translation and implementation of the bio-artificial pancreas were explored to elucidate their perspectives, needs, and preferences.

**Methods:** An interview guide was developed and pilot-tested. Semi-structured interviews were carried out with 20 type 1 diabetes patients. Inclusion was stopped once data saturation was reached. The interviews were audio-taped, and transcribed for content analysis with an inductive approach was conducted to categorize the data, and develop themes within a coding frame.

**Results:** Most patients reported a range of expected advantages of the bio-artificial pancreas as a potential treatment that could be divided into four themes: the ethical value benefits (e.g. better health and psychological outcomes), autonomy (e.g. more freedom and flexibility in their daily lives), privacy (e.g. a therapy invisible to others to avoid stigmatization and without the risk of sharing personal health data) and justice (e.g. suitable for patients without self-management skills required for device-based treatment). Further, preferences regarding informed consent procedures, the implantation site and follow-up care were mentioned. Patients also shared their views on rescinding control of their treatment, and their concerns regarding the irreversibility of the surgical procedure, cell sources used and accessibility of the therapy.

**Conclusions:** Insights from this interview study allow researchers, policy makers and clinicians to align the clinical translation and implementation of the bio-artificial pancreas with patients’ needs and preferences. Alignment is likely to improve chance of successful implementation.

**BOS4_2**
**PSYCHOLOGICAL SCREENING AND FOLLOW-UP CARE FOR LIVING LIVER DONORS: 5-YEAR PROSPECTIVE COHORT DATA FROM A SINGLE ACADEMIC CENTRE**

**Leoniëke Kransenburg**1, Alicia Chorley2, Emma Massey2, Sohal Ismail1, Hayo Ter Burg1, Robert Minnie1, Markus Boehnert1

1Erasmus MC, Psychiatry, Rotterdam, Netherlands, 2Erasmus MC, Surgery, Rotterdam, Netherlands, 3Erasmus MC, Internal medicine, Rotterdam, Netherlands

**Background:** Transplantation with a living donor has proved to be an effective solution for patients on the waiting list for a liver transplantation. To maximise the benefits that living donor liver transplantation offers, careful donor screening is an absolute prerequisite. In our centre, this screening also involves standard psychological screening by a licensed health care psychologist, and if indicated psychological treatment.

**Methods:** We report on the psychological screening and care for all potential living donor candidates who entered the program since 2018. Donors were screened using the ELPAT Psychosocial Assessment Tool (EPAT), both the interviews and the questionnaires. Data on additional psychological care was retrieved from the medical records.

**Results:** One hundred and two donors (54 female, mean age 35.4 (SD 9.7)) underwent psychological screening for living liver donation. Intended recipients were first-degree relative (52), partners (10), other family members (17), friends (9) and unrelated (14, of which 6 undirected and 8 directed). Ambivalence was present in 9 cases. Pressure from others to donate was reported in 3 donor candidates, and 10 experienced some type of moral obligation to donate. All potential donors were given the possibility to opt out from donation during the whole process until surgery was started. Fifty-eight donor candidates had sought professional mental health support and/or used psychotropic drugs in the past. However, the average number of current antidepressants treated, as measured by validated screening questions (PHQ-2 and GAD-2) were low. Of all candidates, 2 were rejected for psychological reasons. From this cohort, 38 eventually donated part of their liver. Of these, 12 received additional psychological care, for various reasons. In addition 3 donor candidates who were medically unfit to donate received counselling to improve coping.

**Conclusions:** The EPAT is a useful tool for living liver donor screening, covering all important psychological domains. Providing psychological treatment on indication proved to be a feasible way for this group to deal with potential psychological complaints. Donors appreciate knowing from the start that it was possible to receive additional psychological care, and 12 out of 38 living liver donors made use of this offer.
PSYCHOSOCIAL EVALUATION OF LIVING KIDNEY DONORS IN QATAR – PROCESS AND OUTCOMES OF THE COMMITTEE FOR OVERSIGHT OF LIVING DONATION

Biadh Fadlallah
Hamad Medical Corporation, Director of Qatar Organ Donation Center, DOHA, Qatar

Background: Transplants from living donors comprise 38% of global kidney transplant activity. They offer better outcomes for many recipients, but several socioeconomic and psychological factors must be addressed in the evaluation of prospective living kidney donors (PKD), to optimize care in local contexts. The Committee for Oversight of Living Donation (COLD) was established in Qatar in 2014 to provide standardized multidisciplinary psychosocial evaluation of all PLKD, to ensure adherence to protocol and ethical standards, and to enable appropriate care provision throughout the evaluation and donation processes.

This study describes the COLD protocol for PKD evaluation and reports outcomes of eight years’ experience evaluating PKD.

Methods: This observational, retrospective cross-sectional study used data manually extracted from the COLD database of all PLKD who presented Sep 2014 – Dec 2022 inclusive. Donors’ demographic data, associated relationships with intended recipients, and outcomes of psychosocial evaluation (acceptance/decline as potential donor) were reviewed and analyzed using descriptive statistics. Reasons for decline were thematically coded.

Results: 896 PLKD were evaluated by the COLD; 50% were Qatari citizens and 50% non-citizens from 43 different countries. 96% declared a relationship with the intended recipient (76% genetically related; 20% emotionally related). Of those unrelated, 22 claimed to be directed altruistic donors and 19 non-directed altruistic.

Conclusion: Of those declined, 17 were genetically related, 7 emotionally related, 22 claimed to be directed altruistic donors and 19 non-directed altruistic. More than half (56%) of those declined were psychological, with the most common reasons for decline were psychological unfitness, insufficient socioeconomic supports, coercion (by employer or family), and medical contraindication.

LONG TERM OUTCOMES OF CHILDREN OF FEMALE KIDNEY TRANSPLANT RECIPIENTS – A RETROSPECTIVE REGISTRY STUDY

Goni Katz-Greenberg1, Lisa Coscia1, Serban Constantinescu2, Michael Moritz3
1Duke University School of Medicine, Medicine, Durham, United States; 2Transplant Pregnancy Registry International, Gift of Life Institute, Philadelphia, United States; 3Lewis Katz School of Medicine, Temple University, Medicine, Philadelphia, United States

Background: Pregnancy and short-term outcomes of kidney transplant recipients (KTRs) have been reported previously. However, there is limited evidence regarding health and development of KTRs’ OS are lacking. We sought to describe these using data from the Transplant Pregnancy Registry International (TPRI).

Methods: Since 1991, the TPRI has enrolled pregnant KTRs. Data are collected via questionnaires, periodic phone interviews and medical record review. We extracted basic data of KTRs and their pregnancies, and all available data on their OS. Each live birth was treated as a separate episode. Each disease/disorder was extracted individually as an OS could have more than one. Descriptive statistics were expressed as absolute numbers (%) for categorical data and as median with interquartile range (IQR) for skewed distribution.

Results: There were 1747 distinct live births in the TPRI, and 1546 OS with>1 year of follow-up (FU) were included (Figure 1). A vast majority (1508 (97.5%)) were from North America, and 805 (52%) of OS were male. Median flu was 15.32 years (6.80-23.51), with 1142 (73.8%) of OS reported as healthy and developing well at last flu. Most common diagnoses were allergies, asthma, and renal disease (2.8%), most commonly due to anatomical malformation. There were 144 reported behavioral and psychiatric disorders (Table 1).

Conclusions: This is the largest cohort of OS of female KTRs to date. While there is apprehension among clinicians regarding outcomes of pregnancy and OS of KTRs, our study shows that the majority of OS are healthy at last flu.

LONG TERM OUTCOMES OF CHILDREN OF KIDNEY TRANSPLANT RECIPIENTS: A Retrospective Registry Study

Goni Katz-Greenberg, Lisa Coscia, Serban Constantinescu, Michael Moritz
1Duke University School of Medicine, Medicine, Durham, United States; 2Transplant Pregnancy Registry International, Gift of Life Institute, Philadelphia, United States; 3Lewis Katz School of Medicine, Temple University, Medicine, Philadelphia, United States

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Conclusions: This is the largest cohort of OS of female KTRs to date. While there is apprehension among clinicians regarding outcomes of pregnancy and OS of KTRs, our study shows that the majority of OS are healthy at last flu. Despite high rate of prematurity and low birthweight, the majority of OS seem to have normal long-term development. The proportion of reported neurological or psychiatric disorders in the OS is overall similar to the general population. Whereas previous data have shown association between a chronically ill parent to a child’s wellbeing, further studies are needed to assess causation in this study population. Lastly, etiologies of renal disease were mainly anatomical or genetic disorders and may impact early child development and/or manifest in early adulthood.
Figure 1. Study Flow Diagram

11747 live births

24 neonatal deaths

11 infant deaths

96 children with < 1 year follow up from birth

70 children with follow up time "not available"

1546 children with > 1 year follow up from birth

Table 1: Baseline characteristics and outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
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<tr>
<td>Mother's race, n (%)</td>
<td></td>
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<tr>
<td>Black/African American</td>
<td>88 (5.7)</td>
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<tr>
<td>White/Caucasian</td>
<td>1088 (70.3)</td>
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<tr>
<td>Asian</td>
<td>96 (6.2)</td>
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<tr>
<td>Other</td>
<td>131 (8.5)</td>
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<tr>
<td>Not available</td>
<td>143 (9.3)</td>
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<tr>
<td>Mother's age at conception, years, median (IQR)</td>
<td>30.2 (26.4-33.7)</td>
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<tr>
<td>Time between last KT to conception, years, median (IQR)</td>
<td>4.4 (2.3-7.8)</td>
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<tr>
<td>Gestational age, weeks, median (IQR)</td>
<td>36.5 (34.3-38.3)</td>
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<tr>
<td>Birth complications, n (%)</td>
<td></td>
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<tr>
<td>Yes</td>
<td>666 (43.2)</td>
</tr>
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<td>No</td>
<td>873 (56.5)</td>
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<tr>
<td>Not available</td>
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<tr>
<td>Birth defects, n (%)</td>
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<td>Yes</td>
<td>97 (6.3)</td>
</tr>
<tr>
<td>No</td>
<td>1442 (93.3)</td>
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<tr>
<td>Not available</td>
<td>7 (0.4)</td>
</tr>
<tr>
<td>Birth weight, grams, median (IQR)</td>
<td>2,693 (2,126-3,090)</td>
</tr>
<tr>
<td>Child's health, n (%)</td>
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<tr>
<td>Health and developing well</td>
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<tr>
<td>Asthma</td>
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<td>Diabetes</td>
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<tr>
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<td>Anatomic (e.g. – hypoplasia)</td>
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<td>Neuro/vision</td>
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<td>Attention-deficit/hyperactivity disorder (ADHD)</td>
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<tr>
<td>Seizure disorder</td>
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<td>Other</td>
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</table>

*Number/percentages will not add to 1546 children and 100%, as individuals can have more than 1 ailment

Background: International travel for organ transplantation (ITOT) may involve ethically legitimate activities as well as organ trafficking or “transplant tourism.” Little information is available on the prevalence of ITOT, limiting efforts to investigate, monitor, and respond to trends. Longstanding calls to address this data gap include recommendations to establish an international registry for clinician case reporting. However, transplant professionals’ willingness to be involved in reporting is unknown. This study aimed to assess the feasibility of an ITOT registry by exploring clinician attitudes towards reporting ITOT.

Methods: With the support of the Declaration of Istanbul Custodian Group, the Transplantation Society and the International Society of Nephrology, an online anonymous survey was conducted [Oct-Dec 2022]. The English language questionnaire items addressed: respondent demographics, recent experiences of cases involving ITOT, and reporting of ITOT cases to national or international registries (preferences, attitudes, and influential factors). Data were analysed using descriptive statistics.

Results: 335 transplant professionals from 73 countries (42% European) completed the survey. Of respondents with experience of ITOT patients, 210 (84%) had cared for people who had donated/received an organ transplant since 2017. Their most recent case experiences involved travel to/from 109 countries (31 European). 54% of respondents indicated they were likely/very likely to submit ITOT cases to an international registry (30.7% unsure; 15.5% unlikely/very unlikely), compared with 76.3% to a national registry (14.8% unsure; 9% unlikely/very unlikely). Several factors influencing willingness to report were identified, with privacy concerns and risk of harm paramount (Table 1); 53.1% preferred to report anonymously.

Conclusions: Collection of data regarding ITOT activities should be a concern for all countries. An international ITOT registry may complement national registries and support ethical practice in ITOT. Effective collection of ITOT data will depend on international collaboration and systems addressing ethical reporting concerns of transplant professionals.
**BRIEF ORALS**

Looking through the glass – fresh perspectives on ethicolegal and psychosocial aspects of donation and transplantation

**BOS4_11**

THE ORGANIZATION OF THE HUMAN ORGAN TRADE: A COMPARATIVE SCRIPT ANALYSIS BETWEEN LEGAL AND ILLEGAL KIDNEY TRANSPLANTS

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**Background:** It is unknown what the similarities and differences are between legal and illegal kidney transplants. The aim of our study is to explore the similarities and differences in activities, actors and locations between legal and illegal kidney transplants, utilizing crime script analysis.

**Methods:** Data was gathered pertaining to the Netcare – and Medicus case, in South Africa, Kosovo, United Kingdom and Israel. The collected materials consisted of law enforcement data and 36 interviews with 45 respondents, most of whom were involved in the investigation and prosecution of these cases. The data was analysed using qualitative content analysis.

**Results:** Our analysis reveals the extensive preparations and high degree of diversity in locations for the pre-operative work-up of donors and recipients. Compared to legal transplants, the studied illegal transplant schemes reveal a similarity in the opportunity structures that facilitate illegal kidney transplantations, utilizing crime script analysis.

**Conclusions:** The illegal transplant activity that is needed to execute illegal transplants. Offenders in the netcare and Medicus case were involved in the investigation and prosecution of these cases. The data was analysed using qualitative content analysis.

**BOS4_12**

IMPLEMENTING A VALUES-DRIVEN POLICY IN A COMPLEX SYSTEM: WHAT HAPPENED WHEN THE SOFT OPT-OUT SYSTEM OF ORGAN DONATION WAS IMPLEMENTED IN ENGLAND?

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1Bangor University, Bangor, United Kingdom, 2Policy Innovation and Evaluation Research Unit, London, United Kingdom

**Background:** In May 2020 England implemented a ‘soft’ opt-out system of consent to organ donation on the assumption that switching the default to one more closely aligned with the preferences of citizens would make organ donation easier.

**Methods:** A mixed-methods evaluation comprising: review of Parliamentary debates and feedback from legislators; surveys and interviews with healthcare professionals; analyses of representative public attitude surveys and public responses to media campaigns; interviews with family members approached about organ donation and the public; and analysis of donor audit data (e.g. consent rates), informed by input from a lay (public) perspective.

**Results:** Implementing a ‘soft’ opt-out system into a well-established and complex opt-in system has been challenging. Consent forms, procedures and audits have become more complicated. Professionals frequently have to move between scenarios with families where opt-out applies, and others where family consent (opt-in) is still required. Bereaved families have no idea when this is required and continue to believe they are the decision makers. There is an increasing mismatch between establishing one’s wishes on the organ donor register and what the family are asked after death by staff. Support for organ donation continues to vary between subgroups of the population. The opt-out system appears to have had little impact so far on these differences. Nonetheless, implementation created a context for mis/disinformation to spread, especially among minority ethnic and faith groups. Disruptions from COVID-19 mean any impact of the law change on consent rates remain unclear.

**Conclusions:** COVID-19 has hampered the ability to identify the effectiveness of the law change. At the same time, the legacy of informed consent has made it difficult to adapt fully to the opt-out system. This has prevented the principle behind the Act that everybody is a potential donor being realised in practice. Rather than presuming that the opt-out system will work as intended, it is likely to be more effective to improve the organ donation system in other ways.
Looking through the glass - fresh perspectives on ethicolegal and psychosocial aspects of donation and transplantation

**BOS4_14 NATIONAL HEALTH INSURANCE COVERAGE OF ORGAN PERFUSION MACHINES (PM) IMPROVES ACCESS TO TRANSPLANTATION**

Helene Logerot1, Seida Salman1, Emilie Savoye1, Carine Jasseron1, Richard Dorent1, François Kerbau1, Michel Tsimaratos1, Corinne Antoine1

1Agence de la Biomédecine, Saint-Denis, France

**Background:** At the level of the national health care system, the insurance cost of managing chronic kidney, liver and lung diseases is significantly in favour of transplantation. Perfusion of harvested organs significantly increases the number of quality grafts available. Although activity is increasing, the overall cost for the healthcare system is offset by the savings in the patients care pathway.

**Methods:** France is a government-managed health care system where organ transplantation is funded both by Diagnosis Related Groups-like system and by specific lump sum for transversal activities related to organ transplantation (OT). Several criteria have been gathered to reach right level of funding: (1) evidence of efficacy, quality and safety of PM, (2) perfusion indications endorsed by transplant societies of each discipline, (3) organization model, (4), European conformity marked technology (5), costs studies. For each organ lump sum, specific costs studies were considering based on cost effectiveness analysis and simulation; integrating identified additional costs of expenditure items as human resources (additional operating time), purchase of PM, consumable, amortization, maintenance and storage.

**Results:** The French National Transplantation Organisation (ABM) has evaluated PM’s additional costs. The Ministry of Health has validated the amounts. Thus, since 2012 for kidneys, 2019 for lungs and 2023 for liver perfusion, the specific lump sums are:

<table>
<thead>
<tr>
<th>Organ perfusion</th>
<th>Transplantation lump sum (€)</th>
<th>2022 activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys (every 3 procedures, 2 kidneys/procedure)</td>
<td>9577</td>
<td>1112</td>
</tr>
<tr>
<td>Lungs (1 ex-vivo perfusion and rehabilitation)</td>
<td>34057</td>
<td>49</td>
</tr>
<tr>
<td>Liver (1 hypothermic ex vivo perfusion)</td>
<td>4840</td>
<td>90</td>
</tr>
</tbody>
</table>

In 2022, PM were used in 88.5% of kidney transplants with expanded criteria donors, 15% of lung transplants, and 7% of liver transplants. In addition, 1,451 donors were improved access to transplants at an average cost of €2,894 per transplant. The final presentation will show comparative results over several years and the share of the PM in the overall funding of OT.

**Conclusions:** France is the first European country to have implemented incentives national funding for the use of PM. The aim is to ensure equity of access to optimal graft preservation for all patients and to improve extended criteria donors graft outcome without extra cost for the transplant centers. The evaluation of this policy confirms its medical and scientific relevance as evidenced by the increase in transplant activity.
### BOS 2: TRANSPLANTING PATIENTS WITH AMYLOIDOTIC CARDIOMYOPATHY: A DREAM FOR FEW

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**Background**: Amyloidotic cardiomyopathy (AC) is a rare indication for heart transplantation. However, few data are available on survival and outcomes. Even more challenging to address is the selection of patients and the timing of transplant.

**Methods**: We reviewed all pts (n=23) receiving HT for AC (1998-2022), collecting data on demographics, clinical characteristics and hemodynamics (by right heart cath) before, within one month and one year after HT. The endpoints were survival and freedom from Cardiovascular death at 1, 5, 10 years (Kaplan Meier) analysis was stratified by era (availability of drugs for transthyretin, TTR, in 2018), and etiology (TRT vs AL).

**Results**: Among 25 pts (19 TTR, 6 AL) received HT, mean 62±19 years, due to more frequent rejection episodes (50% vs 5.9%, p=0.02); no pts in TTR pts. AL were more frequently on steroids at one year (100% vs 59%, p<0.05) due to more frequent rejection episodes (50% vs 5.9%, p=0.02). sepsis was the leading cause of death at 1 year (26.7±22.6% vs 76.6±10.3%, p=0.06) and l0y (0% vs 85.5±9.5%, AIL vs TTR, p=0.03). AL pts death was due to irreversible kidney failure (40% vs 5%), p=0.007) following transplantation. TTR pts had better survival at all time points (y); analysis was stratified by era (availability of drugs for transthyretin, TTR, in 2018), and etiology (TRT vs AL).

**Conclusions**: Our first experience with the Aeson HT was positive. The device pressure sensor’s information may be helpful to monitor the evolution of patients with pulmonary hypertension and guide the proper timing of transplant listing especially in a bridge to candidacy policy.

### BOS 3: THE FIRST IMPLANT OF A BIOARTIFICIAL TOTAL ARTIFICIAL HEART IMPLANTATION IN A PATIENT WITH SEVERE PULMONARY HYPERTENSION

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**Background**: The improvement of the outcomes of medical therapy using the 4 pillars of heart failure medications and device therapy has shifted the indication from mechanical circulatory support in a later phase of the clinical disease course in which the burden of right ventricular failure is higher. Since the onset of biventricular failure is often followed by acute cardiogenic shock, heart transplantation is rarely the timely answer to the patient decompensation and LVAD implantsation is frequently faced with the bedside available solution when the right ventricular is already ongoing.

**Methods**: The Aeson® Total Artificial Heart (TAH) is intended to provide physiologic heart replacement therapy for patients suffering from end-stage biventricular heart failure who are not suitable candidates for heart transplantation due to contra-indications or patient refusal. The device pressure sensor’s information may be helpful to monitor the evolution of patients with pulmonary hypertension and guide the proper timing of transplant listing especially in a bridge to candidacy policy.

**Conclusions**: Outcomes of pts with AC after HT are worse than in the other etiologies. TTR has become frequent indication for HT, with good outcomes regarding patient survival. Further studies are required to better define the indications and outcomes of this procedure.
we compared the outcome of 27 (15%) transplanted on VA-ECMO support to the outcome of 24 (13%, matched for sex, age and anthropometric characteristics) transplanted without support in the same period.

**Results:** VA-ECMO bridged patients were less likely to be women, had more frequently previous cardiac surgery and had higher bilirubin levels. There were no significant differences in age, creatinine levels, mean pulmonary arterial pressure (mPAP) and donor characteristics between the two groups. We found a statistically significant difference in VA-ECMO patients regarding fewer days on waiting list (Table). The Kaplan-Mayer curves showed no statistically significant differences in event-free survival (Figure).

**Conclusions:** data from our study suggests that, despite being on worse clinical condition with more hepatic damage at transplant, there are no significant differences in early and medium-term survival between patients on VA-ECMO support and the other group. The shorter time on waiting list in VA-ECMO population may have a protective role in these patients preventing further organ damage and complication related to the mechanical support itself. Larger case series and more in-depth statistical analyses should be carried out in future studies to confirm this result.

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**Background:** The use of Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) as Bridge-to-Transplant (BTT), although increasing, is controversial. In the past decade, early studies reported VA-ECMO support as an independent risk factor for mortality after heart transplant (HT). However, recently investigations showed improving results at short-term follow-up and to date, long term survival has been poorly investigated. Therefore, it is the aim of this study to analyse short and long term outcomes of VA-ECMO support. Acute kidney injury requiring dialysis and post-operative infections occurred in 35% and 24%, respectively. Bleeding complications were 27%. Sepsis and multi-organ failure resulted as the main causes of death (77%). Hospital mortality was 25.4%. Recipient age at transplant (OR 1.09 [95%CI:1.017-1.17]; p=0.034), preoperative systolic pulmonary arterial pressure >50 mmHg (OR 6.3 [1.23-32.84]; p=0.027), and platelets number (OR 0.98 [0.96-0.99]; p=0.034) independently predicted hospital mortality. Cumulative survival was 67.4%, 56.7% and 48.2% at 1, 5 and 8 years of follow-up. Stratification by decades showed no differences in terms of post-transplant survival (2002-2012: 65.8% and 56.7% vs 2013-2022: 68.4% and 56.5% at 1 and 5 years, respectively; p=0.81 (Figure)).

**Conclusions:** HT after VA-ECMO still maintains suboptimal results. Better stratification tools according to preoperative risk factors can implement these results. Outcomes after HT post- VA-ECMO support don’t seem to be improved during the last 20 years.
Contemporary heart transplantation: scores, pumps, cells and much more

**BOS5_7** HEART TRANSPLANT SURVIVAL OUTCOMES: ROLE OF DONOR-TRANSMITTED Atherosclerotic Donor-transmitted atherosclerosis has been associated with worse outcomes in recipients of heart transplantation. This study aimed to evaluate the impact of donor-transmitted atherosclerosis on outcomes in a large cohort of heart transplant recipients.

**Background:** A growing number of potential heart recipients with UNOS1 status forces to find solutions for the shortage of donor organs by expanding the criteria for selecting donors. Coronary assessment of a cardiac graft is inaccessible in the pre-transplant period; therefore there exists a risk of transmission of the coronary atherosclerotic from a donor to a recipient.

**Methods:** We retrospectively reviewed the medical records of 1155 recipients who underwent Heart transplantation in the Shumakov Center from 2009 to 2018; 985 were men, and 170 women, aged 10 to 74 years. All patients underwent coronary angiography in the early postoperative period and were divided into 3 groups: I – recipients with hemodynamically significant lesions of the coronary arteries (CA), II – pts. with signs of CA atheroma (rough contours or stenoses up to 50%), and III – pts. without signs of CA. The analysis included the following criteria: sex, age, cause of donor’s brain death, UNOS status.

**Results:** In 332 pts. (groups I and II) signs of donor-transmitted atherosclerotic disease were found. In 130 cases the lesions were assessed as hemodynamically significant and percutaneous coronary intervention was performed. In 823 cases there were no signs of atherosclerosis. In recipients with UNOS status 1A (n=355) and 1B (n=436), transmission of atherosclerosis was detected more often than in recipients with UNOS 2 (60% and 40%, respectively). The age of donors in groups I and II was significantly higher than in groups III (p = 0.0001). No association was found between the frequency of donor-transmitted atherosclerosis and the gender of the donor. Acute cerebrovascular accident as a cause of donor’s brain death in groups was: 90% in I, 84% in II, and 80% in III. Five-year survival in I group was 75.6%, II - 72.5%, and III - 74.6%, no significant difference between groups (I/II p=0.849, II/III p=0.389, II/III p=0.421).

**Conclusions:** Donor-transmitted atherosclerosis, including hemodynamically significant lesions of the CA, is associated with the age of the donor. Early endovascular correction of hemodynamically significant lesions neutralizes the potentially negative impact of coronary stenosis on the survival of heart transplant recipients.

**BOS5_9** VALIDATION OF THE CLINICAL UTILITY OF MICRORNA AS NON-INVASIVE BIOMARKERS OF CARDIAC REJECTION: A PROSPECTIVE LONGITUDINAL MULTICENTER STUDY

**Background:** Circulating microRNAs (miRNAs) have been identified as non-invasive biomarkers of cardiac allograft rejection in retrospective studies but their clinical utility to detect rejection has not yet been evaluated in large prospective and unselected cohorts of patients.

**Methods:** We designed a longitudinal prospective study (NCT02672683) including 11 heart transplant referral centers. Patients were included from August 2016 to March 2018. Either de-novo HTx recipients or patients transplanted ≥ 1 year were included at the time of an endomyocardial biopsy (EMB, protocol or for cause). The primary endpoint was to validate the association between the peripheral expression of 3 previously identified circulating miRNA (miR-10a, miR-92a, and miR-155) with allograft rejection on concomitant EMB. Relative miRNA measurements were performed by normalizing miRNA PCR copy numbers by an endogenous control. A sensitivity analysis was performed by applying an absolute quantification method of miRNA using standard dilution curves of microRNA mimics. The association between miRNA and rejection was tested using mixed effect logistic regression.

**Results:** A total of 461 patients were included representing 831 EMB. Overall, 79 rejection episodes occurred, including 25 ACR ≥ 2 R and/or 56 AMR ≥ pAMR 1. In a first pre-specified interim analysis based on 258 EMB from 184 patients including 49 rejection episodes (82% of overall rejections, ACR ≥ 2R = 17, pAMR 1(H+) = 14, pAMR1(I+) = 9, pAMR2 = 11), no association between any of circulating miRNA and rejection was found (Figure 1-A). A sensitivity analysis performed with the absolute quantification method on 191 EMB from 134 patients including 49% of overall rejections confirmed these results (Figure 1-B). The analysis of remaining sera was stopped for futility.

**Conclusions:** In this prospective longitudinal multicenter study of unselected patients, the clinical utility of 3 circulating miRNA as non-invasive biomarkers of cardiac rejection was not confirmed.
Contemporary heart transplantation: scores, pumps, cells and much more

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Background: Cardiac allograft vasculopathy is one of the main factors negatively affecting the long-term results after heart transplantation (HTx), which is characterized by the coronary arteries stenosis and causes the graft loss. MicroRNAs (miRs) are a new class of regulatory molecules that affect various cellular functions and have potential value for diagnostic of post-transplant complications. miR-339 was shown as a promising biomarker of chronic graft rejection. This can potentially reduce the frequency of invasive diagnostic interventions or partially replace them, which will expand the possibilities of a personalized approach to the early diagnosis of post-transplant complications and postoperative management. The aim is to determine the diagnostic value of miR-339 levels for the coronary arteries stenosis of cardiac allograft.

Methods: The study enrolled 53 heart transplant recipients, aged 16 to 70 (48.6 ± 10.9) years. Expression levels of miR-339 were measured in blood plasma by PCR and expressed in relative units. The coronary artery stenosis of cardiac allograft was verified by the results of coronary angiography.

Results: 16 heart recipients (30%) had the stenotic lesion of the coronary arteries of the transplanted heart. 6 of them had the progression of initial stenotic lesion of the coronary arteries of donor heart, and 10 – the coronary arteries stenosis developed after HTx (62.5% of cases). The levels of miR-339 in heart transplant recipients with stenotic coronary arteries are significantly lower than in recipients without ones (p=0.03). When the miR-339 expression level is below 7.5 fold change the relative risk of coronary arteries stenosis is RR=6.0±0.91 [95% CI 1.003–35.909], p=0.04. The sensitivity and specificity were sufficient for use in clinical practice: Se=85.7% and Sp=100.0%. We found that active recipients achieved better results of VO2peak and VO2pred – 52.5±10.5, p<0.001; VE/VCO2 slope – 38.5±8.9, p<0.001 and then continued to improve (1 year, p<0.001; 5 years, p<0.05). After HTx PCS increased (3 months – 41.8±8.5, p<0.001; 1 year – 46.9±3.9, p<0.001; 5 years – 48.1±7.6, p<0.414). In 3 months MCS improved (48.0±2.3, p<0.001) but then started to slowly decrease (p<0.001). One year after HTx 55% of patients reached normal values, 38% (73%) of them were physically active. Physically active recipients achieved better results of VO2peak (3 months, p=0.019; 1 year, p<0.001) and PCS: 1 year (p=0.030) and 5 years after HTx (p<0.001). The miR-101 expression level was measured by PCR in blood plasma before and after the HTx. The plasma level for detection the patients with the risk of ACR after HTx.

Conclusions: Decreasing miR-339 expression level after HTx is associated with the coronary arteries stenosis in heart graft and lower survival rate, which allows us to evaluate miR-339 as a potential biomarker of chronic graft rejection.

Fig. Kaplan-Meier survival curves of heart recipients with miR-339 above and below threshold level

The diagnostic value of mi-R-339 for coronary stenosis of cardiac allograft.

The impact of exercise trainings on physical capacity and quality of life after heart transplantation

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Objective: to estimate the dynamic of physical capacity (PC) and quality of life depending of exercise trainings in recipients after heart transplantation (HTx).

Methods: From 2010 to 2022 HTx was performed in 205 patients (48±14 year-old; 149 – male) who completed cardiopulmonary exercise test before, 3 months, 1 year and 5 years after HTx. Dynamics of VO2peak and VO2/VCO2 slope were measured. Physical activity was defined by questionnaire – IPAQ. Exercise trainings were prescribed to all recipients but less than one third of patients followed recommendations and were physically active (3 months – 67, 1 year – 66, 5 years – n=36). We estimated the dynamic of physical capacity (PCS) and mental component summary (MCS) by SF-36 questionnaire.

Results: PC had significantly increased in 3 months (VO2peak – 15.4±3.4 ml/min/kg, p<0.001; VO2pred – 52.5±10.5, p<0.001; VO2/VCO2 slope – 38.5±8.9, p<0.001) and then continued to improve (1 year, p<0.001; 5 years, p<0.05). After HTx PCS increased (3 months – 41.8±8.5, p<0.001; 1 year – 46.9±3.9, p<0.001; 5 years – 48.1±7.6, p<0.414). In 3 months MCS improved (48.0±2.3, p<0.001) but then started to slowly decrease (p<0.001). One year after HTx 55% of patients reached normal values, 38% (73%) of them were physically active. Physically active recipients achieved better results of VO2peak (3 months, p=0.019; 1 year, p<0.001) and PCS: 1 year (p=0.030) and 5 years after HTx (p<0.001). The miR-101 expression level was measured by PCR in blood plasma before and after the HTx. The plasma level for detection the patients with the risk of ACR after HTx.

Conclusions: After HTx there was an improvement of PC and PCS that continued to increase in long-term but only half of the transplant recipients (55%) reached normal values of VO2peak and most of them were physically active (73%). Physically active patients also achieved higher PCS but no matter of VO2peak raise their MCS started to slowly decrease long-term after HTx. There was no difference depending on post-transplant TTE results and the number of allotraft rejections (p>0.05).

The impact of exercise trainings on physical capacity and quality of life after heart transplantation.

MicroRNA-101 plasma level: diagnostic and prognostic value for cardiac graft acute cellular rejection

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Background: Acute cellular rejection (ACR) causes graft dysfunction after heart transplantation (HTx). Endomyocardial biopsy is gold standard for its in vivo diagnosis. The search for new minimally invasive laboratory technologies for its early detection is extremely relevant. MiRNAs (miR) are a new class of regulatory molecules that have potential value for diagnostic and prediction of post-transplant complications. The aim is to determine the value of miR-101 plasma level for detection the patients with the risk of ACR after HTx.

Methods: The study enrolled 79 heart transplant recipients, aged 16 to 70 years. The miR-101 expression level was measured by PCR in blood plasma before and after the HTx and presented in relative units. The plasma levels of ST2 (proteine biomarker of cardiac graft acute rejection and cumulative cardiovascular events) was measured by ELISA. The diagnostic and prognostic value of miR-101 was evaluated by the receiver operating characteristic analysis.

Results: According to the ISHLT classifications, 36 recipients with ACR (R1G – R3G degree) after HTx were identified. The comparison group consisted of 43 recipients without rejection. MRIR-101 level was significantly lower in heart transplant recipients with ACR than in heart recipients without it (p=0.011). When miR-101 level below 8.36 relative units the relative risk is RR=1.92±0.16 [95% CI 1.39 – 2.63], p=0.001 with Se=39.5% and Sp=96.0%. The risk of ACR with ST2 level above 36.84 ng/ml was RR=2.56±0.26 [95% CI 1.53 – 4.26], p=0.0003. The diagnostic characteristics of miR-101 and ST2 combination
were analyzed. The Se and Sp of the duplex test have increased to 69.2% and 100% respectively, RR=4.00±0.43 [95% CI 1.71 – 9.35], p=0.001. Moreover, miR-101 pre-transplant level in heart recipients with ACR was significantly lower compared to recipients without rejection (p=0.02). The prognostic relative risk of ACR in recipients with miR-101 pre-transplant value below –9.73 relative units was RR=3.00±0.47 [95% CI 1.19 – 7.56], Se=62.5%; Sp=100% (p=0.02).

Conclusions: The measurement of miR-101 plasma level before and after HTx can be helpful for identifying the recipients with the risk of ACR, and optimize the appointment of biopsy and therapy correction. The combination with ST2 improves the diagnostic characteristics of the test.

**Development and Validation of Specific Post-Transplant Risk Scores According to the Transplant Era: A UNOS Cohort Analysis**

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Background: The clinical use of post-transplant risk scores is limited by their poor statistical performance. Neglecting the dynamic evolution of demographics and risk factors over time may be a key issue. We hypothesized that developing specific prognostic models for each transplant era may improve risk stratification.

Methods: We analyzed the UNOS database including first, non-combined heart transplantations with a common allocation scheme (2003-2018). The endpoint was death or retransplantation during the first year post-transplant. We analyzed the evolution of post-transplant outcomes, demographics, and odds ratios of major predictive variables over time. Then, we build (logistic regression, derivation cohort 2/3) and compared (validation cohort 1/3) the statistical performance (discrimination, calibration, reclassification indices) of era-specific models and non-era-specific models (2001-2005, 2006-2010, 2011-2015, 2016-2018). In a sensitivity analysis, we randomly generated 1,000 bootstrap samples to analyze the variability of specific predictive models and compare era and non-era-specific models.

Results: A total of 34,747 patients were included; 3,674 patients (10.6%) met the composite endpoint. We observed a significant improvement in post-transplant outcomes (p < 0.001) and an important evolution in baseline characteristics over time. We found a significant interaction between time and the effect of the following variables: bilirubin, recipient age and prior cardiac surgery (p<0.01). Era-specific models differed from each other, both in terms of variables and odds ratios (Figure 1A). Era-specific models outperformed the statistical performance of non-era-specific models in a majority of samples, both in terms of discrimination, calibration (Figure 1B) and reclassification indices.

Conclusions: We found important evolution in post-transplant outcomes, baseline characteristics and predictive models over time. Era-specific models outperformed the statistical performance of non-era-specific models in a majority of samples. This finding suggests the need for a regular update of post-transplant predictive models to account for the evolving demography of candidates and medical practices.

**BRIEF ORALS**

Contemporary heart transplantation: scores, pumps, cells and much more
Treatable traits lead the way towards better outcomes in lung transplantation

**BRIEF ORALS**

**BOS6_3 INCREASED TOTAL CELL-FREE DNA EARLY AFTER LUNG TRANSPLANTATION IS ASSOCIATED WITH BASELINE LUNG ALLOGRAFT DYSFUNCTION**

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**Background:** Baseline lung allograft dysfunction (BLAD) is the inability to achieve the expected peak lung function within the first year after lung transplantation (LuTx). The underlying cause of BLAD is not yet fully understood, but early graft alteration has been identified as a risk factor. We hypothesized that early levels of absolute and percent plasma donor-derived cell-free DNA (ddcfDNA and %ddcfDNA, respectively), which are biomarkers of graft damage, as well as total cell-free DNA (cfDNA) levels, may have predictive value for the incidence of BLAD.

**Methods:** A total of 16 patients who underwent bilateral LuTx between May 2021 and March 2022 (women 50%), followed-up in a single center were included, with a median age at the time of LuTx of 50.2 years (IQR 37.8 - 63.8). Blood samples were collected monthly from 3 up to 6 months post-LuTx. Samples obtained during rejection or infection were excluded. %ddcfDNA, ddcfDNA (cp/mL) and cfDNA (cp/mL) levels were obtained by the Prospera test. BLAD was defined as the inability to achieve forced expiratory volume in 1 second and forced vital capacity of 80% predicted on two consecutive measurements within the first year post LuTx. Analyses were performed by Mann-Whitney test.

**Results:** 46 samples were analyzed (median 2.9 per patient). 5 of 16 patients had BLAD (31.3%). Median %ddcfDNA value for the non-BLAD group was 0.17% (IQR 0.11 - 0.31) and for the BLAD group 0.31% (IQR 0.22 - 0.60), p=0.21. In absolute values, median ddcfDNA for the non-BLAD group was 24.92 cp/mL (IQR 18.17 - 56.18) and for the BLAD group 70.29 cp/mL (IQR 24.92 - 56.18). Blood samples were collected monthly from 3 up to 6 months post-LuTx. Samples obtained during rejection or infection were excluded. %ddcfDNA, ddcfDNA (cp/mL) and cfDNA (cp/mL) levels were obtained by the Prospera test. BLAD was defined as the inability to achieve forced expiratory volume in 1 second and forced vital capacity of 80% predicted on two consecutive measurements within the first year post LuTx. Analyses were performed by Mann-Whitney test.

**Conclusions:** Increased total cfDNA levels obtained between 3rd-6th month after LuTx were associated with a higher risk of BLAD. Due to the fact that 90% of cfDNA originates in white blood cells, we hypothesize that a proinflammatory status might be a risk factor for BLAD incidence but further investigation is required. Although a trend for elevated ddcfDNA and %ddcfDNA was observed for BLAD, this was not statistically significant.

**BOS6_4 CLINICAL RELEVANCE OF CELL-FREE DNA QUANTIFICATION AND QUALIFICATION DURING THE FIRST MONTH AFTER LUNG TRANSPLANTATION**

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**Background:** Many studies have reported the relevance of donor-derived cfDNA after lung transplantation (LT) to diagnose and monitor acute (AR) or chronic rejection or infection (INF), analysis of cfDNA fragment size is not validated. The aim of this study was to determine the clinical relevance of dd-cfDNA and cfDNA size profiles in events (AR and INF) during the first month after LT.

**Methods:** This is a prospective, single-center study including 62 LT patients at the Marseille Nord Hospital (LARA project). Total cfDNA quantification was performed by fluorimetry and digital PCR, dd-cfDNA by NGS (AlloSeq cfDNA-CareDX®) and the size profile by BIABooster (Adelis®). A biopsy at D30 allowed establishing the following groups: stable, nonstable (AR, INF and AR+INF).

**Results:** Quantification of total cfDNA, for all methods, was not correlated with the patient’s status at D30, percentage of dd-cfDNA was significantly higher for nonstable patients at D30 (p=0.0004). A threshold of 1.72% of dd-cfDNA determined the nonstable patients (NPV: 91.4%). The analysis of small sizes (80-120 bp) identified the INF with a threshold of 3.7% (PPV: 100%). An algorithm combining the two analyses allows to significantly differentiate the type of lesions due to allografts.

**Conclusions:** Our algorithm aims at guiding the performing of biopsies, which are invasive and risky for the patient. This combined noninvasive biomarker of allograft injury requires to be confirmed. For this purpose, a control cohort is being included and a multicenter study is planned.

![Figure 1: Comparison of 3rd/6th month median of percent donor derived cell-free DNA, absolute donor derived cell-free DNA and total cell-free DNA between lung transplant recipients with and without baseline lung allograft dysfunction (BLAD).](image-url)
Background: Donor-derived cell-free DNA (dd-cfDNA) has been investigated as a non-invasive alternative approach to transbronchial biopsies (TBBS) to evaluate lung allograft injury (LAI) following transplantation. The aim of the study was to compare the diagnostic yield of dd-cfDNA to scheduled TBBS systematically evaluated according to the LASHA template.

Methods: Twenty-one recipients were prospectively enrolled between October and November 2022. TBBS were scored according to LASHA template. Alveolar macrophages, oedema, and mild capillary dilation with score <2 were considered nonspecific and classified as unremarkable if not associated with altered microbiological or immunological findings. A comprehensive immunological and microbiological/cytological evaluation was carried out on blood and broncho-alveolar lavage (BAL), respectively. dd-cfDNA was measured (%) by NGS on plasma collected at the same time of TBBS.

Results: dd-cfDNA was under the threshold of 0.85% in 10 patients. In 8 plasma collected at the same time of TBBs.

Conclusions: Plasma dd-cfDNA is highly predictive of LAI, even after a granular histological evaluation. Further studies are needed to confirm the clinical validity of cfDNA, especially for the detection of specific or concomitant pathological lesions of LAI.

Background: Endoscopic surveillance with transbronchial biopsy in lung transplant (Ltx) is crucial, since an early diagnosis of acute cellular rejection (AR) can affect long-term survival. Histological diagnosis of AR is usually made using transbronchial forces biopsies (FB). In recent years, transbronchial cryobiopsy (CB) has been increasingly used, as it obtains larger samples than FB, without crush artefacts. Few studies have compared the two methods in terms of diagnostic accuracy and safety. The aim of this study is to assess the diagnostic yield and safety of CB in comparison with FB, for sampling lung tissue in transplant recipients.

Methods: We analyzed through a retrospective study our case series of the two procedures. From January 2013 to December 2017, 251 FBs were performed in 110 patients, 223 for surveillance purposes and 28 on clinical indication. From January 2018 to October 2022, 218 consecutive CBs were performed in 137 patients, 159 for surveillance purposes and 59 on clinical indication. All biopsies were scored according to the ISHLT criteria. Clinical and functional data, complications, and histologic results were collected.

Results: Diagnostic yield was higher in the CB group for all parameters: grade of AR was detected in 95.0% vs 84.5% in the FB group (p<0.001). Diagnostic rate of airway inflammation was 65.3% vs 51.3% (p=0.005), for chronic rejection 89.0% vs 64.9% (p<0.001). Pneumothorax requiring chest drainage occurred in 3.6% in the CB group and in 4% of patients in the FB group (p non-significant). Moderate and severe bleeding complications CB and FB procedures in 7 (3.2%) and 3 cases (1.3%), respectively (p=0.178).

Conclusions: Transbronchial cryobiopsies improved the diagnostic yield in the monitoring of the lung allograft. The risk of bleeding and pneumothorax has not increased significantly. Prospective studies will better define the role of CB after LTx.

Background: Lung transplantation (LuTX) is the standard of care for patients with chronic progressive, end stage lung diseases. Adherence to prescribed immunosuppressive medication is crucial to prevent graft failure, but it also makes lung-allograft recipients more susceptible to infections. Years of chronic disease and prior hospitalizations on one side, along with intensive-care stay and airway intubation prior to organ donation on the other, facilitate the spread of pathogenic germs in the respiratory tract. This retrospective cohort study aimed to investigate the relationship between the respiratory tract’s germ spectrum and its impact on post-LuTX survival.

Methods: Only patients that received a single or double LuTX from 2014 onwards were considered for this investigation. In addition to a valid and complete follow-up after TX, inclusion criteria were pre- and postoperative sputum samples, as well as intraoperatively performed smear-tests of donor and recipient bronchus. Microbiological findings were categorized into bacteria and fungi. Bacteria were again grouped into gram-positive and gram-negative (aerobic/anaerobic) germs.

Results: Up to this point, 200 patients with valid data on pre-, intra- and postoperative sputum samples, as well as intraoperatively performed smear-tests of donor and recipient bronchus. Microbiological findings were categorized into bacteria and fungi. Bacteria were again grouped into gram-positive and gram-negative (aerobic/anaerobic) germs.
**FUNGAL INFECTION WITHIN THE FIRST YEAR AFTER LUNG TRANSPLANTATION DOES NOT AFFECT LONG TERM SURVIVAL**

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**Background:** Lung transplantation is the only definitive treatment for end-stage lung diseases. However, lung transplantation has the poorest survival rate among all solid organ transplantations. The poor long-term survival after lung transplantation is mainly due to chronic lung allograft dysfunction (CLAD), while one of the most common causes of death within the first year post transplantation is infection caused by microorganisms such as viruses, bacteria and fungi. The majority of fungal infections appear within 3 – 12 months after transplantation. Invasive fungal infections are feared and affect up to approximately 10% of all transplanted patients during the first year after the transplantation. The invasive fungal infections are most commonly caused by Aspergillus species, which create a hypoxic environment in the small airways of the lung allograft, which is believed to increase the risk of rejection. Previous studies state that lung transplant patients with a fungal infection have increased risks of both morbidity and mortality compared to patients without fungal infections.

**Methods:** In the current study we investigated how fungal infections during the first year after lung transplantation impacts the overall survival. A total of 88 lung transplant recipients, transplanted between the years 2011 and 2018 were included. Patient charts were reviewed for collection of data. Out of the 88 patients included, 68 had a fungal infection during the first year after lung transplantation, and 20 did not (table 1).

**Results:** In the group with fungus, there were 33 men and 35 women (age 19 – 68 years). In this group there were 33 patients with aspergillus species, 20 with candida species, four with both, two with pneumocystis species and nine with other fungal infections. In the group with no fungal infection there were 10 men and 10 women (age 16 – 65 years). Analysis comparing the survival between recipients with and without fungal infection during the first-year post lung transplantation, showed no statistically significant difference between the groups (p = 0.57) (hazard ratio: 1.2 (95% CI: 0.6 – 2.3) (figure 1).

**Conclusions:** In this study, long-term survival following lung transplantation was not affected by fungal infections within the first 12 months post transplantation reflecting an equal survival between the groups.

**Table 1: descriptive statistics**

<table>
<thead>
<tr>
<th>Age, mean (range)</th>
<th>Male sex, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fungal infection</td>
<td>52 (19 – 68)</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>49 (16 – 65)</td>
</tr>
</tbody>
</table>

**Figure 1.** Kaplan Meier curve, showing no significant effect on overall survival of patients with fungal infection during the first 12 months post lung transplantation compared to patients without fungal infection.

**POLYOMAVIRUS BK REPLICATION IN URINE DETERMINES A RAPID DECLINE IN KIDNEY FUNCTION AFTER LUNG TRANSPLANTATION**

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**Background:** Different modalities of non-renal solid organ transplantation can develop chronic kidney disease (CKD) as a long-term complication. After lung transplantation (LT), the prevalence of CKD rounds 5-15% depending on the time of evaluation of renal function (RF) after LT. BK polyomavirus replication has recently gained interest as a cause of CKD. Thus, the present study aimed to assess whether the replication of polyomavirus BK in the urine of lung transplant recipients is associated with an increase in the rate of decline of the eGFR slope during follow-up.

**Methods:** We determined BK viruria in 56 LT recipients. Further, they were categorized according to viruria as positive or negative. Demographic and clinical variables were analyzed. The eGFR slope was calculated considering the estimated glomerular filtration rate (GFR) from 2 years before the determination of BK viruria and up to 2 years later. A total of 7 eGFR measurements were used (-2 years, -1-year, baseline, +6 months, +1 years, and +2 years). Linear regression was used to determine the variables associated with the decrease in the eGFR slope. Logistic regression allowed identifying the variables associated with rapid progression (eGFR slope >5 ml/min/1.73 m²/year).

**Results:** 38 out of the 56 TP showed negative viruria, whereas 18 were positive. The least squares mean decrease in the eGFR slope was greater in subjects with positive viruria (-6.50 ml/min/1.73 m²/year vs. -0.31 ml/min/1.73 m²/year, p<0.001). Positive BK viruria was independently associated with a decrease of -6.2 ml/min/1.73 m²/year (p<0.001, Figure 1) in multivariable linear regression. Likewise, these subjects showed a 26.3-fold increase in the risk of being rapid progressors with a sustained decline in the eGFR of > 5 ml/min/1.73 m²/year (p<0.002). Age, the use of calcineurin inhibitors as immunosuppressors, nor albuminuria attenuated the effect of viruria on the rate of eGFR decline.

**Conclusions:** In our study, subjects with BK viruria showed a greater rate of decline of eGFR slope. In addition, subjects with BK viruria showed a rapid progression pattern to advanced stages of CKD.

**Figure 1.** Least squares mean yearly rate of decline in eGFR according to BK viruria. Model adjusted for age, transplantation vintage, ICN through levels, and albuminuria.
Treatable traits lead the way towards better outcomes in lung transplantation

BOS6_10 EVALUATION OF LONG-LASTING LUNG INFLAMMATION IN CIRCULATORY DEATH RAT DONORS USING TISSUE CULTURE AND NORMOTHERMIC REGIONAL PERFUSION

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Background: Lung transplantation after circulatory death (DCD) is an option to treat end-stage diseases. Lungs are highly affected organs and present a long transplantation waiting list, moreover, they have a considerable chance of developing primary graft dysfunction (PGD). In order to expand the donor pool, normothermic regional (in-situ) perfusion is an alternative to ex-vivo lung perfusion. Lung tissue culture can be a tool to evaluate the long-lasting release of inflammatory mediators. This aimed to study the late inflammatory profile of DCD donor lungs, after warm ischemia, using normothermic regional perfusion and tissue culture.

Methods: Male Wistar rats were submitted to circulatory death (19.1% KCl and tissue culture. DCD donor lungs, after warm ischemia, using normothermic regional (ex-vivo) perfusion is an alternative to transplantation. In order to expand the donor pool, normothermic regional (in-situ) perfusion is an alternative to ex-vivo lung perfusion. Lung tissue culture can be a tool to evaluate the long-lasting release of inflammatory mediators. This aimed to study the late inflammatory profile of DCD donor lungs, after warm ischemia, using normothermic regional perfusion and tissue culture.

Results: CS lungs homogenates presented lower concentration of TNF-α than P lungs (CS: 10.75±3.41; P: 5.65±20.48 pg/ml; p=0.0576). There were no differences in IL-10 and IL-6. In the perfusate, the inflammatory mediators concentration increased with time in both groups. Conversely, in the lung tissue culture (24 hours later), IL-6 (CS: 15.99±1.20; P: 7.52±1.86 pg/ml; p=0.4772) were higher in CS indicating a time and preservation dependent inflammatory response. Nonetheless, TNF-α was not altered in the explant quantification, but it is important to consider that it is an early mediator.

Conclusions: Comparing the immediate tissue analysis and the 24h tissue response, the normothermic regional perfusion of the lungs seems to reduce the inflammatory cytokines production and that could indicate a worse scenario in the recipient of cold-stored organs.

Financial support: grant 8887.51368/2020-00, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES

BOS6_11 EFFECT OF DONOR AGE ON LUNG TRANSPLANT SURVIVAL: A MULTICENTER RETROSPECTIVE STUDY FROM THE COLT DATABASE

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Background: Shortage of organ requires lung transplantation (LT) teams to consider older donors. The effects of donor age in LT are not clearly established and data are needed to enable an adequate choice of lung donor.

Methods: We retrieved data from a French and Belgian multicenter lung transplantation cohort. Recipients who underwent heart and lung transplantation, single LT and those who benefited from a retransplantation were excluded. The objective was to determine a correlation between donor age and post-transplant survival.

Results: The analysis was performed on 1191 recipients. Donors over 60 years of age are more frequently female and have a less frequent history of smoking. Lung grafts from donor over 60 years of age are more frequently allocated to recipients of older age, female gender, chronic obstructive pulmonary disease as underlying disease and with cardiovascular comorbidities. The 5-year survival of recipients of lung grafts from donor over 60 years of age was lower than that of recipients of lung grafts from younger donors (62.1% versus 69.3%, respectively, p<0.001). In multivariate analysis, donor age over 60 years was a risk factor for mortality (HR = 1.28, 95% CI [1.01 – 1.53], p = 0.039). Other predictors of survival in multivariate analysis were for recipients female gender (HR = 0.75, 95% CI [0.60 – 0.92], p = 0.026), cystic fibrosis underlying disease (HR = 0.45, 95% CI [0.35 – 0.58], p < 0.001), and a history of ischemic heart disease (HR = 1.57, 95% CI [1.12 – 2.14], p = 0.011).

Conclusions: Donor age greater than 60 years is an independent risk factor for survival after transplantation. The age criterion must be considered in the acceptance decision for a lung transplant.

BOS6_12 IDENTIFYING TREATABLE TRAITS IN RESTRICTIVE ALLOGRAFT SYNDROME: A NESTED CASE-CONTROL STUDY

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Background: Chronic lung allograft dysfunction (CLAD), with its main phenotypes bronchiolitis obliterans syndrome (BOS) and restrictive allograft syndrome (RAS), remains a major cause of mortality after lung transplantation. Several risk factors for CLAD development have been identified. However, most studies hitherto did not assess RAS as a separate phenotype or pooled all phenotypes of CLAD together, making it difficult to distinguish between RAS and BOS. Therefore our aim was to identify (and confirm) risk factors for RAS.

Methods: In this retrospective nested case-control study, all patients transplanted at our center from 2010 till 2021 (n=789) were evaluated for inclusion. CLAD patients were phenotyped according to the 2019 ISHLT consensus. 69 patients with RAS or mixed phenotype were included, and 1 non-CLAD control patient. CLAD patients were phenotyped according to the 2019 ISHLT consensus. The analysis was performed on 1191 recipients. Donors over 60 years of age were more frequently allocated to recipients of older age, female gender, chronic obstructive pulmonary disease as underlying disease and with cardiovascular comorbidities. The 5-year survival of recipients of lung grafts from donor over 60 years of age was lower than that of recipients of lung grafts from younger donors (62.1% versus 69.3%, respectively, p<0.001). In multivariate analysis, donor age over 60 years was a risk factor for mortality (HR = 1.28, 95% CI [1.01 – 1.53], p = 0.039). Other predictors of survival in multivariate analysis were for recipients female gender (HR = 0.75, 95% CI [0.60 – 0.92], p = 0.026), cystic fibrosis underlying disease (HR = 0.45, 95% CI [0.35 – 0.58], p < 0.001), and a history of ischemic heart disease (HR = 1.57, 95% CI [1.12 – 2.14], p = 0.011).

Conclusions: Donor age greater than 60 years is an independent risk factor for survival after transplantation. The age criterion must be considered in the acceptance decision for a lung transplant.
**BRIEF ORALS**

**Treatable traits lead the way towards better outcomes in lung transplantation**

**Results:** Univariate analysis demonstrated that post-transplant pseudomonas isolation, transient anti-HLA antibodies, DSA, invasive pulmonary aspergillosis (IPA) and fungal isolation (with clinical symptoms impeding diagnosis of colonization, but insufficient endoscopic/radiologic features for invasive fungal disease) were associated with increased RAS/Mixed phenotype occurrence. Multivariate analysis confirmed the association for pseudomonas isolation, transient HLA, DSA and IPA.

**Conclusions:** We have identified a set of risk factors associated with RAS that could be therapeutic targets in lung transplant follow-up.

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**BOS6_13**

**EXTRACORPOREAL PHOTOPHORESIS IN CHRONIC LUNG ALLOGRAFT DYSFUNCTION. SINGLE CENTER EXPERIENCE**

**Juan Pablo Reig Maqueda**, Inés Gómez Segui, José Alfonso Cerón Navarro, Beatriz Montull Veiga, Gabriel Anguera DE Francisco, María José Selma Ferrer, Desamparados Pastor Colom, Amparo Solé Jover

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**Background:** Extracorporeal photopheresis (ECP) is a procedure that involves the apheresis and collection of the leukocyte-enriched blood, which is exposed to ultraviolet light in the presence of 8-methoxypsoralen and then, reinfused to the patient. This results in lymphocyte apoptosis and induction of regulatory T-cells. ECP is an accepted therapy in lung transplant recipients (LT) for treatment of chronic lung allograft rejection (CLAD).

**Methods:** We performed a retrospective study of all lung transplant recipients who were treated with ECP for CLAD at Hospital la Fe, Valencia (Spain) from July 2017 to January 2022. ECP treatment was performed with off-line methods and processing one volemia. Treatments were performed weekly (1st mo.), quarterly (till 6 mo.) and then, monthly (6-12 mo.). A positive response to ECP was considered change in the mean decrease of FEV1 6 months after ECP, compared with 6 months prior to ECP. A small group of patients receive ECP due to recurrent acute rejection (RAR) (n=03). Means (paired Student’s t-test) were calculated with SPSS 20.0 software.

**Results:** Thirty-eight patients received ECP for CLAD (28 bilateral LT, 9 single-LT, 1 heart-lung transplant; 27 male & 11 female), with median age of 47 years (range 19-71). CLAD stage at ECP initiation was CLAD 1-2 28%, CLAD 3-4 28%, CLAD subtype obstructive 32%, restrictive 23%, mixed 35%. Immunosuppression at ECP start consisted of tacrolimus and everolimus in 3-4 28%. CLAD subtype obstructive 32%, restrictive 23%, mixed 35%.

**Conclusion:** ECP treatment is associated with a decrease in the mean decline in FEV1 in progressive CLAD patients. ILD-LT recipients might respond more than others. Advanced stage of CLAD at the start of ECP implied more mortality. RAR patients responded, ECP was proved as a safety alternative for LT recipients.
Complications and infections after kidney transplant

**BOST 1**
PREDICTION OF KIDNEY GRAFT SURVIVAL AMONG DECEASED TRANSPLANT RECIPIENTS IN THE UK: AN ARTIFICIAL INTELLIGENCE APPROACH

Hatem Al
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**Background:** Predicting kidney allograft outcome can direct clinical care and resource allocation. The aim of our study was to develop a prediction tool for death censored graft survival using artificial intelligence.

**Methods:** All deceased kidney transplant recipients registered in the UK Transplant Registry database from 2007 till 2020 were retrospectively reviewed. Exclusion criteria: age <18 years old, multiple organ transplant, kidney graft failure within 3 months post-transplant, or missing data about death censored graft survival. Graft failure was defined as the need for maintenance dialysis post-transplant. The data was divided into training and test dataset with ratio 70:30 in order to train the model and then evaluate its performance on the unseen data. Decision based models for survival analysis were used (decision tree, Random Forest and XGBOOST). Evaluation criteria were Harrell C statistic for discrimination, and Integrated Brier score for calibration. Data collected were transplant, factors donor and recipient demographics, serum creatinine at 3 months post-transplant.

**Results:** 22,717 patients were included in our study. For the decision tree model, Harrell C-statistics=0.70 (indicating adequate discrimination), Integrated Brier score=0.02 (indicating excellent calibration), AUC for a 10-year post-transplant period was 0.7 (indicating adequate performance). Random Forest and XGBOOST models slightly improved the Harrell C-statistic to 0.72. The key players in making the predictions were serum creatinine at 3 months post-transplant (importance factor=0.67), followed by donor-recipient age difference. A user-friendly web app can be developed using our model.

**Conclusions:** Decision based models can aid in predicting kidney graft survival post-transplant. Our model can make high discrimination and calibration predictions. A user-friendly web app can be developed using our model. Key players in prediction were serum creatinine at 3 months post-transplant and donor-recipient age difference. A user-friendly web app can be developed using our model.

**BOST 2**
REAL-LIFE IMPLEMENTATION OF A STRATEGY BASED ON CMV-SPECIFIC CELL-MEDIATED IMMUNITY TO GUIDE CMV PREVENTIVE THERAPY IN SOLID ORGAN TRANSPLANTATION

Delphine Kervella, Elena Crespo, Franc Casanova, Ignacio Cidraque, Laura Donadeu, Alba Torija, Maria Meneghini, Nuria Montero, Ina Torres, Jose Zuhila Vergara, Joana Sellares, Francesc Moreso, Oriol Bestard
1 VHIR - Vall d’Hebron Institut de Recerca, Nephrology and Transplantation laboratory, Barcelona, Spain, 2 Vall d’Hebron University Hospital, Nephrology department, Barcelona, Spain, 3 Bellvitge University Hospital, Nephrology department, Hospital de Llobregat, Spain

**Background:** Measuring CMV-specific cell-mediated immunity (CMI) is be a new promising tool to guide CMV preventive therapy after solid organ transplantation (SOT). However, its implementation in clinical practice has not been done yet.

**Methods:** Between January 2017-December 2019, we evaluated a new strategy for both CMV prevention guided by CMV-specific CMI in a real-life clinical scenario in 147 consecutives SOT recipients. In the preemptive cohort, CMV-CMI was assessed at day 10-15 post-transplantation in TV CMV R+ SOT not receiving T-cell depletion induction therapy. In the Stop-prophylaxis cohort, CMV-CMI was assessed in 55 CMV R+ and 17 D+/R- kidney recipients. Decision to discontinue prophylaxis therapy was at clinician’s discretion according to CMV-CMI results. We assessed CMV-CMI against two major CMV antigens (IE-1/pp65) with the T-SPOT®.CMV assay following IE-1 and pp65 thresholds recently published by our group in a RCT to classify patients into High- (HR), Intermediate- (IR) and Low-risk (LR). Primary outcome was occurrence of CMV graft viral load requiring therapy during first year post-transplantation.

**Results:** The preemptive cohort included 40 (53%) liver, 25 (33%) heart and 10 (13%) KT recipients. Mean time between transplantation and CMV was 14±8 days. No (0/24) LR-CMI patients, 5/27 (19%) of IR-CMI and 10/24 (42%) HR-CMI received prophylaxis. No infections occurred in patients on prophylaxis. Infection occurred in 3/24 (4.1%) LR, 3/22 (14%) IR- and 2/14 (14%) HR-CMI patients under preemptive strategy (figure 1A). In the Stop-prophylaxis cohort, mean time between transplantation and CMV-CMI was 117±43 days. Prophylaxis was withdrawn after first CMV in all LR-CMI patients (28/28), 16/27 (75%) IR- and 4/16 (25%) HR-CMI patients. 12 CMV events occurred, 3 in R+ and 9 in R-. All events occurred after prophylaxis completion, with a last CMV-CMI categorizing patients as IR (3/12) and HR (9/12) (p<0.01, figure 1B).

**Conclusions:** CMV-CMI risk stratification in a real-life clinical transplant scenario allowed identification of at-risk patients and proves to be a useful tool to guide type and extension of prophylaxis therapy among D+/R+ SOT.

**BOST 3**
MACHINE LEARNING MODELS IN RENAL TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PREDICTIVE PERFORMANCE IN GRAFT SURVIVAL

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**Background:** Kidney transplantation (KT) is currently the renal replacement therapy of choice for most patients with end-stage kidney disease. Despite many advancements, the variations in outcome and frequent occurrence of graft failure continue to pose important clinical and research challenges. The aim of this study was to carry out a systematic review of the current application of Machine Learning (ML) models in KT and perform a meta-analysis of these models in the prediction of graft outcomes.

**Methods:** This review was registered with the PROSPERO database (CRD42021247469) and all peer-reviewed and preprint original articles that reported the sensitivity and specificity of AI-based models were included in the meta-analysis. The quality of the articles were assessed by the criteria defined by Qiao et al and Risk of Bias assessment was performed using the PROBAST tool. The diagnostic performance of the meta-analysis was assessed by a meta-analysis of the Area under the Receiver Operating Characteristic (AUC) and a Hierarchical Summary ROC plot. 25 studies met the inclusion criteria for the review and 22 studies were included in the meta-analysis. More than 15 different ML models were used to predict graft survival in the included studies. Seven studies compared the predictive performance of ML models with traditional regression methods. 6 studies had a high risk of bias and 3 studies had an unclear risk of bias. The area under the HSROC curve was 0.79 and the summary sensitivity and specificity of ML-based models were 0.79 (95% CI, 0.69 - 0.85) and 0.66 (95% CI, 0.60-0.73), respectively.

**Conclusions:** Our study shows that ML models can accurately predict outcomes following KT by the integration of the vast amounts of non-linear data.
Complications and infections after kidney transplant

**BRIEF ORALS**

### BRIEF ORALS 1

#### BOS7 4

**BURDEN OF REFRACTORY/RESISTANT CYTOMEGALOVIRUS OR CYTOMEGALOVIRUS DRUG INTOLERANCE IN SOLID ORGAN TRANSPLANT RECIPIENTS: EUROPEAN SUBGROUP ANALYSIS**

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**Background:** Contemporary real-world data on management and outcomes of cytomegalovirus (CMV) infection post solid organ transplant (SOT) are scarce. Data were collected to describe the burden of resistant/refractory CMV infection or intolerance to conventional anti-CMV therapies (RRI) among SOT recipients enrolled in the Multinational CMV Outcomes, Treatment Patterns and Health-care Resource Utilization study (OTUS).

**Methods:** OTUS SOT is a multicenter retrospective study of adult patients (pts) who had RRI post-SOT. Eligible pts received SOT after Jan 1, 2014 across 13 transplant centers in the US (Spain, France, Germany, UK). Pts were followed ±12 months from CMV index date (date of RRI identification) or until death, whichever occurred first. A CMV index episode was defined as the first clinical presentation of CMV disease, outcomes, and hospitalizations in pts from the 8 European centers are described.

**Results:** Overall, 112 pts from Europe with ±3 years (mean) of follow-up post-SOT were analyzed. Median time from transplant to first CMV episode: 94.5 days. 109 (97.3%) pts developed RRI during their first CMV episode. Valganciclovir was used for primary and secondary prophylaxis in all pts for whom prophylaxis was used, and as treatment in 89.0% of pts. In the treatment setting, 16 (14.3%) pts received foscarnet and 58 (53.2%) pts required ≥2 anti-CMV therapies. In the treatment setting, 16 (14.3%) pts failed to achieve viremia clearance during the CMV index episode. CMV recurred in 22 (19.6%) pts. 50 (44.6%) pts had CMV-related hospitalizations (23.2%) pts failed to achieve viremia clearance during the CMV index episode. CMV recurred in 22 (19.6%) pts. 50 (44.6%) pts had CMV-related hospitalizations. All-cause mortality: 22.3%. Mortality 1-year post-RRI identification occurred in 16.1% of pts.

**Conclusions:** A relevant portion of pts in the European cohort of the OTUS SOT study who had RRI did not achieve CMV clearance during the CMV index episode and had CMV recurrence and/or adverse outcomes. Therapies that achieve and maintain CMV clearance without treatment-limiting toxicities are needed. Funding: Takeda Development Center Americas Inc.

#### BOS7 5

**PREVALENCE OF CYTOMEGALOVIRUS ANTIViral RESISTANCE IN TRANSPLANT RECIPIENTS**

**Steve Kleibeuker**

*Eurofins Viracor, Lenexa, United States

**Background:** Human cytomegalovirus (CMV) is a significant pathogen after solid organ and allogeneic hematopoietic cell transplantation. Antiviral drug resistance (ADR) to CMV is an important complication for patients on prophylaxis or treatment, and genotypic testing is well-documented for all current anti-CMV drugs. International guidelines recommend that ADR should be suspected, and genotypic testing performed, with persistent or recurrent CMV DNAemia or disease during prolonged (e.g., ≥26 weeks) antiviral therapy (Transplantation 2018; 102:900).

**Methods:** A total of 2750 patient samples submitted to Eurofins Viracor’s reference laboratory for CMV genotypic resistance testing were de-identified prior to retrospective performance. Testing was performed for ganciclovir (GCV), foscarnet (FCN), maribavir (MBV) and/or lenamevir (LMV) resistance based on physician orders. Viral UL54, UL56 and/or UL97 genes were amplified by PCR to produce overlapping fragments, which were subjected to consensus (Sanger) sequencing. Resistance conferring mutations were analyzed by viral genes and patient.

**Results:** Resistance mutations were most common in UL97 with 27.64% and 9.96% of samples positive for GCV and MBV ADRs, respectively. For LMV, ADR in UL56 were present in 7.17% of samples, and mutations at C329 represented 80.95% of mutations. The five most common mutations for each viral gene are shown in Table 1. Patient samples with ADR to GCV were most common, with 29.36% having mutations (587 in UL54 only, 42 in UL56 only, 95 in both UL57 and UL54). Several ADRs conferring resistance to more than one drug were identified, such as F342Y and C480F in UL97 which confer resistance to both GCV and MBV. Of the 2750 patient samples, 826 (30.03%) had resistance to one or more drug. Resistance to 2 drugs was identified in 216 samples and to 3 or more drugs in 35 samples.

**Conclusions:** A high prevalence of CMV ADR was identified in patient samples, although this may be taken in the context of physicians submitting samples from patients with suspected resistant CMV strains. For these patients, rapid monitoring for ADR allows physicians to treat based on objective results rather than empiric drug selection, which is particularly relevant given the presence of mutations conferring resistance to more than one drug.

**Table 1. Prevalence of the most commonly detected resistance conferring mutations by CMV gene and antiviral drug**

<table>
<thead>
<tr>
<th>Drug</th>
<th>UL54</th>
<th>UL56</th>
<th>UL97</th>
<th>UL54</th>
<th>UL56</th>
<th>UL97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luciferase</td>
<td>95.76</td>
<td>88.35</td>
<td>93.56</td>
<td>92.78</td>
<td>89.64</td>
<td>92.63</td>
</tr>
<tr>
<td>UL54</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
</tr>
<tr>
<td>UL56</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
</tr>
<tr>
<td>UL97</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
<td>94.32</td>
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<td>94.32</td>
</tr>
</tbody>
</table>

*No antiviral drug resistance mutations detected for the indicated drug and CMV gene.

#### BOS7 6

**THE RISK OF VENOUS THROMBOEMBOLISM IS ENHANCED AFTER A CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENT**


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**Background:** In immunocompetent patients, past CMV infections have been associated with an increased risk of venous thromboembolism (VTE). In this study, we have investigated in a large prospective cohort of kidney transplanted recipients (KTR) whether the occurrence of a CMV infection which is the most frequent pathogen encountered within the first-year post transplantation could be enhanced by an increased risk of VTE in addition to the risk of the post-operative period, or repeated hospitalizations.

**Methods:** We conducted a study on the multicentric DIVAT database which was carried out prospectively and exhaustively on key dates during post-operative follow-up of clinical and biological data for 68,000 KTR belonging to 8 French transplantation centers (CNIL decision DR-2015-087, N°914184). Multivariable cause-specific time-varying Cox models stratified on centers were used to estimate the relationship between the risk of VTE occurring after well documented first CMV infections (asymptomatic or disease) and which were considered as a time-dependent variable.
Complications and infections after kidney transplant

Results: 15,433 KTR transplanted between 2000 and 2021 were included among whom 11,765 with CMV. CMV infection with a cumulative incidence at 1- and 2 years respectively of 11.6% (95% CI from 11.1% to 12.2%) and 13% (95% CI from 12.4% to 13.5%). Within the same period of survey 2001 VTE occurred in 5.53% (95% CI from 5.17% to 5.92%) and 6.71% (95% CI from 6.31% to 7.14%) at 1- and 2 years respectively. CMV and VTE were significantly associated at baseline and at the end of the follow-up (n=1176) the risk of VTE was 1.61 (95%CI 1.19; 2.17). The risk enhanced at 2.00 (95%CI 1.32; 3.02) after a first asymptomatic CMV infection (n=574) in comparison to similar patients free of CMV infection and independently of recipient age, past history of TVE and post-transplant surgical complications. Finally, the increased risk of VTE occurrence did not change whatever it was a primo or a reactivation of the CMV infection. There are 3 risk markers of CMV and VTE: age, gender and diabetes. The risk increased in patients older than 65 years, male gender and diabetic patients. The risk of VTE occurrence did not change in case of CMV disease, there is an increased risk of VTE. Since the high frequency of CMV infection after a kidney transplantation, transplant physicians should be aware of such association for a rapid diagnosis and adapted treatment.

Background: Proton pump inhibitors (PPIs) are frequently used after renal transplantation and often maintained afterward. However, many studies report complications related to the use of PPIs, especially in terms of nephrotoxicity on native kidneys. Nevertheless, data concerning the use of PPIs in renal transplantation remain scarce.

Methods: We retrospectively analyzed all kidney transplant recipients at the Nantes University Hospital between 01/01/2000 and 31/12/2020. In order to approach a clinical trial methodology, patients were categorized according to whether or not they were taking PPIs at D15, and then analyzed in Intention to Treat. The primary endpoint was graft survival. Secondary endpoints were biopsy proven rejection, all-cause infections, and digestive bleeding complications. Analyses were performed using a multivariate Cox model.

Results: 2379 patients were included, 1401 in the PPI group and 978 in the non-PPI group. The median follow-up time was 6 years. In multivariate analysis, patients in the PPI group did not have a significant excess risk of graft loss (HR = 0.86; CI95% = 0.69 ;1.06). There was a statistically non-significant trend towards an increase in occurrence of rejection (HR = 1.24; CI95% = 0.95; 1.60) and a higher risk of infectious complications (HR = 1.13; CI95% = 1.01; 1.29) in the PPI group. The occurrence of bleeding complications did not differ between groups (HR = 1.12; CI95% = 0.75; 1.69).

Conclusion: In our cohort analyzed in Intention to Treat, the use of PPIs did not impact graft survival nor the occurrence of bleeding complications but increased the occurrence of infectious complications. 

Results: The mean capillary numbers were 38,4±15,2 and 27,6±14,4 for GCs and PTCs respectively. The mean of capillary PI was 0.97±0.08 and 0.87±0.07 for GCs and PTCs respectively. The mean expression of VEGF was 125,1±72,9 and 139,3±72,9 for GCs and PTCs respectively. The mean expression of NO was 90,8±57,9 and 86,4±51,5 for GCs and PTCs respectively. The mean expression of villin was 52,1±32,1 and 53,1±33,3 for GCs and PTCs respectively. The mean expression of proteinuria was 0.3±0.1 and 0.3±0.1 for GCs and PTCs respectively. The mean expression of cholesterol was 5.1±4.2 and 5.3±4.3 for GCs and PTCs respectively. The mean expression of PI of ECs was 1.8±0.2 and 2.0±0.3 for GCs and PTCs respectively. The mean expression of PI of tubules was 1.4±0.1 and 1.7±0.1 for GCs and PTCs respectively. The mean expression of PTC-VEGF was 1.3±0.2 and 1.5±0.3 for GCs and PTCs respectively. The mean expression of PTC-NO was 0.9±0.1 and 1.0±0.1 for GCs and PTCs respectively.

Results: Among 150 patients, 63 (42%) had HC. Biopsies were highlighted with the impact of age and cholesterol on the density of GCs and PTCs. A marked loss of capillary VEGF & NO expression associated with hypertension, IF development, and graft loss (P<0.001 for all). The GC loss was also significantly associated with GVIF & NO expression associated with hypertension, IF development, and graft loss (P<0.001 for all). IF development was found to increase with the decreasing degree of tubular villin and tubular cell PI index. Conclusion: A marked loss of capillary VEGF & NO expression associated with hypertension, IF development, and graft loss (P<0.001 for all). IF development was found to increase with the decreasing degree of tubular villin and tubular cell PI index.

Results: During the study period, 213 kidney transplant recipients were treated with alemtuzumab for rejection. 1691 kidney transplant recipients were included who didn’t receive alemtuzumab as an anti-rejection treatment. Baseline characteristics were comparable (Table 1). Alemtuzumab-therapy was associated with a higher probability of death (HR 1.63, 95%-CI 1.12 to 2.20) and infection-related death (HR 1.82, 95%-CI 1.08 to 3.05), but not with malignancy-related death. Alemtuzumab-therapy was also not associated with a higher incidence of overall malignancies, solid malignancies, skin malignancies or hematological malignancies.

Conclusions: Treatment with alemtuzumab for kidney transplant rejection is associated with a higher probability of death and infection-related death, but not malignancy-related death or the number of malignancies. These results suggest that infections are the most important long-term complication of alemtuzumab for kidney transplant recipients.
Background: Increased urinary excretion of protein and albumin are associated with adverse outcomes in kidney transplant recipients. However, the optimal test for proteinuria and albuminuria at one-year posttransplant to identify patients at risk is uncertain.

Methods: We analyzed 1264 adult kidney transplant recipients with stable graft function in this retrospective, observational cohort study. The predictive performance of one-year posttransplant spot urine protein-creatinine ratio (uPCR), albumin-creatinine ratio (uACR), 24-hour urine protein excretion (24hPE), and 24-hour urine albumin excretion (24hAE) as well as urinary dipstick protein (uDSP) on five-year death-censored graft loss (DCGL) and all-cause mortality were compared.

Results: Patients were followed up for a median of 8.17 (25th-75th percentile, 4.47-11.84) years, during which 58 (4.59%) patients developed graft loss and 83 (6.96%) patients died. The predictive performance of uDSP for DCGL was lower (area under the receiver-operating characteristic curve [AUC] 0.61, P = 0.005) than 24hPE, uPCR, 24hAE, and uACR (AUC 0.65, 0.68, 0.72, and 0.74, respectively, all P < 0.001). Results were similar for the mortality outcome. Elevated uACR was associated with increased DCGL (adjusted hazard ratio [aHR] 7.45, 95% confidence interval [95% CI] 2.05-27.13, P = 0.002) as well as cumulative mortality (aHR 2.93, 95% CI 1.23-6.95, P = 0.012), whereas, uDSP was not associated with DCGL or cumulative mortality.

Conclusions: In patients with stable graft function, measuring albuminuria and uACR showed the best performance in predicting 5-year outcomes after kidney transplantation. Dipstick proteinuria measurement performed poorly on outcome prediction. Our data suggest that albuminuria measured as spot uACR should be the method of choice for routine care and research, while uDSP test does not reliably predict outcomes.

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Background: Tubuloreticular inclusions (TRIs) seen on electron microscopy (EM) are classically associated with lupus nephritis (LN) and systemic viral infections in native biopsies. Traditionally a marker for enhanced type I interferon expression, little is known about their significance post-transplant. We aimed to look at a large cohort of transplant biopsies showing TRIs to investigate associations and outcomes.

Methods: A retrospective analysis was performed on two prospective databases; an in-centre transplant registry and a histopathology database holding data on all kidney biopsies performed at our centre. All patients biopsied since 2015, who had EM examination were included. Where patients had more than one biopsy showing a TRI the earliest one was included. Demographic, clinical and transplant data was collected from the laboratory records. ABO incompatible transplants were excluded. Results: 998 kidney transplant biopsies were performed between December 2005 and December 2022: 1740 (21.7%) had EM performed. Of 1740 EM, 256 (14.7%) had evidence of TRIs on at least one biopsy: Of 256 patients, 34% were female, the median age was 52.3 years (38.9-59.4), 28% had underlying glomerulonephritis as their cause of ESKD, 61% were deceased donors and 68% were of non-white ethnicity. TRIs were associated with serological evidence of autoimmunity (17%), viral infections (28%) and donor specific antibodies (35%), with no association found in 34%. Rejection occurred in 127 (50%), including 38% of patients with no recognized association with TRIs. Allograft outcomes were poor, with all-cause allograft survival and death-censored allograft survival of 54% and 70% after a follow up of 5.7 +/- 3.8 years post index biopsy. A comparison with a matched control group is underway.

Conclusions: In extension to previous work, we show that TRIs appear to be associated with alloimmunity. In this regard they may be a useful biomarker especially in cases where the diagnosis is unclear or biopsy findings are ‘sudddrenched’. Irrespective of aetiology, TRIs are associated with poor outcomes and warrant further consideration.
BRIEF ORALS

Complications and infections after kidney transplant

BOS7_14

IMPACT OF ALLOGRAFT CELLULAR INFLAMMATION ON THE IGA NEPHROPATHY RECURRENTE AFTER KIDNEY T RANSPLANTATION

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Background: The recurrence of IgA nephropathy (rIgAN) after kidney transplantation (KT) is relative frequency and impairs KT outcomes, representing the third cause of loss in KT recipients. Several variables at the time of recurrence, ( e.g. impaired allograft function, heavy proteinuria, steroid withdrawal, and MEST-C histological findings have been associated with a higher risk of graft loss after rIgAN. The presence of allograft clinical or subclinical inflammation has been associated with a higher risk of graft loss, but it is not precisely known how it influences the outcome of patients with rIgAN.

Methods: A multicenter retrospective study was carried out including KT recipients with biopsy-proven IgA nephropathy as the underlying disease in which the Banff criteria were available or could be reviewed. Allograft cellular inflammation was defined according to Banff scores as “t” or “i” ≥2. The main endpoint was progression to CKD stage 5 or death censored-graft loss (DCGL).

Results: 118 KT recipients were included (47±14 ys. at recurrence), 80% male, with a mean time to biopsy of 65±69 mo. and a post-transplant follow-up of 118 ± 70 months. After recurrence, 34 (28.8%) allografts were lost after 35±28 mo., excluding death. By univariate Cox regression, the factors related to CKD stage 5 or graft loss were systolic blood pressure (HR 1.039, 95%CI 1.016-1.064, p = 0.001), glomerular filtration rate (HR 0.948, 95%CI 0.922-0.974, p <0.001), the logarithm of proteinuria (HR 15.836, 95% CI 5.504-45.565, p <0.001), Oxford-C score (HR 3.490, 95% CI 2.137-5.499, p <0.001), Interstitial fibrosis (HR 2.173, 95% CI 1.362-3.468, p = 0.001) and cellular inflammation (HR 2.458, 95% CI 1.237-4.884, p = 0.010). By multivariate analysis, allograft inflammation remained significantly related to CKD stage 5 or DCGL (HR 2.338, 95% CI 1.077-5.075, p = 0.032), independently of systolic blood pressure, glomerular filtration rate, proteinuria and Oxford-C score.

Conclusions: Allograft cellular inflammation influences worsens KT outcomes after rIgAN. We suggest to considering the Banff criteria for acute cellular inflammation to better understand the subsequent evolution of patients with rIgAN.

Kidney allograft immunopathology

BOS8_1

HUMAN LEUKOCYTE ANTIGEN MISMATCHES AND GRAFT OUTCOMES IN THE CONTEMPORARY ERA OF IMMUNOSUPPRESSION: A UK REGISTRY ANALYSIS

Rajas Rashid1, Charlotte Stephens1, Adnan Sharifi1,2

1Queen Elizabeth Hospital Birmingham, Department of Nephrology and Transplantation, Birmingham, United Kingdom, 2University of Birmingham, Institute of Immunology and Immunotherapy, Birmingham, United Kingdom

Background: The impact of human leukocyte antigen (HLA) mismatching on kidney transplant outcomes is unclear. A recent meta-analysis of 23 cohort studies concluded HLA mismatching was a critical prognostic factor for graft loss, especially HLA-DR, but the majority of included studies did not reflect contemporary use of immunosuppression. The aim of this study was to investigate this using contemporary UK transplant registry data.

Methods: A retrospective cohort study was undertaken of prospectively collected registry data of all kidney transplant recipients in the United Kingdom from January 1, 2000 until September 30, 2019 inclusive. HLA mismatch levels were defined by national criteria; level 1 (HLA mismatch 0), level 2 (HLA mismatch 0 DR and 0/1 B), level 3 (HLA mismatch 0 DR and 2B, or 1 DR and 0/1 B), and level 4 (1 DR and 2B, or 2 DR). The primary outcome was death-censored graft loss. Time-to-graft loss was modelled using weighted estimation of Cox regression to account for non-proportional hazards, with covariate adjustment. All analyses were done using R statistical software (version 4.2.2).

Results: A total of 37,251 kidney transplant recipients formed the study cohort. HLA mismatches were as follows; level 1 (12.4%, n=4,592), level 2 (30.4%, n=11,237), level 3 (44.7%, n=16,521), level 4 (12.4%, n=6,400). Increasing level of HLA mismatches were associated with risk for 3-month rejection; level 1 (11.0%), level 2 (13.4%), level 3 (14.4%) and level 4 (18.1%) (p<0.001). In an adjusted weighted Cox regression model with level 1 the reference, there was no increased risk for death-censored graft loss with level 2 (HR 1.18, 95% CI 1.09-1.28) but borderline association with observed with 2 (HR 1.30, 95% CI 0.85-2.05) and 2 (HR 2.338, 95% CI 1.077-5.075, p = 0.032), independently of systolic blood pressure, glomerular filtration rate, proteinuria and Oxford-C score.

Conclusions: In the current era of immunosuppression, level of HLA mismatches does not contribute to long-term death-censored graft survival. Unless clinically indicated (e.g. younger kidney transplant candidates), HLA mismatching should not influence choice of allograft.
BRIEF ORALS
Kidney allograft immunopathology

BOS_2

PATTERNS OF MAJOR-HISTOCOMPATIBILITY-COMPLEX (MHC) CLASS I-RELATED CHAIN A (MICA) ALLOIMMUNE RESPONSES REVEALED BY MACHINE LEARNING ALGORITHMS

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Background: Antibodies against major histocompatibility complex class I–related chain A antigens (anti-MICA) in kidney transplantation (KTx) have been associated with rejection episodes and reduced graft survival. MICA cross-reactive epitope groups (CREGs) are not full described. This study aimed to the unsupervised identification of MICA CREGs in KTx patients, thus providing more information regarding their role in immune responses.

Methods: A cohort of 1208 KTx patients were enrolled from 2006-2022 and tested by single antigen bead assay (One Lambda). Initially, the antibody responses to 9 common MICA between different lots, were analyzed in all patients. In 336 patients, the analysis was repeated adding 6 additional MICA alleles to the antibody response control, studying a total of 15 MICA. Knowing that the immune system usually responds to “shared” immunogenic targets, the clustering patterns of anti-MICA responses without any a priori hypothesis using Principal Component Analysis (PCA), was studied. MICA protein sequence alignment was performed utilizing the IMGT/HLA alignment tool. The response clusters polymorphisms were determined with the 57 verified MICA epitopes in the Registry of HLA Epitopes.

Results: PCA projection, revealed that anti-MICA responses can be explained by two major distinctly related CREGs filling the upper and lower quadrant of the PCA biplot respectively (Figure 1). Protein sequencing alignment of the two clusters polymorphisms were determined with the 57 verified MICA epitopes in the Registry of HLA Epitopes.

Conclusions: Machine learning approaches can be considered for objective clustering and measuring of antigenic distances of anti-MICA responses. Two major bead-array defined CREGs were clearly identified and were explained by specific amino acid differences. Knowledge of MICA associations may guide allograft and immunosuppression strategy selection, thus improving long graft survival and KTx success.
Background: Early graft failure after kidney transplantation (KT) is mainly a result of acute rejection or surgical complications, while long-term graft failure is due to multifactorial conditions. An inflammatory profile in kidney transplant recipients is associated with increased long-term mortality, and specific inflammatory biomarkers have shown association with long-term graft failure. In this study, we have examined the association between early subclinical systemic inflammation scores following kidney transplantation and long-term kidney graft failure.

Methods: We measured 21 inflammatory biomarkers 10 weeks after KT in 1044 patients. Low-grade inflammation was assessed with predefined inflammation scores based on specific biomarkers: one overall inflammation score and five pathway-specific scores representing fibrogenesis, vascular inflammation, metabolic inflammation, angiogenesis, and leukocyte activation. The scores were tested in Cox regression models adjusted for established risk factors. Death-censored kidney graft failure was the primary outcome variable.

Results: Median follow-up time was 9.8 years (interquartile range 7.6-11.4 years). When tested as a continuous variable, the overall inflammation score was associated with long-term kidney graft failure (HR 1.03, 95% CI: 1.02-1.05, p-value <0.001). When the score was assessed as a categorical variable with the 1st quartile as reference, the 4th quartile was also associated with long-term kidney graft failure (HR 1.03, 95% CI: 1.02-1.05, p-value <0.001, table 1, figure 1). In the pathway-specific analyses, fibrogenesis activity and vascular inflammation stood out (table 1).

Conclusions: In conclusion, based on total inflammatory- and pathway-specific scores, we have described a significant association between an inflammatory environment early after kidney transplantation and long-term kidney graft failure. Vascular inflammation and increased fibrogenesis activity stood out among the tested pathways and could be potential targets in future intervention studies.

Table 1: Adjusted Cox regression analyses of inflammation scores and death-censored kidney graft failure

<table>
<thead>
<tr>
<th>Pathway-specific inflammation score</th>
<th>Score as continuous variable (HR, 95% CI, p-value)</th>
<th>2nd Quartile (HR, 95% CI, p-value)</th>
<th>3rd Quartile (HR, 95% CI, p-value)</th>
<th>4th Quartile (HR, 95% CI, p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall inflammation</td>
<td>1.03 (1.02-1.05, p-value=0.001)</td>
<td>1.11 (0.68-1.84, p-value=0.524)</td>
<td>1.23 (0.95-3.00, p-value=0.074)</td>
<td>3.12 (1.71-5.69, p-value=0.001)</td>
</tr>
<tr>
<td>Fibrogenesis</td>
<td>1.05 (1.02-1.08, p-value=0.004)</td>
<td>1.20 (0.97-1.50, p-value=0.029)</td>
<td>2.05 (1.85-2.63, p-value=0.013)</td>
<td>3.73 (0.92-0.20)</td>
</tr>
<tr>
<td>Vascular/general inflammation</td>
<td>1.07 (1.03-1.11, p-value=0.001)</td>
<td>1.50 (0.89-2.38, p-value=0.115)</td>
<td>2.83 (1.80-4.60, p-value=0.002)</td>
<td>5.02 (0.90-0.001)</td>
</tr>
<tr>
<td>Metabolic</td>
<td>1.03 (0.99-1.07, p-value=0.109)</td>
<td>1.40 (0.80-2.40, p-value=0.092)</td>
<td>1.43 (0.64-2.48, p-value=0.047)</td>
<td>2.53 (p=0.212)</td>
</tr>
</tbody>
</table>

Figure 1: Kaplan-Meier plot: association between the overall inflammation score and kidney graft survival.
Kidney allograft immunopathology

**BRIEF ORALS**

**BOS8_7**

**HIGH REJECTION RATES WITH NO INDUCTION+RAPID STEROID WITHDRAWAL IN WELL MATCHED LIVING DONOR KIDNEY TRANSPLANTS WITH PREVIOUS TCELL ALLOREACTIVITY**

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**Background:** Both de novo and preformed alloimmunity drive posttransplant immune-mediated events, that may be predicted by the assessment of donor/recipient HLA molecular mismatch and pretransplant circulating donor-reactive memory T cells (dR_mTc). To investigate the value of these biomarkers to allow safe immunosuppression (IS) individualization, we conducted a prospective, multicentre clinical trial in which first, living-donor kidney transplants (LDKT) were randomized to biomarker-guided IS regimens or to standard-of-care (SoC) therapy.

**Methods:** In this 2-year follow-up trial, run in 6 adult KT centres, IS individualization based on preformed dR_mTc (IFNg ELISPOT) and HLA-DR/DQ Eplet Mismatch (HLA-Matchmaker) (group A) was compared to SoC IS (TAC/MMF/PDN, group B) on a composite endpoint made of loss of renal function, incidence of biopsy-proven acute rejection (BPAR) and de novo DSA. Patients with high dR_mTc frequencies (>25 IFNg spots/3x10^6 PBMC) received Thymoglobulin induction (A1), patients with high DR/DQ Eplet MM received basiliximab and TAC-based triple therapy with higher MMF exposure (A2), and KT with both low DR/DQ Eplet MM and low dR_mTc received TAC/MMF with no induction and rapid (7-day) steroid withdrawal (A3).

**Results:** The study was prematurely halted when 39 LDKT were recruited due to exceeded BPAR rates in the A3 group (4/8, 50%), whereas none occurred in the other 2 biomarker-guided groups (A1, A2) and only 1/8 (13%) in SoC (group B).

All rejections were T-cell mediated (3 Banff IA, 2 IIA) and occurred within the first weeks after transplant (25±32 days) (figure). Assessment of baseline biomarkers revealed that LDKT developing BPAR within group A3, albeit lower than 25, these patients displayed detectable and significantly higher IFNg-producing mTc than those that did not reject (10.8±2.3 vs 2.3±4.0, p=0.05). Conversely, no differences on distinct donor/recipient HLA MM algorithms were observed. Notably, the patient in group B developing TCMR showed high frequencies of dR_mTc (>25 IFNg spots).

**Conclusions:** Rapid steroid withdrawal in absence of induction therapy in a TAC/MMF-based IS regimen should be highly discouraged in presence of low but detectable preformed donor-reactive mTc, despite good donor/recipient HLA molecular matching.

**BOS8_8**

**EUROPEAN SURVEY ON CLINICAL PRACTICE OF DETECTING AND TREATING T-CELL MEDIATED KIDNEY TRANSPLANT REJECTION**

**Priyanka Kosty1, Lucrezia Furian2, Peter Nickerson3, Gianluigi Zaza4, Maria Haller5, Alko De Vries6, Maarten Naesens2**

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**Background:** The 2009 KDIGO guideline for treatment of acute rejection recommends the use of corticosteroids as the initial treatment and suggests using lymphocyte-depleting antibodies or OKT3 if the patient is nonresponsive to corticosteroids or if there is recurrence of acute cellular rejection. OKT3 is unavailable and it is unclear what is the current clinical standard of care in acute T-cell mediated rejection (TCMR) in EU. Adapting treatment guidelines to the current EU reality is necessary, also for novel clinical trial design.

**Methods:** An invitation was sent through ESOT/EKITA newsletters and through a social media campaign to transplant professionals in Europe for taking part in the survey. The survey was web-based through SurveyMonkey and was conducted in 2022.

**Results:** A total of 129 European transplant professionals responded to the survey, most were transplant nephrologists (78.1%). 92 major university hospitals across Europe were represented. There was equal representation of small and large sized transplant centres. There was heterogeneity between centres in the performance of protocol biopsies (always-36.2%; in specific groups-21.3%; never-42.5%). The kidney biopsies performed for the diagnosis of TCMR were evaluated by renal pathologists (91.7%). The common practices observed were that majority of the centres treat borderline changes (BL) and TCMR (Grade IA-B, IIA-B), in indication biopsies (99% for BL; 100% for TCMR), with primarily steroids (69.9% for BL; 100% for TCMR), with primarily steroids as the first line treatment. Thymoglobulin is used as second line treatment for TCMR Grade IA-B (72.1%) & TCMR IIA-B (74.8%). Alentuzumab is not routinely administered since many centres in EU have not approved the drug for clinical use and it is not reimbursed. There were no differences observed between the large and small centres for the management of TCMR. No consensus was observed in the dosages of steroid therapy for the treatment of borderline changes and TCMR.

**Conclusions:** This survey highlights the common practices and diversity in clinics for management of TCMR in Europe. It also highlights the differences in clinical practices in EU from US and Canada.
Background: The histological Banff classification for kidney transplant rejection currently includes limited information on the cell type composition of the immune infiltrate. Improved understanding of rejection’s immune cell composition could help in developing targeted therapies. This study aims to explore the association of intragraft immune cell populations and Banff histology.

Methods: The proportions of nine infiltrating immune cell types were estimated via the deconvolution of two transcriptomic datasets (N=596) of kidney transplant biopsy specimens using a novel signature matrix derived from single cell transcriptomics. Differences in cells proportion between No rejection and AMR, TCMR or Mixed rejection were assessed with Student t-tests. The association between cellular proportions and the ordinal Banff scores (1 vs 2 vs 3 acute lesions) and F and G chronic lesions) was assessed with Kendall’s tau on the first dataset (N=224).

Results: CD4 memory (CD4mem) cells were the only cells whose fractions were significantly higher in No rejection (on average +3.1% p<0.001) compared to Rejection. All other immune cells were significantly higher in Rejection. Mixed rejection was marked by the largest difference with No rejection in NK cells (+1.7% p<0.001), FCGR3A+ myeloid cells (+2.6% p<0.001), B cells (+2.2% p<0.001), and CD4mem (-5.1% p<0.001), although there were large overlaps in the cell composition between the rejection subtypes (Fig. 1A). TCMR demonstrated the highest degree of general inflammation (total immune cells, p<0.001), and CD4mem (-5.1% p<0.001), although there were large overlaps in the cell composition between the rejection subtypes (Fig. 1A). TCMR demonstrated the highest degree of general inflammation (total immune cells, p<0.001), and CD4mem (-5.1% p<0.001), although there were large overlaps in the cell composition between the rejection subtypes (Fig. 1A).

Conclusions: Profiling kidney graft infiltrating immune cells showed an important involvement of monocytes and NK cells in acute rejection phenotypes. We are currently investigating how the complex immune cell composition of rejection relates to transplant outcomes.
REAL-LIFE ASSESSMENT OF NON-INVASIVE MOLECULAR BIOMARKERS FOR PREDICTING CLINICAL AND SUBCLINICAL HISTOLOGICAL LESIONS IN KIDNEY TRANSPLANT RECIPIENTS

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1VHIR - Vall d’Hebron Institut de Recerca, Nephrology and Transplantation laboratory, Barcelona, Spain, 2Vall d’Hebron University Hospital, Kidney transplant unit, Nephrology department, Barcelona, Spain, 3Bellvitge University Hospital, Nephrology department, Hospital de Llobregat, Spain, 4Hospital del Mar, Nephrology and Kidney Transplantation, Barcelona, Spain, 5Hospital Clinic, Nephrology and Kidney Transplantation, Barcelona, Spain, 6Hospital Germans Trias i Pujol, Badalona, Spain, 7Hospital Germans Trias i Pujol, Barcelona, Spain, 8Fundació Puigvert, Kidney transplant unit, Barcelona, Spain

Background: Non-invasive biomarkers are intended to rule out alloimmune-mediated graft damage in kidney transplant patients. While TruGraf®, a gene set signature has been shown to accurately exclude the presence of subclinical rejection, especially TCMR as well as borderline lesions, elevated dd-cfDNA levels accurately capture clinical and subclinical ABMR. This study evaluated the ability of TruGraf® and dd-cfDNA (Viracor TRAC®) to diagnose rejection when assessed at the time of for-cause or surveillance biopsies.

Methods: We performed a multicenter, observational study with 310 unselected, consecutive kidney transplant recipients undergoing either for-cause or protocol biopsies (Banff 2019 classification) with paired blood samples, from Dec. 2021 to Oct. 2022. TruGraf® and Viracor TRAC® were run blinded by a central lab. Of 310 patients, 230 had paired core biopsies.

Results: In the for-cause biopsy group (n=89), mean dd-cfDNA values were different between patients with normal and abnormal biopsies (0.596±0.579% vs 2.106±1.781% (p=0.003) (Figure 1A) and was significantly higher in allo-immune mediated lesions (rejection, BL, MVI) from any other feature such as recurrent GN, IFTA and pristine biopsies (3.905±5.536% vs 0.633±0.552% vs 2.106±4.030% (p=0.003) (Figure 1A) and was significantly higher in patients with normal vs abnormal biopsies (0.596±0.579% vs 2.106±1.781%, 0.812±0.747%, p=0.007, p=0.001 and p<0.001, respectively) (Figure 1B). Viracor TRAC® discriminated between rejection and non-rejection (AUC=0.714) as compared to serum creatinine (AUC=0.584). In protocol biopsies (n=104), mean dd-cfDNA values were significantly different between patients with normal vs abnormal features (0.812±0.747 vs 1.935±3.743 (p=0.029), although with a low AUC of 0.514. These differences were significantly stronger when discriminating allo-immune-mediated lesions (ABMR, TCMR, BL) from any other feature such as recurrent GN, IFTA and pristine biopsies (3.905±5.536% vs 0.633±0.552% vs 1.032±1.781%, 0.812±0.747%, p=0.007, p=0.001 and p<0.001, respectively) (Figure 1B). Viracor TRAC® discriminated between rejection and non-rejection and between ABMR and no ABMR with AUC of 0.758 and 0.861 respectively. In vivo validation was made in an adapted mouse heterotopic heart transplantation model, in which donor animals were from the same genetic background as recipients [C57B6 (H2b)] but KO for MHC-I. This trick allowed stimulating recipient’s NK cells by missing self in the absence of any other allogeneic stimulation. Finally, a monocentric pilot clinical study was conducted in 46 renal transplant patients with MS-induced NK rejection.

Conclusions: Viracor TRAC® showed good performance to capture subclinical rejection, especially ABMR, and to discriminate normal vs abnormal histology in patients with graft dysfunction.

INHIBITION OF MTOR PATHWAY PREVENTS MISSING SELF-INDUCED NK CELLS-MEDIATED REJECTION

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1Lyon University Hospital-INSERM U1111, Lyon, France

Background: Our team recently reported that the inability of graft endothelial cells to deliver HLA-A1-dependent inhibitory signals to circulating recipient NK cells (missing self, MS) was the cause of DSA-independent microvascular inflammation (MVI) leading to chronic vascular rejection. The purpose of this translational study was to identify the signaling pathways involved in NK cells activation and to evaluate the therapeutic potential of their pharmacological blockade.

Methods: The coculture of human purified NK cells with allogeneic microvascular endothelial cells recapitulated MS-induced NK cell rejection in vitro. In vivo validation was made in an adapted mouse heterotopic heart transplantation model, in which donor animals were from the same genetic background as recipients [C57B6 (H2b)] but KO for MHC-I. This trick allowed stimulating recipient’s NK cells by missing self in the absence of any other allogeneic stimulation. Finally, a monocentric pilot clinical study was conducted in 46 renal transplant patients with MS-induced NK rejection.

Results: The coculture model revealed the crucial role of the mTOR pathway for MS-induced activation of NK cells. The addition of an mTOR inhibitor to the cocultures blocked NK cells activation and prevented the destruction of endothelial cells. These results were confirmed in the mouse heart transplantation model, in which the MVI lesions observed in the grafts of untreated controls were completely abrogated in recipients treated with mTOR inhibitor. Finally, the replacement of MMF by an mTOR inhibitor in 16 kidney recipients diagnosed with MS-induced NK rejection resulted in the reduction of graft MVI lesions in control biopsy and an improved graft survival as compared with historical controls (n=30) left on the same immunosuppression (MMF+CNI).

Conclusions: The introduction of an mTOR inhibitor in patients diagnosed with MS-induced NK rejection could reduce rejection lesions and improve graft survival.
Kidney allograft immunopathology

BRIEF ORALS

Zainab Al Fatli*, Anass Bekkaoui, Michiel Betjes, Marlies Reinders, Annelies de Weerd
1Erasmus Medical Center, Nephrology and kidney transplantation, Rotterdam, Netherlands

Background: Animal experimental data suggest a blood pressure lowering effect of mycophenolate mofetil (MMF). However, data from a randomized controlled trial in humans are lacking.

Methods: A randomized controlled weaning trial was performed in low immunologically risk kidney transplant recipients (EudraCT nr.: 2014-001372-66). Recipients were randomized to standard tacrolimus (TAC)/MMF or to TAC monotherapy (TACmono), from 9 months onwards after transplantation, without steroids. Outpatient clinic blood pressure measurements were performed at month 6 (baseline), 9 and 12 after transplantation. At each timepoint, blood pressure was measured 7 times with 5-minute intervals by a research nurse after 30-minutes rest. The WHO developed Daily defined dose (DDD) was used to compare the number and type of antihypertensive drugs. At each timepoint 24-hour urinary sodium, potassium and protein excretion was also assessed.

Results: Between 2015 and 2018, 79 recipients were randomized, of whom 73 completed 12 months follow-up in the blood pressure study (39 TAC/MMF and 34 TACmono). At baseline six months after transplantation, patients were 62 (56-69) years of age with an eGFR of 55±16 ml/min and proteinuria of 14.0 (10.0-23.0) mg/mmol in both groups and MMF dose of 1000 mg daily (1000-1500) in TAC/MMF.

Conclusions: Discontinuation of MMF after kidney transplantation in a tacrolimus/MMF immune suppressive regimen increased the use of antihypertensive drugs significantly. These data support the concept of a blood pressure lowering effect of MMF.

Table 1. Baseline characteristics of kidney transplant recipients randomized to either tacrolimus monotherapy or tacrolimus with mycophenolate mofetil

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TAC mono (n = 39)</th>
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<tbody>
<tr>
<td>Age, median (range in years)*</td>
<td>63 (38-71)</td>
<td>61 (30-80)</td>
<td>0.77</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>25 (74)</td>
<td>28 (72)</td>
<td>0.87</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>28 (6.0)</td>
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</tr>
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<td>Transplant type, n living donor / n transplant (%)</td>
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<td>Proteinuria/protinecreatinine ratio, median (range in mg/mmol)*</td>
<td>12.1 (0.04-5.4)</td>
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<td>CKD G3-G4, mean (SD)</td>
<td>59 (3.2)</td>
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<td>TAC trough level, median in ng/l (IQR)*</td>
<td>7.4 (2.9)</td>
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<td>MMF trough level, median in ng/l (IQR)*</td>
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<td>Daily dose TAC, median in mg (IQR)*</td>
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<td>Daily dose MMF, median in mg (IQR)*</td>
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* normally distributed ** not normally distributed; * p ≤ 0.05; TAC mono: tacrolimus monotherapy; n: number; BMI: body mass index; eGFR: estimated glomerular filtration rate; TAC: Tacrolimus; MMF: Mycophenolate mofetil; IQR: interquartile range

Figure 1. Systolic blood pressure and use of antihypertensive drugs in kidney transplant recipients treated with tacrolimus monotherapy vs. tacrolimus and mycophenolate mofetil.

Antihypertensive drug use was defined as WHO daily defined dose units (DDD). In the intervention arm a 3 months after transplantation, MMF was withdrawn and at month 6 discontinued.

BOS8_13

THE INFLUENCE OF MYCOPHENOLATE MOFETIL ON TOP OF TACROLIMUS ON BLOOD PRESSURE IN A RANDOMIZED COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: Optimal adherence to immunosuppressive regimens is key for prolonged allograft survival. However, granular data on adherence after kidney transplantation is still expandable, while the implementation of assessments in routine care remained limited. Therefore we designed the prospective ADTORQUE trial including a multi-component monitoring over first two years after renal transplantation.

Methods: A total of 226 adult kidney graft recipients consecutively transplanted at the Medical University of Vienna from January 2018 to December 2019 were prospectively monitored for up to 24 month with six study visits (V1-V6). The study visits were scheduled in three month intervals within the first year and at 24 months post-transplant. The adherence monitoring based on multicomponent assessment, complemented by concurrent immune monitoring by the quantification of the Torque Teno virus level in peripheral blood. Medication adherence was assessed by self-reports, electronic drug monitoring, pharmacy refill records, tacrolimus trough level and individual evaluation by a transplant psychologist. Within we present preliminary analysis of the data on the self-reported adherence using the BAASIS© questionnaire.

Results: Non-adherence was detected in 55% of recipients across all time-points: 58 (26%) of the transplant recipients reported non-adherence at least once within the first year post transplantation, while 67 recipients (30%) revealed non-adherence at multiple times. The proportion of non-adherence increased within the first three month post transplantation, from 11% at V1 to 31% at V2. At following visits, and remained at 27%, 27%, 32% and 32% over subsequent visits. Deviations from dose-timings were indicated in 44% of all recipients and constitutes for the most frequent cause for non-adherent ratings. Patient revealed non-adherence once had a significantly higher rate of biopsy proven rejections than adherent patients (21% vs. 7%, p=0.006).

Conclusions: Inappropriate adherence was substantially reported already in early phases post-transplantation, whereby taking doses on time was the main barrier. The analysis of the whole adherence monitoring might provide granular data to define an optimal diagnostic setting for clinical meaningful non-adherence.

Table 1. Baseline characteristics of kidney transplant recipients randomized to either tacrolimus monotherapy or tacrolimus with mycophenolate mofetil

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Reference:

BOS8_14

A COMPREHENSIVE MONITORING OF MEDICATION ADHERENCE OVER THE FIRST TWO YEARS AFTER RENAL TRANSPLANTATION - A PROSPECTIVE, NON-INTERVENTIONAL STUDY

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Background: For a second kidney transplantation (2nd KT), many transplant centers systematically avoid repeat HLA antigen mismatches (RMM) with the previous donor. This precaution comes at the price of a potential increase in waiting time. We hypothesized that, since highly sensitive anti-HLA antibody assays have become standard of care, 2nd KT with 1 or more RMM have no inferior graft survival compared to 2nd KT with no RMM because harmful RMM could now be accurately identified and selectively avoided.

Methods: We performed an analysis of the Collaborative Transplant Study (CTS) registry including data of 6711 patients who had received a 2nd KT between 2010 and 2021, with at least one HLA-A,-B or DR mismatch. 2nd KT were not included (N= 177).

Results: No significant difference in death-censored graft loss (DCGL) was observed between 2nd KT with no RMM compared to 2nd KT with ≥ 1 RMM (HLA Class 1 or Class 2) in univariate and multivariate analysis. However, a higher DCGL was observed for recipients with ≥ 1 Class 1 only RMM and no RMM with significance at 1 year in univariate analysis (P=0.011) (Figure). Multivariate analysis showed a doubling of the risk of 1-year DCGL (HR 2.02; 95% CI 1.40 to 2.91; P=0.001) and a 56% increase of 1-year DCGL was observed between 2nd KT with ≥ 1 RMM (HLA Class 1 only RMM; Class 1 ≥ 1 RMM; Class 2 only RMM compared to no RMM). For recipients with a Class 1 RMM only, no significantly increased risk was observed in 1-year DCGL (HR 1.07; 95% CI 0.81 to 1.40; P=0.64) and 5-year DCGL (HR 0.98; 95% CI 0.79 – 1.21; P=0.64) compared to no RMM.

Conclusions: Our observations suggest that HLA Class 1 RMM with the first donor do not need to be systematically avoided. On the other hand, HLA Class 2 RMM have a detrimental impact on early and late graft survival in patients who receive a 2nd KT at present times, suggesting modern anti-HLA antibody assays lack accuracy to identify harmful Class 2 RMM. Based on our observations, caution remains warranted for the acceptance of HLA Class 2 RMM.

Figure: Kaplan Meier analysis of 5-year death-censored graft survival after a second kidney-only transplant without a repeat mismatch (-RMM) or with a RMM stratified by repeatedly mismatched HLA class 1 or 2 (C1 ≥ 1 HLA class 1 RMM; C2 ≥ 1 HLA class 2 RMM). Log rank test after 5 years: P = 0.054. Log rank after 1 year: P = 0.11. Subjects with both class 1 and class 2 RMM were not included (N= 177).

Background: Detection of HLA antibodies relies on single-based antigen bead (SAB) technology (Luminex), which has been shown to be a more sensitive and specific method compared to enzyme-linked immunosorbent assays (ELISA). We aim to elucidate the impact of more sensitive HLA testing on antibody-mediated rejection (AMR) occurrence and long-term allograft survival.

Methods: In this single-center observational study, we made use of a retrospective cohort consisting of all adult patients (n=1818) who received a kidney transplant between March 2004 and May 2021. In April 2008, our transplant center switched from ELISA to SAB HLA testing. We included 393 (21.6%) patients before and 1425 (78.4%) patients after the transition from ELISA- to Luminex-based testing. Bio-banked sera of both groups were retested with the Luminex screening and identification method.

Results: In 90 of 393 patients (23%) of the ELISA-only and 387 of 1425 patients (27%) of the Luminex-only period, circulating HLA antibodies were detected prior to transplantation. HLA-DSA were observed in 11 and 7.6% of patients of the ELISA-only and Luminex-only cohort respectively. Consequently, the preDSA-to-preHLA ratio significantly decreased in the Luminex-only period (43/90), compared to the ELISA-only period (109/387) (48% vs. 28%, P<0.01). Throughout 61 months of follow-up post-transplantation, 166 of 1818 (9.1%) patients developed AMR. After implementing Luminex-based testing, the risk of AMR was significantly decreased with correction for competing risk (Figure 1). However, death-censored graft survival did not significantly differ between both testing methods.

Conclusions: Transition from ELISA- to Luminex-based testing resulted in a significantly decreased preDSA-to-preHLA ratio, indicating that less preformed DSA positive patients are transplanted since the implementation of SAB HLA testing. Consequently, Luminex-based testing led to a significant decrease in AMR occurrence post-transplantation. Since the decline of AMR did not translate into improved graft survival, Luminex-based testing has the added-value of preventing low-risk AMR cases. Therefore, Luminex’ high sensitivity must be balanced against the waiting time for a suitable organ.

Figure 1: Competing risk analysis: ELISA- versus Luminex-based HLA testing.
DEVELOPMENT AND VALIDATION OF A MULTIDIMENSIONAL PROGNOSTICATION SYSTEM FOR KIDNEY TRANSPLANT PATIENT SURVIVAL: THE MORTALITY BOX

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1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, APHP, Paris, France

Background: Predicting kidney transplant patient mortality has been hampered by registry-based studies and low level phenotyped cohorts without specific design towards mortality prediction. This represents a limitation for decision making and patient care. We aimed to build and validate a robust patient mortality prognostication system.

Methods: We enrolled 1,446 patients transplanted in France between 2004 and 2014 in whom a protocol-based collection including more than 160 parameters from the recipient, donor and graft, biological and imaging data, was performed on the day of transplantation (TX) and during the first year of TX. Multivariable Cox model was used to develop an individual predictive score of mortality using the strongest predictors of mortality. We externally validated the score in a multicentric French cohort gathering 1198 transplanted kidney recipients.

Results: Among the 1,446 kidney transplant recipients included, 364 patients died after a median post-TX follow-up time of 9.6 years (IQR 6.93-12.71). Among the 160 parameters 16 predictors were selected using multivariable Cox regression. The strongest predictors of patient survival were 1) Baseline recipient factors (age, presence of Donor Specific Antibodies at the time of TX, cardiovascular events, psychiatric history, VHC status and Left Ventricular Mass) 2) Post-TX parameters (complications in the first year of TX) and 3) 6 biological variables measured at one year post-TX (HbA1c, Leucocyte counts, Gamma-Glutamyl Transferase, Uric acid, and Urinary protein). The score showed accurate calibration and discrimination for predicting patient mortality up to 10 years (C-statistic = 0.81, CI: 0.79-0.83). Performances of the score in the validation cohort showed accurate calibration and discrimination for predicting patient mortality up to 10 years (C-statistic = 0.81, CI: 0.79-0.83). The score showed a superior prediction performance when compared to previous prognostic systems, reaching 81% prediction accuracy at 10 years. This tool will be a helpful tool in the clinical scenario compared to DBD donors.

Conclusions: We generate and validate the first integrative patient survival score that shows a superior prediction performance when compared to previous prognostic systems, reaching 81% prediction accuracy at 10 years. This tool will enable improved patient monitoring and therapeutic decision making to alter the course of an unfavorable patient survival outcome and may provide a surrogate endpoint in clinical trials. Additional external validation (Europe and US) are in progress.

OUTCOMES OF RENAL TRANSPLANTATION USING DONOR AFTER CARDIOCIRCULATORY DEATH FOR HIGHLY SENSITIZED PATIENTS IN SPANISH AND CATALAN PROGRAMS

Eduardo Melilli1, Jordi Comas1, Francesc Moreso2, María José Pérez-Saez1, Anna Vila-Santandreu1, Fritz Diekmann6, Lluis Guirado7, Nuria Montero1, Jaume Tort1, Josep Maria Cruzado1
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Background: In Spain and autonomous communities, special programs for highly sensitized patients on the waiting list allows for using aging donors and/or donors after cardiocirculatory death (controlled, cDCD). Nonetheless, such donors confer a high risk of delayed graft function that could affect renal and patient outcomes. Our scope was to evaluate how cDCD donors perform in this clinical scenario compared to DBD donors.

Methods: Data from the Registry of Renal Patients of Catalonia were extracted. Inclusion criteria were: cPRA > 90 %, renal transplantation period from 2012 to 2020. A search for pairs of cases (Transplants with cDCD) with a control (Transplants with DBD) was realized by propensity score matching methodology without replacement. Pairs were matched by the age of the donor/recipient, sex, presence of DSA at the time of transplantation, and by year of the transplant. We analyzed the impact of donor type on DGF, bPAR, renal, and patients’ survival up to 36 months after transplantation. We compared survival curves (Kaplan-Meyer) with the long-rank test and performed survival models with multivariate regression cox analysis.

Results: In the period analyzed, 409 hypersensitized patients were transplanted. After match pairs, 278 patients were included (139 DBD vs 139 cDCD). No statistical differences in basal characteristics were observed. Incidence of DGF was higher in patients from a cDCD donor (40 % vs 28 % p= 0.04) and worse renal function at 12 and 24 months (eGFR-CKD-epi 46 ± 20ml/min and 50±20 for DBD vs; p=0.022 and 0.021, respectively) but not at 36 months (44±18 vs 45±12; p=0.3). Acute rejection incidence was similar (24 % vs 25 % for cDCD vs DBD, p=0.8). At 36 months, death-censored graft survival and patients’ survival, were not different according to donor type (83 % vs 84 % and 83 % vs 85 % for DBD and cDCD respectively, NS)

Conclusions: cDCD donors lead to similar outcomes compared to DBD in highly sensitized recipients.
Management and selection of kidney transplant candidates

Dietary oxalic acid intake and plasma oxalic acid concentration in patients with chronic kidney disease

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Background: High oxalic acid concentration may be caused by genetic disorders, enteric diseases, but also by kidney insufficiency per se. It may result in kidney oxalic acid stones, kidney function decline, and failure. This study aimed to investigate whether dietary oxalic acid intake influences plasma oxalic acid concentration in a population undergoing kidney transplantation.

Methods: Dietary oxalic acid intake was assessed using a Food Frequency Questionnaire. Based on frequency and portion size, average daily oxalic acid intake in the past year and in the last 24 hours was calculated. A blood sample for determination of plasma oxalic acid concentration was drawn on the operation ward before transplantation. For multivariable analysis seventeen recipient related variables were gathered.

Results: 418 patients were included. The median age of the participants was 62 year, 60% were male, all had an eGFR <20 ml/min/1.73 m², and 66% were on dialysis with a median dialysis vintage of 13 months. The median plasma oxalic acid concentration was 32.2 µmol/L (range 4.6-243.2). In 98.3% of patients oxalic acid concentration was above the upper limit of normal. The average oxalic acid intake was 199 mg/day (range 4-1599), while it was 138 mg/day in the last 24 hours. Multivariable linear regression analysis showed that plasma oxalic acid concentrations were significantly higher in recipients with higher average (p<0.001) and last 24 hours oxalic acid intake (p=0.002), lower age (p=0.001), lower residual diuresis (p=0.001), higher body mass index (p=0.001), longer dialysis vintage (p=0.032), hemodialysis (p=0.001), and peritoneal dialysis (p<0.001) versus preemptive status.

Conclusions: In pre-kidney transplant patients, plasma oxalic acid concentration is above upper normal limit in 98.3% of patients and is multifactorially determined. As all other factors are not modifiable, the only way to decrease plasma oxalic acid concentration is dietary restriction.

Circulating TNF-α levels in deceased donors associate with posttransplant function in kidney transplantation

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Background: Organ transplantation is a life-saving treatment of end-stage diseases. Yet, shortage of donors and uncertainty for the quality of donor organs limits the full benefit of organ transplantation. Recent research suggests that biomarkers of the TNF-α pathway are associated with kidney function decline. Soluble TNFs, TNFR1 and TNFR2 receptors are inflammatory markers with strong prognostic value of progression from acute injury to chronic kidney dysfunction. In this study, we evaluated donor longitudinal circulating levels of TNF-α, TNFR1 and TNFR2 during donor management and compute relevant associations with 12-month posttransplant function.

Methods: A cohort of 475 plasma samples were obtained from 189 deceased donors (DBD=95, DCD=94). Samples were provided by the Quality in Organ Donor (QUOD) biobank. Plasma samples from living donors (n=20) obtained from the Oxford Transplant Biobank, provided a baseline reading for these analytes. Using Luminex assay, we quantified the circulating levels of TNF-α and receptors in serial donor plasma collected longitudinally during donor management at three time points (time of brain stem death test; B2, start of retrieval; B3, prior to cross clamp; B4) in DBD and two corresponding time points in DCD (prior to withdrawal of life support; B2, start of retrieval; B3). Circulating levels of TNF-α and receptors differ among donor types. In DBDs, initial high levels of TNF-α and TNFR1 following brain death reduced during donor management before reaching their highest level prior to kidney retrieval (time point B4). TNFR2 levels remained roughly constant at all time points (Fig 1). In contrast, in DCDs the levels of circulating analytes show a steady increase that peaked just before withdrawal of life support. Notably, only in DBDs plasma levels of TNF-α (p=0.002) and TNFR1 (p=0.018) strongly associated to 12-month suboptimal function (eGFR<30ml/min) posttransplant (Mann-Whitney U test) (Fig 2). All analytes had baseline levels in living donor plasma prior to kidney procurement.

Conclusion: Our study demonstrates that circulating inflammatory levels differ in DBDs when compared to DCDs. Increased levels of TNF-α mediators in deceased donor may deem donor organs susceptible to posttransplant injury and suboptimal function at 12-m post-transplant function.
Management and selection of kidney transplant candidates

**ASSOCIATION BETWEEN ABDOMINAL CT MEASUREMENTS OF BODY COMPOSITION AND WAITLIST MORTALITY IN KIDNEY TRANSPLANT CANDIDATES**

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**Background:** Obesity is considered a risk factor for developing adverse outcomes in the kidney transplant (KT) population, however, there are inherent limitations of BMI measurements. Objective measures of body composition, measured using abdominal CT scans, may improve pre-transplant risk stratification. The goal of this study was to determine the association between various CT-based body composition measurements and waitlist mortality in KT candidates.

**Methods:** We leveraged a perspective cohort of adult first-time KT candidates (n=836) from 2010 to 2022 who underwent abdominal CT scans during KT evaluation, including L3 vertebral level, at Johns Hopkins Hospital. Body composition measurements were obtained, including skeletal muscle index (SMI) and skeletal muscle radiation attenuation (SM-RA). Sarcopenia was defined as an SMI< 50 cm2/m2 for males and an SMI<39 cm2/m2 for females. Myosteatosis was defined as an SM-RA>41 mean HU for recipient with a BMI≥ 25 kg/m2 and an SM-RA>53 mean HU for recipient with a BMI< 25 kg/m2. Sarcopenic obesity was defined as a BMI≥ 30 kg/m2 for sarcopenic recipients. Fine and Gray proportional subhazard models were used to quantify the associations of each measurement with waitlist mortality. P values <.05 were considered significant.

**Results:** Among 836 KT candidates, the mean age was 55.3 years (SD, 12.8 years) and 38.8% were women. The 1- and 5-year cumulative incidence of waitlist mortality was 1.8% and 14.5%, respectively. For myosteatosis, cumulative incidence of waitlist mortality was higher among those with myosteatosis (cSHR=1.95, 95%CI: 1.29-2.94, p=0.002). Regarding patients with sarcopenic obesity, cumulative incidence of waitlist mortality was higher when compared to their non-sarcopenic obese counterparts (cSHR=1.55, 95%CI: 1.01-2.39, p=0.047). None of the body composition profiles carried a higher risk of waitlist mortality compared to their non-sarcopenic obese counterparts.

**Conclusions:** Cumulative incidence of waitlist mortality is higher among kidney transplant candidates with myosteatosis and those with sarcopenic obesity. Transplant centers should consider using body composition metrics, when a CT scan is available, to improve risk stratification at KT evaluation.

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**EMPLOYMENT BEFORE, AT OR AFTER KIDNEY TRANSPLANTATION IN DENMARK – A NATIONAL CASE-CONTROL STUDY**

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**Background:** Kidney transplant patients have difficulties at maintaining their employment with an estimated proportion of 38% patients in work after transplantation. Prior studies on employment have previously used self-reported employment as main endpoint, with no control group and only sparse information on employment prior to transplantation. This study aimed to establish the rate of employment in kidney transplant patients from 3 years before to 3 years after kidney transplantation and associated predictors for employment after transplantation.

**Methods:** All kidney transplantation patients from 2005-2019 were identified using The Danish Nephrological Register linked with DREAM database for information of government benefits, Statistics Denmark for socioeconomic information and The Danish Health Data Authority National Patient Register for comorbidities. Inclusion criteria were kidney transplantation, age 18-65 years. Exclusion criteria were emigration during period of interest. Each transplant patient was matched with 1-3 controls on age, gender and municipality.

**Results:** In total 2294 kidney transplant patients (median age 49 years, 64 % males) were included with 6790 controls. Employment rate for kidney transplant patients and controls 3 years prior, 1 year prior, at transplantation, 1 year after and 3 years after are shown in Figure 1. At all timepoints kidney transplant patients had a lower employment rate (P<0.001). Associated cause specific hazards of employment after transplantation were male, HR 1.5 (1.3-1.8), non-Danish ethnicity, HR 0.8 (0.5-0.8), education with university degree or higher compared to basic schooling, HR 2.2 (1.6-2.9). Other predictors of employment were hemodialysis compared to preemptive transplantation, HR 0.7 (0.6-0.9), peritoneal dialysis compared to preemptive transplantation, HR 0.8 (0.7-0.97) and diabetes, HR 0.7 (0.5-0.8).

**Conclusions:** Kidney transplant patients have a low employment rate in Denmark with male gender, Danish ethnicity, preemptive transplantation and education associated with improving the hazard of employment and dialysis and diabetes decreasing the hazard of employment.

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Figure 1: Cumulative Incidence of Waitlist Mortality by Myosteatosis Status

Figure 1. Employment rates of kidney transplant patients (cases) and controls according to time of transplantation (baseline).
BRIEF ORALS

Management and selection of kidney transplant candidates

**BOS9_10**

DOES TYPE OF DIALYSIS MODALITY INFLUENCE POST-TRANSPLANTATION OUTCOMES? A POPULATION-COHORT ANALYSIS USING REGISTRY DATA

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**Background:** There is conflicting data with regards to whether kidney transplant candidates using peritoneal dialysis (PD) versus haemodialysis (HD) at the time of kidney transplant surgery have better short- and long-term post-transplant outcomes.

**Methods:** A retrospective cohort study was undertaken of prospectively collected registry data of all kidney transplant recipients in the United Kingdom from January 1, 2000 until September 30, 2019 inclusive. Outcomes studied included short-term and long-term graft outcomes. Time-to-event analyses were performed using weighted estimation of Cox regression models to account for non-proportional hazards, with covariate adjustment as indicated. All analyses were done using RStudio (version 2022.07.2), with survival analyses performed using the coxphw package.

**Results:** A total of 37,194 kidney transplant recipients formed the study cohort, of whom 71.6% (n=26,639) were receiving HD and 28.4% (n=10,555) were receiving PD. Rates of living and donation after brain or circulatory death were similar among patients. PD was more common in the following kidney transplant candidates: younger, females, White ethnicity, non-diabetics and first transplant recipients. Kidney transplant candidates on PD versus HD had lower risk for delayed graft function (13.5% versus 24.4% respectively, p<0.001), but a slightly higher risk for 3-month rejection (15.0% versus 13.8% respectively, p=0.004). Creatinine at 1-year (in umol/L) was slightly better in PD versus HD transplant recipients. Kidney transplant recipients on PD versus HD at the time of transplant surgery have better short- and long-term post-transplant outcomes.

**Conclusions:** Kidney transplant recipients on PD at the time of transplant surgery have better short- and long-term post-transplant outcomes. Kidney transplant candidates using peritoneal dialysis (PD) versus haemodialysis (HD) at the time of transplant surgery have better short- and long-term post-transplant outcomes. Kidney transplant candidates using peritoneal dialysis (PD) versus haemodialysis (HD) at the time of transplant surgery have better short- and long-term post-transplant outcomes.

Figure. Unadjusted Kaplan Meir plot of post-transplant mortality by pre-transplant dialysis modality

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**BOS9_11**

CHARACTERISTICS OF PRE-TRANSPLANT HOSPITALIZATIONS ARE ASSOCIATED WITH ELDERLY PATIENT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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**Background:** In elderly patients, kidney transplantation is not systematically associated with a benefit in terms of survival, compared to dialysis. Screening of comorbidities is not sufficient to identify those at high risk of mortality, possibly due to unmeasured frailty in some patients. The profile of hospitalizations may be a good proxy of this frailty. Thus, our aim was to study if the number and length of hospitalizations during the three years preceding kidney transplantation were associated with post-transplant mortality.

**Methods:** We included all patients older than 65 years the day of transplantation who received a kidney transplant between 2006 and 2016. Recipient and donor characteristics were retrieved from French national registries (Renal Epidemiology and Information Network (REIN) and CRISTAL). Data on hospitalizations were obtained by indirect matching with the National Health Data System. Patients with pre-emptive kidney transplantation were excluded. Cox models were used to identify factors associated with mortality.

**Results:** We included 3882 patients, 930 (24.0%) without pre-transplant hospitalization, and 2952 (76.0%) cumulating a total of 9373 hospitalizations. 67% of patients were male and 14% were older than 75 years. In univariate analysis, patients with history of pre-transplant hospitalization had a lower probability of survival (p<0.001). In hospitalized patients, we observed a dose-response relationship between the number of hospitalizations and survival (Figure). History of hospitalization was associated with a higher mortality (HR 1.26 [1.08:1.48]) after adjustment for recipient comorbidities, duration of dialysis, ECD donors, and cold-ischemia time. For patients with a history of hospitalization, the number of pre-transplant hospitalizations, rather than their cumulative length, was associated with a higher mortality (adjusted HR 1.07 [1.04:1.10]) per one hospitalization increase). Being hospitalized at least once for a cardiac or a respiratory condition was independently associated with a higher risk of mortality.

**Conclusions:** Taking into account the characteristics of pre-transplant hospitalizations during evaluation of elderly candidates to transplantation may help to identify patients with a higher risk of post-transplant mortality.

Figure. Number of hospitalizations and survival after kidney transplantation (in years)

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Background: The association between sarcopenia of kidney transplant recipients and outcome after kidney transplantation has not yet been fully understood and is still considered controversial. The aim of our study was to analyse the impact of pre-transplant sarcopenia on graft function, postoperative complications, and survival of the patients after renal transplantation.

Methods: In this retrospective single-centre study, all patients who underwent KT (01/2013-12/2017) were included. Demographic data, rejection rates, delayed graft function, graft and patient survival rates were analysed. Sarcopenia was measured in computed tomography images by the sex-adjusted Hounsfield Units Average Calculation (HUAC).

Results: During the study period, 111 single KT (38 women and 73 men) were performed. Living donor kidney transplants were performed in 48.6%. In total, 146

BRIEF ORALS

**BOS_12**

SARCOPENIA OF KIDNEY TRANSPLANT RECIPENTS AS A PREDICTIVE MARKER FOR REDUCED GRAFT FUNCTION AND GRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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Background: The association between sarcopenia of kidney transplant recipients and outcome after kidney transplantation has not yet been fully understood and is still considered controversial. The aim of our study was to analyse the impact of pre-transplant sarcopenia on graft function, postoperative complications, and survival of the patients after renal transplantation.

Methods: In this retrospective single-centre study, all patients who underwent KT (01/2013-12/2017) were included. Demographic data, rejection rates, delayed graft function, graft and patient survival rates were analysed. Sarcopenia was measured in computed tomography images by the sex-adjusted Hounsfield Units Average Calculation (HUAC).

Results: During the study period, 111 single KT (38 women and 73 men) were performed. Living donor kidney transplants were performed in 48.6%. In total, 146

**BOS_13**

EFFECTS OF SOCIAL DEPRIVATION ON REGISTRATION ON THE RENAL TRANSPLANTATION WAITING-LIST THROUGH MARKERS OF NEPHROLOGICAL CARE: A MEDIATION ANALYSIS

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Background: Reducing disparities in access to renal transplantation requires identification of factors involved in the access (KT) and lack thereof. Social deprivation status and registration on the renal transplantation waiting-list are associated with socioeconomic status and registration on the renal transplantation waiting-list. This mediation analysis was conducted to estimate the effect of social deprivation on waiting-listing and to identify key mediators of this association.

Methods: From the Renal Epidemiology and Information Network, this retrospective observational multicenter study included all patients eligible for an evaluation for registration according to French recommendations who started dialysis between 1 January 2017 and 30 June 2018. Social deprivation was estimated by quintile 5 (Q5) of the European Deprivation Index (EDI). Registration was defined as being already listed at dialysis start or within the first 6 months. Mediation analysis was conducted to assess the direct effect of the EDI on registration and its indirect effect through markers of the nephrological follow-up, defined a priori in a directed acyclic graph.

Results: Among the 11,655 patients included, 2,410 were registered. Age, sex, comorbidities, dialysis modality and starting dialysis on a catheter or in emergency were not associated with registration on the waiting-list. In the mediation analysis, EDI had a direct effect on registration (OR 0.83 [0.81-0.85]) and an indirect effect mediated by emergency start dialysis (OR 0.97 [0.96-0.98]), hemoglobin < 11 g/dL and or lack of EPO (OR 0.95 [0.95-0.96]) and albumin < 30 g/L (OR 0.98 [0.98-0.99]). Conclusions: Social deprivation is directly associated with a lower chance of being registered on the renal transplantation waiting-list but its effect is also mediated by markers of the pre-dialysis care, suggesting that improving the follow-up of the most deprived patients should help to reduce disparities in access to renal transplantation.
BRIEF ORALS

Cardiovascular and metabolic complications after kidney transplant

BOS10_1

IS A BLOOD PRESSURE BELOW 130/80 MM Hg A UNIVERSAL GOAL FOR ALL RENAL TRANSPLANT RECIPIENTS? AN ANALYSIS OF THE COLLABORATIVE TRANSPLANT STUDY

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Background: In 2018, the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines published new categories for hypertensive blood pressure (BP) of adults, recommending a BP goal of less than 130/80 mm Hg. This goal was adopted in the 2021 KDIGO Clinical Practice Guidance for the Management of Blood Pressure in Chronic Kidney Disease for adult kidney transplant recipients. Thanks to the contribution of many centers around the world over decades, the extensive database of the CTG could be used to verify whether this BP cut-off equally applies to different patient groups.

Methods: More than 57,000 adult patients who received kidney-only transplants since 2000, with a functioning graft one year after transplantation and for whom diastolic and systolic BP were available 1 year after transplantation, were analyzed in 3 categories: normal <130/80, hypertension stage 1 <140/90, and stage 2 ≥140/90 mm Hg. Multivariable Cox regression analyses that included 24 confounding factors were used to analyze the impact of 1-year BP on 10-year death-censored graft survival.

Results: Less than a quarter (23%) of patients had a normal BP below 130/80 mm Hg, with a strong dependence on patient age and sex. When all study patients were analyzed, patients with stage 1 hypertension had only a 7% higher death-censored graft failure rate than patients with normal BP (HR=1.04, 95% CI 1.02-1.05, P<0.001). However, a stratification by recipient age and sex revealed remarkable differences (Figure 1). Cox regression of stage 1 and 2 vs. normal BP also showed strongly different risks with regard to graft number and 1-year serum creatinine, first transplants: HR 1.04 (P=0.27) for stage 1, HR 1.31 (P=0.001) for stage 2; retransplants: 1.23 (P=0.018), 1.60 (P=0.001); 1-year serum creatinine <130 µmol/l: 0.97 (P=0.66), 1.25 (P<0.001); ≥130 µmol/l: 1.14 (P=0.003), 1.42 (P<0.001).

Conclusions: Maintaining BP below 130/80 mm Hg is especially important for <50-year-old women, retransplanted patients, and recipients with impaired graft function.

Figure 1. Influence of hypertension (HT) stage on death-censored graft survival stratified by recipient age (<50, ≥50 y) and sex (pairwise P values vs. normal BP of Kaplan-Meier analyses are shown).

BOS10_2

COMPARISON OF OFFICE, HOME AND AMBULATORY BLOOD PRESSURE IN KIDNEY TRANSPLANT RECIPIENTS WITH AND WITHOUT TELEMEDICINE MONITORING

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Background: Despite extensive cardiovascular screening before kidney transplantation, cardiovascular mortality among kidney transplant recipients (KTR) remains high. The aim of this study was to quantify hypertension control and evaluate concordance between available blood pressure modalities in a sample of KTR with and without telemedicine monitoring.

Methods: For this cross-sectional study 80 KTR were recruited at the Charité Transplant Outpatient Clinic. Study participants had to be adults and transplanted at least 6 months prior to inclusion. Known arrhythmias, hemodialysis shunt on both arms as well as recent adjustment of antihypertensive drugs were defined as exclusion criteria. For each study participant office (OBP), automated office blood pressure “AOBP”, and manual office blood pressure “MOBP”, home (HBPM) and ambulatory blood pressure measurement (ABPM) were performed.

Results: Mean blood pressure for daytime-ABPM, HBPM, AOBP and MOBP was 130/82, 131/85, 126/71 and 129/74 mm Hg. The Bland-Altman plot showed the mean bias ± SD between systolic daytime ABPM and HBPM, AOBP, MOBP as -110 mmHg, 41±31 mmHg, 11±32 mmHg with corresponding limits of agreement -21 and 18 mmHg, -20 and 29 mmHg, -24 and 26 mmHg. Uncontrolled hypertension, as defined by 24h-ABPM, was present in 65% of trial participants. The evaluation of dipping status yielded a physiological dipping pattern in 12.5% of participants whereas 87.5% showed a non-physiological dipping pattern. Clinical features (i.e. edema, nocturia) did not correlate significantly with hypertension status, as defined by 24h-ABPM. Despite showing a tendency towards lower mean blood pressure by MOBP, AOBP and HBPM, the Telemedicine sample displayed no difference in ABPM measurements.

Conclusions: HBPM showed the narrowest limits of agreement compared to the gold standard ABPM. Nonetheless, HBPM showed a low negative predictive value with regards to daytime-ABPM. Furthermore we recorded a high prevalence of non-physiological dipping pattern among KTR. Despite the undeniable advantages of HBPM (tolerability, improved patient adherence and outcomes), systematic integration of ABPM into clinical practice, as proposed by recent hypertension guidelines, should not be withheld for the KTR population.

BOS10_3

PREDICTION OF MACE AND MORTALITY AMONG KIDNEY TRANSPLANT CANDIDATES USING RISK FACTORS, CORONARY ARTERY CALCIUM SCORE AND CORONARY CT ANGIOGRAPHY

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Background: Kidney failure is associated with an increased risk of cardiovascular disease and death. The present study evaluated cardiovascular outcomes and all-cause mortality in asymptomatic kidney transplant candidates who were systematically referred to coronary artery calcium score (CACS) and coronary computed tomography angiography (CTA).

Methods: In a single-centre, observational study all potential kidney transplant candidates > 40 years, with diabetes or need for dialysis > 5 years were systematically referred to cardiac CT. All patients initiating cardiovascular screening prior to kidney transplantation between March 2014 and September 2019 were included. Data on clinical risk factors, major adverse cardiovascular events (MACE) and all-cause mortality was collected from patient records.

Results: A total of 529 kidney transplant candidates were included with a median follow-up of 4.7 years. CACS was evaluated in 437 patients and CTA was analyzed in 411. Both the presence of ≥3 risk factors, CACS ≥ 400 as well as multiple vessel stenoses or left main artery disease predicted MACE (HR 2.09 (95% CI 1.35-3.23), 4.85 (2.20-9.82), 3.70 (1.81-7.57), 4.90 (2.40-10.01)) and all-cause mortality (HR 4.44 (95% CI 2.54-7.76), 4.47 (2.22-9.02), 2.82 (1.34-5.94), 5.41 (2.81-10.41) in univariate analyses. Among patients eligible for CACS and CTA (n = 376), only CACS and CTA were associated with both MACE and all-cause mortality.

Conclusions: Risk factors, CACS and CTA provides prognostic information in kidney transplant candidates. An additional value of CACS and CTA compared to risk factors was observed for prediction of MACE in a subgroup undergoing both CACS and CTA.

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Cardiovascular and metabolic complications after kidney transplant

**BOS10_4**

**INFLUENCE OF LOW- AND HIGH-DENSITY LIPOPROTEIN CHOLESTEROL ON GRAFT FUNCTION IN RENAL TRANSPLANT RECIPIENTS - A COLLABORATIVE TRANSPLANT STUDY REPORT**

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**Background:** Hypercholesterolemia is highly prevalent in renal transplant patients. Therefore, post-transplant screening of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol is routinely performed. When appropriate, post-transplant drug therapy is directed at lowering LDL cholesterol to reduce cardiovascular risk. The extent to which LDL and HDL influence graft function has long been debated. Thanks to the contribution of many centers around the world, the large database of the CTS allows verification of the influence of LDL and HDL on graft outcome.

**Methods:** More than 26,000 adult patients who received kidney-only transplants since 2003, with a functioning graft one year after transplantation and for whom HDL and LDL levels were available one year after transplantation, were analyzed. Taking into account cholesterol-affecting characteristics such as recipient age, sex, and medication with statins, the influence of 1-year HDL and LDL on death-censored graft survival and the incidence of rejection treatment after the first post-transplant year was analyzed. Multivariable Cox regression analysis was used to adjust for additional confounding factors.

**Results:** Regardless of whether patients were treated with statins, transplanted women had approximately 10 mg/dl higher HDL levels than men. Increased LDL values in women were only found in recipients aged ≥50 years. For LDL, there were no significant differences with respect to recipient age or medication with statins; however, in female recipients a significantly higher risk was noted already at a cut-off of 45 mg/dl with respect to recipient age or medication with statins. Notably, patients with an HDL of less than 35 mg/dl had a strikingly increased risk of death-censored graft failure (P<0.001, Figure 1). Regarding the influence of HDL on death-censored graft survival, there were no significant differences between male and female recipients. In contrast, patients with an HDL of less than 35 mg/dl had a strikingly increased risk of death-censored graft failure (P<0.001 vs. ≥45 mg/dl). The impact of HDL on the incidence of rejection treatment after the first post-transplant year was small. Therefore, post-transplant drug therapy is directed at lowering LDL cholesterol to reduce cardiovascular risk.

**Conclusions:** Low HDL serum cholesterol of <35 mg/dl in men and <45 mg/dl in women is a strong predictor of impending rejection or graft failure after kidney transplantation.

**Figure 1. Influence of 1-year post-transplant HDL cholesterol (mg/dl) on subsequent death-censored graft survival.**

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**BOS10_5**

**GLIFLOZIN IN RENAL TRANSPLANTATION: A MULTI-CENTER OBSERVATIONAL STUDY (GREAT-ASTRE)**

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1Tours University Hospital, Tours, France, 2Caen University Hospital, Caen, France, 3Reims University Hospital, Reims, France, 4Strasbourg University Hospital, Strasbourg, France, 5Reims University Hospital, Reims, France, 6Pitié Salpêtrière University Hospital, Poitiers, France, 7Clermont-Ferrand University Hospital, Clermont-Ferrand, France, 8Angers University Hospital, Angers, France, 9Amiens University Hospital, Amiens, France, 10Paris Necker University Hospital, Paris, France, 11Brest University Hospital, Brest, France, 12Limoges University Hospital, Limoges, France, 13Rouen University Hospital, Rouen, France

**Background:** SGLT2 inhibitors (SGLT2i) decrease all-cause mortality, cardiovascular mortality and slow progression of kidney disease in patients with albuminuria. In agreement with the French marketing authorization, SGLT2i can be prescribed to kidney transplant recipients (KTRs), although these patients were not included in large randomized clinical trials (DAPA-CVD, CREDENCE, EMPA-Kidney). GREAT-ASTRE is a real-life multicentric study of KTRs treated with SGLT2i.

**Methods:** We implemented an observational study of all KTRs followed in the 13 kidney transplant centres that collect transplantation-related data in ASTRE database (DR-2012-518). We added visits at initiation of SGLT2i, then at 3 and 6 months (M0, M3, M6). The aim was to identify all KTRs receiving SGLT2i in order to describe the prescribing pattern and determine safety profile. We paid particular attention to urinary tract and genital infections, as well as treatment discontinuation.

**Results:** So far, 265 KTRs have been identified, 95% of them having received a prescription of dapagliflozin 10 mg/day. General characteristics of the patients at initiation are presented in the table. Most initiations took place between 1 and 10 years after transplantation (47.2%), only 10.9% in the first year of transplantation. HbA1c at initiation was <7% in 33% and <8% in 67% of the 185 (69.8%) diabetic KTRs. Serum creatinine level increased following initiation of SGLT2i (M0 : 144±44 µmol/L, M3 : 156±55 µmol/L, p=0.0001), followed by a stabilization at M6 (160±60 µmol/L). A significant decrease in systolic blood pressure was observed between M0 and M3 (146±21 mmHg vs. 140±19 mmHg, p<0.001) and a stabilization at M6 (160±60 µmol/L).

**Conclusions:** GREAT-ASTRE is the largest series of KTRs (diabetic or not) treated with SGLT2i. SGLT2i are frequently prescribed to KTRs, regardless of their diabetic status, without any safety alert in short-term follow-up. Complete follow-up data will be available soon.

**ASTRA ZENECA funded ASTRE database to implement GREAT-ASTRE study.**

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**Table 1. Characteristics of the patients at initiation.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.5 ± 11.9</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>204 (77)</td>
</tr>
<tr>
<td>Dapagliflozin, n (%)</td>
<td>250 (94)</td>
</tr>
<tr>
<td>Time from transplantation (years)</td>
<td>7.99 [2.79 - 11.92]</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>185 (69.8)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.1 ± 5.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>144.6 ± 20.2</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80.9 ± 11.9</td>
</tr>
<tr>
<td>Serum creatinin level (µmol/L)</td>
<td>145.3 [112 - 168]</td>
</tr>
</tbody>
</table>
Background: Between 10 to 30% of kidney transplant recipients develop post-transplant diabetes mellitus (PTDM). PTDM is a major risk factor for cardiovascular events and death in kidney transplant recipients. In a retrospective single-center cohort study we investigated risk factors for development of de novo PTDM from eight weeks after kidney transplantation.

Methods: Inclusion criteria were kidney transplantation from 2015-2019, age > 18 years, no known diabetes prior to or at the eight-week control after transplantation and with at least one year of follow up. At the eight-week control an oral glucose tolerance test (OGTT) was performed for PTDM diagnosis. De novo PTDM was defined as fasting glucose ≥ 7 mmol/L, 2-hours glucose ≥ 11.1 mmol/L at OGTT performed routinely at the one-year visit, or at least two registered dispensations of glucose lowering medication in the Norwegian Prescription Database (NorPD).

Results: In total 632 patients (median age 53 years, 62 % males) with a median follow-up of 2.7 years [1-4] were included of which 54 (8.5%) developed de novo PTDM (31 diagnosed by the OGTT at 1 year and 23 identified by glucose lowering dispensation). In a multiple logistic regression analysis, significant associated factors of PTDM were age (years), OR 1.05 (CI 95%: 1.01;1.09), fasting triglycerides (mmol/L), OR 1.59 (CI 95%: 1.19;2.12) and tacrolimus (g/L), OR 1.22 (CI 95%: 1.02;1.46) concentrations measured at the one-year control visits, accumulated methylprednisolone dose at rejections (g), OR 1.61 (CI 95%: 1.06;2.45) and CMV serostatus (positive donor to recipients, OR 2.12 (CI 95%: 1.02;4.38). Plasma magnesium, gender, BMI and plasma creatinine were not associated with development of PTDM.

Conclusions: In conclusion development of de novo PTDM later than eight weeks after kidney transplantation was associated with increased age, higher triglycerides, higher tacrolimus concentrations, accumulated methylprednisolone dose at rejections and D+/R- CMV-serostatus.
**BRIEF ORALS**

**Cardiovascular and metabolic complications after kidney transplant**

**BOS10.8 DEVELOPMENT AND VALIDATION OF A NEW SCORE TO ASSESS THE RISK OF POST-TRANSPLANTATION DIABETES MELLITUS IN KIDNEY TRANSPLANT RECIPIENTS**

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**Background:** Post-transplantation diabetes mellitus (PTDM) is a serious complication following solid organ transplantation. It is associated with major adverse cardiovascular events, which represent a leading cause of morbidity and mortality in transplanted patients. PTDM is also associated with reduced patient and graft survival. The purpose of this study was to develop and validate a score for predicting the risk of PTDM in kidney transplant recipients.

**Methods:** Single-center retrospective cohort study conducted in a tertiary care hospital, Medellín-Colombia from 2005 to 2019. Data from 727 kidney transplant patients were used to develop a risk prediction model. Significant predictors were identified using time-dependent proportion hazard Cox regression models. To build the prediction model, the score for each variable was weighted by the regression coefficients calculated. External validation of the model was performed using independent external data including 198 kidney transplant recipients from the University Hospital of Tübingen.

**Results:** Among 727 kidney transplant recipients, 122 of whom developed PTDM. The predictive model was based on 5 predictors (age, body mass index; gender, tacrolimus therapy, and hyperglycemia during the first week after kidney transplantation). The model showed good predictive performance (C-Index: 0.72 [95% CI 0.65 – 0.76] in the development cohort). The risk score was then used in 198 kidney transplant recipients in the validation dataset, including 33 patients with PTDM. The results showed good discrimination (C-Index: 0.72 [95% CI 0.62 – 0.84]). The Brier calibration plot demonstrated an acceptable calibration capability in the external validation.

**Conclusions:** We proposed and validated a prognostic model to predict the risk of PTDM. The model performed well in discrimination and calibration, being simple to use and implement. In addition, a nomogram based on the Cox model was established for clinical application.

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**BOS10.9 A PROSPECTIVE COHORT STUDY OF SODIUM/GLUCOSE COTRANSPORTER 2 INHIBITOR-TREATED DIABETIC KIDNEY TRANSPLANT PATIENTS**

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**Background:** Diabetic kidney transplant (DKT) patients suffer from increased burden of cardiovascular (CV) disease. The graft outcome of these patients is not only determined by immunologic injury but also by diabetic kidney disease (DKD) of graft. The SODIUM/GLUCOSE COTRANSFER 2 INHIBIT (SGLT2I) reduces CV events and delays the progression of DKD, and would favor the outcome of these patients. There are limited experiences of the use of SGLT2I on DKT patients.

**Methods:** One hundred and forty-nine DKT patients treated with dapagliflozin have been prospectively followed for more than 6 months (median 15.4 ± 7.0 months) in our institute. Four patients had type 1 diabetes, 58 had type 2 diabetes, and 87 had posttransplant diabetes. Twenty-five patients were on insulin. Baseline serum creatinine was 1.36±0.40 (0.6-2.4 mg/dl).

**Results:** Baseline HbA1c was 7.0±1.9%, which decreased significantly at 3 months (6.8±1.3%, p<0.01) and maintained stable thereafter. Body weight decreased significantly from 65.5±27.1 to 65.1±27.3 kg (p=0.00) at 3 months and slightly more reduced until 12 months. Baseline urine albumin-creatinine ratio was 168.9±511.1 mgg, which decreased significantly in 3 months (132.3±301.2 mg/g, p=0.03), reduced further until 6 months and maintained unchanged until 24 months. The slope of eGFR decline before and after the use of SGLT2I did not differ significantly. Eight patients stopped dapagliflozin due to acute cystitis in 3, weight loss in 2 and patient’s preference in 3. There was no episode of adverse cardiovascular events, which represent a leading cause of morbidity and mortality in transplant recipients.

**Conclusions:** SGLT2I reduced albuminuria and was well tolerated in DKT patients. The long-term benefit of patient and graft outcome would be worth to be evaluated by further follow up.

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**BOS10.10 FIRST USE OF DEEP LONG SHORT-TERM MEMORY NEURAL NETWORK IN PREDICTING KIDNEY GRAFT FUNCTION**

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**Background:** Predicting kidney allograft function represents a major challenge in management of kidney transplant recipients. Currently, there are different models for predicting the risk of graft failure and patient survival, some of which are used for graft allocation and decision-making during kidney transplant procurement. All these models are based on mathematical algorithms and machine learning algorithms. Deep Long Short-Term Memory Neural Network (LSTM) is an artificial neural network (ANN) that can learn from entire sequences of measured data through prolonged periods of time, which makes it suitable for learning patterns and predicting final outcomes. Here we present for the first time the results of the use of Deep LSTM neural network in predicting graft function dynamics for future medical examinations.

**Methods:** A dataset was formed from characteristics of 922 kidney donors and their recipients that underwent a total of 6123 ambulatory controls during which creatinine, eGFR, proteinuria and GFR were measured. This dataset was split into two separate datasets, one was used for ANN model learning, the other for ANN model evaluation.

**Results:** Deep LSTM ANN learned to predict weather graft function (eGFR) on the next medical examination will be better or worse according to stages of chronic kidney disease (CKD). Better meaning one class better than current stage, the same (same CKD stage), worse (CKD stage class higher for one point than previous), or much worse (CKD stage class higher for 2 points or more). It predicted a better CKD stage with an of accuracy 0.67, precision 0.92, specificity 0.88. The same CKD stage with accuracy 0.89, precision 0.7, specificity 0.97, worse CKD stage with accuracy 0.92, precision 0.83, specificity 0.98; and graft failure (much worse CKD) with accuracy 1.0, precision 1.0, specificity 1.0.

**Conclusions:** This study provides evidence that a Deep LSTM neural network was able to learn and predict graft function on future medical examinations with high accuracy, precision and specificity. In the present era of a broad artificial intelligence application, we find that the next step in improving kidney transplant patients care will be the use of neural networks and their predicting abilities.
Cardiovascular and metabolic complications after kidney transplant

**BOS10_12**

**ERECTILE DYSFUNCTION AFTER KIDNEY TRANSPLANTATION IN MALES WITH END-STAGE KIDNEY DISEASE: A META-ANALYSIS**

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**Background:** Patients with end-stage kidney disease (ESKD) on dialysis have a constant uremic status and associated comorbidities, such as diabetes mellitus, peripheral, coronary artery disease, or hypertension, as well as complications related to dialysis. There is also a high prevalence (62%) of erectile dysfunction (ED) in males with chronic kidney disease (CKD). Data regarding erectile dysfunction and kidney transplantation (KT) are controversial, ranging from worsening to improvement of ED after KT. We aimed to evaluate the effect of KT on ED in males with ESKD.

**Methods:** Potentially relevant studies were searched in the following databases: MEDLINE (PubMed), SCOPUS, Embase and Cochrane library from inception until January 2023. Eligible studies compared the same population before and after KT. The primary outcome of our study was to assess the effect of KT on ED. We used a random-effects model for meta-analysis and expressed treatment effects as a risk ratio (RR) with 95% confidence intervals (CI). We used the I2 statistic to assess for inconsistency. An I2 > 50% indicated large inconsistency across studies not explained by chance. All statistical analyses were performed using Review Manager Version 5.2 (The Cochrane Collaboration 2012).

**Results:** 20 articles with a total population of 1681 patients were included, with most patients undergoing hemodialysis before and after KT. Most studies used the International Index of Erectile function (IIEF) questionnaire as the main method to assess sexual function. Our analysis shows that after kidney transplantation, there was an improvement in erectile dysfunction of 234% (RR 2.3) (95% CI 1.36, 4.01), as seen in Figure 1.

**Conclusions:** Our meta-analysis shows improvement of ED in males with ESKD after KT. Our study has a few strong points. First, there was a large study population. Second, we used studies that evaluated the same population before and after KT. However, there are a few limitations to our meta-analysis, such as the observational nature of the studies included. Our findings show a beneficial effect of KT on ED.

![Figure 1 - Forest plot of the RR of patients with improved sexual function vs worsening sexual function post KT](image)

**BOS10_13**

**OUTCOMES FOLLOWING ARTERIO-VENOUS FISTULA LIGATION FOLLOWING KIDNEY TRANSPLANTATION**

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**Background:** Cardiovascular disease remains one of the leading cause of death post-kidney transplantation. Recent evidence suggests an improvement in functional cardiovascular tests following ligation of arterio-venous fistulae (AVF). Ligation of AVF post-successful transplant could improve outcomes; however, this needs to be balanced against removal of venous access, which may be needed should the transplant fail. This investigation aims to: 1. Describe the outcomes following AVF ligation in kidney transplant recipients (KTR), n=190. 2. Compare allograft outcomes against a control group of KTR without AVF ligation, n=380 (1:2 cases:controls) 3. Identify risk factors associated with return to dialysis following AVF tie-off.

**Methods:** Patients and outcomes were identified from a prospectively maintained transplant database. Ligation episodes were captured from health records. All patients, irrespective of indication for ligation were included.

**Results:** 190 patients (70% males, median age 50 (40-59) years, 33% white, 76% receiving a deceased donor transplant and 19% with diabetes) underwent AVF ligation at a median time of 2.5 (2.0-3.3) years post-transplant. Median follow up was 6.4 (5.2-7.1) years post tie-off. 5-yr all-cause and death censored allograft survival was 71.9% and 81.8% respectively. Risk adjusted cox-proportional hazards regression for; a. all-cause allograft survival, showed fistula excision was independently associated with improved risk of all-cause allograft loss, HR 0.44 (0.2-0.61), p=0.0001 (Figure 1); b. death-censored allograft survival, showed fistula excision was independently associated with improved risk of death-censored allograft loss, HR 0.35 (0.23-0.53), p=0.0001 (Figure 1). A diagnosis of diabetes (HR 2.13 (1.23-3.69), p=0.007) and time to tie-off post-transplant (HR 1.09 (1.02-1.16), p=0.008), are associated with all-cause graft loss. Time to tie-off (HR 1.19 (1.10-1.30), p=0.001) and receipt of a living donor transplant (HR 0.33 (0.11-0.89), p=0.045) impacted on risk of death censored allograft loss.

**Conclusions:** AVF ligation post-transplant may have potential graft and patient benefits with careful timing and patient selection.

![Figure 1](image)
CARDIOVASCULAR AND METABOLIC COMPLICATIONS AFTER KIDNEY TRANSPLANT

BOS10_14 PROSPECTIVE RANDOMIZED CONTROLLED TRIAL ANALYZING THE EFFECTS OF DENOSUMAB ON BONE MINERAL DENSITY AND BONE METABOLISM IN RENAL ALLOGRAFT TRANSPLANTS

Amrit Sharma1, Ashish Sharma1, Sanjay Bhadada1, Deepesh Kenwar2, Uma Saikia2, Tulika Singh2, Raja Ramachandran2, Uttam Saini2, Deprakash Choudhary1, Sahil Rally1, Sarbpreet Singh1, Shiva Kumar Sp1
1Post Graduate Institute of Medical Education and Research, Chandigarh, India, 2Post Graduate Institute of Medical Education and Research, Chandigarh, India

Background: The administration of denosumab decreases bone resorption and increases bone mineral density in osteoporosis in non-transplant settings. This study at our centre was done to study the potential benefits of denosumab in terms of bone health in renal transplant patients.

Methods: A single centre (PGIMER Chandigarh India) randomized control study to analyse the effects of denosumab on Bone Mineral Density (Measured by DEXA scan and HRPOCT Scan) and bone turnover markers (PINP, Beta-CTX, BSAP) in denosumab group patients (Received Inj. denosumab 60 mg s.c two dose 6 months apart for 1 year, along with standard immunosuppression), and control group patients (Do not received denosumab but received standard immunosuppression plus calcium 1 gram and vitamin D 500 IU daily).

Results: 30 were randomized into denosumab (n=15) and control (n=15) groups. Mean age in denosumab group was 32.36±3.77 years and 34.57±5.72 years in control group. Other baseline demographics were balanced between two groups. Six monthly DEXA Scans revealed significant fall in BMD at lumbar vertebra in control group (p=0.0001) over 1 year. The denosumab significantly increased BMD at lumbar vertebra (p<0.0001) (Two way repeated measure ANOVA) in denosumab group. In HRPOCT scan significant difference in trabecular thickness (in mm) (p =0.045) was noticed at end of 1 year. Denosumab also resulted in significant fall in bone turnover markers (measured 6 months), PINP (P<0.03), Beta-CTX (p=0.001) and BSAP (p=0.006). Asymptomatic significant fall in serum calcium was noticed (p<0.001) after each denosumab dose but no clinical side effect noticed after denosumab use.

Conclusions: The bone mineral density at lumbar vertebra decreased significantly after renal allograft transplantation which may predispose the patient to risk of fractures in long term. The use of denosumab in two doses 6 month apart effectively countered the reduction and improved bone mineral density in lumbar vertebral region and tibia. Denosumab resulted in favourable reduction in bone turnover markers with no adverse side effect profile.

KIDNEY REJECTION, FUNCTION AND SURVIVAL

BOS11_1 LANDSCAPE OF T-CELL MEDIATED REJECTION RESPONSE TO TREATMENT AFTER KIDNEY TRANSPLANTATION

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1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, 2CHU de Toulouse, Université de Toulouse, Toulouse, France

Background: In the current era of immunosuppression, T-cell mediated rejection (TCMR) seems to be less severe than antibody mediated rejection, however TCMR phenotype can be more complex and the response to therapy has not been investigated in large clinical trials. There is a need to better assess response to treatment in TCMR in order to optimize clinical trial and end points definition.

Methods: This multicenter prospective cohort study included patients who presented a first T-cell-mediated rejection between 2004 and 2021 in four French transplant centers. TCMR cases were reassessed using the latest Banff 2019 classification. Patients with features of concomitant antibody mediated rejection (AMR) were excluded. All clinical, immunological, histological and TCMR therapies were collected at time of rejection and during the follow-up. All patients received a standard of care treatment with 3 steroid pulse and steroid sparing IMmunosuppression +/- anti-thymocyte treatment. Kidney allograft reevaluation was performed including eGFR, proteinuria, DSA and graft biopsy assessment.

Results: A total of 550 patients were included. The TCMR occurred in a median time of 3.4 [1.1-12.3] months post-transplantation. Mean eGFR was 40.0 (20.3) mL/min/1.73m2. The distribution of TCMR grade was 26.4% grade IA, 37.7% grade IB, 23.5% grade IIA, 8.3% grade IIB and 4.1% grade III. The median time between TCMR and kidney allograft revaluation was 3.1 [1.8-7.7] months post-TCMR. At time of reevaluation, mean eGFR was 42.0 (18.5) mL/min/1.73m2. 25.5% of patients had positive anti-HLA DSA. The main diagnoses at reevaluation were: 1) persisting TCMR 10.8%, 2) AMR 10.9%, and 3) borderline lesions 10.8%. After a mean follow-up time of 7.8 (5.3) years post-TCMR, 169 (32.8%) patients experienced graft failure. Patients with persisting features of allograft activity, either TCMR and AMR has decreased graft survival compared with patients with TCMR histological resolution (p<0.05).

Conclusions: In the largest cohort of well phenotyped TCMR, response to treatment is suboptimal for almost 30% of patients and associated with worse prognosis. We provide here the basis for better assess response to treatment after TCMR to better individualize treatment strategies, clinical trials and improve patients outcomes.

BOS11_2 OPERABILITY OF THE BANFF “V” LESION SCORE IN DSA POSITIVE MIXED REJECTION

Karolien Wellekens1,2, Priyanka Koshy1, Tim Debroy1, Evert Cleenders1, Marie-Paule Emonds1, Dirk Kuypers1, Aleksandar Senev1, Elisa Van Loon1, Maarten Coemans1, Maarten Naseems1
1KU Leuven, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium, 2KU Leuven, Leuven, Belgium

Background: According to the Banff Classification of Allograft Pathology, the “v” lesion score appraises the degree of inflammatory cells in the subendothelial space. This lesion score remarkably contributes to the diagnosis of antibody-mediated rejection (AMR) as well as T cell-mediated rejection (TCMR); high “v” scores alone can give rise to TCMR diagnosis independently of other main TCMR features. Here, we aim to investigate the operability of this lesion score in rejection diagnosis.

Methods: In this single-center observational study, we made use of a retrospective cohort database consisting of kidney biopsy samples (n=7601) from all adult patients (n=1868) who received a kidney transplant between March 2004 and May 2021. We retrospectively defined TCMR and AMR by the Banff’19 criteria and related the histological phenotype to DSA status and C4d staining results in perifurcular capillaries.

Results: 386 out of 1020 DSA positive biopsies showed acute rejection subtypes (38%): 155 AMR (40%), 85 TCMR (22%), 49 borderline TCMR (13%), 73 full mixed (AMR-TCMR, 19%), and 24 borderline mixed rejection (AMR-borderline TCMR, 6%). A large number of mixed rejections was however explained by the “v” lesion as a criterion for TCMR. When the “v” lesion was not considered, the proportion of borderline mixed and AMR cases increased with 6% and 5% respectively. In total, we reclassified 35% of the phenotypes (P<0.001).

Conclusions: A significant proportion of DSA positive mixed rejection biopsies meet the TCMR criteria by the “v” lesion, indicating the need to review the sensitivity and specificity of this lesion, and thus its operability in rejection diagnosis in general. Our data suggest not using the “v” lesion to classify rejection phenotypes, but rather applying it as a “risk estimator” as it is proven to be a negative prognostic factor for kidney allograft survival.
Figure 1: Reclassification of phenotypes according to the Banff'19 consensus vs when not taking into account the 'ptc rule'.

**BRIEF ORALS**

**Kidney rejection, function and survival**

**BOS11_3**

**CALLING INTO QUESTION THE ADDED VALUE OF THE PTC RULE IN CLASSIFYING KIDNEY TRANSPLANT REJECTION**

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**Background:** To establish antibody-mediated rejection (AMR) diagnosis in the presence of (borderline) T cell-mediated rejection (TCMR), peritubular capillaritis ("ptc") alone is not sufficient and glomerulitis ("g") must be present. We aim to import the importance of peritubular capillaritis as an exclusion criterion to classify rejection phenotypes in accordance with the Banff Classification of Allograft Pathology.

**Methods:** In this single-center observational study, we made use of a cohort database consisting of kidney biopsy samples (n=7601) from all adult patients (n=1868) who received a kidney transplant between March 2004 and May 2021. We retrospectively defined TCMR and AMR by the histological Banff'19 criteria and reclassified these phenotypes not taking into account the 'ptc rule' ("ptc" or "g" ≥2 / "ptc" or "g" ≥1 in case of C4d positivity). We retrospectively defined TCMR and AMR by the histological Banff'19 criteria and reclassified these phenotypes not taking into account the 'ptc rule' ("ptc" or "g" ≥2 / "ptc" or "g" ≥1 in case of C4d positivity).

**Results:** 386 out of 1020 (38%) DSA+ and 1060 out of 5316 (20%) DSA- biopsies showed acute rejection phenomena. In DSA+ cases, we scored 155 AMR (40%), 85 TCMR (22%), 49 borderline TCMR (13%), 73 mixed (AMR-TCMR, 19%), and 24 borderline mixed rejection (AMR-borderline TCMR, 6%) phenotypes. 187 AMR (18%), 392 TCMR (37%), 333 borderline TCMR (31%), 112 mixed (11%) and 36 borderline mixed (3%) phenotypes were identified in DSA- cases. When the 'ptc rule' was not taken into account for DSA+ cases, we reclassified only 4% of TCMR to mixed and 2% of borderline TCMR to borderline mixed rejection phenotypes; both changes did not reach statistical significance. For DSA- cases, 6% of TCMR and 3% of borderline TCMR phenotypes were reclassified to mixed and borderline mixed rejection respectively (P<0.01).

**Conclusions:** Omitting the 'ptc rule' has a minor impact on final rejection phenotype classification for DSA+ cases. In DSA- cases, further research on how phenotype reclassification is related to outcome and immunological risk factors such as non-HLA antibodies and missing self is ongoing to define whether elimination of the 'ptc rule' in DSA- cases indeed alters the accuracy of the classification. These findings will likewise contribute in determining if we could fully align the historical definition of DSA+ and DSA- microvascular inflammation.
**BOS11_5**  
**ACUTE REJECTION AFTER CONVERSION TO BELATACEPT IN KIDNEY TRANSPLANTATION**

Dominique Bertrand1,2, Nathalie Chavarot1, Jerome Olagne3, Clarisse Greze4, Philippe Gatault1,克莱门·Danthu1,Charlotte Colosio1, Maite Jaureguy2, Agnes Duveau5, Nicolas Bouvier4, Yannick Le Meur4, Leonard Gedon1, Eric Thervet3, Antoine Thierry1, Charlotte Laurent1, Mathilde Lemoine1, Daniele Anglicheau1, Dominique Guerot2

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4. Clermont-Ferrand University Hospital, Nephrology, Dialysis and Kidney Transplantation, Clermont Ferrand, France.  
5. Tours University Hospital, Nephrology, Dialysis and Kidney Transplantation, Caen, France.  
6. Brest University Hospital, Nephrology, Dialysis and Kidney Transplantation, Brest, France.  
7. Reims University Hospital, Nephrology, Dialysis and Kidney Transplantation, Reims, France.  
8. Amiens University Hospital, Nephrology, Dialysis and Kidney Transplantation, Amiens, France.  
9. Angers University Hospital, Nephrology, Dialysis and Kidney Transplantation, Angers, France.  
10. Caen University Hospital, Nephrology, Dialysis and Kidney Transplantation, Caen, France.  
11. Brest University Hospital, Nephrology, Dialysis and Kidney Transplantation, Poitiers, France.  
12. Rouen University Hospital, Nephrology, Dialysis and Kidney Transplantation, Rouen, France

**Background:** After kidney transplantation, conversion to belatacept is an interesting alternative in patients with poor graft function or intolerance to calcineurin inhibitors (CNI). The occurrence of acute rejection has been widely described and studied during de novo use, but much less so in conversion conditions.  

**Methods:** We present here a retrospective multicenter study investigating the occurrence of acute rejection after conversion to belatacept.  

**Results:** Between 2011 and 2021, 901 patients were switched to belatacept after transplantation and 54 of them experienced a biopsy-proven acute rejection, i.e. 6% of the cohort. Among the 54 patients, 47 (87%) developed a T cell mediated rejection rejection (5 borderline, 9 grade Ia, 9 grade Ib, 7 grade IIa, 11 grade IIb, 6 grade III). This rejection episode occurred after a median of 2.6 months (IQR: 2.1-2.6) after switch. In all cases, rejection therapy was offered (high dose steroids in 91.5% of cases) and belatacept treatment was discontinued in 51.2% of cases. Renal function improved in 56.4% of patients. We recorded 18 graft losses (36.9%) within a median of 7.2 months (IQR: 4.1-10.1) after rejection and 8 patients died after rejection. We compared these 47 patients to a multicenter historical cohort (2011-2017) of 262 patients switched to belatacept who did not develop rejection at follow-up, to determine clinical and bio-chemical predictors of acute rejection. After multivariate analysis, the only factors associated with the occurrence of rejection after switch were the use of thymoglobulins as induction (HR: 0.46, 95% CI: 0.21-0.99, p=0.05), tacrolimus treatment before switch (HR: 2.97, 95% CI: 1.23-7.14, p=0.01) and late switch > 6 months (HR: 4.63, 95% CI: 2.33-9.23, p<0.003).  

**Conclusions:** The occurrence of acute rejection after switching to belatacept appears to be less frequent than de novo use. Nevertheless, the risk of graft loss or deterioration of renal function after rejection is significant in patients with already poor renal function.

**BOS11_6**  
**SUBCLINICAL ANTIBODY-MEDIATED REJECTION DETECTED BY EARLY (TWO WEEKS) PROTOCOL BIOPSIES IN HIGHLY IMMUNIZED TRANSPLANT RECIPIENTS**

Carroll Araña1,2, Elena Cuadrado1,2, Johanna Reinoso1,3, Enrique Montagud-Marrahi1,2,3, Jordi Rovira1, Diana Rodriguez-Espinosa1, Judit Cacho1, Angela González1, Jose V Torregrosa1, Ignacio Revuelta1,2, Nuria Esforzado1,2, Frederic Cofan1,2, Beatriz Bayes1, Ana Belan Larque1, Adriana Garcia1,2, J. Luis Caro1,2, Eduard Paleu1, Fritz Dziekmann2,1, Frederico Oppenheimer1,2,  
1. Hospital Clinic de Barcelona, Nephrology and Transplant Unit, Barcelona, Spain.  
2. Fundació de Recerca Clínica Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain.  
3. Laboratori Experimental de Nefrología i Transplantación, LLENTI, Barcelona, Spain.

**Background:** Renal graft recipients with donor-specific anti-HLA antibodies show an increased risk of antibody-mediated rejection (ABMR). Protocol biopsies may help detect subclinical rejection. The aim of this research was to describe the prevalence, severity and outcomes of patients with high immunological risk who underwent early protocol biopsy.

**Methods:** Renal transplant (RT) recipients with pre-transplant calculated (cPRA) ≥90%, who received a cadaveric donor kidney graft between 2015 and 2021 were evaluated. Patients with protocol biopsy within the first two weeks post transplantation were included. Baseline characteristics, immunological parameters, immunosuppressive treatment, presence of delayed graft function and serum creatinine levels throughout follow-up were reported. The prevalence of ABMR was analyzed by early protocol biopsy in the study group.  

**Results:** Out of 155 patients, a total of 128 early protocol biopsies were performed. Thirty-eight patients (29.5%) had at least one episode of rejection excluding borderline during follow-up: 23 (60.5%) corresponded to acute ABMR, of which 17 were diagnosed early (<90 days post-TR), and 6 late. Among patients with early ABMR 11 (64.7%) were diagnosed by protocol biopsies within 2 weeks post-TR (early ABMR). No significant differences in pre-TR immunological data or donor-derived cell-free DNA (dd-cfDNA) compared to those without early biopsy rejection. A higher percentage of uncontrolled astystole in the rejection group. At 1-year follow-up the patients with early ABMR rejection: 2 had graft dysfunction, 2 developed ABMR chronic-active and differences were observed in eGFR: 32±7 vs 48±2 p=0.038 compared to those without early biopsy rejection.  

**Conclusions:** 64.7% of early ABMR were detected by early protocol biopsy in a population at high immunological risk (cPRA≥90%), information not previously reported in this population.

**BOS11_7**  
**A NOVEL TWO STAGE REJECTION PREDICTION MODEL IN KIDNEY ALLOGRAFT USING SERIAL SERIAL GENE EXPRESSION PROFILE AND DONOR-DERIVED CELL-FREE DNA**

Sook Park1,2, Kexin Guo3, Lihui Zhao3, Christabel Rebello3, John Friedewald1

1. Northwestern University, Chicago, United States

**Background:** Non-invasive blood biomarkers for rejection have gained significant attention as an alternative to invasive kidney biopsies. We aimed to develop predictive models using serial samples' gene expression profile and donor-derived cell-free DNA up to 2-year post kidney transplantation (KT).  

**Methods:** We used data from a previously reported prospective multicenter observational study. For 1-year post KT prediction model, we analyzed 212 subjects with 1-year post KT biopsies and at least one serial samples of GEP and dd-cfDNA. We developed a 2-year post KT prediction model using 166 subjects with 2-year post KT biopsies and serial samples. A microarray GEP method and fraction of dd-cfDNA over total cell free DNA were used. Two stage model fitting was performed. The first stage was to fit two linear mixed effect model to calculate random intercept and random slope followed by the second stage logistic regression model.  

**Results:** For 1-year post-KT rejection model, 792 GEP and 1375 dd-cfDNA samples were analyzed. The area under the receiver operating characteristic curve (AUC) of 1-year post KT rejection model was 0.80 (Table 1). A total of 921 GEP and 1,666 dd-cfDNA samples from 166 subjects were used for the 2-year KT rejection model (Table 2). As more serial samples were incorporated into the model, the AUC improved to 0.84 at 2 months (Table 2).  

**Conclusions:** Accumulation of data from multiple serial GEP and dd-cfDNA samples improved 2-year post KT rejection prediction with AUC 0.84. Further study will be needed to validate this novel rejection prediction model and incorporate additional data elements.

**Table 1** The summary of 1-year post KT rejection prediction model

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**Table 2** The summary of 2-year post KT rejection prediction model

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Kidney rejection, function and survival

**BRIEF ORALS**

**BOS11_8** SURVIVAL OUTCOMES COMPARING OLDER LIVING DONOR VERSUS STANDARD CRITERIA DONOR KIDNEY TRANSPLANTATION VERSUS NOT BEING TRANSPLANTED

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**Background:** The literature regarding mortality outcomes for kidney transplant candidates receiving older living donor kidneys versus receiving a younger standard criteria donor (SCD) kidney or remaining on dialysis has not been explored. The aim of this analysis was to explore this using UK transplant registry data, with older living donors defined as a donor aged 60 years and above.

**Methods:** A retrospective cohort study was undertaken of prospectively collected registry data of all waitlisted kidney failure patients receiving dialysis in the United Kingdom. From January 1, 2000 until September 30, 2019 inclusive, all patients listed for their first single kidney transplant were included. The primary outcome was mortality, with survival analysis conducted according to the intention-to-treat principle. Time-to-death from listing was analysed using nonproportional hazard Cox regression models with transplantation handled as a time-dependent covariate. All analyses were done using R statistical software (version 4.2.2).

**Results:** A total of 32,978 waitlisted kidney failure patients formed the primary study cohort, of whom 18,796 (58.5%) received a kidney transplant (1,557 older living donor kidneys and 18,062 SCD kidneys). Older living donor kidney transplantation constituted only 17.0% of all living donor kidney transplant activity (overall living kidney donor cohort: n=9,140). Recipients of older living donor kidneys had reduced all-cause mortality compared to receiving SCD kidneys (HR 0.904, 95% CI 0.845-0.967, p=0.003) and much lower all-cause mortality versus waiting for any SCD kidney transplant or remaining on dialysis (HR 0.160, 95% CI 0.149-0.172, p<0.001).

**Conclusions:** Waitlisted kidney transplant candidates who proceed with living donor transplantation from donors aged 60 years and over have similar all-cause mortality versus waiting for any SCD kidney transplant or remaining waitlisted. Older living kidney donors should be actively explored to expand the living donor kidney pool and are an excellent treatment option for waitlisted patients. Older living donors defined as a donor aged 60 years and above.

**BOS11_9** PREDICTION OF GRAFT SURVIVAL PRIOR TO ACCEPTING AN OFFER FOR LIVING DONOR KIDNEY TRANSPLANT: AN ARTIFICIAL INTELLIGENCE APPROACH

Hatem Ali1, Mahmoud Mohamed2, Bernard Burke3, David Briggs4, Nithya Krishnan1

1University Hospitals of Coventry and Warwickshire, Coventry, United Kingdom, 2North Mississippi medical center, mississippi, United States, 3Coventry University, Coventry, United Kingdom, 4BHSBT, Birmingham, United Kingdom

**Background:** The current available models for evaluation of outcomes of living donor kidney transplant before accepting an offer are poorly developed, and validated. Aim: We aim to use Artificial Intelligence to build a model that can accurately predict death censored graft survival for living donor kidney transplant prior to accepting an offer.

**Methods:** All living kidney transplant patients who were registered in the UNOS database between 1/1/2007 and 1/6/2021, maintained on TAC/MMF immunotherapy were included in our analysis. We excluded patients with age<18 years old and ABO incompatible transplant. We divided the data randomly into training and testing dataset with ratio 80:20. We performed recursive feature elimination to select the important ones for prediction. Features were selected based on their Gini impurity scores. We performed Artificial Neural Network analysis (ANN). We evaluated the model using Harrell Concordance-time-dependent score (for discrimination), and Integrated Brier score (for calibration). We also assessed dynamic AUC for model performance.

**Results:** 54,110 living donor kidney transplant patients were included in the study. Harrell C-Statistic scores were 0.70 at 5 years post-transplant, 0.68 at 10 years post-transplant and 0.68 at 13 years post-transplant, indicating very high discrimination power. Integrated Brier Score was 0.08, indicating very high calibration score for our model. Dynamic AUC scores were 0.71 at 5 years post-transplant and 0.68 at 10 and 13 years post-transplant, indicating adequate performance for our model. The key players in our model were recipient age (variable importance=0.26), donor age (variable importance=0.17), donor ethnicity (variable importance=0.90), followed by dialysis vintage pre-transplantation.

**Conclusions:** The ANN model had high discrimination, calibration, and performance indices for predicting death censored graft survival prior to transplant. It can aid the clinical decision for management of the transplant patients. We are currently developing a user-friendly web application that can be used to apply the ANN model for prediction. Our model can help ranking potential living kidney donors based on graft outcomes. Therefore, our model can help improve current outcomes of kidney paired exchange schemes.
Background: Our aim is to predict occurrence of lifetime kidney failure and development of hypertension among living donors prior to donation.

Methods: All living kidney transplant donors registered in the UNOS database from 1994 till 2020 were retrospectively reviewed. Kidney failure was defined as the need for maintenance dialysis post-donation or being added to the transplant waiting list. The outcome of kidney failure was followed-up for lifetime per donor. Development of hypertension was defined as "requiring long-term medication for treatment of hypertension post-donation". The data was divided into training and test dataset with ratio 70:30 in order to train the model and then evaluate its performance on the unseen data. Decision based models for survival analysis were used (decision tree, Random Forest and XGBOOST). Class weights were used to encounter for class imbalance. Evaluation criteria were Area under the curve (AUC) and accuracy to evaluate model performance for discrimination between the class outcomes. Sensitivity and specificity for identifying each outcome were evaluated.

Results: 159,617 patients were included in our study. For the predicting kidney failure, the xgboost model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.77, sensitivity=0.76 and specificity=0.77. The key-players with the highest weights for predicting kidney failure were "history of cigarette smoking" (weight=-0.35), "biological relationship with the recipient" (weight=-0.13), followed by "donor ethnicity" (weight=0.08). For the predicting development of hypertension, the random forest classifier model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.76, sensitivity=0.76 and specificity=0.76. The key-players with the highest weights for predicting the development of hypertension were "history of cigarette smoking" (weight=-0.15), followed by "donor ethnicity" (weight=0.12). For the predicting development of hypertension, the random forest classifier model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.76, sensitivity=0.76 and specificity=0.76. The key-players with the highest weights for predicting the development of hypertension were "history of cigarette smoking" (weight=-0.35), "biological relationship with the recipient" (weight=-0.13), followed by "donor ethnicity" (weight=0.08).

Conclusions: Decision based models can aid in predicting kidney failure and development of hypertension among potential living donors. User-friendly web app can be developed using our model. Key players in prediction for kidney failure and hypertension were cigarette smoking, biological relationship with the recipient and donor ethnicity.

BRIEF ORALS

BOS11_10 PREDICTION OF KIDNEY FAILURE AND DEVELOPMENT OF HYPERTENSION AMONG POTENTIAL LIVING DONORS: AN ARTIFICIAL INTELLIGENCE APPROACH

Hatem Ali¹,², Mahmoud Mohamed², David Briggs¹, Nithya Krishnan¹,²
¹University Hospitals of Coventry and Warwickshire, Coventry, United Kingdom, ²Coventry University, Coventry, United Kingdom

Background: Our aim is to predict occurrence of lifetime kidney failure and development of hypertension among living donors prior to donation.

Methods: All living kidney transplant donors registered in the UNOS database from 1994 till 2020 were retrospectively reviewed. Kidney failure was defined as the need for maintenance dialysis post-donation or being added to the transplant waiting list. The outcome of kidney failure was followed-up for lifetime per donor. Development of hypertension was defined as "requiring long-term medication for treatment of hypertension post-donation". The data was divided into training and test dataset with ratio 70:30 in order to train the model and then evaluate its performance on the unseen data. Decision based models for survival analysis were used (decision tree, Random Forest and XGBOOST). Class weights were used to encounter for class imbalance. Evaluation criteria were Area under the curve (AUC) and accuracy to evaluate model performance for discrimination between the class outcomes. Sensitivity and specificity for identifying each outcome were evaluated.

Results: 159,617 patients were included in our study. For the predicting kidney failure, the xgboost model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.77, sensitivity=0.76 and specificity=0.77. The key-players with the highest weights for predicting kidney failure were "history of cigarette smoking" (weight=-0.35), "biological relationship with the recipient" (weight=-0.13), followed by "donor ethnicity" (weight=0.08). For the predicting development of hypertension, the random forest classifier model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.76, sensitivity=0.76 and specificity=0.76. The key-players with the highest weights for predicting the development of hypertension were "history of cigarette smoking" (weight=-0.15), followed by "donor ethnicity" (weight=0.12). For the predicting development of hypertension, the random forest classifier model showed AUC=0.82 (indicating adequate discrimination), accuracy=0.76, sensitivity=0.76 and specificity=0.76. The key-players with the highest weights for predicting the development of hypertension were "history of cigarette smoking" (weight=-0.35), "biological relationship with the recipient" (weight=-0.13), followed by "donor ethnicity" (weight=0.08).

Conclusions: Decision based models can aid in predicting kidney failure and development of hypertension among potential living donors. User-friendly web app can be developed using our model. Key players in prediction for kidney failure and hypertension were cigarette smoking, biological relationship with the recipient and donor ethnicity.

BOS11_12 IMPACT OF INDIVIDUAL EPLETS TO ACUTE REJECTION STUDIED BY MACHINE LEARNING METHOD: ANALYSIS OF KOREAN ORGAN TRANSPLANTATION REGISTRY

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¹Seoul National University Bundang Hospital, Department of Internal Medicine, Seoul, South Korea, ²Seoul National University Bundang Hospital, Department of Surgery, Seongnam, South Korea, ³Aju University School of Medicine, Department of Internal Medicine, Suwon, South Korea, ⁴Samsung Medical Center, Department of Surgery, Seoul, South Korea, ⁵Seoul Red Cross Hospital, Department of Internal Medicine, Seoul, South Korea, ⁶YONSEI University College of Medicine, Department of Internal Medicine, Seoul, South Korea, ⁷National Medical Center, Department of Internal Medicine, Seoul, South Korea, ⁸Seoul National University Bundang Hospital, Department of Laboratory Medicine, Seongnam, South Korea, ⁹Korea Organ Donation Agency Laboratory, Seoul, South Korea

Background: Epitope matching has been shown to predict allograft survival and development of de novo donor-specific antibodies. However, statistical superiority of epitope mismatch to predict rejection outcome than that of HLA genotype mismatch were not thoroughly investigated.

Methods: Patients included in the Korean Organ Transplantation Registry (KOTRY) were used. Kidney transplant recipients who received transplants from 2014 to 2021 were enrolled. HLA four-digit genotypes were imputed by matching to the four-digit haplotype distribution as our previous method. The primary outcome measurement was acute rejection, biopsy-proven acute rejection (BPAR), T-cell mediated rejection (TCMR) and B-cell mediated rejection (BCMR) within 1 year. Ten fold cross-validated Extreme Gradient Boost (XGBoost) model and logistic regression were used as statistical method and cross-validated receiver operating characteristics (ROC) curves were compared.

Results: Among 9,150 donor-recipient pairs, four digits HLA estimation were successful in 7,607 pairs. Exact 1:1 matching of HLA haplotype were successful in 1,980 pairs (call 4 digits group). Mean class I and class II epitope mismatches were not thoroughly investigated.

Conclusions: In this Korean population study, individual epitope mismatches predicted acute rejection better than HLA mismatches in the subpopulation who had accurate 4 digits matched subpopulation. Sum of epitope mismatch number did not show better predictability than HLA mismatch numbers.
Background: De novo donor-specific antibodies (dnDSA) may cause antibody-mediated rejection (ABMR) and graft dysfunction. In this study we aimed to assess the value of estimated glomerular filtration rate (eGFR) and protein body-mediated rejection (ABMR) and graft dysfunction. In this study we aimed to assess the value of estimated glomerular filtration rate (eGFR) and protein body-mediated rejection (ABMR) and graft dysfunction.

Methods: All 400 kidney transplant recipients at our center with dnDSA against the last graft (01/03/2000-31/05/2021) were included in this retrospective study. The dates of doubling creatinine, ≥30% eGFR decline and proteinuria ≥500 mg/g were registered from day of first dnDSA occurrence. Patients were classified as ‘completely stable’ (no graft loss, no ≥30% eGFR reduction, no proteinuria ≥500 mg/g) at 5 years after first occurrence of dnDSA.

Results: During 8.3 years of follow-up, graft loss occurred in 33.3% of patients. Creatinine doubled after a median of 2.8 years from dnDSA appearance, and the time from doubling creatinine to graft failure was 1.0 years. Analyzing the time from dnDSA appearance to the event of doubling creatinine and ≥30% eGFR decline was 27.2% (± 2.7%) and 42.9% (±3.1%), respectively. B) At 5 years post-dnDSA, 48.5% (± 2.9%) of patients had proteinuria ≥500 mg/g.

Conclusions: A relevant (28.2%) proportion of patients has a ‘completely stable’ clinical course after 5 years post-dnDSA. A ≥30% decline in eGFR, the time from dnDSA occurrence to this event was 2.0 years, with a positive predictive value of 47.3% to predict graft failure, which occurred after 1.9 years. The median time from proteinuria ≥500 mg/g and ≥1000 mg/g to graft failure was identical (1.8 years). The 5-year incidence of renal outcomes is shown in figure 1. Interestingly, 5 years after first occurrence of dnDSA, 113/400 (28.2%) patients were ‘completely stable’.

Figure 1. Time-to-event renal outcomes: A) By survival analysis, the 5-year incidence of doubling creatinine and ≥30% eGFR decline was 27.2% (± 2.7%) and 42.9% (±3.1%), respectively. B) At 5 years post-dnDSA, 48.5% (± 2.9%) of patients had proteinuria ≥500 mg/g and 32.7% (± 2.7%) had proteinuria ≥1000 mg/g.

A) KAPLAN-MEIER Time-to-event doubling Creatinine and eGFR reduction >>30% eGFR reduction ≥30% Doubling creatinine

B) KAPLAN-MEIER Time-to-event proteinuria (mg/g) Proteinuria ≥ 500 mg/g Proteinuria ≥ 1000 mg/g

Methods: We retrospectively analyzed the outcomes (renal function and histological lesions) of a 6-months TCZ therapy in 6 pKT recipients treated during November 2021 and December 2022. All patients had caAMR according to the Banff classification 2018 (category 2) and all received intravenous TCZ (8mg/ kg/month for 6 months). Collected data included creatinine, eGFR, proteinuria, HLA and non-HLA antibodies at baseline, month +3 (M3) and month +6 (M6) after TCZ initiation. For each patient, a follow-up biopsy was scheduled at the end of the treatment.

Results: Six patients (average age 15 years, 4 male) were included. Immunosuppression at the time of caAMR included tacrolimus with MMF (4 patients, 66.6%) or mTOR inhibitor (2 patients, 33.3%), and daily prednisone. AntiHLA antibodies (DSA) were detected in 3 patients and nonHLA antibodies (AT1R and ETAR) in 2. caAMR diagnostic was based on histological findings in the 3 patients without DSA. Mean time to caAMR was 4 years after transplantation. At the time of caAMR diagnosis, mean eGFR was 40.6±12.8 mL/min/1.73 m². In one patient, TCZ treatment was discontinued after 3 doses due to graft failure. Another patient performed follow up biopsy, which showed persistent caAMR with worsened histological lesions, and subsequently lost his graft. Two patients showed a stable renal function, but histological lesions had worsened (c1, c3, IFTA2). In one patient, with worsened renal function, follow up biopsy was not performed due to intrarenal arteriovenous fistula. In the last patient, the biopsy is yet to be performed. Globally, mean eGFR worsened to 31.4±15.3 mL/min/1.73 m² at M3 and remained stable at M6. Proteinuria, antiHLA and nonHLA antibodies remained stable.

Conclusions: In our experience, TCZ therapy did not appear to be significantly effective in modifying the natural history of caAMR. However, more studies are needed to clarify the role of TCZ in caABMR.
**BRIEF ORALS**

**Transplantation outcomes and complications**

**BOS12.1 SPLIT-LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS IS ASSOCIATED WITH REDUCED GRAFT SURVIVAL DUE TO HEPATIC ARTERY THROMBOSIS**


1University of Melbourne, Surgery (Austin Precinct), Melbourne, Australia, 1Paris Institute for Transplantation and Organ Regeneration, Universitè Paris

**Background:** Primary sclerosing cholangitis (PSC) is a common indication for liver transplantation (LT). In the context of chronic shortages, split-liver transplantation (SLT) has the potential to increase the pool of donors organs. Biliary complications occur with increased frequency following LT for PSC, and in SLT. The aim of this study was to compare graft survival in SLT and whole liver transplantation (WLT) for patients with PSC.

**Methods:** Outcome data for 2656 adult liver transplant recipients were analysed from the Australia-New Zealand Liver and Intestinal Transplant Registry, 2011-2020. Patients were categorised into 4 groups: PSC with SLT (PSC-SLT), PSC with WLT (PSC-WLT), non-PSC with SLT (non-PSC-SLT) and non-PSC with WLT (non-PSC-WLT). Graft and patient survival were analysed using Kaplan-Meier graphs with log-rank tests. Univariate Cox proportional hazards testing, followed by multivariate proportional hazards regression were used to identify variables independently associated with graft loss. Re-transplantation rates for any cause were compared between groups using chi-square.

**Results:** The cohort included 261 PSC patients (PSC-SLT n=26). 5-year graft survival was significantly reduced following PSC-SLT (57.9%), compared to the other groups (see Table). Reduced graft survival post PSC-SLT was significant when compared with PSC-WLT (p=0.002) and non-PSC-SLT (p=0.006). On multivariate analysis, PSC-SLT was the strongest, independent risk factor for graft loss (HR 3.24, 95% CI 1.77-5.92, p<0.001). There were no significant differences in patient survival (p=0.62) or biliary complications leading to graft loss (p=0.061) between groups. Graft loss in PSC-SLT was strongly linked to an increased incidence of hepatic artery thrombosis (HAT) leading to graft failure (PSC-SLT 15.4% vs non-PSC-SLT 2.4%; PSC-WLT 0.4%; non-PSC-WLT 0.7%; p<0.001).

**Conclusions:** PSC-SLT is associated with significantly reduced graft survival compared with PSC-WLT and non-PSC-SLT, and should be avoided where possible. SLT is generally associated with an increased risk of HAT, but this may be further compounded by a hypercoagulable state in PSC. Patients undergoing PSC-SLT may benefit from perioperative anticoagulation and enhanced vascular monitoring protocols to mitigate increased risks of graft loss.

**Table:**

<table>
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<th>Group</th>
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</tr>
<tr>
<td>PSC-WLT</td>
<td>91.1%</td>
</tr>
<tr>
<td>PSC-SLT</td>
<td>73.1%</td>
</tr>
<tr>
<td>Non-PSC-SLT</td>
<td>88.3%</td>
</tr>
<tr>
<td>Non-PSC-WLT</td>
<td>91.6%</td>
</tr>
</tbody>
</table>

**BOS12.2 IDENTIFICATION OF NOVEL LIVER TRANSPLANT BIOPSY PHENOTYPES ASSOCIATED WITH DISTINCT BIOLOGICAL PROFILES AND ALLOGRAFT SURVIVAL**

**Zeynep Demir**, **Olivier Aubert**, **Mylene Sebagh**, **Jean-Paul Duong van Huyen**, **Dominique Debry**, **Valerie Paradis**, **Cyrille Ferry**, **Francois Durand**, **Eric Vibert**, **Christophe Charod**, **Claire Francoz**, **Carmen Lefaucheux**, **Alexandre Loupy**

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**Background:** The heterogeneity of histological lesions in liver transplant (LT) biopsies has not been precisely characterized nor classified so far, especially those associated with circulating anti-HLA DSA. We hypothesized that a probabilistic unsupervised approach applied in a large comprehensive and well annotated prospective LT cohort could bring new insights of liver allograft phenotypes.

**Methods:** We evaluated LT biopsies with concomitant investigation of anti-HLA DSA from pediatric and adult recipients transplanted between 2010 and 2020 in 3 French centers. Using a comprehensive cohort of LT including clinical, immunohistological and outcome data, unsupervised archetypal analysis was done integrating the 27 clinical, histological and immunological parameters assessed for each biopsy. The association between the archetypes identified and liver function tests and allograft survival were investigated. The primary outcome was liver allograft failure while the secondary outcome was the occurrence of biliary strictures.

**Results:** A total of 490 LT biopsies provided by 325 patients were evaluated. The median time from LT to biopsy was 426.5 days (IQR: 137-871).Liver allograft survival rates after biopsy were 89.1% and 80.2% at 5 and 10 years, respectively. The unsupervised archetypal analysis identified 7 archetypes characterized by distinct clinical, immunological and pathological features (Figure). The characteristics defining the archetypes were similar and conserved across pediatric and adult cohorts. The 7 archetypes displayed distinct biological profiles and allograft outcomes: 1) with allograft survival rates ranging from 92.6% to 50% between archetypes 3 years after biopsy (log rank p value=0.001); 2) and biliary strictures free rates: 100% to 66.7% at 3 years after biopsy (log rank p value=0.002). The allograft outcomes were mainly determined by the severity of histological bile duct lesions and/or presence of circulating anti-HLA DSA.

**Conclusions:** Based on an unsupervised analysis, we identified clinically meaningful phenotypes with distinct biological profiles and outcomes, allowing to quantify and refine the currently unclassified liver-graft histological lesions.

**Figure:** Summary of clinical and immuno-histological features characterizing the 7 archetypes.
**BRIEF ORALS**

**Transplantation outcomes and complications**

**BOS12_3**

**MACHINE PERFUSION TECHNIQUES FOR LIVER TRANSPLANTATION - A META-ANALYSIS OF THE FIRST SEVEN RANDOMIZED CONTROLLED TRIALS**

Janina Eden1, Alessandro Parente2, Fabio Tirotta1, Alessia Pini3, Daniele Dondossola1, Tommaso Manzia4, Philipp Dutkowski5, Andrea Schlegel6

1Swiss HPB Centre, University Hospital Zurich, Switzerland; 2Surgery and Transplantation, Zurich, Switzerland; 3HPB and Transplant Unit, Department of Surgical Science, University of Rome Tor Vergata, Rome, Italy; 4Surgery, Rome, Italy; 5Queen Elizabeth Hospital Birmingham, University Hospital Birmingham NHS Trust, Birmingham, United Kingdom; 6Surgery, Birmingham, United Kingdom.

**Background:** The role of machine perfusion on outcomes after liver transplantation has been assessed. This study provides the highest (level 1) evidence on the role of machine perfusion in liver transplantation compared to static cold storage (SCS).

**Methods:** A MEDLINE and EMBASE database search was performed to identify randomized controlled trials (RCTs) reporting the outcomes after retransplantation of machine perfused livers compared to SCS. Data were pooled using random effect models. Risk ratios (RR) were calculated for clinically relevant outcomes including early allograft dysfunction (EAD), complications, graft loss and retransplantation within the first year after liver transplantation.

**Results:** Seven RCTs were identified for end-ischemic hypothermic oxygenated (HOPE, n=4) and upfront normothermic machine perfusion (NMP, n=3), including a total number of 1017 patients (241 HOPE vs. 241 SCS; 282 NMP vs. 253 SCS). Both NMP and HOPE were associated with significantly lower EAD rates (NMP: RR 0.50, CI95% 0.30-0.86, p=0.01, I2: 39%; HOPE: RR 0.48, CI95% 0.35-0.65, p<0.00001, I2: 5%) compared to SCS, only the HOPE-approach, despite performed after cold storage, showed impact on other clinically relevant outcomes. The duration of hospital stay was shortened (Mean Difference: -4.26, CI95%: -7.98-0.55, p=0.02, I2: 95%), and the number of patients with major complications (Clavien Grade IIIb) was reduced by HOPE (RR 0.79, CI95% 0.62-0.99, p=0.04, I2: 0%), together with lower rates of non-anastomotic biliary strictures (RR: 0.43, CI95% 0.20-0.93, p=0.03, I2: 0%) and re-transplantation (RR: 0.21, CI95%: 0.04-0.96, p=0.04, I2: 0%) with substantially significantly better graft survival rates (RR: 0.40, CI95% 0.17-0.95, p=0.04; I2: 0%).

**Conclusions:** This study provides the highest (level 1) evidence on the role of machine perfusion in liver transplantation. The HOPE-technique was found to best protect liver recipients from clinically relevant posttransplant complications and should therefore be routinely considered in clinical practice.

**Figure:** Graphical presentation of the meta-analysis results for the first seven randomized controlled trials on ex-situ machine perfusion in liver transplantation.

**BOS12_4**

**ABSORBABLE SELF-EXPANDABLE BILIARY STENT AS APREVENTIVE TREATMENT OF BILIARY COMPLICATIONS IN LIVER TRANSPLANT**

Víctor López-López1,2, Christoph Kuemmerli2, Alberto Hiciano1, Pedro Cascales Campos3, Alberto Baroja-Mazo1, Kohei Miura3, José Antonio Pons1, Laura Martínez-Arcón1, Francisco Sanchez-Bueno1, Pablo Ramirez Romero1, Ricardo Robles-Campos1

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**Background:** Complications related to the biliary anastomosis in liver transplant (LT) have been reduced in recent years but remain a weak spot of the procedure. In this study, we analyzed the use of a self-expandable absorbable stent to support the biliary anastomosis in LT.

**Methods:** Between July 2019 and September 2022, patients who had LT with duct-to-duct biliary anastomoses were analyzed. The primary endpoint was to assess the technical details and complications of a self-expandable absorbable biliary stent. We also compared biliary complications associated in patients with absorbable stent, T-tube, and no stent. A cost analysis was also performed.

**Results:** A total of 120 patients were included (47 without stent, 54 with absorbable stent, and 19 with T-tube). Overall biliary complications were significantly lower in the absorbent stent group compared to T-tube and no stent groups (p<0.001). Ninety-days biliary complications were significantly lower in the absorbent stent group (1.9%) compared to the T-tube (21.1%, p=0.020) and no stent (29.9%, p=0.001) groups. Hospital stay related to biliary complications after LT was significantly shorter in the absorbent stent group [18[15-21]] compared to no-stent [19[15-24]] and T-tube [22[18-31]] groups. In the absorbent stent group, the mean cost and the excess cost calculated according to the cost prediction calculator and the hospital stay related to biliary complications, were significantly lower compared to non-absorbable stent groups (p=0.004 and p=0.006, respectively).

**Conclusions:** Placement of a self-expandable absorbable biliary stent during biliary anastomosis in LT is a feasible and safe technique. Our study suggests that its use may reduce the rate of early and late biliary complications with a reduction in the costs associated with its management.

**Figure:** Graphical presentation of the absorption rate of the self-expandable absorbable stent (S-ESACS) and the hospital stay related to biliary complications, grouped by the type of stent used in the recipients.
THE ITALIAN EXPERIENCE ON LIVER TRANSPLANTATION FOR UNRESECTABLE PERIHILAR CHOLANGIOCARCINOMA: A NATIONAL SURVEY AND FUTURE PERSPECTIVES

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Background: Perihilar Cholangiocarcinoma (pCCA) is a rare tumor of the liver, associated with poor prognosis even for patients amenable to radical surgery. Since the introduction of the Mayo Clinic protocol, with strict inclusion and exclusion criteria and an extensive preoperative chemo and radiotherapy treatment, liver transplantation (LT) is becoming an innovative therapeutic option.

Methods: All 22 Italian LT Centers were asked to participate in a national survey. From 1984 to 2021, 53 LT for pCCA were performed in 8 Italian centers (Table). Patients were stratified according to whether they were subjected to full neoadjuvant radio-chemotherapy (Group 1, n = 25) or not (Group 2, n = 28), and whether transplantation occurred before (n = 26) or after 2015 (n = 27).

Results: Eighteen patients (18/53, 34%) died because of recurrence of disease, 14/28 in Group 2 (, 50%) and 4/25 in Group 1 (16%). Nine patients died of unrelated causes, 6 in Group 1 (6/25, 24 %) and 3 in Group 2 (3/28, 11%). Three patients received early re-transplantation for technical complications, such as portal vein thrombosis (n. 1) or biliary necrosis (n.1), or for primary non function (n. 1). Overall survival at 1y, 3y and 5y was 78,2%, 49,3% and 43,1% (median 57 months); in Group 1 was 83,8%, 56,6% and 50,6%, while in Group 2 was 72,4%, 41,4% and 35,5% respectively (p = 0.13). Recurrence-free survival at 1y, 3y and 5y was 76,9%, 51,7% and 40,3% (time to recurrence 16,6 months); in Group 1 was 91,2%, 61,1% and 47,2%, while in Group 2 was 58,2%, 42,2% and 36,1% respectively (p = 0.16) (Figure). Competing risk regression analysis showed a 5-year risk of cancer-related death of 19% for patients in Group 1, against 62.3% in Group 2 (hazard ratio 0.31, 95% CI 0.10-0.98, p = 0.047).

Conclusions: The preliminary data from this survey can be the basis for a nationwide discussion about the obstacles to a more widespread implementation of the protocol and its possible evolution.

<table>
<thead>
<tr>
<th>n° LT</th>
<th>Neoadjuvant RT-CT (Group 1)</th>
<th>No Neoadjuvant RT-CT (Group 2)</th>
<th>Before 2015</th>
<th>After 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCONA</td>
<td>2 / 2 (50%)</td>
<td>1 / 2 (50%)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>BOLOGNA</td>
<td>7 / 12 (58%)</td>
<td>5 / 12 (42%)</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>PADOVA</td>
<td>10</td>
<td>7 / 10 (70%)</td>
<td>3 / 10 (30%)</td>
<td>3</td>
</tr>
<tr>
<td>MILANO - TUMORI</td>
<td>8</td>
<td>8 / 8 (100%)</td>
<td>0 / 0 (0%)</td>
<td>5</td>
</tr>
<tr>
<td>PISA</td>
<td>4</td>
<td>0 / 4 (0%)</td>
<td>4 / 4 (100%)</td>
<td>1</td>
</tr>
<tr>
<td>MODENA</td>
<td>2 / 2 (100%)</td>
<td>0 / 2 (0%)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TORINO</td>
<td>5</td>
<td>0 / 5 (0%)</td>
<td>5 / 5 (100%)</td>
<td>5</td>
</tr>
<tr>
<td>MILANO NIGUARDA</td>
<td>10</td>
<td>0 / 10 (0%)</td>
<td>10 / 10 (100%)</td>
<td>9</td>
</tr>
</tbody>
</table>

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**EARLY DIAGNOSIS OF LIVER GRAFT FIBROSIS AND STEATOsis: ARE NON-INVASIVE TESTS THE ANSWER?**

Colin Dumont1,2, Samuele lesari3,2, Pamela Baldin1, Selda Aydin1, Guillame Henin1, Marie Philippart1, Eliano Bonaccorsi Riani1, Olga Ciscarelli1, Laurent Coubeau1, Hubert Pessevaux1, Nicolas Lanther1, Géraldine Dahlvist1

1Ciniques universitaires Saint-Luc, Hepato-gastroenterology department, Brussels, Belgium, 2Fondation IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Kidney Transplantation Unit, Milan, Italy, 3Institut de Recherche Expérimentale et Clinique, UCLouvain, Pôle de Gastroenterologie et Transplantation, Brussels, Belgium, 4Ciniques universitaires Saint-Luc, Anatomopathology department, Brussels, Belgium, 5Institut de Recherche Expérimentale et Clinique, UCLouvain, Laboratory of Gastroenterology and Hepatology, Brussels, Belgium, 6Ciniques universitaires Saint-Luc, Abdominal Transplantation and Surgery department, Brussels, Belgium

**Background:** Detection of graft fibrosis and steatosis is a new challenge to avoid graft loss after liver transplantation (LT). The role of liver biopsy (LB) after LT is changing with the emergence of non-invasive tests, including transient elastography (TE) with controlled attenuation parameter (CAP) and liver stiffness measurement (LSM). Our aim is to evaluate the accuracy of TE in predicting fibrosis and steatosis in post LT.

**Methods:** This prospective analysis was performed on 158 LT patients undergoing protocol LB, from February 2021 to September 2022. Fibrosis was classified according to Metavir score and steatosis was classified in 3 categories (S0: <33%, S1: 33-66%, S2: >66%). LSM and CAP were carried out using Fibroscan® prior to LB. We performed univariate analysis of factors associated with fibrosis and steatosis. We built ROC curves to evaluate the predictive performance of TE. Based on these results, to dichotomize LSM, we chose a cut-off associated at least 0.80 specificity. The Spearman’s rho was used to evaluate the correlation between Metavir and AST to platelet ratio index (APRI) or fibrosis-4 index (FIB-4).

**Results:** 60% of the patients were male, median age was 59. Median BMI was 25 kg/m². Median time since LT was 5 years. Median stiffness, CAP values and IQR/med were 6.00 kPa, 222 dB/m and 14% respectively. Factors associated with fibrosis were pre-LT autoimmune liver diseases (p = 0.05), arterial hypertension (p = 0.024), and low lipids levels (p < 0.001). Factors associated with steatosis were pre-LT non-alcoholic steatohepatitis (p = 0.033) and current body mass index (p < 0.01). Using LSM, AUROC were 0.59 (CI = 0.49-0.68, p = 0.101) and 0.65 (CI = 0.48-0.82, p = 0.099) for the diagnosis of graft fibrosis ≤ F2 and F3-F4 respectively. Using CAP, AUROC were 0.67 (CI = 0.79-0.95, p = 0.005) and 0.71 (CI = 0.61-0.80, p < 0.001) for the diagnosis of graft steatosis > S2 and > S1 respectively. Cut-offs for LSM were 7.95 for ≤ F2 and 9.25 for ≥ F3. Cut-offs for CAP were 198 dB/m for ≤ S1 and 276 dB/m for > S2. We found no correlation between Metavir and APRI or FIB-4.

**Conclusions:** Compared to other non-invasive tests, evaluation using TE with CAP may be useful for the screening of advanced fibrosis, and interestingly for steatosis after LT. It could become a tool to track graft metabolic dysfunction and to propose lifestyle interventions.

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Alfonso Avolio1,2, Marco Pascale1, Vatche Agopian1, Umberto Baccarani1, Patrizia Buzzi1, Lucio Caccamo1, Amedeo Carraro1, Matteo Cescon1, Umberto Cillo2, Luciano De Carli3, Martin de Santibanes4, Paolo Di Simone4, Burcin Eker5, Giuseppe Maria Ettorre6, Mikel Gastaca2, Zhiyong Guo7, Michael Lesurtel8, Laura Liado1, Vincenzo Mazzaferro1, Gilberto Mejia1, Thamara Perera1, Wojciech Polak1, Matteo Ravaiol1, Gonzalo Saps6, Timucin Taner, Giuseppe Tison6, Gianni Vennarecci1, Roberta Angelico1, Gianna Berardi1, Marco Bongini1, Lorenzo Cocchi1, Marco Cossutta, Antonio Cubillas1, Ricardo De Carli1, Daniele Dondossola2, Daniele Ferro1, Maria Grazia-Guix16, Maiciej Krasnodeb, Roberta Angius5, Jacopo Lanari3, Fabio Melandri3, Tommaso Partipilo1, Niv Pencovich1, Riccardo Pravins1, Mikkel Prieto1, Asa Thépabejou1, Pia Clara Pafundi1

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**Background:** The ongoing IMPROVEMENT project aims to develop predictive models of 90-day and 1-year allograft failure after liver transplantation (LT). A descriptive ad interim data analysis was performed to assess the effect of COVID-19 pandemic on complication rate and both graft and patient survival.

**Methods:** We currently evaluated data of 1970 deceased donor adult LTs from 21 LT centres worldwide. Centre- and patients-specific inclusion criteria are detailed elsewhere (https://gennigelgenerator.it/projects/the-improve-ment-study-2/) and on https://ClinicalTrials.gov (Ref. NCT05289609). The study sample was stratified in pre-COVID (Jan 2016-Feb 2020: 1444 cases) and post-COVID period (July 2022-Jan 2023: 526 patients) and the 2 groups were compared. A composite endpoint (Clavien complications and survival rates) was further considered.

**Results:** Donors’ median age was higher in the post-COVID (58 vs 53.5 yrs.; p=0.02), Table 1. The retrieval location has different prevalence according to the pre- and post-COVID period (p<0.01). The retrieval location has different prevalence according to the post-COVID period (p<0.01). The retrieval location has different prevalence according to the post-COVID period (p<0.01). In the post-COVID, DCDs were more often local (46.6% vs 35.5%) and less regional (30.6% vs 41.6%). In the post-COVID, DCDs were more often local (46.6% vs 35.5%) and less regional (30.6% vs 41.6%). In the post-COVID, DCDs were more often local (46.6% vs 35.5%) and less regional (30.6% vs 41.6%). A composite endpoint (Clavien complications and survival rates) was further considered.

**Conclusions:** Preliminary IMPROVEMENT data show a clear evolution in the profile of LT. After the pandemic, a higher-risk donor and/or recipient profile was accepted. Novel techniques, such as PM, were more commonly implemented. The COVID-19 pandemic stimulated transplant surgeons to review local protocols and management practices.
Table 1. Demographic and clinical characteristics of the patients

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>MEDIAN (IQR) N (%)</td>
<td>MEDIAN (IQR) N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DONOR</td>
<td>Age, median (IQR)</td>
<td>58 (41 – 71)</td>
<td>55.5 (45 – 69)</td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>560 (43 %)</td>
<td>216 (43,1)</td>
<td>0.07</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>27.9 (23.4 – 31.3)</td>
<td>27.9 (23.0 – 28.0)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cause of death, n (%)</td>
<td>25 (23.8)</td>
<td>25 (23.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Trauma</td>
<td>5 (4.5)</td>
<td>123 (23.4)</td>
<td>0.7</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>75 (6.5)</td>
<td>213 (41.9)</td>
<td>0.2</td>
</tr>
<tr>
<td>Other</td>
<td>310 (21.5)</td>
<td>120 (24.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>DRL, median (IQR)</td>
<td>1.9 (1.3 – 2.2)</td>
<td>1.8 (1.3 – 2.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>Location of retrieval, n (%)</td>
<td>292 (64.6)</td>
<td>163 (90.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Local</td>
<td>512 (35.5)</td>
<td>121 (23.0)</td>
<td>0.6</td>
</tr>
<tr>
<td>Regional</td>
<td>601 (41.6)</td>
<td>163 (90.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Extra-regional</td>
<td>331 (22.9)</td>
<td>121 (23.0)</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Methods: All adult patients with symptomatic IC after first-time deceased-donor LT between 2011 and 2020 were included. Symptomatic IC was defined as any narrowing of the donor bile ducts documented by MRCP, accompanied by clinical signs or laboratory findings suggestive of cholestasis, in the presence of a patent hepatic artery. An expert radiologist created 4 groups according to a recently described classification of IC after DCD-LT by Croome et al.: diffuse necrosis (DN), multifocal progressive (MP), confluence dominant (CD) and minor form (MF). Graft survival (primary outcome) was assessed by Kaplan-Meier analysis and compared between groups by the Log-rank test. Secondary outcomes were related to the clinical course of IC.

Results: 90 patients (16.8% of total LT) developed symptomatic IC (48 DCD [23.9% of total DCD] and 42 DBD patients [12.6% of total DBD]), of whom DN in 2, MP in 17, CD in 40 and MF in 31 patients. Due to the low number of DN, DN and MP patients were analyzed together (n=19). Graft survival was significantly different between DN/MP and CD patients (P=0.032, figure). Graft survival at 1 and 5 years was 94.7% and 59.8% for DN/MP; 94.9% and 82.3% for CD and 90.2% and 76.5% for MF patients. Graft survival was also significantly different per IC class in DCD (P=0.013) but not in DBD patients. In total, 17 patients (18.9%) were relisted and 12 (13.3%) were retransplanted (26.3% of DN/MP, 7.5% of CD and 12.9% of MF patients). After DCD-LT, MF patients had the shortest cumulative in-hospital length of stay and CD patients had the longest duration of stent therapy. After DBD-LT however, clinical courses of IC classes were less distinct.

Conclusions: IC after DCD-LT can be classified into subtypes with distinct clinical outcomes. Severity and location of IC after DCD-LT are indicative of the risk of graft loss and the need for hospitalization and stent therapy. However in DBD patients, this classification does not have prognostic value.

Figure 1a. Comparison of the Clavien-Dindo complications

Figure 1b. Kaplan-Meier curve for graft survival

BRIEF ORALS: Transplantation outcomes and complications

BOS12_8: RADIOLOGICAL CLASSIFICATION OF ISCHEMIC CHOLANGIOPATHY AFTER DECEASED-DONOR LIVER TRANSPLANTATION

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Background: Ischemic cholangiopathy (IC) is a feared complication after liver transplantation (LT). There is growing evidence that, rather than being a single entity, IC represents a spectrum with distinct radiological patterns and clinical courses. This study aimed to investigate whether IC classified by these radiological patterns can predict the clinical outcomes, in both DCD and DBD-LT.

Methods: All adult patients with symptomatic IC after first-time deceased-donor LT between 2011 and 2020 were included. Symptomatic IC was defined as any narrowing of the donor bile ducts documented by MRCP, accompanied by clinical signs or laboratory findings suggestive of cholestasis, in the presence of a patent hepatic artery. An expert radiologist created 4 groups according to a recently described classification of IC after DCD-LT by Croome et al.: diffuse necrosis (DN), multifocal progressive (MP), confluence dominant (CD) and minor form (MF). Graft survival (primary outcome) was assessed by Kaplan-Meier analysis and compared between groups by the Log-rank test. Secondary outcomes were related to the clinical course of IC.

Results: 90 patients (16.8% of total LT) developed symptomatic IC (48 DCD [23.9% of total DCD] and 42 DBD patients [12.6% of total DBD]), of whom DN in 2, MP in 17, CD in 40 and MF in 31 patients. Due to the low number of DN, DN and MP patients were analyzed together (n=19). Graft survival was significantly different between DN/MP and CD patients (P=0.032, figure). Graft survival at 1 and 5 years was 94.7% and 59.8% for DN/MP; 94.9% and 82.3% for CD and 90.2% and 76.5% for MF patients. Graft survival was also significantly different per IC class in DCD (P=0.013) but not in DBD patients. In total, 17 patients (18.9%) were relisted and 12 (13.3%) were retransplanted (26.3% of DN/MP, 7.5% of CD and 12.9% of MF patients). After DCD-LT, MF patients had the shortest cumulative in-hospital length of stay and CD patients had the longest duration of stent therapy. After DBD-LT however, clinical courses of IC classes were less distinct.

Conclusions: IC after DCD-LT can be classified into subtypes with distinct clinical outcomes. Severity and location of IC after DCD-LT are indicative of the risk of graft loss and the need for hospitalization and stent therapy. However in DBD patients, this classification does not have prognostic value.
**ADD-ON CONTRAST-ENHANCED US WITH DOPPLER US ON POD#1 CAN REDUCE FALSE POSITIVES OF VASCULAR COMPLICATION AFTER LIVER TRANSPLANTATION**

**Woo Kyoung Jeong**

1Samsung Medical Center, Radiology, Seoul, South Korea

**Background:** To investigate advantages of the add-on contrast-enhanced ultrasound (CEUS) on the first post-operative day (POD#1) after liver transplantation (LT) for detection of immediate vascular complications such as hepatic arterial complications (HAC) and acute bleeding.

**Methods:** Among 913 patients who underwent LT and a routine ultrasound (US) examination on the POD#1 were enrolled in the retrospective study. The protocol of the routine US examination consisted of Doppler US followed by CEUS using sulfur hexafluoride microbubbles. An experienced radiologist performed Doppler US with measuring hepatic arterial resistive index (HARI). If HARI was lower than 0.5 or hepatic artery was not detected, it was defined as suspicious HAC. And, CEUS was followed. If microbubbles arrived in the hepatic artery within 15 sec after injection, hepatic artery was considered normal; however, they didn’t arrive in the hepatic artery, it was defined highly suspicious HAC, and CT angiography was recommended. We compared the diagnostic performance between Doppler US and add-on CEUS study. Gold standard is follow-up CT or angiography. In addition, microbubble extravasation into the perihepatic space was investigated after vascular evaluation to detect active bleeding. For statistical analysis, McNemar test was performed to compare the diagnostic performances between Doppler US only and add-on CEUS.

**Results:** Patients with suspicious HAC on Doppler US only were 6.7% of the subject (62/913), and those with highly suspicious HAC on add-on CEUS were 3.9% (36/913). The false positive rate of Doppler only was 2.2%, but that of add-on CEUS was 0.3% (p = 0.0002). Two cases with abnormal CEUS findings but intact Doppler US were proven as unremarkable (2/913). In terms of acute bleeding, 18 patients (18/913) had active bleeding on CEUS, and 10 patients (10/18) underwent surgical removal of hematoma, and the rest was conservative management.

**Conclusions:** CEUS as an add-on test was useful to find acute complication of LT. Especially, it can decrease false positive of hepatic arterial complications on Doppler US presenting decreased HARI.

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**SURVIVAL OUTCOMES OF SALVAGE VS PRIMARY LIVER TRANSPLANTATION FOR EARLY-STAGE HEPATOCELLULAR CANCERS: SYSTEMATIC REVIEW AND META-ANALYSIS**

**Ria-Angel Sharma1, Anya Adair1,2, Gabriel Oniscu1,2, Chris Johnston1,2, Ahmed E Sherif1,2**

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**Background:** Salvage liver transplantation (SLT) after surgical resection (SR) or locoregional ablative therapies (LRAT) is utilised in hepatocellular carcinoma (HCC) patients with very early/early-stage and preserved liver functions. However, recurrence and survival outcomes of SLT when compared to primary liver transplantation (PLT) are disputed by several studies. This systematic review and meta-analysis compared the clinical outcomes of SLT after SR or LRAT with PLT.

**Method:** MEDLINE, EMBASE, CENTRAL and Web of Science databases were searched to identify studies comparing risk estimates of mortality and recurrence for SLT (after SR or LRAT) vs PLT. Selection was based on inclusion criteria to include studies comparing patients with HCC classified as very early/early-stage as per EASL practice guidelines 2022. Risk of bias was reviewed using the Newcastle-Ottawa Scale. A random effects model assessed primary endpoints based on evaluation of heterogeneity.

**Results:** 5734 patients from 16 studies were included. For SLT after SR, the odds ratio of mortality at 1-3 and 5-years were comparable to PLT. However, the odds of HCC recurrence at 1-3, 3-5 and 5-years were higher when SLT after SR was compared to PLT, particularly at 5 years (OR [95% CI] = 1.64 [1.07 - 2.49], as shown in Figure 1. For SLT after LRAT vs PLT, the odds ratios of mortality HCC recurrence and mortality showed no statistically significant difference compared to PLT, but interpretations are limited by high heterogeneity of included studies.

**Conclusions:** Very early/early-stage HCC patients who underwent SLT after SR had higher rate of long-term of recurrence when compared with PLT, which could be explained by increased risk of surgical challenges when SLT is performed. The use of LRAT with SLT showed comparable outcomes to PLT, limited by the heterogeneity and small number of studies included.

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**SALVAGE LIVER TRANSPLANTATION FOLLOWING RESECTION OF COMBINED HEPATOCELLULAR-CHOLANGIOCARCINOMA**

**Matteo Seregari**, Enrico Prosperi1**, Elisa Albertini1, Francesco Tovoli1, Francesca Caputo1, Luca Di Gregorio1, Chiara Bonatti1, Matteo Ravaiol1, Fabio Piscaglia1, Francesco Vasuri1, Matteo Cescon1

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**Background:** Between November 2000 and November 2019, all consecutive patients submitted to HR for HCC-CC were included. SLT was considered after HR in patients with underlying liver cirrhosis ≤ 65 years old and without recurrence of disease for at least 6 months after HR. No evidence of extra-hepatic disease, including lymphatic metastases was required at listing.

**Methods:** During the study period, 48 patients were included. Among them, 6 patients (13.6%) were submitted to SLT in median, SLT was performed 596 days (range: 249-4613) after HR. Overall survival was significantly higher in SLT group compared to those who were not transplanted (131 mo vs. 17.7 mo, p=0.017). Disease-free survival was higher in SLT group but without reaching statistical significance (39.8 vs. 8.3 mo, p=0.122). According to COX-regression analysis, SLT was significantly associated to OS (p=0.048).

**Conclusions:** SLT may be considered as a therapeutic option for patients with HCC-CC and cirrhosis after HR if no recurrence occurs. Biopsy as well as tumor differentiation should be added to the current criteria to better select those patients.
BRIEF ORALS

Transplantation outcomes and complications

**BOS12_14** MODIFYING TACROLIMUS RELATED TOXICITY AFTER LIVER TRANSPLANTATION COMPARING ENVARSUS® AND ADVAGRAF®: A MULTICENTER RANDOMIZED, CONTROLLED TRIAL

Mieke Mulder1,2, Bart van Hoek4, Wojciech Polak3,4, Ian Alwayn5, Brenda de Winter3,4, Sarwa Danwish Murad6,7, Lara Elshove4, Anna van den Burg8, Nicole Erler9, Dennis Hesselink9, Caroline den Hoed9, Herold Metselaar2,4

1Erasmus University Medical Center, Hospital Pharmacy, Rotterdam, Netherlands, 2Erasmus University Medical Center, the Erasmus MC Transplant Institute, Rotterdam, Netherlands, 3Leiden University Medical Center, Gastroenterology & Hepatology, Leiden, Netherlands, 4Erasmus University Medical Center, Surgery, Division of HPB and Transplant Surgery, Rotterdam, Netherlands, 5Leiden University Medical Center (LUMC), Surgery, Leiden, Netherlands, 6Erasmus University Medical Center, the Erasmus MC Transplant Institute, Rotterdam, Netherlands, 7Erasmus University Medical Center, the Erasmus MC Transplant Institute, Leiden, Netherlands, 8Erasmus University Medical Center, Gastroenterology and Hepatology, Rotterdam, Netherlands, 9Erasmus University Medical Center, Biostatistics, Rotterdam, Netherlands, 9Erasmus University Medical Center, Epidemiology, Rotterdam, Netherlands, 9Erasmus University Medical Center, Internal Medicine, Division of Nephrology and Transplantation, Rotterdam, Netherlands

Background: The hypothesis of this study was that meltdose tacrolimus (Envarsus®) compared to extended-release tacrolimus (Advagraf®) will result in less chronic kidney disease (CKD), new-onset diabetes after transplantation (NODAT) and new-onset hypertension.

Methods: In this multicenter RCT, patients were randomized at discharge after liver transplantation (LT) in a 1:1 ratio to 1) Advagraf® (control group) or 2) Envarsus® (interventional group). The primary endpoint was a composite endpoint of any three events at 12 months: CKD defined as eGFR <60 ml/minute/1.73 m2 for >3 months, sustained (>3 months post LT) NODAT or new-onset hypertension. Secondary endpoints included: safety, quality of life, neurotoxicity (tremors), graft and patient survival, rejection, liver steatosis and fibrosis, pharmacokinetics and –dynamics.

Results: A total of 106 patients were included and baseline characteristics were comparable for both groups. In the intention-to-treat analysis, significantly less LT recipients reached the primary endpoint at 12 months in the interventional group compared to the control group (50.9% and 71.2%, p = 0.005). No significant difference was shown between interventional group and control group in the percentage of LT recipients developing NODAT (15.1% and 21.2%, p=0.35) or new-onset hypertension (30.2% and 36.5%, p=0.42). Significantly less LT recipients developed CKD in the interventional group compared to the control group (26.4% and 42.3%, p=0.03). The per protocol analysis showed comparable results and in addition significantly less LT recipients developed new-onset hypertension in the interventional group compared to the control group (27.6% and 42.9%, p=0.04). In total, 95.3% (101/106) of the LT recipients developed serious adverse events (SAEs, n=156). SAEs most frequently reported: fever (23.7%), infections (10.3%) and cholangitis and bile duct obstruction (10.3%).

Conclusions: After 1 year, meltdose tacrolimus (Envarsus®) results in a significant reduction in the prevalence of the composite endpoint and a significant reduction of CKD compared to extended-release tacrolimus (Advagraf®)

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Organ preservation and ischemia reperfusion

**BOS13_1** REMOVAL OF CHROMATIN-ASSOCIATED-MOLECULAR-PATTERN (CAMPS) REDUCES EX-SITU REPERFUSION INJURY IN PORCINE DCD LIVERS PRESERVED WITH NMP

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Background: DCD and extended-criteria donor livers are highly susceptible to reperfusion injury, even when occurring ex-situ in the context of normothermic machine perfusion (NMP) during organ preservation. This ‘ex-situ reperfusion injury’ (ERI), is driven by the release of endogenous alarms and damage signal molecules, in particular chromatin-associated molecular patterns (CAMPs) such as histones, nucleosomes and cell free DNA (cfDNA). CAMPs released into the circulation upon reperfusion propagate inflammation and injury which can result in poor function ex-situ, resulting in subsequent organ discard. We aimed to assess the impact of removing circulating CAMPs during NMP; on ex-situ function and subsequent reperfusion in a large animal DCD liver perfusion model.

Methods: 12 DCD pig livers were included in the study. CAMPs were removed from the circulating perfuse using the NucleoCapture column that was integrated into the perfusion circuit and these livers were compared to NMP controls. Perfuse Nucleosomes/NETs, free histone and cfDNA was measured sequentially during perfusion (including pre and post-column). Perfusion parameters, functional assessment of the livers and histological features were assessed between groups. Statistical analysis was performed using repeated measures ANOVA and t-test/Wincoxons-test.

Results: NucleoCapture significantly reduced early circulating CAMPs across the column: cDNA p<0.009(1hr), Histone p<0.009(1hr) and Nucleosomes p<0.003(2hr). This also corresponded with a significant improvement in early lactate clearance (0.5hrs p= 0.033, 1hr p=0.013, 2hr p=0.043) supported by improved haemodynamic perfusion metrics and less neutrophil infiltration on histological assessment. Warm and cold ischaemic times were comparable between groups. All livers produced bile and metabolised glucose.

Conclusions: NucleoCapture effectively removes circulating CAMPs from the perfuse during NMP, improving graft function and mitigating ERI. Application of this technology during NMP of DCD and extended-criteria donor livers could reduce organ discard due to poor function ex-situ and be pivotal in organ optimisation for transplantation.

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Organ preservation and ischemia reperfusion

**BRIEF ORALS**

**BOS13_2**

**IN SITU AND EX SITU DYNAMIC PRESERVATION VERSUS COLD STORAGE IN LIVER TRANSPLANTATION FROM OLDER DONATION AFTER CIRCULATORY DEATH DONORS**

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**Robert J. Porte**
**Diethard Monbaliu**

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**Introduction:** Dynamic preservation strategies were shown to significantly reduce non-anastomotic biliary strictures (NAS) after liver transplantation (LT) using selected, controlled donation after circulatory death (DCD) livers. Whether this also applies to DCD livers from older donors is unknown.

**Methods:** In this retrospective, multicenter study, we compared outcomes after transplanting livers procured from DCD donors older than 60 years that were preserved either with static cold storage (SCS), sequential dual-hypothermic perfusion, controlled oxygenated rewarming, and normothermic perfusion (DHOPE-COR-NMP), or abdominal normothermic regional perfusion (aNRP) between 2016 and 2022. Incidence of NAS at 1-year, post-transplantation peak aspartate transaminase (AST), early allograft dysfunction (EAD), and 1-year patient/graft survival were compared. Kaplan-Meier curves with log-rank test, Kruskal-Wallis and Fisher’s exact test were used. Median [IQR] or percentage are given, unadjusted p-values are reported.

**Results:** 56 LT were included in the SCS group, 33 in the DHOPE-COR-NMP group, and 27 in the aNRP group. Donor warm ischemia time was shorter in the SCS group (20 [16-24] minutes) compared to DHOPE-COR-NMP (32 [26-35] minutes, p<0.001) and aNRP (36 [31-40] minutes, p<0.001) (DHOPE-COR-NMP vs. aNRP: p=0.58). Cold ischemia times were similar in all groups (SCS 306 [270-344] minutes, DHOPE-COR-NMP 319 [278-352] minutes and aNRP 339 [287-389] minutes). Cold ischemia times were significantly higher compared to grafts with no glucose peak (397 [346-453] versus 154 (IQR:87-206) µg/kg/h; P<0.001). LiMAx scores significantly correlated with ALT (R=-0.755; P<0.001) and AST (R=-0.800; P<0.001) levels at 24 hours. Furthermore, livers that demonstrated a stress hyperglycemia peak (>20mmol/l glucose) had a higher LiMAx score compared to grafts with no glucose peak (P=0.032). LiMAx scores significantly correlated with ALT (R=-0.755; P<0.001) and AST (R=-0.800; P<0.001) levels at 24 hours. Furthermore, livers that demonstrated a stress hyperglycemia peak (>20mmol/l glucose) had a higher LiMAx score compared to grafts with no glucose peak (P=0.032). LiMAx scores significantly correlated with ALT (R=-0.755; P<0.001) and AST (R=-0.800; P<0.001) levels at 24 hours (R=0.585; P=0.045). Conclusions: We demonstrated that LiMAx testing is feasible during aNRP. The LiMAx test is the first objective method that can reliably assess donor liver function during donation after circulatory death (DCD). However, a gold standard for adequate liver function is lacking, and livers are usually subjectively assessed, with the risk of under-utilization. We aimed to assess the maximum liver function capacity (LiMAx) test to objectively grade liver function during aNRP.

**Maximum liver function capacity test (LiMAx) during abdominal normothermic regional perfusion as predictor of graft function after transplantation**

**Ivo Schurink**
**Femke de Goeij**
**Fenna van der Heijden**
**Rutger van Röckes Gilboe**
**Wojciech Polak**
**Luc van der Laan**
**Jeroen de Jonge**

1. Erasmus MC, Department of Surgery, Division of HPB and Transplant Surgery, Erasmus MC Transplant Institute, Rotterdam, Netherlands, 2Leiden University Medical Center, LUMC Transplant Center, Department of Surgery, Leiden, Netherlands

**Background:** Abdominal normothermic regional perfusion (aNRP) enables assessment of donor liver viability during donation after circulatory death (DCD). However, a gold standard for adequate liver function is lacking, and livers are usually subjectively assessed, with the risk of under-utilization. We aimed to assess the maximum liver function capacity (LiMAx) test to objectively grade liver function during aNRP.

**Methods:** aNRP was performed for salvage of extended criteria DCD liver grafts in 18 consecutive donors and grafts were transplanted after positive evaluation criteria (n=13). After one hour of aNRP, the LiMAx test was performed, using the aNRP circuit (Figure 1). LiMAx scores were compared to aNRP variables and post-transplantation outcomes.

**Results:** The LiMAx test was performed successfully in 17 aNRPs donors (94%). LiMAx scores ranged between 35 and 510 µg/kg/h. During aNRP, LiMAx scores of livers with good lactate clearance were significantly higher compared to liver grafts with impaired lactate clearance (396 [IQR:301-451] versus 105 [IQR:70-158] µg/kg/h; P=0.006). Furthermore, livers that demonstrated a stress hyperglycemia peak (>20mmol/l glucose) had a higher LiMAx score compared to grafts with no glucose peak (P=0.032). LiMAx scores significantly correlated with ALT (R=-0.755; P<0.001) and AST (R=-0.800; P<0.001) levels at the end-aNRP.

**Conclusions:** We demonstrated that LiMAx testing is feasible during aNRP. The LiMAx test is the first objective method that can reliably assess liver-specific function during aNRP. We propose a LiMAx score of >240 µg/kg/h during aNRP as a safe cut-off for use of extended criteria donor livers.

Figure 1

---

**Table Post-transplant outcome**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SCS</th>
<th>DHOPE-COR-NMP</th>
<th>aNRP</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1y NAS</td>
<td>12 (21%)</td>
<td>1 (3%)</td>
<td>2 (7%)</td>
<td>0.627</td>
<td>0.13</td>
<td>0.58</td>
</tr>
<tr>
<td>Peak AST (UI)</td>
<td>759 (336-1220)</td>
<td>510 (333-844)</td>
<td>692 (483-1153)</td>
<td>0.622</td>
<td>0.62</td>
<td>0.664</td>
</tr>
<tr>
<td>EAD</td>
<td>9 (18%)</td>
<td>7 (21%)</td>
<td>5 (19%)</td>
<td>0.58</td>
<td>0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1y patient survival</td>
<td>52 (99%)</td>
<td>32 (97%)</td>
<td>26 (98%)</td>
<td>0.85</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1y graft survival</td>
<td>52 (99%)</td>
<td>90 (91%)</td>
<td>25 (93%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P1: SCS vs. DHOPE-COR-NMP; P2: SCS vs. aNRP; P3: DHOPE-COR-NMP vs. aNRP
BRIEF ORALS

OUTCOMES OF LIVERS WITH PROLONGED DURATION OF EX SITU NORMOTHERMIC PERFUSION: CAN LIVER TRANSPLANTATION BE A DAILY ACTIVITY?

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2University of Cambridge, Department of Surgery, Cambridge, United Kingdom

Background: Normothermic ex-situ liver perfusion (NESLiP) gives the opportunity to assess and modify marginal livers. Additionally, it also helps overcoming the time barriers by increasing the preservation time. NESLiP can be employed from the donor hospital until implantation or once the liver arrives at the recipient centre in a cold box. In this study, we discuss our experience of liver grafts subjected to prolonged NESLiP.

Methods: Retrospective analysis of livers undergoing NESLiP at our institute from May 2017 till January 2022. Patients were divided into two groups based on the duration of NESLiP (<10 hours and >10 hours) and outcomes compared. All livers underwent blood-based perfusion.

Results: There were 203 (DBD 80, DCD 123) livers undergoing NESLiP during the study duration resulting in 154 (76%) liver transplants. Thirty-five (30%) out of these were perfused for more than 10 hours before implantation with median 20.2 hours of total preservation. There was no difference in early graft function or renal function.

Conclusions: This experience suggests that prolonged NESLiP is safe. It is useful in managing logistics with increased preservation time.

BRIEF ORALS

GRAFT VIABILITY AND LIVER TRANSPLANT RECOVERY ASSESSMENT USING INDOCYANINE GREEN CLEARANCE TEST: PRELIMINARY ANALYSIS OF A PROSPECTIVE STUDY

Gabriele Sooleoti1, Giuseppe Bianco1, Giuseppe Marrone1, Miriam Caimano1, Alessandro Coppola1, Quirino Lai1, Francesco Frongillo1, Erida Nure1, Francesco Giovinazzo1, Alfonso Avolio1, Salvatore Agnes1
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2Sapienza University, Rome, Italy

Background: Indocyanine green clearance test (RR15) is a prognostic marker for advanced cirrhosis and liver resection. RR15 has not been prospectively evaluated in liver transplantation (LT). Whether grafts from deceased donors with higher RR15 values are less likely to be utilized for LT is the objective of this study. Secondly, the relation between the change in RR15 after LT and function recovery is investigated.

Methods: This is a preliminary analysis from a single-center prospective study on consecutive LT donors and recipients. RR15 was calculated before procurement, at the end of LT, and on day one, three and seven after LT using the pulsedensitymetry method. The procurement surgeon was blinded to the results of the test. Thirty-three LT recipients were prospectively evaluated using a RR15 cut-off of 13.5. No differences in donor characteristics were observed between the lower-RR15 (n=28) and higher-RR15 (n=10) groups. At c-statistics, RR15 cut-off value of 13.5 had a sensitivity of 75% and a specificity of 87% (diagnostic odds ratio, DOR=28), with an AUC=97% (95.0% CI=91.4-100%; p<0.0001).

Conclusions: Donors with impaired indocyanine green clearance have lower chances of being viable for LT. Similarly in LT recipients, impaired clearance on day 7 correlates with EAD, aiding early diagnosis and resource allocation.
Background: During normothermic machine perfusion (NMP), thromboxanes and coagulation factors are exclusively derived from the perfused graft. As some factors are synthesized by the liver and the endothelial cells themselves, these dynamics might reflect on their condition. Further, vascular dysfunction and formation of microthrombi are known pathomechanisms in IRI and ischemic cholangiopathy. Our aim was to investigate factor composition during NMP and their association with liver function and post-transplant outcomes.

Methods: During NMP of 27 livers, including 21 from extended criteria donors, D-dimer, thromboxytes, von Willebrand factor activity (vWF), factor V activity (FV), and factor XII activity (FXIII) in perfusate were assessed. Liver and bile duct biopsies were taken before and after perfusion.

Results: Out of 27 grafts that underwent NMP, 18 livers met viability criteria and were transplanted. Median peak plasma levels were D-Dimer 3.39 µg/mL (IQR: 2.83-3.38), vWF 6 % (IQR: 5-8), thromboxytes 14 G/L (IQR: 13-27), FV 17 % (IQR:8-26), FXIII 32 % (IQR:20-39) and bilirubin 0.85 mg/dL (IQR: 0.66-3.31). Thromboxytes, bilirubin and FV increased steadily, FXIII and D-Dimer peaked and decreased afterwards. There were 11 cases with irregular parameters, 6 livers were declined for failure to produce bile or clear lactate. The 5 transplanted livers passed our standard viability criteria. Three recipients had an uneventful follow-up until now. One transplanted liver (5.81 µg/mL D-Dimer, 96 G/L thromboxytes, bilirubin 5.81 mg/dL, vWF 18 %) performed well on the back-table biopsy, the recipient later developed a biliary leak and biliary CAST due to a portal vein thrombus. Four recipients had complications after DCD liver transplantation. Despite prolonged warm ischemia time without donor age limits. No major differences between D-HOPE and NMP groups were observed. Conclusions: A safe method to perform DCD liver transplants with extended warm ischemia time without donor age limits. Further data are needed to draw definitive conclusions.

References:
1. University of Pisa Hospital, Pisa, Italy, 2University of Milan, Milan, Italy
3. University of Vienna, Department of General Surgery, Division of Transplantation, Vienna, Austria
4. Mayo Clinic, Phoenix, United States
5. Transmedics™ Liver OCS
6. NMP-LT (n=93) SCS-LT (n=199) p-value
7. Median Recipient age (yrs) 63 61 NS
8. Median Donor age (yrs) 52 47 NS
9. Median Preservation time (hrs) 12.5 5.5 <0.05
10. Median warm ischemia time (mins) 26 30
11. Median Allocation MELD 20 21 NS
12. Ischemic Cholangiopathy 1% 20% <0.05
13. UK DCD risk score
14. 1 yr actuarial patient survival
15. 1 yr actuarial graft survival
16. Median donor age for NMP-DCD LT was 52 years ± 9 and 47 years ± 8 for SCS-DCD LT. Median allocation MELD at transplant was 20 for NMP group and 21 for SCS groups. NMP was associated with longer preservation time (12.5 h NMP vs 5.5 h SCS). UK DCD risk score was >10 in 53% NMP vs 44% SCS. IC was observed in 40/199 (20%) of SCS-LT patients, and 84/90 required retransplantation. All IC cases were diagnosed within the first 12 weeks post LT. Zero patients with NMP LT developed IC with median follow-up of 16 weeks. Unadjusted actuarial 1-year graft survival was significantly higher in the NMP-LT (96%) compared to SCS-LT (88%). Conclusions: NMP utilization in a high-volume DCD LT center confirms a significant reduction in the rates of IC despite expanding donor selection with 53% of grafts with UK DCD score >10. Broader use of NMP in DCD LT should be encouraged to improve outcomes and liver utilization.
Background: Liver transplantation (LT) is the treatment of choice for eligible patients with hepatocellular carcinoma (HCC). Despite the use of validated eligibility criteria, HCC recurrences develop in up to 20% of the cases and are associated with poor survival. The aim of the study was to identify clinical predictors of early tumor recurrence in patients with hepatocellular carcinoma after liver transplantation.

Methods: Retrospective cohort study in consecutive liver recipients with HCC between 2016 and 2021. Multivariate logistic analysis was performed to identify clinical predictors of early HCC recurrences. The impact of hypo-oxygenated perfusion (HOPE) on outcome was analyzed after propensity score weighting.

Results: A total of 237 patients were included in this study with an early HCC recurrence rate of 6%. Microvascular invasion (OR 3.737, 95% CI 1.246 – 11.206, p=0.019) and cold ischemia time (OR 1.002, 95% CI 1.000 – 1.005, p=0.049) were independently associated with a lower risk of HCC recurrences (Table 1). After balancing for age, sex, MELD score, donor risk index and Milan Criteria status at listing, patients in the HOPE group had lower rates of tumor recurrence (weighted OR 0.126, 95% CI 0.016 – 0.899, p=0.049) and higher recurrence-free survival (weighted HR 0.132, 95% CI 0.017 – 0.999, p=0.050) (Figure 1).

Conclusions: Reducing cold ischemia time and graft perfusion with HOPE can lead to lower rates of early HCC recurrences and higher recurrence-free survival after liver transplantation.

**Table 1. Bivariate linear model comparing BDIS of livers preserved with SCS or continuous perfusion**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>0.095 (0.01 - 0.63)</td>
<td>0.7</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.67 (0.13 - 3.41)</td>
<td>0.6</td>
</tr>
<tr>
<td>MELD-No score</td>
<td>0.06 (0.02 - 0.16)</td>
<td>0.6</td>
</tr>
<tr>
<td>HCC at listing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outside Milan Criteria</td>
<td>2.31 (0.20 – 0.64)</td>
<td>0.1</td>
</tr>
<tr>
<td>Number of HCC (main)</td>
<td>0.61 (0.07 – 4.02)</td>
<td>0.7</td>
</tr>
<tr>
<td>Diameter of largest HCC (mm)</td>
<td>4.07 (0.19 – 0.07)</td>
<td>0.7</td>
</tr>
<tr>
<td>HCC at last evaluation before LT</td>
<td>0.01 (0.01 – 0.30)</td>
<td>0.7</td>
</tr>
<tr>
<td>Number of HCC (sub)</td>
<td>1.13 (0.44 – 2.95)</td>
<td>0.4</td>
</tr>
<tr>
<td>Diameter of largest HCC (mm)</td>
<td>1.04 (0.55 – 1.93)</td>
<td>0.4</td>
</tr>
<tr>
<td>Donor age (yrs)</td>
<td>1.10 (0.09 – 0.70)</td>
<td>0.1</td>
</tr>
<tr>
<td>Graft fibrosis grade [NAKART]</td>
<td>1.08 (0.14 – 0.46)</td>
<td>0.6</td>
</tr>
<tr>
<td>Donor Risk Index</td>
<td>1.44 (0.4 – 4.76)</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Figure 1** — Kaplan-Meier curves for weighted recurrence-free survival in the HOPE group and Static Cold Storage (SCS) alone group.
Organ preservation and ischemia reperfusion

**BOS13_13**

**THE IMPACT OF DONOR TIME TO DEATH AND FUNCTIONAL WARM ISCHEMIA TIME ON RECIPIENT OUTCOME FOLLOWING DCD LIVER TRANSPLANTATION**

*Abdullah Malik*,1,*,1  Samuel Tingle1, Chris Varghese2, Ruth Owen2, Rodrigo Figueiredo2, Aimen Amer2, Steve White2, Derek Manas1, Colin Wilson1

1Institute of Transplantation, Newcastle upon Tyne, United Kingdom, 2Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

**Background:** UK practice is to abandon donor hepatectomy if functional warm ischemia time (FWIT) exceeds 30 minutes in donors after circulatory death (DCD). During this agonal phase, beginning from treatment withdrawal, donor blood pressure and saturation pressures are expected to drop, reducing flow of oxygenated blood to the liver graft causing ischemic injury. We assessed what impact donor time to death (TTD) and FWIT had on recipient outcomes following DCD liver transplantation.

**Methods:** Data were extracted from the NHS Blood and Transplant registry on all DCD liver graft recipients from 2006 to 2021. TTD was defined as the time from withdrawal of life sustaining treatment to asystole, and FWIT was the time from systolic BP and/or SpO2 falling below 50mmHg and 70%, respectively, to aortic perfusion. The primary endpoint was 1-year graft survival. Potential predictors were fitted into separate hierarchical Cox proportional hazards regression models for TTD and FWIT to avoid collinearity, with multiple imputation for missing data.

**Results:** 1585 DCD liver grafts were included. Median TTD was 13 minutes (IQR 9-17 minutes). TTD occurred between 0-10 minutes in 347 (33.9%), 10-16 minutes in 382 (37.3%), and >16 minutes in 296 (28.9%) recipients. TTD exceeded 30 minutes in 43 donors (2.8%). TTD was not available in 533 donors (34.2%). The incidence of primary non-function did not differ across the 3 TTD categories (6.6% vs. 3.7% vs. 5.1%, p=0.193). TTD (HR 0.82, 95% CI 0.61-1.11, p=0.2) and FWIT (HR 1.00, 95% CI 0.44-2.27, p=0.9) did not predict 1-year graft survival. On sensitivity analysis TTD >30 minutes did not predict 1-year graft survival. Prolonged donor hepatectomy time was significantly associated with 1-year graft loss in the TTD (HR 1.87, 95% CI 1.23-2.83, p=0.003) and the FWIT models (HR 1.89, 95% CI 1.25-2.87, p=0.003). In separate modelling donor TTD, FWIT and hepatectomy time were not predictive of 1-year recipient mortality (all p>0.05). Conclusion: Prolonged hepatectomy time, but not TTD or FWIT, was associated with worse graft survival. Expanding the 30-minute FWIT limit may increase the number of DCD liver grafts retrieved without harming recipient outcomes if hepatectomy time is kept short. Further prospective evaluation of recipient risk from grafts retrieved outside current criteria is warranted.

**BOS13_14**

**HOPE REDUces DURATION OF GLYCOCALYX SHEDDING – ITS DAMAGE MARKER SYNDecAN-1 CAN PREDICT EARLY ALLOGraft DySFUNCTION**

*Laurin Rauter*a, Judith Schiefera, Pierre Raevenb, Thomas Öhlinc, Marija Spasic, Effimia Pompouridou, Julie Dingfelderb, Andreas Salatd, Zoltan Mathea, Georg Gyöleri, Thomas Solimanb, Dagmar Kollmanna, Gabriela A. Berlakovicha

*aMedical University of Vienna, Department of General Surgery, Division of Transplantation, Wien, Austria, bMedical University of Vienna, Department of Anesthesia, Intensive Care Medicine and Pain Medicine, Wien, Austria

**Background:** During liver transplantation, the graft has to endure an ischemic phase and additional injury after reperfusion (IRI), especially mediated by reactive oxygen species (ROS). The endothelial glyocalyx covers the luminal side of the vascular endothelium and regulates vascular permeability, modulates adhesion of leucocytes onto the vascular wall and transduces mechanical shear stress. It is very sensitive to ROS and therefore degraded during graft preservation and reperfusion. Hypothermic oxygenated machine perfusion (HOPE) is a preservation strategy that can reduce IRI-inflicted graft injury compared to static cold storage (SCS). We aimed to measure glyocalyx degradation after HOPE or SCS alone, to evaluate its viability-assessment potential for liver transplantation.

**Methods:** We measured glyocalyx degradation via ELISA for its main component Syndecan-1, in samples from 77 liver transplant patients. 37 grafts were directly transplanted after SCS, 40 grafts additionally underwent HOPE with the Organ Assist® perfusion system, prior to liver transplantation.

**Results:** Sdc-1 concentrations in the graft effluent are significantly lower after HOPE [466 (350-1073) compared to SCS alone [401 (3382-4683)] (p<0.001). Further, Sdc-1 concentrations regenerate faster towards baseline levels on HOPE [466 (350-1073)] compared to SCS alone [401 (3382-4683)] (p<0.001).

**Conclusions:** HOPE reduces the duration of glyocalyx shedding, evident by Sdc-1 release in recipient serum after liver transplantation. Sdc-1 concentration during HOPE can predict early allograft dysfunction. Therefore, Sdc-1 could be a potential viability assessment marker in liver transplantation.

Safety and quality at the core of donation and transplantation

**BOS14_1**

**SETTING EUROPEAN QUALITY AND SAFETY STANDARDS FOR ORGAN DONATION AND TRANSPLANTATION**

*Jaime Marco de Ten*c, Beatriz Dominguez-Gip*, Carl-Ludwig Fischer-Fröhlich2

1European Directorate for the Quality of Medicines and Healthcare-Council of Europe, Strasbourg, France, 2Organizacion Nacional de Trasplantes, Madrid, Spain, 3Deutsche Stiftung Organtransplantation, Stuttgart, Germany

**Background:** Organ transplantation has progressed in recent decades, yet demand for organs exceeds supply. As all substances of human origin, organs entail a risk of disease transmission. It is thus needed to set European quality and safety standards for organ donation and transplantation.

**Methods:** A group of 40 experts nominated by member states of the Council of Europe drafted and agreed on European standards based on a previous edition. In addition, 48 worldwide experts were involved in the revision of certain topics. Standards were revised according to the state of the art, and new and important items were added. Once the text was final, it underwent a stake-holder consultation. 301 comments were received, which were carefully revised, 82% leading to changes in the final text.

**Results:** The result has been the 8th edition of the Guide to the quality and safety of organs for transplantation (contents shown in table 1), published in July 2022.

**Conclusions:** The Guide has demonstrated to be a unique tool for co-ordinators, those responsible for the clinical use of organs, quality managers and health authorities. Its goal is to improve successful and safe transplantation rates.

Table 1: Contents of the 8th edition of the Guide to the quality and safety of organs for transplantation

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduction</td>
</tr>
<tr>
<td>2</td>
<td>Identification and referral of possible deceased organ donors</td>
</tr>
<tr>
<td>3</td>
<td>Determination of brain death by neurologic criteria</td>
</tr>
<tr>
<td>4</td>
<td>Family approach and consent/authorisation for post-mortem organ donation</td>
</tr>
<tr>
<td>5</td>
<td>Management of the potential donor</td>
</tr>
<tr>
<td>6</td>
<td>General donor characterisation, assessment and selection criteria</td>
</tr>
<tr>
<td>7</td>
<td>Specific organ characterisation, assessment and selection criteria</td>
</tr>
<tr>
<td>8</td>
<td>Risk of transmission of infectious diseases</td>
</tr>
<tr>
<td>9</td>
<td>Risk of transmission of cancer</td>
</tr>
<tr>
<td>10</td>
<td>Risks related to the use of organs from donors with other conditions and diseases</td>
</tr>
<tr>
<td>11</td>
<td>Organ procurement, preservation and transportation</td>
</tr>
<tr>
<td>12</td>
<td>Donation after the circulatory determination of death</td>
</tr>
<tr>
<td>13</td>
<td>Living donation</td>
</tr>
<tr>
<td>14</td>
<td>Paediatric donation</td>
</tr>
<tr>
<td>15</td>
<td>Donation of vascularised composite allografts</td>
</tr>
<tr>
<td>16</td>
<td>Biovigilance and surveillance</td>
</tr>
<tr>
<td>17</td>
<td>Achieving and measuring quality in organ donation and transplantation</td>
</tr>
<tr>
<td>18</td>
<td>Measuring outcomes in transplantation</td>
</tr>
<tr>
<td>19</td>
<td>Communication of risk and shared decision-making</td>
</tr>
</tbody>
</table>

Guide was widely used (see figure 1).

Figure 1: Downloads of the Guide as of 30 September 2022
DONOR-TRANSMITTED CANCER IN ORGAN DONATION AND SOLID ORGAN TRANSPLANTATION IN GERMANY FROM 2016-2022

Klaus Böhler, Axel Rahmel, Ana Paula Barreiros
Deutsche Stiftung Organtransplantation, Frankfurt, Germany

Background: Analyzing reported serious adverse events (SAE) and serious adverse reactions (SAR) is an essential part of an effective vigilance and surveillance system in organ donation and transplantation. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is assigned by the German Federal Ministry of Health to manage and monitor SAE and SAR. Donor-transmitted cancer (DTC) can pose an additional risk to the recipients with significant morbidity and mortality.

Methods: All incoming SAE and SAR reported from January 1st 2016 to December 31st 2022 related to a potential malignant disease were analyzed. A DTC was defined as a malignancy already present within the organ at the time of transplantation. The assessment of imputability as proven or probable (P/P) transmission was done according to the grading system of the US Disease Transmission Advisory Committee (DTAC).

Results: 145 reports were analyzed. In 104 reports the final histopathological analyses showed a malignant tumour (104/145; 72%). 16 reports were classified as P/P DTC from the donor to one or more recipients. These 16 cases involved 22 recipients resulting in 11 attributable deaths (11/22; 50%).

Conclusions: Donor-Transmitted cancer is a rare event, but when it occurs can lead to significant morbidity and mortality of the recipients.

<table>
<thead>
<tr>
<th>Malignancy Type</th>
<th>Location</th>
<th>Donors reported</th>
<th>Total recipients</th>
<th>Total recipients with transmission</th>
<th>Total deaths from cancer transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td></td>
<td>43</td>
<td>2</td>
<td>2 (40%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
<td>11</td>
<td>3</td>
<td>4 (50%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>Hematological</td>
<td></td>
<td>9</td>
<td>2</td>
<td>4 (80%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td>8</td>
<td>2</td>
<td>2 (33%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td></td>
<td>2</td>
<td>2</td>
<td>4 (100%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Other Malignancy</td>
<td></td>
<td>31</td>
<td>16</td>
<td>6 (37.5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>104</td>
<td>64</td>
<td>22 (50%)</td>
<td>11 (50%)</td>
</tr>
</tbody>
</table>

* % = recipients with transmission/transmitters from P/P donors. **% = deaths from cancer transmission / total recipients with cancer transmission.

NO SURVIVAL BENEFIT IN KIDNEY TRANSPLANT RECIPIENTS IN THE EUROPEAN SENIOR PROGRAM

Marcel Nah1, Mareen Pigorsch1, Elke Schaeffner1, Vivien Greese1, Kai-Uwe Eckardt1, Michael Kammer1, Ulrich Frei1, Miria Choi1, Lutz Liefeldt1, Robert Öllinger1, Frank Friedersdorff1, Klemens Buddel1, Fabian Halleck1
Charite, Department of Nephrology and Medical Intensive Care, Berlin, Germany, 1Charite, Institute of Biometry and Clinical Epidemiology, Berlin, Germany, 2Charite, Institute for Public Health, Berlin, Germany, 3Medical University of Vienna, Institute of Clinical Biometrics, Center for Medical Data Science, Vienna, Austria, 4Medical University of Vienna, Division of Nephrology and Dialysis, Department of Medicine III, Vienna, Austria, 5Charite, Department of Surgery, Berlin, Germany, 6Charite, Department of Urology, Berlin, Germany

Background: In the European Senior Program (ESP) recipients ≥65 years are waitlisted to receive local kidneys from cadaveric donors ≥65 years without HLA-matching. We compare patient survival of waitlisted (WTL) with survival of transplant (TX) patients in the ESP over 20 years at our center.

Methods: All patients waitlisted with active status in the ESP in our centre between 1999-2019 were included into this survival analysis. The baseline marked either the 65th birthday (inclusion from regular allocation) or any time point thereafter (primary ESP-allocation). To investigate patient survival, landmark analyses were performed at 6, 12, 18 and 24 months after baseline. Patients were analysed in WTL- or TX-group depending on their status at the respective landmark. Survival was estimated using Kaplan Meier analysis. In the age-dependent survival analyses, the median at the respective landmark was used for stratification.

Results: 820 patients were included into the cohort (median age at baseline 67.8 years, 62% male). Landmark analyses at 6, 12 and 24 months including 760, 744, 710 and 662 patients, respectively, showed a survival until landmark of 35%, 32%, 29%, and 31% for TX and 36%, 33%, 33% and 29% for WTL at 10 years, respectively. Age-dependent landmark analyses at 6, 12, 16 and 24 months (Figure 1) stratified by median age at each landmark showed better survival in younger patients below median irrespective of transplant status. Sensitivity analysis in 570 patients who were first listed into the ESP after their 65th birthday (median age 69.9 years) did not show any survival benefit for transplanted patients either.

Conclusions: Our results demonstrate in a large monocentric cohort that kidney transplant recipients ≥65 years receiving an organ from a donor ≥65 years have no survival benefit compared to waitlisted dialysis patients of the same age. A deeper analysis considering major covariates like comorbidities at time of listing and time on dialysis is needed to further validate this finding. A major limitation of our study is that the patients’ quality of life was not recorded.
BRIEF ORALS

DONATION AFTER MEDICAL ASSISTANCE IN DYING IN QUEBEC – THE FIRST FIVE YEARS

Mathew Weiss1,2, Mathilde Dupras-Langlais1, Marie-Josée Lavigne1, Annie-Carole Martel1, Sylvain Lavigne1, Prosanto Chaudhury1,4
1Transplant Québec, Montréal, Canada, 2Canadian Donation and Transplant Research Program, Edmonton, Canada, 3CHUL et Centre Mère-Enfant Soleil, Pediatric Intensive Care, Québec, Canada, 4MUHC - McGill University Health Centre (Glen Site), Multi-organ Transplant Program, Montréal, Canada

Background: Since the 2015 passage of a law allowing medical assistance in dying (MAID), Québec became one of few jurisdictions where deceased organ donation after MAID was possible.

Methods: We reviewed all cases referred for donation after MAID from January 2018 to December 2022, the first five full years of our program. As a retrospective, anonymized report, we did not seek ethics approval. All data is presented descriptively with no comparison statistics.

Results: We received 240 referrals for donation after MAID. We retained and confirmed initial consent for 81 of these references (81/240, 34%). 130/159 non-retained references had a recorded reason: 75/130 (58%) were for medical unsuitability (age, medical history, etc.), 30/130 (23%) were due to patient refusal, and 12/130 (9%) patients withdrew from the MAID process entirely. Seventeen of the 81 retained cases were canceled later in the process, almost all (16/17, 94%) due to medical contraindication discovered during the donation evaluation. One patient died before MAID was realized. The most common underlying diagnostic group was neurodegenerative disorders (85%), followed by cardiopulmonary disorders (6%), or other (9%). The average time from administration of the MAID agents to determination of death was 12.6 minutes (3-28 min); the average WIT was 26.6 minutes (16-43 min). A total of 182 organs (116 kidneys, 20 livers, 46 lungs) were transplanted. Table 1 details the transplanted organs per year. Sixty-four patients became actual donors after MAID (64/240) of all referrals and 79% (64/81) of referrals retained after initial evaluation. MAID donors represented 8% (64/803) of total deceased donors during the study period, increasing from 5% (8/164) in 2018 to 14% (24/173) in 2022. The total conversion rate was 26% (64/240) of all referrals and 79% (64/81) of referrals retained after initial evaluation.

Conclusions: These data describe the substantial increase in deceased organ donation after MAID in the first 5 years of implementation in Québec and show that ODOS can establish a system that honors the wishes of patients pursuing MAID to donate their organs after their death. Future study will focus on how to optimize these systems to ensure these requests are treated in the most ethically and medically effective way possible.

Table 1. Transplanted organs from MAID donor in Québec

<table>
<thead>
<tr>
<th>Year</th>
<th>Kidneys</th>
<th>Livers</th>
<th>Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>16</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2019</td>
<td>24</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>2020</td>
<td>16</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>2021</td>
<td>22</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>2022</td>
<td>18</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

THE SCARCITY OF ORGAN DONORS IN CHILE IS NOT EXPLAINED BY FAMILIAL REFUSAL, BUT BY UNPREPARED ER AND ICU PROFESSIONALS

Francisca Gonzalez Cohens1, Felipe Vera Cid1, Rosa Alcayaga Droguett1, Fernando Gonzalez Fuenzalida1,2
1Departamento de Ingeniería Industrial - Universidad de Chile, Santiago, Chile, 2Campus Oriente de Facultad de Medicina Universidad de Chile, Providencia, Chile, 3Hospital del Salvador, Nephrology, Dialysis, and Kidney Transplantation, Providencia, Chile

Background: Despite appropriate legislation and adequate financial coverage, organ donation rates (ODR) in Chile remain low. Experts blame high familial refusal rates, while dismissing the effect of procurement process inefficiencies in hospitals. Our objective is to study some of those inefficiencies that may lead to the scarce ODR.

Methods: Using a two-step approach, we started by obtaining two datasets, hospital discharges and organ procurements between years 2013-2017. We considered all patients that entered the system with a critical neurological condition according to ICD10, and exited dead; and all possible organ donors (PD) who entered procurement follow-up. We used descriptive statistics to merge and analyze both datasets. Second, we applied a survey on healthcare professionals (HCP, physicians and registered nurses) in ER and ICU of 3 large hospitals in the capital, which aimed at describing procurement process knowledge and behavior. We used descriptive statistics for analysis.

Results: At the first analysis we found that 87% of patients qualifying as PD never entered procurement follow-up and, as 50% of families refused to donate, 6% of all PD became effective organ donors. The survey was answered by 88 HCP. 50% physicians, 70% from ER. 51% declared they’ve actively detected a PD but 43% referred them to the Procurement Unit (PU), thus 22% detected and referred a PD (78% don’t). 10% of the surveyed population was not sure about the validity of brain death diagnosis, and 52% never received formal training on any organ donation topic while studying. 73% thought procurement activity as important, but 40% declared not knowing enough about it. ICU HCP was more knowledgeable than ER (81% vs 23% declared more than sufficient knowledge, p<0.001).

Conclusions: The insufficient knowledge of procurement activity and concepts, especially from ER HCP may explain the lack of PD detection and referral found at a national level. It is also interesting that the HPC% who don’t refer PDs is like PD% lost nationally. Although the small sample may not be fully representative of the target population, the findings provide the insight that the efforts to increase Chilean DDR should be put in educating HCP that participate in the procurement process, or even automating and standardizing the process to stop relying on people’s knowledge.
Safety and quality at the core of donation and transplantation

**BOS14_7**

**CITIZENSHIP STATUS AND KIDNEY FUNCTION OF LIVING DONORS IN THE UNITED STATES**

Ekmol Tantisattawo1,2, Voramol Rochanaroo1, Chanokporn Puchongmart2, Piengpitch Naunspa1, Phuwadith Watanachayakul1

1Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California Irvine School of Medicine, Orange, California, United States, 2Nephrology Section, Department of Medicine, Tibor Rubin Veterans Affairs Medical Center, Veterans Affairs Long Beach Healthcare System, Long Beach, California, United States.

Background: Kidney disease is perceived to greater affect non-citizens residing in countries with a variety of populations like the United States. Whether this disparity exists in living kidney donors (LKD) in the United States is unknown. We aim to evaluate the association between U.S. citizenship status and kidney function after a living kidney donation.

Methods: A retrospective cohort study using OPTN/SRTR database includes LKD undergoing living donation between June 1972 and September 2022. Time-to-event of >35% rising post-donation serum creatinine (Scr) from pre-donation Scr between U.S. and non-U.S. citizens was examined by multiple Cox proportional hazard regression analyses.

Results: Of 136,814 LKD, the mean±SD age was 42±12 years and 61% were female. The majority were U.S. citizens (95%). Over a median time to follow-up of 6.27 months (IQR 4.07, 8.67), 103,938 LKD had post-donation Scr data and 76,542 (73.6%) of these LKD had the event. The incidence rate of the event was 0.092 persons-month. Scr during the pre-donation period was 0.85±0.19 mg/dL and post-donation Scr during routine follow-up visits at 6, 12, and 24 months were 1.22±0.30, 1.19±0.30, and 1.16±0.27 mg/dL, respectively (Figure 1A). There was a graded increase in the mean percentage of elevated Scr from pre-donation Scr at 6, 12, and 24 months post-donation of 46, 43, and 41%, respectively (Figure 1B). Compared to the non-U.S. citizen, the U.S. citizen had a non-significantly higher risk of increased post-donation Scr >35% (HR 1.02, 95%CI 0.99, 1.06, P=0.151). After adjusting for age, gender, race/ethnicity, education level, pre-donation BMI, history of hypertension, SBP, DBP, Scr, and post-donation proteinuria, the U.S. citizen became at greater risk for the event (HR 1.12, 95%CI 1.050, 1.204, P=0.001; Figure 2). There was no effect modification of the adjusted variables in the multivariable Cox regression model.

Conclusions: U.S. citizens are at higher risk of increased post-donation Scr >35% compared to non-U.S. citizens independent of pre- and post-donation factors. While non-U.S. citizen is the minority in the country, exploring factors contributing to this finding from qualitative studies as a mixed method design should explain the mechanism and mitigate the risk of worsening post-donation kidney function among U.S. citizens.

Figure 1: Distribution of pre-donation serum creatinine and serum creatinine at 6, 12, and 24 months post-donation (A) and mean percentage of rising serum creatinine from the pre-donation serum creatinine at 6, 12, and 24 months post-donation (B) Scr, serum creatinine

**BOS14_8**

**KIDNEY FUNCTION DECLINE PREDICTING FACTORS IN LIVING KIDNEY TRANSPLANTATION DONORS**

Zaklina Sterjova1, Lada Trajceska1, Irena Rambabova Bushjetkij1, Goce Spasovski1, Stefan Filipovski1, Galina Severova-Andreewska1, Igor Nikolov1, Mimoza Milenkova1, Aleksandra Canevska Taneska1, Adrijana Spasovska1

1University Clinic of Nephrology, Skopje, North Macedonia

Background: After nephrectomy kidney transplant donors lose 50% of their renal mass. Shortage of donors and long waiting list for deceased donor transplantation expanded the living donor criteria. The aim of this study to identify pretransplant donor related factors associated with renal function decline.

Methods: We retrospectively studied LDKT donors from one transplant center in the period 2013-2022. Data was retrieved from medical history charts and national electronic database system. Demographic characteristics as age, gender and relation to the recipient, patients preference to donate the kidney with higher measured split GFR, the presence of diabetes, hypertension, hyperlipidemia and BMI >30kg/m² were analysed. Estimated GFR by CKD EPI was notified prior donation, one and two years afterwards. In a multivariate regression analysis the reduction ratio of CKD EPI was explored as dependent variable.

Results: We studied 121 donors. The average age at time of transplant was 59.18 ± 10.99 years. Donors’ average eGFR was 91.53 ± 18.62 ml/min. Donor’s age and eGFR were significantly correlated (r = 0.001, r = 0.529). Male donors were 37% (30%), 11% (9%) were unrelated to recipients, 9% (7%) had BMI>30, 17% (14%) diabetes, 53% (44%) hypertension 5% (4%) hyperlipidemia, and 65% (52%) had more than one comorbidity combined. Eight of donors (7%) decided to donate the better kidney. CKD EPI declined to 17±1.62ml/min at first and 66.0±2.12ml/min at the second year. The RR of 24.3±20.60% and 27.6±18.76% raised on yearly bases, respectively. In the univariate analysis of the GFR declination at the first year BMI>30kg/m² was associated with higher reduction of GFR (p=0.318, p=0.003). At the second year the presence of diabetes emerged as a worsening factor of GFR (p=0.227, p=0.034) and BMI>30kg/m² kept its significance (p=0.426, p=0.000). All the other parameters showed no significant associations to the GFR decline. In the multivariate analysis BMI>30kg/m² remained as most powerful predictor at 12 months reduction of eGFR.

Conclusions: Patients with diabetes and especially with obesity are at higher risk of rapid decline in kidney function after kidney donation. Careful assessment prior kidney donation should weight the risks.
Safety and quality at the core of donation and transplantation

**CHARACTERISTICS OF PROSPECTIVE AND EFFECTIVE LIVING DONORS FOR RENAL TRANSPLANTATION: A CROSS-SECTIONAL STUDY**

Sonia Galvis¹, Andrea García López², Nicolas Lozano Suárez², Fernando Giron Luque³
¹Colombiana de Trasplantes, Nursing Department, Bogota, Colombia, ²Colombiana de Trasplantes, Department of Transplantation Research, Bogota, Colombia, ³Colombiana de Transplantes, Department of Transplantation Surgery, Bogota, Colombia

**Background:** Living donor kidney transplantation accounts for 23% of transplants in the country, and most postulated donors do not complete the process. Therefore, the objective of this study was to describe the process of an effective donation, characterizing the potential and effective living kidney donors evaluated in a transplant centre.

**Methods:** In a cross-sectional study, we retrospectively reviewed the medical records of 1488 potential donors, evaluated between 2008 and 2019. A descriptive analysis of donor characteristics was performed. The characteristics of potential and effective donors were compared. And described the living donation process and reasons for non-donation in its distinct phases.

**Results:** Only 36.5% were effective donors, while 63% were disqualified. Of potential donors, 15.4% were not approved by mental health, 31.8% were contraindicated by nephrology or surgery, the medical board did not authorize 11%, and 4.7% of donors were approved but did not complete the process. The most frequent reasons for non-donation due to medical contraindication were arterial hypertension, anatomic anomaly, and proteinuria greater than 30. Effective donors were younger, with lower body mass index and higher frequency of first-degree relationships.

**Conclusions:** Only one-third of potential donors become effective donors. The main reasons for non-donation are clinical, but a critical percentage is disqualified for mental health reasons and for dropping out of the process.

**Figure 1. Approval flowchart from donor nomination to nephrectomy and transplantation.**

**Table 1. Reasons for non-donation.**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number of Donors (n)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Others related to the receiver</td>
<td>4 (0.8%)</td>
<td></td>
</tr>
<tr>
<td>Renal asymmetry or atrophy</td>
<td>4 (0.8%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>44 (8.6%)</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>27 (5.3%)</td>
<td></td>
</tr>
<tr>
<td>Hyperglycaemia or diabetes</td>
<td>17 (3.3%)</td>
<td></td>
</tr>
<tr>
<td>Haematuria</td>
<td>16 (3.1%)</td>
<td></td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>9 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Family background</td>
<td>4 (0.8%)</td>
<td></td>
</tr>
<tr>
<td>Rationale for clinical non-donation</td>
<td>524 (60.2%)</td>
<td></td>
</tr>
<tr>
<td>Rationale for mental health</td>
<td>140 (15.3%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>18 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>CAS</td>
<td>16 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Legal</td>
<td>6 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>Ethical</td>
<td>12 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Ethical and psychological</td>
<td>35 (3.9%)</td>
<td></td>
</tr>
<tr>
<td>Ethical and psychological</td>
<td>35 (3.9%)</td>
<td></td>
</tr>
</tbody>
</table>
Background: Central body fat distribution affects renal function. Abdominal fat measurements using computed tomography (CT) may prove superior in assessing body composition related renal risk in living kidney donors. This study aimed to determine the association between abdominal fat areas and renal function before and after living kidney donation, using CT imaging at L3 vertebral level.

Methods: Between 2002 and 2019, 570 living kidney donors were included in this study. CT-derived abdominal fat areas were determined at vertebral level L3 and indexed for height. Donors underwent glomerular filtration rate measurements (125I-Iothalamate) before (n=588) and 5 years after donation (n=212). Linear regression analyses with crude mGFR and mGFR indexed for body surface area were performed to assess the association of tomographic fat measurements with renal function.

Results: Multivariable linear regression analyses in both male and female donors showed higher levels of total abdominal, visceral, subcutaneous, and intramuscular adipose tissue index were significantly associated with lower crude and body surface area indexed measured glomerular filtration rate levels before donation (body surface area indexed measured glomerular filtration rate: male donors: visceral adipose tissue index: β=-0.04, p<0.001, subcutaneous: β=-0.08, p<0.001, intramuscular: β=-0.05, p<0.001; female donors: visceral adipose tissue index: β=-0.10, p<0.001, subcutaneous: β=-0.08, p<0.001, intramuscular: β=-0.06, p<0.001, total abdominal: β=-0.04, p=0.001; female donors: subcutaneous: β=-0.08, p<0.001, intramuscular: β=-0.65, p=0.003, total abdominal: β=-0.04, p<0.001). Long-term after donation, tomographic abdominal fat measurements remained inversely associated with lower renal function.

Conclusions: This study shows that abdominal fat area, measured by CT analysis, is associated with renal function at time of screening and (in male donors) long-term after living kidney donation. Comprehending the renal outcomes of living kidney donation and accurately identifying their body composition related risk factors can aid clinicians in decision-making and donor counselling during screening for donation.
**BRIEF ORALS**

**BOS15_1 ISLET TRANSPLANTATION VERSUS INSULIN ALONE IN TYPE 1 DIABETIC KIDNEY TRANSPLANT RECIPIENTS: A FRENCH NATION-WIDE STUDY ON BEHALF OF THE TREPID GROUP**

**Meherf Maanaou1,2, Rémi Lenain1, Johann Foucher1, Mikael Chetboun1, Julie Kerr-Conte1, Marie-Christine Vantyghem1, Mikael Chetboun1, Julie Kerr-Conte1, Albanie Bordrin-Sartorius1, Fanny Buron1, Sophie Caillard8, Laurence Kessler1, Sandrine Lablanche1, Thierry Berney7, Marie-Christine Vantyghem1, Marc Hazzan2, Francois Pattou1**

1CHU Lille, Nephrology, Lille, France, 2INSERM, U1190, Lille, France, 3CHU Conte1, Marie-Christine Vantyghem1, Lorenzo Piemonti3, Michael Rickels4, 3IRCCS Ospedale San Raffaele, Milan, Italy, 4University of Pennsylvania transplant Endocrinology, Strasbourg, France, 5CHU Grenoble, Endocrinology, Grenoble, France, 6University of Geneva, Geneva, Switzerland, 7CHU Lille, Endocrinology, Lille, France

**Background:** Islet transplantation is associated with a benefit on glycaemic control compared to optimized insulin therapy in recent clinical trials. However, there is a lack of evidence concerning the long-term impact of islet transplantation on the type 1 diabetic transplant recipients' prognosis. **Methods:** Every type 1 diabetic recipient transplanted with a kidney in France between 2000 and 2017 was included. Patients transplanted with pancreatic islets were compared to controls treated with insulin alone according to a matching method based on time-dependent propensity scores (using the following variables: yera of transplantation, donor age, and recipient age, serum creatinine, HBA1c, BMI, cardiovascular background) which allow to ensure patients comparability at the time of islet transplantation. The primary outcome was graft failure, defined by death or return to dialysis. **Results:** Among 2393 type 1 diabetic patients transplanted with a kidney during the study period, 381 were eligible to islet transplantation, including 47 that were actually transplanted with islets. Median time for islet transplantation was 34.8 months [21.8-48.4]. Probabilities of insulin-independence and islet graft survival at 1, 5 and 10 years were respectively 63.8% [51.5-75.9], 46.3% [33.9-63.2], 38.7% [25.9-58.7] and 89.4% [81.0-96.8], 87.2% [78.2-93.7], 82.6% [86.2-92.4]. After matching, we observed a significant benefit of islet transplantation compared to insulin alone on graft failure, with a HR of 0.48 [0.20-0.94], mainly explained by a protective effect on the risk of death (HR= 0.38 [0.11-0.95]). We finally estimated the life-expectancy for a 10-year follow-up and found 9.61 years [9.02-10.00] in the islet transplantation group versus 8.85 years [7.97-9.56], with a difference of 8.8 months [-2.16-20.44]. **Conclusions:** We observe a significant benefit of islet transplantation on the risk of graft failure and death in type 1 diabetic kidney transplant recipients. These results provide incentives to promote islet transplantation in this population.

**BOS15_2 RELATION BETWEEN PRIMARY GRAFT FUNCTION AND 5-YEAR OUTCOMES OF ISLET TRANSPLANTATION: A RETROSPECTIVE STUDY IN 1210 PARTICIPANTS**

**Mikael Chetboun1,2, Mikael Chetboun1, Elodie Drumez1, Cassandra Ballou1, Mehdi Maanaou1, Elizabeth Payne1, Franca Barton1, Julie Kerr-Conte1, Marie-Christine Vantyghem1, Lorenzo Piemonti1, Michael Rickels2, Julien Labreuche2, Francois Pattou1**

1CHU Lille, Lille, France, 2The Emmes Company, Rockville, United States, 3IRCCS Ospedale San Raffaele, Milan, Italy, 4University of Pennsylvania Perelman School of Medicine, Philadelphia, United States

**Background:** Allogeneic pancreatic islet transplantation (IT) is a validated therapy for diabetes associated with severe hypoglycemia, and after kidney transplantation. This beta-cell replacement strategy currently consists of one or more intraportal infusions of allogeneic pancreatic islets, aiming to restore regulated endogenous insulin secretion and improve blood glucose control. The mechanisms underlying the decline of islet graft function with time are unclear. We evaluated the distinct relation between primary graft function (PGF) measured 28 days after last islet infusion and 5-year IT outcomes in the Collaborative Islet Transplant Registry (CITR), a comprehensive registry that compiles all data from most islet transplant programs in North America, Eurasia and Australia. **Methods:** This retrospective multicenter cohort study enrolled all participants from CITR, the only IT alone (Donor kidney transplantation) (IAK), between 1999 and 2020 with a calculable PGF (exposure of interest), measured 28 days after last islet infusion with a validated composite index of islet graft function (Beta2-score). Primary outcome was 5-year cumulative incidence of uncontrolled IT explored with a competing risk analysis adjusted for all covariates suspected or known to impact outcomes. A predictive model based on PGF was built and internally validated by using bootstraps resampling method. **Results:** In 39 centers, 1210 patients, 712 (59.5%) females, mean age 47±11 years, received a median of 2 (IQR 1-4) islet transplants per kg of body weight (IQR 4.7±13.5). Among them, 211 (17.6%) were islet after kidney recipient and 758 (62.6%) received multiple islet infusions. Mean PGF was 14.3±8.8. The 5-year incidence of unsuccessful IT was 70.7% (95%CI 67.2-73.7), and was higher and linearly related to PGF with an adjusted subhazard ratio of 0.77 (95% CI 0.72-0.82) per 5 units increase of Beta2-score (p<0.0001). Our model based on PGF predicted IT outcome with a good accuracy (median C-statistic 0.70 (range 0.69-0.71)). **Conclusions:** We present the largest multicenter cohort study on islet transplantation and demonstrated a linear relation between PGF and 5-year clinical outcomes of IT, independently from known or suspected prespecified covariates.

**BOS15_3 SIMULTANEOUS ISLET KIDNEY TRANSPLANT – OUTCOMES FROM 2 UK TRANSPLANT CENTRES**

**Andrew Sutherland1, Linda Birtles2, Kirsty Duncan1, Hussein Khambali1, Shareen Forbes1, Martin Rutter1, John Casey1,** **David Van Dellen1**

1Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, 2Manchester Royal Infirmary, Manchester, United Kingdom

**Background:** Simultaneous Islet Kidney (SIK) transplantation is a treatment option for type 1 diabetic patients with an eGFR<20. It is primarily aimed at patients that are deemed unfit for a simultaneous kidney pancreas transplant. Here we report the results of SIK transplants performed in 2 UK centres (Edinburgh and Manchester) between 2018 and 2022. **Methods:** Transplant outcomes from 31 consecutive SIK transplants were analysed retrospectively including patient and graft survival, stimulated c-peptide, HbA1c and insulin dose. Renal transplants were performed on Day 0 and islet transplants from the same donor were performed via a transaortal hepatic portal infusion 24-48 hours later. Selected recipients received a 2nd islet transplant from a different donor. All values are expressed as means ±/− SD and groups compared with a 2-tailed student t-test. **Results:** 15 male and 16 female patients received SIK transplants. All recipients were c-peptide negative pre-transplant. The mean age of recipients was 50.6 years and mean follow-up was 2.7 years. 12 patients received a second IT (1st and 2nd transplant between 1 and 13 months after 1st transplant). Mean islet cell counts and viability for the first transplant were 314,000 +/- 120,000 beta-cell outcomes. Further work is needed to assess the longterm benefits of a SIK transplant versus kidney alone. **Conclusions:** SIK transplant results in excellent renal transplant outcomes and improves glycaemic control. A second islet transplant significantly improves beta-cell outcomes. Further work is needed to assess the longterm benefits of a SIK transplant versus kidney alone.

**BOS15_4 EXPLORING PRESERVATION MODALITIES IN A SMALL HUMAN PanCREAS MODEL TO INVESTIGATE THE EFFECT ON THE ISLET ISOLATION OUTCOMES**

**Antoine Buemi1,2, Nizar Mourad1, Arnaud Devresse1, Tom Darius1, Nada Kanaan1, Pierre Gianello1, Michel Mourad1**

1Cliniques universitaires Saint-Luc (UC Louvain), Bruxelles, Belgium, 2UC Louvain, Ottignies-Louvain-la-Neuve, Belgium

**Background:** In islet transplantation, the use of dynamic hypothermic preservation methods is a current challenge, aiming to include in the the extended criteria pancreas without altering islet isolation results. We here reported a pair comparison of three pancreas preservation methods-cold storage (CS), hypothermic machine perfusion (HMP), and oxygenated machine perfusion (HMP O2)- using a split human pancreas model to assess the impact of the preservation method on islet function and isolation performance. **Methods:** We used a human pancreas split model from discarded donors in which the pancreas head was preserved through the conventional CS method (“control group”) and the pancreas tail was preserved through three different preservation methods: CS, HMP, and HMP O2 (“study group”). After a same ischemia time in both head and tail of each organ, a separate islet isolation was performed in parallel. Dosage characteristics, isolation data and functional tests results of isolated islets at one- and seven-day cultures of both segments were collected.
**Results:** Eight human pancreases were used in each group. Donor demographics, ischemia times and isolation data were similar in all groups (Table 1). Compared to controls, IEQ/gr obtained was higher in both CS and HMP study groups (1219.77±844.3 IEQ vs 230±193 IEQ, p=0.006 and 1476.25±992.2 IEQ vs 251.3±195.6 IEQ, p=0.004 respectively). In contrast, the difference was not significant in the HMP O2 study group vs control (p=0.19) (Table 1, Figure 1). No other significant paired isolation data differences were found. In each paired group (study vs control) and between the three study groups, functional testings of isolated islets were similar, including area under curve of insulin secretion and stimulation index (Table 1, Figure 1).

**Conclusions:** Our results suggest that all preservation methods show similar efficacy in terms of islet secretory function. Despite similar results in CS group and HMP group, the addition of a full oxygenation during the time of hypothermic machine preservation seems to negatively impact the performance on the islet isolation procedure.

**Table 1**

| Donor characteristics and isolation data of CS group, HMP group and HMP O2 group. |
|---------------------------------|-----------------|-----------------|-----------------|
|                                | CS              | HMP             | HMP O2          |
| **Donor Demographics**         |                 |                 |                 |
| Age (years)                    | 50.3±1.4       | 50.3±1.4        | 50.3±1.4        |
| Gender, n                      | Male            | Male            | Male            |
|                               | 4               | 3               | 3               |
| Diabetes mellitus, n           | 0               | 0               | 0               |
| Ischemia, min                 | 44.8±2.8        | 44.8±2.8        | 44.8±2.8        |
| Hypothermic machine preservation, min | 30±5.2        | 30±5.2          | 30±5.2          |
| **Isolation Data**             |                 |                 |                 |
| IEQ (IEQ-gr)                   | 230±193         | 1219.77±844.3   | 1476.25±992.2   |
| Area under curve of insulin secretion (U/MU) |            |                 |                 |
| Stimulation index              | 1.7±0.5         | 1.7±0.5         | 1.7±0.5         |

**Figure 1**

Functional testing of isolated islets after pancreas preservation by three different methods: cold storage (CS, green), hypothermic machine perfusion (HMP, blue) and exogonized machine perfusion (HMP O2, orange). Each study group (CS, HMP, HMP O2) had its own control group (Head, Islet) preserved by a conventional method (CS), following a split organ model in which the two pancreas samples have the same schema times and the same isolation method performed in parallel. At day 1 and day 7, cultured islets from each were perfused with a low concentration glucose solution (0.5 mM Glucose, LSG), followed by a high concentration glucose solution (15 mM Glucose, 15xG). Both areas under curve of insulin secretion (AUC) and stimulation index of each paired group were not statistically significant. (p>0.05).

BRIEF ORALS

Progress and challenges in Pancreas and Islet transplantation
Progress and challenges in Pancreas and Islet transplantation

**BRIEF ORALS**

### BOS15_5

**RE-ANIMATING PANCREATIC GRAFTS SUBJECTED TO PROLONGED COLD ISCHEMIA IN A PORCINE MODEL USING NORMOTHERMIC EX VIVO PERFUSION: A FEASIBILITY STUDY**

Samrat Ray1, Catherine Parmentier1, Masataka Kawamura1, Emmanuel Nellien1, Christian Hobeika1, Tunpun Chiu1, Sujani Ganesh1, Sangeetha Kalimuthu1, Markus Selzner1, Trevor Reichman1

1Toronto general hospital, Multiorgan transplantation, Toronto, Canada.
2Toronto general hospital, Department of Surgical Pathology, Toronto, Canada.

**Background:** Despite promising results in Diabetes mellitus, pancreas transplantation is limited by lower graft acceptability and sparse applicability of “extended criteria grafts”. Transportation of grafts might require prolonged periods of cold storage, having detrimental effects on islet function, limiting usage of such grafts. Accordingly, we aimed to establish feasibility of transplanting in porcine models using pancreato-duodenal grafts subjected to prolonged cold ischemia (>21 hrs) and optimise same using normothermic ex vivo perfusion (NEVP).

**Methods:** Study population consisted of an allo-transplantation porcine model with a 3-day survival plan for recipient. Control group consisted of grafts subjected to cold storage (CS) for 24 hrs (n=2) and 21 hrs (n=4) and test group comprised of grafts subjected to further 3 hrs of NEVP (n=5). Outcome variables of interest and comparison were survival, tissue injury markers, endocrine graft function and histology.

**Results:** Table 1 shows comparison of graft characteristics between 2 groups. Figure 1 (a&b) shows comparison of survival and IV glucose tolerance test between the groups. Mean C-peptide (± SD, pmol/l) (Post-op day 1) was 82.7±84.4 for test vs 60.5±25.2 for control (p=0.78).

**Conclusions:** Bowel necrosis was identified as the cause of graft failure in all cases of prolonged cold storage precluding its feasibility. However, optimising the grafts with NEVP after a period of prolonged cold ischemia seemed promising in re-animating these grafts for transplantation by reviving vascularity and improving endocrine function.

<table>
<thead>
<tr>
<th>Table 1: Graft characteristics</th>
<th>Test (n=5)</th>
<th>Control (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>60% (n=3)</td>
<td>0%</td>
</tr>
<tr>
<td>Gross</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft reperfusion</td>
<td>Patchy subcapsular hemorrhages</td>
<td>Minimal subcapsular hemorrhages</td>
</tr>
<tr>
<td>Bowel reperfusion</td>
<td>Uniform</td>
<td>Patchy</td>
</tr>
<tr>
<td>Necropsy (Corpus)</td>
<td>Preserved on cut section; oedema present (50-60% viability)</td>
<td>Patchy areas of devitalised tissue (&lt;30% viability)</td>
</tr>
<tr>
<td>Necropsy (Bowel)</td>
<td>Well preserved</td>
<td>Transmural necrosis</td>
</tr>
<tr>
<td>Microscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necropsy-Day 3 (Corpus)</td>
<td>Moderate necrosis; islets preserved; acini preserved &gt;50%</td>
<td>Moderate-severe necrosis; acini preserved &lt;50%; islets preserved</td>
</tr>
<tr>
<td>Necropsy-Day 3 (Duodenum)</td>
<td>Mild ischemic damage; crypts preserved</td>
<td>Gross transmural ischemic necrosis; crypts distorted</td>
</tr>
</tbody>
</table>

Figure 1 (a&b): Survival (1a) and Endocrine graft outcome (1b)

### BOS15_6

**SINGLE-CENTER INITIAL EXPERIENCE OF DUODENO-DUODENOSTOMY FOR EXOCRINE DRAINAGE IN PANCREAS TRANSPLANTATION**

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**Background:** Retroperitoneal disposition of the pancreatic graft offers a more physiologic drainage, similar to the native pancreas. We present our experience with duodenoduodenostomy (DD) for exocrine drainage, analyzing intestinal complications and their impact on patient and graft survival.

**Methods:** All pancreatic transplants performed between May 2016 and April 2022 were included. Results were compared with previously published data from our series of duodenojunostomy (DY).

**Results:** A total of 105 transplants were performed using DD. Mean age was 43 years [36 - 38.5], 6% of donors were controlled asystole, and 94% brain death donors. Morbidity was 43.8% in the DD group. Regarding intestinal complications no statistical significance were found between groups (DD: 10 (9.5%) vs DY: 23 (6.8%); p=0.395). The following were identified: intestinal occlusion (n=3); paralytic ileus (n=2); post-transplantectomy duodenal dehiscence (n=1); DD dehiscence (n=2). Seven cases required surgical treatment: adhesiolysis (n=3); transplantectomy (n=1); primary closure of the dehiscence (n=2); reconstruction of the enteric anastomosis (n=1). According to the Clavien-Dindo classification, complications were: 3.8% Grade I, 16.2% Grade II, 3.8% Grade IIIa, and 20% Grade IIb. The average stay was 13 days. After a median follow-up of 30.7 months [IQR 18.1-44], pancreatic graft survival was 85.8% at 1 and 5 years, and patient survival 100% at 1 year, and 97.7% at 1 year, fifth year.

**Conclusions:** Duodenoduodenostomy for enteric drainage in pancreas transplantation is an effective surgical alternative, offering more physiologic exocrine drainage, with similar complication rate and similar patient and graft survival, compared to duodenojunostomy.
Progress and challenges in Pancreas and Islet transplantation

BRIEF ORALS

HEALTH RELATED QUALITY OF LIFE AFTER SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION: HOW GOOD DOES IT GET?

Irene Mosca*, Shruti Sweeney1, Richard Dumbill1, Faysal El-Gilani1, Rumyana Smilevska2, Flavia Nerli2, Venkatesha Udupa1, Isabel Quiroga-Giraldez2, Shrikant Reddy2, Sanjay Sinha2, Rutger Ploeg1, Edward Sharples2, Coral Millburn-Curtis1, Simon Knight1, Alastair Gray2, Peter Friend1

1University of Oxford, Oxford Transplant Centre, Nuffield Department of Surgical Sciences, OXFORD, United Kingdom, 2Oxford University Hospitals NHS Foundation Trust, Oxford Transplant Centre, OXFORD, United Kingdom, 3University of Oxford, Green Templeton College, OXFORD, United Kingdom, 4University of Oxford, Nuffield Department of Population Health, OXFORD, United Kingdom

Background: Better quality of life is considered a major benefit of pancreas transplantation (PT). The existing literature seems to support this notion, however the evidence available is at times contradictory and population sizes are often too small to accrue statistically significant data. The aims of this research were to assess the trajectory of Health-Related Quality of Life (HRQOL) before and up to one year after PT and identify potential predictors.

Methods: This was a single centre prospective longitudinal cohort study on adult patients undergoing PT for type 1 diabetes, recruited from October 2018 to March 2020. Participants completed validated Patient Reported Outcome Measures (PROMs): before transplant, at six weeks, six months and one year after surgery. The study portfolio included general health status and disease specific instruments, to investigate diabetes and renal related HRQOL. Clinical data was collected prospectively at the same time points.

Results: 80 potential participants were recruited, of which 62 received the intervention and 57 reached the end of the study. Nearly 90% were Simultaneous Pancreas/Kidney (SPK) recipients with a median of 3 (1 to 7) chronic complications of diabetes. While interim time points were greatly affected by the pandemic, return rates at one year were adequate (77%). Physical, diabetes and renal-related HRQOL at one year were statistically better than baseline, with a large effect size. This resulted in a statistically significant increment of health indexes. Mental health scores did not improve significantly; despite which these alone reached population norms. Biological male gender, older age, preserved ability to work, sexual function, urinary output at transplantation and a lower number of chronic complications were predictors of higher post-operative HRQOL. Gastrointestinal symptoms, history of psychiatric disorders, severe ophthalmic complications, low Body Mass Index, hypoglycaemia unawareness, HLA sensitisation and longer waiting list time were associated with poorer scores.

Conclusions: PT results in a remarkable improvement of HRQOL, but it does not restore patients to population normative levels. The presence of established chronic complications of diabetes seems to be a key determinant of post-transplant HRQOL.

BRIEF ORALS

HYPERTENSION IN THE DONOR IS ASSOCIATED WITH AN INCREASED RISK OF EARLY PANCREAS ALLOGRAFT FAILURE

Christophe Massel1*, Julien Branchereau1, Georges Karam1, Florent Leborgne2, Karine Autain-Renaudin1, Lionel Badet1, Fanny Bouron1, Xavier Matillon1, Christophe Legendre3, Denis Glotz5, Corinne Antoine1, Magali Giral1, Jacques Dantai1, Diego Cantarovich1

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Background: About 10-20% of pancreas allografts are still lost in the very early postoperative period despite the identification of numerous risk factors that correlate with graft thrombosis.

Methods: We conducted a multicenter study including 899 pancreas transplant recipients between 2000 and 2018. Early pancreas failure occurring before the 30th postoperative day, long-term pancreas survival, kidney survival and patient survival were analyzed and adjusted to several donor, recipient and perioperative transplantation variables using a multivariate cause-specific Cox model also stratified to transplant centers.

Results: Pancreas from donors with hypertension, as well as with high body mass index, were independently associated with an increased risk of early pancreas failure (respectively, HR=2.57, 95% CI from 1.35 to 4.89 and HR=1.11, 95% CI from 1.04 to 1.19). Donor hypertension also impacted long-term pancreas survival (HR=1.88, 95% CI from 1.13 to 3.12). However, when pancreas survival was calculated after the postoperative day 30, donor hypertension was no longer a significant risk factor (HR=1.22, 95% CI from 0.47 to 3.15). As hypertension may correlate to BMI, we assessed the interaction between hypertension and BMI in the donor, which was negative. This confirms that donor hypertension was an independent risk factor for early allograft failure in our cohort analysis.

Conclusion: Donor hypertension was a significant independent risk factor of early pancreas failure. Unknown mechanisms linked to hypertension are possibly involved and will need further studies to allow effective preventive interventions.

Figure A. Cumulative incidence of pancreas failure within the first 30 days after transplantation according to history of donor hypertension (Aalen-Johansen estimator). B. Cumulative incidence of pancreas failure within the first 30 days after transplantation according to history of donor hypertension (Aalen-Johansen estimator).
Progress and challenges in Pancreas and Islet transplantation

NORMOTHERMIC EX VIVO MACHINE PERFUSION OF THE PANCREAS IS SAFE AND FEASIBLE IN A PORCINE MODEL OF PANCREAS TRANSPLANTATION

Catherine Parmentier1, Samrat Ray1, Laura Mazzioluci1, Masataka Kawamura1, Emmanuel Nogueira1, Christian Hobelka1, Tunpang Chu1, Sujani Ganesh1, Markus Selzner1, Trevor Reichman1
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Background: Normothermic machine perfusion (NEVP) has already proved to be superior than static cold storage (SCS) for the preservation of organs like lungs, liver, kidney, and heart but studies with the pancreas are limited. Our group has already established the safety and feasibility of normothermic machine perfusion for porcine and human cold pancreases and successfully established a perfusion and transplantation model in swines. The purpose of this study was to prove the safety and feasibility of NEVP vs SCS.

Methods: Male Yorkshire pigs (30 to 40 kg) were used both as donors and recipients in a model of heart beating donation with limited warm ischemia. The control group (SCS) consisted of 4 donors and 4 recipients, pancreas was procured using our previously established technique, kept in SCS for 5 hours and then transplanted. The study group (NEVP) consisted of 3 donors and 3 recipients, pancreas was procured and kept for 2 hours in SCS. Then subsequently placed on the normothermic machine for a 3-hour perfusion and after reperfusion transplanted into the recipient pig. Recipients in both groups were followed until POD3. Prior to sacrifice a glucose challenge test was performed.

Results:

Table 1. Baseline characteristics of donors and recipients.

<table>
<thead>
<tr>
<th></th>
<th>SCS</th>
<th>NEVP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor Weight (Kg)</td>
<td>41.6 ± 2.4</td>
<td>39.7 ± 1.9</td>
<td>0.31</td>
</tr>
<tr>
<td>Recipient Weight (Kg)</td>
<td>42.5 ± 1.8</td>
<td>39.7 ± 2.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Donor BL amylase (U/L)</td>
<td>1262 ± 201</td>
<td>1734 ± 613</td>
<td>0.19</td>
</tr>
<tr>
<td>Recipient BL amylase (U/L)</td>
<td>1285 ± 278</td>
<td>1697 ± 115</td>
<td>0.06</td>
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<tr>
<td>Donor BL lipase (U/L)</td>
<td>4.5 ± 1</td>
<td>4</td>
<td>0.43</td>
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<tr>
<td>Recipient BL lipase (U/L)</td>
<td>4</td>
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<td>1</td>
</tr>
<tr>
<td>Donor BL LDH (U/L)</td>
<td>733 ± 195</td>
<td>803 ± 12</td>
<td>0.31</td>
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<tr>
<td>Recipient BL LDH (U/L)</td>
<td>728 ± 186</td>
<td>771 ± 218</td>
<td>0.77</td>
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</tbody>
</table>

Figure 1. A. Amylase. B. Lipase. C. Glucose. D. Glucose test. (BL - baseline; POD - postoperative day; PREP10, 30 – Postreperfusion 10, 30 minutes; 91,2,3,4 – postreperfusion 1, 2, 3 and 4 hours).

Discussion: Our study demonstrates that NEVP of the pancreas is feasible and can be performed safely. No injury was observed by NEVP and the results of the perfused group were comparable to SCS. Both groups presented homogenous baseline characteristics and the parameters measured during and after surgery showed no significant differences between the groups. Further studies will focus on the outcome of NEVP in the setting of reduced cold storage time in marginal grafts.

DIFFERENCES IN GLUCOSE HOMEOSTASIS BETWEEN TYPE 1 VS. TYPE 2 DIABETES AFTER PANCREAS TRANSPLANTATION

Richard Knight4, Yan Ye5, Hemangshu Poddar4, Archana Sadhu4, Edward Graviss5, Duc Nguyen1, Stephanie Yi6, A. Osama Gaber7
4Houston Methodist Hospital, Houston, United States

Background: Pancreas transplantation outcomes are equivalent between type 1 and selected type 2 recipients with IDDM. We sought to determine differences in glucose homeostasis between groups by comparing results of glucose tolerance tests in the early post-transplant period.

Methods: A retrospective single center review of IDDM recipients of kidney/pancreas transplants between 2016 and 2022. Type 2 recipients were non-obese with a small insulin requirement. A subset of recipients underwent a modified glucose tolerance test (OGTT) early post-transplantation. Diabetes type was determined using a composite scoring system as previously published [1]. Variables included age at diagnosis of DM, immediate use of insulin or not, c-peptide level, presence of islet autoantibodies or not, and daily amount of insulin. OGTT results were compared between groups by calculating the mean area under the curve (AUC) and peak glucose, insulin, and c-peptide levels.

Results: Demographics of the study group (n=72) included a mean age of 44.5±10years, 65 percent male, and BMI of 25.2±0.3mg/m2. Baseline characteristics of age, gender, race, years of diabetes, dialysis history, and BMI were equivalent between groups. There were 59 recipients with type 1 and 13 recipients with type 2 diabetes. At one-year post-transplant, for type 1 versus type 2 recipients: mean fasting glucose (91±13 versus 88±13 mg/dl) and mean HgbA1c (5.4±0.6 vs 5.5±0.6%) levels were equivalent. As shown in Table 1 and Figure 1; 22 type 1 and 8 type 2 recipients underwent an OGTT between 6-12-months post-transplant. Whereas mean glucose AUC and peak glucose levels were equivalent between groups, both the mean insulin and c-peptide AUC and peak insulin and c-peptide levels of the type 2 recipient groups were significantly greater than that of the type 1 recipients.

Conclusions: The fasting glucose and HgbA1c levels were equivalent between type 1 and type 2 recipients at one year, yet the OGTT results showed that type 2 recipients demonstrated insulin resistance early post-transplant, necessitating a much greater insulin response to a glucose challenge compared to type 1 recipients. Thus, despite equivalent graft outcomes, glucose homeostasis is fundamentally different between these groups.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Total (n=30)</th>
<th>Diabetes type 1 (n=22)</th>
<th>Diabetes type 2 (n=8)</th>
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<tr>
<td>Total AUC glucose (mg/dl) (IQR)</td>
<td>1542 (1399, 1600)</td>
<td>1300 (1250, 1300)</td>
<td>1567 (1500, 1600)</td>
<td>0.54</td>
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<tr>
<td>Total AUC insulin (mU/L) (IQR)</td>
<td>922 (603.5, 1193.5)</td>
<td>1075 (790.5, 960.5)</td>
<td>1165 (1472, 2897)</td>
<td>&lt;0.001</td>
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<tr>
<td>Total AUC c-peptide (nM/L) (IQR)</td>
<td>841 (725.5, 1286)</td>
<td>795.5 (653.5, 963.5)</td>
<td>125 (880.5, 1695)</td>
<td>0.01</td>
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</table>

IQR: interquartile range.
Progress and challenges in Pancreas and Islet transplantation

**BOS15_12** RISK FACTORS FOR GREATER THAN 10 YEARS PANCREAS GRAFT SURVIVAL IN THE UK: SHORT TERM RISK FACTORS ARE NOT ALWAYS THE BEST GUIDE FOR LONG TERM SURVIVAL

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**Background:** The nationally funded Pancreas transplant program in the UK started in 2003-04. Long-term survival of the pancreas is required for improvement of the secondary complications of diabetes. We hypothesise that risk factors affecting long term survival are not necessarily identical to those predicting early failure.

**Methods:** We included all patients, recorded in the UK transplant registry (NHS BT), who had a pancreas transplant between 2004 and 2012, so every patient had the chance to reach 10 year follow up. Factors that correlate with >10 years survival in UK were studied and contrasted with those affecting the early 60-day failures. Binary and Cox regression was used.

**Results:** There were 1512 pancreas transplants, 81% being SPK, 13% from DCD donors, and 4% retransplants. 10 year graft survival was 65%. Among those grafts that failed in the first 60 days, it was more likely that the recipient had prior MI, CVA, or amputation (p=0.02), an older donor (p=0.01), a donor following a CVA (vs. trauma, p=0.01), a heavier donor (p=0.01), a longer CIT (p=0.00), or received a pancreas alone (PAK and PTA vs. SPK, p=0.01). Among grafts with >10 year survival compared to those with less, having SPK (90% vs 78%, p=0.01), shorter (vs. longer, p=0.03) duration of duodenum drainage (16% vs 11% p=0.03), younger donor age (p=0.04) and low waiting time (p=0.001) was more common, whilst fewer recipients had a prior MI, CVA or amputation (p=0.04). The donor type (DCD vs BD, p=0.08), and the duration of diabetes, (p=0.08) marginally affected the >10 year outcome whereas donor BMI (p=0.8), CIT (p=0.8), donor cause of death (CoD) (p=0.4) did not

**Conclusions:** In the UK, where most factors that affect early pancreas failure mirror those predicting long term survival, donor BMI, CIT, and donor CoD are important in early failures but do not affect the long-term outcome if the graft survives at least 60 days. The type of duodenum drainage, donor type, and the duration of diabetes mainly affect the long-term survival but not the early 60 days failures.

**BOS15_13** OUTCOMES OF PANCREAS TRANSPLANTATION ALONE FROM DONATION AFTER CIRCULATORY DEATH

**Rurnya Smiley**1, Shruti Mittal1, Irene Mosca1, Edward Sharples2, Srikanth Reddy2, Isabel Quiroga-Giraldez2, Venkatesha Upuda1, Sanjay Sinha3, Rutger Ploeg3, Peter Friend2, Simon Knight2
1Oxford University Hospitals, Oxford, United Kingdom, 2Department of Surgery, National University of Singapore, Singapore, 3Guys and St Thomas' Hospital, London, United Kingdom

**Background:** Donation after circulatory death (DCD) is not frequently used for pancreas transplantation worldwide, because of a presumed higher risk of complications and lower graft survival. The aim of this study is to compare the outcomes of DCD vs donation after brain death (DBD) in pancreas transplantation alone (PTA) in a single large centre series.

**Methods:** A database of pancreas transplant recipients for the period from July 2004 to August 2022 was analysed. The DBD and DCD cohorts were compared for demographic and transplant variables; Kaplan-Meier for patient and graft survival were performed. Multiple imputation was used to deal with missing data.

**Results:** During the study period 216 PTA were performed, 19 cases were excluded due to early graft loss in the first 30 postoperative days. 197 PTA were included in the analysis: 54 (27.4%) from DCD and 143 (72.6%) from DBD. 197 PTA were included in the analysis: 54 (27.4%) from DCD and 143 (72.6%) from DBD. Amongst the DCD cohort, 73.1% (n=76) survived at least 60 days failures.

**Conclusions:** Outcomes for DCD PTA are comparable to DBD. Donation after circulatory death should be considered for pancreas transplantation and donor selection is paramount. DCD is a safe option to expand the donor pool in many countries.
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1Beaujon Hospital, Assistance Publique-Hôpitaux de Paris, University of Paris Cité, Department of HPB Surgery and Liver Transplantation, Clichy, France, 2Beaujon Hospital, Assistance Publique-Hôpitaux de Paris, University of Paris Cité, Department of Anesthesiology and Critical Care, Clichy, France. -Beaujon Hospital, Assistance Publique-Hôpitaux de Paris, University of Paris Cité, Hepatology and Liver Intensive Care, Clichy, France.

Background: Auxiliary partial orthotopic liver transplantation (APOLT) for acute liver failure (ALF) provides the unique chance of complete immunosuppression withdrawal after adequate native liver remnant regeneration. However, the surgical technique is generally seen as complex and associated with significant morbidity. The aim of this study was to present our current surgical strategy in APOLT focusing on its evolution over time, experience accumulation and assessing the impact of such refinements on clinical outcomes.

Methods: This is a retrospective study on a single center cohort of 48 patients with ALF who underwent APOLT between January 1993 and December 2019. Our surgical technique was standardized in 2012 and implies (i) a restrictive use of a high quality whole liver graft or GI45678 associated with a recipient H145678 (according to the "NewWorld" terminology); (ii) direct anastomosis of graft hepatic artery with recipient right hepatic artery; (iii) end-to-side hepatocochledoceotomy.

Results: Overall patient survival at 1, 3, and 5 years was 81.1%, 74.6%, 71.3%, respectively. Only two patients required re-LT due to graft primary non-function. Complete immunosuppression withdrawal was achieved in 82.1% of patients and none of them required graft explant. The most recent experience after surgical standardization (2012-2019, n=22), compared with earlier experience (1993-2012, n=26), was associated with shorter operative time (median, 325min vs 540min, p<0.001), lower blood loss (median transfused blood units, 3 vs 7, p<0.001), median total cold ischemia time 399±59 min (325-58), rewarming time 67.3±12.1 min (43-112), and mean estimated blood loss 122.8±82.4cc (50-400). No patient was converted to open transplantation. Subcapsular hematoma and penetrating injury of proximal ureter during ureteral anastomosis were observed in one patient, but this improved after conservative management. No anastomosis revision and wound infections occurred. Delayed graft function was not shown in all RKT cases. The mean serum creatinine level at discharge day was 1.3±0.3mg/dL (0.7-2.1).

Conclusions: The promising results of our experience may promote APOLT as a novel and welomed innovation yielding good surgical outcomes. As the first institution to perform a RKT in Korea, our aim is to evaluate and share our surgical and functional results of RKTs performed in our center.

Methods: This is a retrospective study of all RKTs performed between November 2019 and December 2022 at the Severance Hospital. We analyzed the surgical, functional outcomes and complication rates.

Results: During the aforementioned period, 40 patients successfully underwent RKT from living donor. The mean age was 44.3±11.2 years old and male to female ratio was 26:10. Mean body mass index was 21.9±2.9 kg/m² and KT was performed preemptively in 55.6% of cases. Surgical console time was 212.9±41.6 min (154-327) with vascular anastomoses time 39.9±19.9 min (28-58), median inotropic support time 37±31 min (25-41), and rewarming time 67.3±12.4 min (43-112), and mean estimated blood loss 122.8±82.4cc (50-400). No patient was converted to open transplantation. Subcapsular hematoma and penetrating injury of proximal ureter during ureteral anastomosis were observed in one patient, but this improved after conservative management. No anastomosis revision and wound infections occurred. Delayed graft function was not shown in all RKT cases. The mean serum creatinine level at discharge day was 1.3±0.3mg/dL (0.7-2.1).

Conclusions: RCT with regional hypothermia may be a safe and effective, minimally invasive alternative to open KT, yielding comparable clinical outcomes.

Schematic representation of APOLT with end-to-side duct-to-duct biliary anastomosis.
**BRIEF ORALS**

**INNOVATIONS IN SURGICAL TECHNIQUES**

**BOS16_5**

**LAPDOCTOR: TELL ME HOW DIFFICULT WILL BE MY DONOR. MULTICENTRIC VADATION OF A NEW SCORING SYSTEM THAT ANTICIPATES DIFFICULTY OF LDN**

Glentis Spagnoletti, Francesco Emilii Rossini, Roberto Lezzi, Alessandro Pesce, Maria Paola Salerno, Patrizia Silvestri, Aldo Eugenio Rossini, Lucrezia Furian, Barbara Franchin, Alessandro Giacomoni, Leonardo Centonzé, Marco Spada, Zoe Larghi Lauro, Maurizio Iaria, Carmelo Pulitelli, Jacopo Romagnoli

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**Background:** Living donor nephrectomy (LDN) is a surgical procedure performed on healthy individuals, therefore every effort should be made to increase preoperative surgeon’s awareness of potential technical risks and, as a result, safety. We previously developed and validated a new scoring system for preoperative assessment of LDN (LAPDOCTOR vs. HARP-DN). In order to increase the power of the study we further investigated this aspect in the setting of a prospective, multicentric national study.

**Methods:** Difficulty of LDN was graded by the operating surgeon at the end of the operation on the basis of a scale from 1 to 3 (standard, moderately difficult, very difficult) based on the following 8 parameters: availability of laparoscopic space, difficulties encountered in mobilizing the colon, kidney, gonadal vein, adrenal vessel, gonadal vein, renal artery, ureter. One surgeon per center performed all operations and blindly scored them, one radiologist blindly reviewed all preoperative CT scans. The LAPDOCTOR scores were compared with the degrees of difficulty assigned by the operating surgeon to validate the match rate.

**Results:** Between January 2020 and December 2022 120 living donors from five transplant centres were enrolled in the study. Thirty-two percent (39/120) male, mean age 52 ± 11 yrs, BMI 25 ± 3.7 kg/m². The operations were blindly rated standard (51%), moderately difficult (47%) and very difficult (2%) by the surgeons. LAPDOCTOR showed a 95.8% match with surgeon grade (standard vs 53 vs 51 %, moderately difficult 44 vs 47 %, very difficult 2 vs 2%).

**Conclusions:** LAPDOCTOR allows for an accurate preoperative definition of the level of difficulty of LDN. It could be a very useful tool in the pre-operative risk assessment of living kidney donors, now with a multi-center validation.

**BOS16_6**

**HAND ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY (HARP-DN): LESSONS LEARNED FROM 1001 CASES**

Emin Baris Ak äl, Ala Elcircevi, Ilhami Soykan Barlas, Vural Kirac, Mustafa Erdo, Korcal, Sadik Server, Ayse Sinangil, Alattin Yidiz

1 İstanbul Florence Nightingale Hospital, Kidney Transplantation, Istanbul, Turkey; 2 Demiroğlu Science University, Faculty of Medicine, Istanbul, Turkey

**Background:** Hand assisted retroperitoneoscopic donor nephrectomy (HARP-DN) combines the advantages of manual control with the benefits of retroperitoneal access, and offers direct and quicker approach to the vessels in the renal hilum.

**Methods:** We are presenting our series with 1001 cases performed in between February 2009 and December 2022. Paramedian and Pfannenstiel incisions were used for hand port and two 12 mm trocars were introduced from subxiphoid (camera, stapler) and anterior axillary line (assisting hand).

**Results:** There was no mortality. One donor died 2 months after surgery for unknown reasons. None required switched to open procedure. None of the donors required blood transfusion. There was no major intraoperative complication except one renal artery injury during a left-sided HARP-DN. The most frequent intraoperative complication was major peritoneal opening (232 right, 76 left). There were 13 donors (1.3%) with incisional hernia (13 left, 12 Paramedian, 1 Pfannenstiel). There was no incisional hernia in patients with the right-sided HARP-DN group. 14 patients (2.47 %) had surgical site infection (9 left, 5 right) requiring wound care moreover to antibiotic treatment. There was one Clavien-Dindo Grade 3 complication, a donor required surgery for infection. There were thrombosis of transplanted kidney at 3 cases (2 right). There was no significant difference between the right and left sided kidney recipients regarding graft and patient survival. Death censored 1st and 5th year graft survival was 98.2% and 92.4% respectively. 6 out of 10 patients with ureter stenosis required surgical treatment.

**Conclusions:** HARPDN avoided intraabdominal complications for all cases. Right and left sided donor nephrectomy has similar outcome with HARPDN technique.
**Innovations in surgical techniques**

**BOS16_8 FULL-LEFT/FULL-RIGHT LIVER SPLITTING WITH MIDDLE HEPATIC VEIN AND CAVAL PARTITION AND MACHINE PERFUSION**

**Alessandro Furlanetto**, Enrico Gringeri, Nicola Canitano, Domenico Bassi, Francesco Enrico D'amico, Riccardo Boetto, Andrea Lauterio, Luciano De Carlis, Umberto Cillo

1Department of Surgical, Oncological, and Gastroenterological Sciences, Hepatobiliary Surgery and Liver Transplantation Unit, Padua University Hospital, Padua, Italy, 2ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

**Background:** Split liver transplantation is a useful mean to reduce organ shortage and waiting list mortality, but requires logistical efforts and relevant surgical expertise. We hereby describe a novel technique of full-left/full-right (FLG/FRG) liver splitting, with concomitant splitting and reconstruction of the venous and middle hepatic vein, with the aid of dual arterial and portal hypothermic oxygenated machine perfusion (D-HOPE), in order to reduce cold ischemia (CIT) and ischemia-reperfusion injury.

**Methods:** The donor was a 22-year-old with no comorbidities. The recipient for the FLG was a 7-year-old boy affected by methylmalonic acidemia and chronic kidney disease, requiring liver – kidney transplantation. The FRG went to a 64-year-old woman with HCC on HBV-related cirrhosis. Ex-situ splitting allowed to perform a complete partition of the graft and of its outflow (D-HOPE time), lasting 94 minutes, while the single-vessel perfusion time during reconstruction phases lasted 58 minutes for the FLG (artery only) and 173 minutes for the FRG (portal vein only). Both grafts were implanted with piggy-back technique and termi-nal portal, arterial and biliary anastomosis. The pediatric patient also received sternal sparing. The reported lower rate of sternal complications and better respiratory function was attributed to the clamshell incision. We report the influence of the incision on functional outcomes within one-year follow up and late clinical outcomes.

**Results:** The majority of patients received clamshell incision (CLA 71.5%, n=103; BAT 28.5% n=41). Age was similar between the clamshell (median 36 years) and the bilateral anterolateral thoracotomy (median 39 years, p=0.626), while the former was characterized by higher LAS (median 41.1 vs median 37.9, p=0.019). Both FVC and FEV1 were similar between the two groups before surgery, but they became systematically lower in the clamshell group in the four considered follow-ups (Figure 1). On the contrary, we found no correlation with the onset of chronic rejection.

**Conclusions:** The clamshell incision results in more postoperative lung restrictions compared with bilateral anterolateral thoracotomy and this effect persists throughout the first year. However, of note, this condition does not appear to have an impact on rejection incidence and survival rates.

**Figure 1.**
Background: Much of our understanding of acute rejection in vascularized composite allotransplantation (VCA) is drawn from principles in solid organ transplantation. However, there remains much speculation given the unique immunogenicity of skin and involvement of multiple tissue types. Current studies suggest the implication of T cells in VCA rejection, though the exact molecular mechanisms have not yet been elucidated.

Methods: Single cell RNA sequencing (scRNAseq) was performed on 10 fresh skin biopsies (5 face, 5 hand) from one VCA recipient; 2 were categorized as nonrejection (NR) and 8 as acute rejection (AR) by clinical status. Spatial transcriptomics was performed on 8 FFPE skin biopsies (7 face, 1 hand) from 3 VCA patients; 3 were NR and 5 were AR. Data collection is summarized in Table 1. Analysis and visualization was performed using the Seurat and Monocle3 packages in R.

Results: We identified 13 clusters on scRNAseq corresponding to 14 distinct cell types (Figure 1A). Spatial transcriptomics demonstrated colocalization of macrophages, T cells, and NK cells near the basement membrane during a rejection episode (Figure 1B). We then focused on the T and NK cell cluster, further subsetting these cells by relative expression of key genes in the literature (Figures 1C-D). Specifically, we identified 4 subsets of CD8 T cells: GZMK<sup>−</sup> GZMB<sup>+</sup>, GZMK<sup>+</sup> GZMB<sup>−</sup>, GZMB<sup>−</sup> CX3CR1<sup>+</sup>, and “transitional” CD8 T cells, named for their lack of strongly expressed markers and indistinct clustering. To better understand the dynamic states of CD8 T cells in VCA rejection, we performed trajectory analysis starting at GZMK<sup>−</sup> GZMB<sup>−</sup> T cells, which did not express the exhaustion marker LAG3 or cytotoxic markers. Trajectory analysis revealed a shared path through transitional CD8 T cells which then diverged into 2 distinct endpoints: GZMK<sup>−</sup> GZMB<sup>+</sup> and GZMB<sup>+</sup> CX3CR1<sup>+</sup> cells (Figure 1E).

Conclusions: Our analyses demonstrate colocalization of T cells and macrophages near the basement membrane and the involvement of dynamic CD8 T cell states in VCA rejection. Cytotoxic markers such as GZMB and CX3CR1 are seen, however the role of GZMK<sup>−</sup> GZMB<sup>−</sup>-expressing cells is largely unknown. Future studies aim at clarifying CD8 T cell differentiation and their interaction with other cell types during AR.

Table 1: scRNAseq and Spatial Transcriptomics Sample Collection

<table>
<thead>
<tr>
<th>Site</th>
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**BRIEF ORALS**

**BOS16_11 HAND TRANSPLANTATION AT A TERTIARY CARE CENTRE IN INDIA**

George Kurian1,2, Lakshmi Krishnan1, Rajesh Nair1, Anil Mathew1, Zachariah Paul1, Paul Joy1, Subramania Iyer1, Mohit Sharma1, Jimmy Mathew2, Kishore P3

1Amrita Institute Of Medical Sciences Kochi, Nephrology, Kochi, India, 2Amrita Institute Of Medical Sciences Kochi, Kochi, India

**Background:** To assess the outcomes of 13 hand transplant patients who underwent transplant at Amrita institute of medical sciences, Kochi, India.

**Methods:** This is a retrospective, cross sectional observational analysis of 13 hand transplant patients who underwent hand transplant at Amrita institute of medical sciences, Kochi, India.

**Results:** 13 patients underwent hand transplant from Jan 2015 to Dec 2022. 12 patients received bilateral hand transplant and one unilateral. Average age at transplant was 31 years (24 yrs to 52yrs). The mean follow-up of these patients was 2 yrs. The cause of graft loss was due to electrical burns (n=6); crush injury (n=5) and blast (n=2). All patients were induced with ATG and maintenance immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone. The average cold ischaemia time was 320 minutes for each limb and the average warm ischaemia time was 15 minutes. 8 out of the 13 patients had at least one episode of rejection (all were acute cellular rejection). The average number of rejections was 2.5 episodes. Rejection occurred within the first two months. Most rejections were successfully treated with steroids. One patient alone received IVIG and rituximab for rejection and rejection did not recur. The number of rejections was 2.5 episodes. Rejection occurred within the first two months. Most rejections were successfully treated with steroids. One patient alone received IVIG and rituximab for rejection and rejection did not recur. The cause of graft loss was due to electrical burns (n=6); crush injury (n=5) and blast (n=2). All patients were induced with ATG and maintenance immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone.

**Conclusions:** Hand transplant’s long term functional status remains good. With advances in immunosuppression and treatment for the complications this can be offered to a wider population.

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**BOS16_12 DISCORDANT HISTOLOGICAL FINDINGS DURING ACUTE REJECTION IN A COMBINED FACE AND HAND TRANSPLANT RECIPIENT**

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**Background:** The gold standard for rejection diagnosis following vascularized composite allotransplantation (VCA) is skin biopsies and grading via Banff Classification. As rejection is considered a systemic process, it is classically proposed that clinical and pathologic findings will manifest relatively uniformly across allografts—a principle that underlies the use of sentinel flaps for rejection monitoring. We report discordant histologic findings in a face and bilateral hand transplant recipient monitored with multi-site allograft biopsies during an episode of steroid-refractory acute rejection (AR).

**Methods:** Skin biopsies were taken from both the patient’s facial and hand allografts, at multiple time points over a 5-month period, during which there was ongoing clinical rejection. Dermatohistopathologic assessment and Banff grading were conducted at each time point, with findings evaluated in the context of the patient’s clinical presentation.

**Results:** A total of 20 biopsies were collected at eight separate time points. At four of the eight (50.0%) time points, histopathological assessments revealed a discordance in Banff grade between the facial and hand allografts. At three of four discordant time points, the overall Banff grade was greater in the hand relative to the face. This discordance was driven by higher inflammatory infiltrate sub-scores in the hands.

**Conclusion:** We found discordant histological findings during an episode of AR in a face and bilateral hand transplant recipient. These findings warrant re-evaluation of the utility of the Banff Classification system for rejection diagnosis and clinical decision-making in VCA patients and challenge the value of sentinel flaps as a means for rejection monitoring. Further, these findings revealed differing cross-sectional patterns of inflammatory infiltrates in the face and hand allografts at multiple time points, suggesting that despite the systemic nature of AR, different allograft sites do not appear to be affected uniformly by this process.

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**BOS16_13 DEVELOPMENT OF A SHARED DECISION MAKING CONVERSATION AID FOR VCA**

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**Background:** The decision to proceed, or not, with VCA for face or hand transplant is highly complex. Patients and their caregivers require support in thinking, feeling, and talking their way through this decision. A focus on clinical evaluation does not support this need. Shared decision making (SDM) is a process by which patients, clinicians, and caregivers together work to reach a decision that makes sense intellectually, practically, and emotionally. Conversation SDM aids can enable SDM. Our team is developing an online conversation aid for use by hand transplant patients at home and in conversations with their clinicians.

**Methods:** A user-centered design process was used to develop prototype versions of the conversation aid. These prototypes were informed by IRB-approved: Interviews with: 1. 5 VCA transplant recipients regarding their decision making experience. 10 potentially eligible VCA transplant recipients regarding perceptions and expectations of VCA, 21 VCA clinicians regarding VCA practice and patient evaluation. 2. Review of the medical records of (10) patients evaluated for VCA candidacy at an American Academic Medical Center.

**Results:** Medical (e.g., risks of immunosuppression) and nonmedical (e.g., caregiver willingness, practical barriers to undergoing transplant) issues contribute to VCA decisions. Legacy models of SDM are ill-equipped to account for these range of issue types. Purposeful SDM, a novel theoretical model for SDM, that addresses distinct decisional issue types (pros/cons, intra/interpersonal conflicts, problematic situations, and existential matters), guided prototype development.

**Conclusions:** A prototype online conversation aid has been developed for field testing with patients considering hand transplant (figure).

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**BOS16_14 MULTI-LEVEL ANALYSIS OF THE NEOVASCULARIZATION AND INTEGRATION PROCESS OF A NON-VASCULARIZED RECTUS FASCIA FOLLOWING INTESTINAL TRANSPLANTATION**

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**Background:** Failure to close the abdominal wall after intestinal (ITx) and multi-viseral transplantation (MvTx) remains a challenge, associated with increased morbidity. An attractive method is the use of non-vascularized rectus fascia (NVRF) in which both layers of the abdominal rectus fascia are used as an intial patch without vascular anastomosis. The aim of our study is to provide a multi-level analysis (clinical, radiological, histological, contrast-enhanced microCT (CECT) and immunological) of the neovascularization and integration process based on three cases.

**Methods:** Three patients underwent a NVRF transplantation in combination with an ITx between 09/19-09/22. A retrospective analysis was performed. Ethical approval was obtained (S67453).
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Results: The first patient was a 49-year-old female who received a NVRF during combined liver-ITx. At 1 month, doppler confirmed neovascularization of the graft. At 6mo, at time of continuity surgery, the fascia was macroscopi-
cally integrated. H&E on biopsy confirmed integration of the graft with intense fibrotic reaction without rejection. CD31 showed neovascularisation on the interface with the native fascia. CECT analysis revealed presence of micro-
vasculature enveloping the donor fascia as well as penetrating the graft. Fig: The second patient was a 51-year old male who received a NVRF after MvTx. Two weeks later, during a re-operation the fascia showed macroscopic neovas-
cularization. Since the skin could not be closed, a VAC-system was placed on top of the fascia and secondary closure was obtained. The patient died six months post-transplant from a metastasized mesothelioma. The third patient was a 31-year old male who underwent MvTx. Eleven days post-transplant and after re-operation for intra-abdominal collections, primary closure could not be attained and a non-ABO-matched third party fascia was used. Six days later, anti-A natural and immune antibodies were increased suggesting the presence of de-novo specific antibodies against the third party. Twelve days later, the patient died of a mycotic aneurysm. Conclusions: We showed evidence of the neovascularization and integration, by fibrotic reaction, of donor NVRF.

Figure 1a: sagittal view of CECT, red arrow indicating blood vessels in the NVRF (blue).

Figure 1b: 3-dimensional render of neovascularization.

Background: Kidney allograft rejection can occur in clinically stable patients, but long-term significance in pediatric kTx recipients is unknown. Previous single-center studies demonstrated that subclinical borderline (SC-Borderline) or T-cell mediated rejection (SC-TCMR) are associated with an increased risk of acute rejection. However, the prevalence and significance of subclinical antibody-mediated rejection (SC-AMR) and the impact of subclinical rejection phenotypes on graft survival remained to be assessed.

Methods: We used data from pediatric (<21) patients transplanted between 2005 and 2017 from 8 institutions in France and the United States performing surveillance biopsies. Biopsies were identified as surveillance if they were recorded from the hospital charts.

Results: 1400 surveillance biopsies were performed in 772 kTx recipients including 133 (9.7%) SC-Borderline, 46 (3.3%) SC-TCMR, 54 (3.9%) SC-AMR, 8 (0.6%) subclinical mixte rejections. Subclinical rejection was associated with acute rejection with 5-year rejection-free survival of 86%, 79%, 68% and 61% in the no rejection, SC-borderline, SC-TCMR and SC-AMR groups, respectively (p<0,0001). Treatment of SC-Borderline was associated with a lower incidence of clinical rejection. SC-TCMR and SC-AMR were associated with the development of transplant glomerulopathy, p<0,0001. Subclinical AMR only was associated with a lower 5-year graft survival (79% vs. 93% (SC-TCMR), 95% (SC-Borderline), 94% (no rejection)), p=0.002.

Conclusions: Subclinical rejection is prevalent in pediatric kidney recipients without clinical dysfunction and is associated with acute rejection. Subclinical AMR is associated with the development of transplant glomerulopathy and with an increased risk of allograft failure.

Background: Inborn errors of metabolism (IEM) are a group of inherited diseases that cause morbidity and mortality in childhood. Liver transplantation (LT) is curative treatment in some of them.

Methods: Between 2001-2021, 301 children underwent LT. 40 (13.2%) of them were diagnosed with IEM. Crigler-Najjar syndrome (n=0), PFIC (n=36), and Wilson’s disease (n=37) patients were not included. The data were respectively recorded from the hospital charts.

Results: Forty-two LT were performed in 40 patients (2 re-transplantations). The consanguinity rate was 72.5%. Five deceased and 37 living-related donors were used. Tyrosinemia type-1 (TT1) (n=10), HCC (n=1), tyrosinemia type-2 (TT2) (n=2), phenylketonuria (PKU) (n=1), Wilson’s disease (n=6) patients were not included. The data were respectively recorded from the hospital charts.

Conclusions: In IEM, early diagnosis and liver transplantation increase the survival rate, improve the growth, mental-motor development, and quality of life with normal diet.
**BOS17.3 THE UK KIDNEY DONOR RISK INDEX POORLY PREDICTS LONG-TERM TRANSPLANT SURVIVAL IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS**

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**Background:** The UK Kidney Offering Scheme introduced a Kidney Donor Risk Index (UK-KDRI) to improve the utility of deceased donor kidney allocations. The UK-KDRI was derived using adult donor and recipient data. We assessed the UK-KDRI in the respective paediatric cohort from the UK Transplant Registry.

**Methods:** We performed Cox survival analysis on first kidney-only donation after brain death (DBD) transplants in paediatric (<18 years) recipients from 2000 to 2014. Primary outcome was death-censored renal allograft failure >30 days post-transplant. The main study variable was UK-KDRI derived from seven donor risk-factors, categorised into four groups (D1-low risk, D2, D3 and D4-highest risk). Follow-up ended on 31 December 2021.

**Results:** 35% (319/908) patients experienced renal allograft loss with rejection as the main cause (55%). The majority of paediatric patients received donors from D1 donors (64%). There was an increase in D2-D4 donors during the study period while the level of HLA mismatching improved. The KDRI was not associated with allograft failure. In multi-variate analysis, increasing recipient age [adjusted HR = 1.05 (1.03-1.08) per-year, p < 0.001], recipient minority ethnic group [1.28 (1.01-1.63), p < 0.005], dialysis before transplant [1.38 (1.04-1.81), p < 0.005], increasing donor age [1.01 (1.00-1.01) per-year, p = 0.05], donor height [0.99 (0.98-1.00) per centimetre, p < 0.05] and level of HLA mismatch [Level 3: 1.92 (1.19-3.11), Level 4: 2.40 (1.26-4.58) versus Level 1, p < 0.01] were associated with worse outcome. The level of HLA mismatch modulated the risk within UK-KDRI groups [Figure 1]. Donor hypertensin, smoking, CMV, terminal GFR and cause of death were not statistically significant.

**Conclusions:** Adult donor risk scores were not associated with long-term renal allograft survival in paediatric patients. The level of HLA mismatch had the most profound effect on survival. As prediction models become more complex and are used in organ allocation, we advocate that children and young people should also be included in the model development.

Figure 1: Kaplan-Meier curve of death-censored allograft survival dependent on UK-KDRI (D1 v D2,D3,4) and HLA mismatch level (L1.2 v L3,4).

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**BOS17.4 IMPACT OF ANTI-ENDOTHELIN-1 RECEPTOR TYPE A ANTIBODIES IN PEDIATRIC RENAL TRANSPLANTATION**

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**Background:** Non-HLA antibodies (Ab) against specific allogeneic molecules have been identified as a possible cause of graft damage. The detrimental role of anti-AT1R Ab has been demonstrated both in paediatric and adult renal transplantation. However, the potentially harmful role of anti-endothelin-1 receptor Type A (anti-ETAR) Ab remains speculative.

**Methods:** In a cohort of pediatric renal transplant recipients, anti-AT1R and anti-ETAR Ab were measured pre- and post-transplant for at least 2 years. The influence of anti-AT1R and ETAR Ab on chemotaxis of immune cells was also evaluated. Histological and immunohistochemical analyses were performed on protocol biopsies at 6, 12, and 24 months post-transplantation. The relationship between non-HLA antibodies, antibody-mediated rejection and clinical outcomes has been evaluated.

**Results:** Currently, 169 paediatric kidney recipients have been enrolled. More than 500 sera were evaluated. In this cohort 48,4% and 49% of patients had pre-formed anti-AT1R and anti-AT1R Ab, respectively. At all timepoints, 42,2% and 39,1% of patients were negative for anti-AT1R and anti-AT1R Ab, respectively. Anti-ETAR Ab were significantly associated with anti-AT1R Ab. De novo appearance of anti-ETAR or AT1R Ab was detected in 9,4% and 11,7% of patients, respectively. Preliminary in vitro data suggest a positive correlation between T cell migration and anti-endothelin-1 receptor Type A (anti-ETAR) Ab.

**Conclusions:** Our study demonstrates that anti-ETAR Ab are detectable in half of the paediatric renal transplant recipients. Anti-ETAR Ab are highly associated with anti-AT1R Ab. Preliminary data suggest a role of these antibodies on T cell recruitment. The studies underway are expected to determine the possible role of anti-ETAR Ab on the survival of pediatric renal allografts.

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**BOS17.5 SIMULTANEOUS TOTAL INTERNAL BILIARY DIVERSION IN LIVER TRANSPLANTATION FOR PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 1: A STANDARD OF CARE?**

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**Background:** Post Liver transplant (LT) outcomes in patients with PFIC-1 is relatively poor due to progressive graft steatohapatin and fibrosis, intractable diarrhea & growth failure. A total internal biliary diversion (TIBD) if offered simultaneously with a LT may prevent these adverse events and improve their quality of life.

**Methods:** Children with PFIC-1 who were offered a biliary diversion during LT or in the post-LT period were included in this retrospective analysis. Various pre-LT and intraoperative parameters were looked into (Table 1). In the post-LT period, graft function and complications especially pertaining to PFIC-1 were analysed.

The catch-up growth of these children was also plotted against time.

**Results:** Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT. Of 593 pediatric LT performed in our unit from 2011 – 2022, 11(1.8%) were offered for PFIC-1. Four patients did not undergo a TIBD along with LT.

**Conclusions:** Our study demonstrates that anti-ETAR Ab are detectable in half of the paediatric renal transplant recipients. Anti-ETAR Ab are highly associated with anti-AT1R Ab. Preliminary data suggest a role of these antibodies on T cell recruitment. The studies underway are expected to determine the possible role of anti-ETAR Ab on the survival of pediatric renal allografts.
demonstrated that simultaneous TIBD in patients undergoing LT should be standard practice as it helps dramatically improve outcomes in PFIC-1 patients with normal bladder (p<0.05). The frequency of urological complications was higher in the groups of patients with native dysfunctional bladder and patients with ileal conduit m.Bricker than in the group of patients with native dysfunctional bladder. The highest frequency of clinically significant UTI was in the group of patients with native dysfunctional bladder, lower in group of patient with ileal conduit and the lowest in group of patients transplanted into ileal conduit, however are more often in the group of patients transplanted into ileal conduit, as in no case was related to the ileal conduit.

**Conclusions:** Ileal conduit urinary diversion is good and safe alternative in patients with severe lower urinary tract dysfunction. It is ideal conduit m.Bricker as good as normal bladder?

**BOS17_6**

**HYPOTHERMIC OXYGENATED MACHINE PERFUSION IN PEDIATRIC KIDNEY TRANSPLANTATION: A PRELIMINARY SINGLE CENTER EXPERIENCE**

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**Background:** Hypothermic machine perfusion has become the new gold standard in clinical donor kidney preservation, decreasing risk of delayed graft function (DFG), improving graft survival, thanks to the influence of many different pathways involved in ischemia-reperfusion injury (IRI). To date, low data are available about HMP for kidney transplantation (KTx) in pediatric population.

**Methods:** We report a retrospective analysis of our clinical experience using Hypothermic Oxygenated Machine Perfusion (HOMP) in pediatric KTx recipients. Between November 2019 and September 2022, we performed 83 KTx at our institution. We excluded 26 living donor transplantation and we included 57 KTx comparing 16 HOMP versus 41 static cold storage (SCS).

**Results:** Recipients were predominately of male gender (57.6%) with a median age of 12.2 (1.9-21.4) years. We found similar demographics characteristics (Table 1).

**Conclusions:** With the limitation of a retrospective analysis, our data confirm the safety and the efficacy of the use of HOMP in the pediatric setting: the longer CIT did not reflect on graft survival. Based on our preliminary experience, we can speculate and consider HOMP a useful and safe tool in the management of kidney transplantation also in the pediatric field.

**BOS17_7**

**LIVER RETRANSPLANTATION IN CHILDREN**

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**Background:** Liver retransplantation (re-LT) is the only therapeutic treatment for initial graft failure. The purpose of this project was to investigate indications and evaluate outcomes of paediatric re-LT.

**Methods:** Data of paediatric liver transplant (LT) patients who required re-LT between January 1991 and December 2021 were retrospectively analysed. Demographics, clinical and laboratory findings were collected. For survival evaluations, the Kaplan – Meier estimations and the log rank test were used. Significance was set at p<0.05.

**Results:** A total of 887 liver transplantations were performed. Re-LT constituted 73 procedures (8%), of which 10 were second retransplantations. Sixty-three subjects (39 (62%) female, median age at re-LT 13.9 years; range 0.53 – 25.17) were enrolled. Primary indications for LT were mainly biliary atresia (n=23, 37%) and acute liver failure (n=12, 19%). Liver malignancy was seen in 3 patients (5%). The main causes of initial graft loss were biliary complications (n=13, 20%), primary non-function (n=8, 12%), and death (n=6, 9%). Nineteen patients (30%) experienced an early re-LT (<30 days post primary LT) and in forty-four subjects (70%) a late re-LT was performed. Fifty-six re-LT patients (89%) received the second graft from a deceased donor and in 7 cases (11%) the graft came from a living related donor. Early biliary and vascular complications occurred in 8 (13 %) and 6 (9%) patients, respectively. There were 23 deaths (37%) during the median follow-up of 9.3 years (range: 0-30.2). Seventeen patients died with functioning graft. The highest mortality rates were seen among early re-LT patients (n=8, 42%) and re-LT recipients of the 3rd liver graft (n=6, 51%). Patients’ survival rates at 1, 5, and 10 years post re-LT were 72%, 69% and 66%, respectively, and were inferior when compared with long-term survival post primary LT (92%, 90% and 89%, respectively; p<0.001).

**Conclusions:** Retransplantation accounted for 8% of all LTs. Preliminary data showed inferior survival rates after re-LT. Retransplantation with partial graft from a living related donor offers acceptable outcome. Results of detailed comparative analyses identifying factors of poor prognosis after LT and re-LT are essential for improvement of long-term outcomes.

**BOS17_8**

**KIDNEY TRANSPLANTATION IN PEDIATRIC PATIENTS WITH SEVERE LOWER URINARY TRACT DYSFUNCTION: IS ILEAL CONDUIT M.BRICKER AS GOOD AS NORMAL BLADDER?**

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**Background:** The strategy of kidney transplantation (KTx) in children with lower urinary tract dysfunction demands a choice between using dysfunctional bladder or alternatively urinary diversion to ileal conduit m.Bricker.

The aim of the study was to present the outcome of pediatric KTx into an ileal conduit m.Bricker in comparison with patients transplanted into normal or native dysfunctional bladder.

**Methods:** Between 2000 and 2020 there were 789 KTx performed in our institution in patients <18 years old. We divided them in to 3 groups: 89 KTx into ileal conduit m.Bricker (group I); 165 KTx performed into a native dysfunctional bladder (group II) and 535 KTx into a normal bladder (group III). We analysed graft and patient survivals, frequency of urological complications (leaks, ureteral stenosis, vesicoureinary reflux etc) and clinically significant urinary tract infections (UTI). Clinically significant UTI were defined as those with clinical symptoms (altogether: fever, positive cultures, leucocyturia, graft function deterioration) and recurrent. All statistical calculations were performed in MedCalc v 18 software. The cut-off level of statistical significance was assumed on the level 0.05.

**Results:** Comparison of 1-, 5- and 10 - years graft and patient survival curves in group I, II and III showed no statistical difference (p>0.05). The highest frequency of clinically significant UTI was in the group of patients with native dysfunctional bladder, lower in group of patient with ileal conduit and the lowest in group of patients with normal bladder (p<0.05). The frequency of urological complications was higher in the groups of patients with native dysfunctional bladder and for UTI. Leaks as compared with re-LT and in no case was related to the ileal conduit.

**Conclusions:** Ileal conduit urinary diversion is safe and alternative in comparison with native dysfunctional bladder. Urological complications and UTI, however are more often in the group of patients transplanted into ileal conduit, do not put at risk the functionality of the graft and have no impact on patient’s survival in comparison with a conventional KTx.
Background: Pediatric liver transplantations generally represent advanced surgery for selected patients. In case of acute or chronic graft failure, biliary or vessel complications a retransplantation (reLT) can be necessary. In these situations, massive adhesions, critical patient condition or lack of good vessels for anastomosis can be problematic.

Methods: Between 2008 and 2021, 208 pediatric patients received a liver transplantation in our center. Retrospectively, all cases with at least one retransplantation were identified and stored in a excel database. Indication, intra- and postoperative course and overall survival (OS) were analyzed. Early retransplantation was defined < 1 month, late retransplantation > 1 month after primary transplantation.

Results: Altogether 31 patients (14.9%) were retransplanted. In 22 cases only one retransplantation was done, 8 patients received 2 retransplantations and 1 patient needed a fourth graft. Median age for primary transplantation, first, second and third retransplantation was 14 (range: 1-192 months), 8 patients received 2 retransplantations and 1 patient needed a fourth graft. Median age for primary transplantation, first, second and third retransplantation was 14 (range: 1-192 months), 80.5 (range: 1-246 months), 58.5 (range: 14-131 months) and 67 months, respectively.

While bile duct atresia (42%) and acute liver failure (23%) represented the main indications for the primary liver transplantation, acute and chronic graft failure as good preoperative conditioning are essential for success. But with regard to the excellent survival rates even after multiple retransplantations a further discussion over prioritization of patients needing a first liver transplantation is in our opinion ethically questionable.

Conclusions: Pediatric liver retransplantations can be done safe and with good patient outcome. Nevertheless, a carefully patient and graft selection as well as good preoperative conditioning are essential for success. But with regard to the excellent survival rates even after multiple retransplantations a further discussion over prioritization of patients needing a first liver transplantation is in our opinion ethically questionable.
Background: Kidney transplantation is the gold standard treatment for children with kidney failure. Blood group incompatible (ABOi) kidney transplantation is sometimes used in the paediatric population when a compatible transplant is impossible. The aim of this study is to explore kidney graft outcomes following ABOi kidney transplantation and compare that to blood group compatible (ABOc) transplants following the analysis of the United Network for Organ Sharing (UNOS) database.

Methods: Data were retrieved and analysed on blood group incompatible kidney transplants performed in paediatric recipients (<18 years old) from October 1987 until September 2020, from the UNOS database. Statistical analysis was performed using SPSS v28.

Results: There were 23888 ABOc kidney transplants (F=9777, median age 12, IQR 7-15) and 73 ABOi kidney transplants (F=29, median age 14, IQR 9-16) during the study period. The blood groups of those who had an ABOc transplant were, blood group A=10, B=19 and O=44. There were 5 cases of delayed graft function in the ABOi group and 2132 in the ABOc group (p=0.682). There was no graft thrombosis in the ABOc group (p=0.652). There was one case of primary non-function in the ABOi group and 254 in the ABOc group (p=0.543). The median creatinine at discharge following ABOi transplantation was 0.89 mg/dL (IQR 0.6-1.30) whereas the median creatinine following ABOc transplants was 0.90 mg/dL (IQR 0.6-1.42), whereas the median creatinine at discharge following ABOi transplantation was 0.89 mg/dL (IQR 0.6-1.30) [p=0.551]. Kaplan-Meier Survival analysis showed no significant difference between the ABOc and ABOi transplants (Log Rank of <0.487).

Conclusions: In this large comparative study, kidney graft outcomes after ABOi transplantation in children were similar to those after ABOc transplantation. Despite the limitations of large database analysis, this outcome is reassuring when balancing whether to proceed to a blood group incompatible transplantation or not, when other options are limited.

Figure 1: Discrimination (Concordance Harrel’s C-index) of the iBox risk score to predict long-term kidney allograft failure in children with kidney allograft failure in the pediatric population from 1 to 10 years after kidney allograft transplantation.
Background: During the last decade, in Greece, a significant decline in pediatric renal transplantations has occurred, resulting in a prolonged time on dialysis or forcing children to travel abroad to be transplanted. In an effort to bridge this transplant gap, on November 2019, an experienced adult transplant center formed the basis of a pediatric renal transplant program. Methods: We studied the pediatric renal transplant activity of our joint transplant program between November 2019 and December 2022 and reported patients’ characteristics and transplantations’ outcomes. Results: Between November 2019 and December 2022, 24 patients <18 years underwent kidney transplantation in our joint transplant center. Median age of patients was 15 years (IQR 3), while 75% (18/24) were male. Body weight ranged from 29 to 38 kg for patients 10-12 years old (5/24, 21%), 28-58 kg for patients 16-18 years old (9/24, 37%). Living donor transplantations accounted for 19/24 cases (79%), five of which were preemptive. Median time on renal replacement therapy was 78 months (IQR 90). Five of 24 (21%) transplantations were ABO and/or HLA incompatible. There were no major surgical complications, except one hemoptysis, which resolved without sequelae. Acute rejection episodes occurred in 4 patients and were all treated successfully with no impact on renal function. Median hospitalization time was 12 days (IQR 6). At a median follow up of 22.5 months (IQR 11), median eGFR was 56.5 ml/min (IQR 28.8). Between November 2019 and December 2022, 30 pediatric renal transplantations were performed in our country, with our joint transplant center undertaking 80% of them (24/30), thereby increasing the number of pediatric kidney transplantations by 76% compared to the preceding period (January 2016 - October 2019), when only 17 transplantations were performed. Conclusions: The implementation of a pediatric kidney transplantation program in the setting of an experienced adult transplant center, with the collaboration of pediatric transplant physicians, is safe and may result in a significant increase in pediatric kidney transplantations.

References:
1. National & Kapodistrian University of Athens, Medical School, Laiko General Hospital, Athens, Greece, Department of Nephrology and Renal Transplantation, Athens, Greece, “P & A. Kyriakou” Children’s Hospital, Athens, Greece, Department of Nephrology, Athens, Greece, “Medical School National & Kapodistrian University of Athens, Laiko Hospital, Department of Nephrology and Renal Transplantation, Athens, Greece, “Medical School National & Kapodistrian University of Athens, Athens, Greece, “P & A. Kyriakou” Children’s Hospital, Athens, Greece, Department of Anesthesiology, Athens, Greece, “Laiko General Hospital of Athens, Department of Anesthesiology, Athens, Greece, “Laiko General Hospital of Athens, Transplantation Unit, Athens, Greece

Figure 2: Calibration plots at three, five, seven and ten years of the Bob system in the pediatric validation cohort.

BRIEF ORALS
Paediatric Transplantation - Stronger Together

BOS17_14
FIRST REPORT ON THE USE OF A TRANSPLANTED RECTUS SHEATH FASCIA FOR A COMBINED LIVER AND KIDNEY TRANSPLANT IN A PAEDIATRIC PATIENT WITH MMA

Alicia Faessler1*, Miriam Cortes Cerisuelo2, Wajid Jassim2, Hector Vica-Melendez2, Akash Deep2, Vandana Jain2, Andrew Pool2, Stephanie Grunewald2, Judith Van der Voort2, Nicos Kessaris2, Jelena Stojanovic2
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Background: As medicine is advancing, more complex children are becoming multi-organ transplant candidates, bringing new challenges in all aspects of their care. We describe the first case of a small child receiving a combined liver and kidney transplant (CLKT) and an abdominal rectus sheath fascia transplant on a background of Williams Syndrome and Methylmalonic Acidemia (MMA).

Methods: A 3 year old with MMA, and a weight of 12.5 kg, was listed for CLKT. There were many anaesthetic, medical, metabolic and surgical challenges to consider. Pre-operative planning included close collaboration between 9 specialties in 4 hospitals. A long general anaesthetic increased the risk of cardiac complications and metabolic decompensation given the patient’s metabolic background. Gaining an in-depth understanding of the metabolic state of the patient pre- and peri-operatively was crucial in avoiding metabolic decompensation. Hour by hour management protocol was drafted to facilitate transplant and included five domains: 1. Management at the time of organ offer, 2. Before the admission, 3. At admission and before theatre time, 4. Intra-operative management and 5. Post-operative management in the first 24 hours.

Results: The patient’s post-transplant recovery was complicated by sepsis, transient CNI toxicity, de-novo DSAs and difficulty in achieving abdominal closure due to the patient’s small size and organ size mis-match. To achieve abdominal closure, the patient received an abdominal rectus sheath fascia transplant, which to our knowledge, was the first case for this indication. Through a MDT approach and detailed pre-operative planning, a good outcome was achieved and 18 months post-transplant the child has good kidney and stable liver function, no transplant-related complications, improved growth and neurodevelopment, and an excellent quality of life as reported by the parents. This peri-transplant protocol was used for all other patients with MMA we transplanted with excellent outcomes.

Conclusions: Rectus sheath fascia transplant for abdominal closure following CLKT can lead to good results. Using our experience of this complex case and other transplanted MMA patients, and thorough literature review, we recommend MDT approach and propose an hour by hour peri-operative management pathway for MMA patients.

References:
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Background: The prevalence of end stage heart failure and patients that could benefit from heart transplantation requires expansion of the donor pool, relying on the transplant community to continually re-evaluate and expand the use of marginal donor organs. Introduction of new technologies such as the Parag- oxin SherpaPak Cardiac Transport System (CTS) aids in this shift. We seek to analyse the impact of the CTS system on recipient outcomes who receive extended criteria organs in the GUARDIAN Heart Registry.

Methods: Between October 2015-August 2022, 761 adults from 9 US centers receiving donor hearts utilizing either CTS (N=419) or conventional ice storage (ICE, N=342) were analysed from the GUARDIAN Heart registry using summary statistics. A modified EXPAND OCS Trial criteria was used to delineate cohorts of extended criteria donors, which included 176 CTS and 132 ICE (see Table).

Results: Forty percent of the total US donors in the registry population met the extended criteria definition. There were few baseline differences among recipients in the 2 cohorts, most notably both distances travelled, and total ischemic time was significantly greater in CTS, and significantly more donor hearts in the CTS cohort had >4 hours total ischemia time, although baseline VAD was similar.

Conclusions: This subgroup analysis demonstrates that SherpaPak CTS can be safely used to utilize extended criteria donors, with low severe PGD rates. This is encouraging toward use of extended criteria donors in European transplant programs, though further clinical evaluation in Europe is warranted.

Table:

<table>
<thead>
<tr>
<th>ICE</th>
<th>CTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 132</td>
<td>n = 176</td>
</tr>
<tr>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Donor inclusion Criteria</td>
<td></td>
</tr>
<tr>
<td>&gt;3h Total Ischemic Time</td>
<td>66 / 132 (50.0%)</td>
</tr>
<tr>
<td>&gt;2h Total Ischemic Time AND</td>
<td>66 / 132 (50.0%)</td>
</tr>
<tr>
<td>LVF at baseline (%)</td>
<td>23.0 ± 13.7</td>
</tr>
<tr>
<td>Implantable VAD</td>
<td>63 / 132 (48.0%)</td>
</tr>
<tr>
<td>Temporizing IABP</td>
<td>27 / 132 (20.5%)</td>
</tr>
<tr>
<td>Temporary ECMO/VAD</td>
<td>10 / 132 (7.6%)</td>
</tr>
<tr>
<td>Match Characteristics</td>
<td></td>
</tr>
<tr>
<td>Value of Match</td>
<td>56 / 132 (12.3%)</td>
</tr>
<tr>
<td>PHM Mimatch</td>
<td>0.0 ± 0.2</td>
</tr>
<tr>
<td>Distance to Organ (nautical miles)</td>
<td>396.8 ± 295.1</td>
</tr>
<tr>
<td>Total Ischemic Time (minutes)</td>
<td>251.8 ± 155.7</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>All center MCS</td>
<td>48 / 132 (36.4%)</td>
</tr>
<tr>
<td>New IABP Post Tx</td>
<td>18 / 132 (13.6%)</td>
</tr>
<tr>
<td>New ECMO/VAD Post Tx</td>
<td>2 / 132 (1.5%)</td>
</tr>
<tr>
<td>Cardioversion</td>
<td>16 / 132 (12.2%)</td>
</tr>
<tr>
<td>PGD</td>
<td>3 / 132 (2.2%)</td>
</tr>
<tr>
<td>PGD Severe</td>
<td>18 / 132 (13.6%)</td>
</tr>
<tr>
<td>LVF at 4hths</td>
<td>53.1 ± 13.4</td>
</tr>
<tr>
<td>30-day Survival</td>
<td>127 / 132 (96.9%)</td>
</tr>
<tr>
<td>In-hospital Survival</td>
<td>127 / 132 (97.4%)</td>
</tr>
<tr>
<td>1-year Survival</td>
<td>127 / 132 (97.0%)</td>
</tr>
</tbody>
</table>

Conclusions: This analysis substantiates the 2014 definition of severe PGD as a clear risk factor for reduced 1 year survival. The separation of the curves continues to widen beyond the first 30 days post-transplant, continuing through 6 months and even 1 year, suggesting that severe PGD is an initial insult that initiates a sequela of complications. This mechanism warrants further investigation.

Figure: Kaplan-Meier 1-Year Survival Analysis of Thoracic Heart Transplantation after PGD.

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Background: The role of basophils in cardiac allograft rejection is poorly understood. An animal model described the infiltration of basophils in allografts from day 10 to day 20 after heart transplantation (HTx). Anti-thymocyte globulin (aTg) used as induction therapy contains antibodies to antigens expressed by many immune cell subsets, including basophils. While lymphodepletion is considered a therapeutic effect, a decrease in basophil count after administration of aTg has unknown clinical significance. The aim of this study was to investigate an association between basophil count following aTg induction and the development of acute cellular-mediated rejection (ACR) during 1-year follow-up.

Methods: We performed a retrospective single-centre study in HTx patients transplanted between 2010 and 2020. All patients received aTg induction therapy for 5 days. A total of 182 patients were transplanted. During the 12-month follow-up period, 17% of patients had ACR. Both ALC and basophil counts decreased after aTg. Patients with ACR ≥1B had significantly higher median basophil count following aTg induction and the development of acute cellular rejection (ACR) during 1-year follow-up.

Results: A total of 182 patients were transplanted. During the 12-month follow-up period, 17% of patients had ACR. Both ALC and basophil counts decreased after aTg. Patients with ACR ≥1B had significantly higher median basophil count following aTg induction and the development of acute cellular rejection (ACR) during 1-year follow-up.

Conclusions: Lower basophil count after anti-thymocyte globulin induction is associated with a lower incidence of cardiac allograft rejection. This coincides with the timing of basophil infiltration of heart allograft reported in an animal model and indicates the potential contribution of basophils in shaping alloimmune response during the early post-transplant period.
Background: Monitoring allograft rejection and adverse events are crucial after heart transplantation (HTx). The ISHLT guidelines for the care of HTx recipients have included non-invasive surveillance such as testing for donor-derived cell-free DNA (dd-cfDNA). While major studies have been conducted with patient cohorts and centralised testing in the USA, here we explored a European two-site cohort where dd-cfDNA was quantified at local centres by next generation sequencing-based CE-marked assay. We aimed to assess feasibility of assay and evaluate dd-cfDNA values in clinically stable HTx recipients.

Methods: This cross-sectional study in 2 European HTx centres included 50 patients at their scheduled visits. By drawing whole blood into blood collection tubes (Streck), dd-cfDNA fraction in plasma was analysed using AlloSeq cfDNA assay (CareDx). For analysis, clinical stability was defined as asymptomatic patients >28 days post-HTx with normal graft function, without CMV infection, history of rejection, or graft vasculopathy.

Results: Demographic and clinical data are shown in the table. Out of 82 clinical visits, 34 were excluded as they did not meet stability criteria. Median dd-cfDNA value of stable patients was 0.11% (95% CI 0.08%–0.13%), and dd-cfDNA value of 0.20% was exceeded in only 3 visits.

Conclusions: dd-cfDNA testing for donor-derived cell-free DNA is a feasible and non-invasive tool for surveillance in clinically stable HTx recipients.
Background: In advanced heart failure patients, left ventricular assist devices (LVAD) are the optimal treatment option as bridge-to-transplantation. What is the outcome of LVAD use in a low organ donor environment? 

Methods: 60 heart failure patients who underwent LVAD implantation as bridge-to-transplantation were included in the study. The patient characteristics and outcomes of those who managed to reach heart transplantation (HTx) group were compared with those (noHTx group) who did not in a 5-year period after LVAD implantation.

Results: 26 out of 60 patients underwent heart transplantation. The transplantation was performed 691 ± 538 days after LVAD implantation. 5-year survival rates were 70% for the HTx group and 21% for the noHTx group. Patients of the noHTx group were supported with intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) at a higher percentage compared to the HTx group (65% vs. 35%, p=0.02) and had a lower cardiac index (1.6 ± 0.3 L/min/m² vs. 1.9 ± 0.6 L/min/m², p=0.02) at the time of LVAD implantation. Cox proportional hazard regression analysis with time to transplantation as a varying covariate showed that heart transplantation did not have any survival benefit for the follow-up period (CI=0.6 ± 6.2, p=0.263). 5-year survival rate of the transplanted patients was 70%.

Conclusions: LVAD supported patients who did not undergo heart transplantation had a more severe clinical condition at the time of device implantation along with increased mortality during the early post-operative period compared to those who did achieve heart transplantation. Future improvements of the technical characteristics of LVADs is expected to provide additional benefits in low organ donor environment.
**MODERATED POSTER**

**Moderated poster session on infections complications in kidney transplantation**

**MPS2_1**

**BKEVER STUDY: BKV CLEARANCE IN KIDNEY TRANSPLANT RECIPIENTS AFTER REPLACEMENT OF MMF BY EVEROLIMUS AND REDUCTION OF IMMUNOSUPPRESSION**

Sophie Caillard1, Dominique Bertrand2, Malte Jauregy3, Dany Anglicheau4, Laure Ecotiere5, Matthias Buchler6, Nicolas Bouvier7, Betouli Schwartz8, Jean-Philippe Rerolle9, Anne Elisabeth Heng10, Lionel Couzi11, Agnès Duveau12, Emmanuel Morelon13, Yannick Le Meur14, Leonard Golbin15, Eric Thervet16, Ilias Benotmane17, Samira Fat Kremmer18

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**Background:** BK virus nephropathy, a consequence of intense immunosuppression, remains a major problem after kidney transplantation. In this context, developing strategies to avoid BKV nephropathy is currently a major challenge. mTor inhibitors are immunosuppressive drugs which have shown anti-viral effects. Previous non randomized studies suggested an inhibitory role of mTor inhibitors on the proliferation of BK Virus. The aim of our study was to evaluate the effect of everolimus on BKV clearance compared to a simple reduction of immunosuppression in kidney transplant patients who develop a BKV viremia.

**Methods:** we conducted a French randomized multicenter study including 130 patients at the time of apparition of BK viremia. In 65 patients (experimental group), MMF was replaced by everolimus concurrently with a calcineurin inhibitors decrease, whereas in 65 patients, MMF was decreased by 50% (control group). The primary endpoint was the percentage of patients achieving a viral clearance at 6 months and secondary endpoints included BKV replication kinetics, incidence of BKV nephropathy, graft function, incidence of rejection, and tolerance within 2 years after randomization.

**Results:** patients were comparable at baseline within both groups. At 6 months, BKV viral clearance was 56% in the experimental group vs 81% in the control group (p=0.002). The decrease of BK viral load was more rapid in the control group (p=0.001). Trough levels of calcineurin inhibitors were not different between both groups from randomization to month 6 and were in the expected targets. Two grafts were lost throughout the study (one in both group, one from pyelonephritis and one due to rejection). Nine patients developed a proven biopsy BKV nephropathy in the experimental group and 8 in the control group. There was no difference in rejection episodes or de novo donor specific antibodies occurrence between both groups.

**Conclusions:** in this randomized study, replacing MMF by everolimus together with reduction of CNI targets in the same levels was not associated with a more frequent clearance of BK virus at 6 months. Another (preventive ?) strategies should be identified to avoid BK nephropathy in kidney transplant recipients.

**MPS2_2**

**OUTCOME OF KIDNEY TRANSPLANTS FROM VIREMIC AND NON-VIREMIC HEPATITIS C VIRUS POSITIVE DONORS INTO NEGATIVE RECIPIENTS: RESULTS OF THE SPANISH REGISTRY**

Antonio Franco1, Francesc Moreso2, Patricio Mñas Serrano3, Marta Crespo4, Nuria Esforzado5, Asunción Sancho6, Javier Paul7

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**Background:** Hepatitis C virus (HCV) positive kidney donors offer acceptable results. However, in Spain, only 24 out of 43 adult renal transplant units accept kidneys obtained from HCV non-viremic donors and 9 from HCV viremic donors. The aim of this study is to compare patient and graft outcome in recipients from HCV non-viremic and viremic donors.

**Methods:** This is an observational, multicenter, prospective study including all kidney transplants from HCV positive donors into negative recipients reported to the Spanish registry from May 2013 to December 2021. Viral RNA in donor was performed with the Xpert HVC viral load quantitative assay (Cepheid). Recipients from viremic donors received peri-transplant treatment with glecaprevir and pibrentasvir for 8-12 weeks. Donor and recipient age and gender, panel reactive antibodies, HLA mismatch, recipient weight, cold ischemia and the percentage of induction treatment, retransplant recipients, asistolic donors were similar in both groups.

**Results:** We included 116 renal recipients, 75 from 44 non-viremic HCV positive donors and 41 from 25 viremic donors. Primary non function, delayed graft function, acute rejection rate and renal function at the end of follow up were not different between groups. None of the recipients from non-viremic donors (75%) or from viremic donors receiving treatment before transplant (26%) developed viremia but recipients from viremic donors starting treatment after transplantation (n=15) showed viremia in all cases. All recipients from viremic donors had a negative HCV viral load at 14 days and at 12 weeks after transplant. All patients from viremic donors completed treatment with glecaprevir and pibrentasvir without reported adverse events or treatment interruptions. HCV seroconversion was more frequent in recipients from viremic donors (80.0% vs. 16.4%, p=0.001). Patient and graft survival were not different between recipients from viremic (1) and non-viremic donors (2).

**Conclusions:** Donor HCV viremia is not a risk factor for kidney transplant recipients receiving direct-acting antiviral agents in the peri-transplant period but viremia can only be avoided if treatment starts before transplantation.

<table>
<thead>
<tr>
<th>Patient survival at 12 and 24 months</th>
<th>Graft survival at 12 and 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.3% 93.3%(1)</td>
<td>84.7% 80.0%</td>
</tr>
<tr>
<td>94.4% 92.9%(2)</td>
<td>90.7% 83.7%</td>
</tr>
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<td>0.65</td>
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</tbody>
</table>
**MODERATED POSTER**
Moderated poster session on infections complications in kidney transplantation

### MPS2_3 LATE OPPORTUNISTIC INFECTIONS AFTER KIDNEY TRANSPLANTATION IN THE ERA OF CONTEMPORARY IMMUNOSUPPRESSION: ROOM FOR IMPROVEMENT

**Background:** Opportunistic infections (OI) remain a major concern after kidney transplantation (KT). While antimicrobial prophylaxis during the first-year post KT is well codified, focus on late OI is scarce but would prove helpful for preventive strategies. We performed a single-center retrospective cohort study over a ten-year period to describe time-dependent OI after KT.

**Methods:** We defined three groups of patients: (i) late OI occurring beyond the first-year after KT, (ii) early OI within the first-year after KT and (iii) control group without OI surviving at least one year after KT. Primary endpoints were patient and allograft survival. Secondary endpoints were late and early OI description and comparison.

**Results:** One-hundred-eighty-five KT recipients developed at least one OI episode within 21 (8-45) months after KT. Among those, 120 were late (64.9%) and 65 early (35.1%) OI. Three-year patient survival was similar between the late and early OI groups (78.7% and 74.5%, p=0.6, respectively), as was three-year allograft survival (84.3% and 85.2%, p=0.99, respectively). Patient and allograft survival rates were also similar between late OI and control groups (Figure 1). Viruses were the leading cause of OI (65.4%) including mostly zoster in late OI (43.4%) and BK virus nephropathy in early OI (31.6%) (Table 1). Fungal infections were the second cause of OI (23.2%). Pneumocystis was significantly more frequent among late OI (n=12 versus 0, p=0.012), while aspergillosis was significantly predominant among early OI (n=10 versus 3, p=0.01) (Table 1). Old age was significantly associated with early OI (OR 0.97 [95% CI 0.94-0.99], p=0.009) and the sole independent factor associated with mortality.

**Conclusions:** Our results suggest that the period at risk for OI spans beyond the first-year post-transplantation. We did not find significant deleterious effect of late and early OI on patient and allograft survival. Late OI mostly included zoster and pneumocystis, while BK virus nephropathy and aspergillosis were predominant among early OI. Pretransplant screening of aspergillosis, systemic zoster vaccination and life-long pneumocystis prophylaxis should be considered to prevent OI after KT.

### MPS2_4 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE MULTICENTER NATIONWIDE COHORT STUDY

**Background:** Progressive multifocal leukoencephalopathy (PML) is a rare, serious, opportunistic infectious disease caused by JC virus, which usually leads to death in less than a year. Whether PML frequently occurs in kidney transplant recipients is unclear. Belatacept is an analogue of human immunoglobulin CTLA4, used as an immunosuppressive therapy in kidney transplant. In comparison with calcineurin inhibitors, belatacept is associated with an increased risk in some opportunistic infections such as CMV-associated disease, but the relationship between belatacept and PML is unclear. In this study, we aim to estimate incidence of PML in kidney transplant recipients and to identify a possible association between belatacept and PML.

**Methods:** We performed a retrospective, multicentric, national study. We contacted all transplantation centres in the country to retrieve cases of PML. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR (cerebrospinal fluid and/or stereotactic brain biopsy).

**Results:** Between 2006 et 2020, 50 160 kidney grafts were performed. We retrieved the number of grafts performed nationwide using registries from regulatory agencies. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR. Between 2006 et 2020, 50 160 kidney grafts were performed. We retrieved the number of grafts performed nationwide using registries from regulatory agencies. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR. Between 2006 et 2020, 50 160 kidney grafts were performed. We retrieved the number of grafts performed nationwide using registries from regulatory agencies. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR. Between 2006 et 2020, 50 160 kidney grafts were performed. We retrieved the number of grafts performed nationwide using registries from regulatory agencies. We included all patients with neurological symptoms, findings consistent with PML on brain imaging, and at least one positive result for JC virus PCR.
**MPS2_6**

**COMPASSIONATE USE PROGRAMME OF MARIBAVIR FOR ADULT PATIENTS WITH POST-TRANSPLANT REFRACTORY CMV INFECTION**

**Methods:**

**Background:** Maribavir is a benzimidazole riboside that inhibits human CMV replication. Its European indication is “Treatment of adults with post-transplant CMV infection and/or disease who are refractory (with or without resistance) to one or more prior therapy.”

**Methods:** In France, patients were treated with maribavir prior to the European marketing authorization approval, through the compassionate use programme (CUP). To be part of the CUP, patients had to fulfill the eligibility criteria (aligned with the pivotal study inclusion criteria (NCT02931539)) according to the protocol approved by the French health authority. An amendment to this protocol broadened the inclusion criteria in February 2022, with less stringent hematological and renal function cut-off values. The CUP data (from November 3, 2021 to September 30, 2022) at baseline (treatment access request or initiation visit) were analyzed using descriptive statistics to describe patient characteristics, maribavir use, effectiveness and safety data.

**Results:** The analyses were based on 47 patients with a completed treatment initiation study form. At access request, the median age was 58.6 years (range: 23.9 - 88.9). The majority had a solid organ transplant (n=40, 85.1%), mostly kidney transplant (n=35, 75.0%). The proportion of patients with severe renal impairment at baseline (i.e. creatinine clearance ≤ 30 mL/min/1.73²) was 14.9% (n=7). Resistance testing was performed for 44 (93.6%) patients, 30 (68%) of them had an identified mutation. The most frequently identified mutation was UL97, indicating a resistance to ganciclovir/valganciclovir in 23 (76.7%) cases. There were 12 (40%) mutations in the UL54 gene, indicating multidrug resistance to available antivirals.

**Conclusions:** A considerable effort from 41 French hospitals was undertaken to collect data from patients who enrolled the maribavir CUP in France, resulting in a high data completeness above 95%. In the CUP population compared with the pivotal study maribavir cohort, we observed a higher proportion of patients with SOT and identified antiviral resistance to conventional agent at baseline. Future analysis on effectiveness should provide further data.

**MPS2_8**

**KIDNEY TRANSPLANTATION FROM DECEASED DONORS WITH BACTEREMIA**

**Methods:** A retrospective study that included all deceased donor recipients who underwent kidney transplantation between 1/2008 and 12/2021. A total of 102 of 614 recipients (49 male) with a median age of 52[43.5-58] years received a kidney transplant from 82 deceased donors, (45 men), with a median age of 55[46-61] years, with positive blood cultures at the time of organ procurement.

**Results:** The isolated pathogens were Gram-positive bacteria (64.6%), most frequently coagulase-negative staphylococcus, followed by Gram-negative bacteria (19.5%), and fungi 2.5%. Multidrug-resistant (MDR) drug-resistant (XDR) bacteria were observed in 18/82 (22%) of donors. Among 10/18 Gram-negative MDR/XDR isolates, Acinetobacter baumannii was the most common, followed by Klebsiella pneumonia. Two out of the 18 donors had bacteraemia caused by Enterococcus faecium and Staph. aureus, respectively. Six out of 18 donors had positive blood cultures for gram(-)gram(+) MDR bacteria. Early appropriate treatment was administered to 62/82 (76.5%) donors for a median of 5 [4-7] days before organ procurement. All recipients received targeted antibiotic therapy starting pre-operatively in 64/102 (62.7%) patients, whereas 38/102 (37.2%) treatment started post transplantation (median of 4 [3-13] days post transplantation). No evidence of donor pathogen transmission to any recipient was noticed. Delayed graft function occurred in 28/275 (10%) recipients. Patient and graft survival rates over 1-year were 95% and 93.1%, respectively.

**Conclusions:** Kidney transplantation from deceased donors with bloodstream infection is considered safe as long as the pathogen/infected agent is known, provided that recipients receive appropriate antibiotic therapy. It is preferable that targeted treatment be administered to the donor as well.

**MPS2_9**

**ADVANTAGES OF MONITORING CELLULAR IMMUNE RESPONSE AGAINST CYTOMEGALOVIRUS IN RENAL TRANSPLANTATION**

**Methods:** A prospective, observational study was conducted including all patients who underwent renal transplantation at our center between January 2021 and August 2022. These patients were tested for CMV reactivity using QF-CMV test. The aim of the study was to compare prophylaxis duration, the percentage of patients with CMV replication and the kind and duration of treatment of these patients (valganciclovir or IV ganciclovir) depending on the CMV status.

**Results:** 112 kidney transplant patients were included. 68.5% of those (N=74) were QF-CMV reactive; 31.5% (N=34) were QF-CMV non-reactive and 4 patients were QF-CMV indeterminate. The CFM-CMV reactive group was compared to the non-reactive group. There were no differences between the two groups in the variables analyzed at baseline. The QF-CMV reactive group had a CMV infection rate of 17.6% compared to 14.7% in the non-reactive group (p=0.73). Prophylaxis duration was shorter in QF-CMV reactive patients than QF-CMV non-reactive (66 days vs. 85 days for QF-CMV non-reactive, P=0.01). There were no differences in requirement for IV ganciclovir treatment (3 QF-CMV reactive patients vs. 1 QF-CMV non-reactive, P=0.08) or in CMV infection treatment duration (mean 19 days in QF-CMV reactive vs. 13 days in QF-CMV non-reactive, P=0.46).

**Conclusions:** QF-CMV allows for individualized CMV prophylaxis duration, shortening it in QF-CMV reactive patients without increasing the risk of infection or disease. This would reduce the side effects associated with valganciclovir use and lower drug costs.
LONG-TERM IMMUNE DYSREGULATION AFTER RITUXIMAB INDUCTION IN ABO INCOMPATIBLE LIVING-DONOR RENAL TRANSPLANTATION – IMPACT ON CHRONIC BK VIRUS INFECTION

Rolf Weimer*, Hristos Karakizlis1, Fabrice Renner1, Hartmut Dietrich1, Volker Daniel2, Caner Süssal2, Christian Schützler1, Daniel Kämper1, Dominik Leicht1, Michael Wörlen1, Lene Remmer1, Katrin Milchsack1, Hermann-Josef Gröne1, Winfried Padberg6, Gerhard Opelz2

1University of Giessen, Department of Internal Medicine, Giessen, Germany, 2University of Heidelberg, Institute of Immunology , Heidelberg, Germany, 3Köy University, Transplant Immunology Research Center of Excellence, Istanbul, Turkey, 4University of Giessen, Institute of Medical Virology, Giessen, Germany, 5German Cancer Research Center, Heidelberg, Germany, 6University of Giessen, Department of Surgery, Giessen, Germany

Background: We previously described a key role of IL-10 in chronic BK virus infection after renal transplantation. As an increased frequency of BK viremia has been reported after ABOi renal transplantation, we analyzed clinically relevant immune parameters in a prospective renal transplant study up to 5 years posttransplant.

Methods: Mononuclear cell subsets (peripheral blood; regional lymph nodes; protocol biopsies (n=58, 3 months; n=34, 1 year)), intracellular cytokine and in-vitro B cell responses were assessed up to 5 years posttransplant in 85 renal transplant recipients (living donation: n=25 ABO incompatible (ABOi; with rituximab induction) and n=30 ABO compatible (ABOc); deceased donation (DD): n=30, ABO compatible).

Results: The incidence of BK viremia was significantly enhanced in rituximab versus non-rituximab treated patients (P=0.009, 1 year; P=0.029, 5 years). Whereas intracellular IL-10 production was not increased in ABOi patients, IL-10R expression on monocytes was enhanced at 3 months (P=0.009 vs. DD, P=0.037 vs. ABOc) and 5 years (P=0.015 vs. ABOc). Cell subset analysis in protocol biopsies showed rituximab-induced B cell depletion in ABOi patients at 3 months (P<0.001 vs. ABOi and DD), but comparable B cell counts and even enhanced counts of CD3+ T cells (P=0.041), CD68+ macrophages (P=0.021) and CD138+ plasma cells (P=0.033) at 1 year. After rituximab induction in ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years together with impaired B cell responses for 2 years (P=0.010, T-dependent; P=0.053, T-independent). T cell counts were lower in ABOi versus ABOc recipients up to 6 months (CD4+ T cells, 6 months P=0.046; CD8+ T cells, 3 months P=0.011). In regional lymph nodes of ABOi patients, we found a significant rituximab-induced downregulation of CD3+ T cells (P=0.041), CD68+ macrophages (P=0.021) and CD138+ plasma cells (P=0.033) at 1 year. After rituximab induction in ABOi recipients, peripheral blood B cell subsets were profoundly downregulated for at least 3 years together with impaired B cell responses for 2 years (P=0.010, T-dependent; P=0.053, T-independent). T cell counts were lower in ABOi versus ABOc recipients up to 6 months (CD4+ T cells, 6 months P=0.046; CD8+ T cells, 3 months P=0.011). In regional lymph nodes of ABOi patients, we found a significant rituximab-induced downregulation of CD20+ B cells (P<0.0005), of naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation.

Conclusions: An increased frequency of BK viremia in rituximab-treated renal transplant recipients may be explained by increased IL-10R expression, downregulated CD4+ and CD8+ T cell counts, a profoundly delayed B cell repopulation together with compromised B cell responses and compromised antigen presentation due to B cell depletion in the graft and regional lymph nodes.
Background: Immunosuppressed patients show an impaired vaccine response and remain at high risk of severe COVID-19, despite full vaccination. Neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 have been developed for prophylaxis and treatment. No data are available regarding the safety and efficacy of the combination tixagevimab/cilgavimab used as pre-exposure prophylaxis (PrEP) of COVID-19 in kidney transplant recipients (KTRs) during Omicron period.

Methods: Between March 1, 2022, and October 3, 2022, we conducted a multicenter retrospective cohort study including 253 KTRs of whom 98 treated with tixagevimab/cilgavimab 150 mg/150 mg and 155 who received four doses of BNT162b2 mRNA vaccine without prophylaxis [Table 1]. The severity of COVID-19 was classified: no symptoms; mild symptoms (cough, fever, sore throat, asthenia, anorexia, nasal congestion, headache, muscle pain) without radiological findings of pneumonia; moderate/severe symptoms (dyspnea with or without need for oxygen with non-invasive or invasive ventilation, chest imaging showed bilateral pneumonia, shock, multi-organ failure, need for hospitalization).

Results: Only 13.3% of patients developed SARS-CoV-2 infection after the administration of tixagevimab/cilgavimab, (p=0.00013). The largest proportion of infected patients remained asymptomatic (92.3% vs 54.7%), 7.7% had mild symptoms and none of them had severe disease, need for hospitalization or died (p=0.04) [Fig. 1A-B]. Using Kaplan-Meier curves we demonstrated the control group presented an early infection compared to the AZD7442 group (p=0.000014) [Fig. 1C]. Although not statistically significant, the anti-RBD titer at TOEV was lower among infected patients compared to KTRs who did not develop infection [Fig 1D]. No changes in eGFR and proteinuria, assessed before and after the administration, has been observed [Fig 1 E-F].

Conclusions: In conclusion, our study show that tixagevimab/cilgavimab 150/150 mg is effective and safe in preventing infection and severe disease when administered to patients with weak or no response to Covid-19 vaccine.

Table 1 | Patient characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tixagevimab/cilgavimab group (n=98)</th>
<th>Control group (n=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>56 (46-64)</td>
<td>62 (52-68)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male</td>
<td>60 (61.2)</td>
</tr>
<tr>
<td>C/EIR (median: 2.73 mg/L), median (IQR)</td>
<td>45.3 (30-60)</td>
<td>52 (39-69.5)</td>
</tr>
<tr>
<td>BMI, kg/m², median (IQR)</td>
<td>25 (22-28)</td>
<td>25 (23-27.5)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>82 (83.7)</td>
<td>136 (88.7)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>16 (16.3)</td>
<td>24 (15.5)</td>
</tr>
<tr>
<td>Cardiovascular disease, n (%)</td>
<td>33 (33.7)</td>
<td>54 (21.5)</td>
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<tr>
<td>User damage, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HVR-related</td>
<td>0 (0)</td>
<td>10 (6.5)</td>
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<tr>
<td>MVA-related</td>
<td>6 (6.1)</td>
<td>5 (3.2)</td>
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<tr>
<td>History of Sars-CoV-2 infection</td>
<td>17 (17.3)</td>
<td>26 (16.8)</td>
</tr>
<tr>
<td>Type of donor, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decedent</td>
<td>81 (82.7)</td>
<td>142 (91.9)</td>
</tr>
<tr>
<td>Living</td>
<td>17 (17.3)</td>
<td>18 (9.8)</td>
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<tr>
<td>History/kidney transplantation, median (IQR)</td>
<td>147 (147)</td>
<td>200 (162-187)</td>
</tr>
<tr>
<td>Retransplantation, n (%)</td>
<td>13 (13.3)</td>
<td>14 (9)</td>
</tr>
<tr>
<td>Immunosuppressants, n (%)</td>
<td></td>
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<tr>
<td>CNP</td>
<td>97 (99)</td>
<td>145 (97.9)</td>
</tr>
<tr>
<td>Antithymocyte globulin</td>
<td>81 (82.7)</td>
<td>155 (74.3)</td>
</tr>
<tr>
<td>Steroids</td>
<td>94 (95.9)</td>
<td>137 (88.4)</td>
</tr>
<tr>
<td>mTOR</td>
<td>6 (6.2)</td>
<td>24 (15.5)</td>
</tr>
</tbody>
</table>

Table 2 | Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Tixagevimab/cilgavimab group (n=98)</th>
<th>Control group (n=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOH, median (IQR)</td>
<td>0 (0)</td>
<td>4 (2-7)</td>
</tr>
<tr>
<td>Hospitalization, %</td>
<td>4.1</td>
<td>12.8</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Background: Solid organ transplant recipients are at high risk of morbidity/mortality from coronavirus disease 2019 (COVID-19). Studies suggest that monoclonal antibody (MAB) treatment against the SARS-CoV-2 spike protein may decrease hospitalizations. Herein, we report our single center experience with use of MAB for COVID-19 treatment in kidney transplant recipients (KTRs).

Methods: We performed a retrospective review of all KTRs who developed COVID-19 from 7/2020 to 11/2022 at our center. Date of diagnosis, vaccine status, MAB treatment, hospitalization including length of stay and patient outcome was reviewed.

Results: 331 KTRs tested positive for SARS-CoV-2 in the period reviewed. 219/66% KTRs received MAB treatment. Hospitalization was lower in those receiving MAB (10.5% vs 50.9%, p<0.0001, Fig 1a). KTRs who received MAB had better survival than those who did not (99.5% vs 88.7%, p<0.0001, Fig 1b). SARS-CoV2 vaccination was associated with better survival (98.7% vs 87.1%, p<0.0001, Fig 1d). Hospitalization rate was lower in those vaccinated prior to infection (17.6% vs 41.9%, p<0.0001, Fig 1c). The combination of MAB and vaccination decreased hospitalization compared to unvaccinated KTRs who received MAB (8% vs 21.6%, p=0.014, Fig 2a). Utilizing one-way ANOVA we found that length of hospitalization (LOH) was decreased for KTRs who were either vaccinated, received MAB or both compared to those who were unvaccinated and did not receive MAB (Figure 2c, p=0.024). Median LOH for the unvaccinated/no MAB group was 15 days vs 2 days for those vaccinated and treated with MAB.
Conclusions: MAB treatment for COVID-19 and prior vaccination were associated with improved survival and decreased risk of hospitalization in kidney transplant recipients.

Table 1. Summary of Patients by MAB Treatment, Vaccination Status, MAB + Vaccination Status

<table>
<thead>
<tr>
<th>MAB treatment (n%)</th>
<th>No MAB treatment (p=0.05)</th>
<th>p</th>
<th>Vaccinated (n=22)</th>
<th>Not Vaccinated (n=28)</th>
<th>p</th>
<th>MAB + Vaccine (n=21)</th>
<th>MAB + no Vaccine (n=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized, n (%)</td>
<td>23 (10.5)</td>
<td>54 (20.9)</td>
<td>&lt;0.0001</td>
<td>42 (17.6)</td>
<td>39 (14.1)</td>
<td>&lt;0.0001</td>
<td>74 (8.0)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>MAB</td>
<td>196 (89.5)</td>
<td>52 (40.1)</td>
<td>196 (82.4)</td>
<td>6 (18.8)</td>
<td>161 (92.0)</td>
<td>19 (78.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival, n (%)</td>
<td>118 (99.5)</td>
<td>94 (88.7)</td>
<td>&lt;0.0001</td>
<td>226 (98.8)</td>
<td>21 (78.7)</td>
<td>&lt;0.0001</td>
<td>775 (100)</td>
<td>66 (97.3)</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>1 (0.5)</td>
<td>11 (10.3)</td>
<td>2 (0.8)</td>
<td>12 (21.9)</td>
<td>0 (0)</td>
<td>2 (7.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results: Clustering analysis revealed three distinct cytokine profiles. Cytokine profile 1 was characterized by significantly higher concentrations of Th1 (IL-2, IFN-γ, and TNF-α) and Th2 (IL-4, -5, and -10) cytokines in comparison to the other two profiles. This was also significantly associated with higher S1 specific antibody production (p<0.05). Cytokine profile 2 and 3 differed in the concentration of IL-2, -6 and -10, but this did not result in a significant difference in antibody production. The identified cytokine profiles were not driven by the type of alternative vaccination strategies due to their even distribution across the profiles.

Conclusions: Repeated vaccination increased SARS-CoV-2 specific memory T cell cytokine responses in KTRs with an initially poor serological response to previous mRNA-based priming. Balanced memory T cell cytokine profiles were associated with a good SARS-CoV-2 specific humoral immune response. However, there was no significant impact of the type of alternative vaccination strategy on differences in memory T cell cytokine responses and profiles.

METHODS

Background: Kidney transplant recipients (KTRs) elicit an impaired immune response after COVID-19 vaccination, however its exact clinical impact remains unclear. Therefore we analysed the relationship between antibody levels after vaccination and the occurrence and severity of COVID-19 in a large cohort of KTRs.

Methods: All KTRs, living in the Netherlands, were invited to send a blood sample 28 days after their 2nd COVID-19 vaccination by a home-based finger-prick method for measurement of IgG antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein (anti-RBD IgG). Information on COVID-19 was collected from the moment the blood sample was obtained until 6 months thereafter. Multivariable Cox and logistic regression analyses were performed to analyse which factors affected the occurrence and severity (i.e. hospitalization and/or death) of COVID-19.

Results: In total 12,159 KTR were approached of whom 3,828 agreed to participate. Among those, 1,578 (54.7%) became seropositive (i.e. anti-RBD IgG level >50 BAU/mL). Seropositivity was associated with a lower risk for COVID-19, also after adjusting for multiple confounders, including socio-economic status and adherence to COVID-19 restrictions (HR 0.52 (0.31-0.89), p=0.02). Similar results were found for COVID-19 severity.

Conclusions: In conclusion, antibody level after COVID-19 vaccination is associated in a log-linear relationship with antibody level and the risk for COVID-19 (HR 0.52 (0.31-0.89), p=0.02). Similar results were found for COVID-19 severity.

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THI-DOMINANT CYTOKINE RESPONSES IN KIDNEY PATIENTS AFTER COVID-19 mRNA-1273 VACCINATION ARE ASSOCIATED WITH POOR HUMORAL RESPONSES

Yvette den Hartog*, Reshwan Malahe†, Remy van der Molen‡, Marcia Kho§, Marlies Reinders∥, Rory de Vries∥∥, Carla Baan∥∥∥

1University Medical Center Rotterdam, Rotterdam, Netherlands, 2University Medical Center Groningen, Groningen, Netherlands, 3Amsterdam UMC, Amsterdam, Netherlands, 4Radboud University Medical Center Nijmegen, Nijmegen, Netherlands, 5Erasmus MC, Viroscience, Rotterdam, Netherlands, 6University Medical Center Groningen, Department of Nephrology, Groningen, Netherlands

Background: COVID-19 vaccines are poorly immunogenic in kidney transplant recipients (KTR). For the development of virus-specific antibodies, T-cell mediated help to B-cells is required, in which the cytokine IL-21 plays a key role.

Methods: We compared three alternative vaccination strategies to a single dose mRNA-1273 vaccination (control): (1) a double dose of mRNA-1273 vaccination, (2) heterologous vaccination, and (3) temporary discontinuation of the immunosuppressant mycophenolate mofetil (MMF) in KTR with a poor serological response after two or three doses of an mRNA-based vaccine. They were randomized to receive 100 μg mRNA-1273 (n=25), 2x 100 μg mRNA-1273 vaccination (n=25) or Ad26.COV2-S vaccination (n=25). In addition, 50 KTR who received 100 μg mRNA-1273, were randomized to continue (MMF+, n=25) or discontinue (MMF-, n=25) MMF treatment for 2 weeks.

Results: All vaccination strategies resulted in a significant increase in the number of SARS-CoV-2-specific IL-21 producing T-cells and memory B-cells (both p<0.01, measured by ELISpot), except for the memory B-cell response in the double mRNA-1273 group. The IL-21 response was higher in the MMF+ group compared with the MMF- group (160 vs 77 spots/10^6 PBMCs, p=0.04), but did not differ between single mRNA-1273 (200), double mRNA-1273, (173), and Ad26.COV2-S (73). Also, the memory B-cell response did not differ between single mRNA-1273 (35), double mRNA-1273 (20), and Ad26.COV2-S (30), nor between the MMF+ (183) and MMF- (295) groups. Furthermore, both cellular responses correlated with the production of neutralizing antibodies (Spearman’s ρ 0.52 and 0.86, respectively, both p<0.001).

Conclusions: Repeated vaccination enhances SARS-CoV-2-specific memory T and B-cell responses and antibodies in KTR with an initially poor serological response. A higher dose, a heterologous vaccination, or two weeks discontinuation of MMF were not superior in boosting these responses compared to a normal mRNA based vaccination dose. These findings support the recommendation for repeated vaccination in KTR.

REPEATED COVID-19 VACCINATION ENHANCES MEMORY T-CELL IL-21 AND MEMORY B-CELL RESPONSES IN IMMUNOCOMPROMISED KIDNEY TRANSPLANT RECIPIENTS

Reshwan Malahe*, Yvette den Hartog‡, Debbie van Baarle§, Frederike Bemelman∥, Dimitri Diavatopoulos∥, Ron Gansevoort∥, Daryl Geers∥, Corine Geurts van Kessel∥, Luuk Hilbrands∥, Marci Kho∥∥, Ronella de Vries∥∥, Marlies Reinders∥∥∥, Carla Baan∥∥∥∥

1Erasmus MC, 2Department of Internal Medicine, Nephrology and Transplantation, Erasmus MC Transplant Institute, Rotterdam, Netherlands, 3University Medical Center Groningen, Groningen, Netherlands, 4Amsterdam UMC, loca AMC, Amsterdam, Netherlands, 5Radboud University Medical Center, Nijmegen, Netherlands, 6Erasmus MC, Viroscience, Rotterdam, Netherlands, 7University Medical Center Groningen, Department of Nephrology, Groningen, Netherlands

Background: COVID-19 vaccines are poorly immunogenic in kidney transplant recipients (KTR). For the development of virus-specific antibodies, T-cell mediated help to B-cells is required, in which the cytokine IL-21 plays a key role.

Methods: We compared three alternative vaccination strategies to a single dose mRNA-1273 vaccination (control): (1) a double dose of mRNA-1273 vaccination, (2) heterologous vaccination, and (3) temporary discontinuation of the immunosuppressant mycophenolate mofetil (MMF) in KTR with a poor serological response after two or three doses of an mRNA-based vaccine. They were randomized to receive 100 μg mRNA-1273 (n=25), 2x 100 μg mRNA-1273 vaccination (n=25) or Ad26.COV2-S vaccination (n=25). In addition, 50 KTR who received 100 μg mRNA-1273, were randomized to continue (MMF+, n=25) or discontinue (MMF-, n=25) MMF treatment for 2 weeks.

Results: All vaccination strategies resulted in a significant increase in the number of SARS-CoV-2-specific IL-21 producing T-cells and memory B-cells (both p<0.01, measured by ELISpot), except for the memory B-cell response in the double mRNA-1273 group. The IL-21 response was higher in the MMF+ group compared with the MMF- group (160 vs 77 spots/10^6 PBMCs, p=0.04), but did not differ between single mRNA-1273 (200), double mRNA-1273, (173), and Ad26.COV2-S (73). Also, the memory B-cell response did not differ between single mRNA-1273 (35), double mRNA-1273 (20), and Ad26.COV2-S (30), nor between the MMF+ (183) and MMF- (295) groups. Furthermore, both cellular responses correlated with the production of neutralizing antibodies (Spearman’s ρ 0.52 and 0.86, respectively, both p<0.001).

Conclusions: Repeated vaccination enhances SARS-CoV-2-specific memory T and B-cell responses and antibodies in KTR with an initially poor serological response. A higher dose, a heterologous vaccination, or two weeks discontinuation of MMF were not superior in boosting these responses compared to a normal mRNA based vaccination dose. These findings support the recommendation for repeated vaccination in KTR.
**Background:** Sotrovimab, a monoclonal antibody active against the Omicron spike, has been used to prevent severe forms of Omicron induced COVID-19. Clinical data remain scarce in kidney transplant recipients (KTR). Our aim was to assess the impact of subsequent vaccination administration to the antibody (Ab) response (as measured by the Eurowimmuno assay) and severity of SARS-CoV-2 infection in this population. All PCR positive SARS-CoV2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results.

**Methods:** Our aim was to assess the impact of subsequent vaccine administration to the antibody (Ab) response (as measured by the Eurowimmuno assay) and severity of SARS-CoV-2 infection in this population. All PCR positive SARS-CoV2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results.

<table>
<thead>
<tr>
<th>Monoclonal Antibodies</th>
<th>Number of receiving patients</th>
<th>Testing positive days average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sotrovimab</td>
<td>43</td>
<td>12.5 days</td>
</tr>
<tr>
<td>Tigavelivimab/Cilgavimab</td>
<td>24</td>
<td>12.9 days</td>
</tr>
<tr>
<td>Casirivimab/Imdevimab</td>
<td>9</td>
<td>16.9 days</td>
</tr>
<tr>
<td>Bamlanivimab/ Etsevimab</td>
<td>2</td>
<td>28.5 days</td>
</tr>
<tr>
<td>Molnupravir</td>
<td>1</td>
<td>30 days</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>1</td>
<td>40 days</td>
</tr>
</tbody>
</table>

**Results:** We have recorded 117 positive patients in this time frame (49.7 % of total). Among these, 47 patients did not receive early therapy (GROUP A), whereas 70 patients were eligible for monoclonal antibodies therapy (GROUP B). GROUP A patient, who were not eligible for early treatment or who became infected before these drugs were available, on average remained positive for 21 days with longer-lasting symptoms (about one week), reporting 36 surviving patients of whom 6 needed hospitalisation with a positive outcome (12.7%) and 10 patients who died (21% of GROUP A total infected). In GROUP B, on the other hand, we recorded just 3 patients requiring hospitalisation (4.2%) and no deaths. In addition, most of the GROUP B patients reported mild flu-like syndrome symptoms, lasting 3-4 days with an average of 14 days' testing positive (Tab1). No allergic reactions occurred in patients treated with monoclonal antibodies.

**Conclusions:** The advent of early therapies has drastically reduced mortality, morbidity and time to negative outcome in immunosuppressed patients.

Tab 1: Breakdown by type of monoclonal antibody administered and duration of positive test after therapy

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**Moderated poster session on COVID-19**

**MPS3_7 REAL-WORLD EXPERIENCE OF SOTROVIMAB TO PREVENT SEvere COVID-19 IN KIDNEY TRANSPLANT RECIPIENTs: RESULTS FROM A NATIONAL STUDY**

**Nizar Jouer**, Kevin Ou1, Pierre Trémollières2, Lionel Couzi2, Nassim Kamar3, Sophie Caillard4, Claire Presne5, Nathalie Chavaroit6, Dominique Bertrand7, Renaud Snanoudj8, Philippe Gatault9, Camille Pelis-Hoang10, Willy Kini Matondo1, Philippe Grimbert1, Marie Matignon1

1Néphrologie et transplantation rénale, Hôpital Henri Mondor, APHP, Créteil, France, 2Néphrologie, CHU Montpellier, Montpellier, France, 3Néphrologie, CHU de Bordeaux, Bordeaux, France, 4Néphrologie, CHU Toulouse, Toulouse, France, 5Néphrologie, CHU Strasbourg, Strasbourg, France, 6Néphrologie, CHU Amiens, Amiens, France, 7Néphrologie, Hôpital Necker, APHP, Paris, France, 8Néphrologie, CHU Rouen, Rouen, France, 9Néphrologie, Hôpital Bicêtre, APHP, Le Kremlin Bicêtre, France, 10Néphrologie, CHU Tours, Tours, France, 11Néphrologie, Hôpital Tenon, APHP, Paris, France, 12Pharmacie, Hôpital Henri Mondor, APHP, Créteil, France

**Background:** Sotrovimab, a monoclonal antibody active against the Omicron spike, has been used to prevent severe forms of Omicron induced COVID-19. Clinical data remain scarce in kidney transplant recipients (KTR). Our aim was to assess the impact of subsequent vaccination administration to the antibody (Ab) response (as measured by the Eurowimmuno assay) and severity of SARS-CoV-2 infection in this population. All PCR positive SARS-CoV2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results.

**Methods:** Our aim was to assess the impact of subsequent vaccine administration to the antibody (Ab) response (as measured by the Eurowimmuno assay) and severity of SARS-CoV-2 infection in this population. All PCR positive SARS-CoV2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results.

**MPS3_9 SERONEGATIVE TRANSPLANT PATIENTS REMAIN AT SIGNIFICANT RISK OF SARS-COV-2 INFECTION AND COMPLICATIONS; WE ARE NOT OUT OF THE WOODS YET**

**Laszlo Szabo1**, Verity Brooker1, Tarique Sabah1, Mark Ponsford3, Georgios Kountzis1, Stephen Jolles2, Kathryn Bramhall1, Soma Meran3, Usman Khalid1, Ian Humphreys3, Argiris Asderakis1,4,5

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**Background:** Our work in a transplant population has shown that, following the 2nd dose of a SARS CoV-2 vaccine, 43% of Astra-Zeneca (AZ) vaccinated patients seroconverted compared with 52.6% of mRNA/Pfizer leaving a considerable number of patients at risk.

**Methods:** Our aim was to assess the impact of subsequent vaccine administration to the antibody (Ab) response (as measured by the Eurowimmuno assay) and severity of SARS-CoV-2 infection in this population. All PCR positive SARS-CoV2 infections were recorded post 2nd dose and up to the introduction of monoclonal Abs in January 2022. We analysed infections, admissions and ICU stay according to the Ab results.

**Results:** We analyzed 1294 samples in 881 patients. 523 patients had their sample tested after the 3d dose and 167 post the 4th. All but 3 patients received an mRNA vaccine. 380 patients (72.9%) seroconverted after the 3d dose compared to 79% following the 4th. The effect of the type of vaccine (AZ or mRNA) disappeared after the 3d dose, as patients received now an mRNA vaccine. After the 3d dose, 48% of the post 2nd dose Ab-negative patients became positive whilst 8.2% of positive patients became negative. In a multivariate regression analysis increased age (OR 0.96, p=0.001), use of myco-phenolate derivatives (OR 0.29, p=0.001), and prednisolone (OR 0.55, p=0.010) had a negative effect on antibody response. Of note, 20/20 patients who were on rapamycin seroconverted following the 3d dose (11/19 post 2nd). Among the 262 patients with PCR confirmed SARS-Cov-2 infection, from May 2021 to January 2022, 100 had a recent Ab sample. 63/97 (21.2%) of Ab negative patients got infected during this period compared to 37/513 (7.2%) of seropositive ones (p=0.0001, OR 3.46 CI 2.24-5.35). 17/20 patients admitted (OR 4.2) had no demonstrable Ab response at their latest pre-infection sample. 4/5 deaths and 3 of 4 admissions to ICU were in seronegative patients.

**Conclusions:** 20% of transplant patients remain seronegative even after the 4th vaccine dose. MMF and prednisolone are the strongest predictors of a negative response. Seronegative patients are 3.4 times more likely to get an infection and 4.2 times more likely to be admitted compared to seropositive patients. Better treatments are essential to protect the small but significant number of transplant patients at risk of severe disease due to SARS-CoV-2
MODERATED POSTER

SARS-COV-2 ANTIBODIES RESPONSE AFTER VACCINATIONS IN KOREAN KIDNEY TRANSPLANT RECIPIENTS

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Background: Patients with kidney-related disease are at high risk of developing severe COVID-19. The risk of death from SARS-CoV-2 infection is particularly higher in kidney transplant recipients than in healthy individuals. SARS-CoV-2 vaccination is especially important in kidney transplant recipients, but antibodies response is limited due to immunosuppression therapy. We assessed the immune response of antibodies production after vaccinations in Korean kidney transplant recipients.

Methods: We included eighty-five Korean kidney transplant recipients who received full SARS-CoV-2 vaccination. We measured binding antibodies against the SARS-CoV-2 spike (S) protein receptor-binding domain and neutralizing antibody levels using surrogate viral neutralization test. Anti-SARS-CoV-2 S titer was quantitatively detected with a two-antigen sandwich-based electrochemiluminescence immunoassay (ECLIA), using the Cobas 8000 e801 (Roche Diagnostics, Mannheim, Germany). Neutralizing antibody levels were measured by ELISA method (R-FIND SARS-CoV-2 Neutralizing Antibody ELISA, SG Medical, Seoul, Korea).

Results: We divided the subjects into 4 groups (< 1, 1–2.4, 2.5–4.9, and ≥ 5-year) according to the time from renal transplantation to vaccination, and the number of patients in each group was 18, 11, 23, and 33, respectively. The means of anti-SARS-CoV-2 S were 3.2 U/mL, 27.8 U/mL, 370.2 U/mL, and 5.094.2 U/mL (P < 0.001), respectively, showing statistical differences. The neutralizing antibody titers (% inhibition rate) were 2.2%, 11.6%, 45.6%, and 93.0% (P < 0.001), respectively and statistically significant.

Conclusions: The shorter the time from transplantation to vaccination, the lower binding antibody and neutralizing antibody titers. The reason for these results is considered to be due to the strong immunosuppression state in the early stage of post-transplantation by the initial introduction treatment.

| Table 1. Donor demographics and ischemia times of 4 pancreas isolations using continuous purification matched with 8 pancreas isolations using discontinuous purification according to donor age, BMI and organ source |

<table>
<thead>
<tr>
<th>Continuous Purification (n=4)</th>
<th>Discontinuous Purification (n=8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td></td>
<td></td>
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<tr>
<td>Height (mean cm±SD)</td>
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<td>Weight (mean Kg±SD)</td>
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<tr>
<td>Medical History</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus, n</td>
<td></td>
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<tr>
<td>Smoking, n</td>
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<tr>
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<td>Alcohol Abuse, n</td>
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<td>Infections</td>
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<tr>
<td>Malignancy, n</td>
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<td></td>
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<td>Vasopressor use, n</td>
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<tr>
<td>Laboratory Results</td>
<td></td>
<td></td>
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<tr>
<td>Lipase, (mean U/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amylase, (mean U/l)</td>
<td></td>
<td></td>
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<tr>
<td>Hemoglobin, (mean g/dl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemia time, h (±SD)</td>
<td></td>
<td></td>
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<tr>
<td>Cold Ischemia time, h (±SD)</td>
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<td></td>
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<tr>
<td>Warm Ischemia time, min (±SD)</td>
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<td></td>
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<tr>
<td>Total Ischemia time, h (±SD)</td>
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</tbody>
</table>

Abbreviations: BMI, body mass index; CVA, Cerebrovascular Accident; DBD, donation after brain death; DCD, donation after circulatory death; HBP, high blood pressure.
Background: Pancreas transplantation improves and extends the life of patients with insulin dependent diabetes. Pancreata from extended criteria donors have been increasingly used due to the scarcity of available grafts. Normothermic ex situ pancreas perfusion (NESPP) can keep grafts metabolically active, potentially allowing for assessment and organ repair, and could improve outcomes of marginal grafts.

Methods: A novel NESPP technique was developed and tested. Porcine pancreata were removed after a short period of warm ischemia and subjected to 6hrs of NESPP. Perfusion parameters, potential graft assessment markers and graft injury were measured. Next, pancreata subjected to 3hrs of NESPP were transplanted and animals were followed for up to 3 days. Graft function and injury post-transplantation were evaluated.

Results: Using this novel system of perfusion, pancreata were perfused for an extended period of time with minimal edema. Histology at the end of perfusion showed intact islet cells with only mild signs of tissue injury. NESPP transplanted grafts showed immediate function after transplantation, with glucose levels in normal range.

Conclusions: NESPP maintains a physiologic environment and excellent graft function without causing significant graft injury. Porcine pancreas transplantation is feasible and allows for in vivo assessment of pancreas function and injury after NESPP.

Figure 1: Glucose levels after pancreatectomy with/without transplantation and after glucose stimulation test. (A) Glucose levels post-pancreatectomy. (B) Glucose levels after glucose stimulation test in pancreatectomy animals. (C) C-Peptide levels post-pancreatectomy and after the glucose stimulation test. (D) Glucose levels post-transplantation. (E) Glucose levels after glucose stimulation test in transplanted animals. (F) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals. (G) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals. (H) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals. (I) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals. (J) C-Peptide levels post-transplantation and after glucose stimulation test in transplanted animals.
**MODERATED POSTER**

**Moderated e-poster session on pancreas and islet transplantation**

**MPS4_4**

**USING DIABETES TECHNOLOGY TO MANAGE HYPERGLYCAEMIA IN PEOPLE WITH TYPE 1 DIABETES AND FAILING PANCREAS TRANSPLANT**

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**Background:** Advanced hybrid closed loop systems (AHCLS - ‘artificial pancreas’) and similar diabetes technology have demonstrated glycaemic control benefits in people with diabetes, however these studies excluded people with end stage kidney disease (ESKD) or post transplant. There is limited clinical experience on using AHCLS and diabetes technology in people with type 1 diabetes who have had simultaneous pancreas and kidney transplants (SPK) transplants with hyperglycaemia due to failing graft function.

**Methods:** In this case series, we share our experience of using continuous subcutaneous insulin infusion (CSII) therapy, AHCLS and related diabetes technology in 6 people with type 1 diabetes, who developed significant hyperglycaemia post successful SPK or pancreas only transplant between 2021 and 2022. These in range metrics and HbA1c pre and post intervention with diabetes technology was evaluated. All were on multiple daily insulin injections before intervention with diabetes technology. Four people were started on AHCL and 2 people on CSII with ‘flash’ glucose monitoring. Median (range) duration of follow-up was 15.6 months (1-36 months).

**Results:** Six people (5 males) aged between 34 and 50 years with mean (±SD) duration of diabetes at 36 years (±8.2). Five people had a SPK transplant and one patient had a pancreas only transplant. Median (range) duration between transplantation and diabetes recurrence was 3.5 years (3.9-5 years). Median (IQR) time in range (3.9 - 10 mmol/L) glucose improved from 37% (24%-49%) to 56.6% (48%-62%) and HbA1c fell from 72.7 (72-79) to 64 (42-67) mmol/mol (p <0.05 for both) without a concomitant increase in hypoglycaemia. In parallel total daily dose of insulin fell and quality of life feedback assessed by questionnaire positive.

**Conclusions:** Use of ‘artificial pancreas’ diabetes technology improved glycaemic parameters in people with type 1 diabetes with SPK and failing pancreatic graft function. Early use of such therapies within a multidisciplinary clinic framework should be considered to improve diabetes control in this high-risk cohort.

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**MPS4_5**

**EARLY RELAPAROTOMY NEED AND RISK FACTORS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION**

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**Background:** Simultaneous pancreas-kidney transplantation (SPKT) is a well-established treatment for patients with type 1 diabetes mellitus and end-stage renal disease. Despite outcomes have steadily improved as a result of better donor and recipient selection, optimized strategies in immunosuppression and advances in surgical technique, it still displays higher rate of complications and later hospital discharge when compared to kidney transplantation alone.

**Methods:** We performed a retrospective review of all SPKT conducted in our centre between January 2000 and December 2022. Data from medical records was incorporated. The primary endpoint was defined as the need for relaparotomy after SPKT within the initial hospital stay. Hospital length, graft pancreatotomy and mortality rates were also evaluated.

**Results:** 263 patients were included. We analysed recipient characteristics, comorbidities and renal replacement therapy at the time of the transplant, as shown in table 1. Sixty-five patients (25%) required at least one relaparotomy within their initial hospital stay. All-cause relaparotomy rate was 2.04 (1.71-2.44) events per each 100 in-hospital-days. The leading cause for relaparotomy was bleeding (26 patients), followed by intra-abdominal infection in 21, graft thrombosis in 17 and anastomotic leak in 4; other causes were found in 16 patients. Peritoneal dialysis (PD) (IRR: 2.063, p<0.001), SPKT performed between 2000-2011 (IRR: 1.507, p=0.031) and a lower body mass index (BMI) (IRR: 0.881; p<0.001) were found to be independent risk factors for all-cause relaparotomy. Considering relaparotomy cause, lower BMI (p=0.045) and PD (p=0.008) were related with thrombosis, PD (p=0.046) with leak and SPKT performed between 2000-2011 (p=0.020) with infection-driven relaparotomy. Relaparotomy increased hospital length (median 28 vs 15 days; p<0.001), graft pancreatotomy (35% vs 2% patients; p=0.001) and 90-day mortality rate (8% vs 0%, p<0.001).

**Conclusions:** The need for relaparotomy within the initial hospital stay influences short-term prognosis on pancreatic graft and patient survival rates. Efforts should be continuously made to identify and correct potential risk factors. We identified a lower BMI and PD at the time of transplant as independent risk factors for overall relaparotomy.

**Table 1 – Recipient and donor baseline characteristics (N=263)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recipient sex (female), n (%)</th>
<th>Recipient age (y), mean (SD)</th>
<th>Hypertension, n (%)</th>
<th>Diabetes duration, mean (SD)</th>
<th>Recipient BMI, mean (SD)</th>
<th>RRT, n (%)</th>
<th>HD</th>
<th>PD</th>
<th>Pre-emptive</th>
<th>Donor age, mean (SD)</th>
<th>Donor age ≥ 30y, n (%)</th>
<th>BMI – body mass index; HD – hemodialysis; PD – peritoneal dialysis; RRT – renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>126 (48)</td>
<td>35.6 (6.3)</td>
<td>219 (84)</td>
<td>24.2 (6.1)</td>
<td>22.4 (2.8)</td>
<td>71 (59)</td>
<td>59 (22)</td>
<td>12 (5)</td>
<td>20.3 (10.7)</td>
<td>85 (32)</td>
<td>21</td>
<td>100% vs 0%; p&lt;0.001; 35% vs 2% patients; p&lt;0.001; 90-day mortality rate (8% vs 0%, p&lt;0.001)</td>
</tr>
</tbody>
</table>

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**MPS4_6**

**40TH ANNIVERSARY OF PANCREAS TRANSPLANTATION IN SPAIN. LESSONS LEARNED AFTER MORE THAN 650 CASES IN A SINGLE CENTER**

**Joanna Ferrer-Fábregas**, Pedro Ventura-Aguilar, M. Angeles Garcia-Criado, Alba Torroella, Carlos Perez Serrano, Miguel Ángel López-Boado, Rocío García, Antonio J Amor, Enric Esmatges, Miriá Musqueru, Fritz Diekmann, María José Ricart, Laureano Fernández-Cruz, Josep Fuster, Juan Carlos García Valdecasas, Federico Oppenheimer, Beatrúi Bayés, Ramón Rull, Federic Cofán

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**Background:** To determine in our institution the results of pancreas transplantations in diabetic recipients in accordance with the evolution of surgical techniques and immunosuppression protocols over a period of 40 years.

**Methods:** From February 1983 to December 2022, performed pancreas transplants and donor type have been retrospectively analyzed in a prospective database. Pancreatic graft survival and patient survival have been analyzed using Kaplan-Meier curves.

**Results:** During the study period, 654 pancreas transplants were performed, namely: 579 simultaneous pancreas-kidney (SPKT) transplants; 29 pancreas transplants following kidney transplant (PAK); 3 pancreas transplants alone (PTA) and 43 re-transplants, in 98% of cases from brain-dead donors. In 2019, the first SPK from a donor in controlled asystole was performed, with a further 12 cases conducted to date. Induction therapy and maintenance immunosuppression have been continuously modified over time. The type of exocrine drainage has evolved from bladder diversion to enteric drainage (duodenojejunostomy until April 2016 and duodenoduodenostomy from May 2016). Systemic venous drainage was performed in all cases. Pancreatic graft survival in the most recent period, at 1 and 5 years, was: SPK 91% and 83%, PAK and PA 100% respectively. Patient survival at 1 and 5 years was 97% for SPK and 100% for PAK and PA.

**Conclusions:** Pancreas transplantation offers promising results in terms of graft and patient survival i.e with a positive impact on quality of life. Advances in surgical technique and clinical management together with the experience of the multidisciplinary team have all contributed to achieving the current results.
Background: Pancreas retransplantation (P-RETX) after graft loss is still a controversial option, although P-RETX improves quality of life, glycemic control and reversal of end organ damage compared to exogenous insulin therapy. In this study we review our single-center experience in P-RETX.

Methods: The study was designed as a retrospective analysis of a cohort of 256 patients who received pancreas transplant evaluating the incidence and causes of pancreas graft failure (PGF) and the indications and outcomes of P-RETX at our Centre between 1991 and 2022. Donor and recipient characteristics, and patient and graft outcome were analyzed in the institutional database.

Results: Among 256 pancreas transplants (241 (94 %) SPK, 10 (3.9%) PAK and 5 (1.9 %) PTA), 46 (17.9%) pancreas grafts were lost and 33 (12.8%) patients underwent graft repancreatectomy. The main causes for PGF were: 17 (6.6%) vascular thrombosis, 8 (3.1%) acute rejection, 7 (2.7%) pancreatitis, 4 (1.5%) enteric fistula, 3 (1.17%) chronic rejection, 1 (0.3%) bowel occlusion and 1 (0.3%) pancreas lymphoma. Overall, 10 P-RETX were performed mainly after early graft loss (median time until retransplant 15.7 months). Demographic and clinical characteristics of the recipients were similar in the first and second transplant cohorts, but donor selection criteria were stricter, with lower PDRI (pancreas donor risk index) in P-RETX. The rate of graft failure was higher in the P-RETX vs first transplant (40% vs 17.9%). Causes of P-RETX pancreas graft loss were 3 thrombosis, 1 pancreatitis. In the P-RETX 1 patient died with functioning graft.

Conclusions: P-RETX is challenging from a surgical and immunological standpoint, but it represents a viable option for recipients who experience PGF with acceptable patients and graft survival. A thorough evaluation of the candidates needs to be carried out considering not only patient comorbidities, surgical viability, immunological status but also patient motivation.

Background: Pancreatic and lung injury are the main complications of obstructive jaundice. The pathogenesis was attributed to excessive inflammation due to bacterial translocation, and endotoxemia. Individuals with obstructive jaundice may benefit from anti-inflammatory pulmonary enteral formula treatment (eicosapentaenoic acid and gamma linolenic acid). This study examined the safety and efficacy of the enteral formula in the treatment of lung and pancreatic injury due to obstructive jaundice.

Methods: 30 Wisteria-Albino rats were randomly assigned to 3 study groups.

Group 1 constituted the sham (n=10), Group 2 (n=10) and 3 (n=10) underwent ligation and division of the common bile duct. The enteral formula was administered to the treatment group (Group 3) for eight days postoperatively. The inflammatory cytokines and markers were analysed in the serum and tissue samples. Histologically lung and pancreas were evaluated and injuries scored. Morphometric documentation for inflammation and acinar necrosis was obtained by mapping the surface of the head of the pancreas into 10 geographical fields and evaluating each field independently. The mean histological score (1-4) was calculated for each variable in each animal.

Results: TNF alpha levels in serum were significantly lower in Group 1 and Group 3 compared to Group 2 (p<0.001). IL-6 and C-reactive protein levels in serum did not show any statistical significance between the three groups (p>0.083 and 0.130 respectively). Tissue catalase measurements showed no difference among the groups (p>0.503). Tissue myeloperoxidase levels were found significantly higher in Group 2 compared to group 1 (p=0.009). Malondialdehyde content in tissue didn’t differ between the groups (p=0.496). TNF alpha tissue levels were higher (190.36pg/ml) in Group 2, as well as IL-6 (37.9 pg/ml) levels (p<0.001). Pulmonary injury scores showed significant injury in Group 2 in terms of interstitial thickening, inflammatory cell infiltration and presence of necrosis. Histological assessment of acinar necrosis and inflammation of pancreas revealed severe injury in Group 2 compared to other groups (Figure 1).

Conclusions: Our findings highlighted that anti-inflammatory pulmonary enteral formula alleviated pancreatic and lung injury and inhibited inflammation.
Background: Pancreas and islet transplantation are both therapeutic options for patients with complicated diabetes. Unfortunately, the availability of pancreas allografts is inadequate to cover the increasing recipient demand. Strategies to expand the number of available grafts are needed. Normothermic ex vivo perfusion (NEVP) is a method that has the potential to assess, and repair organs. The aim of this study was to assess the feasibility of islet isolation after NEVP of the pancreas.

Methods: Two discarded human pancreases were perfused during 4 hours on a NEVP circuit, previously developed by our group. After the perfusion, organs were immediately processed for islet isolation using the Edmonton Isolation Protocol.

Results: Both organs were successfully perfused for 4 hours with posterior islet isolation. Table 1 shows the donor, graft, and isolation characteristics. The islets morphological integrity was proven by insulin staining. A glucose-stimulated insulin secretion test was performed on both cases figure 1. Islets from both donors responded appropriately, secreting insulin at high glucose concentrations. However, case #1 appeared to demonstrate a more robust response than case #2.

Conclusions: Islet isolation after NEVP is feasible using the standard human isolation protocol and could be used to assess and improve the grafts destined for islet isolation. For this study, only the feasibility of the procedure after perfusion was assessed. To our knowledge, this is the first study reporting islet isolation after NEVP in human pancreas. Future studies will focus on improving the perfusion and thoroughly assessing the islets.

Table 1.

<table>
<thead>
<tr>
<th>Donor</th>
<th>Gender</th>
<th>Age</th>
<th>BMI</th>
<th>Type of donor</th>
<th>CIT</th>
<th>Wet/dry weight ratio before perfusion (Weight in grams)</th>
<th>Wet/dry weight ratio after perfusion (Weight in grams)</th>
<th>Change in ratio (%)</th>
<th>Final trimmed pancreas weight (g)</th>
<th>Digested pancreas tissue weight (g)</th>
<th>Pre-purification yield</th>
<th>Post-purification yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>M</td>
<td>26</td>
<td>22.7</td>
<td>NDD</td>
<td>547</td>
<td>3.5 (270)</td>
<td>4.7 (446)</td>
<td>33% (66%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Case 2</td>
<td>M</td>
<td>55</td>
<td>19</td>
<td>NDD</td>
<td>383</td>
<td>6.5 (348)</td>
<td>3.1 (362)</td>
<td>-48% (4%)</td>
<td>115.3</td>
<td>626 204</td>
<td>220 801*</td>
<td></td>
</tr>
</tbody>
</table>

*Only the purest fractions were quantified
INDIVIDUALIZED HBIG WITHDRAWAL IN AN HISTORICAL COHORT OF LIVER TRANSCPLANT RECIPIENTS IN ITALY

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Background: Since the advent of third-generation Nucleoside-Analogues (3-NA), characterized by strong potency and high genetic barrier, the role of long-term HBIG has been questioned. Scientific Societies suggest that HBIG should be used for a finite duration, specifically in compliant patients without Delta coinfection. The same guidance applies to historical patients. Many liver transplant (LT) centres across Europe still prefer continuing with HBIG-NA long term. Aim of this study is to report the results of HBV prophylaxis according to the ELITA Guidelines in a cohort of historical LT recipients.

Methods: 7 LT Italian Centers consecutively included adherent HBV monoinfected LT recipients with regular follow-up in the study. Patients on Lamivudine were shifted to 3-NA before HBIG-withdrawal. A prospective observational Registry for monitoring serological and biochemical parameters was implemented.

Results: 174 patients were considered for HBIG withdrawal with 3 being excluded, 2 for refusal and 1 for poor-compliance. One additional patient on LAM/HBIG did not tolerate shifting from LAM to Entecavir due to renal tubulopathy. Excluded, 2 for refusal and 1 for poor-compliance. One additional patient on HBIG withdrawal in adherent HBV+/HDV- patients on lifelong HBVDNA at LT was positive in 17%, negative in 69% and unavailable in 14% of the cases. 116 and 68 patients have a follow-up of at least 3 and 6 months, respectively with 113 (97.4%) and 66 (97%) being currently HBsAg-ve. All patients remained HBV-DNA-negative, asymptomatic, with normal liver function tests. Even assuming a very low maintenance dose of 1000 IU every 4 weeks, the cost saving per-patient would be of at least 4,000 Euro for each additional year. For centres who have many patients in follow-up the cost saving would be substantial.

Conclusions: HBIG withdrawal in adherent HBV+/HDV- patients on lifelong 3-NAs is safe and associated with HBsAg negativity in the vast majority of cases. The substantial cost-saving could cover different needs.

DO DONOR LIVER BLOOD TESTS PREDICT LIVER TRANSPLANT OUTCOMES? UK NATIONAL COHORT STUDY

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Background: Safely increasing organ utilisation is a global priority. Donor serum transaminase levels are often used to decline livers, despite minimal evidence to support such decisions. We aimed to investigate the impact of donor ‘liver blood test’ results on transplant outcome.

Methods: This retrospective cohort study used the UK Transplant Registry on adult liver transplantation (2016-2019); adjusted regressions models assessed the effect of donor liver blood tests on outcomes.

Results: 3299 adult liver transplant recipients were included (2530 following brainstem death, 769 following circulatory death). Peak alanine transaminase (ALT) ranged from 6-5927U/L (median=45). Donor cause of death significantly influenced donor ALT; 4.2-fold increase in peak-ALT with hypoxic brain injury versus intracranial haemorrhage (adjusted P<0.001). On multivariable analysis, adjusting for a wide range of factors, transaminase level (ALT or aspartate aminotransferase) failed to predict graft survival (Fig 1), primary non-function, 90-day graft loss or mortality. This held true in all examined subgroups; steatotic grafts, DCD, hypoxic brain injury donors, and donors where ALT was still rising at the time of retrieval. Even grafts from donors with extremely deranged ALT (>1000) displayed excellent post-transplant outcome. In contrast, donor peak alkaline phosphatase was a significant predictor of graft loss (aHR=1.808, 1.016-3.216, P=0.044).

Conclusions: We have found no evidence to support the notion that donor transaminases predict post-transplant outcomes. When other factors are favourable, livers from donors with raised transaminases can be accepted and transplanted with confidence. Such knowledge should improve organ utilisation decision-making and prevent future unnecessary organ discard. This provides a safe, simple and immediate option to expand the donor pool.

Fig 1 - impact of donor ALT/ALP on graft survival (cox regression models with restricted cubic splines)
FACTORS AFFECTING SIGNIFICANT DIFFERENCE BETWEEN RADIAL AND FEMORAL ARTERIAL BLOOD PRESSURE IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Invasive blood pressure monitoring is essential during liver transplantation. Radial and femoral artery are commonly used, although study about the comparison of blood pressure between radial and femoral artery is scarce. In this study, we aimed to evaluate the perioperative factors related to developing significant differences between radial and femoral arterial blood pressure.

Methods: A retrospective study was performed in adult recipients who underwent living donor liver transplantation (LDLT) in 2021 at Samsung Medical Center. After comparing radial and femoral arterial mean blood pressure (MBP) at 3 phases (dissection, anhepatic, and post-reperfusion), we selected data with the largest differences. We defined the significant differences as the 10% of femoral arterial MBP. The recipients were divided into two groups (with and without significant difference group), and perioperative variables were analyzed in each group at post-reperfusion phase.

Results: A total of 128 adults undergoing LDLT were included in our analysis. The largest difference between the radial and femoral arterial MBP was as follows: The median [IQR] of difference, 9.19 [5.93, 12.5] in anhepatic phase; and 10.87 [6.59, 15.28] in post-reperfusion phase. The difference was significantly higher in the post-reperfusion phase than in the anhepatic phase (P=0.003), however, the differences was not significantly different between the dissection and post-reperfusion phase (P=0.095).

In the post-reperfusion phase, 75 recipients showed a significant difference (≥ 10%) and femoral arterial MBP was higher than radial arterial MBP in 121 of 128 total recipients, and 72 of 75 significant difference group. The units of transfused packed RBC (0 [0, 2] vs. 2 [0, 4], P=0.01), units of transfused fresh frozen plasma (0 [0, 0] vs. 0 [0, 2], P=0.05), and vasoactive inotropic score (5 [0, 14.25] vs. 10 [1.5, 20], P=0.037) were significantly higher in significant difference group.

Conclusions: Radial and femoral arterial MBP can differ significantly during LDLT, and it showed significant association with the amount of transfusion and vasoactive inotropic use. Blood pressure measurement based solely on radial artery has the risk of underestimation during liver transplantation.

THE MORBIDITY BURDEN AFTER LIVER TRANSPLANTATION – A TREATMENT-BASED ANALYSIS

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Introduction: Survival after liver transplantation (LT) has improved, now reaching > 90% at 1 year in benchmark cases. However, while post-transplant morbidity remains high, an in-depth analysis of the patient-specific morbidity is currently lacking.

Methods: We retrospectively included all LT performed at our center from 2017 to 2020, except for re-LTs. Complications from the first post-LT year were graded according to the Dindo-Calvien classification and divided into 3 morbidity categories: procedure related (bleeding…) graft related (primary non-function, biliary and arterial complications…) and recipient related (infections, ileus…). The patient specific cumulative morbidity was calculated for each category using the Comprehensive Complication Index (CCI). To test the 3 different morbidity categories, we applied them to low and high-risk donor-recipient scenarios (BAR score<18 and >18).

Results: Out of 287 recipients, 91% had at least one complication during the first post-LT year, including 53% Grade II. While overall and recipient-specific CCI increased from discharge to 1-year, reaching 64.71 and 41.83 points respectively, the graft related CCI only increased after 3 months (26.22 points) mainly including Grade-II complications (Fig 1). The procedure related CCI remained low over the post-LT course but had the highest failure to rescue rate (16.6%). In very high-risk LT scenarios, morbidity increased in all three categories, with the highest increase for procedure related CCI (0 vs 60 points, p<0.001).

Conclusion: Recipient related complications had the highest impact on overall morbidity but transplant related complications had the highest failure to rescue rate. Graft related morbidity only occurred after 3 months with a frequent need of interventional treatment. The proposed morbidity categories may serve as pragmatic study endpoints to validate novel treatment strategies in LT.
EVALUATION THE SIX MONTH ABSTINENCE RULE PRIOR TO LIVER TRANSPLANT: A CLINICAL PRACTICE GUIDELINE

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Background: Until recently in Canada patients with alcohol associated liver disease (ALD) had to be abstinent from alcohol use for 6-months prior to assessment for liver transplantation (LT). This rule has been called into question from evidence, ethical and legal lenses. The purpose of this clinical practice guideline (CPG) is to guide the assessment and management of ALD and LT.

Methods: A committee including medical and surgical experts in liver transplant, addiction, ethics, law, methodology and patient partners developed a CPG according to GRADE Methodology. The steering committee generated and answered questions in the population, interventions, comparison and outcome format.

Results: Five conditional recommendations (very low certainty of evidence) and 2 best practice statements for patients undergoing LT were made. The recommendations included: 1) To not use the six-month rule as a sole criterion for liver transplant in ALD, 2) The definition of relapse should distinguish between: 1. non harmful relapse (e.g. occasional drinking or slip), 2. harmful drinking (e.g. physical, psychosocial implications, binge drinking/escalation drinking) and relapse monitored by biochemical markers when available, 3. During liver transplant workup, assessment of risk factor associated with post-transplant relapse (presence of uncontrolled psychiatric disease, history of smoking and multiple failed attempts of alcohol treatment) and protective factors (social support and employment) should be part of the holistic multidisciplinary assessment to allow for early intervention to mitigate risk factors, 4) The use of validated screening scoring systems and biomarkers for screening post-transplant relapse, 5) Integrated multidisciplinary teams with psychiatrists, addiction services to prevent relapse pre and post-transplant. The best practice statements included: 1) Listed and transplanted ALD patients should be intermittently screened for relapse pre and post-transplantation and 2) We suggest a holistic assessment for patients being evaluated for liver transplant, that not only take into account risk factors or other screening modalities, but a multi prong, multidisciplinary approach.

Conclusions: This CPG provides evidence-based recommendations for listing and transplanting patients with ALD.

IMPACT OF DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION (D-HOPE) ON HEPATOCELULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Ischemia reperfusion injury, which is mitigated by machine perfusion, may increase recurrence of hepatocellular carcinoma (HCC) after liver transplantation (LT). We investigated impact of dual hypothermic oxygenated machine perfusion (D-HOPE) on HCC recurrence in LT.

Methods: Single-center retrospective study in the period 01/2016-12/2020. Pre- and postoperative data of HCC patients undergoing LT were analyzed, comparing recipients of a D-HOPE treated graft with those preserved by static cold storage (SCS). Primary endpoint was recurrence-free survival.

Results: Of 326 patients, 246 received a SCS-preserved liver and 80 a D-HOPE-treated graft (DBD, n=66; DCD, n=14). Donors in the HOPE group were older (72 vs 68 years, p=0.003) and had higher BMI (27 vs 25, p=0.001). All DCD donors were treated by normothermic regional perfusion and D-HOPE. The groups were comparable in terms of HCC features, as it was 5-year recurrence-free survival estimated by metroticket 2.0 model (Figure). Immunosuppression was comparable, except that more patients in the D-HOPE group had induction by basiliximab (54% vs 20%, p<0.001). Everolimus was introduced in 71% of patients in each group. 30 (9.2%) patients had HCC recurrence, which was extra-hepatic in 21 (70%). No DCD recipient had recurrence. At Cox regression, HCC recurrence was associated with previous hepatic resection (HR 4.4, CI 1.7-11, p=0.003), microvascular invasion (HR 5.4, CI 2.6-11, p<0.001) and G3-G4 grading (HR 5.4, CI 2.6-11, p<0.001). HCC recurrence rate was comparable between groups (D-HOPE 10%; SCS 8.9%; p=0.95). D-HOPE did not reduce HCC recurrence, which was confirmed by Bayesian model averaging and competing risk analysis. Excluding DCD recipients did not change results. Recurrence-free survival and other postoperative outcomes, including early (10% vs 10%, p=1) and late (4.5% vs 3%, p=0.145) rejection rate, were comparable, except that in D-HOPE group AST (903 vs 1140, p=0.022) and ALT (496 vs 792, p<0.002) peak was lower.

Conclusions: In our experience, including mainly DBD cases, D-HOPE did not reduce HCC recurrence nor rejection but allowed utilizing livers from extended criteria donors with comparable outcomes. Given low HCC recurrence rate, larger studies may be needed to demonstrate a significant impact of D-HOPE.
MODERATED POSTER

LIVER TRANSPLANT RECIPIENTS WITH AUTOIMMUNE HEPATITIS IN THE SWISS TRANSPLANT COHORT: STUDY HAVE A HIGHER RISK OF GRAFT LOSS AND VASCULAR COMPLICATIONS

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**Background**: Data suggest that patients transplanted for autoimmune hepatitis (AIH) have a higher post-liver transplantation (LT) mortality compared to other liver diseases.

**Methods**: All adult patients with a first LT from May 2008 to December 2020 and included in the Swiss Transplant Cohort Study were classified into seven categories according to their indication to LT: AIH, alcohol-related liver disease (ARLD), viral liver disease (VLD), primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), non-alcoholic steatohepatitis (NASH) and other. Patients with AIH were selected based on clinical, immunological and histopathological criteria; patients with unequivocal etiology were classified in the respective categories, patients with mixed or other diagnoses being classified as “other”. Primary outcomes were death and patient survival; secondary outcomes were post-transplant vascular, biliary and infectious complications. Cumulative incidence of graft loss and death were calculated in the different categories and compared with AIH. The p-value was adjusted according to the Bonferroni method. A Cox proportional hazards model was used to investigate the effect of AIH on complications.

**Results**: 880 LT recipients were included: 23 transplanted for AIH, 254 for ARLD, 303 for VLD, 38 for PBC, 49 for PSC, 61 for NASH, and 152 for other indications. In the AIH group, 65.2% (n = 15) were women, the median age was 49 (IQR 39-58) years and MELD score 20 (15-32); graft loss and death rates were 34.8% (n = 8) and 21.7% (n = 5). There was no significant difference in death rates between AIH and other groups but graft loss was significantly higher in AIH patients (p = 0.002) (Figure). Eighteen (78.3%) AIH patients had a relevant complication, 77.8% (n = 14), 44.4% (n = 8) and 27.7% (n = 5) of them having a vascular, biliary or infectious complication. In multivariate analysis, AIH was independently associated with a higher risk of complications (HR 1.693, 95% CI 1.024-2.799, p = 0.040), along with pre-LT MELD score (HR 1.013, 95% CI 1.002-1.024, p = 0.017), living donation (HR 3.165, 95% CI 2.069-4.841, p < 0.005), and rejection (HR 3.452, 95% CI 2.487-4.791, p < 0.005).

**Conclusions**: Patients transplanted for AIH have a higher risk of graft loss compared to other etiologies, explained by a higher rate of vascular complications.
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**Background:** Rejection is the first cause of allograft loss in pediatric kidney transplant (pTx) recipients. Detection of rejection relies on kTx biopsies performed either because of allograft dysfunction with the risk of late diagnosis or per surveillance protocols allowing early detection of subclinical rejection but resulting in unnecessary biopsies. Dd-cfDNA is a non-invasive biomarker able to improve rejection detection and guide biopsy indications. We aim to assess the association of dd-cfDNA levels with biopsy results in a large cohort of pTx recipients.

**Methods:** All pTx patients with at least one dd-cfDNA assessment at the time of a biopsy were included. Clinical, biological and histological data were collected. Dd-cfDNA were retrospectively measured from plasma samples biobanked at the time of allograft biopsy between 2015 and 2020 or collected in patients receiving dd-cfDNA testing as part as clinical care since 2021.

**Results:** 170 cfDNA measurements in 132 pTx recipients were available at the time of biopsy, including 100 performed for surveillance. Mean age at biopsy was 16 years with a median time from kTx of 21 [11-38] months. Median eGFR was 62 [48.83] mL/min/1.73m², median UPCR 0.21 [0.14;0.36] g/g, and 20% had DSA.

**Conclusions:** We confirm in the largest pediatric kTx cohort to date, the association of dd-cfDNA levels with allograft rejection and its potential interest as a non-invasive biomarker in children. Further studies are needed to assess the added value of dd-cfDNA monitoring to the current standard of care and its ability to reduce unnecessary surveillance biopsies and improve outcomes.

**Figure 1:** Association between dd-cfDNA levels and active tubule-interstitial and microvascular Banff lesions

**Figure 2:** Association between dd-cfDNA levels and biopsy results.
REGIONAL OUTCOMES OF PAEDIATRIC RENAL TRANSPLANTATION IN THE UK: A MACHINE LEARNING ANALYSIS

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Purpose: <25% of UK children commencing RRT receive a pre-emptive transplant in the UK. Disparities have been reported amongst gender and ethnic groups. Paediatric patients on the waiting list have increased over the last 5 years. This study assesses the paediatric renal transplant rates in the UK since the year 2000 and the regional graft outcomes of paediatric renal transplant in the UK and determine the predictors of survival at 1 year, 3 years, and 5 years.

Methods: We harmonized the NHSBT Data to shortlist the paediatric renal transplants performed in the UK from the year 2000-2019. The Predictors of Transplant outcomes were evaluated by five classifiers including logistic regression, SVM, random forest, K-Nearest neighbour matching, and adaptive boosting. Random Forest Model had the best performance validated by RMSE. Rattle R/ JASP was used to derive Variables of importance. Survival outcomes and predictors data mined from MLA were further mined with Cox Regression.

Results: A total of 2610 paediatric transplants were reported to NHSBT (the year 2000-2019). London region did the maximum transplants (N = 854) followed by Northern and Yorkshire (N = 347) and Northern region (N = 340). High Volume center doing living donors had considerably better survival compared to others. On Regression analysis, the better graft survival was correlated to recipient age group >8 years (p <0.001), CIT <12 hr (p= 0.02), Transplant year -2010 onwards (p <0.01), ethnically matched donor-recipient (p= 0.01), HLA NHSBT group 1 and 2 (p=0.04) and high volume centers (> 15 paediatric transplants/annually).

Conclusions: Superior outcomes were reported from high-volume centers and transplants done after the year 2010. Immunologically well-matched kidneys and low Cold Ischemia time (CIT) predict better survival.

KIDNEY TRANSPLANTATION IN CHILDREN WEIGHING 10 KG OR LESS: IS IT A CHALLENGE?

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Koç University Faculty of Medicine, Pediatric Nephrology, Istanbul, Turkey, Koç University Faculty of Medicine, Transplant Immunology Research Center of Excellence, Istanbul, Turkey, Koç University Hospital, Department of Pediatrics, Istanbul, Turkey, Koç University Hospital, Koç University Hospital Organ Transplant Center, Istanbul, Turkey. Koç University Faculty of Medicine, Department of Urology, Istanbul, Turkey

Background: Kidney transplantation (tx), which is considered as the most appropriate treatment for children with end-stage kidney disease, is generally applied in children over 10 kg of body weight. Young children represent the vulnerable population in terms of post-transplant fluid-electrolyte and blood pressure management and immunosuppressive treatment. Infections are a significant risk in these patients and may affect graft survival. We aimed to evaluate the clinical outcomes of transplantation in young children, especially infants weighing less than 10 kg, by comparing them with older children.

Methods: Kidney transplant recipients less than 10 kg were included in this retrospective observational study. This patient group was matched with a pediatric control group in the recipient’s sex and post-transplant follow-up by the nearest neighbor matching method. The primary endpoint was all-cause mortality and graft loss. The secondary endpoints were the occurrence of allo-graft rejection, Cytomegalovirus (CMV), BK virus (BKV), and Ebstein-Barr virus (EBV) infections.

Results: Thirty-four kidney transplant recipients were followed for a median of 36 months after transplantation. Although, there were no statistical differences in both groups in terms of BKV (5 vs. 7; p=0.134), CMV infections (8 vs. 11; p=0.166); EBV DNAemia (11 vs. 1; p<0.001) were common in the patient group than the control group. EBV-related Post tx lymphoproliferative disease (PTLD) occurred in 2 children in the patient group.

Conclusions: The survival rates of infants less than 10 kg were %100 at a median three years follow-up. But the frequency of EBV DNAemia in these patients has increased compared to the other pediatric population. Therefore, close follow-up of these patients is required.
The Effect of HLA Matching in Paediatric Kidney Transplantation

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Background: Impact of HLA-matching in paediatric transplantations is less known. Our study investigated the effects of HLA matches/mismatches between donors and paediatric recipients of kidney transplantation. To our knowledge this is the first systematic review on the topic.

Methods: Study was registered with PROSPERO. MedLine and Embase were searched through Ovid, Cochrane and Web of Science were also searched systematically. Risk of Bias assessment was performed using NHBLI tools by 2 independent researchers.

Results: Search identified 3033 papers, 4 met the inclusion criteria. Graft survival was not affected significantly if there was 0 or 1 mismatch. Similarly having a match of more than 3 HLA A+B alleles increased the graft survival significantly. Incidence of acute rejection was not correlated with number of HLA mismatches (all types) (P > 0.05), however it was negatively correlated with number of HLA DR mismatches (P = 0.02).

Conclusions: The evidence from the papers show that there is no significant difference in graft/recipient survival between 0 or 1 mismatches in kidney transplantation, however a mismatch of 3 or more influences post-transplant outcomes.

Table 1: Effect of HLA matching in paediatric kidney transplantation

<table>
<thead>
<tr>
<th>Study</th>
<th>Total no. of patients</th>
<th>No. of Patients (HLA AB) or Match (P)</th>
<th>Key Findings</th>
</tr>
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<tbody>
<tr>
<td>Reitho 2014</td>
<td>128</td>
<td></td>
<td></td>
</tr>
<tr>
<td>El-Husseini 2005</td>
<td>284</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mckenny 1992</td>
<td>1358</td>
<td>8-18 (M: 1125, F: 233)</td>
<td></td>
</tr>
<tr>
<td>Gaffey 2010</td>
<td>9209</td>
<td>FR mismatches had no significant effect</td>
<td></td>
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STERIOD-BASED VS STEROID-FREE IMMUNOSUPPRESSION IN PAEDIATRIC KIDNEY TRANSPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Corticosteroids are the cornerstone of immunosuppressive regimens in kidney transplantation. In pediatric renal transplantation the side-effect profile of steroids becomes crucial as long-term exposure to high dose steroids affects the development and well-being of the child. Steroid free immunosuppressive regimens are an alternative with a better side effect profile, however to date no systematic review has been carried out evaluating corticosteroid free-regimens safety and efficacy in children.

Methods: Medline, Embase, CENTRAL and Web of Science databases were searched systematically. Risk of bias assessment was performed.

Results: Three studies were included in the meta analysis. No significant difference was seen between graft rejection in the steroid-based or steroid-free regimes (P=0.39) (OR: 0.78 (95% CI: 0.45, 1.36) (fig 1)). Cardiac arrest was reported as a side effect in steroid-based regimes whereas atrial flutter and cardiovascular insufficiency were reported in steroid-free regimes. Infections incidence had heterogeneity between studies and the relation to steroid-based or steroid-free regimes. Anaemia was more common in steroid-free and hypertension was more frequent in steroid-based regimes.

Conclusions: Steroid-free immunosuppressive regimens were as effective at minimizing graft rejection when compared to steroid-based regimes. While regimens are comparable in efficacy, side effect profiles differ between regimes.

CORRELATION BETWEEN CLINICAL OUTCOMES AND QUALITY OF LIFE IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Background: Kidney transplantation is the preferential kidney replacement therapy (KRT) for children with renal failure with well reported physiological and psychosocial advantages over dialysis. There is an abundance of literature regarding clinical outcomes (CO's) associated with KRT but a scarcity of data assessing the impact of these CO's on quality of life (QoL). This study aimed at identifying correlation between CO's and the effect on QoL of paediatric kidney transplant recipients (pKTR).

Methods: Patients attending clinic were offered the opportunity to complete a standardised age-appropriate QoL questionnaire (PedsQL TMv3.0) during clinic attendance in April 2022. Inclusion criteria were pKTR at least three months post-transplant of a single organ (kidney). Questionnaire responses were pseudo-anonymised with QoL scores subsequently matched to individual clinical outcome dataset. The Cronbach alpha co-efficient was calculated for each section of the questionnaire to ensure there was reliable as opposed to error variance.

Results: Of the 46 patients approached to take part, 36 (76% of total post-transplant cohort) met inclusion criteria and completed the questionnaire. The mean patient age and timing post-transplantation were 12.8 years and 5.2 years, respectively. CAKUT (42%) and nephrotic syndrome (22%) were the most prevalent causes of kidney allograft function based on different patient history elements and PROs at their regular outpatient clinic visits. We conducted an unweighted, undirected network-based clustering analysis to identify patient history elements and PROs associated with kidney allograft function and other clinical outcome surrogate parameters (e.g., creatinine).

Conclusions: With this pilot study, for the first time, we demonstrated a clearer differentiation between pediatric patients with high and low kidney allograft function based on different patient history elements and PROs (e.g., defecation-related questionnaire elements).

STERIOD-BASED VS STEROID-FREE IMMUNOSUPPRESSION IN PAEDIATRIC KIDNEY TRANSPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Digital and systematized collection of patient history provides additional information in comparison to traditional methods. Measurement of a patient’s perception of his/her disease and corresponding treatment without interpretation by a third person (i.e., healthcare personnel) defines Patient-Reported Outcomes (PROs). PROs fill an important gap in chronic kidney disease to achieve optimal disease control, treatment, and well-being. Neither PROs nor digital patient history systems are frequently implemented in clinical routine. This pilot study aimed to develop, implement, and analyze a digital system for collection of patient history and PROs of pediatric patients with kidney transplantation (KTX), in context of their graft function during follow-up.

Methods: Pediatric KTX patients received a tablet with 19 questions collecting their recent history (i.e., since the last visit) and PROs at their regular outpatient clinic visits. We conducted an unweighted, undirected network-based clustering analysis to identify patient history elements and PROs associated with kidney allograft function and other clinical outcome surrogate parameters (e.g., creatinine).

Results: A total of 49 pediatric KTX patients were included in this study, with 67% male:female, a median age of 14 (IQR 11-16) and a median post-transplant follow-up time of 5.3 (IQR 2.7-10) years. 45% were living donor recipients, and maintenance immunosuppression was mainly a triple regimen (tacrolimus, mycophenolate mofetil, steroids). The median graft function at baseline was 100 mL/min/1.72 m² (IQR 70-124). We identified a total of four clusters of which two clearly differentiated between patients with high and low kidney allograft function based on different patient history elements and PROs (e.g., defecation-related questionnaire elements).

Conclusions: With this pilot study, for the first time, we demonstrated a clear differentiation between pediatric patients with high and low kidney allograft function based on different patient history elements and PROs. Longitudinal follow-up of pediatric kidney transplant patients with such digital patient history and ePRO systems could aid in the early identification of complications after successful transplantation and facilitate early intervention.
**E-Posters**

**P001 IMPACT OF COVID-19 PANDEMY ON KIDNEY TRANSPLANTATION IN POLAND**

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**Background:** COVID-19 pandemic highly influenced on medical services worldwide. Many medical procedures have been cancelled or postponed. In some cases access to physicians was extremely difficult and in very often cases limited to medical advices over digital communication solutions. One of the most affected medical procedures were qualification for the kidney transplantation, which requires the several medical advices with specialists from different areas and imaging and lab diagnostics on the qualification stage. The aim of the research was check how the numbers of qualified for kidney transplantation patients have been changed in 2020 and 2021 - the years of COVID-19 pandemic in comparison with 2019 data - year without pandemic limitations.

**Methods:** The official data from Polish Transplant Coordinating Centre Poltransplant bulletin from 2019, 2020 and 2021 has been analyzed in terms of the number of patients registered on the waiting list for kidney transplantation. The number of the kidney Tx provided in the country has been taken into consideration as well.

**Results:** During SARS-CoV-2 pandemy the number of qualified and transplanted patients significantly decreased. The most worsened data concerns the new qualifications which decreased about 30% in the first year of pandemic as the effect of all restrictions implemented. Second year of pandemy brought better results of patients newly registered on the waiting list (+11.6%), however still remains on the level lower than in previous years (1178 in 2018 vs. 1160 in 2017). The number of Kidney Tx procedures provided during 2-years pandemy period also decreased significantly and in the second year of the pandemy didn’t increased satisfactorily (0.6%).

**Conclusions:** The period of the pandemy had a great impact on the developement of kidney transplantation in Poland. Restrictions caused by pandemic restrictions have deprived many patients of any chance for treatment. We shall focus on the rapid growth in the number of transplants in the years following the pandemic. On the other hand, the community of transplantologists should induce cooperation with national authorities to implement the best possible procedures of protection the patients referred for transplantation in case of the future epidemnic situation.

**P003 IMPACT OF DIFFERENT IMMUNOSUPPRESSIVE PROTOCOLS ON CLINICAL OUTCOMES IN OBESE KIDNEY TRANSPLANT RECIPIENTS: A PROPENSITY SCORE MATCHED ANALYSIS**

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**Background:** Although obesity has become a relevant clinical problem in the field of transplantation, the impact of different immunosuppressive protocols on clinical outcomes in obese transplant recipients remains unclear. This study aimed to evaluate the obesity-specific impact of calcineurin inhibitor (CNI) or mammalian target of rapamycin inhibitor (mTOR) and its combinations on clinical outcomes in kidney graft recipients.

**Methods:** Data were obtained from the Scientific Registry of Transplant Recipients (SRTR) database. Kidney transplant recipients were categorized to BMI categories and according to immunosuppressive protocols: Tacrolimus/Mycophenolate-Mofetil (Tac-MMF), mTOR-Inhibitor/Tac (mTORi-Tac), mTORi/ Cyclosporin (mTORi-Cyc) and mTORi/MMF. Primary outcome was acute rejection within the first year after kidney transplantation, secondary outcomes included eGFR, graft and overall survival. Propensity score matching, binary logistic regression and Cox regression analysis were used.

**Results:** Among 14,500 patients, graft recipients with advanced obesity (BMI ≥35 kg/m²) exhibited significantly lower rates of acute rejection (AR) in the mTORi-Tac (6.4%) and mTORi-Cyc (8.2%) group compared to Tac-MMF (10.8%). There was no significant association between obesity and the risk of AR on patients receiving therapy with mTORi-MMF (HR: 1.29, 95% CI 0.69–2.43, p value 0.42) and mTORi-Cyc (HR: 1.55, 95% CI 0.92–2.81, p value 0.097), compared to Tac-MMF. Advanced obesity was associated with a significant risk of graft loss in patients receiving therapy with mTORi-MMF (HR: 1.50; 95% CI 1.20–1.88; p<0.001) and mTORi-Tac group (HR: 1.44; 95% CI 1.17–1.76; p<0.001) compared to Tac-MMF, but for not the mTORi-Cyc group (HR 1.15; 95% CI 0.92–1.35, p value 0.28). In the Tac-MMF group, patients with morbid obesity had significantly higher mortality due to cardiovascular disease and infection compared with normal-weight patients.

**Conclusions:** Combination of mTORi and CNI is associated with lower rejection rates and stable long-term kidney function while reducing cardiovascular side effects linked to CNIs in obese kidney graft recipients. These results are critical for the growing number of obese graft recipients and warrant prospective evaluation.

Figure: Cox regression stratified by BMI
**P004 PANCREAS TRANSPLANT ALONE IN UREMIC (PTAU) PATIENTS**

*Yi-Ming Shyr*1

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**Background:** Theoretically, pancreas before kidney transplant (PBK) could be an option for those waiting for both pancreas and kidney grafts. Outcomes of pancreas before kidney transplant (PBK) have never been reported before.

**Methods:** In total, 86 diabetes patients undergoing pancreas transplants were included in this study. Clinical data and outcomes were compared between pancreas transplant subgroups.

**Results:** There were 26 (16%) PBK. The rates of pancreas graft rejection were 3.8% in the pancreas before kidney transplant, 16.7% in the pancreas after kidney transplant (PAK), 29.8% in the simultaneous pancreas and kidney transplant (SPK), and 37.0% in the pancreas transplant alone (PTA) groups. There was no chronic rejection in the PPK and PAK groups. Fasting blood sugar and serum hemoglobin A1c levels after PBK were not significantly different from those of other subgroups. Serum C-peptide levels were significantly higher in the PBK than in the other subgroups. The 5-year pancreas graft survival was 100% for the PBK and PAK, 97.0% for the SPK, and 77.9% for PTA.

**Conclusions:** The inferior patient survival outcome, PTAU is still not recommended unless SPK and PAK is not available. Although PTAU could be a treatment option for patients with diabetes complicated by end-stage renal disease (ESRD) in terms of surgical risks, endocrine function, and immunological and graft survival outcomes, modification of the organ allocation policies to prioritize SPK transplant in eligible patients should be the prime goal.

**P005 PANCREAS TRANSPLANT WITH ENTERIC DRAINAGE: EXPERIENCE OF TAIPEI VETERANS GENERAL HOSPITAL**

*Yi-Ming Shyr*1

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**Background:** Insulin-dependent diabetes mellitus (IDDM) eventually leads to nephropathy, neuropathy, retinopathy and angiopathy after 10 – 30 years. Nowadays, pancreas transplantation is the treatment of choice in tight control of blood sugar for IDDM patients. Simultaneous pancreas and kidney (SPK) transplantation would be an ideal treatment option to resolve both uremia and IDDM. We will present our experience in pancreas transplant.

**Methods:** From September 2003 to September 2020, 164 cases of pancreas transplant were performed, including 37 SPK, 20 pancreas after kidney transplant (PAK), 78 pancreas transplant alone (PTA), 26 pancreas before kidney transplant (PBK) and 1 pancreas after liver transplant (PAL). The clinical courses including blood sugar, C-peptide and HbA1C levels and renal function after operation were recorded. The complications and outcomes were also evaluated.

**Results:** Majority (93%) of the pancreas transplantations in T2DM were for uremic recipients. Complications occurred in 106 (73%) patients, including 70 (48%) with early complications before discharge and 79 (54%) with late complications during follow-up period. Overall, rejection of pancreas graft occurred in 37 (25%) patients. Total rejection rate in T2DM recipients was significantly lower than that in T1DM. The short-term and long-term outcomes for endocrine function in terms of fasting blood sugar and hemoglobin A1c levels and graft survival rates are comparable between the T2DM and T1DM groups.

**Conclusions:** T2DM is not inferior to T1DM after pancreas transplantation in terms of surgical risks, immunological and endocrine outcomes, and graft survival rates. Therefore, pancreas transplantation could be an effective option to treat selected uremic T2DM patients without significant insulin resistance.

**P006 PANCREAS TRANSPLANTATION FOR TYPE 2 DIABETES MELLITUS**

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**Background:** Pancreas transplantation remains the best long-term treatment option to achieve physiological euglycemia and insulin independence in patients with labile diabetes mellitus (DM). It is widely accepted as an optimal procedure for type 1 DM (T1DM), but its application in type 2 DM (T2DM) is not unanimously acknowledged.

**Methods:** In total, 146 diabetes patients undergoing pancreas transplantation were included in this study. Clinical data and outcomes were compared between the T1DM and T2DM groups.

**Results:** Majority (93%) of the pancreas transplantations in T2DM were for uremic recipients. Complications occurred in 106 (73%) patients, including 70 (48%) with early complications before discharge and 79 (54%) with late complications during follow-up period. Overall, rejection of pancreas graft occurred in 37 (25%) patients. Total rejection rate in T2DM recipients was significantly lower than that in T1DM. The short-term and long-term outcomes for endocrine function in terms of fasting blood sugar and hemoglobin A1c levels and graft survival rates are comparable between the T2DM and T1DM groups.

**Conclusions:** T2DM is not inferior to T1DM after pancreas transplantation in terms of surgical risks, immunological and endocrine outcomes, and graft survival rates. Therefore, pancreas transplantation could be an effective option to treat selected uremic T2DM patients without significant insulin resistance.
**Background:** Reported reasons for kidney allograft loss vary widely depending on methods of classification and follow-up duration.

**Methods:** In this single-center study we included all 1477 adult kidney transplants performed between 1997 and 2017 of which all 286 deaths with a functioning graft (DWF) until the end of observation were analyzed case-by-case by an adjudication committee and causes for death assigned based on pre-specified criteria. Additionally, the results were compared to the causes of 303 death-censored graft failures (DCGF) of the same cohort that have already been investigated, to evaluate the impact of causes on overall graft loss. No patients were lost to follow-up.

**Results:** The most frequent causes for DWF were cardiovascular disease (CVD) in 30.8%, malignancy in 28.3% and infections in 21%. Only 9.4% of reasons for DWF were unknown. Sudden cardiovascular death occurred in 40% (35/88) of patients classified as DWF due to CVD. While cardiovascular disease was responsible for >50% of deaths in the first month after transplantation, the number of deaths due to malignancy continuously increased and peaked later than for infections and cardiovascular disease around 8 years after transplantation. Overall graft loss was related to the effect of immunosuppression in 36.2% (infection: 20.9% (123/589); malignancy: 15.3% (90/589)) and CVD in 22.4% (132/589) (Figure 1). In 27.4% (161/589) graft failure was associated with under-immunosuppression (rejection). For infections (80 DWF; 63 DCGF) and CVD (88 DWF; 44 DCGF) a considerable overlap was observed between DWF and DCGF. For patients >70 years of age at transplantation, medical events accounted for 76% of overall graft losses and only 6.5% were associated with rejection.

**Conclusions:** DWF and DCGF share more causes for graft loss than previously reported, and sudden death plays an underestimated role in death with a functioning kidney allograft.
Background: Renal transplantation is the most successful therapy of end-stage renal failure since it is associated with extended life expectancy and quality of life compared to dialysis. As of January 2022, there were in the US, 100,000 patients on the waitlist, with only 24,669 kidneys transplanted the previous year, and an annual death rate of 5,000 patients on the wait-list. Stragertems are sought to expand the donor pool and neonates can be considered a source of kidneys, until now unexplored, since the report by LW Martin in 1969 of the long-term successful transplantation of en bloc anencephalic kidneys to a 17 pound boy.

Methods: To assess the feasibility of neonatal organ donation, we reviewed the neonatal mortality in the US, the physiology of the neonatal kidneys, the ethical, social and medico-legal problems associated with neonatal brain death, and the long-term development of the kidneys after transplantation. The organ procurement and the allocation are also discussed.

Results: Of the 21,000 infants dying in 2020, and taking a conservative approach, 8,600 infants with lethal congenital malformations, 2,380 infants with CNS injuries, and 1,260 infants with respiratory distress could be considered as organ donors. There is ample evidence that en bloc infant kidneys 1- have a catch-up growth, 2- provide excellent long-term function (>25 years) exceeding that of living donor kidneys, 3- are not subjected to hyperfiltration injury, and 4- can be transplanted safely with current techniques at hands.

Conclusions: Ethical, social, medico-legal and technical aspects have been established and are ready for use in neonatal organ donation and transplantation. Policies should be implemented to allow such approach. A simplified allocation system is indicated to avoid long cold ischemia. Neonatal kidneys can improve organ shortage.

Neonatal organ donation for kidney shortage; is this the time?

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Background: The choice between Basiliximab (BSX) or Anti-Thymocyte Globulin (ATG) as induction therapy in non-immunized kidney transplant recipients remains uncertain. Whilst ATG may allow steroid withdrawal and a decrease in tacrolimus, it also increases the risk of viral reactivations due to a prolonged dose-dependent lymphopenia. We investigated outcomes in non-immunized patients receiving a very low dosage of ATG versus BSX as induction therapy.

Methods: In this monocentric study, we analysed non-immunized patients receiving a first kidney transplant between 2015 and 2020. The study outcomes were patient and graft survival, cumulative probabilities of biopsy proven acute rejection (BPAR), infectious episode, CMV infection, post-transplantation malignancy and post-transplant diabetes (PTD). Cox, logistic or linear statistical models were used depending on the studied outcome and models were weighted on propensity scores.

Results: 183 patients were included: 100 receiving ATG (mean total dose of 2.0 mg/kg) and 83 receiving BSX. Maintenance therapy was comparable between groups. Patient and graft survival did not differ between groups, nor did malignancies, infectious complications or CMV viremia. There was a trend for a higher occurrence of a first BPAR in the BSX group (HR at 1.92; 95% CI: 0.77; 4.78, p-value = 0.15) with a significantly higher number of BPAR episodes (17% vs 7.3%, p = 0.0152). PTD occurrence was significantly higher in the BSX group (HR at 4.78, p-value = 0.15) with a significantly higher number of BPAR episodes (17% vs 7.3%, p = 0.0152). PTD occurrence was significantly higher in the BSX group (HR at 4.78, p-value = 0.15)

Conclusion: Induction with a very low dose of ATG in non-immunized recipients was safe and associated with a lower rate of BPAR and PTD without increasing infectious complications.

Very low dose anti-thymocyte globulins versus Basiliximab in non-immunized kidney transplant recipients

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Operating theatre nurses’ main concerns during the operative process of organ donation—A grounded theory

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Background: Organ donation is the result of cooperation between many professionals in a chain of events where it is crucial that every professional involved does her/his utmost to facilitate organ preservation and retrieval. The responsibilities for the Operating Theater Nurse (OTN) range from ensuring that the right instruments are in place to safeguarding the donor’s dignity and rights. The OTN must be flexible since the donation often occurs during nights and involves unfamiliar surgical teams. Little is known about operating theatre nurses’ (OTNs) main concerns during the perioperative organ donation process and how they deal with them. The purpose of this study was to explore OTNs’ experiences of caring for the organ donor during operations where organs are retrieved and to answer the question: what is the main concern during this procedure and how do they deal with it?

Methods: A total of ten OTNs, one man and nine women with a mean age of 51.8 years (range 38-63 years) were interviewed in this Constructive Grounded Theory study. No prior theory exists and the grounded theory stem from the participants’ own experiences. The informants represent two University hospitals and three regional hospitals in Sweden to reflect a diversity of hospital settings and geographical areas.

Results: A core category emerged during the analysis: Optimum organ retrieval, where the generated grounded theory is present in the four main categories: Brace oneself, Facilitate, Retrieve and Completion. Commitment is the force that binds the OTN to a course of action of relevance for optimum organ retrieval. Respect for and the dignity of the donor is essential.

Operating Theatre Nurses’ Main Concerns during the Operative Process of Organ Donation—A Grounded Theory

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A core category emerged during the analysis: Optimum organ retrieval, where the generated grounded theory is present in the four main categories: Brace oneself, Facilitate, Retrieve and Completion. Commitment is the force that binds the OTN to a course of action of relevance for optimum organ retrieval. Respect for and the dignity of the donor is essential.
**P015**  
**RESPONSE TO COVID-19 VACCINATION AND CONTIX-AEGIVIMAB-CILGAVIMAB PROPHYLAXIS IN PATIENTS UNDERGOING LIVER AND KIDNEY TRANSPLANTATION: PRELIMINARY STUDY**

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**Background**: Liver (LT) and kidney (KT) transplant patients are at high risk of mortality from COVID-19 (16-29%), 28%, respectively. Although transplant patients undergo a full vaccination course (3 doses), they are frequently low-responders and long-acting-antibody prophylaxis (LAAB) has been proposed. However, the efficacy of these strategies has not yet been demonstrated in LT and KT. The objective of our study is the evaluation of the antibody response after complete vaccination and the efficacy of prophylaxis with LAAB. 

**Methods**: Since 03/01/2022 all LT and KT patients undergoing follow-up were enrolled. anti-COVID-19 title was obtained by ECLIA Test (Elyx, Roche). In the case of antibody level <100 IU/mL, patients were invited to prophylaxis with tixagevimab-cilgavimab (AZD7442, AstraZeneca). At three months, a follow-up was performed. 

**Results**: Until 31/03/2022 155 patients were enrolled (58 KT; 57 LT), mean age 59.1 (±11.61), with mean antibody value 1127.05 and 1701.14 IU/mL and protective value(responder) in 42 (72.88%) and 45 (79.31%) cases, respectively. Among 32 (27.83%) low-responders, 16 (50%) patients underwent LAAB. After LAAB 4 KT contracted COVID-19, 3 in mild/asymptomatic form and one hospitalized which not required oxygen therapy. In the following three months, in responder patients 83 (72.17%), 6 KT and 8 LT had in mild/asymptomatic COVID-19. No graft-loss, acute rejection, or death have been recorded. 

**Conclusions**: COVID-19 vaccination in KT and LTs can reduce the mortality of transplant patients. In low-responder patients, LAAB prophylaxis is safe and protective, resulting in reduced complications and hospitalization.
**P17**  
**HEPATIC ARTERIAL REVASCULARIZATION IN THE FIRST 72 HOURS FOLLOWING LIVING-DONOR LIVER TRANSPLANTATION: SURGICAL OR ENDOVASCULAR? - A PROPOSED ALGORITHM**

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**Background:** The aim of this retrospective cohort study was to evaluate the feasible treatment modalities for early hepatic artery thrombosis (e-HAT) in the first 72 hours (hrs) following living-donor liver transplantation (LDLT) as well as to design a structured algorithm –based on our 20-year LDLT experience– for management of such a devastating complication during this very early post-transplant period.

**Methods:** The medical records of 34 patients who developed e-HAT following LDLT between August 2001 and September 2021 were retrospectively reviewed. In all cases, the treatment modalities employed and their outcomes were thoroughly evaluated. Revascularization approaches that were used in the first 72 hrs post-transplant were compared in terms of technical success, procedure-related complications, rebound thrombosis, graft failure and 1-year survival rates. Finally, a structured algorithm for management of e-HAT in the first 72 hrs post-LDLT was designed.

**Results:** Overall, the definite technical success and 1-year survival rates of hepatic arterial revascularization (Surgical / Endovascular / Both) were 85.3% (29/34 cases) & 61.8% (21/34 cases) respectively. Nineteen patients developed hepatic arterial revascularization (Surgical / Endovascular / Both) were 85.3% (29/34 cases) & 61.8% (21/34 cases) respectively. Nineteen patients developed hepatic arterial thrombosis (Surgical / Endovascular / Both) were 85.3% (29/34 cases) & 61.8% (21/34 cases) respectively. Nineteen patients developed hepatic arterial revascularization in the first 72 hrs post-LDLT (55.9%). Surgical revascularization was carried out in the first 72 hrs post-transplant in 6/34 cases (17.6%) “Group A” whereas endovascular therapy was carried out within the same time frame in 14/34 cases (41.2%) “Group B”. The definite technical success, rebound thrombosis and 1-year survival rates were 83.3%, 16.7% & 83.3% in group A; and 85.7%, 0% & 57.1% in group B; respectively. Five procedure-related complications were reported in 4 of group B patients (26.6%).

**Conclusions:** In the first 72 hrs post-LDLT, endovascular therapy –including stent placement (early stenting)– is a feasible and effective treatment option for e-HAT; but is associated with a relatively higher risk of procedure-related complications, compared to surgical revascularization. Hence, endovascular therapy can be reserved as a second-line option for treatment of e-HAT in the very early post-transplant period. It can be carried out –with the use of specific technical precautions– in certain situations where surgical revascularization could potentially be more risky, too complex, or absolutely futile.

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**P18**  
**USE OF ECULIZUMAB IN A CASE OF HISTOLOGICALLY PROVEN RECURRENCE OF COMPLEMENT FACTOR H-RELATED PROTEIN NEPHRopathy TO A KIDNEY ALLOGRAFT**

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**Background:** Human complement Factor H (H) -related 5 protein (CFHR5) nephropathy is a hereditary kidney disease endemic in Greek Cypriots and is the commonest cause of C3 glomerulonephritis (C3GN). Great phenotypic heterogeneity is noted among patients and manifestations can vary from isolated microscopic hematuria to end stage kidney disease (ESKD). CFHR5 protein antagonizes complement Factor H (CFH), which is the main circulating regulator of the complement system. To date there is no specific treatment for CFHR5 nephropathy. Although histologic recurrence of the disease after kidney transplantation is usual, graft outcomes are generally good, using standard immunosuppression regimens. Nevertheless, some transplanted patients lose their grafts due to aggressive recurrent disease, usually at the first post-transplant period. Eculizumab is a long-acting humanized monoclonal antibody targeting complement factor C5. Thus, the cleavage of C5 into C5a and C5b is prevented resulting in complement system deactivation. Regarding kidney diseases, until now Eculizumab use is only approved for the treatment of atypical hemolytic uremic syndrome. We describe the case of a 39 yo male patient with histologically proven recurrence of CFHR5 nephropathy in the renal allograft, two months post-transplant. An allograft biopsy was performed due to non-nephrotic range proteinuria and severe kidney function impairment. The patient’s kidney function deteriorated rapidly, leading to the decision to treat him with Eculizumab.

**Results:** Proteinuria was improved and kidney function returned to baseline over the next 3 months. The patient is currently in excellent clinical condition, having no adverse effects from the treatment 10 months after initiation of Eculizumab.

**Conclusions:** To our knowledge, this is the first time that Eculizumab was used as a treatment for CFHR5 nephropathy. Results are promising for kidney transplant recipients with features of clinical and histological recurrence of the disease but also for not transplanted patients with an aggressive form of the disease. Further studies are required to confirm the therapeutic effects of Eculizumab on CFHR5 nephropathy and to identify the subgroup of patients that would benefit from it.

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**P19**  
**PEDIATRIC ORGAN DONATION: SIXTEEN-YEAR EXPERIENCE OF A PEDIATRIC INTENSIVE CARE UNIT / INTENSIVE CARE UNIT IN A LEVEL 3 HOSPITAL FROM 2006 TO 2021**

Sara Rodrigues1*, André Silva1, Marta Grilo1, Margarida Rios1, Augusto Ribeiro2  
1Centro Hospitalar de Entre Douro e Vouga, Santa Maria da Feira, Portugal, 2Unidade Local de Saúde Alto Minho, Viana do Castelo, Portugal, 3Centro Hospitalar de Entre Douro e Vouga, Nogueira de Azeitão, Portugal

**Background:** Pediatric organ donors represent a small but important portion of the deceased donor pool, helping both children and adults in the transplant waitlist. Despite this, pediatric donation remains an overlooked subject of research. Although histologic recurrence of the disease after kidney transplantation is usual, graft outcomes are generally good, using standard immunosuppression regimens. Nevertheless, some transplanted patients lose their grafts due to aggressive recurrent disease, usually at the first post-transplant period. Eculizumab is a long-acting humanized monoclonal antibody targeting complement factor C5. Thus, the cleavage of C5 into C5a and C5b is prevented resulting in complement system deactivation. Regarding kidney diseases, until now Eculizumab use is only approved for the treatment of atypical hemolytic uremic syndrome. We describe the case of a 39 yo male patient with histologically proven recurrence of CFHR5 nephropathy in the renal allograft, two months post-transplant. An allograft biopsy was performed due to non-nephrotic range proteinuria and severe kidney function impairment. The patient’s kidney function deteriorated rapidly, leading to the decision to treat him with Eculizumab.

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**P022**

**ISOLATED GLOMERULITIS IS STRONGLY ASSOCIATED WITH THE ABSENCE OF ANTIBODY-MEDIATED REJECTION BY MOLECULAR DIAGNOSTICS**

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Background: According to the 2018 Banff classification, the Molecular Microscope Diagnostic System (MMDx) is indicated in cases when histology is insufficient to diagnose antibody-mediated rejected (ABMR) due to an absence of diagnostic criteria groups 2 and/or 3. The impact of isolated glomerulitis (g>0, pt<0) on the likelihood of ABMR diagnosis by the MMDx appears critical to the implementation of this new biomarker.

Methods: We analyzed 251 kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from October 2018 to November 2022. Histologic findings were classified concerning the absence of (1) diagnostic criteria groups 2 and 3 (n=18), (2) diagnostic criteria group 2 only (n=18), and (3) diagnostic criteria group 3 only (n=28). In addition, cases with histologically proven ABMR were used for comparison (n=65). High-resolution re-typing was performed from the kidney allograft biopsies if necessary.

Results: The MMDx diagnosed ABMR in 18 of 251 cases (6%) with absent diagnostic criteria groups 2 and 3, 3 of 41 cases (7%) with absent diagnostic criteria groups 2 and 19 of 28 cases (68%) with absent diagnostic criteria groups 3. On the contrary, MMDx confirmed the diagnosis of ABMR in 42 of 65 cases (65%) with histologically proven ABMR but did not in 23 of 65 cases (35%). Among 28 cases with absent diagnostic criteria group 3, only 2 of 19 cases (11%) with ABMR by MMDx but 6 of 9 cases (67%) with no ABMR by MMDx showed isolated glomerulitis (p=0.0048). Among 65 cases with histologically proven ABMR, only 7 of 42 cases (17%) with ABMR by MMDx but 14 of 23 cases (61%) with no ABMR by MMDx showed isolated glomerulitis (p=0.001). Overall, 14 of 65 cases (21%) with isolated glomerulitis showed ABMR diagnosis by MMDx.

Conclusions: Isolated glomerulitis is strongly associated with the absence of ABMR by MMDx not only when diagnostic criteria group 2 is missing but also when diagnostic criteria 3 is missing or ABMR is proven by histology. Our results may help to guide the indication for MMDx in clinical practice. However, the clinical significance of these results needs further investigation.

**Efficacy Outcomes With Tab-Cel in Patients With EBV+ PTLD Following SOT or HCT**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SOT (n=45)</th>
<th>SOT2 (n=45)</th>
<th>All (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders, n (%)</td>
<td>6 (13.3%)</td>
<td>9 (20.0%)</td>
<td>22 (24.4%)</td>
</tr>
<tr>
<td>Clinical benefit rate, n (%)</td>
<td>6 (13.3%)</td>
<td>9 (20.0%)</td>
<td>22 (24.4%)</td>
</tr>
<tr>
<td>Complete responder</td>
<td>1 (2.2%)</td>
<td>5 (11.1%)</td>
<td>7 (7.8%)</td>
</tr>
<tr>
<td>Partial responder</td>
<td>5 (11.1%)</td>
<td>4 (9.0%)</td>
<td>10 (11.1%)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>2 (4.4%)</td>
<td>0</td>
<td>2 (2.2%)</td>
</tr>
<tr>
<td>Progressor/disease</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

**Non-evaluable**

**P023**

**TAB-CEL FOR EBV+ PTLD AFTER FAILURE OF RITUX-IMAB 3 CHEMOTHERAPY FOLLOWING SOLID ORGAN OR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT PLANT ALLELE**

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Background: Poor OS in pts with relapsed/refractory EBV+ PTLD reveals an urgent unmet need for effective therapies. We previously reported interim data from ALLELE (NCT03394365), an ongoing, phase 3 multicenter clinical trial of tabcel, an investigational, off-the-shelf, allogeneic EBV-specific T-cell immunotherapy for EBV+ PTLD after failure of rituximab (R) ± chemotherapy (CT) following SOT or HCT. Here we present updated results with a focus on the SOT cohort.

Methods: Outcomes were assessed in pts with EBV+ PTLD following failure of R (HCT [n=14] and SOT1 [n=13]) and failure of R+CT (SOT2 [n=16]). All SOT types were eligible. Pts receive tab-cel at 2x10^9 cells/kg on days 1, 8 and 15 in a 35d treatment cycle.

Results: Analysis as of Nov 2021 was consistent with previously presented ALLELE data. ORR was 51.2% (22/43) in all pts (BOR of CR [27.9%] or PR [23.3%], 51.7% (15/29) in SOT overall, 46.2% (6/13) in SOT1, and 56.3% (9/16) in SOT2 (Table). Overall median TTR was 1.0 mo; overall median DOR was 23.0 mo. Estimated 1-yr OS rates were 61.1% overall, 56.2% for SOT overall, 47.6% for SOT1, and 64.3% for SOT2. Responders had a longer 1-yr survival vs non-responders in overall (Fig) and SOT groups. There was no change in safety profile compared with previous data (including no related allograft rejection or GvHD).

Conclusions: Updated ALLELE phase 3 data, with additional pts and longer follow-up, confirm that tab-cel provides consistent clinically meaningful outcomes, including improved ORR and both prolonged DOR and OS, in a pt population with poor survival and no approved therapies. Tab-cel was well tolerated without evidence of safety concerns typically observed with other adoptive T-cell therapies.

**P001 P100 P200 P300 P400 P500 P600 P700**
**P024 SUCCESSFUL INTERNATIONAL ADOPTION OF A COMPREHENSIVE, INTEROPERABLE, AND SECURE DIGITAL ORGAN OFFERING MANAGEMENT PLATFORM**

Jonathan Baldanza1, John Walsh2

1InVita Healthcare Technologies, Los Angeles, United States; 2Health Service Executive, Organ Donation and Transplant Ireland, Dublin, Ireland

**Background:** It is well understood that costly inefficiencies exist in the current fragmented donation and transplantation ecosystem. Outdated paper processes and systems operating in silos without seamless sharing of key data can lead to errors, mishandling of critically ill patients, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.

**Methods:** A donation organization responsible for managing country-wide donation and transplant adopted a comprehensive, modern, digital interoperative platform (previously adopted around the world) to manage the donation workflow, shifting from the previous paper process. The platform is a modern web-based system that provides advanced communication tools and has the potential to securely interface with external systems such as hospital EMRs. The donation organization, together with the software provider, coordinated updates to the workflow, processes, and policies, and organized comprehensive training sessions to ensure full compliance and oversee change management of the implementation.

**Results:** The comprehensive secure donation platform streamlines the clinical workflow by providing: 1) access to the latest chart information across multiple workflow, processes, and policies; 2) real-time and retrospective data quality tools to flag potential errors; 3) auditing and additional reporting and compliance tools; 4) notifications and alerts to team members upon key case updates; 5) scheduling and assigning coordination and more.

**Conclusions:** As the donation organization continues use of the new platform they look forward to upcoming reporting on the qualitative benefits of transitioning to the modern software as well as potentially expanding across the donation-transplantation ecosystem with interfacing capabilities.

**P026 PREDICTORS OF NON ADHERENCE TO IMMUNOSUPPRESSION IN RENAL TRANSPLANT PATIENTS AT A UNIVERSITY TEACHING HOSPITAL**

Hemant Sharma1, Georgios Koufopoulos2, Kunal Kapoor1, Thilina Gunawardena1, Bhavesh Devkaran3, Chameera Bandara1, Ernest Ohiha1, Sanjay Mehra1

1Royal Liverpool University Hospital, Liverpool, United Kingdom

**Introduction:** To assess the degree of immunosuppressive medication adherence in kidney transplant patients (KTPs) and to determine the predictors of non-adherence.

**Methods:** From a total of 106 KTPs treated at the RLUH, N=20 (18.6%) patients were identified as being non-adherent on 2 or more hospital incident episodes identified by continued care clinic, clinicians, and pharmacy. Statistical analysis was performed using the student t-test. The predictors were data mined with Cox Regression with time-variable being time to graft dysfunction or Tacrolimus level abnormality > 50% variance of average trough level (6-8 ng/ml).

**Results:** Non-Adherence was observed in 20 (18.6%) patients. The estimated glomerular filtration rate was significantly lower in the no adherence group (28.52 ± 17.02 ml/min) than in the adherence group (62.43 ± 11.72 ml/min, p < 0.05). With regard to the Tac level, a significant difference was also found between the adherers and the Non adherers (5.10 ± 2.19 vs. 3.06 ± 1.04 ng/ml, p < 0.05). Non-adherers were interrogated during clinical encounters by clinicians and interpreter requirement. Polypharmacy (N=15), (Interpreter requirement (N=11), young patients age 18-21 (N=05) and old age>70 (N=04) were the predictors of non-adherence. The patients were re-counselled and social services were involved to minimize recurrence.

**Conclusion:** The KTPs in this study demonstrated that non-adherence was associated with worse graft function and a lower Tac level. Knowledge about the degree of adherence could help the early identification of non-adherent patients and the development of strategies to improve outcomes.

**P027 SUBJECTIVE FRAILTY ASSESSMENT COMPARED TO VALIDATED FRAILTY ASSESSMENT IN DIALYSIS ACCESS/TRANSPLANT SURGERY WORKUP HAS POOR ESTIMATION OF AGREEMENT**

Bhavesh Devkaran1, Hemant Sharma1, Georgios Koufopoulos2, Kunal Kapoor1, Sanjay Mehra1

1Royal Liverpool University Hospital, Liverpool, United Kingdom

**Purpose:** Frailty assessment often rely on subjective frailty assessment, such as ‘the end-of-the-bed’ or ‘eyeball’ test. These assessments have traditionally been accurate in 40% of cases only. Frailty assessment is a part of our institutional clinical workflow. We examined the association between subjective frailty and formal validated score aided frailty estimation in the adult renal failure population.

**Methods:** A cohort of all renal failure patients presenting for dialysis access/ transplant assessment at a satellite unit over one year (December 2020–2021) was analysed. Adult patients aged ≥18 years in the outpatient dialysis access/ transplant assessment surgical clinic were rated with eyeball test in routine clinical assessment as either: frail, pre-frail, or non-frail, which was then compared to a formal frailty assessment using a modified version of the Frailty Phenotype. The association between clinician-estimated frailty and formal frailty assessment was examined.

**Results:** A total of 113 patients were assessed, producing 109 paired frailty assessments. The median age of the patients was 62 years. The Composite Proportions of Agreement of clinician-estimated frailty to formal frailty was poor (0.57). The sensitivity of the Eyeball test was 0.30 & specificity was 0.43. The sensitivity of the Frailty Score was 0.70 & specificity was 0.57. The validated tool has more than twice the odds to estimate frailty OR 2.86 (1.49- 5.46). p=0.002 (2-tailed)

**Conclusion:** Subjective frailty assessment is not a reliable replacement for formal frailty assessment in adults with renal failure. Validated Frailty Tool provide a uniform frailty estimation.
Background: Choriocarcinoma is a rare kind of cancer which may be either gestational or non-gestational. Choriocarcinoma is responsible for about a quarter of all documented neoplastic aneurysms. It is a descriptive case report of choriocarcinoma transmission from a donor, following kidney donation. A 45-year-old woman got a kidney from a 25-year-old woman who was taken to the hospital due to a non-traumatic cerebral hemorrhage. She delivered a healthy baby 48 days before her brain death. The transplant was successfully done. Five weeks post-transplantation, the recipient had pain and erythema in the surgical area. Regarding the high level of B-hCG in her blood, diagnostic tests were performed. Following the confirmation of the cancer, a five-phase chemotherapy plan with various pharmaceutical regimens was initiated. Liver function test values rose after the final round of chemotherapy, and the patient was initiated. Finally, she died due to the hepatic failure and DIC.

Conclusions: Presently, nephrologists do not agree on the best action if this problem occurs, but it seems that a transplanted kidney nephrectomy could be the best solution. If it occurs, a medical history of hypertension is associated with higher rates of mortality during admission, almost doubled compared to admissions with no AKI, admissions with AKI were associated with longer length of stay (median time of 3.83 vs. 7.01 days, P=0.025) and albumin level (OR 0.51, P=0.002), maximum tacrolimus trough level (OR 1.08, P=0.005), hemoglobin level (OR 0.9, P=0.016) and albumin level (OR 0.51, P=0.025) during admission. Compared to admissions with no AKI, admissions with AKI were associated with longer length of stay (median time of 3.83 vs. 7.01 days, P=0.001), in-hospital AKI was associated with higher rates of mortality during admission, almost doubled odds for rehospitalization within 90 days from discharge (OR 1.95, P<0.001), and increased the risk of overall mortality in multivariable mixed effect models. Strategies to prevent AKI during admission in this population should be implemented to reduce re-admission rates and improve patient survival.

Table 1: Multivariable Mixed Effect Logistic Regression Analysis for Readmission within 90 Days in RTRs

<table>
<thead>
<tr>
<th>Effect</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission age</td>
<td>1.01 (0.99-1.03)</td>
<td>0.17</td>
</tr>
<tr>
<td>Gender, F vs. M</td>
<td>0.93 (0.62-1.38)</td>
<td>0.72</td>
</tr>
<tr>
<td>Hypertension, yes vs. no</td>
<td>1.34 (0.91-1.97)</td>
<td>0.14</td>
</tr>
<tr>
<td>In-hospital AKI, yes vs.no</td>
<td>1.95 (1.35-2.81)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SBP min (for every increase of 1 mm Hg)</td>
<td>1.0 (0.99-1.01)</td>
<td>0.93</td>
</tr>
<tr>
<td>Albumin min per 1g/dL increase</td>
<td>0.76 (0.53-1.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Glucose max per 1 mg/dL increase</td>
<td>1.0 (0.99-1.0)</td>
<td>0.94</td>
</tr>
<tr>
<td>Hemoglobin min per 1 g/dL increase</td>
<td>0.92 (0.85-0.99)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

Figure 1. Long-term mortality based on the occurrence and severity of in-hospital AKI in the last admission for each patient.
Background: Post-transplant immune monitoring in renal transplant recipients (RTRs) is lacking.

Methods: We surveyed 132 RTRs, 38 in the first year post-transplant and 94 >1 year post-transplant. A questionnaire administered to these RTRs was divided into physical (Q physical) and mental (Q mental) symptoms.

Results: In multivariable models for the association between Q physical and Q mental scores and different clinical and biochemical variables in the 38 RTRs who filled out the questionnaire 130 times during the first year post-transplant, Prednisone and MPA use are associated with an increased Q physical and Q mental scores, respectively, while MPA use increased the mean Q mental score by 0.72 (95% CI 0.31-1.12, p=0.001). Among the 94 RTRs who each completed the questionnaire only once, the odds for the mean Q mental score to be above the median value were more than 3 times higher for RTRs treated vs. non-treated with MPA (OR 3.38, 95% CI 1.1-10.3, p=0.03). MPA-treated RTRs had higher mean scores for questions related to sleep disorders (1.83±1.06 vs. 1.32±0.67 for not treated, p=0.037), difficulty falling asleep (1.72±1.11 vs. 1.16±0.5, p=0.02), and to depression and anxiety.

Conclusion: Prednisone and MPA use are associated with an increased Q physical and Q mental scores in RTRs. Routine monitoring of physical and mental status of RTRs should be implemented to improve the diagnosis of overimmunosuppression. Dose reduction or discontinuation of MPA should be considered in RTRs who report sleep disorders, depression, and anxiety.

Table 1 | Clinical expression of MPA use in 94 RTRs >1 year post transplant.

<table>
<thead>
<tr>
<th>Questionnaire results</th>
<th>RTRs on MPA (N=75)</th>
<th>RTRs off MPA (N=19)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.88 (1.13)</td>
<td>1.47 (0.7)</td>
<td>0.183</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>1.51 (0.83)</td>
<td>1.47 (0.96)</td>
<td>0.623</td>
</tr>
<tr>
<td>Night sweats</td>
<td>1.24 (0.57)</td>
<td>1.21 (0.92)</td>
<td>0.226</td>
</tr>
<tr>
<td>Joint pain</td>
<td>1.45 (0.83)</td>
<td>1.37 (0.83)</td>
<td>0.481</td>
</tr>
<tr>
<td>Tremor</td>
<td>1.49 (1.01)</td>
<td>1.16 (0.37)</td>
<td>0.198</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>1.83 (1.06)</td>
<td>1.32 (0.67)</td>
<td>0.037*</td>
</tr>
<tr>
<td>Restlessness</td>
<td>1.56 (1.07)</td>
<td>1.21 (0.42)</td>
<td>0.372</td>
</tr>
<tr>
<td>Depression</td>
<td>1.59 (1.15)</td>
<td>1.11 (0.31)</td>
<td>0.09</td>
</tr>
<tr>
<td>Difficulty falling asleep</td>
<td>1.72 (1.11)</td>
<td>1.16 (0.5)</td>
<td>0.021*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.45 (0.98)</td>
<td>1.05 (0.23)</td>
<td>0.064</td>
</tr>
</tbody>
</table>

Background: Renal normothermic machine perfusion (NMP) is an organ preservation method based on the circulation of a warm (35-37 °C) perfusion solution through the renal vasculature to deliver oxygen and nutrients. However, the biological effects of this technique on the marginal kidneys are unclear. We therefore used mass spectrometry to determine the proteomic profile of kidney tissue and urine from eight organs reconditioned for 120 min using a Kidney Assist device.

Methods: Biopsies were taken during the pre-implantation histological evaluation (T-1), at the start of back table preparation (T0), and after 60 and 120 min of perfusion (T60, T120). Urine was collected at T0, T30, T60, and T120. Multiple algorithms, support vector machine learning and partial least squares discrimination analysis were used to select the most discriminative proteins during NMP.

Results: Statistical analysis revealed the upregulation of 169 proteins and the downregulation of 196 in kidney tissue during NMP. Machine learning algorithms identified the top 50 most discriminative proteins, five of which were concomitantly upregulated (LKN, ETPF, NUDT3, CYCS and UQCR1) and six downregulated (CFHR3, C1S, CFI, KNG1, SERPINC1, and F9) in the kidney and urine after NMP. Functional analysis revealed that the most strongly upregulated proteins were involved in the oxidative phosphorylation system and ATP synthesis, whereas the downregulated proteins represented the complement system and coagulation cascade.

Conclusions: Our proteomic analysis demonstrated that even brief periods of NMP induce significant metabolic and biochemical changes in marginal organs, which supports the use of this promising technique in the clinic.

Background: The European Society for Organ Transplantation (ESOT) TLJ 3.0 consensus conference brought together leading experts in the field of transplantation (pathologists, surgeons, nephrologists) to develop evidence-based guidance on the standardization and clinical utility of preplantation kidney biopsy in the assessment of grafts from extended criteria donors (ECD).

Methods: Seven emerging themes of interest have been selected by the Steering Committee (4 histopathologists, 4 nephrologists and 2 transplant surgeons) and underwent in-depth analysis after formulation of PICO (patient/ population, intervention, comparison, outcomes) questions. After a literature search by the Center of Evidence in Transplantation (CET), the relative statements for each key question were produced and rated according to the quality of evidence using the GRADE approach. The statements were subsequently presented in-person at the kick-off meeting in Prague, discussed and voted.

Results: After two rounds of discussion and voting, all 7 statements reached an overall agreement of 100% on the following issues: needle core/wedge/punch technique representativity, frozen/paraffin embedded section reliability, experienced/re-experienced on-call renal pathologist reproducibility and accuracy of the histological report, glomerulocresion/other parameters (interstitial fibrosis, tubular atrophy, wall/lumen ratio, arteriolar hyalinosis) reproducibility, digital pathology/light microscopy in the measurement of histological variables, special staining methods (Periodic Acid Schiff, Silver, Picric Sirius Red, Trichrome) / Haematoxylin & Eosin alone comparison in the measurement of histological variables, glomerulocresion percentage/interstitial fibrosis, tubular atrophy, arteriolar hyalinosis and cv score reliability to predict transplant outcome.

Conclusions: This methodology has allowed us to reach a full consensus on important technical topics regarding pre-implantation biopsy in the process of ECD graft assessment.
Conclusions: Analytical performance validation of AlloSeq cfDNA (CareDx) was executed across three independent laboratories. Each site received the same set of 16 blinded samples to perform cfDNA extraction and the entire AlloSeq cfDNA workflow. Results were compared between sites and against expectations from manufacturer validation to evaluate reproducibility, reproducibility, repeatability, and verify analytical performance metrics.

Results: A total of 247 sample libraries were generated with 10 ng DNA input across 18 runs, with a completion time of <24 hours from sample to result. The first pass rate measured 96.0%, highlighting minimal failures. Overall observed versus manufacturer validation established LOB as 0.18%, LOD as 0.23%, and results from the independent sites in this study verified those limits. Parallel analyses indicated no significant difference (p=0.951) between dd-cfdNA results with or without recipient genotype.

Conclusions: AlloSeq cfDNA proved to be a reliable method for efficient, reproducible dd-cfdNA quantification in plasma from solid organ recipients, without requiring genotyping. In-house access to this technology could facilitate more rapid detection of early signals of allograft injury at transplant centers across Europe.
Background: Renal normothermic machine perfusion (NMP) is a novel strategy to assess pretransplant renal function and injury, but it remains unclear which markers can provide information about renal viability during NMP. Magnetic resonance imaging (MRI) is commonly used to evaluate tissue morphology, metabolism, and function, and recently it has been applied to study ex vivo renal viability. The oxygen-17 (\(^{17}\)O) isotope offers a unique tool for the assessment of regional production of \(\text{H}_2\text{O}\) and the occurrence of this immediate end product of oxidative metabolism can be selectively imaged and quantified by functional MRI sequences. This project aimed to perform direct \(^{17}\)O MRI sequences on porcine kidneys during NMP to assess the feasibility of \(^{17}\)O imaging over time.

Methods: Viable porcine kidneys were retrieved at a local slaughterhouse, subjected to 30min of warm ischemia (WI), and preserved by hypothermia. Kidneys were subsequently perfused for 3h at 37°C. Initially, oxygenation was administered with 95% \(\text{O}_2\) / 5% \(\text{CO}_2\). After 1h of NMP perfusion to the inferior pole of one of the kidneys was blocked for 75min using a balloon catheter and then reperfused for 30min before \(^{17}\)O delivery. \(^{17}\)O was then supplied to the organ and anatomic and dynamic radial \(\text{H}_2\text{O}\) MR images were acquired before, during, and after \(^{17}\)O administration.

Results: \(^{17}\)O-magnitude imaging displayed that kidneys with partial ischemia had decreased signal intensity in the inferior pole after reperfusion, while kidneys without any additional HIT displayed a well distributed signal intensity over the whole organ. This signal shift after reperfusion could not be visualized with other functional MRI sequences such as T2* mapping, a surrogate to assess tissue oxygenation.

Conclusions: This pilot study showed the first evidence of the quantification of regional production of \(\text{H}_2\text{O}\) in isolated perfused porcine kidneys. With this novel MRI method, we were able to image the impact of ischemic injury on the rate of oxidative metabolism in renal tissue, which could not be visualized by any other functional MRI sequence after reperfusion. This suggests that \(^{17}\)O imaging during NMP could offer a valuable new tool for the assessment of renal metabolism and injury.
P044 ARTIFICIAL INTELLIGENCE TOOL FOR KIDNEY PRE-IMPLANTATION BIOPSY “GALILEO”: A STAR IS BORN

Albino Eccher1, Aldo Scarpa1, Antonella Barreca2, Jan Becker2, Ugo Boggi3, David Cucchiari4, Filippo Fraggatta5, Lucrezia Furlan6, Ilaria Girolami7, Stefano Gobbo7, Ersilia Lucenteferro8, Lorna Mascon9, Maarten Naens10, Fabio Pagni11, Liron Pantanowitz12, Gianluigi Zaza13, Angelo Dei Tos14, Giovanni Gambaro1

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Background: Kidney transplantation pathology is a field with complex diagnostic demands and scarcity of experts. Artificial intelligence (AI) can assist by aiding pathologists with the task of kidney donor assessment. Our aim is to present the AI tool called “Galileo”, designed specifically to assist the on-call pathologist with interpreting a pre-implantation kidney biopsy.

Methods: An AI tool called “Galileo” was created to read pre-implantation kidney biopsy digital pathology slides. The application Suite Create was employed for supervised algorithm training by annotating a case series of pre-implantation kidney biopsy slides by expert pathologists based upon ground truth original pathology reports. To overcome interobserver variability among pathologists we focused only on measurable features, such as number and type of glomeruli and vessels.

Results: The performance accuracy of Galileo improved with increasing number and quality of annotations. The pathologist is not replaced, but remains the protagonist when interacting with this AI-based tool which presents the on-call pathologist with an information on the number and type of glomeruli and vessels. The pathologist can actively dismiss the proposed feature result, edit, and validate the information prior to generating a pathology report.

Conclusions: Highly customizable AI solutions are being increasingly developed to address several needs in pathology, such as aiding the interpretation of kidney biopsies in transplant pathology. The AI-based tool called Galileo proved to successfully assist on-call pathologists required to interpret pre-implantation kidney biopsies. Further work is intended utilizing a semi-supervised approach, which would involve training this deep learning model using endpoints such as graft survival over time.

P043 THE OUTCOMES OF ADJUSTED IMMUNOSUPPRESSIVE PROTOCOLS DURING DIFFERENT PHASES OF COVID-19 PANDEMIC IN KIDNEY TRANSPLANT RECIPIENTS

Çağlar Ruhi1, Ali Özer2
1Acibadem University Hospital Atakent, Nephrology/Kidney Transplant, Istanbul, Turkey, 2Acibadem University Hospital Atakent, Transplantation, Istanbul, Turkey

Background: After beginning of the Covid-19 pandemic due to initial reports of high mortality in patients with multiple comorbidities, almost all transplant centres developed different immunosuppressive protocols to decrease the mortality rates in their chronic immunosuppressive kidney transplant patients. In this study, we revealed the outcomes of our immunosuppressive protocols during the different phases of the Covid-19 pandemic.

Methods: In the first phase of Covid-19 due to the high mortality risk of dominant variants until December 2021, the protocol was an increased dose of prednisolone (20mg/day) and complete cessation of calcineurin and MMF. When the dominant variant became Omicron in the second phase, prednisolone 20mg/day, 50% dose reduction of tacrolimus and MMF cessation were applied. The data were evaluated retrospectively in terms of mortality, biopsy-proven rejection, allograft loss, and allograft functions.

Results: Of the 592 follow-up patients at our centre, 132 of them (13.2%) had Covid-19 infection. In the first phase, infection developed in 108 patients (mean age 47.07±12.9 years, 54.6% male, 49% one comorbidity, 9.3% three comorbidities). Mortality was detected in one patient (4.2%), while biopsy-proven rejection and temporary RRT were required in one patient (4.2%), and allograft loss did not occur. Allograft functions of the patients were well preserved (60ml/min vs. 63.1ml/min GFR, 211.5±366.2mg/dl vs. 435.74±1302mg/dl proteinuria, p=NS). In the second phase of Covid-19, infection developed in 108 patients (mean age 47.07±12.9 years, 54.6% male, 49% one comorbidity, 8.3% three comorbidities). Mortality was detected in one patient (4.2%), while biopsy-proven rejection and temporary RRT were required in one patient (4.2%), and allograft loss did not occur. Allograft functions of the patients were well preserved (60ml/min vs. 63.1ml/min GFR, 211.5±366.2mg/dl vs. 116.29±176 mg/dl proteinuria, p=NS)

Conclusions: In the first phase of Covid-19, with aggressive immunosuppressive reduction, lower mortality was achieved in kidney transplant patients than generally reported, while no significant problems were experienced in terms of allograft function and survival. In the second phase, which had a milder course, severe patient and allograft protection could be achieved with moderate immunosuppressive dose reduction.

P046 PREDICTION OF HERPES VIRUS INFECTIONS AFTER SOLID ORGAN TRANSPLANTATION: A PROSPECTIVE STUDY OF IMMUNE FUNCTION

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1Rigshospitalet, University of Copenhagen, Viro-immunology Research Unit, Department of Infectious Diseases 8632, Copenhagen, Denmark, 2Rigshospitalet, University of Copenhagen, Department of Nephrology, Copenhagen, Denmark, 3University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark, 4Rigshospitalet, University of Copenhagen, Department of Cardiology, Section for Lung Transplantation, Copenhagen, Denmark, 5Rigshospitalet, University of Copenhagen, Department of Cardiology, Copenhagen, Denmark, 6Rigshospitalet, University of Copenhagen, Centre of Excellence for Health, Immunity, and Infections, Copenhagen, Denmark, 7University of Copenhagen, Department of Biostatistics, Copenhagen, Denmark, 8Rigshospitalet, University of Copenhagen, Department of Clinical Microbiology, Copenhagen, Denmark, 9Rigshospitalet, University of Copenhagen, Department of Clinical Immunology, Copenhagen, Denmark, 10Rigshospitalet, University of Copenhagen, Department of Surgical Gastroenterology and Transplantation, Copenhagen, Denmark

Background: Herpes virus infections are a major concern after solid organ transplantation and linked to the immune function of the recipient. We aimed to determine the incidence of positive herpes virus (cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus 1/2 (HSV-1/2), and varicella zoster virus (VZV)) PCR tests during the first year post-transplantation and linked to the immune function of the recipient. We aimed to determine the incidence of positive herpes virus (cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus 1/2 (HSV-1/2), and varicella zoster virus (VZV)) PCR tests during the first year post-transplantation and linked to the immune function of the recipient. We aimed to determine the incidence of positive herpes virus (cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus 1/2 (HSV-1/2), and varicella zoster virus (VZV)) PCR tests during the first year post-transplantation and linked to the immune function of the recipient.

Methods: All participants were preemptively screened for CMV, and EBV IgG-negative participants were screened for EBV during the first year.
P047 PREGNANCY OUTCOMES IN FEMALE ABDOMINAL ORGAN TRANSPLANT RECIPIENTS

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*Transplant Pregnancy Registry International, Philadelphia, United States

Background: The Transplantation Pregnancy Registry International (TPRI) has been collecting data for over 32 years in all solid organ transplant recipients. Methods: Data are collected via questionnaires, interviews, online surveys, and review of medical records; retrospective and prospective pregnancy reports are accepted, and recipients worldwide can participate. The figure shows the countries that are represented in the TPRI.

Results: The purpose of this abstract is to present overall outcomes in abdominal organ transplant recipients reported to the TPRI. Results are shown in the table below. Overall outcomes among transplant recipients have remained similar over the last 30 years. The live birth rate is 69-74%, depending on organ transplanted. Each organ group has specific nuances, and it is of utmost importance for recipients to plan pregnancy to avoid mycophenolic acid product exposure as it is a known teratogen and to optimize transplant function in anticipation of pregnancy. The TPRI follows recipients and offspring indefinitely; despite the increased incidences of prematurity and low birthweight, offspring are overwhelmingly reported healthy and developing well at follow-up. The TPRI has over 250 grandchildren, who comprise a second generation providing the ability to study theoretical concerns about potential effects of in utero exposure to immunosuppressive medications on subsequent generations.

Conclusions: For many recipients, pregnancy after organ transplantation is possible with most of the pregnancies resulting in a healthy live birth. The TPRI is a resource for the worldwide transplant community. Healthcare providers who counsel transplant recipients about parenthood and transplant recipients themselves are encouraged to contact the TPRI.

Table 1

<table>
<thead>
<tr>
<th>Organ</th>
<th>Recipients / Total Outcomes</th>
<th>Estimated conception date range</th>
<th>Fetal losses*</th>
<th>Live offspring</th>
<th>Mean Gestational age (wks)</th>
<th>Mean Birth-weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>1367/254*</td>
<td>1967-2022</td>
<td>652</td>
<td>1892 (74%)</td>
<td>35.8</td>
<td>2551</td>
</tr>
<tr>
<td>Kidney-Pancreas</td>
<td>84/154</td>
<td>1989-2022</td>
<td>48</td>
<td>106 (69%)</td>
<td>33.9</td>
<td>2128</td>
</tr>
<tr>
<td>Liver</td>
<td>400/821</td>
<td>1985-2022</td>
<td>221</td>
<td>500 (73%)</td>
<td>36.8</td>
<td>2778</td>
</tr>
</tbody>
</table>

*Includes multiple births, *Includes ectopic, miscarriages, terminations and stillbirth outcomes
Mombeini 2, Atieh Rezaifar2, Haleh Ashraf3, Shahrokh Karbalai2, Abbas Yuki1
1Japanese Red Cross Aichi Medical Center Naoyga Daini Hospital, Transplant Naoyga Daini Hospital, Pharmacokinetics and HLA lab, Nagoya, Japan, 2Japanese Red Cross Aichi Medical Center Naoyga Daini Hospital, Transplant Nephrology, Nagoya, Japan

Background: Production of donor-specific antibody (DSA) is a risk factor for antibody mediated chronic rejection resulting in graft loss. We compared DSA production of everolimus(EVR)-based immunosuppression with mycophenolate mofetil (MMF) based immunosuppression for primary kidney transplant recipients at our single institute.

Methods: From January 2008 to December 2020, 1,231 living donor renal transplant were performed. Among them, 878 recipients who were tested anti-HLA antibody screening in 2021 were enrolled in this study. Pre-DSA patient, and those who received mizorbine were excluded. Immunosuppression included either Tacrolimus(TAC) or Cyclosporine(CSA) and either MMF or EVR. All patients received basiliximab and steroids. Rituximab was given in 233 cases for ABO incompatible transplantation. When immunosuppression was converted to other drug, patients are allotted to regimen which is given at least 1 year from Screening test. De novo DSA was identified using LABScreen single antigen beads. Mean fluorescence intensity (MFI) values >1000 was considered positive. P < .05 was considered significant.

Results: Among 878 patients, there were 445 males and 233 females. Average age was 47.8 years. Distribution of immunosuppression regimen are CSA-MMF 166, CSA+EVR 67, TAC+MMF 382, and TAC+EVR 65. Class I DSA were found in 10 cases and ClassII DSA were found in 39 cases. Incidence of DSA production and MFI values were not statistically different between MMF group and EVR group, properly score matched analysis was performed. Then max MFI value against Class II were significantly less in EVR group (111695 in MMF, 2985 in EVR) (p=0.00763). Patients with MFI >6000 was found only in 1 EVR group and 6 in MMF group (n.s)

Conclusions: Even this is limited analysis, immunosuppression regimen including everolimus may possibly suppress production of anti-HLA Class II after living donor renal transplantation.

P051
A LOW ABUNDANCE OF HLA IN URINARY EXTRACELLULAR VESICLES HINDERS THE IDENTIFICATION OF DONOR-SPECIFIC VESICLES IN URINE AFTER KIDNEY TRANSPLANTATION
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Background: Urinary extracellular vesicles (uEVs) might reflect the integrity and condition of the kidney allograft. The aim of the present study was to identify donor-specific uEVs based on human leucocyte antigen (HLA) mismatching with the recipient.

Methods: Donor-specific CD9 (tetrarospin, general uEV marker) and HLA-A2 double-positive (CD9+/HLA-A2+) uEVs were quantified from the urine of 12 HLA-A2-positive kidney donors and were compared to urine samples collected from 10 healthy controls. uEVs were isolated from 3 mL of urine samples, and immunofluorescence analysis was performed. Then analysis was performed using time-resolved fluoroimmunoassay (TR-FIA), or immunogold-staining electron microscopy (IGS-EM). In addition to unprocessed urine samples, uEV isolates were 266-fold concentrated from the urine by ultracentrifugation (UC). Lastly, cell-derived CD9+/HLA-class-I EVs were spiked into the urine to investigate if the urine matrix (pH, osmotic pressure, ion concentration) affects uEV HLA detection.

Results: CD9+/HLA-A2+ uEV concentrations detected by IFCM could not discriminate HLA-A2+ donor from HLA-A2- recipient urine. In HLA-A2- plasma, we observed 5.2 ± 4.4 x 10^9/mL CD9+/HLA-A2+ EVs, while significantly lower CD9+/HLA-class-I EVs were detected in unprocessed urine samples from HCs (5.6 ± 1.6 x 10^9/mL, p = 0.0046). The TR-FIA signal intensity, reflecting HLA-class-I expression of EVs from plasma (5220 ± 2053), was significantly lower than EVs from urine (2077 ± 55, p = 0.001), and the control with only buffer/PBS (2641 ± 48, p = 0.003). In the IGS-EM, vesicle surface HLA-class-I expression was undetectable in uEV isolates. The spike-in IFCM experiments revealed 4.6 ± 2.3 x 10^9/mL cell-derived CD9+/HLA-class-I EVs, while significantly lower CD9+/HLA-class-I EVs were spiking in the urine to investigate if the urine matrix (pH, osmotic pressure, ion concentration) affects uEV HLA detection.

Conclusions: HLA-class-I cannot be used to identify donor-derived uEV, likely because HLA-class-I EVs are not excreted into the urine under physiological conditions.
**Methods:** The quality of organ donation after death was evaluated using a comprehensive analysis. It is needed to understand how these factors may affect the ground are often factors that affect the quality and safety of the procedure. A many studies have highlighted that the lack of consistent processes for the consent, brain-death identification, conversion rate in DBD donors are areas of all possible donors in the ICU, referral of possible DBD donors, patient/family satisfaction with life scale (SWLS), Connor-Davidson Resilience scale (CDRISC-29). Statistical analysis performed was Spearman and Pearson correlation coefficients.

**Results:** Structural indicators showed a 97% increase in regard to meeting the standards established by the ODEQUS across the selected hospitals in 2020 compared to 2019. However, process indicators showed a 36% increase and indicators of results showed a 9% increase.

**Conclusions:** The necessity of developing of quality indicators in identifying gaps and area for improvement in the organ procurement process that should be redesigned or restructured, hence maximizing the number of donors and organs transplanted. The performance increased by 48%. However, identification of all possible donors (ICU, referral of possible DBD donors, patient/family consent, brain-death identification, conversion rate in DBD donors are areas that need a great opportunity for improvement in order to optimize the process.

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**P055**

**SELECTION OF SAFE DONORS FOR THE LIVING DONOR LIVER TRANSPLANTATION USING EXTENDED RIGHT LOBE GRAFT**

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**Background:** Extended right lobectomy (ERL) for living donor liver transplantation (LDLT) is selectively performed in many transplant centers and showed excellent recipient outcomes as reported in the previous studies. Yet, there is no universally accepted indication for ERL in respect to donor safety. Current study was designed to stratify the risk group of donors according to post-hepatectomy liver failure classification by International Study Group for Liver Surgery.

**Methods:** A total of 79 living donors who underwent ERL for LDLT were included in analysis. Donors were classified as safety and hazard donor groups according to postoperative findings relevant to post-hepatectomy liver failure classification by International Study Group for Liver Surgery.

**Results:** On multivariable analysis, lateral section volume (LLSV) less than 20% of total liver volume (TLV) and non-preservation of segment 4a (S4a) venous drainage were found to be the independent risk factors impairing postoperative liver regeneration. Despite the short-term impairment of liver function in hazard donor groups, all donors recovered and showed satisfactory remnant liver regeneration. However, these findings have implications in establishing selection criteria of donors eligible for ERL donation.

**Conclusions:** In conclusion, LDLT using ERL graft can be safely performed provided that LLVS/TLV is greater than or equal to 20% besides conventional donor selection criteria. Also, efforts to preserve S4a vein must be made in performing ERL graft procurement in LDLT donors.

**Table 4. Univariable and multivariable analyses of risk factors of hazard donor**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Safety group (N=36)</th>
<th>Hazard group (N=43)</th>
<th>p</th>
<th>univariable</th>
<th>multivariable</th>
<th>Odd ratio (95%C.I.)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>164.32</td>
<td>167.57</td>
<td>0.08</td>
<td>-</td>
<td>-</td>
<td>1.00 (0.98-1.03)</td>
<td></td>
</tr>
<tr>
<td>BSAs + 1.70 m2</td>
<td>10 (27.8%)</td>
<td>18 (41.9%)</td>
<td>0.19</td>
<td>1.99</td>
<td>0.91</td>
<td>0.16 (0.00-0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>S4a vein preserved</td>
<td>11 (30.5%)</td>
<td>3 (7.0%)</td>
<td>0.01</td>
<td>3.91</td>
<td>0.00</td>
<td>0.16 (0.00-0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>SLV (ml)</td>
<td>1163.12</td>
<td>1210.42</td>
<td>0.06</td>
<td>0.91</td>
<td>0.32</td>
<td>0.16 (0.00-0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>LLV/TLV (%) &lt; 35</td>
<td>3 (8.3%)</td>
<td>15 (34.9%)</td>
<td>0.05</td>
<td>5.38</td>
<td>0.12</td>
<td>0.16 (0.00-0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>LLVS/TLV (%) &lt; 40</td>
<td>0 (0.0%)</td>
<td>20 (46.5%)</td>
<td>0.01</td>
<td>10.84</td>
<td>0.91</td>
<td>0.16 (0.00-0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>Data are presented as number (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Abbreviations:** BSAs, body surface area; LLV, left lobe volume; TLV, total liver volume; LLVS, left lateral section volume;
P056 SYSTEMIC IMMUNE-INFLAMMATORY MARKER OF HIGH MELD PATIENTS IS ASSOCIATED WITH EARLY MORTALITY AFTER LIVER TRANSPLANTATION

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1Suxon-si, department of liver transplantation and hepatobiliary surgery, Suwon, South Korea

Background: The scarcity of deceased donor livers has led to allocation of grafts to only the most seriously ill patients with a high Model for End-Stage Liver Disease (MELD) score, which has resulted in a high mortality rate after deceased donor liver transplantation (DDLT). The aim of this study is to identify risk factors for posttransplant mortality and thereby reduce futile outcomes in DDLT.

Methods: Between 2013 and 2019, 57 recipients with MELD scores ≥30 underwent DDLT in our center. We reviewed data and identified the risk factors for 90-day posttransplant mortality. The periprocedural clinical and laboratory parameters of patients who did or did not survive for 90 days were subjected to logistic regression analysis. Twelve patients died within 90 days.

Results: Results of univariate analysis indicated that the differences in patient survival were determined by the amount of intraoperative platelets transfused, the presence of posttransplant sepsisemia, and systemic immune-inflammation index (SII) at the time of listing with MELD scores ≥30. Multivariable analysis revealed that an SII ≥870 (× 10^9/L) and posttransplant sepsisemia were independent risk factors for 90-day mortality. Twenty-two patients had SII ≥870, and 13 of these patients had posttransplant sepsisemia. Of the 13 patients, 90-day mortality occurred in 10 cases. However, in 35 patients with SII ≤870, 90-day mortality due to posttransplant sepsisemia was recorded only in 1 patient.

Conclusions: In conclusion, a preoperative SII ≥870 in a patient with a high MELD score may be a significant risk factor for early posttransplant mortality. Because posttransplant sepsisemia in patients with high SII can lead to fatality, a more intensive effort to prevent infection is needed for patients undergoing DDLT carrying such risk factors to avoid futile liver transplantation.

P057 MALIGNANCY AFTER KIDNEY TRANSPLANT - 50 YEARS EXPERIENCE

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1Japanese Red Cross Aichi Medical Center Naogya Daini Hospital, Transplant Surgery, Nagoya, Japan, 2Japanese Red Cross Aichi Medical Center Naogya Daini Hospital, Transplant Nephrology, Nagoya, Japan

Background: Malignancy after organ transplantation is a leading cause of graft and patient loss. Demography of malignancy occurrence was investigated in a single institute.

Methods: Retrospective cohort analysis was performed in renal transplant recipients for last 50years. Medical charts of patients who underwent living or deceased renal transplant during June 1972 to December 2021 were reviewed.

Results: There were 2,246 cases of living donor renal transplant, 315 of deceased donor renal transplant, and 5 pancreas transplant after living donor renal transplant. Among them, 2,233 malignancies in 205 cases (7.9%) were developed. Average period after transplantation was 233 (median 7 years).

Conclusions: A low SAS during kidney transplantation is a major determinant of the risk of DGF.

P058 A LOW SURGICAL APGAR IS A STRONG DETERMINANT OF THE RISK OF DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

Florent Von Tokarski1,2*, Mathilde Labro1, Yanish Sorojebyal1, Bernard Trifil1, Mathilde Lefebvre1, Niloufar Kossari1, Leila Tricot1, Michel Delihouisse1, Morgan Le Guen1, Alexandre Heriti1
1University of Versailles-Saint-Quentin-en-Yvelines, Faculty of Medical School, Montigny-Le-Bretonneux, France, 2Foch Hospital, Department of Nephrology, Dialysis, and Transplantation, Suresnes, France, 3Foch Hospital, Clinical Research Department, Suresnes, France, 4Foch Hospital, Department of Information Systems, Suresnes, France, 5Foch Hospital, Anesthesiology, Suresnes, France

Background: The surgical APGAR score (SAS) is a 10-point scale combining 3 intraoperative variables: lowest heart rate, lowest mean arterial pressure, and estimated blood loss. Although SAS is correlated with morbitimortality in the context of liver transplantation, little is known about its value during kidney transplantation.

Methods: In a monocentric, retrospective study including all adult patients transplanted with a kidney from a deceased donor between 2016 and 2022, we used CHAA software (GE®) to calculate SAS. A low SAS was conventionally defined as ≤7/10. Delayed graft function (DGF) was defined by the need for dialysis within 7 days post-transplant. DGF was explained by a multivariable logistic model, including variables significant at threshold α=0.20 in univariate logistic regressions.

Results: Among 299 patients, 95 (31.8%) had a low SAS. Recipient age (OR=0.85 per 5 years CI95%=[0.77; 0.94], p=0.001), recipient BMI (OR=1.05 per 1 kg/m² CI95%=[1.01; 1.10], p=0.029) and surgery duration (OR=1.03 per 5 minutes CI95%=[1.00; 1.06], p=0.038) were associated with a low SAS after multivariable analysis. DGF developed in 79 patients (26.4%), including 42 (53.2%) with a SAS≤7, and 37 (48.6%) with a low SAS. In multivariable logistic regression, four factors were associated with DGF: a low SAS (OR=2.02, CI95%=[1.1; 3.60], p=0.022), waiting time before transplantation (OR=1.05 per 6 months CI95%=[1.01;1.09], p=0.025), cold ischemia time (OR=1.09 per 2 hours CI95%=[1.00; 1.20], p=0.041) and absence of treatment by renin angiotensin inhibitor (OR=2.38, CI95%=[1.28-4.35], p=0.006). After a maximum follow-up of 6 years, and a low mortality (4.1% by year 1), no association was found between SAS and graft or patient survival.

Conclusions: A low SAS during kidney transplantation is a major determinant of the risk of DGF.

P059 PRETRANSPLANT HBA1C AS AN EASY TO IDENTIFY PATIENTS AT HIGH RISK OF DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION

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1University of Antwerp, Faculty of Medicine & Health Sciences, Laboratory of Experimental Medicine and Experimental Pathology (LEMP), Academic Hospital Antwerp, Antwerp, Belgium, 2Antwerp, University of hospital of Antwerp - Department of Nephrology-Hypertension, Antwerp, Belgium, 3Antwerp, University of hospital of Antwerp - Department of Endocrinology, Diabetology & Metabolism, Antwerp, Belgium

Background: Post-Transplant Diabetes Mellitus (PTDM) occurs in 10-40% of kidney transplant recipients and is associated with an increased cardiovascular risk. Early identification of at-risk patients could allow to take timely measures. However, no widely validated risk score exists to predict the risk of PTDM.

Methods: This retrospective study includes 267 adult patients who underwent kidney transplantation at the Antwerp University Hospital between January 2014 and August 2021. PTDM was diagnosed based on the American Diabetes Association definition at 3 months post-transplant. First, a logistic regression analysis was used to identify risk factors for PTDM. Second, criteria to identify patients with a high risk (>35%) of developing PTDM at 3 months were established.

Results: At 3 months post-transplant, 54 (20.2%) patients developed PTDM. However, no widely validated risk score exists to predict the risk of PTDM.

Conclusions: The HbA1c value at transplantation was the strongest risk factor for PTDM at 3 months post-transplant. Furthermore, a pre-transplant HbA1c of ≥ 5.3% showed to be an easy tool to identify patients at high risk of early PTDM in our population.
**P060**

**COMPARING OUTCOMES IN EXTENDED VERSUS STANDARD CRITERIA LIVING DONOR KIDNEY TRANSPLANTATION: A SINGLE-CENTRE ANALYSIS**

**Nikolaos-Andreas Anastasopoulos** 1, Marina Loucaidou1, Rawya Charif1, Frank Dor1, Vassilios Papalois1

1Imperial College Healthcare NHS Trust, London, United Kingdom

**Background:** Living donor renal transplantation (LDRTx) is considered to be the treatment of choice for treating End Stage Renal Disease (ESRD). Multiple studies have shown the impact of donor and recipient demographics in post-transplant outcomes. We investigated the impact of allocating extended criteria living donor (ECD) renal allografts to extended criteria recipients (ECR).

**Methods:** We retrospectively analysed all the LDRTx pairs between Apr 2017 and Jan 2022. We defined ECD and ECR, as individuals having at least one of the following: age older than 60, presence of diabetes mellitus (DM), hypertension (HTN), atheroma, body mass index (BMI) above 30. We defined four groups for analysis: ECD to ECR, SCD to SCR, ECD to SCR and SCD to ECR. We documented mortality, return to dialysis, perioperative haemorrhage, surgical site infections (SSI), incisional hernias and latest donor renal and recipient graft function from the respective follow up. Jamovi 2.2.5 was used for statistical analysis.

**Results:** We identified 149 pairs of LDRTx. Results are in Table 1. Follow up was 5 years for 21.5%, 3 years for 56.4% and 1 year for 22.1% of the LDRTx pairs.

**Conclusions:** The donor and recipient outcomes of ECD to ECR LDRTx were similar to the other groups which means that extended criteria LDRTx is safe and effective.

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor characteristics</td>
</tr>
<tr>
<td>N = 149</td>
</tr>
<tr>
<td>Age (mean±SD)</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>HTN</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Genetic relationship</td>
</tr>
<tr>
<td>Donor single renal vessels</td>
</tr>
<tr>
<td>Recipient Characteristics</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>Pre-emptive</td>
</tr>
<tr>
<td>Previously sensitised</td>
</tr>
<tr>
<td>CIT (min)</td>
</tr>
<tr>
<td>Donor Outcomes</td>
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<td>Mortality</td>
</tr>
<tr>
<td>Return to Dialysis</td>
</tr>
<tr>
<td>Last eGFR</td>
</tr>
<tr>
<td>Haemorrhage</td>
</tr>
<tr>
<td>SSI</td>
</tr>
<tr>
<td>Incisional Hernias</td>
</tr>
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</table>

**P061**

**PROSPECTIVE ASSESSMENT OF THE NEED FOR AND ADDED VALUE OF MOLECULAR DIAGNOSTICS OF KIDNEY ALLOGRAFT BIOPSIIES – AN EVALUATION IN CLINICAL PRACTICE**

**Thomas Schachtner** 1, Seraina von Moos1, Birgit Helmchen1, Ariana Gasperi2, Thomas Mueller3

1University Hospital Zurich, Nephrology, Zurich, Switzerland, 2University Hospital Zurich, Pathology, Zurich, Switzerland

**Background:** The Molecular Microscope Diagnostic System (MMDx) may resolve inconclusive histology findings, as preserved biopsy material can be examined after histology findings have been obtained. The extent to which this approach can be implemented in clinical practice remains unknown.

**Methods:** We prospectively analyzed 104 consecutive indication kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from April to December 2022. Pathologists and clinicians with experience in molecular diagnostics assessed the need for MMDx by questionnaire when the histology report was available. Clinicians then assessed the added value of the molecular diagnostics when the MMDx report was available.

**Results:** 29 of 104 cases (28%) showed rejection by histology, 42 of 104 cases (40%) showed no rejection by histology, and 33 of 104 cases (32%) showed histologic findings insufficient to diagnose ABMR due to an absence of diagnostic criteria groups 2 and/or 3. Pathologists considered molecular diagnostics indicated in 42 of 104 cases (40%), 9 cases to give extra confidence, and 33 cases for diagnostic clarification concerning rejection. Clinicians considered molecular diagnostics indicated in 54 of 104 (52%) cases, 5 cases to give extra confidence, and 49 for diagnostic clarification concerning rejection. In 54 of 104 cases (52%) showed no rejection by histology, and 33 of 104 cases (32%) showed no rejection by histology. Clinicians considered adjustment of treatment based on the MMDx report in 3 of 11 discrepant cases. Pathologists and clinicians considered molecular diagnostics indicated in 2 of 11 and 3 of 11 discrepant cases respectively.

**Conclusions:** The need for molecular diagnostics goes beyond the recommendation of the 2018 Banff classification for histologic findings insufficient to diagnose ABMR. However, the added value of molecular diagnostics appears to be largely limited to these cases.

**P062**

**EFFECTS OF A QUADRUPLE IMMUNOSUPPRESSANT REGIMEN INCLUDING EARLY ADD-ON EVEROLIMUS AFTER KIDNEY TRANSPLANTATION**

**Hitoshi Iwamoto** 1, Masaaki Ohkura1, Isao Akashi1, Yu Kihara1, Osamu Kono1, Takuya Ueno1

1Tokyo Medical University Hachioji Medical Center, Department of Kidney Transplantation Surgery, Tokyo, Japan

**Background:** Several studies have reported that everolimus (EVR), a mammalian target of rapamycin inhibitor, combined with reduced exposure to calcineurin inhibitors (CNIs), has noninferior results for kidney function, acute rejection, and viral infection, compared with current standard immunosuppressive (IM) drugs that use CNIs and mycophenolate mofetil (MMF). Most protocols containing EVR are triple therapy, in which MMF is converted to EVR. IM regimens with MMF and EVR are very few. This study investigated the beneficial effect of a quadruple IM regimen with MMF and EVR after kidney transplantation (KT).

**Methods:** We evaluated 95 KT patients who used tacrolimus and EVR between May 2014 and December 2020 and followed them for 1-year post-KT. They were divided into two groups by IM regimen: EVR added 7 days after KT (early group; n=52) and EVR added during the stable period (>3 months post-KT, stable group; n=43). The incidence of acute rejection and infection, adverse events, IM drug dose, CNI trough level, and renal function were retrospectively examined.

**Results:** Our current IM regimen comprises tacrolimus, mycophenolate mofetil, MMF, and basiliximab, and EVR is administered 7 days post-KT. Before this current regimen, EVR was started when renal function was stable for >3 months after KT. On average, EVR was started 137.8 days after KT in the stable group. Tacrolimus and mycophenolate mofetil doses were reduced after EVR addition in both groups. One-year post-KT, the mean serum creatinine level in the early vs. stable group was 1.56±1.40 vs. 1.49±0.68 mg/dL (p=0.072), and the estimated glomerular filtration rate was 47.7±19.13 vs. 43.6±16.9 mL/min/1.73 m² (p=0.282), with no significant differences. The incidence of biopsy-proven T-cell-mediated rejection was significantly lower in the early group (p=0.02). There were no significant differences in stomatitis and peripheral edema between the groups. The incidences of cytomegalovirus infection and neutropenia were significantly lower in the early group (p=0.007, both).

**Conclusions:** Our quadruple immunosuppressant regimen including early add-on EVR yielded acceptable outcomes.
Background: Child transplantation is a widely accepted life-saving intervention for pediatric patients needing organ transplants. We studied the kidney transplantation performed in Iran between 2018 - 2020, and described the deceased donor transplants performed in the same period.

Results: During the three years, 349 children, i.e., patients under age 18, became deceased-organ donors, all following a diagnosis of brain death. In 51.9%, the etiology of brain injury was trauma, of which 20.3% were due to hypoxia. Comparing different years, significant differences were found in relation to the etiology of brain death and receipt of defibrillation. The significant differences were found in relation to the etiology of brain death and gender, BMI, and age. 605 kidneys, 308 livers and 62 hearts were transplanted from 349 donors in 2018-2020. During this period, 326 children were listed for a kidney transplant and 138 for a liver. In this period, there were 223, 283 and 307 children on the heart-waiting list each year and 21 (2018), 21 (2019) and 18 (2020) transplants performed; so, to clarify for example in 2020 only 6-10 % of children on the waiting list received a heart transplant each year. This indicates a significant gap between the heart transplant waiting list and donor availability, with 78 children on the waiting list and donor availability. 2018-2020.

Conclusions: Organ donation rates are comparatively reasonable, but the lack of specialist centers for children’s intensive care is still an issue. The establishment of specialized management centers for deceased donation in children under 18 years is required for donation rates to improve.

**Waiting list**

- “I tried with joy when I got the call to show up at the hospital for the transplant.”
- “After all the exams and ranking I was over the moon. I saw the light at the end of the tunnel. Then the months start to pass and then a year the joy starts to turn into a mere-mentioning anticipation. Soon after the panic attacks begin...what if they never call me?”

**After transplant**

- “After the transplant I came back to life and felt like a normal person again.”
- “Slowly I feel better and better. full of strength. My body began to give the right answers to my desire to do.”

**Current life description**

- “In the early days I lived with the fear of rejection and I was careful of everything, I didn’t exaggerate in my daily routine and I promised myself to live my life much more peacefully, having received a gift.”
- “The change was immediately evident given that I no longer did dialysis, being busy three days a week in the hospital away from my family for almost 5 years had a huge impact on my life and not having to do it anymore gave me back a presence in the family that had been missing for too long.”

**Conclusions:**

Transplant experience is characterized by a non-linear timeline different from the chronological steps foreseen by the medical procedure, overlooked as a “healing moment”. Use of creative activities in health care situations, characterized by high intensity, uncertainty and loneliness, can empower people and increase their well-being, self-efficacy and personal growth allowing emotional release. Our study confirms the limitations of children from living donors or who experienced rejection; it is a monocentric experience and the interviews were conducted only in Italian. More research is needed to study the impact of forms of storytelling as an intervention.
virtues are necessary for coexistence in nature and society we live in. Students did a group work to express their ideas to preserve nature and make a just and warm community. In the fourth part, students searched for actual sharing care and routine follow-up.

Conclusions: Students wrote that through these classes, they have learned the value of themselves and others and that we are living together. Through this experience, when students grow up and become adults, we expect them to have more affirmative attitude toward organ donation after brain death.

Conclusions: Transplant patients who have experienced COVID-19 should be carefully monitored for the occurrence of graft arterial and vein embolism. Early detection of these complications in patients after organ transplantation gives an opportunity to save the organ. Thermostrephylaxis with low molecular weight heparin is highly important and should be continued in high-risk patients (obese, with persistent d-dimer levels) for a minimum of 2 weeks (preferably 4-6 weeks) after reaching the convalescent status.

Background: The transmission of hepatitis C virus (HCV) from viremic donors to seronegative recipients of kidney transplantation is well documented. Pre-transplant administration of direct-acting antivirals prevents viremia, but the seroconversion rate is high. The aim of this study is to assess HCV transmission through the graft tissue.

Methods: In this prospective observational study, we determined the presence of HCV in the tissue of 15 kidneys from 8 deceased viremic donors (D16 transplanted to a seropositive recipient) before transplantation. Tissue samples were extracted in the operating room and Viral RNA determination in donor plasma and tissue was performed with the Xpert HCV viral load quantitative assay (Cepheid). Results: Plasma viral load in all donors was significant, and in recipients it was undetectable on days 1 and 7 post-transplantation. However, 13 of the 15 recipients (86.6%) had seroconverted within one month. HCV was detected in 9 of the 15 (60.0%) histological samples analyzed. Viral RNA was detected in D5, but not in D6, from the same donor, probably due to the scant sample and borderline viral. Data showed in table

Conclusions: HCV was detected in a large proportion of kidney grafts from viremic donors, which could facilitate its transmission to recipients.

<table>
<thead>
<tr>
<th>Donor</th>
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<th>Day 7</th>
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<tr>
<td>D2</td>
<td>R2</td>
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<td>D3</td>
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<td>D11</td>
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<td>D15</td>
<td>R15</td>
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</tr>
<tr>
<td>D16</td>
<td>R16</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

P66

DE NOVO CANCER IN LIVER TRANSPLANT RECIPIENTS - A SINGLE CENTER EXPERIENCE

Mariana Mihaila1, Gabriela Smiră1, Teodor Cabel1, Vladislav Brasseuane1, Irinel Popescu1
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Background: De novo malignancies following liver transplant are a serious threat in liver transplant recipients. The excess risk of post-LT de novo malignancy occurrence is now well known; the estimated risk for de novo malignancy is 1.4-4.9 times greater in LT recipients compared with the general populations. However, the incidence and type of DNM also depends on different risk factors, including patient demographics, cause of the underlying chronic liver disease, behavior (smoking and alcohol abuse).

Methods: We evaluated 1000 liver transplant recipients; 206 LT for HCC were excluded.

Results: 42 (5.28%) patients developed de novo neoplasms: 1pts - 2 types of cancer:- skin and cervix cancer. Interval between transplant and diagnosis of de novo cancer (month) were: min 6 month and max 11 years. The cancers were: solid tumors such as pancreatic cancer, lung cancer, colorectal cancer, gastric cancer, esophageal cancer, renal cell carcinoma, bladder cancer, thyroid cancer, oral cancer, brain tumors and laryngeal cancer and non-solid tumors: primarily PTLD/non-Hodgkin Lymphoma (NHL) and leukemia. However, the incidence and type of DNM also depends on different risk factors, including patient demographics, cause of the underlying chronic liver disease, behavior (smoking and alcohol abuse).

Conclusions: All liver transplant recipients should receive counseling on smoking cessation, limitations on alcohol use (complete abstinence in patients with ALD), sun protection and avoidance, regular skin assessments, adherence to routine cancer screening tests, and regular follow-up.

P67

PANCREAS ALLOGRAFT THROMBOSIS AS A POST-COVID-19 COMPLICATION IN DIABETIC PATIENT

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Background: The SARS-CoV-2 pandemic has caused a huge overload on the healthcare system worldwide [1]. From March 4th 2020 until December, 07th 2021 the total number of COVID-19 cases in Poland reached 3.684.671 million. According to the Polish Ministry of Health 85.700 infected patients died, most of them had been suffering from concurrent disease. [2] The mortality rate from COVID-19 in Polish population is ~2.5%. An increase of thrombotic and thromboembolic complications has been associated with COVID-19 in both arterial and venous systems. [3,4] Patients after transplantation suffering from COVID-19 are at a higher risk of mortality (42-24%) and complications than the average population. [5]

Methods: Hospital database analysis and literature search

Results: Recently, in our Center, there was a case of a PTA recipient with diabetes 11 that developed venous and arterial thrombosis 4 months after COVID-19, resulting in graft necrosis and finally in pancreas graftectomy [Figure A-F]. Our 6-year post-PTA patient had no history of thromboembolism or other risk factors apart from diabetes 1 and a history of COVID-19. Furthermore, in 2020 and 2021, 2 cases of infarction of a transplanted kidney in patients suffering from COVID-19 were described. Moreover, both cases occurred in obese transplant recipients with diabetes 1. The first case - a man with DM 11 13 years after kidney and pancreas transplantation who had a segmental infarction of the kidney [6], and the second case was a woman with DM 11 6, 5 months after kidney transplantation, who lost the graft as a result of a renal artery infarction. [7] Identifiable risk factors linking these cases are the post-transplant status for 11 diabetes and obesity.

Conclusions: Transplant patients who have experienced COVID-19 should be carefully monitored for the occurrence of graft arterial and vein embolism. Early detection of these complications in patients after organ transplantation gives an opportunity to save the organ. Thermostrephylaxis with low molecular weight heparin is highly important and should be continued in high-risk patients (obese, with persistent d-dimer levels) for a minimum of 2 weeks (preferably 4-6 weeks) after reaching the convalescent status.

Conclusions: Transplant patients who have experienced COVID-19 should be carefully monitored for the occurrence of graft arterial and vein embolism. Early detection of these complications in patients after organ transplantation gives an opportunity to save the organ. Thermostrephylaxis with low molecular weight heparin is highly important and should be continued in high-risk patients (obese, with persistent d-dimer levels) for a minimum of 2 weeks (preferably 4-6 weeks) after reaching the convalescent status.

P068

TRANSMISION DE VIRUS DE LA HEPATITIS C DE DONANTE VIRÉMICO A RECEPTOR SERONEGATIVO A TRAVÉS DEL INJERTO TEJIDO. UN ESTUDIO PROSPÉCTICO

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1 Hospital General Alicante, Nefrologia, Alicante, Spain, 2 Hospital General Alicante, Microbiologia, Alicante, Spain, 3 Hospital General Alicante, Nefrologia, Alicante, Spain

Background: The transmission of hepatitis C virus (HVC) from viremic donors to seronegative recipients of kidney transplantation is well documented. Pre-transplant administration of direct-acting antivirals prevents viremia, but the seroconversion rate is high. The aim of this study is to assess HCV transmission through the graft tissue.

Methods: In this prospective observational study, we determined the presence of HCV in the tissue of 15 kidneys from 8 deceased viremic donors (D16 transplanted to a seropositive recipient) before transplantation. Tissue samples were extracted in the operating room and Viral RNA determination in donor plasma and tissue was performed with the Xpert HCV viral load quantitative assay (Cepheid). Results: Plasma viral load in all donors was significant, and in recipients it was undetectable on days 1 and 7 post-transplantation. However, 13 of the 15 recipients (86.6%) had seroconverted within one month. HCV was detected in 9 of the 15 (60.0%) histological samples analyzed. Viral RNA was detected in D5, but not in D6, from the same donor, probably due to the scant sample and borderline viral. Data showed in table

Conclusions: HCV was detected in a large proportion of kidney grafts from viremic donors, which could facilitate its transmission to recipients.

<table>
<thead>
<tr>
<th>Donor</th>
<th>Recipient Plasma Viral Load (IU/mL)</th>
<th>Kidney Viral Load (IU/mL)</th>
<th>Seroconversion</th>
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<tbody>
<tr>
<td>D1</td>
<td>R1</td>
<td>Undetectable</td>
<td>Positive</td>
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<tr>
<td>D2</td>
<td>R2</td>
<td>Undetectable</td>
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</table>


Background: Brain death (BD) causes hemodynamic and hormonal impairment, compromising organ quality. Hormone replacement therapies, using thyroid hormones and cortisol, have shown positive results. After BD, female kidneys tend to present higher inflammation in comparison to male. This was associated with the rapid decrease in female sex hormones, like estradiol (E2), considering that E2 plays an important role in female response to stress. In that context, we aimed to investigate the role of E2 and its association with methylprednisolone (MP) in kidneys of female rats after BD.

Methods: Female Wistar rats were submitted to BD by rapid inflation of an intracranial balloon catheter and maintained for 6h. Rats received MP (MP, 4 mg/ml i.v.–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml i.v.–2 ml/h) after 3h of BD until the end of experiment. Sham-operated (S) rats were used as controls. After 6h, plasma and kidney tissue samples were collected for further analyses.

Results: In kidney homogenate, IL-6 (S:26.97±8.52; BD:74.87±25.65; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.0076) and VEGF (S:2.45±2.32; BD:23.45±28.72; MP/E2:2.75±2.99; MP:3.18±4.95 pg/mg/protein - p=0.024) were increased after BD, and both molecules were reduced after treatments. Regarding TNF-α, there was no difference between S and BD, but there is a significant reduction with both treatments (S:2.45±2.32; BD:23.45±28.72; MP/E2:2.75±2.99; MP:3.18±4.95 pg/mg/protein - p=0.024). Plasma measurements showed no difference in urea after BD and a reduction with important MP (S:131.4±14.2; BD:133.3±15.19; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.024). Plasma measurements showed no difference in urea after BD and a reduction with important MP (S:131.4±14.2; BD:133.3±15.19; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.024). Plasma measurements showed no difference in urea after BD and a reduction with important MP (S:131.4±14.2; BD:133.3±15.19; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.024). Plasma measurements showed no difference in urea after BD and a reduction with important MP (S:131.4±14.2; BD:133.3±15.19; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.024). Plasma measurements showed no difference in urea after BD and a reduction with important MP (S:131.4±14.2; BD:133.3±15.19; MP/E2:13.62±3.91; MP:13.27±4.12 pg/mg/protein - p=0.024).

Conclusions: Results suggest that both treatments are able to reduce kidney acute inflammation. These data indicate that MP and its association with E2 has a potential beneficial effect in inflammation triggered by BD in kidneys from female donors, suggesting that this treatment may improve organ quality. This study was financed by 2020/11211-6, Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP.
Background: One severe complication following solid organ transplantation is antibody- and/or cell mediated rejection of the graft. Early detection of rejection is therefore of paramount importance to improve outcome of solid organ transplantation. The present study was conducted to determine the analytical performance of the Devyser kit designed for sensitive detection of dd-cfDNA (donor-derived cell free DNA) following kidney transplantation.

Methods: Three artificial dilution series mimicking recipient and donor were manufactured to determine the analytical performance of the assay. The DNA samples were fragmented to correspond to cell free DNA (~166 bp) using NGS dissociation dissociation and ENGAGE by the manufacturer according to manufacturer instructions. The dilution points for each dilution series were the following: 0.05%, 0.1%, 0.2%, 0.3% 0.4%, 0.5%, 1%, 10%, 20% and 30%. A total of 443 samples were amplified and sequenced using the Devyser kit. All NGS-data were analyzed using the Devyser software employing the ADVYSER software. The stability of the cfDNA in plasma collected in two different kinds of collection tubes were also evaluated prior and post plasma isolation. The integrity of cfDNA was evaluated using Agilent TapeStation Cell-free DNA ScreenTape Analysis.

Results: All samples were tested and sequenced on three different Illumina MiSeq instruments and the fastq files were analyzed using the ADVYSER software. The following analytical parameters were established during the study; Limit of Blank (LOB), Limit of detection (LOD), Limit of Quantification (LOQ), Linearity, lot-to-lot uniformity, within-and between run. Even in samples with low DNA concentration, ddcfDNA as low as 0.1% was detected.

Conclusions: The present study shows that a novel assay for solid organ transplantation based on NGS, exhibits excellent sensitivity, accuracy and precision and is suitable for monitoring dd-cfDNA.

Background: Available tacrolimus formulations exhibit substantial inter- and intra-individual variability in absorption and metabolism. The present non-interventional cohort study aimed to assess the tolerability and effectiveness of the once-daily tacrolimus formulation, LCPT, in hepatic allograft recipients in real life.

Methods: This study was conducted in Austria and the Czech Republic between 07/2016 and 08/2019. Patients aged ≥18 years received LCPT per the approved label and local clinical routine. All the participants provided informed consent. Patients newly treated with tacrolimus (de novo) directly after transplantation were observed for six months. The relevant clinical variables were tacrolimus trough level (TL), total daily dose (TDD), number of dose adjustments, kidney and liver function, and tolerability.

Results: Of the 70 analysed patients, 72.9% were male and 85.7% were aged 18 years. The mean (SD) time to achieve tacrolimus target TL was 6.4 (4.6) days after 4.4 (4.0) dose adjustments; thereafter, TL remained stable throughout observation at approximately 8 ng/mL. The LCPT TDD at initiation was 8 mg, and decreased by a median of 4.1% to 5 mg at six months. Liver function continuously improved, and kidney function remained stable. LCPT was well-tolerated with 24 adverse events in eight patients (17 related to immunosuppression, mostly mild renal insufficiency, and hematological adverse events); two serious unrelated adverse events were reported (atrical flutter and liver dysfunction).

Conclusions: TL was rapidly attained with few dose adaptations after LCPT initiation in de novo liver transplant patients. Liver function rapidly improved, whereas kidney function remained normal. LCPT was well-tolerated in this population.
Background: Studies investigating the role of cell-free deoxyribonucleic acid (cfDNA) in kidney allograft dysfunction have primarily focused on the ability of donor-derived cfDNA (ddcfDNA) to detect rejection. Higher plasma ddcfDNA levels have been shown to be diagnostic of antibody-mediated rejection (ABMR). As ABMR is an established determinant of long-term graft outcomes, we hypothesised that higher levels of ddcfDNA would associate with poorer outcomes. We aimed to examine the long-term prognostic value of plasma ddcfDNA and total cfDNA, measured immediately prior to indication kidney transplant biopsies.

Methods: A retrospective review was performed of kidney transplant recipients (KTRs) who underwent prospective cfDNA quantification by droplet digital polymerase chain reaction, at the time of transplant indication biopsy between 2014 and 2017. Absolute (copies per millilitre, cp/mL) and relative (%) ddcfDNA levels, and total cfDNA concentration, were analysed against long-term survival outcomes.

Results: Of 49 unique KTRs (mean follow-up 5.8 years), there were 6 deaths and 6 failed grafts. Total cfDNA was higher (4736.6cp/ml vs 1639.91cp/ml, p=0.04) and relative ddcfDNA was lower (0.21% vs 0.52%, p=0.047) in KTRs and 6 failed grafts. Total cfDNA was lower (4736.6cp/ml vs 1639.91cp/ml, p=0.04) and relative ddcfDNA was lower (0.21% vs 0.52%, p=0.047) in KTRs that died. The optimal cutpoint (by Youden’s index) for mortality was 4040.66cp/mL (area under the curve, AUC 0.76) for total cfDNA, and 0.31% (AUC 0.75) for relative ddcfDNA. On multivariate analysis, increased KTR mortality was predicted by total cfDNA above the cutpoint (hazard ratio, HR 7.45, 95% CI 1.18-47.1), and by relative ddcfDNA below the cutpoint (HR 20.53, 95% CI 1.4-299.8). Total cfDNA was lower in KTRs with death-censored allograft failure (912.43cp/ml vs 1803.09cp/ml, p=0.02). All cases were identified by total cfDNA levels, and total cfDNA concentration, were analysed against long-term survival outcomes.

Conclusions: Death was significantly associated with higher total cfDNA and lower relative ddcfDNA. Allograft failure was significantly associated with lower total cfDNA. These associations are a novel finding in KTRs. Relative ddcfDNA has been used to identify transplant rejection, but cfDNA and ddcfDNA may indicate prognosis more widely.

Mortality Predicted by Total cfDNA

- Total cfDNA → High → Low
- Log-Rank Test p-value < 0.01
- Hazard Ratio (total cfDNA > 4040.66) = 7.45 (1.18 - 47.1)

Number at risk (number of events)

- Total cfDNA
- Time (years)
- 11 (0) 9 (2) 0 (3) 3 (4) 0 (4)
- 38 (0) 38 (0) 38 (0) 15 (2) 0 (2)

- Time (years)
P082  CLINICAL OUTCOMES AND QUALITY OF LIFE IN CHILDREN WITH METHYLMALONIC ACIDEMIA AND END-STAGE KIDNEY DISEASE: A PROMISING FUTURE

Charalampos Kapogiannis1, Colin Higgins1, Stephanie Grunewald2, Anupam Chakrapani2, Vandana Jain3, Nigel Heaton4, Nicos Kessaris1,5, Jelena Stejanovic1

1Great Ormond Street Hospital for Children, Department of Paediatric Nephrology, London, United Kingdom, 2Great Ormond Street Hospital for Children, Department of Inherited Metabolic Diseases, London, United Kingdom, 3King’s College Hospital, Department of Paediatric Liver, Gastroenterology and Nutrition, London, United Kingdom, 4King’s College Hospital, Institute of Liver Studies, London, United Kingdom, 5Guy’s Hospital, Department of Nephrology and Transplantation, London, United Kingdom

Background: Methylmalonic Acidemia (MMA) is characterised by accumulation of methylmalonic acid in body tissues due to defects in Methylmalonyl-Coenzyme (CoA) mutase or Cobalamin (Vit B12). It leads to end stage kidney disease (ESKD) and severe neurological deficits. To minimize disease-related complications and improve quality of life, isolated Kidney (KT), Liver (LT) or Combined Liver-Kidney Transplantation (CLKT) can be considered. This is the first study reporting correlation of these transplant strategies on quality of life (QoL) and clinical outcomes.

Methods: This single centre, retrospective observational study, evaluated the clinical outcomes and QoL of children with MMA and ESKD, comparing transplanted and non-transplanted patients from 2015 onwards. Percentage change in serum MMA. Creatinine and e-GFR were analysed using IBM SPSS software. Statistical significance was considered at 95% confidence level (p<0.05). Mann Whitney U test was used to compare current clinical outcomes and QoL between transplanted and non-transplanted groups. Validated PedsQL Transplant Module and End Stage Renal Disease Module questionnaires were used. Scores were calculated and compared using a scale from 0 to 100, with higher values representing better QoL.

Results: This study included 5 girls and 4 boys with MMA; median age of 10 years. Transplantation was performed in 6 out of 9 children (2 KT, 2 LT, 2 CLKT), median age of 6.5 years. A statistically significant difference in mean percentage reduction in serum MMA was observed between transplant and non-transplant groups (63.21% Vs 74.7%, p<0.05). In the transplantation subgroups, CLKT demonstrated the highest percentage reduction in serum MMA levels (93.32%), followed by LT (59.74%) and KT (37.58%). CLKT showed the highest percentage improvement in serum creatinine (71.43%). PedsQL mean score values of 75 and 74.7 were observed in non-transplanted and transplanted patients respectively. CLKT should be considered as the first choice type of transplant in children with established ESKD. Short term follow up identified no statistically significant improvement in QoL in this cohort.

Conclusions: Children with MMA and ESKD benefit from transplantation, with reduced MMA-values post-transplant and subsequently reduced toxic effects on all organs. CLKT should be considered as the first choice type of transplant in children with established ESKD. This single centre, retrospective observational study, evaluated the clinical outcomes and QoL of children with MMA and ESKD, comparing transplanted and non-transplanted patients from 2015 onwards. Percentage change in serum MMA. Creatinine and e-GFR were analysed using IBM SPSS software. Statistical significance was considered at 95% confidence level (p<0.05). Mann Whitney U test was used to compare current clinical outcomes and QoL between transplanted and non-transplanted groups. Validated PedsQL Transplant Module and End Stage Renal Disease Module questionnaires were used. Scores were calculated and compared using a scale from 0 to 100, with higher values representing better QoL.

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P085  FUROSEMIDE ATTENUATES TUBULOINTERSTITIAL INJURY AND ALLOWS FUNCTIONAL TESTING OF PORCINE KIDNEYS DURING NORMOTHERMIC MACHINE PERFUSION

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Background: Normothermic machine perfusion (NMP) is a promising pretransplant kidney quality assessment platform, but it remains of crucial importance to increase its diagnostic potential whilst ensuring minimal additional injury to the already damaged kidney. Interventions that alter tubular transport could influence renal function and injury during perfusion. This study aimed to determine whether furosemide and desmopressin can affect renal function and injury during NMP.

Methods: Eighteen viable porcine kidneys (n = 6 per group) sustained 30 min of warm ischemia and 3-5 hours of oxygenated hypothermic perfusion before being subjected to 6 hours NMP. Each organ was randomized to receive either no drug, furosemide (750 mg), or desmopressin (16 μg) during NMP.

Results: Compared to other groups, the addition of furosemide resulted in significantly increased urine output, fractional excretion of sodium and potassium, and urea clearance during NMP (Figure 1). Urinary neutrophil gelatinase-associated lipocalin levels decreased significantly with furosemide supplementation compared to other groups. The addition of desmopressin did not result in any significantly different outcome measurement compared to the control group.

Conclusions: This study suggests that adding furosemide could affect renal function while attenuating tubulointerstitial injury during NMP. Therefore, furosemide supplementation may provide renal protection and serve as a functional test for pretransplant kidney viability assessment during NMP.

Figure 1. Urine production (A), fractional excretion of sodium (B) and potassium (C), creatinine clearance (D), urea clearance (E), and delta urinary neutrophil gelatinase-associated lipocalin (F) during normothermic machine perfusion. Means and standard deviations are shown. Deltas are the differences between the end and the start of perfusion. CrCl, creatinine clearance; FEK, fractional potassium excretion; FENa, fractional sodium excretion; NGAL, neutrophil gelatinase-associated lipocalin; UreaCl, urea clearance. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.
Background: Oxidative damage from ischemia/reperfusion injury (IRI) in organ transplantation is initiated by a burst of reactive oxygen species (ROS) generated by reverse electron transport (RET) in mitochondria. RET is driven by succinate dehydrogenase (SDH)-mediated oxidation of the mitochondrial metabolite succinate, which accumulates extensively in ischemic tissues. We use translational models of kidney transplantation to identify conserved metabolic changes between mice, pigs, and humans, and examine the efficacy and mechanism of protection afforded by inhibition of SDH by disodium malonate (DSM).

Methods: Mouse and pig kidney IRI (bilateral renal pedicle clamping) and pig and human ex vivo normothermic machine perfusion models were used to temporally quantify changes in succinate metabolism. Further mouse experiments examined key metabolic pathways and the impact of DSM treatment, through untargeted metabolomics analysis and bulk RNA sequencing.

Results: Kidney succinate metabolism was highly conserved between mice, pigs, and humans during IRI. DSM treatment prior to kidney IRI in mice inhibited complex II and was protective, reducing elevations in serum creatinine and oxidative markers. DSM treatment rapidly reprogrammed metabolism, reducing ROS production but may also pharmacologically precondition kidneys by rewiring their metabolism in a protective fashion. Whether these transcriptomic changes are solely attributable to DSM-mediated SDH inhibition is unclear, however these analyses identify key enzyme targets for further investigation. Together, these data increase our understanding of the mitochondrial mechanisms underpinning IRI and facilitate clinical translation of DSM as a safe and effective therapy in organ transplantation.

Conclusions: DSM not only ameliorates oxidative damage through inhibition of ROS production but may also pharmacologically precondition kidneys by rewiring their metabolism in a protective fashion. Whether these transcriptomic changes are solely attributable to DSM-mediated SDH inhibition is unclear, however these analyses identify key enzyme targets for further investigation. Together, these data increase our understanding of the mitochondrial mechanisms underpinning IRI and facilitate clinical translation of DSM as a safe and effective therapy in organ transplantation.
Background: Kidney transplantation is the best treatment for End Stage Renal Disease (ESRD). However, post-transplant diabetes mellitus (PTDM) occurred in 15% of cases. To better prevent PTDM, we studied its prevalence at different time points, its dynamics of occurrence, and influencing factor.

Methods: We used data from the French national Astre database, including patients transplanted between 2008 and 2017. The occurrence of PTDM was defined by fasting blood glucose ≥1.26g/L or HbA1c ≥6.5% or the use of antidiabetic treatments. The remission of PTDM was defined by normal fasting blood glucose and HbA1c and no more need of antidiabetic treatments. The remission of PTDM was defined by fasting blood glucose ≥1.26g/L or HbA1c ≥6.5% or the use of antidiabetic treatments.

Results: We included 7215 kidney transplants in the study. The prevalence of PTDM among the 2698 transplants was 27.3% at 3 months (M3); 21.3% at 1 year; 19.8% at 2 years; and 19.9% at 3 years. The trajectory analysis used to study the dynamics changes was based on 1825 transplants and revealed 4 groups: 67% with no PTDM, 6% with late PTDM developed after M3, 10% with PTDM remission after M3, and 17% with early and persistent PTDM. Early and persistent PTDM was associated with higher BMI at transplantation time and lower rejection-free survival. Late PTDM was associated with a history of cardiovascular disease or higher BMI. Weight gain is associated with PTDM at 1 year. Corticosteroid are associated with early, persistent and late PTDM. Used or change immunosuppressive drug between post-transplantation and emphasized the importance of the first-year post-transplant, which seems to be decisive for the progression of PTDM to onset or remission. Corticosteroid use and weight gain before or after transplantation have to be restricted and late PTDM. Used or change immunosuppressive drug between post-transplantation and emphasized the importance of the first-year post-transplant, which seems to be decisive for the progression of PTDM to onset or remission.

Conclusions: This study confirmed the high prevalence of PTDM in post-transplantation and emphasized the importance of the first-year post-transplant, which seems to be decisive for the progression of PTDM to onset or remission. Corticosteroid use and weight gain before or after transplantation have to be restricted and late PTDM. Used or change immunosuppressive drug between post-transplantation and emphasized the importance of the first-year post-transplant, which seems to be decisive for the progression of PTDM to onset or remission.
Background: In older patients with end-stage renal disease recent studies report similar long-term survival between receiving a kidney transplant (KT) or remaining on dialysis. Health-related quality of life (HRQOL) improves early after KT, but the long-term impact of KT on HRQOL in the elderly is not known. In a population of older recipients, we aimed to investigate the longitudinal HRQOL development from waitinglist until five years after KT.

Methods: Patients ≥ 65 years, who were enlisted for KT between January 2013 and November 2016 were included. Self-reported HRQOL was assessed using the Kidney-Disease Quality of Life Short Form version 1.3 (KDQOL-SF) survey. After enrolment, scores were obtained every 6 months until KT, with the last value representing baseline. Post-KT scores were obtained at 6 months and at 1-, 3- and 5-years. Linear mixed-effect models were used to detect HRQOL changes over time and to identify predictors of long-term HRQOL outcomes.

Results: Among 289 enrolled participants ≥ 65 years, 222 (77%) received a kidney. HRQOL substantially improved during the first year after KT, thereafter needed as a possible benefit in graft survival and decrease in PTLD may exist.

Conclusions: KT offers a long-term HRQOL benefit also in older recipients. Living donor transplants are associated with a sustained HRQOL improvement and should be preferred, if possible.

Figure: Health-related quality of life development until 5 years after kidney transplantation. Comparison between recipients of living donor versus deceased donor transplants.

Figure: Data from a single-center study analyzed 1,616 adult KT patients that used tacrolimus-based immunosuppression between 1979 and 2017. We calculated mean tacrolimus trough concentration between the first 6th month and 1 year after KT and investigated association of tacrolimus levels with malignancy and death-censored graft failure using Cox regression analysis.

Results: Overall, malignancy occurred in 120 (7.4%) KT patients. Tacrolimus levels ≥ 7.0 ng/mL had a higher risk for malignancy compared to tacrolimus levels < 5.5 ng/mL (HR 1.899, 95% CI 1.015-3.517; P = 0.047). The systematic review found comparable recipient survival rates, serum creatinine concentrations and viral infection incidences in patients treated with and without basiliximab.

Conclusions: No statistical benefit was found in patients using basiliximab. However, the current evidence on basiliximab is limited and further studies are needed as a possible benefit in graft survival and decrease in PTLD may exist.

Figure: Basiliximab vs No Basiliximab 1-year graft survival.
**P094 CHALLENGES EXPERIENCED BY ADULT LIVER DONORS AFTER LIVING DONOR LIVER TRANSPLANTATION: AN INTEGRATIVE REVIEW**

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**Background:** Living donor liver transplantation (LDLT) is a complex experience that can challenge health and quality of life of donors. With the growing demands to LDLT worldwide, it is timely to review the current state of knowledge regarding challenges and experiences of the living donors following LDLT. Therefore, this integrative review aimed to describe challenges experienced by living donors following LDLT.

**Methods:** Using Whittomere and Knaff's methods, we searched 5 databases (PubMed, Embase, Web of Science, CINAHL, PsycINFO) to identify studies that explored post-LDLT experience of living donors. Inclusion criteria were studies (1) relevant to post-transplant phase of the adult-to-adult LDLT; (2) published in peer-reviewed journals; (3) written in English; and (4) presented one or more of the following variables: (a) psychological outcomes (e.g., anxiety), (b) physical outcomes (e.g., pain), (c) social outcomes (e.g., employment), or (d) needs (e.g., information needs). Study findings were further synthesized using a qualitative-led synthesis.

**Results:** Of 1171 articles, 26 studies were included for review (21 quantitative and 5 qualitative studies). Living donors reported varying challenges to their physical and mental health, which were beyond the challenge of post-surgical complications (e.g., wound infection). Identified challenges were fatigue, anxiety, depression, altered body image, changes in employment/income, relationship with recipients, etc. Major factors associated with these challenges were recipients' health outcomes and uncertain prospects for donor's own health.

**Conclusions:** Findings of this review highlight the current state of the science in physical and psychosocial challenges of living donors after LDLT. Future studies are warranted with more robust methods, such as longitudinal cohort studies, to enhance understanding and supports for living liver donors, a growing but under-researched population.

**Keywords:** Living donors, Liver transplantation, Adult, Physical, Psychosocial, post-transplant outcomes

**P095 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: IS THERE A CURATIVE TREATMENT FOR DISSEMINATED RECURRENT?**

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**Background:** Liver transplantation (LT) is the best treatment in selected patients with both cirrhosis and hepatocellular carcinoma (HCC). Despite strict adherence to accepted selection criteria for transplantation, HCC still recurs in 6-18% of patients post LT, and it is associated with significantly lower survival in these patients compared to those without recurrence. Currently, the clinical management of HCC recurrence is challenging as standardized protocols for post-LT surveillance and consensus treatment guidelines are lacking.

**Methods:** A retrospective observational study was carried out on patients undergoing LT for cirrhosis and HCC between January 2010 and December 2022, selecting patients with recurrence of the HCC.

**Results:** 117 patients were transplanted for HCC, all with subsidiary liver cirrhosis. The most frequent cause of cirrhosis was etiologic (40.4%). During follow-up, 4 patients (3.41%) developed recurrence of hepatocarcinoma. The mean age of the 4 relapsed patients was 58.8 ± 6.4 years. Two were male (50%) and two were female (50%). All recurrent patients were included for LT according to the Milan criteria. Average time from HCC diagnosis to transplant was 12.43 ± 5.52 months. In this period, 100% of the patients received adjuvant treatment. The surgery was uneventful in all cases. The median time from LT to HCC recurrence was 17 months (ICR 14 - 37.5). During this time, 2 patients had acute graft rejection and were treated with corticosteroid therapy and increased doses of immunosuppression. All cases were presented as disseminated peritumoral disease. No significant differences were found in terms of tumour marker values at the time of transplantation and at the time of recurrence. As for the treatment of recurrence, two cases were treated palliatively and died within two months due to rapid progression. Two patients remain alive on systemic treatment with tyrosine kinase inhibitors (sorafenib), one of them with tumour progression and the other with stable disease.

**Conclusions:** There is a clear benefit in terms of survival with the current criteria for candidate selection, although the recurrence rate is not negligible and its treatment is still a challenge. So far, the goal for disseminate recurrence is to prolong survival and treatment is for palliative intent, rather than pursuit of cure.
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Background: In the Spanish scenario of high donation rate and short waiting list, introduction of new graft preservation strategies is controversial. We present our experience with D-HOPE (dual hypothermic oxygenated perfusion) protocol for ECD (extended criteria donors) since October 2021.

Methods: We present a retrospective descriptive study of the use of hypothermic liver machine perfusion in the period between October 2021-October 2022. Indications: 1 ECD, DCD (death cardiac donors) or DBD (brain death donors): age over 65 years, BMI (body mass index) over 30 Kg/m2, UCI (intensive care unit) more than 7 days, Sodium 155 mmol/l, liver enzimas (AST 150 UI/ml, ALT 170 UI/ml), cardiac arrest, macrovesicular steatosis (biopsy) 30% 2 Prolonged hepatectomy, We reproduce a usual technique for organ procure-ration, static cold storage for transport and backtable surgery, with posterior connection to the perfusion system, with a goal of perfusion time of 2 hours.

Results: We transplanted 7 patients with livers from 7 brain death donors with median age 63, BMI 25, MELD-Na 19, preoperative portal vein thrombosis 27% (28%), Transplant duration 395 minutes; cold ischaemia time including D-HOPE 400 min; all cavec- tomy technique (no piggy-back), no portocaval shunt, no Kehr drain. No PNF.

Conclusion: The technique is feasible; the principal drawbacks are that one member of the surgeon team must prepare the device before the arrival of the organ and the implantation surgery can be delayed one hour. The results observed show the complications of liver transplantation technique, none of them attributable to the perfusion procedure.

We need more experience to have statistically significant data.
P100 'WALKING IS FUN BUT WALKING TOGETHER IS EVEN MORE FUN': AN EVALUATION OF THE WALK&TALK PROGRAM IN THE NETHERLANDS

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Background: In 2019, the first Walk&Talk group was established in the Netherlands. Walk&Talk is a physical intervention for and organized by transplant recipients (TRs). The aim of Walk&Talk is to promote physical activity and peer support among TRs and their significant others. Upon request, transplant professionals can join. Walk&Talk is financially supported by Chiesi Pharmaceuticals.

The aim of this study was to evaluate the development of the Walk&Talk program, the satisfaction of Walk&Talk participants, and its effect on wellbeing.

Methods: A mixed-methods study was performed among Walk&Talk participants using a brief survey (n=38) after each walk and semi-structured interviews with ten participants (summer 2022). Data were analysed using descriptive statistics and content analysis.

Results: Seven Walk&Talk groups have been established since the start of the program. Each group organizes a monthly walk of about one hour. Although most groups consist of a total of 20 participants, five to ten participants are present at each Walk&Talk. Some TRs were joined by a significant other, most often their partner. Coordinators (n=4) were motivated to take on this role because they wanted to promote physical activity among TRs. Participants (n=6) mainly wanted to get in touch with other TRs and/or their partners. Overall, participants were satisfied with the frequency, duration, and intensity of the walk. Although transplant professionals did not join the walks frequently, participants appreciated their presence when they did as this setting made them feel more comfortable discussing personal, transplant-related problems. Regarding the effect of Walk&Talk on wellbeing, participants indicated that the program helped them to get in touch with other TRs and their significant others. By talking to their peers, they felt heard and experienced a strong feeling of mutual understanding. This helped them process the transplant experience, which consequently made them feel stronger mentally. As most participants were already physically active, only a few participants indicated that it improved their physical fitness.

Conclusions: Walk&Talk is an easy-to-start physical intervention for TRs and their significant others that enhances peer support, which may have a positive effect on their psychosocial wellbeing.

P101 BROADENING CRITERIA FOR DONOR LIVERS: SUCCESSFUL LIVER TRANSPLANTATION OF TWO DONOR LIVERS WITH PORTAL VENOUS GAS

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Background: Maximising the utilisation of the deceased donor organ resource for liver transplantation (LT) is critical. Portal pyaemia, evidenced by the presence of portal venous gas (PVG), is typically associated with intestinal ischaemia and is generally a harbinger of poor outcome. Donor PVG is traditionally a contraindication to transplantation.

Methods: We present two cases of successful LT utilizing donors livers with pre-transplantation findings of PVG.

Results: Both cases were brainstem death donors having experienced a preceding cardiac arrest. CT scans demonstrated gastric ischaemia and PVG. Donor 2 had evidence of ischaemic hepatitis that improved over time. Neither donor showed signs of uncontrolled infection at the time of organ offer. At organ retrieval there was no evidence of ischaemia on evaluation the liver and entire gastrointestinal tract. The donors had routine broad spectrum antibiotics prior to donation. The retrieval was uncomplicated with blood washed from the organs with UW solution, including back table PV flush as routine. Recipient 1 was a 42-year-old woman with autoimmune hepatitis, and recipient 2 a 54-year-old woman with non-alcoholic steatohepatitis. Both recipients recovered well post-operatively with no infective complications. Recipient 1 was found to have a cystic duct stump leak, which was treated with good effect with an ERCP and stent. At 90-day follow-up, both were clinically well with additional no complications.

Conclusions: Our patients are the first reported cases of successful LT using donors with PVG. With careful evaluation, donors with PVG can be used for LT and that this can prevent underutilisation of the donor resource.

P102 IMPACT OF HEMOADSORPTION ON PHARMACOKINETICS OF IMMUNOSUPPRESSIVE DRUGS IN A SHEEP MODEL

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Background: Potential removal of immunosuppressive drugs (ID) during extra-corporeal hemoadsorption in organ transplantation patients may have important clinical implications. The current study aimed to investigate the impact of extra-corporeal hemoadsorption on the pharmacokinetics (PK) of ID in a sheep model.

Methods: Healthy sheep were administered seven different ID (tacrolimus (TAC), ciclosporin A (CYA), mycophenolate mofetil (MMF), everolimus (EVER), basiliximab (BAS), methylprednisolone (MP) and prednisolone (PRE)) in clinically relevant doses and combinations. Animals were treated either with CytoSorb® hemoadsorption (intervention group, n=5), or a sham extracorporeal circuit (control group, n=3). Blood samples for PK measurements were collected over the treatment period of six hours in both groups. In the intervention group samples were collected pre (inlet) and post (outlet) adsorber. Additionally, for TAC, CYA, EVER, MMF and MP a population pharmacokinetic analysis (NONMEM® 7.5) was performed to investigate the adsorption characteristics.

Results: For PRE and BAS negligible clearance was observed in pre- versus post adsorber measurements. For all other substances a saturable adsorption submodel with linear decrease of the adsorption effect over the adsorbed amount best described the measured data. Calculated maximum absolute adsorbed amounts (95 % confidence interval) for TAC, CYA, MMF, EVER and MP were 0.040 (0.008 - 0.053), 1.15 (0.39 – 1.91), 4.17 (2.00 – 6.35), 0.0163 (0.007 – 0.028), 53.4 mg (20.9 – 85.9), respectively. This equals an adsorption of less than 5% of the daily administered dosages for all tested substances.

Conclusions: In this large animal model, CytoSorb® hemoadsorption had very limited effect on the clearance of ID. These findings provide reassuring information for the safe use of the device in patients receiving ID and may be further complemented by therapeutic drug monitoring according to clinical judgment.
Background: Adolescent thoracic transplant (Tx) recipients require life-long medical management and are at increased risk of psychological distress, social isolation and impaired social and cognitive functioning compared to healthy peers. This is concerning as adolescent recipients are undergoing critical developments in their identity and independence as they prepare to transition to adult care. iP2Peer (iP2P) is an established online support mentorship program enabling trained young adult mentors to provide modelling and reinforcement to adolescent mentees with the same chronic illness. This study assessed the experiences and perspectives of adolescent thoracic Tx mentees participating in the program.

Methods: The iP2P program in thoracic Tx was piloted at two Canadian pediatric Tx centers. Adolescent mentees (12-17 years old) who received a heart or lung transplant were matched one-to-one with trained mentors (18-25 years old) who were successfully managing their Tx. Mentee-mentor pairs connected virtually over 15 weeks through video calls and text messaging. A qualitative descriptive approach was used and individual interviews were conducted with mentees following the iP2P program. Interviews were audio recorded, transcribed verbatim and subject to thematic and content analysis.

Results: Mentee participants included 13 heart and 2 lung Tx recipients (median age: 15 years) with diverse gender and ethnic backgrounds. Three themes emerged: (1) Seeking a sense of normalcy in personal Tx journey, (2) Enabling meaning-making through reciprocal story sharing, and (3) Nurturing confidence and disease self-management skills. Mentees reported high satisfaction with the iP2P program, and all would recommend iP2P to other adolescent thoracic Tx recipients. “It definitely helped me. I feel like [other Tx recipients] had any troubles, it would definitely help them as well.”

Conclusions: The iP2P program is promising intervention to improve quality of life for adolescent thoracic Tx recipients. Next steps involve examining the implementation effectiveness outcomes of the iP2P program and interviewing mentors to capture their perspectives. Findings will inform a future multi-centre randomized controlled trial evaluating the iP2P program across solid organ Tx clinical populations.

P104 IMPROVEMENT GAPS TO DEAL WITH THE SHORTAGE OF LUNGS FOR TRANSPLANTATION FROM A MIDDLE INCOME COUNTRY’S PERSPECTIVE

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Background: In Argentina 78% of the lung waiting list have been waiting longer than 1 year. During 202, only 5.9% of our actual donors were lung donors. Regardless of donation activity in Argentina, we have a clear problem on achieving the lung donation rates expected.

Methods: A cross-sectional study was performed using digital self-report surveys. Critical care specialists and transplant coordinators from different regions in Argentina were surveyed. The surveys included questions directed to obtain information regarding donor management, selection criteria and resource availability that demonstrated an impact on increasing lung procurement. The objectives of the study were 1) To identify the potential causes for the low lung procurement rate in Argentina. 2) To develop strategies to the actual problems.

Results: From the total surveyed 23.7% do not use advanced haemodynamic monitoring. When using CVP to guide decisions only 35.8% consider main- taining a CVP lower than 10 mmHG during the maintenance. In donors with driving pressure < P600, 87.60% of the surveyed population would discard a patient with 1 of these expanded selection criteria used. The main opportunities for improvement seem to be: 1) Training the physicians involved in the donor’s management in the management of potential lung donors seems to be a way of increasing the lung donor rates. 2) The donor selection criteria used should be reviewed together with the transplant teams in order to achieve an increase in the adherence to the expanded selection criteria.

Conclusions: The main opportunities for improvement seem to be: 1) Training the physicians involved in the donor’s management in the management of potential lung donors seems to be a way of increasing the lung donor rates. 2) The donor selection criteria used should be reviewed together with the transplant teams in order to achieve an increase in the adherence to the expanded selection criteria.

How do they use mechanical ventilation

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Table 1: Efficiency in considering expanded selection criteria

P105 "WE’VE ALL GONE THROUGH THE SAME JOURNEY": EFFECTIVENESS OF A MINDFULNESS-BASED RETREAT FOR MOTHERS OF PEDIATRIC HEART TRANSPLANT RECIPENTS

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Background: Mothers of pediatric heart transplant (HTx) recipients are at high risk for psychosocial concerns and lower quality of life (QoL), which may impact familial, social and health outcomes. Mindfulness is proposed as an evidence-based intervention to support maternal coping, distress tolerance and QoL. This study investigated the implementation and preliminary effectiveness of a mindfulness-based retreat (MBR) for mothers of pediatric HTx recipients.

Methods: A two-day MBR was piloted with mothers of pediatric HTx recipients. Quantitative and qualitative data were analyzed independently and then amalgamated to evaluate implementation and effectiveness outcomes.

Results: Sixteen mothers participated in the MBR held at a Canadian retreat centre. The MBR demonstrated high feasibility, fidelity and adoption, and perceived social support. QoL and mindfulness were completed 24 hours before the MBR (T1), immediately after the MBR (T2) and three months after the MBR (T3). Qualitative interviews exploring participants’ experiences were conducted at T2 and T3. Quantitative and qualitative data were analyzed independently and then amalgamated to evaluate implementation and effectiveness outcomes.

Conclusions: The main opportunities for improvement seem to be: 1) Training the physicians involved in the donor’s management in the management of potential lung donors seems to be a way of increasing the lung donor rates. 2) The donor selection criteria used should be reviewed together with the transplant teams in order to achieve an increase in the adherence to the expanded selection criteria.

E-PORTEES P001 P100 P200 P300 P400 P500 P600 P700
Conclusions: Results support the MBR as a feasible and effective intervention that improves maternal coping, social support and QoL, contributing to family-centred care in pediatric HTx. Findings inform future studies exploring the sustainability and transferability of the MBR for caregivers and family members affected by pediatric chronic illnesses.

**P107 ADIPONECTIN / LEPTIN RATIO AS AN INDEX TO DETERMINE METABOLIC RISK IN PATIENTS AFTER KIDNEY TRANSPLANTATION**

**Karol Graňák**1, Monika Beliančinová1, Patricia Kleinová1, Margareta Pytliaková1, Ivana Dedinská1

1Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia

Background: It has been confirmed that adiponectin / leptin (AL) ratio correlates better with cardiometabolic risk factors than hormone levels alone. The aim of our study was to determine the risk of developing post-transplant diabetes mellitus (PTDM) and other metabolic conditions depending on the A/L ratio after kidney transplantation (KT).

Methods: In the prospective analysis, studied sample of 104 patients was divided into three groups: 1. control group, 2. patients who developed a pre-diabetic condition after KT (impaired glucose tolerance, fasting hyperglycemia) and 3. patients who developed de novo PTDM. Pre-transplantation, at 3, 6 and 12 months after KT, we recorded basic characteristics of donor and recipient. We also monitored levels of adipokynesins and calculated A/L ratio.

Results: During observed period, we recorded significant increase in A/L ratio in control group (P=0.0013), on the contrary, a significant decrease in PTDM group (P=0.0003). Comparing the individual subgroups divided according to the values of the A/L ratio in 1 year after KT, we found that patients with an A/L ratio < 0.5 compared to those with a value > 1 were significantly longer in the dialysis program, had a higher body mass index, waist circumference, poorer graft function, higher proportion of prediabetes and PTDM in 1 year after KT. Using Cox regression Hazard model, we identified age at time of KT (HR 2.8226, P=0.0225), triglycerides at 1 year (HR 3.5735, P=0.0174) and A/L ratio < 0.5 as independent risk factors for prediabetes and PTDM 1-year post-transplant (HR 3.1724, P=0.0114).

Conclusions: This is the first study to evaluate the relationship between A/L ratio and the risk of PTDM and associated metabolic conditions after KT. We found out that A/L ratio < 0.5 is an independent risk factor for prediabetes and PTDM 1-year post-transplant.

**Table 1. Cox regression Hazard model**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the time of KT &gt; 54 years</td>
<td>1.095</td>
<td>0.972-1.236</td>
<td>0.307</td>
</tr>
<tr>
<td>BMI &gt; 30 kg/m²</td>
<td>1.376</td>
<td>1.097-1.717</td>
<td>0.008</td>
</tr>
<tr>
<td>Urea after KT &lt; 20 mg/dl</td>
<td>1.203</td>
<td>1.015-1.417</td>
<td>0.028</td>
</tr>
<tr>
<td>Urea ratio after KT</td>
<td>1.201</td>
<td>1.050-1.370</td>
<td>0.006</td>
</tr>
<tr>
<td>Baseline urea after KT</td>
<td>1.000</td>
<td>0.900-1.105</td>
<td>0.999</td>
</tr>
</tbody>
</table>

**Figure 1. The risk of developing prediabetes and PTDM depending on the A/L ratio**

- **A** baseline: B: 1 year after KT

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**P108 BLUEPRINTING EXTENDED REALITY AND TANGIBLE RESOURCES FOR SURGICAL EDUCATION; EXPERIENCES AND POTENTIALITIES FROM THE ENTICE PROJECT**

**Panagiotis Antoniou**1,2, Vassilios Tsioukas1,3, Ion-Anastasios Karolos4,5, Alkinoos Athanasioiu6, Sofia Lachanoudi1, Annta Varel7, Konstantinos Tagaras1, Panagiotis David8, Stathis Sidiropolous9, Natalia Stathakarou10, Tobias Karlsson11, Evangelos Chondrokostas12, Panagiotis-Marios Fillipidis13, Charalampos Bratsas13, Charalampos Chatzimallis13, Vasilis Voulgarakis13, Eirini Schiza13, James Pickering14, Constantinos Pattichis15, Panagiotis Bamidis16, Georgios Tsoullas16,17

1School of Medicine, Aristotle University of Thessaloniki, Lab of Medical Physics and Digital Innovation, Thessaloniki, Greece, 2School of Rural Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece, 3Anaptixiaki Metelitiki Vouli E Ellados, Thessaloniki, Greece, 4Karolinska Institute, Stockholm, Sweden, 5Open Knowledge Foundation Greece, Thessaloniki, Greece, 6VILABS CY, Limassol, Cyprus, 7University of Cyprus, Nicosia, Cyprus, 8University of Leeds, Leeds, United Kingdom, 9School of Medicine, Aristotle University of Thessaloniki, Department of Transplantation Surgery, Thessaloniki, Greece, 10Center for Research and Innovation in Solid Organ Transplantation, Transplantation Surgery, Thessaloniki, Greece

Background: Surgical training is an active learning process. Cognitive apprenticeships and lean consultations prepare surgeons for operation. Virtual, augmented and mixed reality (VR/AR/MR – collectively XR) have found use in surgical training due to their active nature. Also, 3D printing has also been added to the arsenal of surgical training. A core challenge in immersive media for healthcare training is the divide between the subject and the medium. Evidence demonstrate that XR resources may inhibit learning by distracting the learner, focusing on visuals instead of education. The goal of the Evaluating Novel Tangible & Intangible Co-creative Experiential (ENTICE) medical education project is to provide a platform of immersive XR technology where the educational goal maintains primary importance.

Methods: Co-creative workshops with surgical anatomy experts and technologists developed the resource material. Strict adherence to AGILE methodologies developed 3 highly relevant XR and 3D printed resources of hepatic and surgical anatomy supporting specific learning objectives. A bespoke evaluation plan created the toolset for estimating educational efficacy and learner acceptance of the immersive modality for surgical anatomy education.

Results: Several insights have been recognized from the project’s activities on design and implementation of immersive surgical resources. A) Participatory knowledge sharing, like cognitive apprenticeships, facilitates direct and tacit knowledge transfer. B) Predetermined educational content will always facilitate better training even with reduced impressiveness. The ability to pick-up an anatomical structure and manipulate it and sequencing of 3D models according to the lesson plan impact more than graphical fidelity. Evaluation of the platform by attending, residents and medical students was overall positive, based on interview evaluation.

Conclusions: The presented work blueprints a cohesive participatory process for XR and 3D print resource development. We aim to use and evolve this blueprint, creating a versatile portfolio of immersive XR and tangible resources, which will be helpful both in terms of education, as well as surgical planning.

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**Fig. 1: A surgical education resource. The user manipulates objects in VR, to demonstrate important features.**
ADIPONECTIN / LEPTIN RATIO AS A PREDICTOR OF ACUTE REJECTION IN EARLY POST-TRANSPLANT PERIOD IN PATIENTS AFTER KIDNEY TRANSPLANTATION

Karol Grafáš1, Matej Vručnáč1, Monika Beliančinová1, Patricia Kleínová1, Margareta Pýtliková1, Ivana Dedinská1, Expedition Faculty of Medicine, Comenius University, Martin, Slovakia

Background: Adipokines are largely involved in the regulation of immune system activity. While leptin is the main pro-inflammatory marker of adipose tissue, adiponectin is characterized by anti-inflammatory effects. The aim of our study was to determine the risk of acute graft rejection in post-transplant biopsy depending on the adiponectin / leptin (A/L) ratio in patients after kidney transplantation (KT).

Methods: 104 patients were included in the prospective analysis, in whom the levels of adipokines were examined pre-transplant, in the 3rd month after KT and in other kidney diseases.

Results: After adjusting for differences in the basic characteristics of the donor and recipient, we identified a subgroup with A/L ratio < 0.5 pre-transplant (HR 1.6126, P = 0.0133) and 3 months after KT (HR 3.0954, P = 0.0237) as independent risk factor for acute graft rejection. In the subsequent specification of the rejection episode, we identified the risk of ratio A/L < 0.5 for KT [HR 2.2353, (P = 0.0357)] and 3 months after KT [HR 3.0954, (P = 0.0237)] as independent risk factor for the development of antibody-mediated rejection with DSA positivity.

Conclusions: This is the first study to investigate the relationship between A/L ratio and immunological risk in terms of the development of rejection changes in patients after KT. In our study, we found that A/L ratio < 0.5 is an independent risk factor for the development of antibody-mediated rejection and de novo DSA production in the third month after KT.

Table 1. Cox proportional hazard model, end point: acute rejection in protocol biopsy group

<table>
<thead>
<tr>
<th>Rejection (A+RRx)</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyper A:L base line</td>
<td>0.1795</td>
<td>0.0014-1.247</td>
<td>0.1508</td>
</tr>
<tr>
<td>Hyper A:L base line</td>
<td>2.7644</td>
<td>2.2055-13.3961</td>
<td>0.0209</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio base line &lt; 0.5</td>
<td>2.9616</td>
<td>1.69-5.978</td>
<td>0.0039</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio base line ≥ 0.5</td>
<td>1.8993</td>
<td>0.3730-2.7343</td>
<td>0.6403</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio base line &gt; 1</td>
<td>1.1250</td>
<td>0.8402-2.2400</td>
<td>0.9799</td>
</tr>
<tr>
<td>Hyper A:L 2 MI</td>
<td>0.2317</td>
<td>0.0238-2.3583</td>
<td>0.2198</td>
</tr>
<tr>
<td>Hyper A:L 2 SM</td>
<td>2.9393</td>
<td>0.4254-19.7972</td>
<td>0.4192</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio SM &gt; 0.5</td>
<td>1.3510</td>
<td>0.1610-5.7064</td>
<td>0.8172</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio SM &gt; 0.5</td>
<td>1.3599</td>
<td>0.1273-12.1656</td>
<td>0.6832</td>
</tr>
</tbody>
</table>

Table 2. Cox proportional hazard model, end point: antibody-mediated rejection in protocol biopsy group

<table>
<thead>
<tr>
<th>A/LR</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Hyper A:L base line</td>
<td>0.1386</td>
<td>0.0337-0.6109</td>
<td>0.0137</td>
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<tr>
<td>Hyper A:L base line</td>
<td>2.5731</td>
<td>4.6949-11.020</td>
<td>0.0700</td>
</tr>
<tr>
<td>Adiponectin/leptin ratio base line &lt; 0.5</td>
<td>2.3953</td>
<td>1.4994-3.8331</td>
<td>0.0057</td>
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<tr>
<td>Adiponectin/leptin ratio base line 0-0.5</td>
<td>0.8730</td>
<td>0.5193-1.4926</td>
<td>0.6083</td>
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<tr>
<td>Adiponectin/leptin ratio base line &gt; 1</td>
<td>0.9272</td>
<td>0.2793-1.3999</td>
<td>0.8570</td>
</tr>
<tr>
<td>Hyper A:L 2 MI</td>
<td>2.6127</td>
<td>0.2919-37.551</td>
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</tr>
<tr>
<td>Hyper A:L 2 SM</td>
<td>2.1660</td>
<td>0.2052-21.604</td>
<td>0.1569</td>
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<tr>
<td>Adiponectin/leptin ratio SM &gt; 0.5</td>
<td>1.6994</td>
<td>1.0364-2.7754</td>
<td>0.0397</td>
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<tr>
<td>Adiponectin/leptin ratio SM &gt; 0.5</td>
<td>0.7274</td>
<td>0.0876-9.1315</td>
<td>0.7046</td>
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</table>

ANTICOAGULATION DECREASE THE VENOUS THROMBOSIS IN KIDNEY TRANSPLANTATION FROM UNCONTROLLED DONATION AFTER CARDIAC ARREST WITH HIGH RESISTENCE INDEX

María Molina1,2, Marina Urrutia-Jou1, Gregorio Romero1, Javier Paul-Martínez1, Carlos Calameras1, Josep Riera1, Laura Cahus3, Omar Enrique Taco Sánchez1, Inés Perezpaya1, Esther González Monte 1,2, Patrícia Kleinová1, Karol Graňák1, Hana Kwoun*1, Min Suk Chae2

1Incheon St. Mary's Hospital, College of medicine, the Catholic University of Korea, Anesthesiology and Pain medicine, Seoul, South Korea, 2Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Anesthesiology and Pain medicine, Seoul, South Korea

Background: Persistent left superior vena cava (PLSVC) is the most common congenital thoracic venous anomaly. It is usually found incidentally on examination or during invasive procedures. In most cases, the blood flows back to the right atrium through the coronary sinus without hemodynamic abnormalities and it is usually asymptomatic. There is some controversy regarding the clinical use of PLSVC. In a few cases, a PLSVC may be used for hemodialysis or large bore intravenous access.

Case report: A 62-year-old woman with a previous hepatocarcinoma for hepatocellular carcinoma and liver cirrhosis developed hepatic failure. Owing to her worsening condition, she needed liver transplantation (LT). However, a superior vena cava thrombus was found during the right atrium and proximal superior vena cava on preoperative transesophageal echocardiography. Usually, right-sided venous catherization is performed for LT preparation, but the embolic risk was very high in our patient. Fortunately, she had already been diagnosed with PLSVC. Therefore, we decided to perform fluoroscopy-guided catheterization through the PLSVC. For the safe use of a PLSVC catheter during surgery, the rapid infusion system pressure, coronary sinus inflow pressure, and intraoperative transesophageal echocardiography were monitored. The patient successfully underwent LT.

Conclusions: Based on a literature review and this case, PLSVC can be used clinically when accompanied by a detailed history, preoperative imaging examination, and close intraoperative monitoring. We suggest that a PLSVC is a feasible alternative to central venous access for LT.
Background: Anastomosis of multiple renal arteries in kidney transplantation is technically demanding. Previously this condition was considered a relative contraindication to use of the donor, due to an increased risk of vascular and urologic complications.

Methods: Between August 1990 and December 2022, we have performed 736 renal transplants, among which 116 patients (15.8%) of the multiple donor arteries were encountered and total 126 cases of procedure was done. We reviewed these cases for the type of vascular reconstruction and outcome of 16 interposition graft cases using branched internal iliac artery.

Results: The type of reconstruction were illustrated as follows: ligation of an upper polar artery in 38 cases, double barrel anastomosis in 42 cases, end to side anastomosis between a polar artery and main renal artery in 14 cases, separate anastomosis of two renal arteries to the branch of the internal iliac artery in 1 case, use of the inferior epigastric artery of the recipient for the recipient for end to end anastomosis to lower polar artery in 15 cases, interposition graft using branched internal iliac artery in 16 cases. We reviewed the 16 cases of the internal iliac artery interposition. Anastomosis between donor renal artery and recipient's internal iliac artery produced complications at bench and in the recipient.

Conclusions: Our method enables to select an appropriate recipient's interposition arterial branch to be anastomosed that is compatible with donor's multiple renal artery and is easy to perform. Anastomotic arterial pseudoaneurysm formation or rupture is thought to be possible low compared with that of the double barrel anastomosis. And multiple arterial anastomosis are conducted in conditions where an appropriate recipient's interposition arterial branch is not available and a simple anastomosis to end arterial anastomosis is done in recipient's body. This technique would reduced warm ischemic time, therefore renal damage could be diminished.

Results: A total of 3 patients were treated using NU. One patient (64 yr, female) had reduced renal quality by providing a basis for analizing SstO2 in patients undergoing LDLT. A low SstO2 (< 66%) 1 h after graft reperfusion was more highly predictive of early kidney dysfunction than the values measured in other intraoperative phases. A decline in the SstO2 was also related to kidney dysfunction.

Conclusions: Kidney dysfunction after LDLT is associated with patient morbidity and mortality. Our results may assist in the detection of early kidney dysfunction by providing a method for analyzing SstO2 in patients undergoing LDLT. A low SstO2 (< 66%), particularly 1 h after graft reperfusion, was significantly associated with early kidney dysfunction after surgery. SstO2 monitoring may facilitate the identification of early kidney dysfunction and enable early management of patients.

Results: Our method enables to select an appropriate recipient's interposition arterial branch to be anastomosed that is compatible with donor's multiple renal artery and is easy to perform. Anastomotic arterial pseudoaneurysm formation or rupture is thought to be possible low compared with that of the double barrel anastomosis. And multiple arterial anastomosis are conducted in conditions where an appropriate recipient's interposition arterial branch is not available and a simple anastomosis to end arterial anastomosis is done in recipient's body. This technique would reduced warm ischemic time, therefore renal damage could be diminished.

Results: Workshops confirmed that none of the major religions are against organ and tissue donation and reinforced the idea that information and knowledge about donation and its value are basic for a positive donation attitude. However, each religion has some particularities that TC should know before a donation activity. Workshops confirmed that none of the major religions are against organ and tissue donation and reinforced the idea that information and knowledge about donation and its value are basic for a positive donation attitude.

Background: Trust and credibility of the society in donation is a key factor for Spanish model success. In 2019 a “Donation and religions” Project was conceived as a multidisciplinary approach to discuss donation and transplantation concepts with religious leaders. With the aim to improve knowledge about religious or cultural aspects that could encourage dialogue and reduce refusal for donation.

Methods: The project developed 7 activities: 2 open conferences (inception and conclusions) and 5 closed workshops. Moderated by Transplant Coordinators (TC) of Catalan hospitals and experts in religious diversity, each workshop focus in a particular confession: Catholicism, non-Catholic Christian, Judaism, and Oriental religions (Hinduism, Sikhism, others). Finally, 60 religious or cultural leaders, 5 Transplant Patients Associations, 11 TC and 5 religious experts participated.

Results: Workshops confirmed that none of the major religions are against organ and tissue donation and reinforced the idea that information and knowledge about donation and its value are basic for a positive donation attitude. However, each religion has some particularities that TC should know before a donor family interview. For Catholics, donation is widely accepted and reinforced by the last three Popes declarations. However, for some Buddhist aspects related with death (atavistic) could be difficult donation, or for Hinduism, is still difficult to recognize brain death as the death of the person. To improve society knowledge and facilitate community dialogue, 6 leaflets explaining organ donation and religions and a TC Tool Guide for family approach was developed, according to the specific cultural or religious beliefs. In 2022, donation rate in Catalonia increased until 46 pmp donors and 18% of families refuse donation (2% of negative due to religious reasons, compared with 2-8% during previous years).

Conclusions: Until now very few common donation dialogues have been promoted between TC and religious leaders. The Project facilitate an inclusive multidisciplinary forum for all religions creating a shared space to exchange knowledge and facilitate productive dialogue. The elaboration of informative leaflets and TC guides will facilitate donation dialogues and awareness in our society.
Conclusions: scores significantly influence 10-year allograft survival and IFTA development in 6 is associated with increased steroid resistance. Only Glomerular and vascular likely reversible and responsive to steroids and LDAs. A sum score greater than response to LDAs at 3,58 months. While all individual Banff scores affected the grade 2B patients. Only 63% of cases with steroid-resistant TCMR showed a the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for the histological reversal of rejection.

Methods: 105 patients with acute TCMR were included in the study. A total of 562 follow-up biopsies were re-examined. All patients were treated with corticosteroids, and lymphocyte-depleting agents (LDA) were used in steroid-resistant AR patients. Results: Of 105 recipients, 12 had borderline, 27 had grade 1A, 23 had grade 1B, 29 had grade 2A, and 14 had grade 2B acute TCMR. The steroid treatment was successful in 43 (41%) patients. Totally 62 cases did not respond to steroids. Of 62 steroid-resistant cases, 20 received OKT3, and 42 received ATG. The highest steroid response was noted in the borderline and grade 1A groups, with 91% and 55% rates, respectively. Only 25% of grade 1B and 34% of grade 2A patients have shown steroid response, while only 7% of grade 2B cases respond. The mean time between the index and the follow-up biopsy with the histological reversal of steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients. It was 1,68 months for grade 2A and 3 months for the histological response after steroid therapy was 1 month for borderline, grade 1A, and grade 1B patients.
DONOR, RECIPIENT AND SURGEON SEX AND SEX-CONCORDANCE AND THEIR IMPACT ON LIVER TRANSPLANT OUTCOME

Laura Mazilescu1, Isabel Bernheim1, Jürgen Treckmann1, Sonia Radünz2
1Departments of Transplant and General Surgery, Departments of Transplant and General Surgery, Essen, Germany, 2University Hospital Essen, General, Visceral and Transplant Surgery, Essen, Germany

Background: Patient sex is associated with differential outcome of many procedures although the exact mechanisms remain unknown. Recently, worse outcome for female patients treated by male surgeons following common surgical procedures was reported. Especially in transplant surgery, surgeon-patient sex-concordance is rarely present for female patients and outcome may be negatively affected.

Methods: We performed a single-center retrospective cohort study, including all adult patients undergoing first-time deceased-donor liver transplantation between 2013 and 2018 at our transplant center. Recipient, donor, and surgeon sex were evaluated and short- and long-term outcome was analyzed with regards to sex and sex-concordance of patients, donors, and surgeons.

Results: We included 425 recipients in our study; 50.1% of organ donors, 32.7% of recipients, and 13.9% of surgeons were female. Recipient-donor sex concordance was present in 82.7% of female recipients and in 65.7% of male recipients (p=0.0002). Recipient-surgeon sex concordance was present in 11.5% of female recipients and in 85.0% of male recipients (p=0.0001). Donor risk index (DRI) of female donors was significantly higher (1.908 [0.9730-2.678] vs.1.672 [0.9730-2.855], p<0.0001), and female recipients received organs with significantly increased DRIs (1.837 [1.040-2.855] vs. 1.746 [0.9730-2.678], p=0.0272). Five-year patient survival was comparable between female and male recipients (70.0% vs. 73.3%, p=0.3978). Recipient-donor sex concordance did not significantly affect survival of female or male recipients. Five-year patient survival was comparable between female and male recipients (70.0% vs. 73.3%, p=0.7238).

Conclusions: Female recipients and female surgeons are underrepresented in liver transplant surgery. Societal factors influencing outcome of female patients suffering from end-stage organ failure need to be further examined and acted upon to possibly improve the outcome of female liver transplant recipients.

SUBNORMOTHERMIC EX VIVO MACHINE PERFUSION FOR THE PRESERVATION OF DCD PORCINE KIDNEY GRAFTS

Laura Mazilescu1,2, Masataka Kawamura1, Rohan John3, Lisa Robinson3, Markus Selzner3
1University Health Network, Ajmera Transplant Centre, Toronto, Canada, 2University Hospital Essen, Departments of Transplant and General Surgery, Essen, Germany, 3The Hospital for Sick Children Research Institute, Program in Cell Biology, Toronto, Canada

Background: To enhance the usage of marginal kidney grafts, ex-vivo machine perfusion represents a solid alternative to static cold storage (SCS) and hypothermic machine perfusion (HMP) has already been integrated in the clinic. The ideal ex-vivo machine perfusion approach and the optimal temperature for perfusion remain controversial. In the current study, we assessed the advantages of normothermic ex-vivo kidney perfusion (NEVKP) and subnormothermic perfusion (SEVKP) in a porcine kidney autotransplantation model.

Methods: All pig kidneys were exposed to 60 min of warm ischemia followed by 7.5 hrs of either HMP (4°C), SEVKP (22°C) or NEVKP (37°C) (n=5 in each group). After contralateral nephrectomy, grafts were autotransplanted and animals were followed for 3 days. Ex-vivo perfusion parameters and kidney function were compared between groups.

Results: All animals survived the follow-up period. Grafts preserved by NEVKP showed comparable postoperative function to those preserved by SEVKP. In the HMP group, daily values were higher than in the other two groups. In the HMP vs SEVKP group, there was a significant difference in daily SrCrea on all postoperative days (POD; POD1 - 5.4±0.5 mg/dl vs 4.6±0.5 mg/dl; POD2 - 8.9±1.5 mg/dl vs 5.3±1.8 mg/dl; POD3 - 10.5±3 mg/dl vs 4.6±2.2 mg/dl). On POD3, creatinine clearance was increased in the NEVKP and SEVKP groups (NEVKP vs SEVKP vs HMP: 15.4±12.5 ml/min vs 19.2±10 ml/min vs 4.4±1.5 ml/min). Oxygen consumption was reduced during SEVKP (NEVKP vs SEVKP vs HMP: 805±103 ml/min vs 19.2±10 ml/min vs 4.4±1.5 ml/min). Urinary NGAL was lower in the NEVKP vs SEVKP vs HMP (1.5±0.9 vs 1.8±0.9 vs 5.4±1.5). Serum NGAL was lower on POD3 in the NEVKP and SEVKP groups compared to the HMP group (1.5±0.9 vs 1.8±0.9 vs 5.4±1.5). Serum NGAL was lower in the NEVKP and SEVKP groups compared to the HMP group after transplant.

Conclusions: Despite reduced metabolic activity during SEVKP, grafts preserved with SEVKP vs NEVKP demonstrated comparable function directly after transplantation. Both groups showed improved kidney function and less kidney injury compared to graphs preserved with HMP. Further studies are warranted to explore which technology represents a better platform to assess and repair expanded criteria kidney grafts.

Figure 1: (A) Serum creatinine during the 3 days follow-up. (B) Creatinine clearance at baseline and postoperative day 3.
Feedback highlighted these as: disparities in level of care offered between centres and patients; lack of psychological care for patients and their families pre- and post-transplant, leading to a strong adverse impact on their experience, wellbeing and relationships; lack of clear, consistent advice and communication. Some patients felt they had to fight to get the care they needed, even whilst seriously ill. Post-transplant support was reported as lacking for those in need of ongoing care for their specialist condition. Figure 1 shows inequitable psychological provision across cardiothoracic transplant services.

**Conclusions:** Access to transplant services and patient experience is inequitable across the country. This is exacerbated by gender, ethnicity and socio-economic factors.

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**Table 1. Organ Utilisation Group Patient Survey**

<table>
<thead>
<tr>
<th>Question asked</th>
<th>Star rating ([1-5])</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral for listing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessment for transplant/living donation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The care you received from your transplant centre whilst on the waiting list as a potential living donor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The care you received from your local hospital or specialist whilst on the waiting list as a potential living donor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your hospital stay before, during and immediately after transplantation/living donation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your follow-up care within a year of transplant/living donation</td>
<td></td>
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<td>Experience of moving between different parts of the healthcare system when speaking to different healthcare professionals involved in your care</td>
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**P124** OUTCOME OF 40 LIVING DONOR LIVER TRANSPLANTATIONS IN A NEWLY ESTABLISHED ADULT LIVING DONOR LIVER TRANSPLANT PROGRAM IN THE NETHERLANDS


1Erasmus MC, Department of Surgery, Division of HPB & Transplant Surgery, Rotterdam, Netherlands, 2Erasmus MC, Department of Anesthesiology, Rotterdam, Netherlands, 3Erasmus MC, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, 4King Faisal Specialist Hospital and Research Center, Organ Transplant Center, Riyadh, Saudi Arabia

**Background:** Liver transplantation is the only cure for end stage liver disease. Expanding indications, with a stable supply of deceased donor grafts has led to organ shortage. Even the increasing acceptance of marginal grafts did not solve this problem. Wait list mortality reported by Eurotransplant remains at 18%, not including delisted recipients. Living donor liver transplant (LDLT) is a solution to overcome organ shortage. The development of LDLT led to superior outcomes compared to deceased grafts. In 2019 we started an adult LDLT program, here we present our outcomes.

**Methods:** We prospectively reviewed recipients who underwent LDLT between January 2019 and December 2022. Demographics, etiology, graft characteristics, and Operative variables were assessed. Outcome was evaluated on the basis of morbidity and mortality. All complications of ≥ 3 on the Clavien-Dindo grading system were included as morbidity.

**Results:** Forty LDLT have been performed. Most donors were related to their recipients, 36 (94%) of donors donated their right liver lobes; 2 left lobe donations and 2 domino LDLT also took place. The median hospital stay was 6 days. There has been no significant donor morbidity, and no donor mortality. The MELD score for LDLT recipients varied between 6 – 22. Twenty six (65%) LDLT recipients had roux-en-Y biliary reconstructions. Eight (20%) biliary complications were reported in LDLT recipients, all were successfully managed with minimally invasive techniques, no revision of a biliary anastomosis was required. One LDLT recipient required re transplantation 16 months post LDLT after developing a hepatic artery thrombosis 1 week post-transplant. The other 39 LDLT recipients have good graft function, there has been no recipient mortality.

**Conclusions:** With meticulous preparation, appropriate case selection and continuous training of team members by experienced staff a newly established LDLT program can achieve good outcomes.

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**P126** POST REPERFUSION SYNDROME IN PEDIATRIC LIVER TRANSPLANTATION: EXPERIENCE OF A CENTER (LYON)


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**Background:** The post reperfusion syndrome (PRS) is well known in adults liver transplantation, although there are few data for pediatrics. The aim of our study was to evaluate the incidence, and the associated factors in a pediatric population.

**Methods:** We conducted a retrospective study including over 10 years all transplanted patients (2011-2021) in our pediatric liver transplant center. The parents gave their written consent. The procedures were performed with preservation of the recipient’s vena cava and vascular exclusion of the liver. Reperfusion of the graft was done through the portal vein. We retain as the definition of PRS: drop in MAP ≥ 30% of at least 1 minute during the 5 minutes following graft reperfusion, without changing the dose of Norepinephrine infusion. We studied the following factors: Patient’s age and weight, type of graft (DV vs. DD), weight vs. split, donor age, type of graft, warm and cold ischemia, type of injury, graft weight ratio (WGR) and massive transfusion (>40ml/kg during the procedure).

**Results:** We analyzed the data of 145 patients, middle age 6.3 years [0.5-16], middle weight 23kg (58 %< 20kg). They received respectively: 64 whole and 81 parting verses. Incidence of PRS observed was 19%. PRS is not associated with massive transfusion occurrence. Donor infusion of Norepinephrine >1µg/kg/min before the graft removal, and the WGR are significantly associated with the occurrence of PRS (p<0.001). The weight of the recipient is not significantly associated with the occurrence of PRS (p=0.071), perhaps taking into account an insufficient number. Age of the donor, type of graft, warm and cold ischemia time, preoperative and T30 haemoglobin, WGR and mass transfusion (>40ml/kg during the procedure).

**Conclusions:** We analyzed the data of 145 patients, middle age 6.3 years [0.5-16], middle weight 23kg (58 %< 20kg). They received respectively: 64 whole and 81 parting verses. Incidence of PRS observed was 19%. PRS is not associated with massive transfusion occurrence. Donor infusion of Norepinephrine >1µg/kg/min before the graft removal, and the WGR are significantly associated with the occurrence of PRS (p<0.001). The weight of the recipient is not significantly associated with the occurrence of PRS (p=0.071), perhaps taking into account an insufficient number. Age of the donor, type of graft, warm and cold ischemia time, preoperative and T30 haemoglobin, WGR are not significantly associated with PRS. In multivariable logistic regression, donor’s administration of norepinephrine was significantly associated with the occurrence of PRS p<0.003, OR 7.7 [2.0-29.6], as well as WGR p<0.002, OR 1.7 [1.2-2.4].

**Conclusions:** Reperfusion syndrome has a prevalence of around 20% in pediatric liver transplantation. The dose of Norepinephrine infused in the donor and the weight graft ratio increase the PRS occurrence. The risk of having a PRS is 7 times greater when the donor received NOR>1µg/kg/min.
Background: After nephrectomy, living kidney donors (KD) develop an episode of Acute Kidney Injury (AKI). Renal Functional Reserve (RFR), defined as the capacity to increase the glomerular filtration rate (GFR), plays a key role in functional recovery. The aim of this study was the dynamic evaluation of RFR, radioisotopic GFR (rGFR) and urinary injury biomarkers before donation, in the immediate preoperative period and 1 year after to investigate their predictive performance.

Methods: 112 KD were evaluated at different time points sCr, rGFR and sequential scintigraphy with 99mTc-MAG to determine left vs. right renal function and the urinary biomarkers NGAL, Nephrocheck (IGFBP7/TIMP2) and extracellular vesicles expressing the stem cell marker CD133 (CD133+uEVs) detected by flow cytometry.

Results: At study admission, mean sCr was 0.7 mg/dL, rGFR 98 mL/min, in scintigraphy the mean % of right kidney function was 47. After all left nephrectomies, renal function worsened (AKI episodes) with mean sCr values of 1.2 mg/dL. After 7 days, renal recovery was observed in all KD. After 1 year, rGFR was measured and compared with the split rGFR of the right kidney before donation with a mean compensatory increase of 18 mL/min and in % 35. Pre-donation RFR was 21.5 mL/min. Multivariate linear regression confirmed that KD age and baseline rGFR represented 2 independent factors able to predict renal function 1 year after. ROC curve evidenced a value of 45 mL/min to predict rGFR higher than the median after 1 year (sensitivity: 73.53%; specificity: 59.38%). There was no correlation between pre-donation RFR and post-donation AKI, whereas a strong linear correlation between RFR and the compensatory GFR increase after 1 year was observed (r=0.66). Of note, after 1 year KD still maintained a percentage of rGFR (16.5 mL/min). Injury biomarkers were all negative 7 days and 1 year after: moreover, the percentage of CD133+uEVs was significantly increased 7 days after nephrectomy (24% vs. 4.5%), suggesting a regenerative potential of the remnant kidney.

Conclusions: The dynamic evaluation of renal function after nephrectomy represents the next steps for a safer follow-up of KD. Even though a longer observational period is needed, RFR, rGFR and urinary injury biomarkers may allow a better clinical management even in “medically complex” ones.
Conclusions: 3 pts died for sepsis 3 weeks after transplant and 1 pt died for HHV8-induced artery-thrombosis solved surgically. 28 pts (44%) underwent early post-transplant non-function and underwent re-LT after 3 days while only 1 pt had hepatic dysfunction within 48h and the median ICU stay was 5 days [3-9]. Two pts had primary delayed kidney transplantation (KT) and 3 (6%) were then listed for sequential transplantation. Of note, 10 pts (16%) were known to be pre-LT colonized by multidrug-resistant (MDR) bacteria. Median liver cold ischemia time was 447 min [369-504]. The Piggy-back technique was possible in 18/63 (29%) and 9 pts (14%) underwent temporary porto-cava shunt while only 6 pts (10%) received drug-resistant (MDR) bacteria. Among 1754 LT, 63 LT for PCLD (3.6%) have been carried out, of which 45 (71%) SLKT. 48 (76.2%) female; median age 52 years [48-56]; BMI 24 kg/m² [23-26]. GFR was 11 mL/min [7-17] in pts who received SLKT (29/45 on pre-LT dialysis). 58 (92%) pts underwent LT for abdominal fullness with sarcopenia (median liver weight 3950g [2450-6750]; largest cyst size of 7 cm [5-9]); 19 (30%) had refractory ascites. 9 pts (2%) had pre-transplant cyst inter-vascular connections. Analysing pre-disease laboratory parameters is aimed defining possible predictive factors of severe disease. Material and Methods: After Local Ethical Committee approval, the data of KTX patients that are followed up by our center between 2020 and 2022 were retrospectively collected. All pts had either cadaveric or living related donor KTX and all received induction immunosuppression followed by standard maintenance immunosuppression. Covid19 test was done by polymerase chain reaction. Laboratory tests that were done before Covid19 infection were analysed and parameters that are well known to be affected by acute disease, such as acute phase reactants, CRP, procalcitonin, ferritin, d-dimer were excluded. Data is presented as mean (stdev) for continuous variables and as frequencies for discrete values. Statistics were performed using parametric tests and p<0.05 was considered significant.

Results: A total of 43 KTX patients had documented Covid19 infection in our center since March-2020. Eleven patients required hospitalization, of whom 8 had severe disease with extensive lung involvement and 5 of these eventually succumbed into death due to lung failure. Of note, 2 dead and 3 severe pts were vaccinated. Table 1 shows significant predictive factors of mortal cases. Conclusion: Retrospective evaluation of our KTX pts with Covid19 infection revealed significant decreased lymphocyte count and lower platelet count before the actual disease.

Table 1: Significant predictive factors for mortality

<table>
<thead>
<tr>
<th>NONE (42)</th>
<th>MILD (32)</th>
<th>HOSP (5)</th>
<th>DIED (6)</th>
<th>P (anova)</th>
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<tr>
<td>Lym(#)</td>
<td>1.29±0.92</td>
<td>1.29±0.97</td>
<td>1.18±0.91</td>
<td>0.75±065</td>
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<tr>
<td>Lym(%)</td>
<td>15.2±12.6</td>
<td>14.6±11.8</td>
<td>17.6±11.5</td>
<td>8.9±7.1</td>
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<tr>
<td>PLT</td>
<td>284±113</td>
<td>243±90</td>
<td>257±56</td>
<td>151±76</td>
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<td>PCT</td>
<td>0.17±0.1</td>
<td>0.15±0.07</td>
<td>0.17±0.07</td>
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Background: Covid19 virus related mortality is known to be higher among pts with KTX, because pts with KTX are not only immunosuppressed but they also have higher incidence of known risk factors, such as advanced age, hypertension, other cardiovascular diseases and diabetes. Severe disease in immunocompromised individuals may reflect the inability to mount an effective immune response, even after vaccination. The spectrum of Covid19 disease ranges from asymptomatic infection to pneumonia, cytokine storm, and death. Analysing pre-disease laboratory parameters is aimed defining possible predictive factors of severe disease.

Background: polycystic liver disease (PCLD), usually associated with polycystic kidney disease (PCKD), is a benign condition that leads to abdominal fullness and portal hypertension. Liver transplantation (LT) or simultaneous liver-kidney transplantation (SLKT) remains the curative treatment for severe polycystic disease. We aimed at describing pre- and post-transplant characteristics of patients (pts) who underwent LT/SLKT for PCLD/PCKD.

Methods: Pts who underwent LT/SLKT for PCLD/PCKD in our Center from 01/01/2010 to 30/09/2022 were enrolled. Follow up was closed on 31/12/2022.

Results: Among 1754 LT, 63 LT for PCLD (3.6%) have been carried out, of which 45 (71%) SLKT. 48 (76.2%) female; median age 52 years [48-56]; BMI 24 kg/m² [23-26]. GFR was 11 mL/min [7-17] in pts who received SLKT (29/45 on pre-LT dialysis). 58 (92%) pts underwent LT for abdominal fullness with sarcopenia (median liver weight 3950g [2450-6750]; largest cyst size of 7 cm [5-9]); 19 (30%) had refractory ascites. 9 pts (2%) had pre-transplant cyst inter-vascular connections. The Piggy-back technique was possible in 18/63 (29%) and 9 pts (14%) underwent temporary porto-cava shunt while only 6 pts (10%) received drug-resistant (MDR) bacteria. Median liver cold ischemia time was 447 min [369-504].
Background: Malignancy is a significant, life-limiting long-term complication after lung transplantation (LuTx) and the second commonest cause of death, during the first 10 years after LuTx. We aimed to investigate its incidence and effect on the long-term outcome.

Methods: This is a single center retrospective observational study. Between 1996 and 2022, n=627 lung transplantations (LuTx) were performed in our department. We used our institutional database to identify those diagnosed with malignancies after LuTx and examined the malignancies’ incidence and the related mortality.

Results: A number of n=59 malignancies occurred in n=55 (8.8%) LuTx recipients. The post-LuTx malignancies incidence was 9.4% (59/627). We report following rates based on their location: n=17/55 (28.8%) of all recipients diagnosed with malignancies, skin, n=10/55 (18.5%) gastrointestinal, n=9/55 (15.5%) pulmonary, n=6/55 (8.8%) of these, n=13/55 (4.8%) other multiple synchronous. During this study period, a total of n=328 deaths after LuTx was determined. N=29 (8.4%) of all deaths were malignancy induced, corresponding a total malignancy induced mortality of 4.6% (141 were transferred to the University Hospital). Of all deaths, 13% (23) were attributed to LuTx complications. Malignancies’ origin, primary COPD diagnosis, type and specific age-group were significantly survival-related (p values <0.05). The most affected organ was skin and showed the best prognosis. PTLD had the fastest and pancreatic the most delayed onset.

Conclusions: This is the first report of its kind in a large cohort of german LuTx recipients. The prevalence ranking of the three commonest malignancies was skin > colorectal > PTLD. Post-LuTx malignancies were the second commonest cause of death. Further studies are needed, while post-LuTx malignant disease remains a serious impairment of long-term LuTx survival.

LIVER TRANSPLANTATION AT THE KOREA UNIVERSITY: ANALYSIS OF 500 CASES AND INTRODUCING OUR UNIQUE MULTI-INSTITUTIONAL NETWORK

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Background: Liver transplantation (LT) is an established therapeutic modality for patients with life-threatening liver disease. Since the first case in 1994, over 500 cases liver transplantation have been performed at the Korea University medical center which is comprised of 3 tertiary hospitals (Anam, Guro and Ansan hospital). The aim of this study was to analyze our experience of over 500 cases of liver transplantation. In addition, we report our experience of creating a multi-institutional network or team (named the “Korea University Remedy Ensemble” or “KURE”) to help prepare, to perform and especially to improve the outcomes of liver transplantation at our medical center. Methods: We reviewed the records of 518 adults who received LT between March 1994 and July 2022 from 3 tertiary centers. Patient outcomes were analyzed. In addition, we divided the patients into 2 groups according to the date of transplant before and during the “KURE” era, respectively. Outcomes were compared between the two groups. Results: More patients underwent deceased donor LT than living donor LT (n=265 vs n=253). The 1-, 3-, 5-year overall survival was 90.4%, 83.1%, 81%, respectively. And there was no significant difference between deceased donor and living donor LT. Similarly in HCC patients, the 1-, 3-, 5-year disease free survival was 90.5%, 84.2%, 83.0%, respectively. However the disease free survival in patients undergoing living donor LT was significantly lower (p=0.031) probably due to the large tumor burden in these patients. Of the 518 patients, 191 were transplanted during the “KURE” era. Operative time, amount of blood transfusion, non-biliary complications (above Clavien-Dindo grade 3), acute rejection, 30- and 90 day mortality and therefore overall survival all significantly improved during the “KURE” era. Conclusions: Survival outcomes were comparable to other major centers and significantly improved during the “KURE” era. The “KURE” network can be a model for nearby tertiary institutions to improve their transplant outcome in certain regions of Korea.

CONTRAST ENHANCED MAGNETIC RESONANCE ANGIOGRAPHY IN THE EARLY PERIOD AFTER RENAL TRANSPLANTATION

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Background: Our objective was to evaluate the usefulness of three-dimensional contrast enhanced MR angiography (3D CE MRA) for assessment of renal parenchyma itself, arterial inflow stenosis, and peritransplant fluid collection in the early period after renal transplantation.

Methods: Between April 2019 and July 2022, a consecutive series of 62 renal transplantations was examined with 3D CE MRA 14 days after transplantation. MR angiography studies were analyzed for the volume of renal parenchyma, presence of arterial stenosis, renal infarction, and peritransplant fluid collection. The degree of renal transplant artery inflow stenosis was graded qualitatively as <50% = mild, 50-70% = moderate, >70% = severe. According to severity of arterial stenosis on MRA, the following variables were compared: demographic factor, graft survival, post-operative renal function, incidence of acute rejection (AR).

Results: Kidney volume, measured with MRA, varied from 148 to 421 (226±146.8 ml). It is higher than that of pre-operation CT volume (171±132.8) (P = 0.005). Twenty (31.3%) of the 64 patients had normal CE MRA which were significantly different in patients with arterial stenosis from those of others (P<0.005).

Conclusions: The incidence of renal parenchyma infarction, peritransplant fluid collection and arterial flow stenosis is unexpectedly high in the early period after kidney transplantation. MR angiography and MR imaging allows rapid global assessment of renal transplant arterial system and peritransplant fluid collection. It can also help detect or exclude many of the various causes of renal transplant dysfunction.
P139 PASSENGER LYMPHOCYTE SYNDROME PRESENTED AS HEMOLYTIC ANEMIA AFTER SMALL BOWEL TRANSPLANTATION: A CASE REPORT

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Background: The passenger lymphocyte syndrome (PLS) induces hemolytic anemia after minor ABO mismatched organ transplantation. We experienced a case of PLS with hemolysis after small bowel transplantation.

Methods: A 65-year-old man underwent massive small bowel resection and right colectomy for superior mesenteric artery embolism in January 2021. Around 30cm jejunum was left and he got end jejunostomy and was completely dependent on parenteral nutrition. He received small bowel from deceased donor on June 2021. His blood type was B Rh+ and donor was O Rh+. We used simulet 20mg, anti-thymocyte globulin (ATG) 1.5mg/kg for 5 times and prednisolone 1000mg as an induction and then tacrolimus with trough level 13-15ng/ml and reduced dose of prednisolone as a maintenance. Patient was stable and transfusion was not needed during the surgery.

Results: After operation, hemoglobin level was decreased gradually from 10.4mg/dl preoperatively to 5.6mg/dl at POD#6. There wasn’t any bleeding sign on physical exam and CT angiography. A platelet count was decreased together, 60K at POD#6. We thought it might be ATG related bone marrow suppression and gave him RBCs and platelets with supportive care. The platelet low count was but sustained greater than 60K and recovered over 100K at POD#23 and last transfusion was POD#9. However, hemoglobin drop was repeated and transfusion was needed weekly till POD#27. In isoagglutinin test, anti-B IgG was detected at 1:8 titer. A haptoglogin was lower than 20mg/dL suppressed.

Conclusions: At POD 36, there’s no edema or ulcer and normal villi was observed on endoscopy. He is stable and on a diet program to reduce parenteral nutrition. Most of PLS is self-limiting but often poor outcomes have been reported, awareness and suspicion is important.

In case of PLS it is common problem the anomaly of kidney vasculature, pelvicalyceal system, isthmus. These pitfalls are not a contraindication for organ donation anymore. There different techniques of organ procurement but in developing surgical era we must utilize minimal invasive approaches in these patients also as to affect their recovery period and return to their daily activity.

P142 LAPAROSCOPIC HAND-ASSISTED DONOR HEMINEPHRECTOMY IN LIVING DONOR WITH HORSESHOE KIDNEY (CASE PRESENTATION)

Islam Madadov*4

1National Scientific Center of Surgery named after A.N.Syzganov, Kidney Transplantation, Almaty, Kazakhstan

Background: Case of kidney transplantation from 65-years old female donor with horseshoe kidney (HSK) for her 39-years old son with end-stage renal disease (ESRD), by using laparoscopic hand-assisted heminephrectomy technique.

Methods: 39-years old male with ESRD, for the last 2 years on haemodialysis, admitted to our center for kidney transplantation. Technical challenge was due to that donor had a horseshoe kidney with parenchymal isthmus, with 4 arteries on right half and 2 arteries on the left with retrocaval position of the latters (Pic.1). Recipient had concurrent arterial hypertension and otherwise there were no contraindications for transplantation during preoperative evaluation. Donor was his mother 66-years old, with arterial hypertension 1 stage (BP max 142/90 mm/hg), during preoperative evaluation otherwise healthy. Due to the lack of others younger related donors, we inform patients about potential risks of donation and after informed consent taken we prepared patients for surgery.

Results: Patient underwent laparoscopic hand-assisted donor heminephrectomy. Firstly isthmus was sewed in the middle and tied on both sides after left half of HSK was devascularized and then the isthmus was quickly transected just above the suture line, preventing bleeding from the right half. Warm ischamic time 1 was 92 seconds. Resected isthmus was sutured on back-table by interrupted suture and utilizing haemostatic sponge. Surgery was completed otherwise uneventfully. Patient was discharged postop 4 day.

Conclusions: In case of HSK it is common problem the anomaly of kidney vasculature, pelvicalyceal system, isthmus. These pitfalls are not a contraindication for organ donation anymore. There different techniques of organ procurement but in developing surgical era we must utilize minimal invasive approaches in these patients also as to affect their recovery period and return to their daily activity.

Pic. 1. HSK with aortocaval transposition, multiple arteries, parenchymal isthmus.
**P143** DONOR-DERIVED MULTIDRUG-RESISTANT ORGANISMS INFECTION COMPLICATIONS IN LIVER TRANSPLANT RECIPIENTS

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1Minsk Scientific and Practical Center for Surgery, Transplantatology and Hematology, Minsk, Belarus

**Background:** Due to prolonged intensive care unit stay, various medically invasive treatments or surgical interventions and history of broad-spectrum antibiotics use, donor-derived multidrug-resistant organisms (MDRO) infectious complications became a serious problem. MDRO contamination may result in overt infection or an asymptomatic, undiagnosed carrier state. With the development of MDRO complications after liver transplantation (LT), the risk of death increases by 5-9 times and one-year survival decreases to 23-30%. The aim of this study was to assess the impact of MDRO contamination of preservation fluid (PF) on the rate of post liver transplant surgical site infection (SSI) complications in countries with high prevalence of Carbapenem-resistant flora.

**Methods:** In prospective single-center study, 271 LT recipients were included (study period – 2019-2021). A routine study of liver graft preservation fluid during back-table was introduced. Within 24 h, if bacterial growth is detected, the MALDI-ToF analysis will be performed. If MDRO is detected, the sample is sent for a PCR test for the presence of resistance genes. Thus, within 48 hours after organ retrieval, the presence or absence of PF contamination, the pathogen, its sensitivity and the resistance genes were detected. Primary clinical outcomes: SSI rate, SSI mortality rate.

**Results:** Incidence of healthcare-associated infection (HCAI) following LT was 19% (52/271), of those, sepsis - 13% (7/52); SSI rate – 14% (37/271); SSI mortality rate – 16% (6/37). The prevalence of culture-positive preservation fluid was 22% (60/271). MDRO was detected in 5% (15/271). In 10 cases (3.7%) it caused donor-derived MDRO SSI with 60% (6/10) sepsis mortality rate. Preservation fluid contamination increased the risk of SSI in 4 times (OR=6.3; p<0.001) and the prevalence of Carbapenem-resistant pathogens in PF caused 41-fold increase of the SSI risk of in (OR=41.2; p<0.001).

**Conclusions:** Contamination of the preservation fluid increases the risk of SSI after LT. The resistance profile of a pathogen affects the duration, structure, and outcome of infectious complications. Timely diagnosis and infection control measures are fundamental to preventing donor-derived MDRO infectious complications.

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**P144** SERUM CYSTATIN C IN RENAL TRANSPLANTATION: BEYOND GFR ESTIMATION, A PROGNOSIS MARKER?

Lydia Ounoughi1, Christophe Mariat1

1CHU Saint-Etienne, Saint-Priest-en-Jarez, France

**Background:** In renal transplantation, death with a functioning graft remains one of the main causes of graft loss. In the general population, renal function impairment is strongly associated with cardiovascular and all-cause mortality. Whether this association holds true for kidney transplant recipients (KTR) is unclear. This uncertainty is likely to be due, in part, to the fact that glomerular filtration rate (GFR) estimation based on serum creatinine (SCr) does not always provide an accurate evaluation of the graft function in KTR. As compared to SCr, we have previously shown in a large cohort of KTR that serum cystatin C (SCysC) is a much better marker of GFR. Hence, we sought to study the ability of the 1-year post-transplant renal function to predict all-cause mortality according to the methods used to assess GFR.

**Methods:** Four hundred and ten consecutive KTR for whom a measurement of GFR by inulin clearance was available at one-year post-transplant were included. SCreat and SCysC were measured with standardised methods. We studied the association between 1-year inulin clearance value, MDRD Study equation value and CKD-EPI SCysC equation value with all-cause mortality.

**Results:** During a median follow-up of 17 years, 212 KTR died. Mean ± SD inulin clearance at 1-year posttransplant was 47 ± 13 mL/min/1.73m2. Patients who died during the follow-up had a significantly lower GFR value at one-year post-transplant as compared to patients who did not. This was true irrespective of the methods used to evaluate GFR. However, while patients’ survival categorized according to MDRD study median value observed after one-year post transplant was not different, long-term survival was significantly improved in patients with the highest GFR values estimated by the CKD-EPI SCysC equation (which was even more discriminant than inulin clearance, fig. 1).

**Conclusions:** Our preliminary results suggest that cystatin C used as a GFR estimate is superior to serum creatinine to predict risk of mortality in renal transplant patients. CystC predictive value is likely to be explained by a better ability to approximate the so-called “true GFR” (given by inulin clearance) but also by other determinants not directly related to the level of renal function.

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Oral Presentations

P500

[Image -92x255 to 949x734]
Background: Normothermic machine perfusion (NMP) is a novel method for ex situ preservation and/or testing of (extended) criteria donor livers prior to transplantation. During NMP, the liver is metabolically active, which enables functional assessment of the liver, including the production of hemostatic proteins. The aim of the study was to investigate the production, and activity of hemostatic proteins during long-term NMP of human livers up to 7 days.

Methods: Three discarded human donor livers underwent NMP with a perfusate based on red blood cells, albumin, colloids and parenteral nutrition, using a modified Liver Assist device (XVIVO, Groningen, Netherlands) for up to 7 days. Heparin was added to the perfusion fluid continuously. Perfusate samples were collected before the start of perfusion and daily thereafter. After in vitro heparin neutralization, international normalized ratios (INR) were analyzed. In addition, we measured antigen and activity levels of factor II and V, antithrombin, and fibrinogen, as well as levels of proteins induced by vitamin K absence (PIVKA-II).

Results: Perfusate INR values declined over time, which was accompanied by detection of substantial quantities of all analyzed coagulation proteins (Figure 1). Antigen and activity levels of factor V and antithrombin increased to a similar extent resulting in a specific activity comparable to pooled normal plasma (PNP). The specific activity of factor II and fibrinogen was substantially decreased compared to PNP. The lower specific activity of factor II was accompanied by elevated levels of PIVKA-II.

Conclusions: During ex situ NMP of human donor livers, hemostatic proteins are produced in substantial quantities, resulting in stable perfusate protein levels after a few days of perfusion, and forming a plasma like perfusate. This may indicate establishment of an equilibrium between the production and clearance of these proteins. However, this might also result in coagulation problems during perfusion, that needs to be addressed with a different anticoagulation approach.
NO QUICK-FIX IN DETECTING SARCOPENIA IN PATIENTS ENLISTED FOR KIDNEY TRANSPLANTATION - MEASUREMENTS OF PSOAS MUSCLE

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1University of Oslo Faculty of Medicine, Institute of health and society, Oslo, Norway. 2Oslo universitetssykehus HF, Rikshospitalet, Department of Transplantation medicine, Oslo, Norway

Background: Frailty is associated with inferior outcomes after kidney transplantation (KT). Age related reduction of muscle mass, sarcopenia, can serve as a marker of physical frailty. Heart-, lung- and liver transplant recipients, low psoas muscle area has been associated with increased mortality and risk of post-operative complications. Any association between pre-transplant psoas muscle area and outcomes after KT has not been described. We aimed to evaluate the association between pre-transplant psoas muscle area and postoperative complications and death in KT recipients older than 55 years.

Methods: A single center retrospective case-control study was performed. Data from 639 de novo kidney transplanted recipients >55 years transplanted between January 1st 2011 and December 31st 2015 were evaluated. Twenty-one cases who were admitted to the intensive care unit (ICU) for more than 24 hours during the first seven days after KT were identified and compared with 42 controls without any ICU stay. The cases and controls were matched with respect to gender, age and comorbidity. Psoas area was assessed using CT scans taken as a part of the routine work-up for kidney transplantation and a psoas muscle index (PMI) was calculated as total psoas area divided by the square of the body height. Sarcopenia was defined based on our data as PMI less than the gender specific median or less than the gender specific 25 percentile.

Results: Good quality CT scans were available in 60 recipients. Results are presented in table 1. We found no statistical difference in PMI of cases and controls. There were no associations between pre-transplant PMI and post-transplant ICU admission or death.

Conclusions: Our findings indicate that a single pre-transplant measurement of psoas muscle area as an indicator of sarcopenia has limited value in the risk evaluation of KT candidates above 55 years of age.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>&gt; 24 hr. ICU (N=21)</th>
<th>No ICU (N=41)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>66.8 ± 7.3</td>
<td>66.8 ± 6.9</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>15 (75 %)</td>
<td>30 (75 %)</td>
<td>1.00</td>
</tr>
<tr>
<td>Psoas area (cm²)</td>
<td>21.99 ± 5.77</td>
<td>22.59 ± 6.49</td>
<td>0.72</td>
</tr>
<tr>
<td>PMI (cm/m²)</td>
<td>7.3 ± 1.7</td>
<td>7.4 ± 1.8</td>
<td>0.82</td>
</tr>
<tr>
<td>Sarcopenia, median</td>
<td>11 (52 %)</td>
<td>21 (51 %)</td>
<td>1.00</td>
</tr>
<tr>
<td>Sarcopenia 25</td>
<td>6 (29 %)</td>
<td>9 (22 %)</td>
<td>0.76</td>
</tr>
<tr>
<td>Comorbidity score</td>
<td>5.05 ± 4.69</td>
<td>2.73 ± 2.58</td>
<td>0.02</td>
</tr>
<tr>
<td>Time between CT scan and Tx (months)</td>
<td>23.4 ± 4.9</td>
<td>18.3 ± 2.6</td>
<td>0.07</td>
</tr>
<tr>
<td>Living Donor</td>
<td>2 (10 %)</td>
<td>9 (23 %)</td>
<td>0.39</td>
</tr>
<tr>
<td>Dialysis vintage (months)</td>
<td>28.1 ± 22.3</td>
<td>19.6 ± 18.8</td>
<td>0.15</td>
</tr>
</tbody>
</table>

UTILIZATION AND CLINICAL OUTCOMES OF SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION FROM OLDER PANCREAS DONORS

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Background: Donor pancreas utilisation rates for transplantation are inferior to that of other organs. Despite the revised NHSBT donor age limit (DBD=61-years/DCD=56-years), pancreas utilisation rates from donors >45-years remain low due to the perceived poor outcomes. Hence, we aimed to investigate the outcomes of simultaneous pancreas kidney (SPK) transplants from donors >45-years & their utilisation rate in our cohort.

Methods: Our centre’s data on all SPK transplants performed and named SPK offers received between 01-01-2010 to 31-12-2020 was retrospectively analysed. The primary aim was to compare the pancreas graft loss (3-month & 1-year) and long-term survival between SPK transplants done from donors aged ≥45-years (D≥45) & >45-years (D>45). The secondary aim was to compare the utilisation rates between the two groups. Appropriate univariate & multivariate analysis were performed.

Results: 276 transplants were done and the baseline characteristics as in table-1. The 3-month & 1-year pancreas graft loss were comparable between D≥45 & D>45 cohorts (6.8% vs. 14.03%, p=0.21; 10.9% vs. 19.29%, p=0.09, respectively). Among the 2574 named offers received, 55% were from D≥45 group (median donor age 54-years; IQR 50-57). The offer decline rate was significantly higher in the D≥45 group (96.34% vs. 83.57%, p<0.0001). 13.1% (180/1371) of the offers in the D≥45 group were declined solely based on the donor’s age.

Conclusions: We are the first to report utilisation and outcomes from older donors. We are likely to be more selective in accepting these donors. Survival outcomes from this under-utilised cohort are equivalent to younger donors, thereby supporting the usage of older pancreas donors to improve organ utilisation.

Table-1:

<table>
<thead>
<tr>
<th>Donor/recipient transplant characteristics</th>
<th>Donor age ≥45 (n=55)</th>
<th>Donor age &gt;45 (n=180)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median donor age (DD)</td>
<td>67 (63-72)</td>
<td>66.8 (63-72)</td>
<td>0.89</td>
</tr>
<tr>
<td>Median donor weight in kg (DD/DCD)</td>
<td>84 (74-94)</td>
<td>83 (74-94)</td>
<td>0.60</td>
</tr>
<tr>
<td>Proportion of non-Caucasian donors (NHB)</td>
<td>10.2% (6/59)</td>
<td>7.6% (17/222)</td>
<td>0.59</td>
</tr>
<tr>
<td>Proportion of non-CAOO donor (Number)</td>
<td>56.2% (32/57)</td>
<td>55.9% (123/222)</td>
<td>0.68</td>
</tr>
<tr>
<td>Proportion of local donor (Number)</td>
<td>26 (16/57)</td>
<td>23.7% (52/222)</td>
<td>0.48</td>
</tr>
<tr>
<td>Proportion of multiple use in donor (Number)</td>
<td>56.2% (29/81)</td>
<td>71.6% (157/219)</td>
<td>0.33</td>
</tr>
<tr>
<td>% of heavy alcohol (n=222) (donor)</td>
<td>67.8% (89/133)</td>
<td>62.5% (127/202)</td>
<td>0.47</td>
</tr>
<tr>
<td>Median recipient age in years (DD)</td>
<td>42 (34-53)</td>
<td>40 (34-52)</td>
<td>0.11</td>
</tr>
<tr>
<td>Median recipient PMI in kg/m² (DD)</td>
<td>24.6 (21-26)</td>
<td>24.4 (21-26)</td>
<td>0.77</td>
</tr>
<tr>
<td>Median transplant period in days (DD)</td>
<td>40 (30-50)</td>
<td>40 (30-50)</td>
<td>0.28</td>
</tr>
<tr>
<td>Median duration of diabetes in years (DD)</td>
<td>28.1 (20-36)</td>
<td>27.2 (21-31)</td>
<td>0.43</td>
</tr>
<tr>
<td>Proportion of transplant recipients (Number)</td>
<td>34 (50/64)</td>
<td>31.5% (64/203)</td>
<td>0.10</td>
</tr>
<tr>
<td>Median waiting time in days (dd)</td>
<td>9 (6-14)</td>
<td>9 (5-14)</td>
<td>0.20</td>
</tr>
<tr>
<td>Proportion of HCC (Number)</td>
<td>37 (29/64)</td>
<td>38.8% (20/52)</td>
<td>0.69</td>
</tr>
<tr>
<td>Proportion of non-Caucasian recipients (Number)</td>
<td>3 (5/64)</td>
<td>7.7% (4/52)</td>
<td>0.80</td>
</tr>
<tr>
<td>% of recipients with non-Bejannoni MHL (Number)</td>
<td>34 (57/64)</td>
<td>31 (42/52)</td>
<td>0.68</td>
</tr>
<tr>
<td>Median CP in month (dd)</td>
<td>69 (66-77)</td>
<td>69 (66-77)</td>
<td>0.87</td>
</tr>
<tr>
<td>Median WFR in months (dd)</td>
<td>38 (30-40)</td>
<td>38 (30-40)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Figure-1:

Graft Survival-Pancreas (Death censored)

Graft Survival-Kidney (Death censored)
DUAL INHIBITION OF THE COMPLEMENT SYSTEM AND TOLL-LIKE RECEPTORS PREVENTS SYSTEMIC AND LOCAL KIDNEY INFLAMMATION IN MICE EXPERIENCING BRAIN DEATH

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Background: Brain death (BD) induces a potentially harmful systemic inflammation, which may reduce organ quality for transplantation. The complement system (CS) and Toll-like receptors (TLRs) are key for the innate immune system both for recognition and response. The cluster of differentiation 14 (CD14) is a co-receptor for several TLRs, necessary for TLR signaling. We hypothesized that dual inhibition of CS and TLRs by complement protein 5 (C5) and CD14 inhibition will prevent innate immune-mediated inflammation during BD.

Methods: BD was induced with a fluid-filled intracranial balloon in wild-type C57/BL6 mice. Prior to BD, mice were left untreated (n=8), treated with a C5 inhibitor (n=7), a CD14 inhibitor (n=7), or both inhibitors (n=7). Sham mice did not experience BD and were left untreated (n=8). Blood and kidneys were collected three hours after BD. Inflammatory plasma cytokines were analyzed using a 25-plex immunoassay, kidney mRNA expression by qPCR.

Results: In plasma, significantly induced expression of interleukin-6 (IL-6), human IL-8 homolog, IL-12, monocyte chemotactant protein (MCP-1), and macrophage inflammatory protein (MIP-1α, and MIP-1β) compared to sham (all p<0.01). In kidneys, significantly induced IL-6, IL-8, TNF, MCP-1, P-Selectin, and VCAM-1 (all p<0.01). C5 and CD14 single inhibition significantly reduced BD-induced activation of all markers in plasma (all p<0.01) and in kidneys (p<0.05), except for P-Selectin in CD14 inhibition group. Dual inhibition of C5 and CD14 further reduced all plasma cytokines to levels comparable with sham animals (all p<0.05). In kidneys, dual inhibition was comparable to single inhibition.

Conclusions: The innate immune system is crucial for inducing inflammatory reactions during BD. Inhibition of both the CS and TLRs is necessary to efficiently prevent BD-induced systemic inflammation and to reduce local kidney inflammation. CS and TLR inhibitors are clinically available and clinical studies should be performed on deceased BD donors to enhance donor organ quality.

THE QUALITY OF LIFE OF LIVING LIVER DONORS POST-DONATION: AN AMBIDIRECTIONAL COHORT STUDY

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¹Erasmus MC, Department of Hepato-Pancreato-Biliary (HPB)/Transplant Surgery, Rotterdam, Netherlands, ²Erasmus MC, Department of Psychiatry, Rotterdam, Netherlands, ³Erasmus MC, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands, ⁴King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

Background: Living donor liver transplantation (LLDT) is an option for the donor liver shortage. A systematic review showed some impaired quality of life (QoL) parameters 3 months post-donation. This study compares the QoL of living liver donors (LLD) post-donation to pre-donation and to the QoL of the general Dutch population.

Methods: Donors are included from May 2004 to May 2023. Donors filled in Short Form-36 Health Survey (SF-36), and EuroQol-5 Dimension-S Levels (EQ-5D-5L) pre-donation, and 3-, 12-months post-donation. These 3 time points were compared with a reference (Dutch population) and with each other. Subgroup analyses were done for sex, age (<40 vs ≥40), donor hospital stay (<7 vs ≥7 days), and donor and recipient complications. For these factors and body mass index, multiple linear regression analyses were done.

Results: Forty-eight donors are included. For SF-36, mean Physical Component Score (PCS) was 91.5 pre-donation, 87.4 3 months post-donation, and 89.9 12 months post-donation. Mean Mental Component Score (MCS) was 87.6 pre-donation, 87.3 3 months post-donation, and 85.3 12 months post-donation. There were no significant differences between the 3 time points and all means were significantly higher than the reference (PCS: P=0.004, P<0.001, P<0.001; MCS: P=0.004, P<0.001, P=0.002). Subgroup analyses showed a significantly 6.3 higher PCS pre-donation in older donors (P=0.02). Multiple linear regression showed no predictors of PCS and MCS. For EQ-5D-5L, mean Visual Analog Scale (EQ-VAS) was 82.5 pre-donation, 89.3 2 months post-donation, and 84.9 12 months post-donation. Mean composite Trade-off (cTTO) was 0.97 pre-donation, 0.98 3 months post-donation, and 0.89 12 months post-donation. There were no significant differences between the 3 time points. Mean EQ-VAS 3 months post-donation (P<0.001) and cTTO at all 3 time points (P=0.03, P<0.001, P=0.04) were significantly higher than the reference. Subgroup analyses and multiple linear regression showed no significant differences or predictors.

Conclusions: QoL of LLDs 3 months after LLDT returned to their pre-donation QoL. Older donors report better physical QoL pre-donation than younger donors. QoL of LLDs is often higher compared to the general Dutch population. Our results show a faster QoL recovery than the current literature.

Table 1. SF-36 results

<table>
<thead>
<tr>
<th>Time point</th>
<th>Physical function</th>
<th>Physical role</th>
<th>Social function</th>
<th>Role emotional</th>
<th>Energy fatigue</th>
<th>Role physical</th>
<th>Mental health</th>
<th>General health</th>
<th>Vitality</th>
<th>Physical component score (PCS)</th>
<th>Mental component score (MCS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-donation</td>
<td>82.0 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
</tr>
<tr>
<td>3 months post-donation</td>
<td>82.0 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
</tr>
<tr>
<td>12 months post-donation</td>
<td>82.0 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.2 (50-96.6)</td>
<td>86.9 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
<td>86.3 (50-96.6)</td>
</tr>
</tbody>
</table>

Figure 1. Scatter plot of the EQ-VAS.
SUCCESSFUL KIDNEY TRANSPLANTATION WITH ARTERIAL RECONSTRUCTION FROM A DEACEDED DONOR WITH MARFAN'S SYNDROME – A CASE REPORT

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Background: Despite growing awareness of recognizing potential organ donors and enhancement in transplantation procedures, the shortage of organs persists. This leads us to careful recognition of any contraindications for donation. Marfan’s syndrome is a genetic disorder caused by a mutation in the extracellular matrix protein fibrillin-1 which leads to systemic dysfunction of connective tissue. Pathological manifestations of the syndrome include cardiovascular, skeletal and ocular systems. To our knowledge, transplantations from donors with Marfan’s syndrome were only scarcely reported. The safety and efficacy of such organ donation remain unexplored.

Methods: A 56-year-old woman with aortic dissection, with a previous diagnosis of Marfan’s syndrome and arterial hypertension, was declared brain dead on the 5th day after emergency surgery. After careful recognition, she was considered a potential organ donor. Both kidneys and liver were harvested. At organ procurement it was also discovered that the right kidney has two independent arteries, which required arterial reconstruction. Subsequently, both kidneys were successfully transplanted performing an arterial anastomosis without the use of an aortic Carrel patch.

Results: Postoperatively, no major complications occurred. The recipient of the kidney with arterial reconstruction needed one course of hemodialysis.

Conclusions: Although transplantations of organs from donors with Marfan’s syndrome might face technical difficulties and challenges, it seems they are both safe and efficient. This is illustrated by the case presented. The recipient of the kidney with arterial reconstruction needed one course of hemodialysis.

DIVERSITY OF CIRCULATING B CELL SUBSETS IN RENAL TRANSPLANT RECIPIENTS EARLY POST-TRANSPLANTATION

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1Renal Transplant Unit, School of Medicine, Aristotle University of Thessaloniki, General Hospital “Hippokration”, Thessaloniki, Greece, 2Department of Medicine, Thessaloniki, Greece, 3Aristotle University of Thessaloniki, Laboratory of Biological Chemistry, School of Medicine, Thessaloniki, Greece, 4Center for Research and Innovation in Solid Organ Transplantation, Transplantation Surgery, Thessaloniki, Greece

Background: B lymphocytes are actively involved in kidney transplantation. We aimed to assess frequency alterations of circulating B cell subsets 6 months posttransplant compared to pretransplant time point and associate them with stratification to donor type.

Methods: 39 kidney transplant recipients with good kidney function, eGFR>55ml/min/1.73m2, B/39(21%) living donor, 21/39(79%) deceased donor, age 55(20–60) years, 8/39(21%) female, was the study group. The frequencies of 12 B cell subgroups were determined by multiparameter flow cytometry from T0 to T6. After careful recognition, the study was completed.

Results: Analysis of B subset frequency from T0 to T6 revealed a statistically significant reduction in naïve (CD19+ IgD–CD27–) p=0.013, transitional Bregs (CD19+CD24+CD38++) p=0.001, plasmablasts (CD19+IgD+/-CD27+CD38+) p=0.001, transitional Bregs and plasmablasts p=0.001 was detected. B subsets differed significantly between time points or groups did not correlate with age, gender or dialysis vintage.

Conclusions: B cell subsets analysis in kidney transplant recipients with good function, showed that both the deceased donor and living donor recipient groups had lower frequencies of naïve cells 6 months after transplantation. In addition, only the deceased group maintained low frequencies of transitional Bregs and plasmablasts, while the remaining subsets remained unchanged.

Atherosclerosis and Intrarenal Resistance Index in Kidney Transplant Recipients

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1University Medical Center Groningen, Surgery, Groningen, Netherlands, 2University Medical Center Groningen, Groningen, Netherlands, 3Erasmus MC, Rotterdam, Netherlands

Background: Atherosclerosis of the aortoiliac vessels can adversely affect kidney perfusion after kidney transplantation. Atherosclerosis severity can be determined using the calcium score (CaScore). Potential problems with post transplantation kidney perfusion can be determined using the Intrarenal resistance index (RI). This study investigated the association between aortoiliac CaScore and RI in kidney transplant recipients.

Methods: Kidney transplant recipients (2004-2019), for whom the CaScore and RI were determined, were included in this meta-analysis. CaScore was measured in 3 aortoiliac segments using non contrast CT imaging. RI was determined using Doppler ultrasound. Multivariable linear regression analyses were performed to determine the association between CaScore and RI, adjusted for confounding variables.

Results: Mean age of the 389 included patients was 59 (±13) y. Mean RI (unitless) was 0.71 (±0.09) and median CaScore (unitless) was 3340 (399-7833).

In univariable linear regression analyses with RI as the dependent variable, CaScore (P<0.001), age (P<0.001), gender (P=0.002) and history of diabetes (P=0.003), were also positively associated with RI, whereas preoperative recipient diastolic blood pressure (P=0.007), were inversely associated. In multivariable analyses, CaScore and RI remained significantly associated. In multivariable analyses, CaScore and RI remained significantly associated.

Conclusions: A significant association was found between CaScore and RI, independent of adjustment for multiple potential confounding factors, leading to a better insight into the development and interpretation of RI. Aortoiliac atherosclerosis should be considered when interpreting the RI and determining the possible cause of malperfusion and graft failure after kidney transplantation.
Background: Kidney transplant recipients in immunosuppression are at particularly high risk of serious Covid-19 disease. Both the disease itself, as well as the reduction of the dosage of immunosuppression medications, may affect graft function after the recovery from the disease. In this retrospective cohort study, we investigated the role of Covid-19 disease on transplant function in vaccinated and not vaccinated recipients.

Methods: We recorded the vaccination status before the onset of Covid-19 disease in 544 patients followed in our clinic, eGFR and proteinuria were recorded on 101 patients before and 6-12 months after they had contracted the Covid-19 disease.

Results: Out of 544 patients, 156 (28.7%) have contracted Covid-19 and in 54 patients followed in our clinic, eGFR and proteinuria were recorded on 101 patients before and 6-12 months after they had contracted the Covid-19 disease. In 101 infected patients (48±14 years old), eGFR was similar before Covid-19 and after recovery [52.4(25.9) vs 54.5(26.9) ml/min/1.73m²], and proteinuria also remained stable [180(261) vs 176(243) mg daily]. No significant differences were observed when we examined particularly the not vaccinated patients [46 of 101, 45.5%] at the time of infection, as eGFR was similar before and after recovery [57.7(31.2) vs 57.8(34.5) ml/min/1.73m²] and proteinuria increased only slightly after the infection [170(216) vs 119(196) mg, p<0.05] as statistically significant.

Conclusions: Graft function, as assessed by eGFR and proteinuria, was not affected, in the long term, by Covid-19 disease in kidney transplant recipients, independent of their vaccination status.

LIVER OR THYROID CANCER IN LIVING LIVER DONORS SHOULD BE MONITORED AFTER DONOR HEPATECTOMY

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Samsung Medical Center, Seoul, South Korea, 2Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Background: Living liver donors (LLDs) are screened for transmissible diseases including cancer. Outcomes following donation are excellent, but concern exists regarding the development of malignancy, and cancer risk is unknown. We investigated the actual cancer incidence of LLDs compared with a matched healthy control group from the general Korean population using data from the Korean National Health Insurance Services (NHIS).

Methods: 12,372 LLDs who donated a liver graft between 2002 and 2018, and were registered in the Korean Network for Organ Sharing. They were compared to matched healthy control group selected from the Korean NHIS.

Results: Cancer diagnosis was identified in 175 LLDs (1.4%) and 1,014 controls (0.8%). The incidence of liver and thyroid cancer in the LLD group is higher than in the healthy control group. The incidence of 11 specified cancers incidence was not different between the two groups.

Conclusions: Present study suggests that liver and thyroid cancer screening in the LLDs should be routinely required after donor hepatectomy.
Background: Cytomegalovirus (CMV) infection is the most common viral complication after kidney transplant (KT) which is associated with significant morbidity, graft rejection, failure & mortality in KT recipients. Medical frailty has been associated with poorer post-operative outcome. Neutrophil-to-lymphocyte ratio (NLR), a novel inflammatory marker, has also been associated with worse prognosis in KT. Yet, there is limited data investigating the relationship of these variables with CMV infection risk in KT recipients.

Methods: A single-centre, retrospective study of KT recipients was conducted between April 2017 to December 2017. Data on the recipient characteristics, frailty (5-point Modified Frailty Index) at the time of transplantation, inflammatory markers up to 3 days post-transplant, patient outcomes including CMV incidence were recorded up to 1 and 3-year time points. Area under curve of NLR (AUCNLR) on day of KT to day 3 after KT were calculated as a single numeral value for each individual recipient. Mann-Whitney & Chi-square test were used to analyse the relationship between the variables & 2-month CMV infection.

Results: Of 92 KT recipients included in this study, CMV infection occurred in 29 (31.5%) patients. There is a significant difference in AUCNLR between the CMV & non-CMV group (p=0.016) with a cut-off value of 41.4. There is also significant association between frailty and CMV (p=0.008) with a cut-off frailty score of 2. When stratified by AUCNLR and frailty, statistical significance is demonstrated across all 4 groups (p<0.001) (Table 1).

Conclusion: Preliminary analysis suggests frailty & reduced NLR are associated with a higher risk of post-transplant CMV infection in KT patients. Our findings corroborate the existing research in that frailty is linked with worse post-operative outcomes. NLR from 0-3 days and MFI score at index admission are readily accessible tools for clinicians to predict CMV infections – a potential for personalised and stratified management.

Table 1: Outline of patient cohorts' CMV outcomes based on classification of AUCNLR & frailty

<table>
<thead>
<tr>
<th>Total Cohort</th>
<th>2-month CMV incidence</th>
<th>Percentage of CMV-positive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>AUCNLR=41.4, Frail (MFI≥2)</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>AUCNLR=41.4, Non-frail</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>AUCNLR=41.4, Frail</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>AUCNLR=41.4, Non-frail</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>n = 92</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>
Background: Recent advances in CT image analysis technology have contributed to the improvement of diagnostic performance and preoperative evaluation in various fields. For the kidneys, renal and renal cortical volumes can be estimated, allowing quantitative and objective evaluation. While graft nephron mass and donor-recipient size ratio are known to affect early renal function after living donor transplantation, this study aimed to identify donor and recipient factors from CT images that correlate with early renal function after living donor transplantation and to develop a prediction model for early renal function.

Methods: We evaluated 160 pairs of donors and recipients who underwent living donor renal transplantation at the Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital from April 2020 to December 2021. Three items, actual kidney weight, predicted renal volume and predicted renal cortical volume with CT image analysis technology, were used as donor factors, and five items, preoperative weight, ideal weight, height, body surface area, and BMI, were used as recipient factors. These factors and serum creatinine levels at 1 month postoperatively were analyzed using Pearson correlations, and a predictive model of serum creatinine levels at 1 month postoperatively was created by multiple regression analysis.

Results: The recipient’s early postoperative serum creatinine level correlated with the donor’s predicted renal cortical volume and recipient weight ratio, and a predictive model of serum creatinine levels at 1 month postoperatively was created by multiple regression analysis.

Conclusions: Donor renal cortical volume calculated from CT image analysis provides a reasonable prediction of early post-transplant renal graft function.

Background: In the clinical risk management of our donation and transplantation network, serious adverse reactions (SARs) and serious adverse events (SAEs) reported. Data related to SAEs and SARs reported in the period 2012-2021 have been analyzed, detailing type of event reported, type of risk associated to the event (neoplastic, infectious, organological, others), seriousness/severity of the event, phase of the process in which the event occurred, type of donor involved (deceased/organ donor) and time period involved.

Results: In the period 2012-2021, 283 adverse SAEs and SARs have been reported. In most cases (65%) it was an adverse event. The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). In 10 years only 8 events have been associated to the events were primarily related to adverse event. The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). In 10 years only 8 events have been associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively). The type of risks associated to the events were primarily related to management and organizational issues (68 and 56 respectively).

Conclusions: Although radiomics in kidney transplantation is still in its infancy, it has the potential for large-scale implementation. Its greatest potential lies in the correlation with conventional established diagnostic evaluation for living donors and potential in predicting and detecting rejection and graft failure post-operatively.
Conclusions: Our data suggests that the FTR concept would offer a tool for analyzing the missing link between patient morbidity and mortality. We think that the precise analysis of causes of FTR would allow quality improvement of post-operative care in the field of pediatric LDLT.

Methods: Bone marrow harvesting was performed on the iliac crest and lumbar and dorsal vertebrae of the deceased donor for patient #1 and mobilized leukapheresis from sibling donor for patient #2. First we obtained the enriched CD34+ selection using the CLiniMACS system (Miltenyi Biotec) and afterwards the CD45RA+ cell depletion. Lineage-specific chimerism analysis and immune cell recovery was monitored.

Results: Patient #1 15-year-old boy with intestinal epithelial dysplasia. After two previous intestinal transplants. T cell depleted bone marrow graft from the same fully HLA mismatched deceased donor was done. After the infusion of CD34+ cells and CD3+CD45RO+ T cells, any degree of graft versus host disease has been observed, as well as no sign of rejection, with chimerism between 0,05 and 5,1%. Tacrolimus was withdrawn after 8 months. The patient receive only sirolimus as immunosupresor to maintain drug concentrations at 8 ng/ml. No signs of rejection or toxicity were observed after 38 months of follow-up. Patient #2 49-year-old woman diagnosed with chronic kidney failure secondary to rapidly progressive glomerulonephritis. She had received three kidney graft previously. We performed CD34+ haematopoietic progenitors and CD45RA- memory lymphocytes infusion in match related HLA living donor kidney transplant. Mixed hematopoietic chimerism was demonstrated during the first 3 months after SOT of between 0.1% and 40% of CD3+ cells. The patient continued on monotherapy with tacrolimus. The patient did not have acute rejection, graft versus host disease, viral infection or renal failure. Contrastive to previous reports, we did not observe any degree of graft versus host disease or chronic rejection.

Conclusion: We describe for the first time the use of non-myeloablative conditioning and a CD45RA+ T cell-depleted graft to induce transitory mixed chimerism using both hematopoietic progenitors and a solid organ, for tolerance induction purposes.

Method: Induction of tolerance by donor hematopoietic stem cell transplantation together with SOT is an active approach to avoid the chronic use of pharmacological immunosuppression and their adverse effects.

Objective: To present a model for inducing transient mixed chimerism in 2 patients undergoing SOT employing a non-myeloablative conditioning regimen and a partially T cell-depleted graft consisting of CD34+ hematopoietic progenitor cells and CD45RA- memory lymphocytes.

Donors used

Carlos Jiménez1, María Ovidia Lopez1, M Elena González-García1, Esther Boluda1, Mercedes Gasior1, Raquel De Paz1, Jose Maria Alonso2, Rosa Maria Morera1, Moises Saiz1, Antonio Marcos3, Jose Luis Vicario7, Antonio Balas7, Francisco Hernández Oliveros5, Antonio Perez7

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Induction of tolerance by donor hematopoietic stem cell transplantation together with SOT is an active approach to avoid the chronic use of pharmacological immunosuppression and their adverse effects.

Objective: To present a model for inducing transient mixed chimerism in 2 patients undergoing SOT employing a non-myeloablative conditioning regimen and a partially T cell-depleted graft consisting of CD34+ hematopoietic progenitor cells and CD45RA- memory lymphocytes.
ASSESSMENT OF DD-CFDNA IN KIDNEY TRANSPLANTATION AS A MARKER OF GRAFT INJURY - A PROSPECTIVE STUDY

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Background: Cell-free DNA (cfDNA) refers to DNA fragments originating from donor organ cell injury and death, increasing donor derived-cfDNA (dd-cfDNA) plasma levels - a correlation between this increase and graft injury was shown previously.

Methods: We prospectively assessed dd-cfDNA role as a kidney graft injury marker, defining 2 cohorts: longitudinal cohort (LC), with samples collected from all de novo kidney transplant recipients at months 1, 2, 3, 4, 6, 9 and 12 post-transplant; biopsy cohort (BC), with samples collected at biopsy time for clinical indication and 4 and 8 weeks afterwards.

Results: Twenty-four patients were included (8 from BC). Median age was 57 years (IQR 42-60). Remaining characteristics are listed in figure 1. As expected, ds-cfDNA was higher in BC and remained low and stable in most LC patients (figure 2). In 44 LC samples, only 3 had dd-cfDNA > 1%; one sample (2.03%) was miscollected only 5 days after transplant with delayed graft function, so tubular injury may be culprit, though persistent elevation at month 3 (4%) in the same patient remains unexplained. In another sample, a dd-cfDNA of 1.4% at month 1 coincided with COVID infection. In the 8 BC patients there was a clear dd-cfDNA segregation between rejection status (median 3.59% with vs 0.56% without; p=0.025). This wasn’t observed with serum creatinine (sCr). In those with rejection (5/8), dd-cfDNA at biopsy varied between 1.73-8.03%, all reducing to <1% at 1 month. Four of these 5 had de novo donor-specific antibodies (DSA). In the only antibody-mediated rejection case, dd-cfDNA normalized during follow-up, as DSA and proteinuria disappeared. The highest dd-cfDNA case (8.03%) had the lowest graft function by end of follow-up (sCr 4.39 mg/dL). The only non-rejection biopsied case with a dd-cfDNA > 1% (1.45%), had contemporaneous significant BKV viremia (peak 52k copies), successfully treated with stable renal function and dd-cfDNA reduction.

Conclusions: In our data, dd-cfDNA was higher when dysfunction was caused by rejection and outperformed sCr distinguishing stable (LC) from injury (BC) cases. Reduction of dd-cfDNA after biopsy didn’t correlate with function improvement. Furthermore, the magnitude of the elevation may correlate with rejection severity, de novo DSA and prognosis. This needs validation with more cases and follow-up.

<table>
<thead>
<tr>
<th>Age (IQR)</th>
<th>Median (IQR)</th>
<th>Biopsy; N=8</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Total; N=24</td>
<td>57 (42-60)</td>
<td>57 (47-62)</td>
<td>48 (38-59)</td>
</tr>
<tr>
<td>Female R, n (%)</td>
<td>10 (43)</td>
<td>6 (28)</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Retransplant, n (%)</td>
<td>5 (21)</td>
<td>3 (10)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Living donor, n (%)</td>
<td>7 (29)</td>
<td>5 (21)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Proportion DSA, n (%)</td>
<td>3 (13)</td>
<td>2 (13)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>Number of dd-cfDNA, median (IQR)</td>
<td>62</td>
<td>44</td>
<td>18</td>
</tr>
<tr>
<td>Number of dd-cfDNA, median (IQR)</td>
<td>3 (2-3)</td>
<td>3 (2-4)</td>
<td>2 (2-3)</td>
</tr>
<tr>
<td>Indication for biopsy</td>
<td>-</td>
<td>-</td>
<td>2: graft dysfunction; 1: proteinuria</td>
</tr>
<tr>
<td>Months since KT, median (IQR)</td>
<td>1.2 (0.9-0.4)</td>
<td>1.0 (0.7-1.2)</td>
<td>0.4 (2.4-13.6)</td>
</tr>
<tr>
<td>sCr, median (IQR)</td>
<td>1.64 (1.27-2.42)</td>
<td>1.42 (1.23-1.99)</td>
<td>2.63 (1.47-8.28)</td>
</tr>
<tr>
<td>Proteinuria*, median (IQR)</td>
<td>0.24 (0.04-0.64)</td>
<td>0.24 (0.20-0.46)</td>
<td>0.51 (0.20-4.05)</td>
</tr>
<tr>
<td>Acute rejection, n</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
</tbody>
</table>
EX VIVO NORMOTHERMIC CIRCULATION (PNEV) OF GRAFTS FROM DCDs. AN EXPERIMENTAL STUDY OF BIOCHEMICAL AND METABOLIC CONDITION

Victoria Gomez1, Jose Antonio López Plaza1, Marina Mata1, Sarah Hosgood2, Jose Lopez-Menendez2, Federico Soria1, Ana Sañaz-Gonzalez2, Francisco Javier Burgos3
1Hospital Universitario Ramón y Cajal, IRYCIS, Universidad Alcalá, Urology, Madrid, Spain, 2Cambridge University, Cambridge, United Kingdom, 3Hospital Universitario Ramón y Cajal, IRYCIS, Universidad Alcalá, Cardiovascular Surgery, Madrid, Spain, 4Hospital Universitario Ramón y Cajal, IRYCIS, Universidade Alcalá, Experimental Veterinary Surgery, Madrid, Spain, 5Hospital Universitario Ramón y Cajal, IRYCIS, Universidad Alcalá, Pathology, Madrid, Spain

Background: Organs from donors after circulatory deaths (DCD) show an increased susceptibility to prolonged periods of warm and cold ischemia resulting in increased rates of delayed graft function and non-functioning grafts. Efforts should be directed towards improving the methodology for their use and optimizing their viability during preservation. Ex vivo normothermic perfusion (EVNP) would maintain the aerobic metabolism of the graft by providing it with oxygen and nutrients.

Methods: In a porcine model, kidneys were exposed to 30 minutes of warm ischemia and randomized to 1 of 2 study groups with a short (4 hours) or long (18 hours) period of static cold storage (SCS) followed by a 2-hour period of EVNP using a cardiopulmonary bypass and blood perfusion solution. Viability assessment included renal and tubular function, tissue barrier, histology, oxygen consumption and Hosgood viability score (macroscopic appearance of the graft, renal blood flow and urine output) that determines low (1-2), moderate (3-4) or high risk (5). Renal damage molecules (KIM1, NGAL), inflammation (NFkB, iNOS) and cell stress response (SOD1) were estimated by immunohistochemistry.

Results: Data are presented for 12 grafts undergoing PNEV. HyperGlu [437.0 (428.0; 461.0)] mg/dl, hyperNa [163.0 (141.0; 168.0)] mEq/L and hyperK [6.4 (4.4; 8.4)] mmol/L were observed in the second hour of EVNP (7.0; 8.5 mEq/L), and decreased markedly in the second hour (4.8-4.9 mEq/L) accompanied by a progressive increase in lactate and a deterioration in the macroscopic appearance of the graft. Severe alkalosis and hypcapnia resulted in increased oxidative stress. SOD1 staining also increased after normothermic preservation indicating strong antioxidant response of the tubular cells. However, histological study showed minimal tubular changes and increased Bowman’s space as a sign of oedema. The grafts had a viability score of at least, 4 points corresponding to a “moderate” risk.

Conclusions: The need for cardiovascular by-pass equipment and the use of blood-preserving solution poses logistical challenges that limit the clinical application of EVNP. Optimization of PNEV should result in a decrease in the risk score of grafts for transplantation.

EARLY DETERMINATION OF FAST TACROLIMUS METABOLIZER STATUS IDENTIFY RISK OF REJECTION AND ALLOGRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

Christophe Masset1, Florent Leborgne2, Marine Lorent1, Magali Giral1, Claire Kerleau1, Claire Garandeau1, Aurelie Houzet1, Simon Ville1, Delphine Kervella2, Diego Cantarovich3, Gilles Blanco4, Jacques Dantel1
1Institut de Transplantation-Urologie-Nephrologie (ITUN), Nantes University Hospital, Nantes, France, Nantes, France, 2INSERM UMR 1245 - SPHERE, Nantes University, Tours University, Nantes, IDBC Pacé France, Nantes, France

Background: Fast tacrolimus metabolizers kidney transplant recipients have a lower allograft function, but determination of Metabolic Status (MS) patients can be difficult to assess in real life setting due to dosages modifications during the first months post-transplantation. We investigated allograft outcomes and function (eGFR) evolution depending on MS (Fast metabolizers: MS+ or not: MS), and the reproducibility of MS status in the first months post-transplantation.

Methods: eGFR up to 5-years post transplantation was analysed using a linear mixed effect model at T=1-month (main analysis); we also studied subcohorts at T=1-6-months. Long-term allograft survival, occurrence of biopsy proven acute rejection (BPAR) and de novo Donor Specific Antibodies (dNDSA) were also assessed after adjustment on confounding variables.

Results: 1979 patients were analysed at T=1-month, 44.9% were MS+. This status was reproducible during the first months for >80% of them. The 10-years allograft survival was significantly reduced for MS+ patients at T=1-month (83.4%, 95%CI = [80.1% to 86.8%] vs 74.2%, 95%CI = [69.4% to 79.3%]). MS+ patients had a higher risk of occurrence of BPAR (HR = 1.40, CI95% = [1.09; 1.81], p = 0.0058), and a trend to a higher risk of dNDSA (HR = 1.32, CI95% = [0.97; 1.76], p = 0.0747). The confounder-adjusted mean eGFR at T=1-month was lower for MS+ (-3.97 ml/min/100g, CI95% = [-5.55; -2.40]). Moreover, their eGFR increase between one and six months was reduced and their long-term eGFR kinetic was also worse.

Conclusions: MS+ status deleterious effect on allograft occurs since the first month due to BPAR and probably to tacrolimus nephrotoxicity. Physicians may consider an immunosuppression adaptation in the early post-transplant period in these patients.

SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT (IPSILATERAL VERSUS CONTRALATERAL, A SINGLE UNIT EXPERIENCE

Lorenzo Petagna1, Hussein Khamblia1, Giuseppe Giuffrida1, Isaac Jabang1, Jennifer Kingston1, Antonio Giuliani3, Tommaso Manzia4, Zia Moinuddin1,2, Bence Forgacs1,2, David van Dellen1,2
1Manchester Royal Infirmary, Manchester University NHS Foundation Trust, Dept of Renal & Pancreas Transplantation, Manchester, United Kingdom, 2University of Athens, Manchester, United Kingdom, 3Azienda Ospedaliera Regionale “San Carlo”, Potenza, Potenza, Italy, 4Tor Vergata University Hospital, Rome, HPB and Transplant Surgery Unit, Rome, Italy

Background: In simultaneous pancreas kidney transplantation (SPK) grafts are conventionally implanted contralaterally (cSPK), with the pancreas allograft (PG) on right iliac fossa and kidney allograft (KG) on the left. Ipsilateral implant (iSPK) of both grafts on the right side has been previously described but remains underutilised, potentially due to concerns regarding technical complications. We aimed to assess feasibility, safety, outcomes and allograft survival of iSPK versus cSPK.

Methods: A retrospective analysis of a contemporaneous database of SPK transplants was performed. Grafts laterality was noted (iSPK or cSPK) with the pancreas allograft (PG) on right iliac fossa and kidney allograft (KG) on the left. Ipsilateral implant (iSPK) of both grafts on the right side. The grafts had a viability score of at least, 4 points corresponding to a “moderate” risk.

Conclusions: The need for cardiovascular by-pass equipment and the use of blood-preserving solution poses logistical challenges that limit the clinical application of EVNP. Optimization of PNEV should result in a decrease in the risk score of grafts for transplantation.
Administration of vaccine booster in the first six-month post transplantation was safe immediately after kidney transplantation, however remaining positive. Admin-

Conclusion:

Results:

Methods:

Background: Humoral response following mRNA vaccine is broadly accept-

allograft rejection occurred in 10.8% (n = 14) of the immune event, anti-spike titer decreased by 37.9% at M1, 44.4% at M3 and

Methods: All KTR from 2 French university hospital vaccinated previous to transplantation with available serological assessent at the time of transplan-

and recipient pairs from a previously reported prospective multicenter trial. HLA Matchmaker software was used to assess eplet mismatch and antibody

Banff scores.

Table 1A) Association between HLA Class I Eplets Mismatch Load and Banff Scores

Table 1B) Association between HLA Class II Eplet Mismatch Load and Banff Scores

Background: Metabolic acidosis (MA) is frequently diagnosed in patients after kidney transplantation (KTx). Results of both experimental and clinical studies suggest that MA may contribute to faster progression of chronic kidney disease. Data on such relationship in KTx patients are very limited. The aim of this clinical, single center, retrospective, observational study was to examine the relation-

Molecular HLA mismatch load. Logistic regression was used to estimate the odds ratio for 1-unit change in HLA mismatch scores and Banff scores.

Results:

Blood HCO3

Results:

Methods: Blood HCO3 was measured in 486 patients (290 male; 196 female) aged 48 ± 12 years at least one year after KTx and subsequently all patients were observed during 7 years. MA was defined as blood HCO3 concentration lower than 22 mmol/L. The endpoints in Kaplan-Meier survival curves analysis were death and initiation of dialysis therapy or retransplantation. Differences in survival curves were analyzed with log-rank test and were considered as significant when p<0.05. Relative risks (RR) were presented with 95% CI. Results: In patients with MA the risks of initiation of dialysis therapy or retransplantation was significantly higher than in patients without MA [RR=2.51 (1.71-3.68), p<0.001]. Risk of cumulative endpoint of the study (death and initiation of dialysis therapy or retransplantation) was also higher in patients with MA [RR=2.28 (1.73-3.00), p<0.001].

Conclusions: MA increases mortality and progression of chronic graft failure in patients long term after kidney transplantation.

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METABOLIC ACIDOSIS INCREASES MORTALITY AND PROGRESSION OF CHRONIC GRAFT FAILURE IN PATIENTS LONG TERM AFTER KIDNEY TRANSPLANTATION

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Background: Conventional HLA serologic mismatch does not provide detailed risk of histologic rejection in kidney allograft. We hypothesized that molecular level of HLA mismatch load can predict future rejection at histologic level.

Methods: We assessed the association between molecular HLA mismatch load and Banff scores from kidney biopsies performed within 2-year after kidney transplant (KT). High resolution HLA typing was performed on 71 donor and recipient pairs from a previously reported prospective multicenter trial. HLA Matchmaker software was used to assess eplet mismatch and antibody


doi:10.1093/ctr/cct263

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EVOLUTION OF HUMORAL RESPONSE TO SARS-COV-2 VACCINATION AFTER KIDNEY TRANSPLANTATION IN PATIENTS PREVIOUSLY VACCINATED WHILE ON THE WAITING LIST

Pierre Brasard1, Nizar Joher2, Gilles Blancho1, Philippe Grimbert1, Anne Le Bouter1, Claire Garandeau1, Aurelie Houzel1, Diego Cantarovich1, Magali Giral1, Jacques Dautel1, Marie Matignon1, Christophe Masset1

1Institut de Transplantation-Urologie-Néphrologie (ITUN), Nantes University Hospital, Nantes, France, Nantes, France, 2Department of Nephrology and Transplantation, Assistance Publique Hôpitaux de Paris, Hôpital Henri Mondor, Creteil, France, 3Laboratory of virology, Henri Mondor hospital, Creteil, France

Results: 121 KTR were included in the analysis, among whom 50 received a booster during the first six months post-transplantation. In absence of any immune event, anti-spike titer decreased by 37.9% at M1, 44.4% at M3 and 63.9% at M6 post-transplantation; however, not reaching negativity in any patient. In those who received a booster vaccine after transplantation and with available serological assessment afterward, only 20% did not presented an increase in anti-spike titer. Allograft rejection occurred in 10.8% (n = 14) of the cohort; but only one patient out of seven presented a rejection after the vaccine booster. 35 patients presented a SARS-Cov-2 infection during the follow-up, but only one patient out of seven presented a rejection after the vaccine booster.


doi:10.1093/ctr/cct259

P174

ASSOCIATION BETWEEN HLA MOLECULAR MISMATCH AND HISTOLOGICAL REJECTION IN KIDNEY ALLOGRAFT

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1New York Institute of Technology College of Osteopathic Medicine, New York, United States, 2Northwestern University, Organ Transplant Center, Chicago, United States, 3University California, San Diego, San Diego, United States, 4Northwestern university, Chicago, United States

Background: Humoral response following mRNA vaccine was strongly decrease immediately after kidney transplantation, however remaining positive. Admin-

cistral inflammation (i) (OR 1.04, 95% CI [1.01-1.07], p=0.01), glomerulatons (g) scores (OR 1.05, 95% CI [1.00-1.10], p=0.046), and arteriolar hyalinosis (OR 1.03, 95% CI [1.00-1.07], p=0.04) (Table 1B). Conclusions: The degree of HLA class I and II eplet mismatch is associated with histologic evidence of rejection. Future study in a bigger cohort will be needed to address personalized immunosuppression approaches to prevent rejection depending on the HLA eplet mismatch load.


doi:10.1093/ctr/cct262

Table 1A) Association between HLA Class I Eplets Mismatch Load and Banff Scores

Table 1B) Association between HLA Class II Eplet Mismatch Load and Banff Scores

E-POSTERS
**P176** LIVER GRAFT REDUCTION THROUGH EX-VIVO RIGHT POSTERIOR SECTIONECTOMY: SINGLE CENTER EXPERIENCE IN PREVENTING LARGE-FOR-SIZE SYNDROME

Andrea Della Penna1, Markus Quante1, Steffen Hartleif2, Maren Peters2, Dennis Giffler1, Silvio Nadalin1
1Tübingen University Hospital, Department of General, Visceral and Transplant Surgery, Tübingen, Germany, 2Universitätsklinikum Tübingen - Klinik für Kinderheilkunde und Jugendmedizin, Pediatric Gastroenterology and Hepatology, Tübingen, Germany

**Background:** Transplantation of an extremely large liver into a small recipient can lead to Large for Size Syndrome (LFS) characterized by graft compression, impaired graft perfusion, and dangerous increase of intrabdominal pressure and consequently high risk of graft loss. To address this issue, in particular in situations of non-splittable grafts, one possible solution is to reduce the size of the transplanted liver. Especially the reduction of the right lobe of the liver has been shown to be effective in preventing LFS when significant size-mismatch between donor and recipient is expected. Recently, Pu et al. described an ex-vivo technique for performing graft reduction through a right posterior sectionectomy (RPS), reporting positive results in five patients. In this regard, we want to share our own experience using this graft reduction technique.

**Methods:** Single center reduced size liver transplantations (DDLT) performed during the period January 2018 to April 2022 using the ex-vivo RPS technique in young and pediatric recipients.

**Results:** In the study period, 7 patients underwent reduced-size DDLT through the ex-vivo RPS technique. Median age of recipients was 8 (range 2-18), with a M/F ratio of 1/6. Median weight and height were 36 kg (range 11-73) and 141 cm (range 89-163) respectively, and median body mass index (BMI) was 18 (range 13-27). All but one patient was transplanted as high urgency and received grafts through primary allocation. Grafts were non-splittable and had median ET-DRI score of 1.17 (range 1.09-1.89) as whole liver, and 1.99 (range 1.64-2.84) as partial liver. Median Graft-to-Recipient Weight Ratio (GRWR) was 4.7 (range 2.2-10.3) before and 2.2 (range 1.1-5.5) after RPS. Only one patient required delayed fascial closure. There were no cases of LFS postoperatively. One patient died 34 days after transplantation due to brain edema and herniation, and another patient required re-transplantation 22 days after initial transplantation due to severe ITBL and graft failure. Remaining patients had normal functioning grafts at their last follow-up.

**Conclusions:** The ex-vivo RPS-technique represents in our opinion a feasible surgical strategy to prevent LFS, in particular in small recipients and in the setting of high urgency or impossibility to split the graft.

**P177** EFFECT OF RECONSTRUCTION TYPE OF DUAL ARTERIES ON LONG-TERM OUTCOME IN LIVING DONOR KIDNEY TRANSPLANTATION

Won-Bae Chung1,2, Young-Heun Shin1, Taeseung Lee3
1Jeju National University Hospital Center, Surgery, Jeju-si, South Korea, 2Seoul National University Bundang Hospital Center, Surgery, Seongnam-si, South Korea

**Background:** Dual renal arteries (DRA) in living donor kidney transplantation (LDKT) are causing technical challenges. Various reconstruction methods are applicable depending on the anatomy. One group has reported that the end-to-side DRA reconstruction method was inferior to other methods in graft survival. We tried to analyze the outcome according to the reconstruction method in the case of the DRA in LDKT.

**Methods:** Among the 374 patients who underwent LDKT at SNUBH from 2005 to 2021, 79 donors had DRA. Cases with 3 or more renal arteries were excluded. In the case of DRA, they were reconstructed to 5 different methods. (figure 1A). If two arteries were of similar size, they were connected side-to-side to make a single lumen (n=11), or each artery was connected to an internal or external iliac artery respectively (n=15). Additionally, we used internal iliac artery (IIA) and its branch for DRA anastomosis (n=29). If one artery was smaller than the other, the smaller artery was connected to the main renal artery end-to-side fashion (n=9), or the small artery was anastomosed to the inferior epigastric artery (n=15). The outcomes of each group were compared to the control group, a single renal artery (SRA) anastomosis (n=280).

**Results:** As for the short-term result, post-operative GFR did not differ among all the groups (P=0.167), (figure 1B). The 10-year graft survival was significantly lower in end-to-side and side-to-side groups compared to the SRA group (P<0.01 each), (figure 1C). The graft survival of IIA anterior and posterior division group did not show a significant difference compared to SRA group (P=0.878). (figure 1D). There was no significant difference in patient survival according to reconstruction type (P=0.162).

**Conclusions:** Our study showed that long-term graft survival was decreased in end-to-side and side-to-side reconstruction groups. This suggests that the reconstruction of those two methods should be avoided in DRA transplantation. Further study needs on the possible cause of these two methods being inferior to the others.

**P180** THE PREVALENCE OF DYSLIPIDEMIA BEFORE AND AFTER SUCCESSFUL LIVER TRANSPLANTATION

Marcin Adamczak1, Damian Gojowy1, Joanna Urbaniec-Stompor1, Joanna Adamusik1, Gabriela Wojcik1, Henryk Karkoszka2, Robert Krol3, Andrzej Wieczek1
1Medical University of Silesia, Department of Nephrology. Transplantation and Internal Medicine, Katowice, Poland, 2Medical University of Silesia, Department of General, Vascular and Transplant Surgery, Katowice, Poland

**Background:** Liver transplantation (LTx) is the only successful treatment for end-stage liver disease. Long term results of LTx not only depend upon graft survival but it may be also affected by superimposed cardiovascular morbidities. This single center, retrospective clinical study was aimed to assess the prevalence of lipid disorders in patients before and after successful LTx.

**Methods:** One hundred eleven patients (mean age 49.7±12.2 years) who underwent LTx because of liver cirrhosis and survived at least 2 years with functioning graft were included in this study. The prevalence of dyslipidemia was assessed before and two years after LTx in relation to etiology of liver disease, including alcohol toxicity, viral infections or autoimmune diseases.

**Results:** The prevalence of hypertriglyceridemia before and after at least 2 years after LTx was in the whole studied group 13.5% and 40.5%, respectively (P<0.001). Similarly hypercholesterolemia and hypertriglyceridemia together with hypercholesterolemia was noted before and after LTx in 17.1% and 51.4% (P<0.001) and 7.2% and 27.9%, (P<0.001), respectively. In patients with the autoimmune cause of liver cirrhosis the prevalence of dyslipidemia was significantly lower than in patients with the alcoholic liver disease: hypertriglyceridemia (18.5% vs 66.7%, respectively; P<0.001), hypercholesterolemia (29.6% vs 70.0%, respectively; P=0.002) and hypertriglyceridemia together with hypercholesterolemia (14.8% vs 46.7%, respectively; P=0.008).

1. The prevalence of dyslipidemia is significantly increased in patients after LTx in comparison to the pre-transplant results. 2. High prevalence of dyslipidemia is especially common in patients transplanted due to alcoholic liver cirrhosis and may contribute to the increased risk of cardiovascular complications in these patients.
P181 IMPACT OF HUANG’S CLASSIFICATION ON MANAGEMENT OF BILIARY STRICTURES IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Biliary complications remain the Achilles heel of living donor liver transplantation (LDLT). The anatomical variations in donor biliary anatomy have been shown to impact post-transplant biliary complications. The objective of this study was to assess the frequency of various anatomical variations and rates of successful management in patients who developed biliary complications.

Methods: All patients who underwent a right lobe graft LDLT at our centre between 2012 and 2018 were reviewed. Patients with incomplete data were excluded. Out of these, patients with biochemical and radiological evidence of post-transplant biliary stricture formation were included in the study (n=78). Huang classification was used for identification of graft biliary anatomy. We looked at clinical resolution rate for biliary strictures.

Results: Median age was 53 (14-70) and median follow up was 24 months. Among 78 patients who developed biliary strictures, the right lobe donor anatomy was Huang A1 in 50 (64.1%), A2 in 4 (5.1%), A3 in 16 (20.5%), and A4 in 8 (10.3%) grafts. Only 9 (30.8%) patients needed percutaneous biliary intervention after ERCP. The stricture resolution was seen in 49/50 (98%) patients with A1 biliary anatomy and 100% in A2 and A4 anatomy. Only 14/16 (87.5%) patients had resolution of strictures in the A3 Huang group. Patients in the A3 group required a median of 3 (1-10) ERCPs and 3/16 (18.8%) needed percutaneous biliary drainage.

Conclusions: Huang A3 graft biliary anatomy might be associated with lower rates of stricture resolution requiring multiple endoscopic and percutaneous biliary interventions.

Table 1: The frequency and outcomes in anatomical variants of the biliary system based on Huang’s classification.

<table>
<thead>
<tr>
<th>Anatomical Variant</th>
<th>Frequency</th>
<th>Structure Traversed Number (%)</th>
<th>Median of ERCPs (range)</th>
<th>Percutaneous transhepatic biliary drainage Number (%)</th>
<th>Stricture Resolution Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang type A1</td>
<td>50 (64.1)</td>
<td>43 (86)</td>
<td>04 (1-8)</td>
<td>06 (12)</td>
<td>49 (98)</td>
</tr>
<tr>
<td>Huang type A2</td>
<td>04 (5.1)</td>
<td>04 (100)</td>
<td>2.5(2-4)</td>
<td>00 (0)</td>
<td>04 (100)</td>
</tr>
<tr>
<td>Huang type A3</td>
<td>16 (20.5)</td>
<td>11 (68.75)</td>
<td>03 (1-10)</td>
<td>03 (18.8)</td>
<td>14 (87.5)</td>
</tr>
<tr>
<td>Huang type A4</td>
<td>08 (10.3)</td>
<td>05 (62.5)</td>
<td>03 (1-0)</td>
<td>00 (0)</td>
<td>08 (100)</td>
</tr>
</tbody>
</table>

P183 CLINICAL OUTCOME OF LUNG TRANSPLANTATION IN CONNECTIVE TISSUE DISEASE RELATED INTERSTITIAL LUNG DISEASE

Ala Wool1, Hyeyoung Hong2
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Background: Interstitial lung disease (ILD) is a term for about half of the cause of lung transplantation. Idiopathic pulmonary fibrosis (IPF) is most common idiopathic interstitial pneumonia, other interstitial lung disease also ended to lung transplantation. Connective tissue disease (CTD) may affects the pulmonary system as interstitial lung disease. Although their severity and prevalence differ for each disease, some of them ended to death or lung transplantation. CTD patients are usually accompanied by other comorbidities, and transplantation in those patients is still challenging.

Methods: The electronic medical records of lung transplantation patients from January 2010 to December 2021 are reviewed and analyzed retrospectively. The clinical characteristics of CTD-related ILD (CTD-ILD) were compared with those of IPF.

Results: Total 400 patients underwent lung transplantation during the study period. CTD-ILD (n=61), mean age 51.1 years were younger (P=0.004) than IPF (n=194, mean 29.4) and more like to be female (P<0.01). The myositis (n=17, 27.9%) was most common subtype followed by systemic sclerosis (n=15, 24.8%), rheumatoid arthritis (n=13, 21.3%), Sjögren’s disease (n=11, 18%), and mixed connective tissue disease (n=2, 3.3%). The 5-year survival of transplantation associated CTD-ILD (58.7%) was significantly (p=0.057) different from that of IPF (45.6%). The multivariate cox-regression analysis reveals that the age (Hazard ratio 1.05, P <0.001) at transplantation was associated with the mortality, not the pre-transplantation diagnosis (P=0.302).

Conclusions: The lung transplantation in connective tissue disease-related interstitial lung disease showed comparable clinical outcome with that of idiopathic pulmonary fibrosis.

P184 48HR NORMOTHERMIC MACHINE PERFUSION WITH URINE RECIRCULATION FOR DISCARDED HUMAN KIDNEY GRAFTS: A CASE SERIES

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Background: Normothermic machine perfusion (NMP) has reshaped organ preservation in recent years. Despite great success in liver, lung and heart preservation, the role of NMP in renal transplantation has not been clearly defined. In this preclinical study, prolonged normothermic perfusions of discarded human kidney grafts were performed in order to investigate its feasibility, perfusion dynamics and identify potential quality and assessment indicators.

Methods: Five human discarded kidney grafts were perfused normothermically for 48-hours using the Kidney Assist device with a red-blood-cell based perfusate. For fluid management, urine recirculation was applied. Perfusion dynamics, perfusate and urine composition as well as pro- and anti-inflammatory markers were measured and analyzed.

Results: Donor age ranged from 41 to 68 years. Four kidneys were from brain dead donors, one from a donor after cardiocirculatory death. Four donors died due to a cerebrovascular accident, one due to anoxic brain injury. All kidney grafts were successfully perfused for 48-hours. Median arterial flow ranged from 405 to 841 mL/min. All kidneys excreted urine until the end of perfusion. While sodium levels were consistently lower in urine compared to perfusate samples, this was only seen for chloride and potassium in a single organ (KTX 2). Lactate metabolism was recorded in two organs (KTX 2 and 5). AST, LDH as well as pro-inflammatory cytokines increased over time, especially in kidneys KTX 3 and 4. Injury marker dynamics differed between different donor types and donor history.

Conclusions: Ex-situ normothermic machine perfusion of discarded human donor kidneys is feasible for 48-hours applying urine recirculation. Urine production was achieved throughout the perfusion irrespective of donor demographics. Lactate metabolism, pH and injury marker dynamics in prolonged perfusion might be indicators for organ quality.

Table 1. Demographics

<table>
<thead>
<tr>
<th>KTX 1</th>
<th>KTX 2</th>
<th>KTX 3</th>
<th>KTX 4</th>
<th>KTX 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor Age (years)</td>
<td>62</td>
<td>68</td>
<td>51</td>
<td>41</td>
</tr>
<tr>
<td>Donor type</td>
<td>DBD</td>
<td>DBD</td>
<td>DCD</td>
<td>DBD</td>
</tr>
<tr>
<td>Cause of death</td>
<td>CVA</td>
<td>CVA</td>
<td>CVA</td>
<td>CVA</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.9</td>
<td>1.06</td>
<td>1.17</td>
<td>1.98 (RRT)</td>
</tr>
<tr>
<td>CIT total (hours)</td>
<td>27</td>
<td>19.5</td>
<td>19</td>
<td>28</td>
</tr>
<tr>
<td>Reason for discard</td>
<td>malignancy</td>
<td>poor organ quality</td>
<td>poor perfusion</td>
<td>poor perfusion</td>
</tr>
<tr>
<td>Remuzzi Score</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meier cumulative survival curves for idiopathic pulmonary fibrosis (IPF) and connective tissue disease-related interstitial lung disease (CTD-ILD)
Background: AB0 incompatible kidney transplantation has become a genuine treatment method for end-stage renal disease. Non-inferiority in the long-term graft function compared to AB0 compatible transplantation has been shown. However, the assumed burden due to complications owing to increased immunosuppression inherent to AB0 incompatible transplantation has not yet been quantified. The aim of this study was to determine if AB0 incompatible recipients have additional morbidity and whether this burden is justified or whether kidney paired donation programs should be advocated.

Methods: From January 2000 to March 2020 45 AB0 incompatible living kidney transplantation were performed at a tertiary care hospital. Patients were matched with AB0 compatible recipients according to sex, age, underlying disease, year of transplantation and duration of dialysis. Number and duration of readmissions, surgical complication rates according to Clavien-Dindo and its comprehensive complication index (CCI), kidney function, occurrence of new onsets of diabetes and tumours were assessed.

Results: Readmission rate during the time span from transplantation to March 2020 was not significantly higher in AB0 incompatible recipients. The median time of hospital stay for readmissions CCI during primary hospital stay and CCI for readmissions at 3, 6, 12 and >12 months after transplantation were comparable. Incidence of tumour and new onset diabetes after transplantation were also comparable. Incidence of tumour and new onset diabetes after transplantation were also comparable. Incidence of tumour and new onset diabetes after transplantation were also comparable.

Conclusions: AB0 incompatible recipients do not suffer from a higher burden compared to AB0 compatible recipients. We currently recommend not delaying transplantation in AB0 incompatible pairs.

**PLASMA FGF21 CONCENTRATION IN KIDNEY TRANSPLANT RECIPIENTS**

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1Medical University of Silesia, Department of Nephrology, Transplantation and Internal Medicine, Katowice, Poland

Background: Fibroblast growth factor 21 (FGF21) is a protein hormone involved in the regulation of energy expenditure. Results of clinical studies suggest that plasma FGF21 concentration increases with the progression of chronic kidney disease (CKD). The aim of the present clinical study was to analyze the effect of successful kidney transplantation (KTx) on plasma FGF21 concentration and to study the factors related to plasma FGF21 concentration in patients long-term after KTx.

Methods: The first part of the study, i.e. the 6 months prospective observation, included 40 CKD patients directly before KTx [26 women and 14 men aged 47.0 (39.2 – 54.0) years]. In the second part of the study 184 patients long-term after KTx [72 women and 112 men aged 52.0 (48.0 – 54.0) years] and 50 healthy subjects (HS) [28 women and 22 men aged 52.0 (48.0 – 58.0) years] were enrolled.

Results: In CKD patients directly before KTx plasma FGF21 concentration were significantly higher than in HS [1013.0 (689.6-1635.8) pg/ml vs 239.5 (219.0-294.5) pg/ml respectively, p<0.001]. At 14, 30 days and 6 months after KTx, a significant decrease of plasma FGF21 was observed [322.5 (197.3-579.6) pg/ml; 355.0 (268.5-547.6) pg/ml; 344.0 (264.1-405.6) pg/ml (p<0.001), respectively]. In patients long-term after KTx, a negative correlation was found between plasma FGF21 concentration and estimated glomerular filtration rate and a positive correlations between plasma FGF21 concentration and BMI and serum concentration of triglycerides, insulin, interleukin 6, CRP and cystatin C.

Conclusions: Plasma FGF21 concentration in CKD patients measured directly before KTx is higher than in HS. 2. Successful KTx leads to a significant decrease of plasma FGF21 concentration 2. Plasma FGF21 concentration in patients long-term after KTx is related to the degree of graft function impairment and degree of metabolic abnormalities of these patients.

**PROGNOSTIC BIOMARKERS IN KIDNEY TRANSPLANTATION: A META-EPIDEMILOGICAL STUDY**

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1Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France

Background: Despite the increasing number of biomarkers studies published in the transplant literature for the past 20 years, very few have proved clinical benefit and have been implemented in clinical practice. We hypothesized that suboptimal design, data, methodology and reporting might have contributed to this phenomenon. Our goal was to perform a meta-epidemiological study of the prognostic biomarker studies in kidney transplantation.

Methods: We formed a consortium of experts in systematic reviews, nephrologists and methodologists. A systematic literature search was performed in PubMed, Embase, Scopus, Web of Science, and Cochrane Library between 2005 and 2022. All original studies investigating the association between a biomarker and kidney-allograft failure were included. Any uncertainty in the full text assessment was resolved through weakly group discussions. Reviewers performed the critical appraisal for each study, identified the key domains, and scored the risk of bias of each study using: i) study basic characteristics, ii) transparency indicators, and parameters related to iii) the biomarker, iv) methods, v) results, vi) results interpretation.

Results: A total of 7,372 publications were screened and 804 studies met the inclusion criteria. A total of 1143 biomarkers were identified among the included studies. Most biomarkers were from blood (n=821, 71.8%), intra-graft (n=169, 14.9%), or urine (n=81, 7.1%). The number of studies per year was increasing. The top three countries in terms of publications were the USA (n=168 studies, 20.9%), France (n=66, 8.2%), and Germany (n=54, 6.7%). The median number of patients included was 232 (IQR: 96-629). The median follow-up post-transplant was 4.8 years (IQR: 3.0-6.2). 595 studies (74.0%) used data from a single center. Only 38 (4.7%) studies were externally validated. 346 studies (43.0%) did not adjust their biomarker for key prognostic factors. Data sharing, code sharing, and registration occurred in 71 (8.8%), 9 (1.1%), and 37 (4.6%) studies, respectively. 158 studies (20.0%) emphasized the clinical relevance of the biomarker while non-significant.

Conclusions: Biomarker kidney transplant studies lack validation, rigorous design, methods and interpretation, and transparency. Higher standards are needed for biomarker research.

**INCREASED TACROLIMUS TROUGH LEVELS IN KIDNEY TRANSPLANT RECIPIENTS WITH COVID-19**

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1Issad Hassan University Hospital, Algiers, Algeria, 2Faculty of pharmacy - University of Algiers 1, Algiers, Algeria

Background: Kidney transplant recipients (KTRs) with coronavirus disease-19 (COVID-19) have similar clinical manifestations to general population. However, KTRs are more vulnerable to develop severe forms and the mortality rate is higher in this category compared to general population, this is due partly to the use of immunosuppressive agents. The variability of tacrolimus levels in KTRs is to determine the impact of COVID-19 infection on tacrolimus trough concentrations (C0) in KTRs.

Methods: In this single-center retrospective observational study, data were collected from patient medical records, and therapeutic drug monitoring data. Tacrolimus trough concentrations (C0) in KTRs measured directly before KTx was 4.8 years (IQR: 3.0-6.2). 595 studies (74.0%) used data from a single center. Only 38 (4.7%) studies were externally validated. 346 studies (43.0%) did not adjust their biomarker for key prognostic factors. Data sharing, code sharing, and registration occurred in 71 (8.8%), 9 (1.1%), and 37 (4.6%) studies, respectively. 158 studies (20.0%) emphasized the clinical relevance of the biomarker while non-significant.

Conclusions: Biomarker kidney transplant studies lack validation, rigorous design, methods and interpretation, and transparency. Higher standards are needed for biomarker research.
THE OUTCOMES OF FISTULA TRACT EMBOLIZATION FOR ANASTOMOTIC BILIARY LEAKAGE AFTER LIVING DONOR LIVER TRANSPLANTATION

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Methods: We retrospectively reviewed the medical records of patients who underwent LDLT in Seoul National University Bundang Hospital between March 2012 and December 2021. When post-transplant bile leak developed at the biliary anastomosis site, we usually inserted PCD for intra-abdominal bile collection and placed biliary stent at leakage site through the endoscopic or transhepatic approach. Although PCDs were removed after bile leakage was resolved, we also tried to remove PCD early after fistula tract embolization in some patients with a high output bile leakage if the controlled fistula tract was formed. We investigated the outcomes of this strategy.

Results: Among 118 LDLT patients, bile leak occurred in 12 (10.2%) patients. All patients with bile leak received endoscopic or radiologic interventions for biliary stenting and 9 patients (75%) also needed PCD insertion. In 4 patients, PCDs were removed after bile leak was resolved. However, 5 patients (55.5%) had a lasting amount of bile leakage before removal of PCD. The median amount of bile leakage right before PCD removal was 20(1.5-165)cc/day Those patients had PCD during 22 days of the median duration before removal. The internal biliary stents were removed endoscopically 1-3 months after PCD removal. In this treatment strategy, there were neither severe complications and nor recurrent bile leak requiring re-insertion of PCD.

Conclusions: This case series shows that PCD for bile leakage after LDLT could be removed early with tract embolization following internal stent insertion. It does not increase the morbidity of patients and can improve their quality of life. However, because this study was just case series with small number of patients, the results should be validated with large scale studies.

Fig 1. Fistulogram and embolization

DONORS’ AGE MODIFIES THE IMPACT OF PRE-DONATION ESTIMATED GLOMERULAR FILTRATION RATE ON CENSORED GRAFT SURVIVAL

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1Centro Hospitalar Universitário do Porto, Nephrology and transplantation, Porto, Portugal. 2Instituto Português de Sangue e Transplantação, Porto, Portugal. 3Centro Hospitalar Universitário do Porto, Urology, Transplant Unit, Porto, Portugal

Background: A living donor (LD) kidney transplant (KT) is the preferred treatment for ESRD, but not all LD organs are equal. We sought to evaluate the effects of clinical characteristics of LD associated with worse graft outcomes in our cohort, namely age, pre-donation estimated glomerular filtration rate (eGFR), hypertension, dyslipidemia, smoking, proteinuria, and obesity.

Methods: We studied 352 recipients (R) of LDKT from 1998 to 2020, followed until death, graft failure (GF), or attaining 15 years (Y) of follow-up. Firstly, considering R and KT variables, we identified independent predictors of censored (GF) control by eGFR through a stepwise analysis with backward elimination of variables with a P-value ≥0.05. Then, adjusting for these predictors, we explored the aforementioned LD variables as predictors of censored GF in a multivariable model. Lastly, using the same model, we analyzed the interaction between eGFR and LD age categories for the prediction of censored GF.

Results: Most of the R were males (67%), with a mean age of 40.4±13.8 Y. The R from LD with higher eGFR (>90) were significantly younger (36.8±13 vs 43.1±14.6, p=0.04) and had significantly better-censored graft survival (GS) at 15y after KT (75% vs 46%, p<0.001). In younger LD (age <50), R from LD with eGFR<90 experienced the greatest risk of CGF, with adjusted HR (95% CI) of 3.370 [1.362-8.343], compared to recipients from LD with eGFR>90. Differently, when LD were older (age ≥50), no difference in the risk of GF was observed between eGFR categories [eGFR<90 vs ≥90: adjusted HR 1.661 (0.623-4.429)]. The longitudinal pattern of graft function by LD eGFR and age showed, since the first years after KT in R from younger D, significant differences between those with lower and higher eGFR while that differences did not hold in R from older LD. Importantly, none of the remaining LD factors evaluated were independent predictors of CGF.

Conclusions: In our cohort, pre-donation eGFR was associated with post-KT outcomes but LD’s age significantly interacted with this effect. Only in younger LD had an eGFR<90 impact on GS drawing attention to the need for an age-adjusted eGFR cutoff for LD admissibility. The dissimilarity in outcomes driven by pre-donation renal function between younger and older LD may result from different pathophysiologic mechanisms being measured as eGFR.
and >9) as determined by the 2019 Banff classification. The chronicity index is
years) were divided into three groups based on their chronicity index (1-4, 5-8,
A total of 43 patients (24 males, 19 females, average age 47.0 ±14.5
Methods:
who underwent biopsy.

determine the significance of urinary VSIG4 levels in kidney transplant patients
inflammation and drive epithelial-mesenchymal transition in various diseases.
The protein V-set Ig domain-containing 4 (VSIG4) has been found to regulate
changes in the transplant kidney. Given the relationship between the chronicity
index and allograft loss, the levels may serve as a marker for graft outcome.

Conclusions:

In conclusion, urinary VSIG4 levels are associated with chronic
changes in transplant kidneys. Given the relationship between the chronicity
index and allograft loss, the levels may serve as a marker for graft outcome.
**EARLY RESULTS OF A SCREENING PROGRAM FOR SKIN CANCER IN LIVER TRANSPLANT RECIPIENTS: A COHORT STUDY**

Delal Akdag¹, Allan Rasmussen¹, Susanne Dam Nielsen¹, Dina Leth Møller², Katrine Togdverd-Bo³, Emily Wenande¹, Merete Haddersdal¹, Hans-Christian Pommergaard¹

¹Rigshospitalet, Department of Surgery and Transplantation, Copenhagen, Denmark, ²Rigshospitalet, Department of Infectious Diseases, Copenhagen, Denmark, ³Bispebjerg and Frederiksberg Hospital, Department of Dermatology, Copenhagen, Denmark

**Background:** Skin cancers are the most common type of cancers reported in liver transplant recipients with greatly increased risk compared to the general population, likely due to immunosuppressive treatment. Timely and regular dermatological assessment may reduce rates of advanced skin cancer. However, evidence for use of screening programs in liver transplant recipients is lacking. The aim of the study was to describe the early results of a screening program for skin cancer in Danish liver transplant recipients initiated in 2018.

**Methods:** In this prospective cohort study, we included liver transplant recipients enrolled in a skin cancer screening program four years after initiation (January 1st, 2018 to December 31st, 2021) in our center. Overall prevalence and incidence of skin cancer and preneoplastic lesions were determined. Risk factors were assessed using Cox-regression analyses.

**Results:** Of 245 liver transplant recipients, 219 (89.6 %) were referred to a screening program for skin cancer at a specialized dermatological department. In 32 (15.4 %) liver transplant recipients, 118 skin cancers / preneoplastic lesions were diagnosed during the screening period. The incidence rate of skin cancer / preneoplastic lesions was 100.3 per 1000 person-year. Age at transplantation and time since transplantation were independently associated with increased risk of skin cancer / preneoplastic lesions.

**Conclusions:** Early results from a screening program for skin cancer in liver transplant recipients demonstrated a high referral rate to dermatological assessment with a prevalence and incidence comparable to the literature. Later data with additional follow-up is needed to provide more insight into the effects of the screening program.

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**SYSTEMATIC REPORTING AND INVESTIGATION OF POSSIBLE INFECTION OF DONOR ORIGIN IN DECEASED ORGAN DONATION IS ESSENTIAL FOR BEST TRANSPLANTATION PRACTICE**

Ines Ushiro-Lumb⁴, Olive Mcgowan¹, Derek Manas¹, Richard Baker¹

¹NHS Blood and Transplant, Organ and Tissue Donation and Transplantation, London, United Kingdom

**Background:** Post-transplant events that may have an impact on allograft recipients must be centrally reported to our national organ donation and transplantation organisation; this should be done as soon as a donor-related transmission event becomes a possibility. Notification triggers prompt dissemination of information to transplant centres and initiates a systematic investigation. A report with findings, actions, and recommendations is essential; co-operation from all stake holders and a multi-disciplinary approach are key to improved practice and better patient outcomes.

**Methods:** The outcome of extensive investigations over a period of 10 years, where donor-derived transmission of infection was deemed to be possible, probable, or proven is hereby summarised. The methods used may vary depending on the pathogen involved, and good knowledge of the specific disease process is required.

**Results:** During this period 14,949 donors enabled 38,380 organ transplants, with an approximate 0.3% rate of donor-related transmission of infection events per proceeding donor. The agents most implicated were Human Herpes Viruses, mainly herpesvirus type 1, 2, and 8, followed by Hepatitis E Virus (table 1); of note, herpesvirus type 8 alone was responsible for a quarter of all cases and was the most frequent imputable pathogen. Cases where the donor was excluded as possible source of infection in the recipient, or where imputability could not be ascertained, are not included in this summary.

**Conclusions:** Although infrequent, unintended transmission of infection of donor origin may be associated with significant recipient morbidity and mortality. It is essential that all those involved in organ donation and transplantation remain attentive to potential occurrences, so that they can be detected, notified, and appropriately managed. Critical analysis of these events is important for the identification of possible deficiencies, need for change and learning. In our practice, this is continuously used to inform best practice and guidance.

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Table 1: Number of events investigated (2012-2022) and the corresponding implicated infectious agent, where recipient infection of donor origin was classified as proven, probable, or possible.

<table>
<thead>
<tr>
<th>Implicated Organism</th>
<th>Imputability grade</th>
<th>Proven</th>
<th>Probable</th>
<th>Possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida albicans</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
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Note: Figures denote number of events investigated and not number of recipients involved in each event.

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**Factors that Influence the Development and Implementation of Prehabilitation for Kidney Transplant Candidates: A Mixed-Methods Contextual Analysis**

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**Background:** The overall fitness of kidney transplant candidates (KTCs) is often compromised due to chronic kidney disease, comorbidities and dialysis. Prehabilitation, comprised of exercise, nutritional and psychological interventions, may be an effective way to improve the overall fitness of KTCs. However, implementation of a multicomponent intervention is challenging. This study aimed to gain insight into contextual and implementation related factors that are of influence on the development and implementation of prehabilitation for KTCs.

**Methods:** A contextual analysis using the Context and Implementation of Complex Intervention Framework was performed to gain a deeper understanding of current practices, preferences, possible barriers and facilitators for prehabilitation by using qualitative and quantitative methods. In-depth interviews (n=22) and focus group meetings (n=7) were performed with KTCs, their significant others, kidney transplant recipients and healthcare providers (HCPs). In addition, a survey (n=87) was conducted among waitlisted KTCs.

**Results:** In current practice, care for KTCs has a medical focus. In addition, dieticians and social workers are often involved. Both KTCs and HCPs indicated that little attention is paid to physical activity. Ninety-two percent of the KTCs encountered one or more problems regarding physical activity, nutritional status and/or psychological wellbeing. Perceived barriers to engage in healthy lifestyle behaviors were mainly fatigue and a lack of motivation and/or knowledge. Perceived facilitators included social support and guidance from a healthcare professional. Furthermore, 79% of the KTCs indicated that they felt the need for a prehabilitation program, in which 73% would like to improve their strength and endurance, 48% to obtain a healthy nutritional status and 30% to cope with stress and fatigue. The majority of KTCs (64%) preferred a personalized, home-based-training program, with guidance from a healthcare professional.

**Conclusions:** The high percentage of KTCs encountering physical and psychological problems, the limited attention for physical activity in current practice and the felt need for prehabilitation, suggests that prehabilitation may be a promising intervention to improve the overall fitness of KTCs before transplant.

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**Vigilance Data in Organ Donation and Solid Organ Transplantation in Germany: Donor-Derived Disease Transmission from 2016-2022**

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**Background:** Diligent reporting and analysis of all serious adverse event (SAE) and serious adverse reaction (SAR) cases can help to identify risks of transmitting donor-derived disease to transplant recipients. The German organ procurement organization (Deutsche Stiftung Organtransplantation – DSO) is the delegated body assigned by the German Federal Ministry of Health responsible for the management of the national SAE/SAR system.

**Methods:** A team of qualified physicians of the DSO analyzed all SAE and SAR reported from January 1st 2016 to December 31st 2022. In case of a possible transmission of a disease to one or more recipients, an assessment of imputability was done according to the grading system of the US Disease Transmissions Advisory Committee (DTAC).

**Results:** Between 2016 and 2022, 21060 organs were transplanted from 8519 donors. In the same period, the DSO received 543 SAE/SAR reports. 52 of the 543 reports (9.6%) were proven or probable (P/P) transmissions of infectious diseases, malignancies or other diseases to 74 recipients. 17 of 74 (17/74; 23%) recipients died due to the transmitted disease. Infections were the most frequently reported P/P disease transmission occurrences (26/52; 54%). 16 cases (16/52; 31%) were P/P transmissions of malignancies to 22 recipients resulting in 11 attributable deaths (11/22; 50%).

**Conclusions:** Donor-Derived disease transmission is a rare event (52/8519; 0.6%), but when it occurs can lead to significant morbidity and mortality, especially when malignant diseases are transmitted. Reporting of SAE and SAR can identify possible risks in organ donation and solid organ transplantation and help to improve donor characterization and to increase awareness of transmission events.

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**Pre-Transplant Proportions of Polyfunctional Donor-Reactive T Cells Are Associated With Acute T-Cell Mediated Rejection of the Kidney Transplant**

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**Background:** Acute T-cell mediated rejection (aTCMR) still remains a clinical problem after kidney transplantation despite significant improvements in immunosuppressive regimens. Polyfunctional T-cells, i.e. T-cells producing multiple pro-inflammatory cytokines, are believed to be the most relevant T-cells in an immune response. The aim of this study was to determine whether pre-transplant proportions of polyfunctional donor-reactive T-cells are associated with aTCMR.

**Methods:** In a case-control study, 49 kidney transplant recipients with a biopsy-proven aTCMR in the first year after transplantation were included, as well as 51 controls without aTCMR. Circulating donor-reactive T-cells were identified by the expression of CD137 amongst CD8 T-cells being a short-term co-culture with donor antigen-presenting cells. Proportions of interleukin (IL)-2, tumor necrosis factor (TNF)-α and interferon (IFN)-γ cytokine-producing cells and combinations thereof were determined. Polyfunctional donor-reactive T-cells were further characterized by dissection into different T-cell subsets encompassing the spectrum of naïve to terminally-differentiated effector T-cells.

**Results:** Prior to kidney transplantation, proportions of donor-reactive CD4+ (0.03% versus 0.02%, P=0.01) and CD8+ (0.18% versus 0.10%, P=0.01) CD137high-expressing (CD137++) T-cells were significantly higher in recipients with a biopsy-proven aTCMR versus non-rejectors. Polyfunctionality was highest (P=0.03) in this subset of CD137-expressing T-cells. These cells were predominantly of the EM/EMRA-phenotype, with polyfunctional donor-reactive CD137++CD4+ T-cells predominantly co-expressing CD28 whereas approximately half of the polyfunctional CD137++CD8+ T-cells co-expressed CD28. In addition, at the time of aTCMR, polyfunctional donor-reactive CD137++CD4+, but not CD8+ T-cells, were specifically decreased by 75% compared to before transplantation in recipients with as well as those without an aTCMR.

**Conclusions:** Prior to transplantation, the proportion of polyfunctional donor-reactive CD137++ T-cells is associated with the occurrence of a biopsy-proven aTCMR within the first year after transplantation.
Expression of activation-induced markers (AIMs) after T-cell receptor-mediated activation is used to identify alloreactive T cells but whether these markers recognize similar subsets of alloreactive T cells is largely unknown. 

Methods: Alloreactive T cells were characterized following a short-term co-culture of responders peripheral blood mononuclear cells (PBMCs) with allogeneic CD3-depleted PBMCs or autologous CD3-depleted PBMCs as a negative control (background signal). T cells were analyzed by multi-parameter flow-cytometry using a combination of monoclonal antibodies directed to commonly used AIMs (CD69, CD134, CD154 and CD137) and CD45RA and CCRI for T cells subset analysis (naive, central memory (CM), effector memory (EM) and terminally differentiated CD45RA-expressing effector memory (EMRA)). Both supervised and unsupervised data analysis (FlowSOM) were performed.

Results: Median proportions of CD137, CD134 and CD134 total (including single as well as co-expressing other AIMs) alloreactive CD4 T cells amounted to 0.34%, 0.52%, 0.16%, respectively with a low background signal. CD69 expression on CD4+ T cells was high (median 4.16%) with a substantial background (median 3.24%). CD137 expression was preferentially found on EM (P<0.05) while CD154 and CD134 were preferentially found on CM cells (P<0.05). Of all CD137-expressing CD4+ T cells 36.3% were EM versus 19.6% and 7.1% for CD137- and CD154-expressing CD4+ T cells, respectively, with minimal overlap between EM alloreactive CD4+ T cells identified by different AIMs. Proportions of alloreactive CD4+ T cells co-expressing AIMs (59%) were higher in the CM subset when compared to single-AIM expressing (47%) (P<0.05). Alloreactive CD8+ T cells can be best detected using CD137, as CD134 and CD154 were preferentially found on CM cells (P<0.05). Of all single CD134+ T cells 40% were EM versus 21% CD134 and 12% CD134-expressing CD4+ T cells, respectively, with minimal overlap between EM alloreactive CD4+ T cells and CM alloreactive CD4+ T cells when compared to single-AIM expressing (47%) (P<0.05). Alloreactive CD8+ T cells can be best detected using CD137, as CM and CD154 were hardly expressed.

Conclusions: AIMs are differentially expressed according to the differentiation status of alloreactive CD4+ T cells but in general overlap between these different AIMs is surprisingly low. Identification of alloreactive CD4+ T cells by AIMs should therefore include at least CD137, CD134 and CD154.
MICROSURGICAL ANASTOMOSIS BETWEEN LOWER POLAR ARTERY AND INFERIOR EPIGASTRIC ARTERY IN KIDNEY TRANSPLANT: SINGLE CENTRE EXPERIENCE

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Background: The reported incidence of multiple renal arteries (MRA) is approximately 20%, and roughly 6% of them are lower polars arteries (LPA). The LPA supplies the upper urinary tract, therefore at kidney transplantation (KT) reconstruction of LPA is essential to avoid necrosis of the ureter. Among the possible reconstructive techniques for LPA, its anastomosis with recipient’s inferior epigastric artery (IEA) has been seldomly described in literature, with approximately 10% experiencing vascular or urological complications such as arterial thrombosis, partial infarction, urinary fistula, and graft loss.

Methods: Single-centre retrospective analysis of 9 KTAs (7 living donors, 2 deceased donors) with LPA-IEA anastomoses, focused on postoperative complications, and patient and graft survival. The IEA was exposed before approaching recipient’s iliac vessels. The LPA-IEA anastomosis was performed after main vessels were anastomosed and declamped, thus reducing ischemic time according to sequential reperfusion technique. The LPA-IEA anastomosis was performed end-to-end with 7-0 Prolene single stitches, using 5x magnifying loupes with glasses. Doppler US was performed intraoperatively, before discharge, and at follow-ups (FU) with blood exams.

Results: Recipients’ demographics: average age and BMI respectively 45 ± 5 years and 26 ± 5.4 males and 5 females, all ABO compatible (A=4, AB=2, B=2, O=1). Average FU was 76.3 months (4-139). Neither vascular complications nor ureter necrosis occurred. Other complications: acute rejection treated with steroids (n=1), delayed graft function (n=1), lymphocele (n=1). Patient and graft survivals were 100% at most recent FU, and mean creatinine levels within acceptable range.

Conclusions: Reconstruction of LPA is mandatory in KTAs. The LPA-IEA anastomosis, when accurately performed (i.e., microsurgical technique), carries excellent and durable results.

INTRAOPERATIVE MEASURES OF VASCULAR FLOW IN LIVER TRANSPLANT. WHAT CAN THEY REALLY FORESEE?

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Background: The increase in orthotopic liver transplantation (OLT) along with the organ shortage calls for success in every transplant we perform. The goal of our study is to determine the relation between hepatic artery and portal vein flows and the complications in short and large term outcomes.

Methods: A retrospective observational unincentric study was performed, including 126 OLT patients between January 2019 and October 2022. Factors recorded included: demographic characteristics, comorbidities of the recipient, intraoperative variables, postoperative morbidity and mortality and graft and patient survival. Following successful implantation and at point of hemodynamic stability hepatic artery and portal vein flows were measured. Qualitative measures were described using frequencies and percentages. Quantitative measures were expressed as mean ± standard deviation (SD) or median and interquartile range. For the statistical analysis we used Student’s t and Mann-Whitney U tests and Spearman correlation value. Results were considered significant when the corresponding p-value was less than 0.05.

Results: A total of 126 patients were included with a median follow up of 12 months. The mean hepatic artery flow (HAF) was 351 ml/min whereas the portal vein flow (PVF) was 1750 ml/min. Neither HAF, PVF, nor the length of stay in intensive care unit or hospitalization show a significant correlation. Also, biliary, suprarenal or portal complications were not affected by HAF or PVF. However, the HAF was statistically significant (P= 0.005) for the arterial complications. There were differences between allograft and patient survival after 3, 6 and 12 months considering PVF as a significative predictor. Similarly, PVF was also a significative predictor of reoperations, with a percentage in our sample of 20.64%. The mortality rate was 15.08%.

Conclusions: According to our results PVF is a reference standard that can statistically significantly predict patient and graft survival at 3, 6 and 12 months after OLT. More prospective and larger studies are required in order to establish a cutoff point in PVF that can serve us as guidance to achieve better results in every OLT.

PATIENTS’ EXPERIENCES OF PATHWAY CARE AFTER KIDNEY TRANSPLANTATION: FINDINGS FROM AN ITALIAN ETHNOGRAPHIC RESEARCH

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Background: Adherence to immunosuppressive therapy is essential in patients who have received a kidney transplant to prevent organ failure. Therefore, it is crucial to consider the patient’s perspective to recognize the factors that compromise a patient’s adherence to treatment. This qualitative ethnographic research has aimed to identify the possible factors that may promote or, conversely, may impact “adherent” behavior, such as unmet needs, to benefit the supportive care process for transplant patients.

Methods: Twelve adult patients receiving transplant in the previous two years were interviewed via face-to-face video recording at a time and place based on participants’ preferences. The interviews were conducted using a semi-structured approach to collect and analyze cultural meanings associated with the condition and its treatment, with a focus on how patients behaved during immunosuppressive therapy. A thematic analysis of the interview texts was to find common themes within the data by identifying interpretable categories and subcategories about the organization, clinical and psychological care and relational and social factors, and was performed by expert researchers.

Results: Two main categories of patients were identified, depending on whether the illness was viewed as a part of the person’s identity or as an “alternate” stage of life relative to “regular” life. Patients who view their illness as an identifying attribute are more likely to “normalize” it as an essential component of who they are. The transplant recipients were generally satisfied with their transplant education, but they identified communication gaps in all areas of the transplant process, including the transplant waitlist, surgery, life changes post-transplant and immunosuppressive therapy and its effects/consequences. The main categories of unmet needs by the current assistive care process for transplant care are needs related to self-awareness, for information on the disease and lifestyle. Moreover, there emerged the need for patients to receive better psychological support and communication with HCPs.
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MESENCHYMAL STEM CELLS INFUSION DURING LIVER RESECTION AND TRANSPLANTATION – REGENERATION AUGMENTATION AND IMMUNE MODULATION: CASE REPORT

Denis Efimov*, Alakssei Shcherba, Sergey Korotkov, Leanid Kirsukov, Alia Symonovich, Evgeniya Primakova, Paul Bychkovskiy, Olga Lebedz, Svetlana Krivenko, Oleg Rummo

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Background: Mesenchymal stem cells (MSCs) have been demonstrated exciting therapeutic effects in drug-induced liver failure, while only a few studies have been reported in liver surgical models. We have previously shown that intraportal local infusion of allogeneic adipose tissue MSCs during liver transplantation (LT) is safe and feasible with promising immunomodulatory effect.

Case description: The patient M., 54 yo, was diagnosed with right liver lobe mass (histologically – alveococcosis) required right extended hemihepatectomy and pressure gradient decrease (from 12 to 3 mmHg), no clinical improvement was observed. On the 45th postoperative day (POD) after LR, left hepatic vein stenosis (pressure gradient 28 mmHg) was revealed; successful endovascular stent placement was performed. On the 178 POD, inferior vena cava (IVC) stenosis (just before the entrance in the right atrium) with Budd-Chiari syndrome was diagnosed. Despite successful endovascular IVC stent placement and pressure gradient decrease (from 12 to 3 mmHg), no clinical improvement was happened and subsequent deterioration of portal hypertension (ascites, esophageal varices) was observed. The patient was listed on LT. 10 months after LR, LT was performed (intraoperative features: 20 l of ascites, pericardotomy for upper caval anastomosis; bloodloss 3 l). Due to the high risk of acute kidney injury and infectious complications, an alternative immunosuppressive therapy was provided with future liver remnant of 14%, demanded ALPPS procedure. To augment liver regeneration, intraportal infusion of 20 million MSCs into the left portal vein during the 1st and 2nd stage of ALPPS procedure was performed (FLR volume increased by 84% between LR stages; posthepatectomy liver failure was not observed). On the 45th postoperative day (POD) after LR, left hepatic vein stenosis (pressure gradient 28 mmHg) was revealed; successful endovascular stent placement was performed. On the 178 POD, inferior vena cava (IVC) stenosis (just before the entrance in the right atrium) with Budd-Chiari syndrome was diagnosed. Despite successful endovascular IVC stent placement and pressure gradient decrease (from 12 to 3 mmHg), no clinical improvement was observed. On the 45th postoperative day (POD) after LR, left hepatic vein stenosis (pressure gradient 28 mmHg) was revealed; successful endovascular stent placement was performed.

Conclusions: The results suggest that it is relevant improving HCPs attention to patients’ psychosocial, communication and relational needs and might become integral for improving patient transplant outcome.
P213  AWARENESS CAMPAIGN FOR ORGAN DONATION THROUGH SOCIAL MEDIA AND PODCASTS: AN INNOVATIVE APPROACH

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Background: Organ donation is a critical aspect of healthcare and raising awareness on its importance is crucial to increase the number of donors. Despite its importance, there is often a lack of public awareness and understanding of the process. This project aimed to increase awareness of organ donation through a multi-faceted communication campaign utilizing a web site, social media and podcast.

Methods: The campaign was designed to target a broad audience (people 25-54 years) and provide accessible, engaging information on organ donation. Social media platforms (Facebook, Instagram) were utilized to spread awareness and promote educational content, through infographics, questions and answer and emotional videos. A podcast series was also produced, featuring interviews with transplant medical experts, organ living donors, and recipients. A transplant stories’ patients tell themselves and by a famous Italian artist were used to convey the message in a podcast format. The impact of the awareness campaign was evaluated based on the number of listeners, time spent listening of the podcast, and web site visualization and social media followers.

Results: The focus of the communication campaign was on the important role of donors (“Anonymous Heroes”) and the public calling “Are you ready to save a life?”. The number of podcast listeners was over 15,300. The average time spent listening to the podcast was over 80% indicating high engagement and interest among the listeners. Podcast series reached 6th position nationwide among all podcasts in the health and wellness category. Furthermore, a web site visits, from June 2020 to January 2023, around 40,000 and 953,774 people has reached from social. In the same period in Italy, thanks to all communication campaigns, donation declarations of willingness to donate has reached the largest absolute number of consents.

Conclusions: This approach highlights the potential of social media and podcast as effective tools for increasing public awareness and understanding of organ donation. The use of transplant patient stories and famous artists can help to personalize and amplify the message, leading to greater engagement and impact.

P214  HORMONAL PROFILE OF FEMALES INFLUENCES INTESTINAL REPERCUSSIONS IN POTENTIAL BRAIN-DEAD DONORS

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Background: Female donors’ organs have been associated with worse prognostics after transplant, which seems to be associated with the hormonal imbalance produced by brain death (BD). Female sex hormones are known to regulate the inflammatory response. As such, here we investigated the effects of previous sex hormones reduction, like menopause, on gut inflammation using a BD model in female rats.

Methods: Female Wistar rats were separated in 4 groups: BD - high estradiol concentration rats (proestrus phase to heat period) underwent BD and were maintained for 6h, BD-OVx - ovarioctomized rats (10 days before BD induction day) and underwent BD (6h), Control - non-manipulated rats, Control-OVx - ovarioctomized rats not submitted to BD. Serum was analyzed for VEGF, TNF-α, IL-1β, IL-6 and MIP-1α concentrations. Intestine was removed for histopathological analysis; analysis of neutrophil presence/activity (myeloperoxidase - MPO) and microvascular permeability. Mesentery was exposed for blood flow analysis, and sampled for immunohistochemistry and PCR analysis (eNOS, iNOS and ET-1).

Results: Both BD and BD-OVx had greater intestine leukocyte infiltration (BD: 0.23±0.01, BD-OVx: 0.23±0.02, Control: 0.16±0.01, Control-OVx: 0.13±0.01). Reduction of villus height (BD: 388.9±18.1, BD-OVx: 348.7±19.6, Control: 453.1±31.1, Control-OVx: 433.1±20.9 µm; P=0.03) and increased MPO activity compared to respective controls, accompanied by the increase of serum TNF-α, IL-1β, IL-6 and MIP-1α concentrations. Intestine was removed for histopathological analysis; analysis of neutrophil presence/activity (myeloperoxidase - MPO) and microvascular permeability. Mesentery was exposed for blood flow analysis, and sampled for immunohistochemistry and PCR analysis (eNOS, iNOS and ET-1).

Conclusions: BD produced a systemic inflammation that altered intestine integrity in female rats. Menopause-like model (ovariectomy) had greater villus injury associated with iNOS increase, besides BD induced acute drop of female hormones has worsened the intestinal edema. Grant 2023/00728-S, 2021/13020-6, São Paulo Research Foundation (FAPESP).
DONOR-DERIVED CELL-FREE DNA AND GENE EXPRESSION PROFILE IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Background: Rejection is the major cause of graft failure after pancreas transplantation, but pancreas biopsy is a risky technique. Molecular biomarkers, such as donor-derived cell-free DNA (dd-cfDNA) and gene expression profile (GEP), have emerged as an alternative to monitor graft rejection in other solid organ transplants. We hypothesized whether these techniques could complement the non-invasive diagnostic performance of currently available biomarkers of pancreas graft dysfunction.

Methods: We performed a longitudinal analysis of samples from 38 pancreas transplant recipients. Plasma was collected in PaxGene tubes pre-transplant, and afterwards at 1h, 24h and 7 days post-transplant, and at time of pancreas biopsy – either per protocol at 3 weeks and 12 months, or for clinical indication. The Allonext assay was used to report the dd-cfDNA as a % of the donor-derived fraction as compared with total cfDNA by using panels of >500 SNPs. GEP was analysed with the TruGraf® algorithm, which analysed differential expression of 120 genes. GEP results were provided as a probability score normalized on a 0–100 scale. The TruGraf® assay has a previously defined probability threshold of 50 to differentiate the TX (no rejection) from the not TX phenotype.

Results: Dd-cfDNA increased significantly during the first hour after pancreas transplantation (4.30±2.53%), and reduced progressively (at 24h 2.41±1.79%, at 1 week 0.65±0.47%, at 3 weeks 0.47±0.28%). Patients with biopsy-proven acute rejection (P-BPAR) episodes presented higher values of dd-cfDNA (2.1±2.46% vs 0.50±0.88%; p<0.027). In patients with pancreas acute rejection, GEP diagnosed the rejection episode in 56.8%, with a sensitivity of 74.1% (95% CI 53.7-88.9) and a specificity of 83.3% (95% CI 59.8-92.5) with negative predictive value of 86.7% (95% CI 77.3-92.6). Sub-clinical rejection (lipase <3xs normal) was diagnosed in 57.1%, with a specificity of 86.1% (95% CI 71-95). The combination of both parameters presented a negative predictive value of 82.3% (67-91%), with thirteen patients with P-BPAR (72.2%) presenting either test positive.

Conclusions: Dd-cfDNA and GEP can improve the detection of pancreas acute rejection episodes. GEP may provide non-invasive monitoring for sub-clinical rejection of the pancreas. graft.

SARCOPENIA BUT NOT FRAILTY IS ASSOCIATED WITH A SPECIFIC METABOLOMIC SIGNATURE IN KIDNEY TRANSPLANT CANDIDATES

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Background: Sarcopenia and frailty are conditions frequently neglected in the evaluation of kidney transplant (KT) candidates. They might contribute to poor health outcomes after transplantation. Our aim was to analyze which metabolites were associated with frailty and sarcopenia in a cohort of KT candidates.

Methods: Frailty and sarcopenia, measured by physical Frailty Phenotype and EGWSOP-2 criteria, respectively, were evaluated. Serum samples were analyzed through targeted metabolomics. Seventy-five metabolic markers were tested utilizing weighted logistic regressions. The models were adjusted by age, sex, body mass index, diabetes mellitus, type of renal replacement therapy and family/social support. The Benjamini–Hochberg procedure was applied to control the false discovery rate.

Results: 173 KT candidates (72.3% male, mean age 60.7 ± 13.1 years) were evaluated. Regarding frailty and sarcopenia, 66.5% of KT candidates presented with any grade of frailty (57.8% were pre-frail and 8.6% were frail) and 27.2% with sarcopenia. Patients with frailty (both pre-frail and frail patients together) were more frequently female (77% of women vs. 62.4% of men presented with any grade of frailty, p<0.047) but same age as robust ones (61.04 vs 60 years, p=0.078). Similarly, sarcopenia was more frequently detected in women (41.6 vs. 21.6% in men, p=0.008). Phenylalanine, creatinine, serotonin, tyrosine, carnitine, and tryptophan were associated with sarcopenia (Figure). No metabolite was associated with frailty in this cohort.

Conclusions: Frailty and sarcopenia are frequent among KT candidates and women are at special risk for both of them. Although frailty was not associated with any specific metabolic pattern, sarcopenia was found to have a metabolic signature associated with the metabolism of phenylalanine, tyrosine and tryptophan. This metabolic signature might serve as therapeutic target for pharmacological and non-pharmacological treatments in the context of CKD patients.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>OR (95% CI)</th>
<th>FDR-corrected p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylalanine</td>
<td>0.186 (0.064-0.509)</td>
<td>0.0624</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.245 (0.099-0.575)</td>
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</tr>
<tr>
<td>Serotonin</td>
<td>0.589 (0.416-0.820)</td>
<td>0.0021</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>0.256 (0.101-0.619)</td>
<td>0.0031</td>
</tr>
<tr>
<td>Carnitine</td>
<td>0.430 (0.241-0.753)</td>
<td>0.0033</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>0.212 (0.073-0.589)</td>
<td>0.0035</td>
</tr>
</tbody>
</table>

Figure: TruGraf® classification A) according to the diagnosis of acute rejection in the biopsy-proven cases evaluated, and B) according to the Barnt classification scheme. C) TruGraf® discrimination ability biopsies performed for cause in recipients of SPK. D) TruGraf® discrimination in patients with sub-clinical (lipase <3xs normal) pancreas acute rejection. SPK – simultaneous kidney-pancreas transplant.
Background: Kidney transplantation is the best therapeutic option for renal replacement therapy in patients with chronic renal failure but a lot of these patients are highly sensitized, and their transplantation options include joining specific lists, undergoing desensitization protocols, or entering cross-transplant programs. The aim of this study is to know the probability of kidney transplantation after desensitization in patients with incompatible HLA kidney transplantation.

Methods: We studied all patients HLA incompatible with living donor that received a desensitization protocol with Rituximab, plasma exchange or immunoabsorption and CMV specific immunoglobulins and Immunosuppression with Tacrolimus, mycophenolic acid derivatives and steroids. Efficacy of desensitization was to achieve a cross-match by CDC negative, flow cytometry negative and MFI of DSA < 1000.

Results: We analyzed 38 patients, median age 46.2±13 years old, 20(52.6%) women; Time in wait list 72±80 months ( seven patients were pre-emptive), CPRA 72.2±262, RIS (relative intensity score) 8±6.7, number of mismatches (A,B,DR) 3.5±1.3, number of total antibodies 1.5±0.75. MFI Class I 7272±3920, MFI Class II 6422±4066. Cross-match positive before conditioning were CDC in 19, 3.5±1.3, number of total antibodies 1.55±0.75. MFI Class I 72.2±262%, RIS (relative intensity score) 8±6.7, number of mismatches (A,B,DR) 2%, 0% and 11.1% respectively (p=0.024). In ROC curves MFI Class I lower (p<0.001), RIS 5.9±4 vs 15±7.9 (p=0.008), age 48.7±13.1 years old (p=0.048). The percentage of patients with efficacy of desensitization was lower in those that cross-match was positive by CDC comparing with flow cytometry and DSA: 42%, 0% and 11.1% respectively (p=0.024). In ROC curves MFI Class I area 0.966 (p=0.01) with a sensibility of 87% and 1-specificity 0.48 for MFI and DSA: 42%, 0% and 11.1% respectively (p=0.024).

Conclusions: Higher levels of MFI in Class I, RIS and cross-match positive by CDC are factors conditioning the efficacy of desensitization using this protocol.

P221 EVALUATING THE USE OF CONTINUOUS GLUCOSE MONITORING (CGM) EARLY AFTER KIDNEY TRANSPLANTATION

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Background: Prediabetes and Post Transplant Diabetes mellitus (PTDM) affect about 20-30% of kidney transplant recipients (KTR) and have been associated with an increased risk for cardiovascular morbidity and mortality in this population. Despite the poor performance of fasting plasma glucose (FPG) and HbA1c in detecting prediabetes and PTDM, the systematic integration of the “gold standard” oral glucose tolerance test (oGTT) remains challenging. The goal of this study was to evaluate the prognostic and diagnostic capacity of CGM regarding PTDM and prediabetes in the early phase after kidney transplantation.

Methods: CGM with the “Free Style Libre Pro IQ Sensor” was carried out in 21 KTR from day 10 to day 90 post transplantation. On day 90 a blood sample with FPG and HbA1c was drawn and an oGTT performed.

Results: Three months posttransplant, one patient developed PTDM (by all aforementioned diagnostics), twelve patients prediabetes (5 by oGTT, 8 by FPG) and eight showed no abnormality in the glycemic tests performed. One dropout was registered due to patient inconvenience with the sensor. CGM mean glucose from day 10 to day 90 was highest for the PTDM-patient, followed by the prediabetic and the normoglycemic ones. There were no sensor-associated adverse events.

Conclusions: Prediabetes and PTDM are highly prevalent at day 90 post kidney transplantation. CGM-metrics from day 10 to day 90 show an association with glycemic testing at day 90, though higher patient numbers are needed for conclusive statistical analyses. Importantly, feasibility and tolerability of the CGM were excellent allowing the general applicability in the transplant population.

P222 CALCINEURIN-INHIBITOR-FREE IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION IMPROVES RENAL FUNCTION: A SINGLE CENTER EXPERIENCE

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Background: Calcineurin inhibitor (CNIs)-associated nephrotoxicity after liver transplantation (LT) is inevitable; however, the safety of both CNI-sparing protocols and CNI-free immunosuppression is still under debate. Thus, this retrospective analysis was designed to evaluate effects of CNI-discontinuation after long-term follow-up of liver transplant recipients.

Methods: 453 outpatients are currently being followed up after LT in our center. 35 (7.8%) of those were switched to CNI-free immunosuppression after 63 (4-125) months for renal (n=25) or neurological (n=10) impairment or the occurrence of cancer (n=9) to monotherapy with Everolimus (n=10), Sirolimus (n=7) or to Everolimus combined with Mycophenolate Mofetil (n=18). Target trough levels of Everolimus or Sirolimus were 4-6 ng/ml.

Results: While serum creatinine decreased by 17.7% after 6 months of CNI-free immunosuppression from 1.7±0.6 mg/dl to 1.4±0.4 mg/dl the SCR increased by 11.7% from 65.9±11.3 ml/min to 74.6±13.7 ml/min. Most interestingly, kidney function recovered best in patients with serum creatinine of <2 mg/dl. Non-biopsy proven mild rejection occurred in only one patient (2.8%). Two patients (5.7%) were switched back to CNI for proteinuria. The infection rate was comparable in both groups.

Conclusions: CNI-free immunosuppression is safe and has a positive effect especially in patients with serum creatinine of <2 mg/dl.
PROGNOSTIC VALUE OF CREATININE REDUCTION RATIO AT DAY 2 AFTER KIDNEY TRANSPLANTATION

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1Foch Hospital, Department of Nephrology, Dialysis, and Transplantation, Suresnes, France, 2University of Versailles-Saint-Quentin-en-Yvelines, Faculty of Medical School, Montigny-Le-Bretonneux, France, 3Foch Hospital, Clinical Research Department, Suresnes, France, 4Foch Hospital, Urology, Suresnes, France, 5Foch Hospital, Department of Information Systems, Suresnes, France, 6Foch Hospital, Anesthesiology, Suresnes, France

Background: Slow graft function (SGF) after kidney transplantation can be identified by a low Creatinine Reduction Ratio calculated at POD2 (CRR2), a subtle marker of how allograft function recovers, using the immediate trajectory of serum creatinine (SCr) instead of a threshold value.

Methods: CRR2(%) is defined by ([Cr1-Cr2×100]/Cr1), where Cr1 is POD1 SCr (collected the first morning following transplantation) and Cr2 the SCr 24H after. In a monocentric, retrospective study, including all patients receiving a kidney transplant (taken from a deceased donor) between 2016 and 2021, we analyzed the outcome of patients with delayed graft function [DGF, defined by the need of dialysis by POD7], SGF (defined by a CRR2<30% and no need for dialysis), or immediate graft function [IGF, defined by a CRR2>30% and no need for dialysis]. Patient and graft survival were computed over time using a Kaplan-Meier analysis, and a Cox model was used to quantify the impact of graft functions on the risk of graft loss or death.

Results: Among the 301 patients included in the study, 79 (26.2%) developed DGF, 145 (48.2%) recovered SGF, and 77 (25.6%) had an IGF. Median follow-up was 41.4 (Q1;Q3=19.9;58.0) months. Graft survival was significantly different between groups (Log-rank test, p=0.006) (Figure). Compared to IGF, DGF tripled the risk of graft loss (OR 3.26, 95% CI [1.60;6.21], p=0.025). Likewise, patient survival was significantly influenced by the mode of graft function recovery: compared to IGF, SGF was associated with an OR of 3.65 for patient survival. Compared to IGF, SGF was associated with an OR of 3.65 for patient survival. DGF with an OR of 6.70 for patient survival was significantly influenced by the mode of graft function recovery.

Conclusions: CRR2 is a swift, precise, and relevant marker for the quality of graft function recovery. It discriminates SGF (incidentally, the commonest (95%CI=[1.96;22.88], p=0.002).

OPTIMIZING PATIENT THRIVING DURING THE TRANSPLANT PROCESS

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Background: Over 900,000 transplants have been conducted in the United States to date. Although transplantation is viewed as the optimal treatment for end-stage organ disease, many patients report mental health needs due to symptoms of anxiety, depression, and high levels of stress amongst others. These symptoms have been observed pre- and post-transplant, signifying the value of mental health interventions to help patients successfully navigate the steps to transplant as well as post-transplant to enhance their quality of life.

Methods: Informed by clinical practice and research, current practices and interventions used for managing the mental health needs of transplant patients are presented using case study examples as well as supporting research about the usefulness of these practices for different organ types. Additionally, a review of research on strength-based approaches for enhancing patients’ quality of life and well-being during the transplant process is addressed.

Findings revealed the importance of early mental health symptom identification, such as depressive symptoms given the potential for negative physiological and psychological outcomes. Evidence-based interventions such as cognitive behavioral therapy, acceptance and commitment therapy, and behavioral modifications have been effective for symptom reduction, improving medication adherence and reducing post-graft failure. Strength-based strategies such as resilience, and interventions focused on increasing patients’ positive attitudes have been found to be beneficial, although this area is understudied.

Conclusions: Transplant-specific mental health providers are integral to the transplantation process as they are valuable for mitigating the mental health concerns co-occurring pre- and post-transplantation. Effective interventions can be advantageous for improving patients’ outcomes and quality of life. Future work in this area should focus on groundbreaking evidence-based practices for helping patients and consider the cultural relevance of these practices. Also central to the provision of optimal mental health care is harnessing strengths that are already prevalent in this patient population.

IS IMPLANTABLE DOPPLER PROBE USEFUL AS A VASCULAR MONITORING DEVICE IN KIDNEY TRANSPLANT PATIENTS: A RETROSPECTIVE COHORT, SINGLE CENTRE STUDY

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Background: Vascular complications account for 30-35% of the total kidney grafts lost during the first three months after implantation. Early detection of vascular complications allows an opportunity for a prompt intervention that is critical to reducing graft loss. This study aims to evaluate the usefulness of implantable Doppler probe as a vascular monitoring device in kidney transplant patients.

Methods: Implantable Doppler probe is used intermittently for the postoperative monitoring of kidney transplant patients at our centre. We conducted a retrospective description of prospectively maintained medical data by comparing the clinical outcomes in the kidney transplant patients that had postoperative Implantable Doppler probe monitoring against those with standard care clinic observation. The medical data of 324 kidney transplant patients at our unit between Jan 2016 and Oct 2021 was studied and divided into two groups. Group 1 consisted of 194(60%) kidney transplant patients that had postoperative Implantable Doppler probe monitoring while Group 2 comprised 129(40%) kidney transplant patients with standard care clinical observation. The groups were compared in terms of the number of vascular complications identified, the number of departmental ultrasound scans required postoperatively, and the 03-month graft loss.

Results: In all patients, vascular complications were identified in 13.5%, and the resultant graft loss was 2.1%. Both the groups were similar in demographical characteristics. In Group 1 more vascular complications were identified (17.5% vs. 9.3%, RR = 1.88), fewer ultrasound scans were requested in the first 24 hours postoperatively (71.1% vs. 83.7%, RR = 0.84), and lower graft loss (1.5% vs. 3.1%, RR = 0.49) was recorded as compared to Group 2. All probes were removed safely after 72 hours, and no complication related to the device was reported.

Conclusions: The monitoring device may be used as an additional adjunct for graft monitoring in kidney transplant patients. Further controlled studies are warranted to evaluate this device in clinical practice.
Background: The shortage of organs available for donation is the most limiting factor in kidney transplant practice today. In the continuous quest to reduce graft loss due to vascular complications, new monitoring technologies are being investigated. A related study is proposed to assess the feasibility of a novel blood flow monitoring device, the Implantable Doppler (ID) probe in kidney transplant surgery.

Methods: This Public Patient Involvement consultation was aimed at exploring the views and expectations of the stakeholders (kidney transplant recipients, surgeons, clinicians, and nurses with direct experience of the ID probe) on the protocol development of the feasibility study. Its objective was to reveal areas of improvement in the study protocol, understand the perceptions of stakeholders regarding research in the postoperative graft surveillance, identify potential confounding factors to the research and challenges to implementation of ID probe in clinical practice. Semi-structured interviews containing open-ended questions were conducted with the stakeholders (n = 12). Thematic analysis of the data was done at the latent level by an inductive approach using a six-phase guide by Braun and Clarke using NVivo 12 software.

Results: Three key themes emerged. (1) Experiences with the ID probe as a monitoring device reflected that it was well received by the patients. However, there was a clinical equipoise among the healthcare professionals. (2) Recognition of the need for research in the early postoperative graft monitoring displayed the stakeholder’s understanding regarding the role of a blood flow monitoring device to improve the surgical outcomes. (3) Recommendations for the smooth conduct of the proposed study includes suggestions for improvement in the study protocol, informative sessions for the patients and nurses, and innovative ideas to improve the monitoring device.

Conclusions: The PPI consultation provided valuable insights to inform the research design of the proposed feasibility study. Useful strategies and a patient centred approach identified were incorporated to mitigate the potential challenges to the conduct of the research.

P229

URINE-DERIVED STEM CELL ATTENUATED RENAL FIBROSIS AFTER ISCHEMIA REPERFUSION VIA KLOTHO ACTIVATION

Jae Wan Jeon1, Dae Eun Choi2, Kang Wook Lee3, Ki Ryang Na4, Young Rok Han5, Eun Lee1, Hyeyun Park3, Yoon-Kyung Chang5, Kyoungar Yoo5, Boram Kim5

1Chungnam National University Sejong Hospital, Nephrology, Sejong, South Korea, 2Chungnam National University Medical Science, Daejeon, South Korea, 3Chungnam National University, Nephrology, Daejeon, South Korea, 4Chungnam National University Hospital, Organ Transplantation Center, Daejeon, South Korea, 5Daejeon St. Mary Hospital, Nephrology, Daejeon, South Korea

Background: After renal IRI, regeneration and recovery of the renal tubular cell occurs. However, if the renal repair process is maladaptive, it progresses to renal fibrosis. The role of stem cells in kidney regeneration or fibrosis has not been fully elucidated. We evaluated the urine driven stem cells(UDSCs) for renal inflammation and fibrosis after renal ischemia reperfusion(IR).

Methods: 10 week old balb/c nude male mice were used. sham, sham with UDSC, IR, IR with UDSC. UDSC were infused 3 times via tail vain at 6,7,8th day after renal IR. Urine NGAL/creatinine(Cr) were checked. The kidneys tissue were harvested at day 14 day. In vitro, TGF-β treated HK2 cell were co-cultured with UDSC. Klotho siRNA silencing was performed in UDSC.

Results: Urinary NGAL/Cr were significantly increased in IR mice after 14 day IR, compared to sham mice. Urinary NGAL/Cr significantly decreased in UDSC treated IR mice, compared to IR mice. In H&E stain, renal tubulo-Interstitial injury were significantly decreased in UDSC treated IR mice, compared to IR mice. In masson trichrom stain, renal fibrosis area were significantly decreased in UDSC treated IR mice, compared to IR mice. The renal expression of Klotho were significantly increased in UDSC treated IR mice, compared to IR mice. The renal expression of Klotho were increased in UDSC treated IR mice, compared to IR mice in vitro, UDSCs were stem cells that expressed Klotho protein more strongly than other mesenchymal stem cells (MSCs). UDSCs also suppressed fibrosis by inhibiting transforming growth factor (TGF)-β in HK-2 human renal proximal tubule cells in an in vitro model. Klotho siRNA silencing reduced the TGF-β inhibiting ability of UDSCs.

Conclusions: UDSC attenuate renal fibrosis after renal IRI. Klotho-secretion of UDSC play a role in these anti-fibrotic effects.

P228

COMPARISON OF COVID-19 AFTER KIDNEY TRANSPLANTATION BEFORE AND AFTER THE OMICRON VARIANT EPIDEMIC IN JAPAN

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Background: With the emergence of the Omicron variant, the novel coronavirus infection (COVID-19) has evolved into the largest epidemic wave both domestically and internationally. The Omicron variant has been reported as more infectious and less severe in the general population, but its characteristics and clinical course in kidney transplant recipients are not clear.

Subjects: Patients who developed COVID-19 in the first to fifth domestic waves (April 2020 to December 2021: predominantly wild-type, alpha, and delta variants, n=27) and the sixth to seventh waves (January to August 2022: predominantly omicron variant, n=132) among the 1,498 kidney transplant recipients who were receiving care at our hospital as of June 2022.

Results: The incidence in the sixth to seventh waves was 9.7 times higher than in the first to fifth waves (1.2% vs. 11.6%, p<0.01). The sixth to seventh waves had significantly fewer patients who needed oxygen therapy (48.2% vs. 6.8%, p<0.01) and more patients who received three or more doses of the vaccine (18.5% vs. 81.8%, p=0.01). In the inverse probability weighting analysis, use of antivirals within 5 days of onset was associated with a decreased risk of needing oxygen therapy (adjusted OR 0.19, 95%CI [0.04-0.83], P=0.03). In the inverse probability weighting analysis, use of antivirals within 5 days of onset was associated with a decreased risk of needing oxygen therapy (adjusted OR 0.19, 95%CI [0.04-0.83], P=0.03). In the inverse probability weighting analysis, use of antivirals within 5 days of onset was associated with a decreased risk of needing oxygen therapy (adjusted OR 0.19, 95%CI [0.04-0.83], P=0.03). In the inverse probability weighting analysis, use of antivirals within 5 days of onset was associated with a decreased risk of needing oxygen therapy (adjusted OR 0.19, 95%CI [0.04-0.83], P=0.03).
P230
DELETION OF PTP4A1 AMELIORATE RENAL FIBROSIS INDUCED BY UO/U IN MICE

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Background: Inhibitors of protein tyrosine phosphatase (PTP) have been investigated as potential anti-fibrotic agents. PTP4A1 belongs to a sub-class of three prenylated PTP. PTP4A1 has known as promoting growth and migration of tumor cells. The role of PTP4A1 has little known in kidney. We evaluated whether the PTP4A1 could be a target of renal fibrosis.

Methods: 10 week old male background PTP4A1 KO mice and wild type mice were divided into 4 groups; wild, PTP4A1 KO, wild with UO, and PTP4A1 KO with UO. Mice were sacrificed at 7 days after surgery and kidney tissue were collected, molecular study and histologic examination were performed.

Results: PTP4A1 KO with UO mice showed decrease of renal tubule-interstitial damage and fibrosis compared to wild type UO mice. PTP4A1 KO with UO reduced the renal expression of α-SMA and TIMP-1 in UO kidney, compared to wild type with UO mice. Wild type with UO kidney showed decrease of renal expression of E-cadherin, compared to sham mice. However, PTP4A1 KO UUO showed increase of renal expression of E-cadherin, compared to wild type UUO. In vitro, silencing of PTP4A1 in TGF-β treated HK2 cell showed increase of renal expression of E-cadherin, compared to wild type HK2 cell. In silico, monitoring of AKT and GSK3β phosphorylation in TGF-β treated HK2 cell showed decrease of AKT and GSK3β phosphorylation.

Conclusions: PTP4A1 KO ameliorate renal fibrosis in UUO kidney.

P231
THE LONG-TERM RISKS OF KIDNEY DONATION (RENAL RESERVE, HYPERTENSION): OBSERVATIONS FROM A 15-YEAR FOLLOW-UP PERIOD AT THE MILITARY MEDICAL ACADEMY

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Background: The research papers published over the past decade have increased the knowledge concerning the long-term risks after kidney donation. We conducted a retrospective study in our kidney donors in the period from 2004 to 2020, taking into account the renal reserve assessment and the frequency of occurrence and/or worsening of hypertension.

Methods: Our study was conducted as a retrospective case-control study. It included all living kidney donors who underwent donor nephrectomy since 2004 and for whom the medical documentation was available. The parameters of interest were observed before donor nephrectomy, 6 months post-op and 1, 5, 10 and 15 years post-op as well. The control group consisted of donor nephrectomy patients themselves.

Results: The average age of our patients at the time of donation was 55.87, with almost two thirds of them under the age of 60. After donor nephrectomy, the kidney function is decreased. In the first year, a statistically significant decrease in total glomerular filtration (eGFR CKD EPI) was registered, while in the later follow-up period was not the reason for faster deterioration and/or worsening of hypertension.

Conclusions: The donor’s age hasn’t been proved to be a significant factor which impacts the average time span preceding the occurrence of chronic kidney disease (CKD). In patients under the age of 45, not a single CKD was developed. In patients aged 60 and over, 32% developed CKD. Hypertension in the follow-up period was not the reason for faster deterioration and/or the onset of CKD compared to patients without hypertension. Kidney donors are ideal for studying the relationship between the reduced renal reserve and the risk of cardiovascular disease (CVD) occurrence.

P232
PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN A BELGIAN COHORT OF LUNG TRANSPLANT CANDIDATES: THE PROGRESS STUDY

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Background: Lung transplant (LT) candidates are at high risk of osteoporosis (OP), due to both their respiratory condition and frequent oral glucocorticoids use. However, few is known on the prevalence and management of OP in LT candidates. This study aims to evaluate the prevalence and therapeutic management of OP in LT candidates and to determine the risk factors associated with OP.

Methods: We included 196 patients (103 women) among 388 screened for LT at CHU UCL Namur between January 1998 and December 2020. We collected data on bone mineral density (BMD), measured by Dual-energy X-ray absorptiometry (Hologic) at the lumbar spine, total hip and femoral neck, fragility fracture (FF), and OP risk factors along with other factors suspected of affecting BMD such as inhaled (i) glucocorticoids (iGCs) use, pulmonary function tests, hypoxemia and pulmonary disorder type.

Results: OP, as defined by BMD values (T-score ≤ -2.5) and/or FF, was observed in 118 patients (59.6%), among which 54 (45.6%) had only a T-score ≤ -2.5, while 36 (30.5%) had only an FF, with predominant vertebral fractures (77.8%). OP patients were older (median [IQR]) 59.0 years [54.2-62.0] vs 57.0 [53.6-62.0]) and had lower body mass indexes (mean ± SD) 22.2 ± 4.6kg/m² vs 24.3 ± 4.6kg/m² than non-OP. Seventy-eight OP patients (66.1%) reached the ten-year probability of major osteoporotic fracture intervention threshold. Among them, 53 received only calcium and/or vitamin D and 25 an add-on therapy, mostly a bisphosphonates (n=23, 92.0%). Thirty-six OP patients (30.5%) were untreated. OP patients were more prevalent in COPD patients (n=102/153, 66.1%) than in those with ILD (n=12/33, 36.3%) or any other pulmonary diseases (n=4/12, 33.3%). Finally, OP patients used more iGCs, had lower FVC and severely impaired FEV1/FVC ratio. Oral GCs treatment was associated with FF, regardless of the daily dosage.

Conclusions: Most of LT candidates have OP. OP diagnosis before LT in these patients is crucial for a better management of their bone fragility risk after transplantation. GCs use is a major OP risk factor in this category and should raise the OP awareness related to LT patients.

Risk factors for OP, OR (CI) – p value

<table>
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<th>Factors</th>
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<th>p value</th>
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<tr>
<td>BMI</td>
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</tr>
<tr>
<td>FEVI/FVC ratio</td>
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<td>0.49</td>
</tr>
<tr>
<td>COPD</td>
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</tbody>
</table>

Abbreviations: BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEVI, forced expired volume in one second; FF, fragility fracture; GCs, inhaled glucocorticoids; IQR, interquartile range; OP, osteoporosis; OR, odds ratio; P, pulmonary volume; SD, standard deviation; yrs, years.
Background: Optimizing the time in need to allocate organs is a priority to rationalize timing in the articulated and complex process of donation and transplantation. For this purpose, on February 14th 2022 the protocol named “Reduction of organ allocation times project” has been introduced. The main aspects entered by the protocol were: identification of a minimum data set, organ-specific, in need for the evaluation; identification of a procedure as long as to permit transplant centers rapid and easy access to data; identification of a procedure with the aim of rationalizing transplant centers’ evaluation of the organs. The goal of this paper is to compare the average organ allocation time before and after the use of the protocol.

Methods: From February 14th 2022 to August 14th 2022 organ allocation times were evaluated for about 22% of actual DBD donors (145 donors casually selected). A proportional stratified sample has been considered. In priority organ allocation scheme of the donors selected, recipients enlisted on a national allocation organ programme for at least one thoracic organ, liver, kidneys and eventually pancreas, had to occur. In order to calculate allocation times the time of the first organ offered and the time of the last organ accepted have been taken into consideration. The resulting average allocation time has been confronted with the one calculated taking into account a similar sample (casually selected) of 2021, the year prior to the protocol entry.

Results: During the period in which the protocol has been used, the average organ allocation time was 292 minutes (median: 251 minutes), while during the previous period, it was 364 minutes (median: 334 minutes).

Conclusions: The analysis shows how the entry of the protocol strikes its goal with an average reduction of the time needed for the organ allocation process up to 72 hours. However, continuous effort in order to reduce more the allocation times in order to make the process smoother and prompt is necessary.

Background: Deceased donor kidney transplantation (DDKT) is unpredictable; any transplant centre (Ctr) may receive many offers in a short timeframe for which there may not be enough capacity (CAP) to transplant (Tx) in a timely fashion. Such situations pose logistical and ethical challenges. Prolonged cold ischaemia times (CIT) with adverse outcomes may result. Declining an offer could result in patients losing out on a unique Tx opportunity. There may otherwise, for lungs and small bowel offers, which increased by about 86% and 145% respectively. To date, UK-NHS has not started using the FOEDUS portal yet, to offer organs abroad; on the contrary, Eurotransplant stated offering up to 80 organs and resulting the leading organization offering organs abroad (21 % of the total offers). In 2022, a total of 97 organs offered and accepted through FOEDUS web portal, while, in 2021, 285 organs were offered, registering an increase by 35 %. Excluding kidneys and multispecimen organs offers, all the other organ offers improved significantly. In particular, we observed a significant increase in lungs and small bowel offers, which increased by about 86% and 145% respectively. To date, UK-NHS has not started using the FOEDUS portal yet, to offer organs abroad; on the contrary, Eurotransplant stated offering up to 80 organs and resulting the leading organization offering organs abroad (21 % of the total offers).

Results: In 2022, a total number of 386 organs were offered through FOEDUS web portal, while, in 2021, 285 organs were offered, registering an increase by 35%. Excluding kidneys and multispecimen organs offers, all the other organ offers improved significantly. In particular, we observed a significant increase for lungs and small bowel offers, which increased by 86% and 145% respectively. To date, UK-NHS has not started using the FOEDUS portal yet, to offer organs abroad; on the contrary, Eurotransplant stated offering up to 80 organs and resulting the leading organization offering organs abroad (21% of the total offers). In 2022, a total of 97 organs offered and accepted through the portal were actually transplanted, compared with 57 transplanted in 2021, with an increase by 70%. Considering the data of the new organizations participating in the program, UK-NHS performed 4 transplants and Eurotransplant 27. In 2022, as well as in 2021, Italy was the Country that performed the higher number of transplants with organs accepted through the FOEDUS portal: 23 in 2021, 29 in 2023.

Conclusions: Extending the use of the FOEDUS web portal to other organizations is an advantage for the patient enlisted for organ transplantation as long as we proved to increase the number of organ offers and transplants among Europe. The allocation rule based on the principle first comes first serves improved the chance to find the most suitable recipient in the shortest time.
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ASSOCIATION BETWEEN ADULT DBD KIDNEY OFFER DECLINE RATES AND RISK-ADJUSTED WAITING TIMES IN THE UNITED KINGDOM

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Background: Deceased organ donor age and co-morbidities are increasing, meaning that donated organs are more challenging to successfully transplant. There is a variation in appetite for accepting donor offers across the 23 adult kidney transplant centres in the UK. We explore whether 'risk appetite' predicts the average time that a patient waits for a standard criteria DBD donor kidney transplant.

Methods: Data were extracted from the UK Transplant Registry held by NHS Blood and Transplant as published in the NHSTB Kidney Annual Report 2020/21. Offer decline rates were calculated by centre using adult kidney-only offers from standard criteria DBD donors, between 1 April 2018 and 31 March 2021, who had at least one kidney retrieved, offered directly and on behalf of a named individual patient and resulted in a transplant. Adult risk-adjusted1 median waiting times by centre were calculated for patients listed between 1 April 2015 and 31 March 2018 using a Cox-proportional hazards model. The Pearson’s correlation coefficient was used to measure the association between centres offer decline rate and risk-adjusted median waiting time.

Results: The overall decline rate in the UK for an adult standard criteria DBD donor kidney offer was 53%, ranging from 29% to 62%. The median risk-adjusted waiting time to transplant for adult patients registered on the kidney-only waiting list is 563 days, ranging from 374 days to 729 days. Figure 1 shows a significant linear relationship between offer decline rate and waiting time (r=0.4, p=0.05). This is a positive relationship, with a higher offer decline rate associated with a longer waiting time.

Conclusions: Risk-adjusted waiting time and offer decline rates increase together even for these apparently favourable donor offers. This may lead to patients being disadvantaged, depending on the centre where they were listed. 

Figure 1: Adult kidney adjusted waiting time by DBD standard offer decline rates

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**P241** MISMATCHED HUMAN LEUCOCYTE ANTIGENS BETWEEN BLOOD DONORS AND WAITLEISTED TRANSPLANT PATIENTS LEADS TO TRANSFUSION SPECIFIC HLA-B ANTIBODIES

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**Background:** HLA (human leucocyte antigens) sensitisation affects access to kidney transplantation; the median wait time for highly sensitised patients is twice that of unsensitised patients. Red cell transfusion provokes alloimmune anti-HLA antibodies and is a potentially modifiable source of HLA sensitisation. It has been shown to cause broad HLA sensitisation. Here we show it can cause transfusion specific antibodies (TSAs) and degree of mismatch can predict the formation of antibodies.

**Methods:** We identified waitleisted kidney transplant candidates who received a blood transfusion. The corresponding blood donors were identified, contacted and retrospectively HLA typed (REC 18/WM/0161). Donors and recipients were typed to split specifically antigen level. We compared HLA antibodies, as determined by single antigen bead assays pre- and post-transfusion and identified the transfusion specific antigen(s). (TSA) against donor or antigen(s).

**Results:** We identified 55 patients who received 111 typed blood transfusions (median 2, range 1-5). 17 patients (30.9%) had HLA antibodies prior to transfusion. Post-transfusion, 36 patients (65.5%) had at least one new HLA-antibody specific to the transfusion-induced specific antigen(s). (TSA) against donor or antigen(s). The mean number of transfusion specific antibodies was 1.95 (±1.43). Of the 41 TSAs which developed 11 (26.8%) targeted class II antigens. The most common locus targeted was HLA-B, with 9 patients (18%) developing 17 HLA-B antibodies. The mean total HLA-A, -B, -DR and -DQ mismatch was 5.87 (±1.26). The HLA mismatch at HLA-B was predictive of developing an HLA-B TSA, with a mean mismatch of 1.86 and 1.63 for TSA+ and TSA- patients respectively (p=0.026).

**Conclusions:** We have shown that red cell transfusion increases HLA-sensitisation in waitleisted patients. Poorly matched transfusions result in many patients developing a TSA. Most TSAs targeted Class I HLA but a significant proportion targeted Class II antigens. All 17 of the pre-sensitised patients and 19/38 (50.0%) without known sensitisation. Post-transfusion, 36 patients (65.5%) had at least one new HLA-antibody specific to the transfusion-induced specific antigen(s). (TSA) against donor or antigen(s).

Yitian Fang1, Anton Nikolaev2, Lisanne van Ooijen3, Gisela Ambaghtsheer4, Jeroen Essers5, Jenny Dankelman6, Gijs van Soest7, Ron de Bruijn8, Robert Minne1
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**Background:** Normocytic machine perfusion (NMP) provides a platform to assess donor organ quality prior to transplantation, which is significant when using marginal donor kidneys. As novel imaging techniques, photoacoustic imaging (PAI) can identify different tissue molecules and laser speckle contrast imaging (LSCI) can visualize the movement of particles. The aim of this study is to investigate the value of PAI and LSCI as kidney quality assessment tools during NMP.

**Methods:** Two independent studies using slaughterhouse porcine kidneys were conducted. In the 1st study, kidneys (n=16) were subjected to 30 minutes (n=8) and 75 minutes (n=8) warm ischemia time (WIT) respectively. Volumetric PAI of the renal cortex was acquired for each kidney during 120 minutes of NMP. The PAI data were used to quantify oxygen saturation (SO2). In the 2nd study, all kidneys (n=10) were subjected to 30 minutes WIT. LSCI was used to measure one-sided microcirculation in the first 100 minutes of NMP, followed by measurement on both ventral and dorsal aspects after clamping one renal artery branch to induce ischemia.

**Results:** In the 1st study, kidneys with 30 minutes WIT showed significantly higher SO2. (Figure 1A). Blood flow, creatinine clearance and oxygen consumption compared to the kidneys with 75 minutes WIT. Renal cortical SO2 had a positive correlation with renal blood flow (r=0.82, p<0.001) and oxygen consumption (r=0.73, p<0.001). The 2nd study, the increase of renal cortical perfusion could be visualized with LSCI (Figure 1B). LSCI fluxes correlated linearly with renal blood flow (R²=0.90, p<0.001). Kidneys had comparable creatinine clearance, fractional excretion of sodium and total sodium reabsorption after occlusion of the inferior renal artery branch as before, while the decrease in renal cortical perfusion could be visualized and quantified by LSCI.

**Conclusions:** PAI and LSCI are promising imaging techniques in real-time kidney perfusion measurement during NMP. PAI can be a valuable addition to evaluate renal metabolism and LSCI can visualize cortical microcirculation. The combination of using PAI and LSCI can help assess pre-transplant kidney quality.

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**P242** PROGESTERONE EFFECTS ON INTESTINAL CHANGES CAUSED BY ICHENMIA AND REPERFUSION PROCESS

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**Background:** Intestinal transplantation is becoming the standard treatment in patients with nutritional impairment, and patient graft survival rates have improved over time. However, bowel transplantation is still associated with significant mortality and morbidity, which may be directly linked to the ischemia and reperfusion process. Progesterone depresses the inflammatory response and reduces the free radicals development in the intestine. Thus, our aim was to evaluate the impact of treatment with progesterone on the intestinal ischemia and reperfusion (IR) process.

**Methods:** Male Wistar rats were divided in 3 groups (n=7): Sham (SH) group, animals submitted only to surgical procedure; IR group, animals submitted to ischemia (30 min) and reperfusion (2h); P4 group, animals submitted to ischemia/reperfusion and treated with progesterone (P4) (2mg/kg, i.v.) at the moment of flow reestablishment. The decrease in renal cortical perfusion could be visualized by insertion of a 2-F balloon catheter in the descending aorta leading visceral ischemia. Intestinal transit, vascular permeability and serum inflammatory mediators (ELISA) were measured at the final of the experiment period.

**Results:** IR decreased intestinal transit compared to sham group (SH 71.5%±2.6; P<0.001) and reduces the free radicals development in the intestine. Thus, our aim was to evaluate the impact of treatment with progesterone on the intestinal ischemia and reperfusion (IR) process.

**Conclusions:** Male Wistar rats were divided in 3 groups (n=7): Sham (SH) group, animals submitted only to surgical procedure; IR group, animals submitted to ischemia (30 min) and reperfusion (2h); P4 group, animals submitted to ischemia/reperfusion and treated with progesterone (P4) (2mg/kg, i.v.) at the moment of flow reestablishment. The decrease in renal cortical perfusion could be visualized by insertion of a 2-F balloon catheter in the descending aorta leading visceral ischemia. Intestinal transit, vascular permeability and serum inflammatory mediators (ELISA) were measured at the final of the experiment period.

Yitian Fang1, Anton Nikolaev2, Lisanne van Ooijen3, Gisela Ambaghtsheer4, Jeroen Essers5, Jenny Dankelman6, Gijs van Soest7, Ron de Bruijn8, Robert Minne1
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**Conclusions:** PAI and LSCI are promising imaging techniques in real-time kidney perfusion measurement during NMP. PAI can be a valuable addition to evaluate renal metabolism and LSCI can visualize cortical microcirculation. The combination of using PAI and LSCI can help assess pre-transplant kidney quality.

Figure 1. A. Oxygen saturation of the kidneys with 30 minutes (top) and 75 minutes (bottom) WIT; B. Laser speckle contrast images of the kidneys during 100 minutes of NMP.
THE EXPERIENCES OF HEALTH CARE PROFESSIONALS APPROACHING FAMILIES FOR ORGAN DONATION CONSENT: A MIXED-METHOD SYSTEMATIC REVIEW

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Background: Healthcare professionals (HCPs) play an essential role in organ donation (OD) particularly when approaching families to discuss consent to OD. The percentage of families agreeing to deceased donation varies globally and therefore gaining insights in the complexities of approaching families is paramount. We conducted a mixed-method systematic review to synthesize the evidence reporting HCPs’ experiences in approaching potential donor families for donation after brain or circulatory death.

Methods: Fourteen bibliographic databases were searched to identify studies describing HCP experiences when approaching potential donor families or associations between HCP experiences and consent rates. Independent reviewers extracted the data and assessed the methodological quality using the Mixed Methods Appraisal Tool. Data were analysed using parallel-results describing HCP experiences when approaching potential donor families or associations between HCP experiences and consent rates. Independent reviewers extracted the data and assessed the methodological quality using the Mixed Methods Appraisal Tool. Data were analysed using parallel-results convergent synthesis design using thematic synthesis.

Results: We identified 12,698 unique references of which 86 studies met the inclusion criteria. The methodological quality of studies varied. Despite the common assumption that staff experiences can be improved by training and education, quantitative studies showed that consent rates did not increase significantly following OD training. HCP experiences were categorised according to broad themes including personal, organisational, patient, family, death and approach. HCP experiences were conceptualised as a paradox due to the challenges to negotiate the boundaries between life and death. Organisational and personal aspects shape the experiences of professionals broadly. The complexities of the family approach were evident in the variety of definitions of HCP experiences and experienced interactions between HCPs and the donor family, which may explain why there is no uniform approach across settings and countries.

Conclusions: The review highlights the challenges faced by professionals when negotiating policy and practice globally. Findings inform the development of recommendations for good practice and training to support staff involved in the OD process worldwide. This will require strategies of international collaboration and cooperation taking into account legal and sociocultural factors of countries.

NORMOTHERMIC MACHINE PERFUSION ALTERS RENAL GENE EXPRESSION PATTERNS

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Background: Renal normothermic machine perfusion (NMP) is gaining interest because of its potential for viability assessment and graft repair before transplantation. During NMP, in vivo-like conditions are pursued. However, physiology during NMP is still incompletely understood, and it is likely that in vivo functional markers, such as creatinine clearance or fractional sodium excretion, are not appropriate for ex vivo viability assessment. Therefore, a better understanding of ex vivo physiology is warranted to further develop NMP as an assessment tool. We aimed to unravel ex vivo organ biology by analyzing the RNA profiles of kidneys in vivo and during NMP.

Methods: Thirty landrace pigs were anesthetized and prepared for a bilateral nephrectomy. During surgery, an in vivo biopsy was taken. One kidney was exposed to 75 minutes of warm ischemia (WI), while the contralateral kidney sustained no WI. Kidney grafts were cold preserved for 6 hours, followed by 6 hours of NMP. Cortical biopsies were taken at 0, 1, 2, 3, and 6 hours of NMP. RNA sequencing was performed in all biopsies and aligned to a reference genome. Sequencing results were analyzed using the Seurat pipeline in R. Clusterprofiler was used for functional analysis of identified gene clusters.

Results: A total of 27,626 genes were identified. Unsupervised clustering analysis revealed distinct clustering between the different time points and exposure to WI (Figure 1A). Only two significantly differentially expressed genes (DEG) were identified after cold preservation compared to in vivo (P adj < 0.05) (Figure 1B). However, during NMP, gene expression profiles changed considerably. Functional enrichment analysis of protein-coding genes revealed downregulation of genes involved in mitochondrial respiration and upregulation of inflammatory processes during NMP. Kidneys exposed to WI showed upregulation of the genes related to stress responses compared to the kidneys with no WI.

Conclusions: These results show that in vivo renal function significantly differs from function during NMP, emphasizing that the interpretations based on our in vivo reference frame should be carefully weighed. Additionally, the duration of NMP and the timing of viability assessment are of great importance, as the active physiological processes change over time.

Figure 1. (A) UMAP of all samples. (B) Upset plot of DEG (P adj < 0.05) of all timepoints compared to in vivo gene expression. Bars indicate overlapping DEG between timepoints. DEG: differentially expressed genes. WI: warm ischemia. NMP: normothermic machine perfusion.
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Background: “Baseline kidney function”, the change point between initial rapid improvement after kidney transplant and subsequent stabilization, is often used in clinical decision-making and clinical trials but is not well defined. We aimed to characterize the evolution of kidney transplant function in the first year after transplant and objectively define the “change point” of baseline function.

Methods: The retrospective cohort consisted of 921 recipients, who were alive with a functioning graft at 1 year after transplant. Only eGFR observations within the first year were included (N = 46 575 in total; median = 47 observations per transplant; IQR = 39–58 observations). Segmented regression models with one change point were used to estimate change point timing, eGFR value at change point, rate of change before and after change point for each transplant. Associations of the eGFR evolution with recipient/donor characteristics and graft failure rate were assessed with linear and Cox regression respectively.

Results: The change point occurred at an eGFR value of 45.2±16.4 mL/min/1.73m², at a median time of 10 days since transplant (IQR = 4.4–21.5 days). The change point occurred earlier (-8.4 days; P=0.002) in case of a living donor, compared to deceased donors after transplant (P<0.001). The initial increase in kidney function was steeper (+11.3 mL/min/1.73m²/day; P<0.001) and the change point occurred earlier (-8.4 days; P=0.002) in case of a living donor. Among cases with a deceased donor, the change point occurred later in case of donation after cardiac death (DCD), compared to brain death (DBD) (+4.9 days; P=0.007). While the eGFR value at change point was higher in case of a living donor (+10.7 mL/min/1.73m²; P<0.001), the subsequent rate of change was lower compared to both DCD and DBD (+1.32 mL/min/1.73m², at a median time of 10 days since transplant (IQR = 4.4–21.5 days).

Conclusions: This study indicates that donor characteristics importantly determine kidney function evolution and timing of the “change point” within the first year after transplant. Long-term outcome is less affected by the shape of the kidney function trajectory during the first year, and rather explained by the eGFR value reached at one year post-transplant.

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Background: Previous research indicates an inferior SARS-CoV-2 spike-specific T-cell response, following COVID-19 vaccination in kidney transplant recipients (KTR) compared to controls. Here, we perform an in-depth longitudinal phenotypical study of these T-cell responses in KTRs and controls.

Methods: For this study, we selected 21 KTR and 21 controls who mounted a positive T-cell response after second mRNA-1273 vaccination. Of the KTR, 11 also mounted a positive antibody response (KTR+), whereas 10 did not (KTR-). Peripheral blood mononuclear cells (PBMCs) were isolated 28 days and 6 months after second vaccination. Spike-specific IFN-γ producing T-cells were enumerated using an SARS-CoV-2 spike-specific IFN-γ ELISPOT assay. SARS-CoV-2 spike-specific T-cells were phenotypically characterized using a flow cytometry based activation-induced markers (AIM) assay.

Results: Compared to controls, the number of IFN-γ producing T-cells was comparable in KTR+, and lower in KTR- 28 days after the second vaccination (532.5 (265.0 – 689.2) vs. 375.0 (91.2 – 492.1) and 100.0 (65.0 – 371.7) –6. SFCs/10⁶ PBMCs; p=0.07). IFN-γ T-cell levels decayed less rapidly towards six months in KTR- compared to controls (-78.3 vs. -260.0 SFCs/10⁶ PBMCs; p<0.001 and CD8: 0.35% vs. 0.09%; p=0.003). Interestingly, these CD4+ T-cells tended to be more often from the terminally differentiated effector memory (TEMRA) phenotype compared to controls (4.1 vs. 2.3% p=0.07). IFN-γ T-cell levels decayed less rapidly towards six months in KTR- compared to controls (-78.3 vs. -260.0 SFCs/10⁶ PBMCs; p=0.50, p=0.08). The CD4+ T-cell percentages, however remained stable in controls and declined only in KTR, with an equal rate in KTR+ and KTR- (Figure 1).

Conclusions: In KTR who did not mount a positive antibody response after COVID-19 vaccination, a different T-cell phenotype was found compared to controls in addition to lower T-cell levels. Moreover, a decay of CD4+ T-cell percentages, however remained stable in controls and declined only in KTR, with an equal rate in KTR+ and KTR- (Figure 1). This study indicates that donor characteristics importantly determine kidney function evolution and timing of the “change point” within the first year after transplant. Long-term outcome is less affected by the shape of the kidney function trajectory during the first year, and rather explained by the eGFR value reached at one year post-transplant.

Definitions:
- eGFR: estimated glomerular filtration rate
- KTR: kidney transplant recipient
- KTR+: kidney transplant recipient who mounted a positive antibody response after second mRNA-1273 vaccination
- KTR-: kidney transplant recipient who did not mount a positive antibody response after second mRNA-1273 vaccination
- DCD: donation after cardiac death
- DBD: donation after brain death
- IFN-γ: interferon-γ
- ELISPOT: enzyme-linked immunospot assay
- AIM: activation-induced markers
- TEMRA: terminally differentiated effector memory

Graphical Abstract:
- A) Time course of IFN-γ producing T-cells
- B) Time course of CD4+ T-cell percentages
- C) Time course of CD8+ T-cell percentages

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Background: Primary sclerosing cholangitis (PSC) represents 5% of the indications for liver transplantation (LT). Recurrence of PSC (rPSC) is reported in 8-27% of cases and it has a great impact on graft and patient survival.

Methods: The clinical data of 35 patients with PSC who underwent LT in our center in the last 20 years were retrospectively evaluated.

Results: 25 were male (71.4%) with a history of IBD before LT (67%). Tacro-limus + steroid was the most frequent immunosuppressive schedule (84.8%). Graft and patient survival at 5 years were respectively 73.6% and 88%. 5 patients (15.1%) underwent re-LT: 3 for rPSC, 2 for immunological damage (with an average and median time of respectively 37 and 31 months). A female patient transplanted for the first time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT. The time interval between 2nd and 3rd LT was much shorter than the time at the age of 17 years, redeveloped aggressive rPSC, with the need for a third LT.

Conclusions: Re-LT is the only treatment option for aggressive rPSC. Our patient successfully underwent 3rd Re-LT combined with aHSCT with no evidence of rPSC at over 18 months follow-up: this may represent a successful approach as a preemptive strategy in selected cases of re-LT for rPSC.
Background: Response to vaccination is a complex procedure, implicating humoral and cellular immunity. The aim of our study was to assess differences in cellular immunity between Renal Transplant Recipients (RTRs) classified as “responders” and “non-responders” to vaccination with Tozinameran.

Methods: Thirty-nine RTRs on stable immunosuppression, naive to COVID-19 infection, who had not developed protective humoral immunity three weeks after the 2nd vaccine dose (T2), were evaluated 48h before (T1) and 3 weeks after (T2) the 3rd dose. Nab levels >0.3 AU/ml (chemiluminescence immunoassay) and/or enzyme-linked immunosorbent spot (ELISpot) values >30 SFC/5x10^6 PBMCs were regarded as response. Results were correlated with cellular immunity. Concentrations of CD4+, activated CD4+, CD8+, activated CD8+ T-cells, CD3+CD16+CD56+ (NKT), activated NKT cells, CD3-CD16+CD56+ (NK) cells, CD19+, CD19+CD27- (Naïve), CD19+IgD+CD27- (Marginal), CD19+CD24+CD38+ (Transitional), CD19+CD27+CD38+ (Plasmablasts) and CD19+CD27+ (Memory) B cells were measured with flow cytometry at T1 and T2.

Results: The number of responders significantly increased from T1 [17/39, responders: Nab(-) - ELISpot(+)] to T2 [34/39, responders: Nab(+) and/or ELISpot(+)] (x^2=16.2, p<0.0001). No difference was observed between responders and non-responders regarding age, renal function, calcineurin inhibitor levels, dialysis and transplantation vintage. Compared to non-responders, responders presented increased concentrations of: NK, activated CD8+ and NKT at T1 and of: total B cells, marginal and memory B-cells at T2 (table). A notable increase in naïve B-cells, as well as a significant drop in activated CD4+ and activated NKT cell numbers from T1 to T2 ([56.3(69) vs 1123.6(751) μL, p<0.001, 10.38(12) vs 5.71(7)/μL, p: 0.007 and 2.6(3) vs 1.28(3), p: 0.028 respectively) was evident only in the group of patients that were regarded as responders at T2.

Conclusions: The 3rd Tozinameran dose substantially improved RTRs’ immune response, inducing a prominent stimulation of the B lymphocyte compartment.

### Table

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<th>Cellular Subpopulation</th>
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<td></td>
<td>Responders</td>
<td>Non-Responders</td>
<td></td>
</tr>
<tr>
<td>Activated CD8+</td>
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<td>9.49(10)</td>
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<tr>
<td>Activated NKT cells</td>
<td>T1</td>
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<td>1.73(2)</td>
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<tr>
<td>NK cells</td>
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<td>198.9(163)</td>
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<tr>
<td>B-cells</td>
<td>T2</td>
<td>87.63(101)</td>
<td>26.86(42)</td>
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<tr>
<td>Marginal B-cells</td>
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<tr>
<td>Memory B-cells</td>
<td>T2</td>
<td>28.31(42)</td>
<td>10.57(19)</td>
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</table>
ATYPICAL HAEMOLYTIC UREMIC SYNDROME (AHUS) RECURRENT AFTER KIDNEY TRANSPLANTATION IN PATIENTS WITH ECULIZUMAB PROPHYLAXIS

Constantino Fernández Rivera1, María Calvo Rodríguez1, Marta Blanco Parado1,2, Diego Sierra Castro1, Catuxa Rodriguez Magariños1, Sara Domenica Erazo Guerrero1, Tamara Ferreiro Hernando1, Leticia García Gago1, Andrés Lopez Muñiz1, Mercedes Cao Vilarino1
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Background: The outcome of kidney transplantation in patients with aHUS before the use of eculizumab was poor and it was conditioned to the appearance of recurrence of the disease. Nowadays, this outcome has changed with the use of eculizumab. The aim of this study is to know the incidence of aHUS recurrence after kidney transplantation in patients with eculizumab prophylaxis.

Methods: We studied all patients with aHUS and that had received a kidney transplantation from 1981. Recurrence was defined as the appearance of hemolytic anemia (low levels of Hemoglobin, thrombocytopenia, increase of LDH and haptoglobin no detected) and a deterioration of renal function. When a deterioration of renal function was detected, a biopsy was performed in all patients. Biopsy of surveillance was done at first week and at six months after kidney transplantation only in patients with eculizumab. We compared the incidence of recurrence between patients with and without eculizumab and we analyzed the risk factors for this recurrence.

Results: We studied 46 kidney transplantation (mean age 39±14.8 years old) to 33 patients (13 with eculizumab) from 1981 to 2023. 33 were first kidney transplant and 13 second, third or fourth kidney transplantation. Eculizumab was used from 2016 and dose and mode of administration was made as data sheet. After a follow up of 69.6±84 months, 14 patients showed recurrence of aHUS, all of them didn’t receive eculizumab (p=0.003). Recurrence was associated with: mean age 32±11.2 vs 42±15.3 years old; p=0.03, CMV infection (83.3% vs 33.3%; p=0.04) and the time to start dialysis from diagnosis of aHUS 1.1±0.5 vs 9.7±23 months (p=0.04). We didn’t find relationship with variants of complement proteins, cold ischemia time, immunosuppressive agents, acute rejection and others. The probability of recurrence was 24.1 at 6th month and 39.0% at first year. We withdrew eculizumab in four patients, in two cases due to lost allograft (chronic rejection at five years and thrombosis at first month) and two in patients without variant transplantation from 1981. Recurrence of aHUS occurred in patients with eculizumab. We didn’t observed aHUS recurrence in kidney transplant recipients when prophylaxis with eculizumab was performed.

Conclusions: We didn’t find aHUS recurrence in kidney transplant recipients when prophylaxis with eculizumab was performed.

P257 HUMAN LIVER TRANSPLANTATION: EVALUATION OF IMMUNE T CELLS WITH TISSUE RESPIRATORY FUNCTIONS

Bost Romain1,2, Mackowiak Claire1,2, Robin Aurélié1,2, Barbara Alice1,2, Pellerin Luc1,2, Ephrem Salame4,5, Gombert Jean-Marc1,2, Barbier Louise1, Herbelin André1
1INSERM U1313, FHTI SUPORT, Poitiers, France, 2University of Poitiers, Poitiers, France, 3University hospital of Poitiers, Poitiers, France, 4Digestive surgery and liver transplantation, university hospital of Tours, Tours, France, 5University of Tours, Tours, France

Background: The immune system plays a crucial role in several “domestic” processes, including repair, which consists of two successive phases: inflammation and its resolution characterized by new tissue formation and/or remodeling. Sterile inflammation in organ transplantation is an important feature of ischemia-reperfusion (IR) injury. Although immune cells have been shown to play an important role in IR injury, their potential role in ensuring tissue repair and the return to homeostatic conditions is not yet well-documented. Here, we analyzed the influence of human liver transplantation (LT) on the relative proportion and activation of blood T cells known for their regulatory and repair functions (i.e., T regulatory cells (Treg), and innate T cells (ITC)).

Methods: The study was conducted from a prospective biological collection of 20 LT recipients. Peripheral mononuclear cells (PBMC) were isolated from blood collected at different times: at the end (EoT) of LT, at one day (D1) and seven days (D7) after LT, and stored prior to multiparametric spectral flow cytometry analysis.

Results: Analysis of PBMC showed a D7 post-LT increase in the relative proportion of Treg within T cells, compared to D0. This late phenomenon was not found when considering the other conventional T cell subsets and ITC. Moreover, D7 post-LT increase of Treg was accompanied by an activation status, as testified by their upregulation of CD69 surface expression, compared to D0. Interestingly, D7 post-LT increase of Treg correlated with the release of IFN-γ and TNF-α at the EoT of interluekin-33 (IL-33), an antigen/cytokine known to drive expansion of Treg. Considering ITC, relative proportions of invariant natural killer T cells (iNKT), γδ-T cells and mucosa-associated invariant cells (MAIT) were found to have increased between D0 and EoT, prior to decreasing up until D7 post-LT. Remarkably, the early cell activation observed between D0 and EoT for 10% of MAIT and γδ-T cells, respectively, was maintained until D7 post-LT.

Conclusions: Our preliminary data reveal a late/maintained activation state of blood Treg and ITC after LT, suggesting their contribution to inflammation resolution and tissue repair. Current liver IR studies using IL-33-deficient mice are under investigation to directly test the role of IL-33 in this phenomenon.

P258 TAILORED IMMUNOSUPPRESSION WITH LCPT EXTENDED RELEASE TACROLIMUS BASED ON NFAT-REGULATED GENE EXPRESSION

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Background: There is a narrow therapeutic window for immunosuppression (IS) with calcineurin (CNI) inhibitors. The immunosuppressive effect of CNIs differs between individuals. Therefore, the drugs’ trough levels do not reflect IS and should be replaced by pharmacodynamic monitoring. Since nuclear factor of activated T-cells (NFAT)-depending gene expression correlates with cyclosporine induced IS, this study was designed to evaluate the effect of LCP extended release tacrolimus (Tac) on NFAT regulated residual gene expression (RGE).

Methods: Gene expressions of interleukin-2, interferon-γ and granulocyte-macrophage colony-stimulating factor and three reference genes were measured with droplet digital polymerase chain reaction (ddPCR) in whole blood samples at day 2, 7, 14, month 1 and 6 until 1 year after LT in 23 patients transplanted between February 2019 and June 2020. The RGE after Tac intake was calculated as RGE = cpeak/c0, where c0 is the adjusted number of transcripts at the Tac predose level and cpeak is the number of transcripts at peak level. IS consisted of LCPT extended-release Tac introduced directly after LT, mycophenolic acid, and a corticosteroid-taper for 3 months.

Results: Tac peak levels and RGE showed a strong inverse correlation (r=-0.8). Our descriptive analysis shows that although patients show a Tac trough level within the targeted therapeutic window, low RGE can result in a higher risk for infection. Mean individual trough effect of Tac on the 3 target genes with all timepoints pooled was 33% (26-56%) in patients without infection and 81% (53-95%) in patients with infection (p=0.011), mean individual peak effect was 48% (44-64%) in patients without infection and 91% (90-94%) in patients with infection (p<0.001).

Conclusions: Tailored IS monitored with NFAT-RGE is promising to decrease infectious complications by optimization of the IS level in LT recipients on LCP extended release Tac.
**Background:** A metabolic collapse at reperfusion, impairing the kidney's energy metabolism, was recently proposed as mechanism behind delayed graft function. More specifically, a potential Krebs cycle defect was identified. Since perfusate/tissue metabolite abundances can result from different underlying biochemical pathways, we further elucidate the complex biochemical processes on a whole organ level by applying tracer metabolomics during isolated normothermic kidney perfusion.

**Methods:** Pig kidneys exposed to no, 22h of cold or 1h of warm ischemia were perfused with a red cell based perfusate for 4 hours. Key nutrients (glucose, glutamine and glutamate) were completely replaced by their fully labelled 13C isotopes (based on the number of labelled atoms per metabolite) were measured by Liquid Chromatography Mass Spectrometry. Changes in both the relative abundances of metabolites as well as the contribution of 13C-isotopes to the pool of the respective metabolite (fractional contribution) and isotopologue percentages were determined.

**Results:** The isolated kidney incorporated 13C-atoms from glucose into amino acids (alanine, glycine, serine, and glutamate) and lactate, released back into the perfusate. Differences between ischemic conditions at 2h of perfusion were seen for m1 and m2 isotopologues of serine and glycine. Furthermore, the kidney’s gluconeogenic capacity was impaired in ischemic kidneys. Additional analyses of tissue Krebs cycle intermediates from glucose, glutamine and glutamate labelling experiments showed a truncated Krebs cycle in healthy kidneys displaying an active aspartate-glutamate cycle, while ischemia reverses this towards the glutamate-aspartate cycle.

**Conclusions:** Combining tracer metabolomics and normothermic organ perfusion is a powerful non-invasive tool to understand how perturbations like ischemia change underlying biochemical processes.
Background: Clinical operational tolerance (COT), defined as the absence of immunosuppressive treatment (IS) without graft immunological damage, was initially observed in non-compliant liver transplant (LTx) recipients or in recipients immunosuppressive treatment (IS) without graft immunological damage, was initially observed in non-compliant liver transplant (LTx) recipients or in recipients immunosuppressive treatment (IS) without graft immunological damage, was initially observed in non-compliant liver transplant (LTx) recipients or in recipients with (de-novo) malignancy or uncontrollable infection. Several clinical trials failed however to establish a protocol for IS withdrawal in clinical practice out of these conditions. Here we describe a clinical approach to actively minimize and eventually complete IS withdrawal in LTx recipients over time.

Methods: Patients who achieved tacrolimus (TAC) 1mg/day monotherapy eventually complete IS withdrawal in LTx recipients over time. These findings indicate that active minimization and even complete IS withdrawal are feasible in clinical practice in very selected LTx patients under close biological/histological surveillance. Further studies would validate these results.

Results: During the period 01/01/1994-31/12/2017, 866 adults received a LTx. The 1mg/day TAC regimen was achieved in 164 (19%) recipients, all included in the stepwise IS reduction approach. Patients’ demographics and IS reduction dynamics are displayed in Table 1. At the end of follow-up on 07/31/2022, IS was further reduced in 110 (67.1%) recipients as follows: in 50: 5-6mg/week, in 17: 1-2mg/week; and 19 patients (11.6%) reached COT status. No demographics differences were observed between these 4 groups. Reduction had not yet been attempted in 38 patients (1mg/day recently started), while in 16 (9.6%) the strategy failed; however, LTx normalized after resumption of the previous IS regimen. Histology from recipients on progressive reduction or complete withdrawal did not show increase of fibrosis or evolution towards chronic rejection.

Conclusions: These findings indicate that active minimization and even withdrawal of IS are feasible in clinical practice in very selected LTx patients under close biological/histological surveillance. Further studies would validate these results.
Background: Insufficient physical activity increases the risk of all-cause mortality and cardiovascular disease among kidney transplant recipients. The aim of this review is to examine the published studies on physical activity in kidney transplant recipients.

Methods: In this study, all databases (ClinicalKey, Cochrane, Ebsco, Ovid, Proquest, Science Direct, Scopus, Springer, Turkey Citation Index, Ulakbilim, Wiley Online Library, Web of Science etc.) were searched using the keywords “Physical Activity” “Kidney Transplant Recipients” were reviewed.

Results: A total of 70 publications were reviewed. When repeated publications were removed, 67 articles were reached. The publications were written between 2007-2022. The most publications belonged to the year 2021 (n=10). When analyzed by research type, two publications were research protocols, twelve were interventional, eight were cross-sectional, four were cohorts; five were longitudinal, thirteen were descriptive, seven were prospective, four were qualitative, five were articles, and twelve were review articles. The level of physical activity was low in kidney transplant recipients. It was determined that the subjects of weight gain, nutrition, cardiopulmonary functions, fluid intake, graft function, quality of life and self-efficacy were studied together with physical activity. Interventions studies were conducted for three, six and 12 months. Studies have shown that interventions increase physical activity levels after three months, and more research is needed for long-term results.

Conclusions: As a result of the examinations, it was found that the physical activity level was low in kidney transplant recipients. When analyzed according to research types, interventional studies are limited. It was determined that randomized controlled studies are needed to improve physical activity levels.

Evet Cleenders1, Priyanka Koshy2, Elisabet Van Loon3,4, Katrien Lagrou5, Graciela Andrei6, Dirk Kuypers1, Olga Mineeva-Sangwo7, Robert Snoeck1, Geert Verbekel1, Maarten Coemans1,2, Maarten Naessens1,2

1KU Leuven, Nephrology and Renal Transplantation Research Group, Leuven, Belgium, 2KU Leuven, Leuven Biostatistics and Statistical Bioinformatics Centre (L-BioStat), Leuven, Belgium, 3University Hospitals Leuven, Department of Imaging and Pathology, Leuven, Belgium, 4University Hospitals Leuven, Department of Nephrology and Renal Transplantation, Leuven, Belgium, 5KU Leuven, Laboratory of Clinical Microbiology, Leuven, Belgium, 6Rega Institute for Medical Research (KU Leuven), Department of Microbiology, Immunology and Transplantation, Leuven, Belgium, 7KU Leuven, Nephrology and Renal Transplantation Research Group, Leuven, Belgium

Background: Systematic screening for BK polyomavirus-DNAemia (BKPyV-DNAemia) has been advocated to aid prevention and treatment of polyomavirus associated nephropathy (PyVAN), an important cause of kidney graft failure. The added value of performing a biopsy at time of BKPyV-DNAemia, to distinguish presumptive PyVAN (negative SV40 immunohistochemistry) and proven PyVAN (positive SV40) has not been established.

Methods: We studied an unselected cohort of transplantations (N = 950), performed between 2008-2017. The diagnostic performance of BK viral load in plasma for positive SV40 staining in a contemporaneous biopsy was assessed. Using Cox regression we investigated associations of recipient/donor characteristics and treatment with rates of the following events: first occurrences of BKPyV-DNAemia and positive SV40 staining, BKPyV-DNAemia resolution and graft failure. Associations of BKPyV-DNAemia resolution and graft failure with histological scores at time of first BKPyV-DNAemia were assessed.

Results: BKPyV-DNAemia was detected in 250 (26.3%) transplant recipients, and positive SV40 in 91 cases (9.6%). Among 210 patients with a concomitant biopsy at time of first BKPyV-DNAemia, 60 (28.6%) biopsies were SV40 positive. Plasma viral load showed high diagnostic value for concurrent SV40 positivity (ROC-AUC 0.951, 95%CI 0.920 - 0.977, Figure 1A) and intrarenal BKPyV load (pvl score) (0.979, 95%CI 0.969 - 0.989). SV40 positivity is highly unlikely when plasma viral load is below 4 log10, copies/ml (negative predictive value 0.989, 95%CI 0.979 - 0.994, Figure 1B). In SV40 positive patients, higher plasma and intrarenal BKPyV load were associated with slower viral clearance from the blood (Hazard Ratio [HR] 0.712, 95%CI 0.604 - 0.839, and HR 0.268, 95%CI 0.116 - 0.621, respectively), whereas the dichotomy positivity/negativity of SV40 did not predict viral clearance.

Conclusions: Although intrarenal BKPyV load offers some prognostic value for viral clearance on top of plasma viral load, the latter provides good guidance on when a biopsy is unnecessary to exclude PyVAN. Our study supports the current guidelines that a biopsy is not required for the primary management of patients with BKPyV-DNAemia, and that the difference between presumptive and proven PyVAN is of limited clinical value.
Askiti*1, Moeke2, Leuvenink3, Michel Struys2, Rob Henning1, Gertrude Nieuwenhuijs-

Background: Amongst ischemia and reperfusion injury (IRI), mitochondrial may release mitochondrial DNA (mtDNA). mtDNA can serve as a propagator of further injury during and after kidney transplantation. Aim of this study was to measure the perioperative plasma kinetics of mtDNA during living donor kidney transplantation (LDKT) and the potential of plasma mtDNA levels as markers of graft outcome parameters.

Methods: This was a post-hoc analysis of plasma samples of the Volatile Anaesthesia Protection of Renal Transplants-1 (VAPOR-1) study. All donor-recipient couples of the Volatile Anaesthesia Protection of Renal Transplants-1 (VAPOR-1) trial were included (n=57). Systemic venous, systemic arterial and renal venous samples were taken at multiple timepoints in the peri-operative period. Real-time PCR analysis was used to measure 3 mtDNA genes: displacement loop (D-loop), NADH ubiquinone oxidoreductase subunits 1 and 6 (ND1 and ND6).

Results: Levels of mtDNA genes changed over time and differed between sample origin. Donor mtDNA levels were significantly lower compared to recipients at pre-transplantation (all P<0.001). Systemic venous D-loop levels significantly increased from pre-transplantation till day 9 post transplantation (P<0.05). Systemic arterial mtDNA genes all significantly increased at 2 hours post transplantation (all P<0.001). Renal venous mtDNA levels at 30 sec after reperfusion were significantly higher compared to later timepoints (P<0.05). Different association to graft outcome parameters was found after correction for multiple testing. Several donor, recipient and transplant characteristics had a significant effect of the dynamics of mtDNA over time.

Conclusions: These results demonstrate mtDNA release during the LDKT procedure. Furthermore, mtDNA release differed over time. In addition, different concentrations of mtDNA were measured in different sample origin, demonstrating the importance of timing and sample origin to study the diagnostic potential of mtDNA.

E-POSTERS P100 P300 P400 P001 P200 P500 P600 P700

P272 VALGANCICLOVIR VS LETERMORV PROPHYLAXIS AND RISK OF CYTOMEGALOVIRUS DNAEMIA IN A RANDOMIZED PHASE 3 TRIAL

Klemens Budde*1, Nassim Kamar1,2, Marta Crespo1, Catherine B. Small1, Franco Citterio1, Nicole Stauffer2, Valerie L. Teal3, Christopher L. Gilbert4, Barbara Haber5

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Background: Valganciclovir (VGCV), indicated for cytomegalovirus (CMV) prophylaxis in adult donor CMV-seropositive/recipient CMV-seronegative (D+/R-) kidney transplant recipients (KTRs), is limited by myelosuppression and need for dose adjustment for creatinine clearance (CrCl) <60 mL/min. Letermovir (LET) is non-myelotoxic and needs no dose adjustment for CrCl. This large, randomized Phase 3 non-inferiority study (NCT03443889) demonstrated that CMV prophylaxis with LET was non-inferior to VGCV in adult D+/R-KTRs and significantly safer as measured by rate of leukopenia or neutropenia (IDWeek 2022). A post-hoc analysis was conducted to understand the impact of renal function on CMV DNAemia and CMV disease (CMV end-organ disease or syndrome confirmed by an adjudication committee) during prophylaxis.

Methods: Adult KTRs were randomized (1:1) within 7 days post-KT to receive LET daily at the approved dose with acyclovir (400 mg twice daily) vs VGCV (900 mg daily; adjusted for CrCl) through Week 28 (~200 days). CrCl was calculated by Cockcroft-Gault equation at each visit; doses of VGCV were adjusted if needed according to the manufacturer. CMV DNA was obtained at each visit through Week 28 post-transplant (Roche COBAS® AmpliPrep/COBAS TaqMan® [CAP/CTM] assay; LLOQ 137 IU/mL).

Results: 586 D+/R-KTRs were randomized and received ≥1 dose of prophylaxis. The rate of quantifiable CMV DNAemia through Week 28 post-KT was 2.1% with LET vs 8.8% with VGCV. The rate of CMV disease through Week 28 post-KT was 0% with LET and 1.7% with VGCV. The proportions of LET- and VGCV-prophylaxed KTRs with CrCl <60 mL/min were 68% and 70% at week 1 and 37% and 38% at Week 28, respectively. Figure 1 shows CrCl over time by treatment arm. Dose adjustments of LET occurred in 0% of LET-prophylaxed KTRs, and dose adjustments of VGCV occurred in 63% of VGGV-prophylaxed KTRs, of whom 27% had >10 adjustments. The proportion of KTRs with quantifiable CMV DNAemia or CMV disease by CrCl quartile (Table 1) was higher in patients receiving VGGV prophylaxis with low CrCl. No association was observed for KTRs receiving LET.

Conclusions: In D+/R- KTRs, LET dosing independent of renal function avoids the burden of dose adjustments for renal function and is associated with a reduced risk of CMV DNAemia and CMV disease during prophylaxis compared with VGGV.

Figure 1. Creatinine Clearance Over Time

Weeks Post-transplant

Mean (95% CI)

P270 COVID-19 INFECTION IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS AFTER IMMUNIZATION WITH THE BNT162B2 COVID-19 MRNA VACCINE

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Background: Evidence from adult studies has shown that immunocompromised renal transplant recipients (RTR) belong to a high risk group for complicated COVID-19 infection. Data on the clinical course of the disease in the pediatric population especially after vaccination are limited.

Methods: We retrospectively analyzed the incidence and clinical course of PCR confirmed SARS-CoV-2 infection in a cohort of 20 (13 males/7 females) pediatric RTR. In the vaccinated patients we measured spike protein of SARS-CoV-2 IgG antibody using chemiluminescent microparticle immunoasay (Architect/Aility,Abbott). IgG results ≥50 AU/ml were considered positive.

Results: 17/20(85%) RTR were vaccinated with the BNT/1622 Covid-19 mRNA vaccine and 3/20(15%) declined vaccination. 13 patients received 2 vaccine doses and 4 patients 3 doses. 11/17 (65%) patients had positive antibody titer (mean 2209.26 AU/ml) and 6/17(35%) patients had negative antibody titer. 14 patients developed COVID-19 disease; 11/17(65%) vaccinated patients (mean time post vaccination: 6 months) and 3/3(100%) of the unvaccinated patients. The mean post vaccination antibody titer of the infected RTR was 1741.22 AU/ml versus 3087.33 AU/ml in the not infected group (p=0.53). After approval of remdesivir for treatment of COVID-19 infection, 6 patients received remdesivir as per our local protocol for immunocompromised patients. The mean symptom duration was 3 days (range 1-7 days) in the vaccinated patients, 2.6 (range 2-3 days) in the unvaccinated patients and 4.2 (range 3-7 days) in the patients that received remdesivir.

Conclusions: None of our patients developed pneumonia nor oxygen requirements. The major symptom was rhinits in 11/17(68%) patients while fever >38°C had 6/14(42%), low grade pyrexia <38°C 3/14(21%), cough 5/14(36%), diarrehas 2/14(14%), headache 2/14(14%) and myalgias 2/14(14%). We observed a transient creatinine increase in 4/11(36%) vaccinated and 1/3(33%) of unvaccinated patients. None developed acute rejection, however 2 patients developed graft rejection, both 6 months after COVID-19 infection.

Figure 1. Creatinine Clearance Over Time

Weeks Post-transplant

Mean (95% CI)

P269 PERI-OPERATIVE KINETICS OF PLASMA MITOCHONDRIAL DNA LEVELS DURING LIVING DONOR KIDNEY TRANSPLANTATION

Marie Krones1, Nora Sprakman1,2, Femke Hoogstra-Berends1, Henri Leuvenink1, Michel Struys1, Rob Henning1, Gertrude Nieuwenhuis-Mosker1

1University Medical Center Groningen, Clinical Pharmacy and Pharmacology, Groningen, Netherlands, 2University Medical Center Groningen, Anesthesiology, Groningen, Netherlands, 3University Medical Center Groningen, Surgery, Groningen, Netherlands

Background: During ischemia and reperfusion injury (IRI), mitochondria may release mitochondrial DNA (mtDNA). mtDNA can serve as a propagator of further injury during and after kidney transplantation. Aim of this study was to measure the perioperative plasma kinetics of mtDNA during living donor kidney transplantation (LDKT) and the potential of plasma mtDNA levels as markers of graft outcome parameters.

Methods: This is a post-hoc analysis of plasma samples of the Volatile Anaesthesia Protection of Renal Transplants-1 (VAPOR-1) study. All donor-recipient couples of the Volatile Anaesthesia Protection of Renal Transplants-1 (VAPOR-1) trial were included (n=57). Systemic venous, systemic arterial and renal venous samples were taken at multiple timepoints in the peri-operative period. Real-time PCR analysis was used to measure 3 mtDNA genes: displacement loop (D-loop), NADH ubiquinone oxidoreductase subunits 1 and 6 (ND1 and ND6).

Results: Levels of mtDNA genes changed over time and differed between sample origin. Donor mtDNA levels were significantly lower compared to recipients at pre-transplantation (all P<0.001). Systemic venous D-loop levels significantly increased from pre-transplantation till day 9 post transplantation (P<0.05). Systemic arterial mtDNA genes all significantly increased at 2 hours post transplantation (all P<0.001). Renal venous mtDNA levels at 30 sec after reperfusion were significantly higher compared to later timepoints (P<0.05). No association to graft outcome parameters was found after correction for multiple testing. Several donor, recipient and transplant characteristics had a significant effect of the dynamics of mtDNA over time.

Conclusions: These results demonstrate mtDNA release during the LDKT procedure. Furthermore, mtDNA release differed over time. In addition, different concentrations of mtDNA were measured in different sample origin, demonstrating the importance of timing and sample origin to study the diagnostic potential of mtDNA.
Table 1. Proportion of KTRs with quantifiable CMV DNAemia or CMV disease by C1r/C1s quartile

<table>
<thead>
<tr>
<th>C1r/C1s Quartile at Week 28, mL/min</th>
<th>LET arm Failures</th>
<th>VGV arm Failures</th>
<th>LET Failures quartiles 1-2 vs 3-4</th>
<th>VGV Failures quartiles 1-2 vs 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (0-55)</td>
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<td>2 (1.7%) of 117</td>
<td>17 (13.1%) of 130</td>
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<td>2 (&gt;55-97)</td>
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<td>0</td>
<td>3 (2.0%) of 116</td>
<td>5 (4.3%) of 117</td>
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<tr>
<td>3 (&gt;97-145)</td>
<td>1</td>
<td>4</td>
<td></td>
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<tr>
<td>4 (&gt;145)</td>
<td>0</td>
<td>0</td>
<td>0 (0.0%) of 116</td>
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</tr>
</tbody>
</table>

CMV Disease through Week 28 by Week 28 C1r/C1s Quartile

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<td>4 (&gt;145)</td>
<td>0</td>
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<td>0 (0.0%) of 116</td>
<td>0 (0.0%) of 117</td>
</tr>
</tbody>
</table>

*Participants without a C1r/C1s at Week 28 are not included.

P274 LONGITUDINAL DYNAMICS OF SARS-COV-2 SPIKE-SPECIFIC ANTIBODY RESPONSES IN PATIENTS ON WAITING LIST AND AFTER LUNG TRANSPLANTATION

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Background: Patients with end-stage lung diseases on the MHH waiting list for lung transplantation (LTX) have been vaccinated against SARS-CoV-2 spike protein with usually 3 doses of the mRNA vaccine. They are supposed to develop robust antibody and T cell responses when immunized prior to LTX without the influence of immunosuppression. We hypothesized the induction of high spike-specific IgG levels protected against SARS-CoV-2 infection and severe COVID-19. To gain information about the humoral response in waitlist patients (WL-LTX) vaccinated prior to LTX, we compared spike S1-, RBD- and S2-domain- specific IgG levels in WL-LTX patients pre vs. post LTX.

Methods: Plasma obtained pre- (n=70) and post-LTX (n=28) of WL-LTX patients was analyzed by Luminex-based multiplex assays. Threshold for positivity was set separately for each spike domain based on the median MFI +2σ in healthy, unexposed pre-pandemic controls. Patients with previous known SARS-CoV-2- infection were excluded.

Results: 95.7% of WL-LTX patients had seroconverted for either RBD-, S1- or S2-specific IgG pre-LTX and 92.86% were positive post-LTX. S1-, S2- and RBD-specific IgG MFI values did not significantly differ between pre- vs. post-LTX. Subanalysis of matched plasma samples (n=25) revealed that 52% of WL-LTX patients showed a higher IgG response pre- than post-LTX for all three spike protein domains and 28% showed even elevated antibody levels post-LTX. Lastly, S2-specific IgG MFI values were significantly elevated compared to RBD-specific IgG MFI values, both pre- (S2 vs. RBD p=0.0001) and post-LTX (S2 vs. RBD p=0.0225).

Conclusions: The majority of WL-LTX patients mounted high SARS-CoV-2 spike-specific IgG responses following vaccination pre LTX. Based on the more efficient antibody production against the S2 domain compared to RBD- and S1-domains, S2-specific IgG responses should be included also in the general evaluation of humoral immune responses to SARS-CoV-2. WL-LTX patients exhibited superior antibody responses to vaccination compared to LTX-recipients first vaccinated after LTX. Pre-transplant responses were maintained in some patients following transplant. Collectively, these results support patients, both on the waiting list and after LTX, benefitting from additional booster vaccinations after transplantation.

P273 A NEW KIDNEY OFFERING SCHEME IN THE UK - 3 YEAR REVIEW

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Background: On 11th September 2019 a new kidney offering scheme (NKOS) was introduced in the UK to reflect the changing donor pool which had led to a higher rate of offer declines and an increasing use of DCD donors. The scheme was designed to meet several key objectives identified through reviewing the past Kidney Allocation Scheme introduced in April 2006, comparing alternative schemes across the world, looking at the philosophies in allocation, and understanding whether improvements could be made in histocompatibility and immunogenetics.

Methods: The 2019 NKOS allocates all kidneys from both DBD and DCD donors and gives absolute priority to difficult to match and long waiting patients, better kidney longevity matching for those patients with 19% of transplant recipients being highly sensitised compared to 12% in the previous scheme. Older patients and long waiting recipients have also benefited. The introduction of longevity matching has contributed to a reduction in declines due to donor related reasons. No statistical difference is reported in in declines due to donor related reasons. No statistical difference is reported in

Results: There were 5139 kidney-only transplants performed during the first three years of the new scheme. Of these, 3226 were from DBD donors and 1913 from DCD donors. There has been a significant benefit to difficult to match and ethnic minority patients, better kidney longevity matching and improved equity of access across different patient groups. Initial analysis reveals that the scheme is meeting these objectives.

Conclusions: The scheme was designed to increase access to transplant for difficult to match and ethnic minority patients, better kidney longevity matching and improved equity of access across different patient groups. Initial analysis reveals that the scheme is meeting these objectives.
Managing immunosuppression after kidney transplant failure remains controversial. Continuous balancing between sensitization and risk of infections remains challenging. Our aim was to evaluate the benefits and harms of continuing immunosuppression when aiming for re-transplantation.

Methods: We evaluated retrospectively all patients wait-listed for re-transplantation after kidney transplant failure between 2006 and 2022 in our institution. From 2015 the institutional policy recommended to continue immunosuppression if aiming for re-transplantation. The outcomes studied were calculated PRA (cPRA) at the time of re-transplantation, time on waiting list until re-transplantation, the rate of infection-related hospitalizations, and delayed graft function of the repeat transplant. For comparison, the patients were classified in two groups based on whether calcineurin inhibitor had been continued (CNI-continued) or withdrawn (CNI-stopped) before re-transplantation or at the end of the follow-up.

Results: Altogether 110 of 134 cases analyzed proceeded to retransplantation. CNI was continued in 60 patients and withdrawn in 74 patients. In the CNI-stopped group, there were more non-sensitized (PRA 0%) patients (20% vs 8.6%, p=0.04), fewer highly sensitized (PRA >80%) patients (35% vs 70.3%, p <0.001) and a lower mean cPRA compared to CNI-stopped group (Figure 1). Mean transplant waiting time was shorter in the CNI-continued group (557 vs 893 days, p <0.001). There were 0.93 infection-related hospitalizations per 1000 patient-days in the CNI-continued group compared to 1.68 in the CNI-stopped group (p<0.01). In the CNI-continued group, 60% had no hospitalizations due to infection compared to 24% in CNI-stopped (p<0.001). Delayed graft function of the retransplant was more common in the CNI-stopped than in the CNI-continued group (50% vs 26%, respectively, p = 0.02).

Conclusions: Continuation of calcineurin inhibitor seems beneficial among patients referred to retransplantation after kidney graft failure, as it was associated with lower sensitization, shorter waiting time, and lower risk of delayed graft function, whereas the risk of infection-related hospitalizations was not increased.

Figure 1. Comparison of the last PRA levels measured before the re-transplantation or at the end of the follow up.

Comparison of cPRA levels between the two groups

P277 THE PROSPECTIVE EFFECT OF LIVING AND DECEASED RELATED DONOR TRANSPLANTATIONS IN PATIENTS’ IMMUNE PROFILE

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Background: Phenotypic changes in lymphocytes have been described following renal transplantation (RT), including both CD4 and CD8 subpopulations.

Aim: Prospectively assess of T lymphocyte phenotypic alterations, after RT and compare differences between deceased (DR) and living (LR) donor recipients.

Methods: One hundred six RTRs were included in the study, 78/106 (74%) DR, age 52.5(15) years and 28/106 (26%) LD, 35(21) years. Lymphocytes, CD4, CD8, CD4/CD8, CD4/CD28, and CD4/CD25/CD127 were evaluated at peripheral blood, by flow cytometry, at certain time points: RT and 3, 6, 12 months (T0, T3, T6, T12, respectively).

Results: During follow up, at T3, T6, T12, eGFR was 61(23.6), 62(31.1), 63.5(23.9) ml/min/1.73m2, p=NS and 59.1(24.8), 61(25.3), 62(22.7), p=NS, in DR and LR group, respectively. eGFR showed no significant difference between DR and LR at any time point. At any time point, T0, T3, T6, T12, lymphocytes were significantly increased in DR compared to LR groups, p=0.001, p<0.0001, p=0.002, p<0.0001, similarly CD4, p<0.0001, p=0.001, p=0.001, and CD8 cells, p=0.002, p<0.0001, p=0.005, p=0.006, respectively. Tregs were increased at T0, T3, T6, not at T12, p<0.0001, p=0.001, p=0.01, respectively. At this point, Tregs were increased in RTRs with eGFR>50ml/min/1.73m2, 23.3(9.3) vs. 27.2(16.6), p<0.03. CD4CD28null, CD8CD28null, CD16+CD56+ (NK) and CD4+CD25+FoxP3+ (Tregs) were evaluated at peripheral blood, by flow cytometry, at certain time points: RT and 3, 6, 12 months (T0, T3, T6, T12, respectively).

Conclusions: Immune profile, was improved in both groups, DR and LR, however a significantly better effect managed in LR, although elimination of CD28 molecule could not be restored. Interestingly, Tregs were associated only by renal function one year following RT.

<table>
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<tr>
<th></th>
<th>DR</th>
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<td>130(800)</td>
<td>1600(918)</td>
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<td>414(249)</td>
<td>600(607)</td>
<td>729(615)</td>
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<td>286(163)</td>
<td>390(223)</td>
<td>450(275)</td>
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<td>198(125)</td>
<td>125(131)</td>
<td>142(149)</td>
<td>149(158)</td>
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<td>Tregs</td>
<td>20(13)</td>
<td>24(23)</td>
<td>27(25)</td>
<td>20(16)</td>
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<td>LR</td>
<td>1350(750)</td>
<td>2250(1300)</td>
<td>2150(1275)</td>
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<td>Lymphocytes</td>
<td>56(244)</td>
<td>904(817)</td>
<td>880(635)</td>
<td>863(442)</td>
<td>p&lt;0.001</td>
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<td>CD4 cells</td>
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<td>630(341)</td>
<td>623(614)</td>
<td>639(558)</td>
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<td>145(213)</td>
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<td>Tregs</td>
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<td>35(44)</td>
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**Results:**

Methods: All 636 HCC patients diagnosed were pathologically confirmed. As a result of examinations, we determined the treatment protocol (LT, surgical resection, locoregional treatment methods). Systemic chemotherapy treatment was given to HCC patients with distant organ metastases. During follow-up period, patients had routine laboratory tests, alpha-fetoprotein test and ultrasonography examinations every 3 months and computed tomography or magnetic resonance scans done every 6 months.

Results: Between November 1988 and February 2023, 965 patients were diagnosed with hepatocellular carcinoma. As a treatment protocol, locoregional therapy (TACE, RFA, TARE) was performed to 652 patients, systemic chemotherapy (sorafenib) was given to 156 patients, LT was performed to 107 patients, and surgical resection was performed to 20 patients. The mean survival of all LT recipients, who diagnosed HCC was 137.45 months. One year, 5 years and 10 years survival rates of these patients were 92.0%, 71.1% and 61.4% respectively. The mean survival time of 50 HCC patients who underwent surgical resection was 156.6 months. One year, 5 years and 10 years survival rates of these patients were 86.0%, 75% and 57% respectively. Locoregional treatment was performed to 652 patients. The mean survival time was 27.9 months. One year, 5 years and 10 years survival rates of these patients were 33%, 48% and 18% respectively.

Conclusions: Appropriate treatment methods must be selected with detailed evaluation in experienced centers in HCC patients. In patients who cannot undergo surgical resection or liver transplantation, in the absence of distant organ metastases, locoregional treatments can provide longer survival times than those reported in the literature.

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**P79**

**TARGETED DELETION OF HYPOXIA INDOUCIBLE TRANSCRIPTION FACTOR-1A GENE IN CD4+ T CELLS IMPROVES VASCULARIZED COMPOSITE ALLOTRANSPLANTATION OUTCOME**

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**Background:** This study aims to determine the impact of the deletion of the HIF-1α gene in CD4+ T cells on the immune response and allograft outcome after VCA. Both regulatory T cells (Tregs) and effector T cells (Teff) play a role in the acceptance of the allograft and the deletion of the HIF-1α gene influences the differentiation and function of various T cell populations. The study will investigate how the deletion of HIF-1α gene affects the immune response and allograft outcome.

**Methods:** In this study, mice with a deletion of the HIF-1α gene in CD4+ T cells were created using the Cre-lox-P system. The immune response was evaluated in an in vivo model of vascularized composite allotransplantation. The assessment included measures of Tregs and Teff cell activation, inflammatory cytokine levels, and allograft acceptance.

**Results:** The results show that the recipient with HIF-1α deficiency in CD4+ showed longer allograft survival than wild-type recipient under the same immunosuppressive regimen of either CTLA4i and Rapamycin or anti-CD154 and CTLA4i. These effects can be at least partially elucidated by reduced allo-reactive T cells. Lower levels of pro-inflammatory cytokines (such as IL-6 and TNF-α), and a significantly increased Helioc+ Tregs population with improved suppressive capacity.

**Conclusions:** The findings of the study suggest that manipulating the differentiation of CD4+ T cells through the HIF-1α pathway could be a promising strategy to enhance the outcome of allotransplantation. This approach holds the potential to positively impact allograft survival and the immune response, leading to improved transplant outcomes.

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**LONG TERM SURVIVAL OF THE HEPATOCELLULAR CARCINOMA WITH OR WITHOUT LIVER TRANSPLANTATION**

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**Background:** Hepatocellular carcinoma (HCC), which is frequently diagnosed at late stages, 5-year survival rate of less than 12%. The gold standard treatment is liver transplantation (LT) or surgical resection. Various local regional treatment strategies (transarterial chemoembolization (TACE), radiofrequency ablation (RFA), and radioembolization (TARE)) can be performed to the treatment of tumors inappropriate for surgical resection and LT. We evaluated the differences between the outcomes of the treatment protocols.

**Methods:** All 636 HCC patients diagnosed were pathologically confirmed. As a result of examinations, we determined the treatment protocol (LT, surgical resection, locoregional treatment methods). Systemic chemotherapy treatment was given to HCC patients with distant organ metastases. During follow-up period, patients had routine laboratory tests, alpha-fetoprotein tests and ultrasonography examinations every 3 months and computed tomography or magnetic resonance scans done every 6 months.

Results: Between November 1988 and February 2023, 965 patients were diagnosed with hepatocellular carcinoma. As a treatment protocol, locoregional therapy (TACE, RFA, TARE) was performed to 652 patients, systemic chemotherapy (sorafenib) was given to 156 patients, LT was performed to 107 patients, and surgical resection was performed to 20 patients. The mean survival of all LT recipients, who diagnosed HCC was 137.45 months. One year, 5 years and 10 years survival rates of these patients were 92.0%, 71.1% and 61.4% respectively. The mean survival time of 50 HCC patients who underwent surgical resection was 156.6 months. One year, 5 years and 10 years survival rates of these patients were 86.0%, 75% and 57% respectively. Locoregional treatment was performed to 652 patients. The mean survival time was 27.9 months. One year, 5 years and 10 years survival rates of these patients were 33%, 48% and 18% respectively.

Conclusions: Appropriate treatment methods must be selected with detailed evaluation in experienced centers in HCC patients. In patients who cannot undergo surgical resection or liver transplantation, in the absence of distant organ metastases, locoregional treatments can provide longer survival times than those reported in the literature.

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**EFFECTS OF COLONIZATION WITH MULTIDRUG-RESISTANT BACTERIA ON PNEUMONIA ETIOLOGY IN THE FIRST YEAR AFTER KIDNEY AND HEART TRANSPLANTATION**

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4. Chang Gung Memorial Hospital, Department of Nephrology, Taoyuan, Taiwan
5. Chang Gung Memorial Hospital, Department of Pathology, Taoyuan, Taiwan

**Background:** Our aim was to analyze if previous colonization with multidrug resistant (MDR) bacteria has effects on etiology of pneumonia in kidney (KTx) and heart (HTx) transplant recipients during the first year after transplantation.

**Methods:** Our retrospective study enrolled KTx and HTx recipients transplanted between January 2019 and December 2020 with 12 months follow-up. Pneumonias were identified according to American Society of Transplantation Infectious Diseases Community of Practice guidelines. Surveillance cultures including nasal, throat and rectal swab, and urine culture were used.

**Results:** Our study included 106 KTx and 30 HTx recipients with bacterial pneumonia occurrence of 6.6% (7/106) and 13.3% (4/30), respectively (Table 1). Surveillance cultures detected colonization with MDR bacteria in 40.6% (43/106) of KTx and 53.3% (16/30) of HTx recipients. The most frequent MDR isolate in KTx was extended-spectrum beta-lactamase-producing (ESBL) Klebsiella pneumoniae (18/53, 34.0%) and vancomycin-resistant enterococci (VRE) (8/53, 15.0%), and in HTx recipients MDR Pseudomonas aeruginosa (7/25, 28.0%), VRE (5/25, 20.0%) and K. pneumoniae ESBL (5/25, 20.0%). In five patients etiological pathogens were detected and those were Gram-negative bacilli (GNB). In KTx recipients with pneumonia (N=7), there were no MDR bacteria as proven etiological pathogen. In all HTx recipients with pneumonia (N=4), GNB were MDR and in 75% (3/4) of HTx recipients they were present as previous colonization in surveillance cultures.

**Conclusions:** GNB are responsible for the majority of bacterial pneumonias in our patient population. MDR GNB were more frequent etiological pathogens in HTx recipient majority of whom were previously colonized with the same bacteria. Despite small number of HTx recipients with pneumonia included, understanding the current epidemiology in different SOT recipients may help to better prevent and treat these infections.

<table>
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<th>Characteristic</th>
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<th>Heart</th>
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<td>Transplantations</td>
<td>106</td>
<td>30</td>
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<tr>
<td>Median age at transplantation, y (range)</td>
<td>53.5 (8-77)</td>
<td>55.5 (5-67)</td>
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<td>Gender (male) (%)</td>
<td>77 (72.6)</td>
<td>22 (83.3)</td>
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<td>Bacterial pneumonia, n (%)</td>
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<tr>
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</tr>
<tr>
<td>&gt;1-6 months</td>
<td>5 (71.4)</td>
<td>1 (25.0)</td>
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<tr>
<td>&gt;6-12 months</td>
<td>2 (28.6)</td>
<td>1 (25.0)</td>
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DELAYED REGULATORY T CELL THERAPY FOLLOWING ALEMTUZUMAB INDUCTION

Conor Hennessy1, Matthew Brook1, Joanna Hester1, Alaa Alzahrani1, Salim Hammad1, Kathryn Wood1, Peter Friend1, Paul Harden1, Fadi Issa1

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Background: In the OIST study, phase 1 trials of Treg therapy showed feasibility and safety in kidney transplantation. The goal of the TWO study is to expand on this and demonstrate further safety and efficacy of Treg therapy using a modified protocol of delayed Treg infusion following lymphodepletion with alenetuzumab induction to promote a Treg-skewed immune phenotype.

Methods: This was designed as a prospective single centre randomised controlled trial to explore delayed Treg therapy in living donor kidney transplant recipients. Patients were randomised to receive either 5-10x10^6 autologous Tregs per kg at week 28 post transplantation, or standard immunosuppression. Both groups received alenetuzumab induction and initial immunosuppression with tacrolimus and mycophenolate mofetil. Primary outcomes were rejection and patient survival. Trial recruitment was paused in March 2020 due to the COVID-19 pandemic. Alenetuzumab induction was discontinued due to the uncertainty around safety of alenetuzumab in the context of COVID infection and the protocol was modified. Here we report data from the original protocol.

Results: We present here the outcomes of the cohort of 9 patients who underwent alenetuzumab induction under the original TWO study protocol. Two patients withdrew due to temporary suspension of the living donor transplant programme during the pandemic, and on resumption alenetuzumab could not be used. Seven patients completed the trial following alenetuzumab induction. Post-transplant patient and graft survival was 100%. Acute rejection free survival was 100% in the Treg arm compared to 75% in the control arm at 18 months post-transplant. Alenetuzumab resulted in prolonged depletion of T cells, with only 2/7 patients returning to pre induction CD4+ T cell levels at the 18-month visit. A trend towards transient increases in Treg numbers at weeks one and two post infusion were observed in patients receiving Treg therapy. Increases in naive and transitional B cells were also observed in the Treg groups, similar to previous reports in operational tolerance.

Conclusions: Autologous Treg therapy is feasible and safe and can be delayed following lymphodepleting induction immunosuppression.

ADDITIONAL PAPER: DAVE DIONE ON REAL-WORLD IMMunosuppressive Therapy Patterns for Renal Transplant Patients in France: 10 Year Follow-Up Data From the OIST Study

P282

Radu Vadensis1, Dany Anglicheau2, Antoine Durbach3, Denis Goltz4, Melanie Charron1, Francois-Emery Cotte1, Fayssou Fouda1, Isabelle Bardoulat6, Mickael Arnaud4

1BMS, Medical Affairs, Paris, France, 2Necker Hospital, Nephrology & Transplantation, Paris, France, 3Hervé Mondor Hospital, Nephrology & Transplantation, Creteil, France, 4Saint Louis Hospital, Nephrology & Transplantation, Paris, France, 5Bristol-Myers Squibb, market access, Rueil Malmaison, France, 6IQLIQA, Paris, France

Background: Immunosuppressive (IS) therapy modification is often required to maximise long-term patient and graft survival for kidney transplant recipients. Real-world data on IS strategies are limited. This analysis aims to describe real-world patterns of IS use and survival outcomes among renal transplant patients in France from OISTER, a long-term observational study.

Methods: A retrospective cohort of 29,709 adult patients receiving a renal graft and subsequent treatment with ≥1 IS therapy between 2009 and 2019 was identified from the French National Health Data System (SNDS). Patients were followed from first kidney transplant up to first event of interest (i.e., death, graft loss) or last observation available.

Results: Calcineurin inhibitors (CNI) were the most common first-line IS therapy (96.1% of patients, Table 1), while mammalian target of rapamycin inhibitors (mTORi) (1.2%) and belatacept remained marginal. In subsequent lines of therapy, CNI use remained dominant, whereas the use of mTORi, belatacept and combination IS regimens increased (Table 1). Nearly 25% of patients on first-line IS had treatment modifications (8% in 2nd line, and ≥2% in ≥3rd line). During the study period, belatacept was unavailable until 2012 and since 2017, belatacept initiations were limited by supply issues. The 1-month, 1-year and 5-year patient survival rate were estimated at 99.1%, 96.8%, and 89.0%, respectively. Unsurprisingly, older age at transplantation negatively impacted 5-year survival: 73.1% in patients aged ≥70 years vs. 97.8% in 60-69 years. The 5-year graft survival rate was comparable across age groups (range: 84.2-87.3%), although decreased slightly in higher age groups (82.3 % in 60 years and 80.6 % in 70 years).

Conclusions: This study provides a wide picture of IS therapies used for kidney transplant maintenance nationwide. The observed therapeutic strategies are aligned with French and international recommendations. In clinical practice, patient and graft survival at 5 years in renal transplant patients was excellent, most patients were alive with a functional graft. Graft survival remained comparable irrespective of age at transplantation, underlying that there was no discrimination with regard to the quality of the graft transplanted.
**Factors Associated with Growth in Pediatric Kidney Transplant Recipients: A Retrospective, Single-Center Cohort Study**

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**Background:** Catch-up growth after pediatric kidney transplantation (KT) is usually insufficient to reach normal adult height. Moreover, the incidence of overweight and obesity increases post kidney transplantation (KT). We aimed to describe growth patterns and predictive factors in children post KT.

**Methods:** We retrospectively reviewed the records of 28 children who underwent KT in our center between 2002-2022. Height (hSDS) and body mass index (BMI/SDS) z-scores at various time points and possible predictors were assessed.

**Results:** Median age at KT was 11.2 years (3.6-14), 20 were male, mean time on dialysis was 5.95 years. KT from a living donor (LRD) was performed in 18 patients. Mean follow-up time was 4.88 (1.10) years. rhGH was administered pre-KT in 15/28 patients and in 3 post KT. Following the first post KT, steroid free, alternate day and daily steroid regimes were adopted for 9, 11 and 8 patients, respectively. Mean hSDS at the time of KT, one year after and at last visit were -1.76, -1.87, and -1.77 (p<0.05). Mean BMI/SDS at the respective times were 0.13, 0.65 and 0.05 respectively (p<0.05). At last visit, 29% and 17% of children showed moderate and severe height deficit. hSDS at last visit was associated with preoperative hSDS at a difference of 1 hSDS pre and last visit post KT (ΔhSDS) was associated with the type of KT [mean ΔhSDS for LRD and DTD -1.45 (95% CI -1.87, -1.03) and -2.66 (95% CI -3.4, -1.93) respectively, p<0.002] and steroid regimen [mean ΔhSDS for daily and alternate day steroid treatment -0.39 (95%CI -0.77, -0.03) and 0.55 (95%CI -0.7, 1.17) respectively, p<0.037]. There was no association between ΔhSDS and rejection episodes or rhGH administration pre-KT. At the time of KT and at last visit 25% and 10.7% were overweight, respectively, whereas only 1 patient was preoperative but none at last visit. The overall incidence of overweight and obesity had reduced at last visit compared to pre-KT (p<0.01).

**Conclusions:** Linear growth post KT remained limited, resulting in short stature in nearly half of children. Strategies to improve height post pediatric KT could include height optimization pre-KT, steroid withdrawal/avoidance protocols, and LRTD.

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**Characterisation of Graft Infiltrates Following Regulatory T Cell Therapy in Kidney Transplant Recipients**

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**Background:** Post-transplant diabetes mellitus (PTDM) is an important and potentially avoidable complication after kidney transplantation. In this study we assessed graft infiltrates in patients receiving Treg therapy, using the Nanostring GeoMx digital spatial profiling platform.

**Methods:** Adoptative Treg therapy was found to be safe and feasible in clinical practice. The TWO study is a Phase 1b randomised control trial of Treg therapy in living donor kidney transplant recipients which seeks to further expand on the safety data and explore the efficacy of this novel treatment strategy.

**Results:** In this study we assessed graft infiltrates in patients receiving Treg therapy, using the Nanostring GeoMx digital spatial profiling platform. Protocol biopsies were retrieved from patients 9 months post-transplantation in patients who received Tregs 5 days post-transplant as an alternative to induction immunosuppression. These were compared to graft infiltrates in control patients with biopsy-proven rejection, or protocol biopsies from control patients not receiving cell therapy. Multiplexed protein expression was assessed on sections of interest identified using CD3, CD4 and FOXP3 immunofluorescence.

**Conclusions:** The dense focal infiltrates seen in the cellular therapy group appeared to express an overall signature of immune regulation, in contrast to those in rejecting transplants. Defining the characteristics of these infiltrates is important in understanding how treatment with cell therapy alters tissue rejection responses.
De novo GEM is a rare complication of kidney transplantation that detrimentally impact on graft survival. Several clues indirectly suggest that this entity might represent a particular form of AMR directed against minor histocompatibility antigen expressed on podocyte surface.

Conclusions: De novo GEM is a rare complication of kidney transplantation that detrimentally impact on graft survival. Several clues indirectly suggest that this entity might represent a particular form of AMR directed against minor histocompatibility antigen expressed on podocyte surface.

Results: De novo GEM were diagnosed later and had a more severe impact on graft survival than recurrence (Log rank p respectively: 0.006 and 0.0007). Compared to patients with recurrence, those with de novo GEM had characteristics associated with alloimmunization with more female, past transfusion, and cyclosporine rather than tacrolimus. Furthermore, analysis of graft biopsies found more microvascular inflammation (glomerulitis and/or peritubular capillaritis, associated with AMR in Banff) in the de novo GEM group. Finally, although there was a trend for a higher proportion of patients with anti-HLA DSA at diagnosis in the de novo GEM (20%) vs recurrence (13%) group, this difference was not significant (p=0.51). Rather than ruling out our hypothesis, this result could indicate that the humoral alloimmune response that drives de novo GEM is directed against minor (non-HLA) polymorphic antigens.

Conclusions: De novo GEM is a rare complication of kidney transplantation that detrimentally impact on graft survival. Several clues indirectly suggest that this entity might represent a particular form of AMR directed against minor histocompatibility antigen expressed on podocyte surface.
Further studies are needed to determine whether adiponectin and leptin play a pathophysiological mechanism for the occurrence of NODAT in the early period after LT. This may be because beta cell dysfunction, rather than IR, is the main cause. Adiponectin and leptin did not affect the occurrence of NODAT in the first year after LT. The levels of adiponectin before or after LT were not associated with the development of NODAT. However, adiponectin and leptin were associated with the occurrence of IR by 1.25-fold (CI: 1.08-1.45).

Results: A poor knowledge of screening before or after LT was not associated with the occurrence of NODAT. However, the occurrence of NODAT included BMI before LT (OR 1.1, 95% CI: 1.02-1.22), acute graft rejection, infectious or cardiovascular complications. Risk factors for NODAT occurrence was not associated with higher mortality, increased rates of pregnancy. Only 47% knew that heterozygosity status could be a cofactor of liver disease.

Conclusions: AATD is a poorly known disease among LT practitioners in France. A better knowledge of screening methods, diagnosis and treatment of the disease would allow a better management of the patients and their relatives.

Background: Alpha-1 antitrypsin deficiency (AATD) is one of the most common genetic diseases in Europe with a prevalence of heterozygosity of 1.6%. Although it is also responsible for liver damage leading to end stage liver diseases, AATD is not always diagnosed, even in the most severe patients who are candidates for liver transplantation. The pathogenesis of NODAT is most likely similar to that of the type 2 diabetes mellitus, with insulin resistance (IR) and beta-cell dysfunction being the main driving factors. Adiponectin and leptin dysregulation are associated with the occurrence of IR and diabetes in the general population, but their role in LT patients remains unclear.

Methods: The study included patients undergoing LT without prior glucose intolerance or overt diabetes. Metabolic parameters (including adiponectin and leptin) did not affect the occurrence of NODAT in the first year after LT. This may be because beta cell dysfunction, rather than IR, is the main cause. Adiponectin and leptin were associated with the occurrence of IR by 1.25-fold (CI: 1.08-1.45).

Conclusions: AATD is a poorly known disease among LT practitioners in France. A better knowledge of screening methods, diagnosis and treatment of the disease would allow a better management of the patients and their relatives.

Background: Alpha-1 antitrypsin deficiency (AATD) is one of the most common genetic diseases in Europe with a prevalence of heterozygosity of 1.6%. Although it is also responsible for liver damage leading to end stage liver diseases, AATD is not always diagnosed, even in the most severe patients who are candidates for liver transplantation (LT). Considering the recent advances in potential treatment and the understanding of AATD involvement in progression of liver disease, we aimed to investigate the level of knowledge on AATD and the current practices of liver transplant physicians in France. 

Methods: A practice survey of 22 multiple-choice questions in the form of a questionnaire created and distributed via Google Form was sent by e-mail to the members of the French think tank in LT, GREF2.

Results: Adherence to the survey was 54%, including 89% hepatologists, 7.5% liver surgeons and 3.5% anesthesiologists. 81% of practitioners rated their level of knowledge as very low, low, or average, and only 12% answered the question of disease prevalence correctly. Half of the responders had >15 years of experience in high-volume LT centers. Only 57% of practitioners routinely performed AATD screening before LT. LT AAT dosage was used in 97% of cases for the screening, but 47% knew that it is decreased by hepatocellular insufficiency and 20% by pregnancy. Only 47% knew that heterozygosity status could be a cause of liver disease progression. Furthermore, 62% of practitioners with > 5 years of experience considered their level of knowledge to be low but systematically screened before LT in 75% of cases compared to 44% for practitioners with between 5 and 15 years of experience and 61% for practitioners with > 15 years.

Conclusions: AATD is a poorly known disease among LT practitioners in France. A better knowledge of screening methods, diagnosis and treatment of the disease would allow a better management of the patients and their relatives.

Background: The development of new-onset diabetes after transplantation (NODAT) has the greatest negative impact on long-term survival after liver transplantation (LT). The pathogenesis of NODAT is most likely similar to that of type 2 diabetes mellitus, with insulin resistance (IR) and beta-cell dysfunction being the main driving factors. Adiponectin and leptin dysregulation are associated with the occurrence of IR and diabetes in the general population, but their role in LT patients remains unclear.

Methods: The study included patients undergoing LT without prior glucose intolerance or overt diabetes. Metabolic parameters (including adiponectin and leptin) were measured before and 3, 6, and 12 months after LT to determine the incidence and risk factors for NODAT.

Results: The study involved 152 people, of whom 29 (19.1%) developed NODAT. Patients with alcoholic liver disease had a higher incidence of NODAT with 19 (26%) compared to 10 (12.7%) patients in the rest of the population (p=0.041). NODAT occurrence was not associated with higher mortality, increased rates of allograft rejection, infectious or cardiovascular complications. Risk factors for the occurrence of NODAT included BMI before LT (OR 1.1, 95% CI: 1.02-1.22), BMI 12 months after LT (OR 1.15, 95% CI: 1.01-1.31), and beta cell function 3 months (OR 0.98, 95% CI: 0.97-0.99), 6 months (OR 0.99, 95% CI: 0.97-1.00) and 12 months (OR 0.98, 95% CI: 0.97-1.00) after LT. Adiponectin and leptin levels before or after LT were not associated with the development of NODAT. However, elevated leptin concentrations were found to be a risk factor for the development of IR in cirrhotic patients. A leptin increase of 1 µg/mL increased the odds ratio for the occurrence of IR by 2.1 (CI: 1.08-1.45).

Conclusions: NODAT was a common complication in the first year after LT, but no association between NODAT and adverse events was found. The levels of adiponectin and leptin did not affect the occurrence of NODAT in the first year after LT. This may be because beta cell dysfunction is a factor rather than IR, is the main pathophysiological mechanism for the occurrence of NODAT in the early period. Further studies are needed to determine whether adiponectin and leptin play a role in the occurrence of NODAT in the long-term course after LT.
THE IMPACT OF POSTREPERFUSION SYNDROME ON RECIPIENT MORTALITY AND GRAFT FAILURE IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Post-reperfusion syndrome (PRS) during liver transplantation (LT) is known to be related to higher morbidity and mortality after surgery. However, most of the studies that investigated effect of PRS on prognosis could not control various pharmacological interventions immediately before or after reperfusion. Furthermore, they are mainly based on deceased donor LT (DDLT), and thus the effect of PRS on prognosis in the living donor LT (LDLT) is unclear. By utilizing our institution’s standard protocol in LDLT and minimizing prophylactic use of pharmacological interventions before or after reperfusion, we aimed to investigate the effect of PRS on graft failure and post-transplant mortality in LDLT.

Methods: With approval of IRB, medical records of adult recipients (age ≥ 19 years) who received LDLT between April 2010 and December 2019 at Samsung Medical Center were retrospectively reviewed. Primary outcome was the effect of PRS on mortality and graft failure. Secondary outcome was the effect of PRS on other post-operative outcomes including the lengths of ICU and hospital stay, rejection.

Results: A total of 399 patients were enrolled. The incidence of PRS was 35.3%. To reduce confounding variables, patients were divided to two groups, No PRS group and PRS group, and then matched at a 1:1 ratio with the factors that are known to be associated with prognosis. Before matching, only the length of ICU stay showed significantly longer in PRS group than no PRS group (P=0.001). After matching, 120 paired sets of patients were generated and all postoperative outcomes including death, graft failure, and the lengths of ICU and hospital stay did not show significant difference. Cox regression analysis on postoperative outcomes including death, graft failure, and the lengths of ICU and hospital stay did not show significant difference. After matching, 120 paired sets of patients were generated and all postoperative outcomes including death, graft failure, and the lengths of ICU and hospital stay did not show significant difference.

Conclusions: In this study, PRS did not affect mortality and graft-failure in LDLT. Only the length of ICU stay showed statistical difference before matching.

CHARACTERIZING ADHERENCE PROFILES BASED ON C0 MONITORING IN KIDNEY TRANSPLANT PATIENTS: ILLUSION OR REALITY?

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Background: Many authors claim the relationship between adherence and immunosuppressive drug concentrations, and trough level monitoring has been proposed as a tool to characterize patients’ adherence. Our objective was to explore the relationship between exposure to calcineurin inhibitors (CNIs) and adherence over time in kidney transplant patients followed-up for up to three years after transplantation.

Methods: Adherence was repeatedly estimated with the 4-Item Morisky-Green-Levine Medication Adherence Scale (MMAS) in 712 kidney transplant recipients followed-up in the EPIGREN and EPHEGREN cohorts between 2007 and 2017. Non-adherence was defined for a MMAS score >0. Adherence time-profiles were explored by mixed effect modeling with latent processes. The relationship between drug exposure and adherence was explored by comparing the proportion of subtherapeutic trough concentrations (C0) between patients with: (i) adherent vs. non-adherent time-profiles; (ii) simultaneously have subtherapeutic C0 and a MMAS score >0. The intra-patient coefficient of variation (CV) of C0 was calculated for cyclosporine and tacrolimus in patients with adherent and non-adherent profiles.

Results: Two profiles of adherence over time were characterized: the first subgroup of patients (85%) displayed a good and stable adherence, while patients of the second subgroup (15%) displayed a poorer adherence, worsening over time. The proportion of subtherapeutic C0 was comparable between groups for both cyclosporine and tacrolimus. No patient was found to simultaneously have subtherapeutic C0 and a MMAS score >0. The intra-patient coefficient of variation (CV) of C0 was not associated with adherence for either molecules (non-adherent vs. adherent patients: 42.8 vs. 49.5% for tacrolimus and 52.9 vs. 51.6% for cyclosporine).

Conclusions: No relationship was found between exposure to CNIs and adherence over time. The TDM of CNIs can allow identifying episodes of non-adherence in patients who display very low C0, but is of limited interest to characterize adherence profiles. The characterization of adherence profiles is relevant only when TDM is associated with patient interviews.
Evaluation of Post Reperfusion Baseline Biopsies for Kidney Transplant Outcome

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Methods: To determine the predictive value of histologic findings in post reperfusion kidney transplant biopsies, we evaluated the degree of glomerulosclerosis, interstitial fibrosis and tubular atrophy (IF/TA), arteriosclerosis (AS) and acute tubular injury (ATI) in 383 biopsy specimens collected from 2006 to 2016 after deceased (n=243) and living donation (n=95). All baseline biopsies were scored by a blinded renal pathologist. Survival analysis was performed using multivariate Cox regression analysis and binary regression analysis to investigate an association with delayed graft function (DGF).

Results: Mean follow-up time was 4.1 years. DGF was reported in 108 (32%) cases. As expected, ATI and arteriosclerosis were significantly associated with DGF (OR: 2.65, CI: 1.52-4.67, p = 0.001 for moderate AS). Survival analysis revealed IF/TA as the only histologic lesion being associated with death-censored graft failure over the entire observation period, determined by multivariate Cox regression analysis in three different models adjusted for known clinical risk factors as e.g., donor age, donor history of hypertension, cold ischemia time and terminal serum creatinine >1.5mg/dl (Hazard ratio: 1.04, CI: 1.01-1.08, p = 0.032). The median survival of kidney transplants with IF/TA > 0% was 110 months compared to 98 months for those without evidence of IF/TA. None of the histologic lesions had a significant effect on one-year graft survival.

Conclusions: ATI as histological hallmark of ischemia-reperfusion damage and the extend of arteriosclerosis were associated with DGF. IF/TA provides independent information on graft survival but cannot be used alone as a prognostic tool given the still acceptable survival time. The inclusion of histologic markers in a combined tool with clinical features may be promising.

A Lengthened Euthanasia Eliminates the Burden of Organ Donation Related Premortem Inquiries and In Hospital Performed Euthanasia

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Background: Organdonation after euthanasia (ODE), has been performed since 2012 in the Netherlands. ODE exposes the euthanasia donor (ED) to a non-familiar environment in the last moments of life. Decoupling of euthanasia and organ donation (OD) has been shown to be feasible in ODE starting from home. Preparations for ODE with premortem inquiries may also be experienced as burdensome. We describe a modified ODE to reduce the ODE related physical and mental burden.

Methods: A patient with a neurodegenerative disease suffered from aggravating symptoms. She lived her life mainly solitary at night and isolated. She requested for euthanasia and had a sincere wish to donate her organs. Assessments were performed and euthanasia was consented. There were no objections for OD in her medical history. She explicitly preferred not to have any exposure to hospital surroundings and medical professionals in the preparation and performance of OD.

Results: To facilitate her wish to donate, she consented to come to the hospital, would be deeply sedated in a private room as start of the euthanasia, and thereafter general anesthesia (GA) was provided to maintain sleep and secure vital functions, immediately followed by additional testing (laboratory, CT scanning, echocardiography, bronchoscopy). Allocation was to be awaited in the next hours. After allocation and settlement of the OD procurement team, last acts of euthanasia resulted in a respiratory arrest, 14 minutes later followed by a circulatory arrest, and declaration of death after 5 minutes ‘no touch’. The functional warm ischemia time (WIT) was 19 minutes. The body was immediately transported to the operation room. OD procurement followed successfully.

Conclusions: A further decoupling of OD and euthanasia in ODE is feasible. The OD related burden is transferred from the ODE patient to medical professionals, especially to the euthanasia provider, who must attend at the ED from beginning of euthanasia till death declaration. From the perspective of the ED this may result in a significant reduction of moral-ethical and logistical distress. GA followed by last acts of euthanasia might also hasten death, reducing the functional WIT without doing harm to the ED. ODE patients should be informed about the alternative pathways of ODE, decoupling euthanasia and postmortem OD.
Background: Thanks to advances in surgical techniques and immunosuppression, patient and graft survival after organ transplantation have increased significantly. Most of the female patients who had kidney transplants in childhood want to become pregnant when they reach reproductive age. Among this patients, concerns regarding adverse immunosuppression effect on the fetus and consequence of pregnancy of allograft function represent significant sources of anxiety. We retrospectively analyzed pregnancy outcomes after liver and kidney transplantation at our transplant center.

Methods: Since November 3, 1975 we have performed 3404 kidney transplantations (KT) and 720 liver transplantations (LT) at Baskent University. Among KT recipients 394 were pediatric and 348 of LT patients were pediatric (age <18 years old). On March 15, 1990, Dr. Haberal performed partial LT in children, a first in Turkey, Europe and the region. Mean age of the pediatric KT recipients was 13.8 ± 6.7 (range 1.5-18 years) and of the pediatric LT recipients was 7.44 years (range 4 months – 17 years). Of 394 pediatric kidney transplant patients 177 were female and 156 of 348 pediatric LT patients were female. All of KT and LT’s were living related kidney transplant and all recipients were relatives with their donors.

Results: In total 28 kidney and liver transplant recipients became pregnant. Of these patients, 10 were LT recipients and 18 were KT recipients. The mean age at which the patients gave birth was 30 years (range 24-38 years). The mean time between the organ transplantation and delivery of the patients was 10.63 years (range 2-22 years). Recipient patients were immunosuppressed with tacrolimus or cyclosporine together with prednisone during pregnancy. The mean delivery time of the babies was 35.5 weeks (range 24-39 weeks). One patient delivered vaginally, and the other patients delivered cesarean section. Except for 1 baby, all of the other babies were born healthy. One baby died at 24 weeks due to praecentia previa. No significant complications or organ rejection occurred during or after delivery in any of the mothers.

Conclusions: Liver and kidney transplant female recipients can have a safe pregnancy and give birth to healthy children if they are followed up and treated in experienced centers.

P303 UROLOGIC COMPLICATIONS AFTER KIDNEY TRANSPLANTATIONS AND THEIR MANAGEMENT
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Background: Urologic complications are most common surgical complications encountered after kidney transplant, causing significant morbidity and mortality. Rates of urologic complications after kidney transplant range between 2% and 12.5%. In parallel with the evolution of minimally invasive percutaneous techniques and acquired experience, there has been a major shift from surgery to interventionial radiologic procedures in the management of these complications. In our transplant center, thanks to interventional radiologic procedures in the management of these complications and acquired experience, there has been a major shift from surgery to interventionial radiologic procedures in the management of these complications.

Methods: Between November 1975 and January 2023 our transplant team has performed 3404 kidney transplantations. From 1975 to 1983, we performed ureteroneocystostomies using the modified Politano-Leadbetter technique. From December 1983 to January 1993, we performed corner-saving technique. We analyzed types of urologic complications after kidney transplantation in 1141 patients. Then, in September 2003, we began using corner-saving technique. We analyzed types of urologic complications (KT) and 720 liver transplantations (LT) at Baskent University. Among KT recipients 394 were pediatric and 348 of LT patients were pediatric (age <18 years old). On March 15, 1990, Dr. Haberal performed partial LT in children, a first in Turkey, Europe and the region. Mean age of the pediatric KT recipients was 13.8 ± 6.7 (range 1.5-18 years) and of the pediatric LT recipients was 7.44 years (range 4 months – 17 years). Of 394 pediatric kidney transplant patients 177 were female and 156 of 348 pediatric LT patients were female. All of KT and LT’s were living related kidney transplant and all recipients were relatives with their donors.

Results: In total 28 kidney and liver transplant recipients became pregnant. Of these patients, 10 were LT recipients and 18 were KT recipients. The mean age at which the patients gave birth was 30 years (range 24-38 years). The mean time between the organ transplantation and delivery of the patients was 10.63 years (range 2-22 years). Recipient patients were immunosuppressed with tacrolimus or cyclosporine together with prednisone during pregnancy. The mean delivery time of the babies was 35.5 weeks (range 24-39 weeks). One patient delivered vaginally, and the other patients delivered cesarean section. Except for 1 baby, all of the other babies were born healthy. One baby died at 24 weeks due to praecentia previa. No significant complications or organ rejection occurred during or after delivery in any of the mothers.

Conclusions: Liver and kidney transplant female recipients can have a safe pregnancy and give birth to healthy children if they are followed up and treated in experienced centers.

P304 PREVALENCE OF POST-COVID-19 CONDITION IN PATIENTS WITH CHRONIC KIDNEY DISEASE, ON DIALYSIS AND LIVING WITH A KIDNEY TRANSPLANT
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Background: The prevalence of post-COVID-19 condition (PCC) is estimated to be 13% in healthy individuals. We analyzed the prevalence and disease burden of PCC in patients with chronic kidney disease (CKD), dialysis patients and kidney transplant recipients (KTR).

Methods: Patients participated in the RECOVAC study, in which SARS-CoV-2 antibodies were measured in CKD G4/5, dialysis patients and KTR after the second and third COVID-19 vaccination in the Netherlands. A questionnaire was sent to 4868 participants one year after initial vaccination asking for the presence of long-lasting symptoms after diagnosis in COVID-19 positive patients, or since the start of the pandemic in COVID-19 negative patients. PCC was defined according to the WHO clinical case definition. Blood samples at one month after the second and third vaccination were analysed with anti-RBD IgG ELISA. COVID-19 diagnosis was assessed by questionnaire or positive anti-nucleocapsid IgG antibodies. Logistic regression analysis was used to compare the presence of one or more long-lasting symptoms between COVID-19 positive and negative patients. In COVID-19 positive patients, we likewise identified predictors of PCC by backward selection and estimated the association between log-transformed antibody levels and PCC.

Results: 2747 patients were included, of which 222 patients with CKD G4/5, 390 dialysis patients and 2135 KTR. PCC was present in 25%, 16%, and 21% of CKD G4/5 patients, dialysis patients and KTR with high or very high long-lasting symptom burden in 57%, 61% and 71%, respectively. In COVID-19 negative patients, long-lasting symptoms were present in 15%, 13% and 18%, respectively. COVID-19 positive patients (n= 1004) were at higher odds of having one or more long-lasting symptoms compared with COVID-19 negative patients (n=1743) (OR 1.33 [1.09-1.61], p<0.05). Predictors of PCC were chronic lung disease (adjusted OR 2.04 [1.18-3.50], p<0.01) and hospital/ICU admission (adjusted OR 5.03 [3.22-7.86], p<0.001). Log anti-RBD IgG antibody level was negatively associated with PCC (adjusted OR: 0.79 [0.65-0.94], p=0.008).

Conclusions: Patients with CKD G4/5, dialysis patients and KTR are at risk for PCC with a high symptom burden, especially if antibody levels after COVID-19 vaccination are low.
**P305 EFFECT OF A NATIONWIDE INTERVENTION TO REDUCE HEPATECTOMY TIMES IN DUTCH ORGAN PROCUREMENT TEAMS**

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**Background:** Donor hepatectomy time > 60 minutes is associated with poorer transplantation outcomes. The Dutch organ procurement committee executed a nationwide audit to evaluate hepatectomy times of procedures performed from December 2017 until February 2018. Liver procurements exceeded the 60-minute threshold in more than 50% of cases. Subsequently, a nationwide improvement program ("intervention") was enrolled to reduce hepatectomy time, ideally below 40 minutes. Aim of this study was to determine whether this intervention successfully reduced hepatectomy time.

**Methods:** A nationwide, retrospective database study of organ procurement procedures, both DBD and DCD was conducted. All procedures from January 2013 until October 2022 were included. Donor hepatectomy time was defined as time between start of abdominal flush and hepatectomy. The intervention period, from March 2018 till June 2018, was excluded from analysis. We compared hepatectomy times before and after the intervention, of procurement teams who were affiliated to a liver transplant center (n=3) with those not affiliated to a liver transplant center (n=2).

**Results:** In total 1749 liver procurements were analyzed, of which 876 before and 873 after intervention. Median hepatectomy time significantly decreased from 50 (39-63) to 35 (28-43) minutes, p<0.01 for affiliated procurement teams and from 67 (52-84) to 34 (28-42), p<0.01 for non-affiliated procurement teams. Before intervention 24.1% of the hepatectomies in the Netherlands were performed within 40 minutes. This increased to 69.5% after the intervention (p<0.01). Before intervention, simultaneous procurement of thoracic organs was significantly associated with increased hepatectomy time (B=0.31 95% CI: 0.24-0.38, p<0.001), while this was not the case after intervention (B=0.03 95% CI: -0.35-0.10 p=0.37). There was no significant difference in preventable surgical damage before or after the intervention (p=0.27).

**Conclusions:** The nationwide audit and the subsequent intervention resulted in a significant decrease in hepatectomy times for all procurement teams. Therefore, we recommend implementing such procurement analysis in all EU countries. Monitoring and intervention, if needed, will assure the same procurement standards, and increase donor liver quality.

**P306 THE COST-EFFECTIVENESS OF PROPHYLAXIS IN CYTOMEGALOVIRUS SEROPOSITIVE (CMV R+) KIDNEY TRANSPLANT RECIPIENTS OVER THE FIRST YEAR POST-TRANSPLANTATION**

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**Background:** The medico-economic benefits of prophylaxis over preemptive strategy in cytomegalovirus (CMV) seropositive kidney transplant recipients (R+) are still debated. This study aimed to evaluate the cost-effectiveness and cost-utility of oral ganciclovir prophylaxis vs. preemptive strategy on CMV-infection-free survival over the first year post-transplantation.

**Methods:** Clinical, biological and economic data were collected from 188 CMV R+ kidney transplant recipients: 101 patients benefited from prophylaxis and 87 from preemptive strategy. The impact of the strategy on CMV infection free survival was explored using a time-dependent Cox proportional hazard model (using R software). Costs were calculated from the hospital perspective. Quality-adjusted life years (QALYs) were determined using the EQ5D. Incremental cost effectiveness and cost utility ratios (ICER and ICUR) were estimated in euros by nonparametric bootstrapping for each case of infection avoided and for each QALY gained over 1 year.

**Results:** Prophylaxis significantly decreased the risk of CMV-infection over the first year post-transplantation (HR=0.22, CI95%=[0.12-0.37], p<0.01). Compared with the preemptive strategy, prophylaxis allowed resources saving (€-1155 per patient), and was more effective (0.42 infection avoided per patient), resulting in an ICER = €-2769 per infection avoided. Prophylaxis was superior to the preemptive strategy, with a net gain of 0.046 QALY per patient and costs saving of €1422 for 1 QALY gained.

**Conclusions:** In this study, the most cost-effective strategy for the management of CMV infections in R+ kidney transplant recipients was prophylaxis, despite the high cost of ganciclovir. Prophylaxis had a positive effect in quality of life at reasonable costs and resulted in net savings. Further studies comparing prophylaxis and preemptive strategies should be conducted to confirm the medico-economic superiority of prophylaxis in CMV R+ kidney transplant recipients.

**P307 RENAL TRANSPLANTATION IN HYPERSENSITIZED PATIENTS. DESENSITIZATION VS. PATHI**

Catuxa Rodriguez Magarinos1, Marta Blanco Pardo1, Sara Domenica Erreaz Guerrero1, Constantino Fernández Rivera1, Andres Lopez Muñiz2, Diego Sierra Castro1, Maria Calvo Rodriguez2
1Hospital Universitario de A Coruña, A Coruña, Spain, 2Erasmus University Medical Center Groningen, Groningen, Netherlands

**Background:** Higher sensitized patients suffer from greater difficulties to access kidney transplantation. We have designed the present study to analyse and compare two methods that facilitate access to transplantation for these patients: HA-desensitization in living-donor kidney transplantation and PATHI (Spanish allocation system for high sensitized patients)

**Methods:** Sensitized patients undergoing renal transplantation were studied during two different action protocols: pre-transplant desensitization with a living-donor and the national PATHI program (cPRA>98%). We analysed time on waiting list, the degree of cPRA and the prognosis: patient and graft survival, acute rejection and infectious complications.

**Results:** 51 patients are studied (27 desensitized and 24 PATHI). The time on the list was longer in PATHI (115 +/ 79 vs 87 +/ 87, p=0.24), higher number of incompatibilities in desensitization group (3.6 +/ 1.1 and 2.8 +/ 1.6) and longer follow-up in desensitization group (78+/66 vs 34+/27 months, p=0.001). Delayed graft function 14.8% in desensitized patients and 66.7% in PATHI (p=0.001). The incidence of CMV at one year was 30.2% in desensitized and 13.4% in PATHI (p=0.95) with AMBR in 2 patients in desensitization and 4 in PATHI. Graft survival at 1 and 3 years was 88.3% in desensitization and 90% in PATHI p 0.75. Patient survival of 96.3% and 91.7% at one year and 3 years in desensitization vs 94.4% at one year and 3 years in PATHI, p=0.69. The incidence of CMV at one year was 30.2% in desensitization vs 21.9% in PATHI p=0.45. The incidence of BK at one year was 0% in desensitization vs 10.5% in PATHI, p = 0.01.

**Conclusions:** The time on the waiting list is longer in PATHI and the number of incompatibilities is higher in desensitization group. Follow-up is longer in desensitization, so the results in the medium-long term must be interpreted with caution. We did not find significant differences in survival, higher frequency of rejection mediated by tests in PATHI without statistically significant difference. Higher CMV in desensitization without statistical significance and higher incidence of BK in PATHI.
KIDNEY TRANSPLANTATION IN JEHOVAH’S WITNESSES: ETHICAL IMPLICATIONS, MANAGEMENT PROPOSAL AND REVIEW OF LITERATURE

Marika Morabito1, Linda Liepa1, Federica Masci1, Marta Ripamonti1, Federico Nicolò1, Elia Zani1, Cristianò Parise1, Giuseppe Letto1, Giulio Carcano1
1University of Insubria and Ospedale di Circolo e Fondazione Macchi, Emergency and Transplant Surgery, Varese, Italy; 2University of Insubria, Center for Clinical Ethics, Biotechnology and Life Sciences Department, Varese, Italy

Background: For Jehovah’s Witnesses (JW) religious principles organ transplant is permitted but blood transfusions are proscribed: blood is a symbol of life and only God can give or take life. JW represents a challenge for the surgeon: even if often not necessary, there is no proof that transfusions can be avoided systematically and safely. Especially for non-lifesaving organs, doubts remain on the wisdom to engage in such a complicated procedure. Moreover, denial of transfusions may be considered an additional risk factor for premature graft loss and might discourage transplant physicians from enrolling JW in their waiting lists. Aim of this study is to describe a single center experience and analyze the issues still present on surgical decision-making.

Methods: From 2013 to 2022, 17 JW received a Kidney Transplant (KTx) at our institution. Grafts procured from deceased donors were allocated to JW on the basis of regionally allocation rules. Living donations were performed too. To secure JW needs, various techniques have been developed for reducing the extent of bleeding and recovering the blood loss intraoperatively. Systematic review of the literature was carried out, analyzing publications from 1990 to 2023.

Results: We have established an operating protocol focused on the patient’s cardiovascular system, verifying the ability to deal with transient states of anemia by satisfying the oxygen demands of peripheral tissues. Continuous circuit blood salvage and reinfusion was employed during surgery as were recombinant erythropoietin and intravenous iron during the posttransplant period. About literature review, of 536 articles found, only 18 items were included after the text analysis.

Conclusions: Most JW can safely receive a KTx without increasing the risk of graft failure. Ethical debate is still open on the risk of reduced chance of graft survival, which may be seen as a violation of the rights of non–JW recipients who have one or more surgical complications. In addition, hypertension (HTN) and diabetes mellitus (DM) was diagnosed in 10 (11.6%) and 3 (3.5%) living donors, respectively. Creatinine clearance was > 90 mL/min in 47 (54.2%), 60 to 90 mL/min in 34 (39.5%), and ≤ 60 mL/min in 5 donors (5.8%).

LIVING KIDNEY DONATION CONTINUES TO EXIST AS A STANDARD THERAPEUTIC OPTION FOR ESRD PATIENTS AND HARBOURS A MINOR RISK. POST-OPE.RATIVE COMPLICATIONS CAN BE REDUCED WITH VIGILANT SELECTION OF DONORS AND APPROPRIATE POST-SURGICAL MANAGEMENT

COMPARISON OF PERFUSATE COMPOSITION DURING NONMORPHIC LIVER PERFUSION - TRANSPLANTED VERSUS NON-TRANSPLANTED LIVERS

Jule Dingfelder1,2, David Pereyra1,2, Laurin Rauter1, Sertac Kacar3, Gerd Silberhumer1, Andreas Salat1, Zoltan Mathe1, Thomas Soliman1, Dagmar Kollmann1, Georg Gyoeri1, Gabriela A. Berlakovich1
1Medical University of Vienna, Department of General Surgery, Division of Transplantation, Vienna, Austria

Background: An increase in perfusate components during normothermic machine perfusion (NMP) could be indicative for the synthesis capability of the graft and extent of preservation injury. Our aim was to compare perfusate composition of transplanted (tx) with not transplanted livers (non-tx) during NMP.

Methods: During NMP of 27 livers, blood gas analysis (BGA) of perfusate and bile was performed, as well as perfusate analysis for factor XIII activity (FXIII), fibrinogen, bilirubin, sodium, and lactate dehydrogenase (LDH). Viability assessment was based on lactate clearance, perfusate and bile glucose, perfusate and bile pH, and bile production.

Results: In total 31 livers underwent NMP, 20 were transplanted following viability assessment while 11 livers did not meet the criteria for transplantation. The two groups did not differ significantly in donor age (p = 0.06) and BMI (p = 0.197), but WIT was significantly longer (p = 0.016) and gGT was higher (p = 0.003) in the non-tx group. Perfusate sodium (p = 0.0001; 60 minutes, p = 0.005) and bicarbonate (60 minutes, p = 0.011) levels were lower in non-tx livers. The pH was higher in tx livers at T = 0 (p = 0.012), 30 (p = 0.001), and 60 (p = 0.024) minutes. Non-tx livers presented with higher FXIII activity at T = 0 min (p = 0.041), 60 min (p = 0.007), 120 min (p = 0.008), and 240 min (p = 0.069). FXIII act was increasing in non-tx livers but remained stable in tx livers. Bilirubin (5 min, p = 0.02), AP (5 min, p = 0.027), LDH (5 min, p = 0.049), AST (5 min, p = 0.02; 60 min, p = 0.04; 120 min, p = 0.008; 240 min, p = 0.014; ALT (120 min, p = 0.009; 240 min, p = 0.043), gGT (5 min, 0.002; 60 min, p = 0.013), LDH (5 min, p = 0.05; 60 min, p = 0.011; 120 min, p = 0.009) was significantly higher in non-tx livers. Fibrinogen levels trended higher in tx livers (not significantly) and were increasing over the course of the perfusion in both groups.

Conclusions: Damage markers in perfusate confirmed the decisions during viability assessment. Interestingly, FXIII in perfusate was higher in non-tx livers and presented with different dynamics. Fibrinogen was increasing over the course in all livers, tx livers presented with higher fibrinogen levels, which might indicate a higher regenerative capacity.
Zaira Ivette Castañeda Amado, Nestor Toapanta, Manel Perello, Joana Sellares, Irina Torina, Maria Meléndez, Jose Zurìaga Vergara, Jhusela Rosas, Cesar Sanchez Carrillo, Oriol Bestard, Francesc Moreo

1Hospital Universitari Vall d’Hebron, Barcelona, Spain

Background: The convenience of the use and type of T-cell depletion Induction immunosuppression in kidney transplants (KT) from cDCD donors is not well-established yet. We aimed at characterizing main clinical outcomes in a large consecutive cohort of KT patients from cDCD according to different induction immunosuppressive therapies.

Methods: From 2015 to 2021 we performed 302 KT from cDCD and we considered recipients of a single KT with cPRA 0%. Induction immunosuppression was based on Thymoglobulin (rATG) from 2015 until 2019 and Grafalon thereafter. During this time period there were recipients treated with Basiliximab to avoid longer cold-ischemia time (CIT). Maintenance immunosuppression was based on tacrolimus, MMF, and steroids. Valganciclovir prophylaxis was employed for CMV and BK virus infection was not significantly different between groups.

Results: Main baseline, clinical, demographic and immunological, donor/recipient characteristics were not different between groups (table 1). Post-transplant lymphocyte kinetics showed a significantly lower cellular depletion and faster recovery among Grafalon-treated patients compared to rATG. After adjusting for donor KDPI and functional warm and CIT, treatment with Grafalon was associated with lower risk of DGF (OR: 0.39; 95%CI: 0.16-0.97; p=0.043) and Thymoglobulin (OR: 0.52; 95%CI: 0.24-1.14; p=0.101). Furthermore, when adjusting for DGF and HLA mismatches, treatment with both Grafalon (OR: 0.14; 95%CI: 0.04-0.57; p=0.006) and rATG (OR: 0.37; 95%CI: 0.14-0.95; p=0.04) were associated with a lower risk of rejection. Notably, incidence of CMV and BK virus infection was not significantly different between groups. However, when adjusting for CMV serological risk (D+/R-), patients treated with Grafalon showed a trend to a lower risk of late-onset CMV infection than rATG and basiliximab (OR: 0.48; 95%CI: 0.22-1.02; p=0.059). One-year patient and graft survival were not different between the three groups.

Conclusions: In our cohort, grafalon is associated with less lymphocyte depletion, maintaining an excellent safety profile in term of the incidence of AR and viral opportunistic infections such as CMV.

Background: ACLI is an acute liver disease related to bile duct obstruction leading to liver inflammation response and apoptosis. Gpbar-1 is a cell surface receptor that is involved in the regulation of multiple metabolic pathways. However, the function of Gpbar-1 in the context of innate immune activation in ACLI remains unclear.

Methods: The liver tissues and blood samples from Twenty ACLI patients and twenty healthy subjects were collected and subjected to biochemical test, HE staining, western blot and immunohistochemistry assay to verify liver damage and expression of Gpbar-1. WT and si-Gpbar-1 mice with ACLI induced by BDL were used in vivo, and primary KCs with or without Gpbar-1-siRNA were used in vitro. We used animal and cell experiments to verify macrophage-mediated ACLI and the regulatory mechanism between Gpbar-1 and NLRP3-ASC inflammasome.

Results: In this study, Gpbar-1 knockout significantly exacerbated BDL-induced acute hepatic damage, inflammatory reaction and liver apoptosis compared with WT mice in vivo. The KCs with knockdown of Gpbar-1 were more susceptible to lipopolysaccharide (LPS) stimulation than normal KCs. Gpbar-1 activation by its ligand suppressed LPS-induced pro-inflammatory response in KCs. M1 polarization in vitro was accelerated under LPS-stimulated Gpbar-1-knockdown KCs. From a therapeutic viewpoint, the administration of KCs expressing Gpbar-1 directly increases intracellular cAMP levels and phosphorylation of PKA, thus disrupting the NLRP3-ASC inflammasome. The pro-inflammatory nature of Gpbar-1 deficiency was almost neutralized by NLRP3 inhibitor CY-09 in KCs. M1 polarization in vitro was accelerated under LPS-stimulated Gpbar-1-knockdown KCs. From a therapeutic viewpoint, the administration of KCs with Gpbar-1 deficiency aggravated BDL-induced ACLI, which was effectively rescued by inhibition of NLRP3-ASC inflammasome.

Conclusions: Our studies reveal that Gpbar-1 plays a crucial role as a novel regulator of immune-mediated ACLI by inhibiting NLRP3-ASC inflammasome, with therapeutic implications for the management of human ACLI.

Table 1. Clinical, demographic and immunological, donor/recipient characteristics on different groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Thymoglobulin (n=77)</th>
<th>Grafalon (n=106)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63 (53-71)</td>
<td>62 (50-78)</td>
<td>0.642</td>
</tr>
<tr>
<td>Sex [male (%)]</td>
<td>79 (94)</td>
<td>80 (93)</td>
<td>0.800</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>73 (58-94)</td>
<td>70 (59-91)</td>
<td>0.743</td>
</tr>
<tr>
<td>Donor terminal [hematocrit] (median)</td>
<td>0.7 (0.4-0.8)</td>
<td>0.7 (0.5-0.8)</td>
<td>0.880</td>
</tr>
<tr>
<td>Donor KDP, %</td>
<td>79.2 ± 2.2</td>
<td>79 ± 2.2</td>
<td>0.590</td>
</tr>
<tr>
<td>Functional warm ischemia time (hrs)</td>
<td>20 (16-24)</td>
<td>25 (17-29)</td>
<td>0.771</td>
</tr>
<tr>
<td>Recipient age (years)</td>
<td>62 (43-75)</td>
<td>62 (43-78)</td>
<td>0.720</td>
</tr>
<tr>
<td>Recipient sex [male (%)]</td>
<td>79 (94)</td>
<td>80 (93)</td>
<td>0.800</td>
</tr>
<tr>
<td>Recipient BMI (mg/Kg)</td>
<td>20.4 (19-28)</td>
<td>21.4 (17-29)</td>
<td>0.606</td>
</tr>
<tr>
<td>HLA-DR/B DKK-4, %</td>
<td>88 (100)</td>
<td>89 (100)</td>
<td>0.687</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>40 (52)</td>
<td>34 (32)</td>
<td>0.204</td>
</tr>
<tr>
<td>Peptic-renal cancer, %</td>
<td>19 (16)</td>
<td>8 (8)</td>
<td>0.087</td>
</tr>
<tr>
<td>Cardiovascular disease, %</td>
<td>88 (100)</td>
<td>89 (100)</td>
<td>0.606</td>
</tr>
<tr>
<td>QoL (0-100)</td>
<td>90 (80-100)</td>
<td>90 (80-100)</td>
<td>0.391</td>
</tr>
<tr>
<td>MELD/SOF (mm)</td>
<td>54 ± 8</td>
<td>51 ± 5</td>
<td>0.126</td>
</tr>
<tr>
<td>Cold-buff temperature (hrs)</td>
<td>10 (7-14)</td>
<td>12 (9-11)</td>
<td>0.012</td>
</tr>
<tr>
<td>DGF, %</td>
<td>35 (26)</td>
<td>12 (15)</td>
<td>0.028</td>
</tr>
<tr>
<td>Graft survival after transplant (days)</td>
<td>210 (192-292)</td>
<td>212 (192-292)</td>
<td>0.004</td>
</tr>
<tr>
<td>Acute rejection, %</td>
<td>23 (31)</td>
<td>27 (36)</td>
<td>0.032</td>
</tr>
<tr>
<td>TTE-MRI (mm/m)</td>
<td>2.2 (1.7-3.2)</td>
<td>2.2 (1.6-3.8)</td>
<td>0.007</td>
</tr>
<tr>
<td>Type of all (STEM grade1/STEM grade2/STEM grade3)</td>
<td>2.6/3.4/2.6</td>
<td>2.5/3.4/2.6</td>
<td>0.940</td>
</tr>
<tr>
<td>CMV transaminase (T/Control)</td>
<td>49 ± 28</td>
<td>28 ± 16</td>
<td>0.212</td>
</tr>
<tr>
<td>Tching CMV replication (copies/ml)</td>
<td>6.2 ± 1.5 ± (4.1 - 11)</td>
<td>2.1 ± 1.5 ±(4.1 - 11)</td>
<td>0.002</td>
</tr>
<tr>
<td>Liver-invasive peritoneal carcinomatosis metastasis</td>
<td>45 (20)</td>
<td>45 (20)</td>
<td>0.584</td>
</tr>
<tr>
<td>Liver venous occlusion (mm)</td>
<td>15 ± 5.5</td>
<td>15 ± 5.5</td>
<td>0.404</td>
</tr>
<tr>
<td>Tching CMV replication (copies/ml)</td>
<td>2.1 ± 2.3 ± (3.5 - 8.5)</td>
<td>2.1 ± 2.3 ±(3.5 - 8.5)</td>
<td>0.004</td>
</tr>
<tr>
<td>BR rejection, %</td>
<td>9.5 ± 3.6</td>
<td>2.1 ± 1.5</td>
<td>0.017</td>
</tr>
<tr>
<td>Acetylcholine response (ng)</td>
<td>3.4 ± 2.3</td>
<td>2.1 ± 1.5</td>
<td>0.004</td>
</tr>
<tr>
<td>Liver reperfusion rate (%)</td>
<td>95.4 ± 9.0</td>
<td>95.4 ± 9.0</td>
<td>0.920</td>
</tr>
<tr>
<td>1-year death-censored graft survival (%)</td>
<td>93 ± 90</td>
<td>85 ± 90</td>
<td>0.597</td>
</tr>
</tbody>
</table>
Conclusions: 
Between groups. There was however a significant decrease in urine excretion reached the target BP. There was no difference in changes of eGFR, creatinine, (TGFβ-1) and procollagen-type-III-amino-terminal propeptide (PIIINP).

Methods: 
Flow cytometry was performed on 31 long-term kidney recipients who retained graft function for more than 20 years. Specific T lymphocyte subtypes studied were CD4CD28null, CD8CD28null, and CD4CD25FoxP3 (Tregs). We performed the same analysis on 31 kidney recipients one year after kidney transplantation, matched for age and eGFR, who served as a control group.

Results: 
Long-term kidney recipients (53±10 years old) maintained graft function for a median of 25 years, while their estimated GFR was 53±22.0 ml/ min/1.73m2. In comparison with one-year kidney recipients, long-term patients had increased CD4 T lymphocytes, both in percentage [51.5(17.4) vs 42.9(18.8) %, p<0.013] and absolute cell number [1200(801) vs 535(329) cells/μl, p<0.001]. The CD3CD28null cells/μl were increased [402(441) vs 236(344), p<0.049] while Tregs almost doubled [41(49) vs 21(15), p<0.001] in long-term patients. 

Conclusions: 
In long-term kidney survivors, alterations observed in T cell subpopulations may render these patients more susceptible to specific common risk factors for morbidity and mortality, independent of their graft function.
Background: Extraembryonic mesenchymal stem cells (MSC) possess multi-potency and remarkable immunomodulatory features with robust and constitutive anti-inflammatory and anti-fibrotic properties, making them suitable for the treatment strategy of different acute and chronic liver disorders. The aim of this study was to evaluate the safety and the therapeutic potential of systemic intravenous chorionic plate MSC (CP MSC) infusion for the treatment of decompensated liver cirrhosis.

Methods: MSC were obtained from the placenta of a healthy woman in labour who signed an informed consent and was delivered by caesarean section. The chorionic plate as a source of MSC was chosen based on the high differentiation potential of this cell population (differentiated in adipoergic, chondrogenic and osteogenic directions), as well as on the basis of more significant secretion of hepatocyte growth factor in relation to MSC from other tissues of the placenta (>100 000 pg/ml vs 11 427 [3378; 19182] for CP MSC vs other placental MSC. We report an experience of 5 prospective clinical cases (age – 39 [37; 42]; MELD score – 24 [22; 25]) of intravenous systemic CP MSC infusion (~2mln/kg, see table) in decompensated liver cirrhosis patients. Inclusion criteria: age under 18, total bilirubin >100 mmol/l, Child C liver cirrhosis, inpatient treatment demand.

Results: Systemic administration of CP MSC did not cause side effects, was not associated with complications of administration or worsening of the clinical picture. There was one lethal outcome on the eighth day after administration due to profuse esophageal varices bleeding. In 4 patients, stabilization of the course of liver failure was observed, which made it possible to continue treatment at the outpatient stage, one patient subsequently underwent liver transplantation.

Conclusions: In selected patients systemic CP MSC infusion may stabilize the decompensation of liver cirrhosis. To make it evident, the future clinical trials are required.

### Table 1: Binary logistic regression analysis on delayed graft function

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cell count. ×10^6</th>
<th>Passage</th>
<th>Viability %</th>
<th>Criopreservation (yes/no)</th>
</tr>
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<tbody>
<tr>
<td>K.</td>
<td>178,1</td>
<td>2</td>
<td>99</td>
<td>no</td>
</tr>
<tr>
<td>M.</td>
<td>138,0</td>
<td>2</td>
<td>97</td>
<td>no</td>
</tr>
<tr>
<td>L.</td>
<td>145,9</td>
<td>3</td>
<td>96</td>
<td>yes</td>
</tr>
<tr>
<td>P.</td>
<td>174,5</td>
<td>3</td>
<td>99</td>
<td>yes</td>
</tr>
<tr>
<td>H.</td>
<td>141,78</td>
<td>3</td>
<td>99</td>
<td>yes</td>
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<table>
<thead>
<tr>
<th>B</th>
<th>Sig. (Exp(B))</th>
<th>95% C.I. (Exp(B))</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBD</td>
<td>&lt;0.001</td>
<td>9.688</td>
</tr>
<tr>
<td>DCD</td>
<td>&lt;0.001</td>
<td>30.149</td>
</tr>
<tr>
<td>Recipient BMI</td>
<td></td>
<td>35.149</td>
</tr>
<tr>
<td>Donor age</td>
<td></td>
<td>13.880</td>
</tr>
<tr>
<td>Donor sex</td>
<td></td>
<td>67.931</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>&lt;0.001</td>
<td>2.230</td>
</tr>
<tr>
<td>Preemptive transplantation</td>
<td>&lt;0.001</td>
<td>0.094</td>
</tr>
<tr>
<td>Residual diuresis (mL per day)</td>
<td>0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Glucocorticoid (μg/mL)</td>
<td>0.001</td>
<td>1.000</td>
</tr>
<tr>
<td>Glyceric acid (μg/mL)</td>
<td>0.001</td>
<td>1.200</td>
</tr>
<tr>
<td>Constant</td>
<td>0.001</td>
<td>1.000</td>
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### Table 1: Binary logistic regression analysis on delayed graft function

<table>
<thead>
<tr>
<th>B</th>
<th>Sig. (Exp(B))</th>
<th>95% C.I. (Exp(B))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual diuresis (mL/day)</td>
<td>0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Donor age</td>
<td>0.002</td>
<td>1.039</td>
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<td>Donor sex</td>
<td>0.001</td>
<td>1.051</td>
</tr>
<tr>
<td>Donor age</td>
<td>0.001</td>
<td>1.014</td>
</tr>
<tr>
<td>Donor sex</td>
<td>0.001</td>
<td>1.014</td>
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<td>Residual diuresis (mL/day)</td>
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<td>0.999</td>
</tr>
<tr>
<td>Donor age</td>
<td>0.002</td>
<td>1.039</td>
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<tr>
<td>Donor sex</td>
<td>0.001</td>
<td>1.051</td>
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<tr>
<td>Donor age</td>
<td>0.001</td>
<td>1.014</td>
</tr>
<tr>
<td>Donor sex</td>
<td>0.001</td>
<td>1.014</td>
</tr>
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### Figure 1: Multivariable Cox Proportional Hazards analysis on graft failure censored for death

### Figure 1: Multivariable Cox Proportional Hazards analysis on graft failure censored for death
P321 PREGNANCY AFTER KIDNEY TRANSPLANTATION - IMPACT OF FUNCTIONAL RENAL RESERVE ON ALLOGRAFT OUTCOME AND MATERNAL HEALTH

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Background: Women of childbearing age show increased fertility after kidney transplantation. Of concern, preeclampsia, preterm delivery, and allograft dysfunction contribute to maternal and perinatal morbidity and mortality. Patients after KTX have an underlying chronic kidney disease and it can be difficult to discriminate whether the cause of deterioration of allograft function is related to pregnancy.

Methods: We performed a retrospective single-center study, including 40 women with post-transplant pregnancies after single or combined pancreas-as-kidney transplantation between 2003 and 2019. We took into account recent changes regarding the definition of preeclampsia as new onset of hypertension and proteinuria or new onset of hypertension and/or significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation. Outcomes of kidney function up to 24 months after end of pregnancy were compared with a matched-pair cohort of 40 transplanted patients without pregnancies to address the question if changes in allograft function depict the consequence of pregnancy itself rather than non-pregnancy-related risk factors.

Results: With a maternal survival rate of 100\%, 39 out of 46 pregnancies ended up with a live-born baby. eGFR slopes to the end of 24 months follow up showed mean eGFR declines in both groups (-5.4±14.3 mL/min in pregnant versus -7.6±14.1 mL/min in controls). We identified 16 women with adverse pregnancy events (APE), defined as preeclampsia with severe end organ dysfunction. An impaired hyperfiltration during pregnancy was a significant risk contributor for both, APE (Figure) and deterioration of kidney function (p<0.01). In addition, a declining renal allograft function in the year before pregnancy was a negative predictor of worsening allograft function after 24 months follow up. No increased frequency of de novo donor-specific antibodies after delivery could be detected.

Conclusions: Overall, pregnancies in women after kidney transplantation showed good allograft and maternal outcomes. The use of biomarkers such as sFlt-1 and PI GF need to be explored in future studies.

Impact of hyperfiltration during pregnancy. Maximal renal reserve (A), change from baseline eGFR (B), change of proteinuria (C). *= p<0.05, **= p<0.01, ns=not significant.

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Background: The most common way to anastomose donor’s single renal artery (DSRA) to recipients is using the internal iliac artery (IIA) or external iliac artery (EIA) in kidney transplantation (KT). One study showed no significant difference in long-term outcomes between the two groups in 38 deceased donor kidney transplant recipients. However, this study had some limitations. The number of patients was small, and living donor KT was not included. Therefore, we attempted to compare the outcomes of two groups using IIA and EIA in deceased and living donor KT.

Methods: 381 patients with DSRA who underwent KT at Seoul National University Bundang hospital from 2005 to 2021 were investigated retrospectively. Among 381 patients with DSRA, 288 patients underwent living donor kidney transplantation (LDKT) and 93 patients received deceased donor kidney transplantation (DDKT). In 212 cases of 288 LDKTs, the donor’s renal artery was anastomosed end-to-end to the recipient’s IIA, and in 76 cases, the EIA was anastomosed end-to-side fashion. In 27 cases of 93 DDKTs, the donor’s renal artery was anastomosed end-to-end to the recipient’s IIA, and in 66 cases, the IIA was connected end-to-side. To compare the short-term result between the IIA and EIA groups, the estimated glomerular filtration rate (GFR) was collected for the first 40 days after surgery, and for the long-term result, graft survival and patient survival for 15 years of the two groups were compared.

Results: Baseline characteristics showed differences in the follow-up period, age, and prevalence of diabetes mellitus (p<0.01, p<0.001, p<0.002, respectively) (Table 1). The post-operative 40-day GFR of the IIA group was higher than the EIA group in the LDKT (p=0.005). On the other hand, there was no difference in GFR between the two groups in the case of DDKT (p=0.852) (Figure 1). There were no differences between two groups in graft survival and patient survival in both LDKT (p=0.636, 0.419) and DDKT (p=0.520, 0.814) (Figure 2).

Conclusions: Our study showed no difference in graft survival and patient survival between the two groups when the DSRA was anastomosed to the recipient’s IIA or EIA in LDKT and DDKT. Therefore, it is desirable to select an appropriate reconstruction method according to the anatomy of donor and recipient in KT.

Table 1

<table>
<thead>
<tr>
<th>Patients’ Characteristics</th>
<th>Internal (n=288)</th>
<th>External (n=93)</th>
<th>p-value</th>
</tr>
</thead>
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<tr>
<td>Length of follow-up, years, mean (SD)</td>
<td>6.1 (±4.1)</td>
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<td>Age, mean (SD)</td>
<td>52.8 (±12.1)</td>
<td>60.1 (±10.5)</td>
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<td>Sex, n (%)</td>
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<tr>
<td>Male</td>
<td>135 (50.5)</td>
<td>94 (66.2)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>154 (49.5)</td>
<td>48 (33.8)</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m(^2), mean (SD)</td>
<td>23.0 (±3.8)</td>
<td>24.2 (±4.2)</td>
<td>0.355</td>
</tr>
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<td>Pre-transplant diaylsis, n (%)</td>
<td>152 (53.8)</td>
<td>58 (58.9)</td>
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<td>HDN, n (%)</td>
<td>181 (75.7)</td>
<td>117 (82.4)</td>
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<td>DM, n (%)</td>
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<td>58 (40.8)</td>
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<td>ABO, n (%)</td>
<td>56 (46.9)</td>
<td>22 (15.5)</td>
<td>0.063</td>
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</tbody>
</table>
**P323**

**SHORT-TERM HEPATITIS B IMMUNOGLOBULIN (HBIG) COMBINED WITH ENTECAVIR IN PREVENTING HBV RECURRENT IN LIVER TRANSPLANTATION**

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**Background:** The combination of nucleoside analogs (NAs) and long-term hepatitis B immunoglobulin (HBIG) is considered to be the standard regimen for preventing hepatitis B virus (HBV) recurrence following liver transplantation (LT). However, the long-term usage of HBIG causes many side effects. The aim of this study was to evaluate the effect of NAs entecavir combined with short-term HBIG in preventing HBV recurrence following LT.

**Methods:** This retrospective study assessed the effect of a combination of entecavir and short-term HBIG in prophylaxis of HBV recurrence among 56 LT recipients who had undergone the procedure due to HBV-associated liver disease at our center between December 2017 and December 2021. All patients received entecavir treatment combined with HBIG for the prevention of hepatitis B recurrence, and HBIG treatment was withdrawn within one month. The patients were followed up to determine levels of HBsAg, HBsAb, HBV-DNA and the recurrence rate of HBV.

**Results:** Only one patient appeared positive for HBsAg at 2 months post-LT. The overall HBV recurrence rate was 1.8%. The HBsAb titers of all patients were lower than those of HBV-DNA negative patients. Only one patient appeared positive for HBsAg at 2 months post-LT. The group with cognitive impairment performed significantly worse in the executive flexibility domain than in the other domains (comparison with verbal memory (t(32) = 2.93, p = .015; with attention (t(32) = 3.69, p < .010).

**Conclusion:** The prevalence of cognitive impairment is common in non-decremented patients after kidney transplantation and appears to be intermediate between dialysis patients and the normal population. The duration of dialysis before transplantation has no influence on cognitive performance. Creating a neurocognitive profile is helpful and important, as the therapy for the treatment of cognitive impairment is based on the cause of the disease, based on the reduction of vascular risk factors (consistent antihypertensive therapy, optimal control of blood pressure). There is no difference between groups in duration on dialysis before transplantation (t(57) = -0.82, p = .208) or in time since transplantation (t(57) = -1.04, p = .305). The group with cognitive impairment performed significantly worse in the executive flexibility domain than in the other domains.

**P324**

**ASSESSMENT OF COGNITIVE IMPAIRMENT IN KIDNEY TRANSPLANTATION AND ITS RELATED RISK FACTORS**

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**Background:** Association of cognitive impairment with chronic kidney disease especially in ESRD-Disease has been reported over the last decade. Data about cognitive function in transplanted patients is rare. Individuals after kidney transplantation are more likely to be affected by cognitive impairment than age-matched comparison groups. The goal of our study is to examine the extent of cognitive impairment after kidney transplantation and to derive a distinct profile of cognitive function using standard neurocognitive tests, as this is important for developing management strategies.

**Methods:** Participants completed standardized neurocognitive assessment and were then classified as having no, mild, moderate or severe cognitive impairment based on an established algorithm. For statistical analyses, we compared two groups (no vs. any impairment) using χ²-tests for dichotomous variables, and unpaired (between groups) as well paired (between domains) t-tests for continuous variables.

**Results:** 59 patients (43 men, 16 women, mean age 55±13 yrs) took part in the study. 26 (44%) of the patients had no, 9 (15%) a mild, 15 (25%) a moderate and 9 (15%) a severe cognitive impairment. There was no difference between groups in duration on dialysis before transplantation (t(57) = -0.82, p = .208) or in time since transplantation (t(57) = -1.04, p = .305). The group with cognitive impairment performed significantly worse in the executive flexibility domain than in the other domains (comparison with verbal memory (t(32) = 2.93, p = .015; with attention (t(32) = 3.69, p < .010).

**Conclusion:** The prevalence of cognitive impairment is common in non-decremented patients after kidney transplantation and appears to be intermediate between dialysis patients and the normal population. The duration of dialysis before transplantation has no influence on cognitive performance. Creating a neurocognitive profile is helpful and important, as the therapy for the treatment of cognitive impairment is based on the cause of the disease, based on the reduction of vascular risk factors (consistent antihypertensive therapy, optimal adjustment of any existing diabetes, etc.) and seems to be of crucial importance and priority.
P329 X-RAY ANALYSIS OF DONOR LUNGS IN EX-VIVO LUNG PERFUSION SYSTEM (EVLPS). A PILOT STUDY WITH ASSESSMENT OF THE BRIXIA SCORE TO PREDICT TRANSPLANTABILITY

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Background: Ex-vivo lung perfusion (EVLP) is a safe and effective technique for lung evaluation and reconditioning of marginal donor lungs (DLs). The assessment of the DLs during EVLP is crucial for the transplantability decision making. There is a limited number of studies regarding the radiographic analysis of DLs within EVLP. Furthermore, there are only few X-Ray grading scores available. The Brixia score is a proven radiological score for the severity grading of lung abnormalities with confirmed predictive power of the clinical outcome that was successfully used in pneumonia patients during the Covid19 pandemic. It was the aim of our study to evaluate the X-Ray findings of DLs within EVLP and investigate the prognostic potential of this score regarding transplantability and clinical outcome.

Methods: This is a retrospective observational pilot study. Between 2016 and 2022, n=30 LuTx with EVLP DLs were performed. X-Rays with the best radiographic quality and exposure of the last eleven consecutive EVLP-DLs were chosen and blindly evaluated regarding the severity of interstitial and alveolar infiltrates. The Brixia score was assessed. Furthermore, the clinical outcome (transplantability, severe primary graft dysfunction PGD, survival, ICU and hospital stay) and EVLP parameters (delta pO2) of these were analyzed and compared to the Brixia score for each case.

Results: A range of Brixia score values from 4 to 18 was determined. Eight DLs were transplanted (mean delta pO2 394 mmHg, mean Brixia score 6.5) while three were rejected (mean delta pO2 213 mmHg, mean Brixia score 8). The two EVLP-DL cases with the highest Brixia score were transplanted after EVLP. Postoperative PGD Grade 3 at 72 hours was recorded in one case without correlation to the Brixia score (Brixia score 4). Interestingly, the case with the highest Brixia score had the highest pCO2 value as well, and was transplanted with good clinical outcome. All patients survived to hospital discharge with a mean ICU and hospital stay of 9 and 30 days respectively.

Conclusions: In this pilot study the Brixia score did not predict transplantability or postoperative outcome during EVLP. Additional studies are needed to further evaluate the use and clinical prognostic power of radiologic assessment with this promising score in the EVLP lung assessment.

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Background: Living donor kidney transplantation is the best therapeutic option for end stage chronic kidney disease. The assessment of the potential donor is exhaustive and a significant percentage of the initial studies will not progress to kidney donation. We aim to assess the characteristics of these donor candidates and the reasons for rejection of these kidney donors.

Methods: retrospective study and analysis of all patients evaluated for kidney donation at Fundació Puigvert during the last 20 years.

Results: a protocolized study for donation has been initiated in 837 candidates, 509 nephrectomies have been performed and 328 candidates have been rejected. The discard proportion has remained stable during these years (39.2% discards). The age of those dismissed is 54.7 ± 10.9 years, 37.2% are men. The age of potential donors, both accepted and discarded, has increased among years. In those discarded, the donor-recipient relationship is: spouse (36.5%) > siblings (30.7%) > parent-son/daughter (22.3%) > others (18.6%). The main reasons for dismissal are change of opinion of the donor (23%), kidney pathology of the donor such as lithiasis or renal mass (17%), medical pathology of the donor (12.7%), cadaver transplant (9%) and vascular complexity of the donor (9%). The complementary diagnostic test that determines the highest proportion of dissimuls is abdominal computer tomography.

Conclusions: - The percentage of discarded donors remains stable among years, although their age of living donor candidate is increasing. - The percentage of discarded donors is not different based on age or gender or donor-recipient relationship. - The main reason for rejection is the donor’s decision. The experience in the evaluation of these donors will possibly avoid unnecessary studies in this group.
Comparing Physical Function among Patients on Dialysis, Kidney and Kidney-Pancreas Transplant Recipients Using PROMIS Scores

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1University Health Network, Toronto, Canada

Background: Patients treated on dialysis have impaired physical function (PF) which is associated with poor outcomes. Kidney-pancreas (KP) and kidney transplant (KT) provide better outcomes; however, many transplant recipients have low PF. PF can be assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) PF item bank, administered as either computer adaptive testing (CAT) or short form. Here we aim to assess PF among patients on dialysis, KP and KT recipients.

Methods: Secondary analysis of data from our research database, which include cross-sectional convenience sample of adult patients on dialysis, KT and KP recipients. Demographic data are self-reported, clinical data are from health records. Patients completed the PROMIS-29 profile domains, which include the PF domain. Higher PF scores correspond to better physical function outcomes. Scores were compared using ANOVA and linear regression adjusted for age, sex, ethnicity, comorbidity and time since starting current treatment modality.

Results: Of 755 participants, 285 dialysis, 93 KP and 407 KT, 472 (60%) were male, mean(SD) age was 55(16) years. Sex distribution was similar between treatment groups; patients on dialysis were significantly older than transplant recipients (mean[S.D] age 64[14] vs 52[10] vs 51[16] years for dialysis vs KP vs KT, respectively; p<0.001). Females had lower mean(SD) PF scores 42(10) vs 44(11)(p=0.01). Age was negatively correlated with PF score (r=-0.39, p<0.001). Mean(SD) PF was significantly different in all 3 groups: 37(9) vs 44(8) vs 48(10)(p=0.01). PF in both KT and KP remained significantly better after adjusting for potential confounders (coefficients [95% confidence interval] 4.92[6.7-2.2] and 8.68[4.9-9.6] for KP vs KT, respectively, p<0.001 for both). The difference between KP vs KT was also significant in the adjusted model.

Conclusions: These results suggest that both KP and KT recipients have better physical function compared to patients on dialysis, but all groups remain significantly better after adjusting for potential confounders (coefficients [95% confidence interval] 4.92[6.7-2.2] and 8.68[4.9-9.6] for KP vs KT, respectively, p<0.001 for both). A history of dialysis profoundly impacted transplant utility (i.e. transplant delay for any cause) with hazard ratios of 1.59 (Netherlands) and 1.51 (UK) (both p<0.0001). The benefits of preemptive transplantations were granular, with both superior short- and long-term outcomes. For example, Dutch recipients with a dialysis vintage had a >5-fold higher 90-days mortality risk, and a respectively 1.67 and 1.54-fold higher risk for long-term graft loss or death. Data for Dutch recipients of a living donor graft cohort indicated a critical tipping point at approx. 6-months of dialysis. No tipping point was observed for procedures with deceased donor grafts, nor for UK recipients of a living or deceased donor graft.

Risk Management and Safety of the Pediatric Transplant Patient: The Role of the Nurse in the Preparation of the Caregiver

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Background: Discharge represents a critical moment for the caregiver, characterized by two types of uncertainty: lack of preparation for future experiences and lack of adequate information (M. Boughton, 2009). The literature shows that from 40% to 80% of the medical information that a patient/caregiver receives, is immediately forgotten, and nearly half of the information retained is incorrect (Farris, 2015). If we are talking about foreign patients, discharge becomes an even more difficult moment, given the linguistic and cultural barrier. The aim of our study is to respond to the caregiver’s need for information, especially for the management of home drug therapy, to reduce the related risks. The ultimate goal is to develop an audiovisual application that is always available, to clarify any parental doubts regarding the dilution, preparation and administration of therapy.

Methods: The project is designed for a patient of Kazakh origin undergoing liver transplantation, with an illiterate parent. After obtaining informed consent, videos were produced and additional audio files were recorded by a Kazakh-speaking interpreter. At the time of administration of the various therapies, in addition to the classic sound alarm that attracted the attention of the parent, an illustrative video was available on the preparation of the drug and its administration. This work was then developed in 4 different languages to allow the training of as many caregivers as possible.

Results: All the parents obtained a good level of training after a total of 10 days (7 of practical/theoretical training and 3 of re-evaluation). Thanks to the teach-back method, all doubts were clarified and understood. Thanks to this new educational method, we obtained a reduction in the caregivers’ uncertainty at discharge regarding the management of the therapy and an improvement in the well-being of the caregiver himself. All this translated into a reduction in calls to the transplant coordination to resolve doubts regarding the management of home therapy (the patients included in the project never contacted the coordination for this issue) and in a drastic reduction of errors regarding drug dosages.

Conclusions: According to the results obtained during the project period, the new method of communication and caregiver training used was found to be effective.
TREATMENT OF COMPLEX UROLITHIASIS IN ORTHOTOPIC KIDNEY TRANSPLANT BY ENDOSCOPIC COMBINED INTRARENAL SURGERY (ECIRS)

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Background: Urolithiasis treatment has evolved greatly with technological advances in endoscopic material and miniaturization of percutaneous surgery instruments. However, there are still complex cases that can pose a challenge for the urologist, such as lithiasis treatment in patients with an orthotopic kidney transplant or any type of urinary diversion.

Methods: We report a case of a 46-year-old male with a personal history of spina bifida and lumbosacral myelomeningocele. Tubeless cutaneous ureterostomy is performed for this reason at 6 months of age. Eventually, the patient develops chronic kidney disease secondary to chronic tubulointerstitial nephritis due to recurrent urolithiasis. Consequently, our patient received an orthotopic left kidney transplant in 2014. Pyeloureteral anastomosis to native ureter was performed. During follow-up the patient maintains a stable kidney function (baseline Creatinin 1.64 mg/dl) and in a control CT scan a staghorn lithiasis is visualized, which occupies renal pelvis and superior calyx. Given the complexity of the case, endoscopic combined intrarenal surgery is proposed (ECIRS). For that purpose, retrograde flexible ureteroscopy is performed, with partial laser fragmentation of the lithiasis. Mini percutaneous nephrolithotomy is added to complete stone fragmentation using ultrasonic and shockwave energy (ShockPulse-SE Lithotriptor®). At the end of the procedure, 18Fr nephrostomy tube and mono J catheter are placed.

Results: Immediate postoperative period went by with no incidents. Nephrostomy tube was removed on the third day after surgery (Creatinin 2.03 mg/dl), and 24 hours after it was removed. The patient was discharged on the 6th day after surgery. Mono J catheter is removed 16 days after surgery. At the present time, kidney function has returned to baseline values (Creatinin 1.76 mg/dl) and ultrasound scan was performed, without new lithiasis or ureterohydronephrosis.

Conclusions: Endoscopic combined intrarenal surgery is feasible, safe and useful for the treatment of complex urolithiasis. In particular cases such as orthotopic kidney transplant or cutaneous ureterostomy, surgical planning is crucial to succeed in lithiasis treatment and minimize surgical risks.

THE RISK FACTOR FOR DELAYED GRAFT FUNCTION IN THE DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: Delayed graft function (DGF) is a common and significant complication in deceased donor kidney transplantation (DDKT). DGF is characterized by a temporary or permanent loss of kidney function after transplantation, which is associated with increased morbidity and mortality for transplant patients. But the exact cause of DGF is not well understood. The aim of this study is to identify the risk factors associated with DGF after the DDKT.

Methods: Between June 2011 and December 2022, 88 patients underwent DDKT at department of surgery at Konyang university hospital, Daejeon, Korea. We compared two groups according to delayed graft: no delayed graft function group (n=75), delayed graft function group (n=13). The following characteristics were evaluated retrospectively through the medical records.

Results: The 5-year patient survival in the DGF group was 69.2% compared to 94.1% of the no DGF group (P < 0.001). The 5-year survival rate was 76.9% and 97.1% in the DGF group and no DGF group (P=0.005) respectively. The eGFR level by period of recipients was significantly more increased in no DGF group (1week: 61.4±25.5 ml/min vs. 22.0±12.2 ml/min, P=0.001, 12th months; 73.0±22.2 ml/min vs. 47.8±14.5 ml/min, P=0.001) but the eGFR level of recipients at 60th months was not significantly different in both groups (79.8±21.5 ml/min vs. 79.7±13.6 ml/min, P=0.899). Also, we found that significant independent risk factors associated with DGF after DDKT were extended criteria donor (OR = 6.002, 1.586-22.729 95%CI, P=0.008) and recipient BMI >25 kg/m2 (OR = 4.881, 1.249-19.074 95% CI, P=0.023) in multivariate analysis. During the follow periods, pneumonia increase in the DGF group (30.8% vs. 16.0%, P = 0.041) and AVN occurred 2 cases (15.4%) of DGF group (P = 0.020).

Conclusions: We should anticipate a high possibility of DGF after DDKT, when recipient’s BMI is high or using the graft from extended criteria donor.

ISCHEMIA-FREE KIDNEY TRANSPLANTATION: A PILOT STUDY

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Background: We previously performed the first case of ischemia-free kidney transplantation using normothermic machine perfusion in 2018. Here we report the first pilot study to compare the short-term outcome between ischemia-free kidney transplantation and the traditional kidney transplantation.

Methods: We have performed 9 cases of ischemia-free kidney transplantation since 2018. For each pair of donor kidneys, the right kidney was used in ischemia-free kidney transplantation by normothermic machine perfusion, the left kidney was used in traditional kidney transplantation by cold storage. The clinical data of donors and recipients were collected, and the recipients were followed up for at least 1 year. The incidences of delayed graft function (DGF), recovered time of DGF, acute rejection, bleeding, infection, the 1-month serum creatinine levels and the biomarkers of kidney injury after reperfusion were also significantly reduced in ischemia-free group (p<0.01). The 5-year patient survival in the DGF group was 69.2% compared to 94.1% of the no DGF group (P < 0.001). The 5-year survival rate was 76.9% and 97.1% in the DGF group and no DGF group (P=0.005) respectively. The eGFR level by period of recipients was significantly more increased in no DGF group (1week: 61.4±25.5 ml/min vs. 22.0±12.2 ml/min, P=0.001, 12th months; 73.0±22.2 ml/min vs. 47.8±14.5 ml/min, P=0.001) but the eGFR level of recipients at 60th months was not significantly different in both groups (79.8±21.5 ml/min vs. 79.7±13.6 ml/min, P=0.899). Also, we found that significant independent risk factors associated with DGF after DDKT were extended criteria donor (OR = 6.002, 1.586-22.729 95%CI, P=0.008) and recipient BMI >25 kg/m2 (OR = 4.881, 1.249-19.074 95% CI, P=0.023) in multivariate analysis. During the follow periods, pneumonia increase in the DGF group (30.8% vs. 16.0%, P = 0.041) and AVN occurred 2 cases (15.4%) of DGF group (P = 0.020).

Conclusions: We should anticipate a high possibility of DGF after DDKT, when recipient’s BMI is high or using the graft from extended criteria donor.
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HLA INCOMPATIBILITY AND PANEL REACTIVE ANTIBODIES PRIOR TO RENAL TRANSPLANTATION CAN ADVERSELY AFFECT RENAL FUNCTION OUTCOME AND IMMUNE PROFILE

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Background: The presence of Panel Reactive Antibodies (PRA) prior to renal transplantation (RT) and HLA incompatibility influence graft function and may cause immune profile alterations. The aim of this study was to estimate the effect of HLA class I and II incompatibility and the prevalence of PRA on lymphocyte changes and renal function outcome during the first year post-transplant.

Methods: One hundred six Renal Transplant Recipients (RTRs) were typed for HLA class I and II and assessed for PRA presence just before RT, subsequently followed for 12 months. Lymphocytes, CD4, CD8, CD4+CD28null, CD8CD8-28null, CD3-CD16+CD56+ (NK) and CD4+CD25+ FoxP3+ (Tregs) were estimated with Flow cytometry on peripheral blood samples collected just before RT and at 3, 6, 12 months post transplantation (TI), T1, T2, T3 respectively.

Results: RTRs with at least 2/4 common HLA class II antigens (either DR or DQ), N=80/106 (75.4%), were younger at RT, 38.9±14 vs. 47.4±14yrs, p=0.04. At time point T1, they had increased lymphocytes 2200(1012) vs. 1600(863) p=0.001, CD4 897(697) vs. 5954(485) p=0.008, CD8 cells 429(397) vs. 471(247) cells/μL, p=0.04, and Tregs 24(21) vs. 17(17), p=0.05. No difference was noticed regarding HLA class I incompatibility or other T cell subpopulations. RTRs with PRA(−), N=80/106 (78.3%), with no clinical differences compared to PRA(+) and non-PRA patients. In this regard, the median (IQR) NT-proBNP just before RT was 111.7(53.8) vs. 71.5(29.6) ng/l, p=0.04.

Conclusions: MHC class II incompatibility and presence of PRA seem to affect RTRs T cell subpopulations independently, at different time points, with no interaction with age. No influence was noticed to graft function during 12mo follow-up.

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N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE LEVELS AS A PREDICTOR OF ADVERSE RENAL AND CARDIOVASCULAR OUTCOMES IN STABLE RENAL TRANSPLANT RECIPIENTS

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Background: Cardiovascular (CV) morbidity and mortality are highly prevalent in renal transplant recipients (RTRs). Assessments of CV status using N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations could help to identify patients at risk for death or CV events and as a predictor for deterioration of graft function. The aim of the study was to investigate the biomarker NT-proBNP for the prediction of adverse renal and cardiovascular outcomes in stable RTRs.

Methods: 305 stable RTRs with a median age of 53 years, (60.6% male) transplanted between 1994 and 2018, were enrolled in the study. At baseline, troponin, NT-proBNP, carotid-femoral pulse wave velocity (cfPWV) and pulse pressure (PP) were measured. NT-proBNP was measured during a routine baseline visit in stable RTR without cardiac symptoms and heart failure (HF) exacerbation. The median NT-proBNP concentration (292ng/l) was used as cut-off. Patients were divided into two groups (high (>292ng/l) and low (<292ng/l) NT-proBNP) and followed for 54 months. During this time CV events (stroke, myocardial infarction, peripheral artery thrombosis), death, graft loss and deterioration of renal graft function (increase creatinine ≥30% or proteinuria (urine protein creatinine ratio (UPCR) increase ≥500mg/g)) were monitored.

Results: At baseline, significant differences were observed between groups in terms of creatinine, eGFR, NT-proBNP, UPCR, PP, and PWV. In the group with baseline NT-proBNP ≥292ng/l, more patients had coronary artery disease/peripheral obliterans artery disease (CAD/POAD) and HF. Baseline NT-proBNP correlated only weakly with age (R=0.41), cfPWV (R=0.31) and eGFR (R=0.52). During follow-up, patients with high NT-proBNP experienced more frequently an increase creatinine ≥30% (28.7% vs 15.8%), doubling creatinine (11.1% vs 2.6%) and an increase of UPCR (22.2% vs 8.5%). Furthermore, high NT-proBNP at baseline was associated with graft loss (16.3% vs 0.6%), death (11.7% vs 0.6%) and CV events (7.2% vs 3.9%) during follow-up.

Conclusion: Age, arterial stiffness and eGFR only have a weak impact on NT-proBNP in stable RTR. Higher NT-proBNP is associated with poor outcomes and might be useful not only for the identification of patients with high-risk CV events but also for the prediction of deterioration of allograft function.
Background: Minimally invasive surgery (MIS) has been in use in solid organ transplantation for the last three decades. However, in kidney transplantation, this approach is generally favoured for the donor surgery rather than for the recipient’s. Our centre used a novel MIS approach, mini-inguinal access kidney transplant (MIKAT) technique that additionally spared vessels and nerves of the abdominal wall during transplantation in 50 kidney transplants.

Methods: Between November 2020 and May 2022, a consecutive series of 50 patients underwent MIKAT performed by a single senior surgeon. The surgical procedure (see figure) involves an incision of the cutaneous and subcutaneous layer, restricted to 6 to 8 cm, between the anterior superior iliac spine and the pubic tubercle. Instead the muscles receive an 8 cm J shape para-rectal dissection from the pubic tubercle. The dissection to create a retroperitoneal pouch is then suspended ex-situ during the vascular anastomosis time, and can be concurrently cooled to reduce the warm ischaemia, whereas the Lich-Gregoir technique is used for the urethral anastomosis.

Results: The mean (+/- SD) age of the recipients was 52 +/- 6 years (range 21-71), the body mass index was 24 +/-0.2 (range 17-28), the procedural time was 136 +/- 18 minutes (range 98-170 minutes), anastomoses time of 40 +/-4 minutes (range, 24-43 minutes), skin incision (+/- SD) of 7.5 +/- 0.7 cm (range 6-8 cm). Despite one patient experiencing an occult ureteral dehiscence requiring surgical revision, no infection or hernia at incision site were observed. Furthermore, no vascular complications occurred during follow-up period of 9 months.

Conclusions: The mini-inguinal incision results in minor tissue trauma that does not add to possible delayed wound healing induced by peri and post-transplant immunosuppression protocols. Kidney transplant recipients deserve the best surgical approach to guarantee best outcomes not just in terms of graft function but also health-related quality of life.
**P347**  
A FEASIBILITY STUDY EXPLORING THE IMPACT OF A LOW ADVANCED GLYCATION END-PRODUCT DIET ON SKIN AUTOFLUORESCENCE IN KIDNEY TRANSPLANT RECIPIENTS

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**Background:** Advanced glycation end-products (AGEs) are uremic toxins that result from hyperglycaemia and oxidative stress. AGEs are also formed in food, especially during cooking using dry-heat methods. AGE accumulation can be measured by skin autofluorescence (SAF) and increased SAF is a strong predictor of death and graft loss in kidney transplant recipients (KTR). The aim of this feasibility study was to investigate whether a low-AGE diet leads to a reduction in SAF levels in KTR.

**Methods:** Thirty-eight KTR were randomly allocated to a usual diet (control group, n=19) or a low-AGE diet (intervention group, n=19) and then followed-up for 6 months. The goal was to reduce dietary AGE intake <8000 kiloheats/day. SAF was measured at baseline and 6 months. Rate of change in SAF (i.e., SAF trend) was calculated using the SLOPE function in Microsof Excel. Dietary AGE intake, biochemistry and nutritional assessments were reconstructed.

**Results:** There were no significant differences between the intervention and control groups at baseline in SAF, dietary AGE intake, estimated glomerular filtration rate (eGFR), demographics, and clinical, biochemical and nutritional characteristics. Baseline SAF was negatively associated with eGFR (r = -0.387; p = 0.02), energy intake (r = -0.464; p = 0.003) and fat intake (r = -0.438; p = 0.006). Seventeen participants in the control group and 13 participants in the intervention group completed 6 months of follow-up (Figure 1). Adherence to the low-AGE diet was moderate (69%). Dietary AGE intake decreased significantly in the intervention group but remained high in the control group. Body weight, energy, and fat intake decreased in the intervention group but there was no significant change in SAF (Table 1). The mean SAF trend observed was a decrease of 0.45±1.19 and 0.22±0.75 AU/year in the intervention and control groups, respectively (p=0.7 for comparison between groups).

**Conclusions:** In this feasibility study, we observed a high drop-out rate in the intervention group, which may explain our finding that reduction in dietary AGE intake did not seem to have any significant effect in decreasing SAF levels. This highlights the need for a larger trial to determine the effect of dietary AGE intake in decreasing SAF levels in KTR.

**P349**  
EXTENDED RELEASE TACROLIMUS IN SIMULTANEOUS KIDNEY PANCREAS TRANSPLANTATION (SKPT): PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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**Background:** Extended release tacrolimus (ER-T) is a novel formulation of drug using a MetaDose delivery technology that enables improved absorption of tacrolimus throughout the gastrointestinal tract and better bioavailability, leading to lower peak blood concentrations. ER-T is reported to have comparable efficacy and safety profiles to immediate release tacrolimus in kidney recipients and it allows more compliance to the young population.

Although ER-T is largely and safely used as immunosuppressive drug in kidney transplant recipients, few studies have been done on ER-T efficacy and safety in SKPT. Given that SKPT recipients are at risk of low early absorption of immunosuppressive drug because of surgery (intestinal anastomosis of pancreatic graft) and diabetic gastroparesis, we think that ER-T based immunosuppressive protocol could be more effective in this group of patients.

**Methods:** We started to use ER-T in SKPT since January 2022 in patients with 0 panel reactive antibody (PRA). Our immunosuppressive protocol included basiliximab (20 mg in day 0 and 4), steroids, mycophenolic acid (720 mg bid from day 1) and ER-T starting on postoperative day 2 (median starting dose: 0.03 mg/Kg), aimed to reach trough level of 8-10 ng/ml.

**Results:** Five patients underwent SPKT (M/F: 3/2, median age 47 years) in 2022, median follow-up was 6 months (range 3-11 months). All patients had uneventfully recovery with no surgical complication and neither rejection episodes. Graft function was excellent for both kidney and pancreas. Dosage in mg and trough level are summarized in tab.1. ER-T reached acceptable trough level at postoperative day 6 (median 6 ng/ml), with low administration of drug (median dose was 4 mg/4).

**Conclusions:** Our preliminary study shows that ER-T associated to basiliximab, steroids and micophenolic acid can be safely used in SKPT. The low dose required to rapidly achieve trough level reflects the improved absorption provided by the MetaDose formulation even in SPKT patients.

**Tab.1.** Trend of ER-T dose (mg) and tacrolimus trough level (ng/ml) early post SKPT.
E-POSTERS

P350 EVALUATION OF DONOR’S QUALITY OF LIFE AFTER KIDNEY DONATION: SINGLE CENTER EXPERIENCE

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Background: Living kidney donation is considered a supreme act of altruism, especially because it has a favorable effect solely to the recipient. Therefore, it is essential to ensure kidney donors ideal pre- and post-operative conditions, as well as excellent long-term health and life quality. The purpose of our study was to evaluate the quality of life of kidney donors as well as to identify the association with potential influencing factors.

Methods: Over a pre-specified one-year time period (01/01/2022 to 31/12/2022), we recorded, in a cross-sectional study, information on demographic, laboratory and morbidity parameters in clinically stable donors, attending the Outpatient Kidney Donor Clinic of our department. We also assessed the donors’ quality of life through the questionnaire SF-36. The SF-36 questionnaire aims, through 36 questions, to study eight different health-related parameters, which are summarized in two general categories, that of physical (PCS) and mental (MCS) functioning.

Results: The study population consisted of 199 stable kidney donors, who had donated at our center between 2000-2022. The majority (72%) were females, with mean age 62.8±10.3years and estimated glomerular filtration rate (eGFR) 83.6±14.1mL/min/1.73m². The total PCS and MCS score (52.5±52.7 respectively) was excellent and comparable to that of the general population (52.6±53.3 respectively). In addition, the analysis, performed 2.93±3.53 years after kidney donation, showed that men had significantly higher PCS and MCS scores (56.57 and 58.27 respectively) compared to women (55.03 and 53.3 respectively). Furthermore, younger age, both at the time of donation and evaluation, was correlated to a better quality of life on the physical scale (p=0.038 and p=0.07 respectively), whereas laparoscopic nephrectomy was strongly associated with increased mental health compared to open surgery (p=0.001).

Last but not least, comorbidities, BMI, and donor-recipient relationship did not seem to affect donor’s quality of life.

Conclusions: Overall, it seems that, postdonation, kidney donors have very good quality of life, which is mainly influenced by non-modifiable factors such as gender and age.

P351 HAEMODYNAMICS IN THE EXTERNAL ILIAC ARTERY: THE UTILITY OF CARDIOVASCULAR IMAGING FOR INVESTIGATING TRANSPLANT RENAL ARTERY STENOSIS

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Background: Magnetic resonance angiography (MRA) is a sensitive, non-invasive test for transplant renal artery stenosis (TRAS) but lacks specificity; up to 45% of TRAS cases identified by MRA have the diagnosis refuted at formal intra-arterial digital subtraction angiography. Using cardiovascular imaging (CVI) software, it is possible to assess haemodynamics in the external iliac artery (EIA) proximal (Point A) and distal (Point B) to the transplant artery anastomosis.

Methods: 787 MRAs were performed at our centre between January 2019 and February 2021. To date, 279 MRAs have been reviewed using CVI software. MRAs were excluded from the study if the software did not generate a typical arterial wave form (fig 1) or if the origin of the internal iliac artery was within the measurement points A and B on the external iliac artery. Accurate measurements were performed on 88 MRAs. 65 MRAs showed no evidence of TRAS and were analysed further. Paired sample t-tests were used to assess the relationship between measurements at point A and B.

Results: The maximum pressure gradient was greater at Point A than Point B (0.64 ± 0.64 mmHg, 95%CI -0.32 – 0.07, p=0.0027) (fig 2). There was no difference in maximum velocity between Point A and Point B (45.94 ± 43.72 cm/s, 95%CI -15.37 – 10.94, p=0.74). Maximum flow was greater at Point B than Point A (8.70 ± 4.37 ml/s, 95%CI -0.32 – 0.07, p=0.001).

Conclusions: This study demonstrates that, in recipients with no TRAS, there are statistically appreciable differences in haemodynamics at points proximal (A) and distal (B) to the transplant artery anastomosis on the external iliac. Determining why these differences exist, and normal parameters, may improve the specificity of MRA. Analysis of MRA-measured haemodynamics in a cohort of patients with IADSA-confirmed TRAS is underway.

P352 IMPACT OF PEG35-BASED SOLUTION ON STEATOTIC LIVER COLD PRESERVATION: INSIGHTS INTO MITOCHONDRIAL PROTECTION AND CELL SIGNALING

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Background: The need for liver transplants has increased the use of steatotic livers, which are more susceptible to injury during preservation. PEG35 is a commonly used oncotic agent in organ preservation solutions, but its impact on liver preservation is not well understood.

Methods: To investigate this, the study aimed to evaluate the protective effects of three preservation solutions (UW, HTK, and IGL-2) on steatotic livers during hypothermic preservation. Male obese rats were used for liver preservation for 24 hours at 4°C using the solutions. IGL-2 was also compared to Belzer-MPS for hypothermic preservation with HOPE. A control group of SHAM livers was included for comparison.

Results: The results showed that after 24 hours of preservation at 4°C, ATP levels decreased significantly in the UW and HTK groups compared to the control and IGL-2 groups. The IGL-2 group had improved ATP levels and increased autophagic markers such as LC3B and beclin1. Cold preservation increased oxidative stress, measured by endoplasmic reticulum stress, lipid peroxidation, and protein oxidation, but the damage was reduced in the IGL-2 group. The IGL-2 solution, which contains higher amounts of GSH, showed significantly lower oxidative stress and better antioxidant activities compared to the other solutions. These benefits were confirmed when IGL-2 was used in HOPE with Belzer-MPS. The IGL-2 solution showed less presence of inflammation mediators and improved energetic status, reducing oxidative stress and lipoperoxidation, and resulting in less inflammation. The data suggests that IGL-2 is a suitable solution for static and dynamic preservation techniques as a unique solution.

Conclusions: Steatotic liver preservation with the PEG35-based IGL-2 solution showed better results in reducing damage during static and dynamic preservation, but further research is needed.

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P353  VAR-TELLS: AN INNOVATIVE CELLULAR PLATFORM TO OPTIMIZE THE RESPONSE OF TRANSPLANTED PATIENTS ON THERAPEUTIC IMMUNOSUPPRESSION TO VACCINATION

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Background: Solid Organ transplantation is the best option for patients with vital organ failure. Because the donor is genetically distinct from the recipient, the latter needs to receive immunosuppressive drugs that block T cell activation (calcineurin inhibitor, CNI) to prevent graft rejection. However, CNI that act regardless of T-cell receptor (TCR) specificity, also inhibit T cells involved in the response against pathogens and vaccines, making transplant patients extremely vulnerable to infectious complications, as illustrated during the recent SARS-CoV-2 pandemic. Elaborating on the recent success of Chimeric Antigen Receptor (CAR)-T cells, we propose an innovative approach named Vaccinant Chimeric Receptor (VAR)-T cells aiming at optimizing the vaccine responses of immunocompromised transplant recipients without increasing their risk of rejection.

Methods and Results: Lentivector have been designed to induce the expression on the surface of purified CD4+ T cells of a chimeric receptor made of the vaccine antigen on the extracellular side and the signal domains of CDS3 and CD28 in the intracellular side. In vitro experiments conducted with human and murine cells suggested that when contacting antigen specific B cells, VAR-T cells simultaneously deliver BCR dependent- and receive VAR dependent-signal 1 of activation. As a result, VAR-T cells upregulated the surface expression of costimulatory molecules, which represent the second mandatory signal triggering the differentiation of cognate B cells into Ab-producing plasma cells. In vivo experiments demonstrated that CDS3KO mice (devoid of T cells) transferred with OVA- or SARS-CoV-2 Spike-VAR-T cells efficiently generated detectable levels of, respectively anti-OVA or anti-Spike antibodies. Additional experiments are under way to specifically confer to VAR-T cells resistance to CNI.

Conclusions: VAR-T cells represent a promising innovative cellular platform to optimize the response of transplanted patients on therapeutic immunosuppression to vaccination.

P355  POST-TRANSPLANT THROMBOTIC MICROANGIOPATHY (PT-TMA) AFTER ABO-INCOMPATIBLE LIVING KIDNEY TRANSPLANTATION: TWO CASES WITH LOW ISOAGGLUTININ TITLES

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Background: PT-TMA is a rare condition but it was shown that ABO-incompatibility (ABOi) is a risk factor for de novo TMA after kidney transplantation (KTx).

Methods: We describe 2 cases of PT-TMA after ABOi living KTx.

Results: Case 1: A 49-years-old male, blood type A Rh+, with chronic kidney disease (CKD) secondary to a mesangial proliferative glomerulopathy without immunofluorescent study. The donor was a female, blood type B Rh+, and 7/8 HLA mismatches were present. Five days before KTx, IgM and IgG isoagglutinin were 1:4. He received a single dose of 375 mg/m2 of rituximab (RTX) and on day 0 isoagglutinins stayed ≤1:4, with normal blood count and lactate dehydrogenase (LDH). Induction was done with basiliximab, mycophenolate mofetil (MMF), tacroliimus (FK) and methylprednisolone (MP). On day 1, Hb was 7.4 g/dL, platelets 85 x 10^3/uL, LDH 313 U/L, FK levels 28,2 ng/mL. He suspended FK, but blood count and LDH get worse, with consumed haptoglobin, negative direct Coombs and isoagglutinin titers remained <1:2 since KTx day. He developed PT-TMA with consumption coagulopathy, kidney biopsy showed presence of TMA. Case 2: A 57-years-old male, blood type B Rh+, with CKD secondary to a mesangial proliferative glomerulopathy without immunofluorescent study. The donor was female, blood type B Rh+, with CKD secondary to atrophic left kidney. The donor was female, with blood type AB Rh+. They had 8/12 HLA mismatches. Isoagglutinin titers were 1:8 and he received a single dose of RTX. Induction was done with basiliximab, MMF, FK and MP. On day 1, Hb was 7.3 g/dL, platelets 64 x 10^9/L, LDH 471 U/L, FK 5.5 ng/mL. He started PE (total of 7 sessions). Due to dysfunctions, we started eculizumab. After two doses, blood counts improved. His kidney graft biopsy was postponed due to thrombocytopenia. Isoagglutinin titers remained <1:2 since KTx day.

Conclusions: ABOi is a risk factor for PT-TMA. In both cases isoagglutinin titers were low and none received PE before KTx. Both received eculizumab with improved kidney function.
DESENSITIZATION WITH IMLIFIDASE IN CROSS-MATCH-POSITIVE, HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS: A SINGLE-CENTER EXPERIENCE

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Background: HLA sensitization is a significant immunological barrier in kidney transplantation, resulting in prolonged waiting times and inferior patient survival. Imlifidase acts by eliminating all IgG subclasses, leading to a rapid conversion of a positive crossmatch (XM) to negative. Here, we report the first three cases treated with imlifidase in our centre.

Methods: Three highly sensitized patients (cPRA ≥ 97%) received priority for deceased donor kidney transplant after their HLA incompatible living donor was matched to the national waiting list. Single antigen bead analysis, CDC and Flow XMs were performed pre- and post-imlifidase administration. Immunosuppression regimen included rabbit anti-thymocyte globulin, rituximab, and intravenous immunoglobulin (IVIG) in addition to mycophenolate mofetil, tacrolimus and methylprednisolone.

Results: The first patient was a 49-year-old male with preformed HLA class II donor specific antibodies (DSA) with a cumulative mean fluorescence intensity (cMFI) of 35858 and positive B-Flow XM. At 2 h post-imlifidase dose, the XM was negative. DSAs rebounded on day 9, whereas renal function continued to improve. No kidney biopsy was performed. On day 259, creatinine level was 0.93 mg/dl. The second patient was a 43-year-old female with preformed HLA class I & II DSA (cMFI: 64158) and positive CDC and T/B Flow XMs. Both XMs were negative at 2 hours post-imlifidase. The patient developed antibody-mediated rejection and the graft was removed during surgery. Renal graft biopsy revealed intense IgM expression on glomerular and peritubular capillaries with preformed HLA class I & II DSA (cMFI: 73377) and positive CDC and B-Flow XM. Both XMs were negative at 2 hours post-imlifidase. The patient was successfully treated with plasma exchange and IVIG. On day 185, creatinine level was 0.78 mg/dl. The third patient was a 24-year-old female with preformed HLA class II DSA (cMFI: 84158) and positive CDC and T/B Flow XMs. Both XMs were negative at 2 hours post-imlifidase, both XMs were negative. The patient developed hyperacute rejection and the graft was removed during surgery. Renal graft biopsy revealed intense IgM expression on glomerular and peritubular capillaries in the absence of IgG, findings suggestive of IgM-induced hyperacute rejection.

Conclusions: Imlifidase offers a rational therapeutic approach for kidney transplantation to highly sensitized patients. Besides IgG, other antibodies that are not routinely screened prior to transplantation, may have harmful effects on the renal graft.

LUMINAL INTESTINAL PRESERVATION FOLLOWING BRAIN DEATH MAY REDUCE INNATE IMMUNE SYSTEM ACTIVATION

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Background: Organs obtained from brain dead (BD) donors often have worse outcomes. Activation of the complement system and translocation of intestinal bacteria could be causative. We aimed to examine activation of the complement system following BD and evaluate the effect of adding luminal intestinal preservation to vascular preservation.

Methods: BD was induced in 30 pigs (four groups: control (n=7), BD alone (n=8), BD + luminal intestinal polyethylene glycol (PEG, n=7) and BD + luminal intestinal University of Wisconsin solution (UW, n=6)) using a previously validated method. All animals were observed for 6 hours before organ retrieval. In the PEG and UW groups, 2000 ml of the selected solution was instilled into the duodenum during the organ procurement. Repeated measurements of C3a, Terminal Complement Complex (TCC), IL-8 and TNF were performed in plasma at baseline, BD, 30, 60, 120, 240 and 360 minutes after BD, and following the intestinal intervention (480). Plasma lipopolysaccharide binding protein (LPS-BP) was measured at baseline, BD, and 480 minutes after BD. All were normalised to albumin concentration.

Results: All animals were kept circulatory- and respiratory stable until organ procurement. At 480 minutes, C3a was significantly higher in BD, BD+PEG, and BD+UW groups compared to control group (all p<0.05) (fig. 1A). TCC was significantly higher in the combined BD group compared to control at 360 minutes, at 480 minutes, the BD and BD+UW groups. TCC was significantly higher compared to the control group (all p<0.05) (fig. 1B). IL-8 and TNF were significantly higher in the BD group compared to all other groups at 480 minutes (p<0.003 and p<0.001) (fig. 1C and D). LPS-BP expression increased following induction of BD in all groups except BD+PEG, which at 480 minutes were significantly lower (p<0.002) (fig. 1E and F) compared with all other groups.

Conclusions: The complement system is activated following BD independently of intestinal and luminal preservation and may lead to inflammation. Luminal intestinal preservation during organ procurement led to reduced cytokine and LPS-BP expression, which may be due to reduced bacterial translocation occurring during surgery independent of BD. Luminal PEG intervention may be combined with early innate immune system inhibition in BD donors to prevent systemic inflammation.
**Background:** Introduction of living-donor liver transplantation (LDLT) have significantly reduced waiting list mortality. However, a higher morbidity is observed after LDLT, including an increased rate of anastomotic bile leaks (ABL). This study aimed to investigate the incidence, management and outcomes of ABL following hepaticojejunostomy creation in paediatric LDLT.

**Methods:** Retrospective cohort study of 331 children (<18 years of age) who underwent a primary LDLT between 2005 and 2020. Patients with duct-to-duct anastomosis were excluded from the analysis.

**Results:** The incidence of ABL in analysed group was 11.4% (n=33). In 3 patients additional leak on the cut surface was also recognized. All patients with ABL were treated surgically. In 23 cases existing hepaticojejunostomy was reinforced with additional sutures and in 5 cases complete reanastomosis was necessary due to major anastomotic leak. Primary surgical intervention was successful in 87.3% of patients (n=29). Remaining 4 patients required further surgical interventions with a good result. Five patients (15.1%) with ABL developed anastomotic biliary stricture afterwards.

**Conclusions:** ABL is a common early complication after LDLT. Early surgical approach to ABL treatment is legitimate and effective. Such approach ensures good result with acceptable frequency of anastomotic biliary strictures.

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**P360 REDUCED CARDIOVASCULAR DISEASE ASSESSMENT FOR KIDNEY TRANSPLANT RECIPIENTS – A RETROSPECTIVE COHORT STUDY**

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**Background:** Screening for asymptomatic cardiovascular (CV) disease in potential kidney transplant recipients (KTR) remains controversial. There is insufficient evidence that cardiovascular screening prior to transplantation does not significantly improve patient outcomes. Since 2015 our centre has reduced CV screening for potential KTR, particularly removing the requirement for cardiac stress testing in asymptomatic patients. The aim was to assess the perioperative and one year post transplant CV event incidence in our KTR following this change of practice.

**Methods:** This was a single centre retrospective cohort study using a prospectively designed clinical database. The study included all KTR aged ≥ 18 years who had received a transplant between January 2015–December 2021. Key demographic details, perioperative/early (≤3-month post-transplantation) and one-year post-transplantation CV events were recorded. Logistic regression identified variables of statistical significance that predicted CV events.

**Results:** A total of 895 individuals received a kidney transplant between January 2015 and December 2021, 193 (22%) of the KTR had a formal previous CV diagnosis. A total of 18 patients had a perioperative/early CV event representing 2.0% of the KTR. There was a 5.7% incidence of CV events in this cohort one year post transplantation. The results of the logistic regression analysis of multiple clinical variables exploring predictive variables and CV event one-year post-transplantation are shown in Table 1.

**Conclusions:** This study demonstrates comparable rates of CV events early and one-year post-transplantation CV event incidence in our KTR following this change of practice.

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**P361 INCIDENCE OF ANTIBODIES AGAINST HUMAN NEUTROPHIL ANTIGENS-3A IN KIDNEY TRANSPLANT CANDIDATES**

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**Background:** Human Neutrophil Antigens 3 (HNA-3a/3b) are expressed on neutrophils, lymphocytes, platelets and other tissues including kidney endothelium. Approximately 95% of Europeans are HNA-3a and 36% HNA-3b positive. Interestingly, ~5% are homozygous for HNA-3b and therefore at risk of developing HNA-3a antibodies (anti-HNA-3a). Anti-HNA-3a have been frequently associated with transfusion-related acute lung injury (TRALI) and immune neutropenias. Their role in kidney transplantation (KTx) is still not fully elucidated. In limited cases, is reported an association of anti-HNA-3a with unexplained positive T/B Flow crossmatches (T/B-FCM) in patients without HLA donor specific antibodies (HLA-DSA) as well as early rejection and poorer outcome post KTx. The aim of this study was to determine the incidence of anti-HNA-3a antibodies in patients with or without T/B-FCM and to analyze if the detection of Human Leucocyte Antigens (HLA) x Major-histocompatibility-complex (MHC) class I-related Chain–A antibodies (anti-MICA).

**Methods:** Anti-HNA were tested in 368 patients (107 females) registered in the kidney transplant waiting list of the University of Athens. An initial screening for anti-HNA-3a antibodies was performed using the normalized background values<10 and Mean Fluorescence Intensity–MFI>1000 as a positive result for anti-HNA-3a.

**Results:** Anti-HNA-3a were detected in 6 patients (5 females), 1.63% of the total cohort and 4.67% of the females, with mean MFI=7277 (1404-15420) and NBG=57.5 (13-105). Although all females had previous pregnancies, only one had anti-HLA. There was no correlation with anti-HLA or anti-MICA. Decreased donor kidneys were offered, so far, in only 2 of 6 cases according to their ranking on the match list. In both cases, although no HLA-DSA or anti-HLA antibodies were detected, the T/B-FCM were unexpectedly positive with 2 and 3 different donors respectively, resulting in graft refusal.

**Conclusions:** Monitoring of anti-HNA is important in order to identify patients with high risk to develop early rejection and graft loss although have no evidence of transfusion history. In such cases, HLA-DSA or anti-MICA, to evaluate unexplained positive T/B-FCM and to decide for patient selection for the virtual crossmatch program. The data are limited and further work is required to understand better the immunological risk associated with anti-HNA-3a and their clinical significance.

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**P362 THE IMPACT OF APPLYING UCSF CRITERIA TO PATIENTS UNDERWENT LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN A LOW VOLUME CENTER**

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**Background:** There are many studies in patients with hepatocellular carcinoma applying the expanded Milan criteria. The University of California San Francisco (UCSF) criteria are considered as the most promising expansion rules so far. Based on UCSF criteria, we selected the patients underwent liver transplantation for hepatocellular carcinoma since 2008. Here we reported the long-term outcomes of patients underwent liver transplantation for hepatocellular carcinoma to assess the validity of the UCSF criteria instead of Milan in a single center. The University of California San Francisco (UCSF) criteria was developed in multi-center, multinational study. In the current study, we aimed to assess the impact of applying UCSF criteria to patients underwent liver transplantation for hepatocellular carcinoma.

**Methods:** Between 2008 and 2020, a total of 201 liver transplantation were performed, of which 39 were liver transplantation for hepatocellular carcinoma patients. Among them, living donor transplantations were 29 cases and deceased donor transplantations were 140 cases. Based on radiologic examination prior to operation, patients were prospectively categorized into 2 groups: within Milan (n = 32) and beyond Milan within UCSF (n = 7). Clinical outcomes were reviewed retrospectively.

**Results:** Mean age of patients was 51.2 years, and 28 patients were male. Mean MELD score was 11.2 ± 8.7. Mean follow-up period was 63.7 ± 54.6 months. The 5-year overall survival rates in ‘within Milan’ and ‘within UCSF’ groups were 84.4% and 74.7%, respectively (p<0.041). The 5-year disease-free survival rates in ‘within Milan’ and ‘within UCSF’ groups were 56.0% and 76.0%, respectively (p<0.001). Generally, 5-year disease-free survival rate in total patients was acceptable (39.76%). However, 7 expanded patients from Milan were revealed very poor long term both 5-year overall survival rate and disease-free survival rate (7.1%, 6.8%, 0%, respectively). Based on the survival analysis, the overall survival and disease-free survival rate were lower when applying UCSF criteria compared to Milan criteria.

**Conclusions:** The Milan criteria are still optimal in seeking for long term good results in patients with hepatocellular carcinoma. When the UCSF criteria are applied to hepatocellular carcinoma patients, the overall long-term results are acceptable, however there is a higher risk of recurrence compared to the Milan criteria.
Background: N-terminal Pro-Brain Natriuretic Peptide (NT-proBNP) as a cardio-related biomarker indicated an increasingly valuable prognosis in renal transplant recipients (RTRs). This study aimed to develop and validate a nomogram based on preoperative data with NT-proBNP for predicting major adverse cardiovascular events (MACEs) in RTRs.

Methods: A retrospective study was conducted using data from 582 RTRs in The First Affiliated Hospital of Sun Yat-sen University from January 2015 to September 2020. The LASSO-Cox regression analyses were used to identify potential predictors. Then nomogram was developed and evaluated with respect to discrimination, calibration, and clinical usefulness and compared with previous predictive models. Finally, NT-proBNP was added to previous models for evaluation of model improvement.

Results: Overall, 58 (9.9%) patients developed MACEs during 2.8 (2.0 - 3.8) years of follow-up. Five variables including Log₂NT-proBNP (HR=1.43, 95%CI 1.25 to 1.64), Age (HR=1.05, 95%CI 1.03 to 1.08), BMI (HR=1.08, 95%CI 1.02-1.15), Diabetes (HR=3.00, 95%CI 1.67 to 5.39), Retransplant (HR=2.72, 95%CI 1.16 to 6.42) were incorporated in the nomogram. Area under the receiver operating characteristic curve was 0.864 at 6 months, 0.859 at 1 year, 0.838 at 3 years, with good consistency and clinical value showed by calibration curve and decision curve analysis respectively. The nomogram exhibited a higher predictive capacity than previous models in this cohort, and previous models were remarkably improved when adding NT-proBNP.

Conclusions: A nomogram including preoperative NT-proBNP may predict cardiovascular risks in renal transplant recipients more accurately than conventional models.

Background: Polymavirus are small DNA viruses that can infect humans and animals like rabbits, rodents, and birds. In renal Tx recipients, BK virus can lead to tubulointerstitial nephritis, ureteral stenosis and hemorrhagic cystitis in bone marrow Tx. The current consensus on management of BKV viremia is to decrease immunosuppression and to regularly follow up BK viral polymerase chain reaction (PCR) along with renal functions to prevent allograft BKV nephropathy (BKVN) which increase the risk of graft failure. The challenging part in managing BKV infection is the balance between the fear of rejection, due to reduction of immunosuppression, and maintaining the same level of immunosuppression-causing more BKV viremia and consequently BKV nephropathy (BKVN). BKV is one of the most common infections in renal transplant patients. Our study aimed at evaluating the effect of BK virus reactivation on both graft and patient survival in renal transplant recipients.

Methods: A single-center retrospective analysis of 492 patients who received their renal transplant between January 2010- October 2017.

Results: A total of 492 patients (337 males, 155 female) with a mean age of 54.1 ± 13.7. 73 years. About 14.8% of the patients had BK Viruria out of which 33 patients developed BK viremia. 10 patients were biopsy-proven BKVN and three of them had graft loss. The mean duration between transplantation and viruria was 8.92 ± 11.55 months, between viruria and viremia was 2.83 ± 3.16 months, and between viremia and development of BKVN was 3.29 ± 4.88 months. Finally, the duration between BKVN and development of graft failure as a result of BKVN was 14.49 ± 19.39 months. There was no statistically significant difference between the overall graft survival or patient survival for patients with positive BKV infection and that of negative BKV infection. No statistically significant difference in the incidence of acute rejection between both BKV infected group and the non-infected group.

Conclusions: Patients who developed BKV infection have a poorer graft function when compared to other renal transplant patients who did not. However, no significant statistical difference between both groups regarding both graft and patient survival.
Donors undergoing laparoscopic nephrectomy were divided into two groups: the nefopam group (n = 36; 40mg IV nefopam) and the acetaminophen group (n = 36; 2g IV denogan). Ultrasound-guided RSB was performed preoperatively in all enrolled donors. The primary outcome of the study was total opioid consumption of IV-PCA during postoperative day (POD) 1. In addition, the numeric pain rating scales (NRS) of flank (visceral pain) and umbilicus (parietal pain) at rest and cough quality of recovery-15 questionnaire (QoR15) were investigated on POD 1.

Results: There were comparable in demographic findings. Total opioid consumption of IV-PCA was higher in the acetaminophen group than in the nefopam group (70.2±29.0 mL vs. 44.5±19.3 mL; p=0.001). NRSs of flank and umbilicus at rest and cough were lower in the nefopam group than in the acetaminophen group in post-anesthesia care unit. Sub-division score related to severe pain was better in the nefopam group than in the acetaminophen group in QoR15.

Conclusions: Nefopam may provide better analgesic effect to reduce opioid requirement rather than acetaminophen in living kidney donors with pain relieved by RSB. Further randomized controlled studies are needed to determine an effective and safe dose in advanced multimodal analgesia for living donors.

Background: Due to their immunocompromised status, lower immune responses to SARS-CoV-2 mRNA vaccination have been observed in solid organ transplant (SOT) recipients. However, scarce data is available regarding the impact of the different immunosuppressive treatments (IS). T-cell exhaustion abrogates effective proliferative and functional antigen specific immune responses. Therefore, characterizing different exhaustion T-cell phenotypes could identify patients more likely to respond to booster vaccination.

Methods: Within a large, prospective, multicentre study investigating serological and cellular memory immune responses specific to SARS-CoV-2 in 148 SOT undergoing three booster mRNA vaccination we assessed functional and phenotypic immune profiles related to distinct maintenance immunosuppressive therapies such as TAC/MMF, MMF-monotherapy, TAC monotherapy and TAC/ mTORi. Antigen-specific neutralizing antibodies (NAb), memory B and Th1/Th2 cell exhaustion markers (PD-1, TIM3 and CD57) in CD4 and CD8 T-cells were assessed in 700 biological samples at 5 different time points.

Results: After three doses of SARS-CoV-2 mRNA vaccine, 32.3% of SOT did not achieve a successful neutralizing antibody response. 12.5% (2/16) TAC/ mTORi patients did not achieve NAb versus 40% (24/78) and 50% (4/8) in patients in TAC/MMF and MMF (p=0.038 and p=0.023, respectively). Similarly, all functional T and B memory immune responses were significantly lower in patients on TAC/MMF than TAC/mTORi (p<0.05 for all). SOT patients not developing NAb after three booster vaccines exhibited a significantly more exhausted CD4+ T-cell phenotype prior to vaccination than those with NAb (p<0.001 PD1+CD57+, p<0.001 CD57+, p<0.001 PD1+ and p<0.048 TIM3+CD57+). Patients with an exhaustion phenotype were non-responders for T and B memory immune responses and were receiving TAC/MMF IS. Patients with severe breakthrough infection (BTI) exhibited a significantly more exhausted CD4 T-cell phenotype than those with mild/asymptomatic BTI (Figure).

Conclusions: T-cell exhaustion phenotypes seem to drive poor antiviral immune responses after SARS-CoV2 booster vaccination and favour severe BTI if infected, this feature being more likely observed among patients under TAC/MMF IS.
P377 CIRCULATING IRISIN LEVELS IN KIDNEY TRANSPLANT PATIENTS

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Background: There is increasing evidence that skeletal muscle acts as a secretory organ. Irisin is a myokine, which promotes insulin sensitivity, body weight, and glucose tolerance in mice. There has been controversy regarding its role in glucose metabolism and development of diabetes in humans. Irisin serum concentrations were not previously analyzed in transplant patients and in post-transplant diabetes mellitus (PTDM).

Methods: We analysed irisin serum levels in 47 patients without diabetes (M28, F19, mean age 48.5 years) before and after kidney transplantation (KT) performed in our centre between 2020 and 2022. We present preliminary results. Blood samples were obtained before KT and at the following time points: 1, 2, 3, 4 and 5 weeks after KT. The serum was separated after centrifugation, mixed with aprotinin and stored at −80 °C pending analysis. Quantification of serum irisin was based on competitive enzyme immunoassay kits.

Results: We found an outstanding increase in ISL measured after KT reaching more than 1000 times in 44% of patients (21/47). All measurements of irisin serum levels before KT were lower than 25 ng/ml (median 8.4 ng/ml). The increase appeared at the first measurement (one week after KT) and remained stable for at least a month. Median values of all measurements after KT procedure in the group with increase in ISL was: 1220 ng/ml (min-max: 158-5884) and in the group without increase was: 6 ng/ml (min-max: 2-20). Factors connected to large growth were obesity, with BMI>30 (p=0.04), longer cold ischemia time (p=0.05), time spent on dialysis before KT (p=0.02) and subsequent KT - 2nd and 3rd (p=0.0006). In the group characterized by an increase in irisin, glycemic disturbances requiring permanent insulin therapy occurred at a rate of 19% (4/21), while in the group without an irisin increase, 27% (7/26), difference not statistically significant. We did not find the influence of the type of calcineurin inhibitor and delayed graft function on the increase of the irisin level.

Conclusion: Irisin serum levels are increased in some KT recipients. Whether the increase has an impact on the reducing risk of post-transplant diabetes requires further study.

P379 MACHINE-PERFUSION FOR LIVER TRANSPLANTATION IN HIGH VERSUS LOW/MID-VOLUME CENTRES: AN INTERNATIONAL SURVEY

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Background: Machine perfusion (MP) was developed to expand the available donor pool and improve liver transplantation (LT) outcomes. Despite optimal results in clinical trials, the real-life scenario of the MP benefit in LT center with low/mid-volume activity is still being determined.

Methods: An online 22-item survey on MP for LT outside clinical trials was distributed to worldwide LT centres representatives. Variables of interest included MP logistics, technicalities, and outcomes. Responding centres were grouped into high-volume centres (HVCs) (>55 LTs/year) and low/mid volume centres (LVCs) (≤55 LTs/year). Results from HVCs and LVCs were compared.

Results: Sixty-seven centres were included, 36 HCVs and 31 LCVs. Between HVCs and LVCs, significant differences were found regarding: I) the existence of an established MP program (80.6% vs. 41.9%, p=0.02), II) the presence of a dedicated perfusionist (58.3% vs 22.6%, p=0.006), III) the duration of MP (>4 hours: 47.2% vs. 16.1%, p=0.01), IV) the routine MP use (20-40% vs. 5-20%, p=0.002), V) the graft utilization (75% vs. 51.6%, p=0.009), VI) the 90-day patient survival rates (90-100% vs. 50-90%, p=0.001) and VII) the subjectively perceived benefit of MP (always vs. only in selected ECDs, p=0.009). Concordance was found for indications of MP use, type of MP technology, viability tests, graft salvage rate, 90-day graft loss and major complications.

Conclusions: This study captured a picture of the real MP use in LT practice. Significant disparities have surfaced between LVCs and HVCs regarding the logistics, utilization and results of MP, including patient survival. Further studies are required to define the future role of MP worldwide.

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Background: World Health Organization (WHO) is advocating for the de-velopment of self-sufficiency in organ donation and transplantation (D&T) worldwide. European countries represent 8 from the 10 worldwide countries with highest organ donation rates. Nevertheless, many countries in the region still present low rates with great opportunities for improvement. The International Registry for Organ Donation and Transplantation (IRODAT registry) is the oldest worldwide registry for organ donation and transplantation activity, reporting information since 1996 from 106 different countries.

Methods: A retrospective analysis of the organ donation activity from the information reported from European countries between 2019 to 2022 in the IRODAT registry has been conducted. European countries have been selected according to the World Health Organization’s classification. Data from the actual deceased organ donors per million population (PMP) rate, living organ donors PMP rate and actual donors after circulatory death PMP rate was analyzed.

Results: From the 53 countries in the European region, 43 have submitted data to our registry. COVID pandemic showed a big impact in the programs’ activity, with 30 countries having a decrease in their deceased donation rates during 2019 and persist until 2021. In the analysis of total deceased donation activity, 3 countries (7%) did not report deceased donation in the period studied, and only 23 countries (52%) reported more than 15 donors PMP in at least 1 of the 3-year period studied, with 20 of them maintaining this level during 2021.

Conclusions: To achieve self-sufficiency in organ transplantation in the European region, more efforts should be allocated to develop efficient deceased donation programs. Despite WHO’s third guiding principle which mentions that donation from deceased persons should be developed to its maximum therapeutic potential, many European countries have living donation programs with poor or no deceased donation activity at all.

Background: Incisional hernia (IH) remains one of the most common complications following abdominal organ transplantation with no consensus on the optimal management. This study is a narrative review on the incidence, risk factors, diagnosis, and management of IH post-transplantation.

Methods: A literature search using the EMBASE and MEDLINE from 1.1.2016 to 15.8.2020 was conducted. Included studies reported on IH after open abdominal organ transplantation. The outcomes included in our analysis were the incidence of IH, significant patient risk factors, the diagnostic approach used to detect IH, and proposed strategies for the management of IH. 33 publications that involved 9336 transplant patients who developed IH were included.

Results: The incidence of IH ranged from 1.7% to 43% in liver transplant patients and was reduced following kidney transplantation (1.1%-7.0%). Patient risk factors predisposing to IH were body mass index >30, age >50, smoking history, previous open abdominal surgery, open surgical repair, a Mercedes or inverse T incision and surgical site infections. The most common diagnostic approach for IH is clinical examination, followed by US or CT imaging in cases of complex IH. Following IH repair, recurrence rates ranged from 0-76.9%, and complication rates from 12%-52.9%, the most common of which were surgical site occurrences (16.0 - 79.2%) including infection (0 - 65.4%) and seroma formation (0-8%). Management of IH should include preoperative optimization of patients through weight reduction, smoking cessation and adjustment of insulin or other antidiabetic medications and smoking cessation. Mesh repair, either open or laparoscopic, is the gold standard for the treatment of IH, resulting in a significantly lower recurrence rate than primary closure. There is no consensus on the type and positioning of mesh, and very limited studies have reported on other peroperative factors such as wound closure.

Conclusions: Prehabilitation and MDT approach are important in ensuring good outcomes following IH repair. Further prospective studies and the establishment of a relevant registry are required to propose a consensus pathway for IH repair in the transplanted population.

Background: Transplantation of kidneys from patients dying from uncontrollable circulatory arrest outside hospital (uCD) has been published from several large populations. Overall, 2087 patients show a 65.1%-76.0% frequency of DGF and a 6.8%-12.3% frequency of PNF. The high frequency of DGF, in combination with the labour-intensive and expensive methods for utilizing these donors, is the main reason why uCD kidneys are rare among all DCD kidney transplantations in Europe. Based on animal data in pigs, we have strong reason to believe that a novel developed method significantly can reduce the frequency of delayed graft function (DGF), increase the quality of renal grafts, and increase the donor pool for successful kidney transplantation. The present study protocol describes a first-in-human trial, in which uCD kidneys are reconditioned and preserved using this new perfusion method and then transplanted to patients on the waiting list for uCD donors.

Methods: This is a first-in-human phase 1-2a safety study in eight patients, using only one kidney from each uCD donor in four patients, followed by both kidneys from two uCD donors in four more patients. Patient safety data, including patient death, DGF, and PNF will be closely monitored. The effect on the kidney function in the device solutions, will be studied. Kidneys from the uCD donor will be retrieved up to 4 hours after death, followed by ex vivo perfusion, using lys-plasminogen and IPI to remove/prefet clot formation and allow oxygenation of the kidneys. Results: We have extensive preclinical and clinical data published in Transplantation and will use the protocol in humans. The primary objective is to perform a safety study with minimal risk for patients. Preclinical data from pigs suggests a low risk of complications. A limited number of patients will be used. Proof of Concept (PoC) will be declared if 50% or fewer patients (≤4 of 8) experience DGF and less than 13% will have primary non function (PNF) i.e., substantially lower than published data. The protocol will be presented. Inclusion of patients is estimated to start August 15th 2023.

Conclusions: Kidneys from extended uCD donors, allowing warm ischemia times of > 4 hours, will be transplanted to patients. The novel method has the potential to change organ allocation and abolish organ shortage, globally.

Background: Adipokines, such as leptin and adiponectin, are adipocyte-specific secretory cytokines. They play an important role in the metabolic regulation of body weight. Alterations in leptin and adiponectin concentrations are associated with CKD-related cardiovascular problems. Data on the association between inflammatory processes and leptin and adiponectin in people after kidney transplantation are unclear. The aim of this study was to investigate the levels of adipokines and assess its relation to nutritional and inflammatory parameters in overweight/obese and normal weight kidney transplant recipients (KTRs).

Methods: The 66 KTRs in stable clinical condition were enrolled in the study (mean time after Tx was 137 ± 83 months). Assessment of nutritional status was determined by the level of s-albumin, body mass index (BMI), percentage of body fat (%F), lean body mass (LBM), Fat Tissue Index (FTI) and lean Tissue Index (LTI). Analysis of body composition was performed using the BCM (Fresnius SA). The routine laboratory parameters (creatinine, urea, potassium, lipids, albumin, blood whole morphology) were measured in serum. Leptin, adiponectin and hsCRP levels were measured by ELISA method. eGFR was calculated by CKD-EPI formula. The statistical analysis was done used Statistic 13.0.

Results: Overweight and obesity were found in 85% and decreased LTI in 84 % KTRs. The most high leptin level and increased ratio leptin to adiponectin in people after kidney transplantation are unclear. The aim of this study was to investigate the levels of adipokines and assess its relation to nutritional and inflammatory parameters in overweight/obese and normal weight kidney transplant recipients (KTRs).

Conclusions: Obesity and its association with high level of leptin, decreased adiponectin and biochemical signs of inflammation may increase cardiovascular risk in KTRs. Results suggests need nutritional education that could prevent the consequences of adipose tissue accumulation in KTRs.
we found a slight increase in inflammatory lesions, and most patients that had a better creatinine at M12 but it wasn’t statistically significant. At M12, months, but no correlation was found between the presence of CV, Ah1, Medial tubular vacuolisation and higher means of tacrolimus during the 3 months. Every metaboliser patients had mixed lesions (toxicity and rejection), 1 patient recurrence of IgAN, 1 patient an acute pyelonephritis. We found a significant correlation between Tubular vacuolisation and higher means of tacrolimus during the 3 months, but no correlation was found between the presence of CV, Ah1, Medial Vacuolisation, IFTA and higher means of serum tacrolimus. Patients with Ah1 at M3 had a better creatinine at M12 but it wasn’t statistically significant. At M12, we found a slight increase in inflammatory lesions, and most patients that have a slight tubular atrophy.

Conclusion: Protocol biopsy is a safe and useful procedure, perfectly stable patients can present a pathological biopsy, even if the elementary lesions are moderate and at early stages. Subclinical rejection was found in our study in 8% of a moderate immunological risk population mainly treated with ATG and Tacrolimus. These results encourage us to continue our strategy.

Table. Selected results (* normal vs overweight/obese KTRs p<0.05).

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<th>Leptin ng/ml</th>
<th>Adiponectin pg/ml</th>
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<th>hsCRP mg/dl</th>
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**P382**

**SHOULD INFECTION IN DECEASED ORGAN DONORS INHIBIT THE DECISION FOR KIDNEY TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE**

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**Background:** The decision to accept a deceased organ donor with infection can be a subject of controversy among physicians due to the possibility of transmitting the disease to the recipient. Here, we report the impact of the infections of deceased donors to 87 recipients in our centre.

**Methods:** We retrospectively collected data from 68 deceased donors who donated their kidneys to 87 recipients in our centre from 1/1/2016 until 1/9/2022. The donors had been diagnosed with microbe, urinary tract infection or both diseases. The minimum follow-up of recipients was 3 months.

**Results:** One of the 87 recipients was a donor diagnosed with UTI, while the donors of 16 (18.3%) recipients suffered from both microbe and UTI. The median stay of donors in the ICU was 10 days. Infection by the same pathogens developed in none of the recipients. No serious adverse effects of the antibiotic regimen on recipients were reported. The one-year survival rate of renal recipients was 96.8%, while the one-year survival rate of renal grafts was 95.4%.

**Conclusions:** Although the harmful effects of donor-derived infections on renal recipients have been described, the careful acceptance of some infected donors could be a safe and reasonable way to expand the donor pool in countries with long waiting lists for kidney transplantation.

**P381**

**PROTOCOL BIOPSY IN LIVING KIDNEY DONOR TRANSPLANTATION**

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**Background:** The benefit of protocol biopsies is supported by the fact that histological lesions precede biological disturbances; We were the first center in our country that established protocol biopsies at 3 and 12 months. The aim of our study was to demonstrate the utility of the screening at 3 months by reporting a significant rate of pathological findings.

**Methods:** We conducted a descriptive, prospective study, which included patients transplanted with AB0 compatible living donors who have stable creatinine and no significant proteinuria. Out of a total of 67 patients, we retained 62 pts who benefited at M3 from routine testing for DSA, graft ultrasound Doppler and biopsy, biopsies were analysed twice, locally and a second time in France or Belgium in a reference center. The Mean of serum tacrolimus during the 3 M was calculated for each patient and correlated to the histological lesions. At M12, a 2nd screening was performed to evaluate the evolution of patients.

**Results:** The mean age was 34yoc, sex ratio:1:69, The causal nephropathy was underterminated for about ½ of patients, 85% of pts had no DSA even if 54% experienced sensitizing events. ATG was used in 76% of cases, a minimisation strategy of CNI was adopted. Elementary lesions were classified according to Banff 2017, we found 13% of CNI toxicity, 8% subclinical rejection, 2 hyper metaboliser patients had mixed lesions (toxicity and rejection), 1 patient recurrence of IGAN, 1 patient an acute pyelonephritis. We found a significant correlation between Tubular vacuolisation and higher means of tacrolimus during the 3 months, but no correlation was found between the presence of CV, Ah1, Medial Vacuolisation, IFTA and higher means of serum tacrolimus. Patients with Ah1 at M3 had a better creatinine at M12 but it wasn’t statistically significant. At M12, we found a slight increase in inflammatory lesions, and most patients that have a slight tubular atrophy.

**Conclusion:** Protocol biopsy is a safe and useful procedure, perfectly stable patients can present a pathological biopsy, even if the elementary lesions are moderate and at early stages. Subclinical rejection was found in our study in 8% of a moderate immunological risk population mainly treated with ATG and Tacrolimus. These results encourage us to continue our strategy.
P386  DEVELOPMENT OF RENAL ALLOGRAFT LYMPHANGI-ECTASIA AFTER 14 YEARS FROM KIDNEY TRANSPLANTATION

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**Background:** Renal lymphangiectasia is known to be a very rare disease, and in particular, it is confirmed that very few cases occur in the setting of transplant kidney. Here, we report a rare case of renal lymphangiectasia after kidney transplantation.

**Methods:** A 43-year-old man received living donor kidney transplantation due to IgA nephropathy, treated with two episode of acute and chronic antibody-mediated rejection, on post-transplant 1 year and 7 year respectively.

**Results:** On post-transplant 14th year, he presented with abdominal distension, and dyspnea gradually progressing for 2 months. Serum creatinine level was elevated to 1.6mg/dL from baseline 1.1mg/dL. Computed tomography (CT) and Magnetic resonance imaging (MRI) showed multi-septated cystic lesions around the graft kidney with a large amount of ascites. Ascites profile showed transudative, non-chylous, suggesting lymphatic fluid. (Protein 289.3mg/dL, Serum ascites albumin gradient(SAAAG) 3.1g/dL, Triglyceride 3mg/dL). There was no evidence for infectious or malignant disease. At first, tacrolimus was switched to sirolimus, which has an anti-lymphangiogenic effect, consequently the amount of ascites was significantly reduced and abdominal distension improved, and the patient was eventually discharged from the hospital on the 5th day after changing the medication. However, 3 weeks after discharge, he returned to the hospital with abdominal distension, and again a large amount of ascites was confirmed. In this time, surgical approach with laparotomy and argon coagulation and helixor injection through Hemo-vac drain inducing adhesion were done. Also, lymphatics embolization was performed using lipiodol. Afterwards, the abdominal distension and ascites resolved. However, massive ascites recurred just after 1 week from procedures, therefore, allograft nephrectomy was inevitable.

**Conclusions:** Post-transplant renal lymphangiectasia is a rare but critical complication of allografts, still poorly understood. However, massive ascites due to lymphangiectasia could result serious situation, so efforts to active treatment is required.

Fig 1. Abdominal computed Tomography

Fig 2. Kidney magnetic resonance imaging

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P387  LONG-TERM OUTCOME OF PEDIATRIC LIVER TRANSPLANTS: THE IMMUNOSUPPRESSION AND PSYCHO-SOCIAL DEVELOPMENT

Rey-Heng Hu*, Ming-Chih Ho, Cheng-Maw Ho, Chih-Yang Hsiao, Yao-Ming Wu, Po-Huang Lee

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**Background:** To review the long-term outcome of pediatric liver transplantation at NTUH, with attention to immunosuppression regimen and psycho-social development.

**Methods:** 174 liver transplants were performed at age <18 y/o. All patients were followed till December 2021 or death. Their medical records were reviewed for biologic outcome and immunosuppression regimen. Psycho-social developments were studied for 51 patients with final age ≥15 y/o by questionnaire.

**Results:** Of the 174 patients, 10 were excluded due to death within 6 months. The 5 and 10 year patient survival are 85% and 75%. Most of the transplants were performed between 0.5 to 2 y/o. 19 patients are on CsA-based therapy and the other 145 patients are under TAC-based immunosuppression. Most of them are with two combined immunosuppressants. There is no significant change of TAC dose along with age, and then the standardized TAC daily dose decreased along with time. At age of 15 (n=49), the average TAC level was 2.82 ng/ml, and 1/5 of cases with level below the detectable limit. This level is far lower than that in adult liver transplant patients. For patients with age ≥15 years, 87% of them are with compatible academic degree in their learning process. 20% patients need special education program in their junior-high or high school stage. 23% patients had one to two years delay in their education process. Around 17 % of patients had the feeling to be discriminated by their peer group.

**Conclusions:** The long-term survival of pediatric liver transplantation is good. The age standardized TAC dose decreased with age, but there is no parallel decrease of TAC concentration. The long-term TAC level is very low. Though they survived with normal liver function and body built, but significant percentage of patients have obstacle/delay in their learning process, and they have the feeling of being discriminated psychologically.
Background: Loading protocol with daily mycophenolate mofetil (MMF) dosage of 3 gram for 5 days resulted in superior accomplishment of target MPA level and reduction of acute rejection. However, with lower MMF dosage usage in Asian population, data regarding MPA-AUC in early phase after KT is lacking.

Methods: We performed a prospective cohort study in patients who underwent KT at Siriraj Hospital between July 2019 and March 2020. All enrolled patients received MMF loading protocol of 2 gram daily for 7 days after KT then adjusted to 1 – 1.5 gram per day. Full MPA-AUC was measured at 3rd and 5th day after KT. MPA-AUC was also measured at 1 month after transplantation by mean of abbreviated AUC model. The CMV, BK infection and rejection were monitored for 2 years after KT.

Results: We enrolled 37 patients with mean age of 38.9 ± 11.8 years. Most (75.7%) received deceased donor KT. At 1-month post KT, 62.4% patients received daily MMF dosage of 1.5 gram. Achievement of therapeutic MPA-AUC (≥ 30 mg.hr/L) at 3rd, 5th and 30th day after KT were revealed in 82.9%, 80% and 85.3% of patients, respectively. However, high MPA-AUC (≥ 60 mg.hr/L) at 3rd and 5th day was observed in 37% and 51.4% patients, respectively. Most of patients whose BW < 65 kg (96%), but 50% of patients with higher BW had MPA-AUC ≥ 30 mg.hr/L at 3rd day. Early acute rejection was found in 2 patients. Both patients had MPA-AUC at 3rd day < 40 mg.hr/L (15.4%). CMV and BK viremia was found in 40.5% and 16.2% of patients, respectively. Patients who had CMV viremia tended to have higher MPA-AUC at 3rd day after KT (62.2 ± 34.4 vs 47.1 ± 22.7 mg.hr/L; p = 0.13).

Conclusions: A MMF loading protocol of daily 2 gram in Thai KT patients resulted in early therapeutic MPA-AUC achievement, especially in patients with BW < 65 kg. Monitoring MPA exposure at day 3 after KT is advantageous for prevention of transplant complication.

P390
PREVALENCE OF EARLY ACHIEVEMENT OF THERAPEUTIC LEVEL OF MYCOPHENOLATE AFTER A LOADING PROTOCOL AMONG THAI KIDNEY TRANSPLANT RECIPIENTS

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Background: Loading protocol with daily mycophenolate mofetil (MMF) dosage of 3 gram for 5 days resulted in superior accomplishment of target MPA level and reduction of acute rejection. However, with lower MMF dosage usage in Asian population, data regarding MPA-AUC in early phase after KT is lacking.

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Conclusions: A MMF loading protocol of daily 2 gram in Thai KT patients resulted in early therapeutic MPA-AUC achievement, especially in patients with BW < 65 kg. Monitoring MPA exposure at day 3 after KT is advantageous for prevention of transplant complication.

P391
PREGNANCY AFTER LUNG TRANSPLANTATION IN THE NETHERLANDS

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Background: Data on pregnancy after lung transplantation (LTX) is scarce. Most data on pregnancy after solid organ transplantation comes from pregnancies after kidney or liver transplantation. Data from the American National Transplant Registry Pregnancy Registry (NTPR) shows that these pregnancies (n=46) are associated with a high risk of complications such as (pre)eclampsia, graft rejection, kidney function decline, preterm birth and maternal mortality. The primary aim of this study was to examine neonatal and maternal outcomes of pregnancy after LTX in the Netherlands.

Methods: In this retrospective multicenter cohort study all patients with a pregnancy after LTX in the Netherlands were eligible. Data on demographics, pregnancy complications, kidney function (slope) and lung function, was collected from medical files. Due to small sample size mainly descriptive statistics were used.

Results: We included 11 pregnancies of 8 women. For 7/8 women cystic fibrosis (CF) led to LTX and 1/8 pulmonary hypertension. Hypertension during pregnancy occurred in 3/11 pregnancies and preeclampsia in 2/11. One patient with pre-existent CF-related diabetes had progressive renal insufficiency during pregnancy. In one patient post-transplant lymphoproliferative disorder (PTLD) was diagnosed in the second trimester. Lung function remained >80% of FEV1 % of baseline at last follow-up in all patients. One woman died 3.5 years after her first pregnancy and 2 years after her second due to PTLD (distinct from the former PTLD patient). All children were born alive, 10/11 were born preterm and their median gestational age was 35 weeks (range 27-38). All children had a birth weight <3500 grams with a median weight of 2340 grams (range 1020-3300). Median follow-up after pregnancy was 5 years (range 2-months-7 years). All children were reported as healthy on last follow-up. However, no specific tests were performed.

Conclusions: This cohort study in the Netherlands found that pregnancy after LTX led to an increased risk for pregnancy complications for both mother and child. This is in line with existing research. In the longer term results show no deterioration of lung function after pregnancy and healthy children. However, 13% of the mothers died, which is in line with the survival of women with a pregnancy after liver of kidney transplantation.

Table 1. Characteristics of pregnancies after lung transplantation in the Netherlands

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Time to conception (years)</th>
<th>Gestational age (weeks)</th>
<th>Birth weight (grams)</th>
<th>Neonatal outcome</th>
<th>Maternal outcome</th>
<th>Lung function last before 3rd trimester (N/FEV1 of baseline)</th>
<th>Lung function at last follow-up (N/FEV1 of baseline)</th>
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<tr>
<td>1a</td>
<td>37</td>
<td>PAH</td>
<td>5</td>
<td>36</td>
<td>2340</td>
<td>alive</td>
<td>heart (PTLD)</td>
<td>5/5 years after birth</td>
<td>5/5 years after birth</td>
</tr>
<tr>
<td>50</td>
<td>45</td>
<td>PAH</td>
<td>6</td>
<td>56</td>
<td>2390</td>
<td>alive</td>
<td>heart (PTLD)</td>
<td>5/5 years after birth</td>
<td>5/5 years after birth</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>CF</td>
<td>5</td>
<td>31</td>
<td>2420</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
</tr>
<tr>
<td>2b</td>
<td>38</td>
<td>CF</td>
<td>5</td>
<td>38</td>
<td>2490</td>
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<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
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<tr>
<td>67</td>
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<td>5</td>
<td>37</td>
<td>3300</td>
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<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
</tr>
<tr>
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<td>35</td>
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<td>5</td>
<td>35</td>
<td>2500</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
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<tr>
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<td>7</td>
<td>31</td>
<td>1370</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
</tr>
<tr>
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<td>27</td>
<td>CT</td>
<td>7</td>
<td>31</td>
<td>2117</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>CT</td>
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<td>26</td>
<td>2320</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
<td>9/9 years after birth</td>
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<tr>
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<td>33</td>
<td>CT</td>
<td>12</td>
<td>27</td>
<td>2120</td>
<td>alive</td>
<td>(pre) eclampsia</td>
<td>9/9 years after birth</td>
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</tr>
</tbody>
</table>

Background: Transplantation of kidneys to highly sensitized patients has become a common practice in recent years. Desensitization is commonly used in sensitized recipients, but its relation to non-infectious complications is unclear. The aim of the study was to evaluate the effect of desensitization on early complications in kidney transplantation.

Methods: Based on the Korean Organ Transplant Registry (KOTRY) data, a retrospective analysis was conducted of 5038 living donor kidney transplants (LDKTs) between 2014 and 2021. A comparison was made between the outcomes of 1819 sensitized patients and those of other recipients. The incidences of early complications such as delayed graft function (DGF), urinary leak, hemorrhage, thrombosis and embolism at graft vessels, wound infection, and vascular stenosis and their associated risk factors were analysed.

Results: The desensitized group had a higher rate of hemorrhage (2.1% vs. 0.8%, P < 0.001) and DGF (1.2% vs. 0.6%, P = 0.03). Desensitization did not appear to be responsible for any other complications. Except for desensitization, other demographic and baseline factors were not associated with hemorrhage. Univariate and multivariate analysis revealed that diabetic (OR 2.0, P = 0.028) and/or desensitized (OR 2.0, P = 0.03) recipients had higher DGF. DGF eventually resulted in graft failure (GF) for 12 of the 40 patients. In desensitized recipients, GF was more likely to occur, and the period between transplantation and GF was shorter. A higher rate of early acute rejection was observed in patients who underwent desensitization (OR 1.4, P < 0.001).

Conclusions: More frequent postoperative bleeding and DGF were observed in desensitized kidney transplant recipients. The only risk factor for bleeding was desensitization. In regards to DGF, DM was also considered a risk factor. DGF and GF may be associated with the increased incidence of early acute rejection in desensitized recipients.

E-POSTERS

P393 EARLY COMPLICATIONS AFTER DESENSITIZED LIVING DONOR KIDNEY TRANSPLANTATION: ANALYSIS OF KOREAN ORGAN TRANSPLANTATION REGISTRY (KOTRY) DATA

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1Seoul National University College of Medicine, Seoul, South Korea

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Background: Enhanced Recovery after Surgery (ERAS) is well established in many specialties but has yet to be widely adopted in liver transplantation. The aim of this survey was to understand current national practices and sentiment towards ERAS in liver transplantation.

Methods: A web-based survey was designed and sent to consultant surgeons, anaesthetists, hepatologists and transplant coordinators at all UK adult liver transplant centres between February and April 2022. Respondents were requested to answer the survey in the context of uncomplicated liver transplant. Data was analysed according to individual responses and where appropriate, grouped according to transplant centres.

Results: All disciplines, at all seven centres were represented in the responses. No units had a formal ERAS pathway for all recipients. Of the 116 eligible respondents, over half (54%) were considering implementing ERAS within 18 months. Perceived barriers to implementation included the complexity of post-operative management and the complex nature of liver transplant surgery (51%, 47% respectively); lack of a standardised protocol (49%) and embedded unit culture (48%). The majority of respondents (93%) regularly inserted NG drainage tubes whereas fine bore tubes were rarely or selectively inserted by most (76%). Only 12% of respondents routinely used portocaval shunts or portosystemic bypass. The commonest time to extubation was 2-6hr (44%). Opiate based PCA was most commonly used (79%), with routine discontinuation of PCA between 48-72hr for 55% of respondents. Routine discontinuation of PCA between 48-72hr for 55% of respondents. Routine discontinuation of PCA between 48-72hr for 55% of respondents.

Conclusion: Despite slow uptake of ERAS in liver transplantation, appetite is increasing. The captured national practices and opinions of transplant specialists are now being used to help with standardisation of a local ERAS protocol for liver transplant recipients.

Background: Post-transplantation cancer is common, associated with increased healthcare costs and a leading cause of post-transplant mortality but remains poorly understood. Limitations include translation of data from different countries (e.g., United States), lack of contemporary population cohorts and epidemiological data being siloed across different registries and/or data warehouses. Epidemiology of Cancer after solid Organ Transplantation (EpCOT) overcomes these limitations by creating a comprehensive record-linked national dataset of solid organ transplant recipients.

Methods: EpCOT has gained approval for record linkage between the UK Transplant Registry (held by NHS Blood and Transplant) and Hospital Episode Statistics secondary care episode/national cancer registry/civil registration deaths (held by NHS England). Deterministic record linkage, conducted by NHS England, has created an anonymised linked dataset available for analysis by the research team combining all individual datasets. The project obtained institutional support, ethical approval, and Section 251 legal approval back in 2014 but has taken 9 years to reach fruition.

Results: The EpCOT study cohort consists of 63,817 solid organ transplant recipients who received their first solid organ transplant in England between January 1st 1985 and December 31st 2015. Up-to-date clinical outcome data to 2022 is available, allowing the research team to study our pre-specified research questions which include: 1) compare observed and expected risks of specific causes of deaths between transplant and general population cohorts, 2) investigate survival and causes of death after cancer in post-transplant patients versus the general population, 3) compare observed and expected risks of specific cancer types post-transplantation versus the general population, and 4) estimate risk of morbidity requiring hospitalization for transplant recipients.

Conclusions: The EpCOT dataset is the largest record linked resource available to study post-transplantation cancer at a comprehensive national level. It is designed to help address some of the unmet need to further our understanding of the morbidity and mortality associated with post-transplantation cancer and will be ready for analysis from August 2023.
BACKGROUND: Supply-demand mismatch of appropriately sized liver grafts for transplantation is particularly pronounced in small children. Advanced surgical techniques in reducing cadaveric and living donor liver grafts allow for access to life-saving transplantation. Living donor left lateral segment liver grafts have been successfully transplanted into small children in South Africa since 2013; however, this type of partial graft remains too large for children below 6 kilogram (kg) in body weight and requires reduction. We report the first case in Africa of a reduced monosegment, blood group incompatible, living donor liver transplant in a 4.5 kg child with fulminant liver failure.

METHODS: An ex-prem male twin, at a corrected age of 3 weeks and a weight of 4.5 kg was referred to our unit in fulminant liver failure. Despite listing as a Status 1A recipient, no cadaveric donors became available. Both parents were found to be unsuitable for living donation. An altruistic donor consented to urgent donation and was found to be suitable. Computerized tomography (CT) volumetry calculated a 289 g left lateral segment graft which amounted to a graft to recipient weight ratio (GRWR) of 6.4%. The donor surgery involved the procurement of a standard left lateral segment graft, followed by an in-situ reduction of segment III parenchyma without dissecting around the segment III vascular pedicle. Further reduction of the graft on the lateral aspect of segment II followed to achieve a GRWR of 3.5%. The recipient transplant involved a standard implantation technique used for a left lateral segment graft. Cold and warm ischemic times amounted to 50 min and 20 min respectively. Primary vascular inflow and outflow. Total operative time was 5 hours 30 min.

RESULTS: The donor was discharged after 6 days without complications. The recipient suffered no technical surgical complications except for an infected cut-surface biloma and biliary anastomotic stricture and remains well and alive 10 months post-transplantation.

CONCLUSIONS: This case report describes the first hyper-reduced monosegment liver transplant performed in Africa. This development is a critical landmark in ensuring access to liver transplantation for small infants on the continent.

#$E-POSTERS#
**Background:** The European Committee for Organ Transplantation of the Council of Europe (CD-P-TG) proposed a “Critical Pathway” with the aim to develop a common systematic approach and lay the foundations to standardize data used to measure efficiency and effectiveness of deceased tissue donation (1). We present the 2022 deceased tissue donation activity of a third level university hospital (VHUH) on of the largest tissue procurement centers of Spain classified according to the new pathway.

**Methods:** The “Critical Pathway” defines the steps of tissue deceased donation process following the definition similar to organ donors (2): Possible tissue donor-PTD- (person who has died or in a situation of imminent death); Potential tissue donor-PTT- (Dead PTD with no apparent absolute contraindication whose body has been preserved according to requirements for tissue procurement); Eligible tissue donor-ETD- (PTT consented donor medically suitable and meets specific criteria for the donation for at least one type of tissue) and Actual tissue donor (ATD) (ETD from whom at least one tissue was recovered with the intention of clinical application)

**Results:** A total of 1792 PTD were identified (male 58.8%, median age 76 (min 0- max 103) years old, 876 of whom (48.8%) became PTT. Three-hundred and thirty-four (38.1 % ) PTT became ETD, 99.7% of whom progress to ATD (18.5% of all PTD) generating a total of 330 corneal, 47 musculoskeletal, 39 skin, 14 blood vessel and 28 heart valve tissue grafts. Figure 1.

**Conclusions:** Despite an optimized donation process (few modifiable causes of loss), VHUH tissue donation potentiality is hampered by the profile of the possible donor (aged and high percentage of medical contraindications). Training in family approach could be implemented as a measure to increase efficiency.


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**Figure 1. Critical Pathway for deceased tissue donation VHUH**
Background: The c.825C>T single-nucleotide polymorphism (rs5443) of the guanine nucleotide-binding protein subunit β3 (GNB3) results in increased intra-cellular signal transduction via G-proteins. The present study investigated the effect of the GNB3 c.825C>T polymorphism on cardiovascular events among renal allograft recipients posttransplant.

Methods: Our retrospective study involved 436 renal allograft recipients who were followed up for up to 8 years after transplant. The GNB3 c.825C>T polymorphism was detected with restriction fragment length polymorphism (RFLP) polymerase chain reaction (PCR).

Results: The GNB3 TT genotype was detected in 43 (10%) of 436 recipients. Death due to acute cardiovascular events occurred more frequently among recipients with the TT genotype (4 [9%]) than among those with the CC/CT genotypes (7 [2%]; p=0.003). Rates of myocardial infarction–free survival (p=0.004) were significantly lower among T-homozygous patients. A multivariate analysis showed that homozygous GNB3 c.825C>T polymorphism exerted only a mild effect for the occurrence of myocardial infarction (relative risk, 2.2; p=0.065) or acute PAOD (relative risk, 2.4; p=0.05) after renal transplant.

Conclusions: Our results suggest that the homozygous GNB3 T allele exerts noticeable effects on the risk of MI and acute PAOD only in the presence of additional nonmodifiable risk factors.
**Background:** Posttransplant kidney survival depends on several risk factors: Viral infections (cytomegaly (CMV) and polyoma BK (BKV)), or the development of specific antibodies (DSA) seems to determine the graft's longevity. Viral infections (cytomegaly (CMV) and polyoma BK (BKV)), or the development of specific antibodies (DSA) seems to determine the graft’s longevity.

**Methods:** Patient and graft survival (recorded by Kaplan Meier curves and logrank testing) was determined within an observational, single centre study including patients transplanted from 2010 to 2016 with a follow up until 2022. All patients presented in the outpatient-clinics with a standardized posttransplant work-up including (1) viral screening (BKV, CMV), and (2) screening the HLA antibody-status (no-HLA-ab, non-specific HLA-ab (NDSA) and donornonspecific HLA-ab (DSA)) every 6 months in case of DSA free patients, and every 3 months in case of DSA + patients (for 2 years, and on the long-term every year per indication). CMV prophylaxis was administered according to the current recommendations.

**Results:** A full dataset was obtained from 336 patients. Viral infection with CMV or BKV (in terms of positive PCR, first event of CMV or BKV counted) had no impact on the overall patient and graft survival (Chi²= 1.3, p = 0.254). The patient and graft survival differed between the three groups no-HLA, NDSA, DSA (Chi²= 9.8, p=0.007), with a worse outcome for DSA+ patients. The cohort was further stratified for infection in addition to the DSA status (Figure 1). Log rank testing revealed a worse survival for DSA+ patients with viral infections (Chi²=20.3, p=0.001).

**Conclusions:** Applying standardized viral screenings and CMV prophylaxis after transplantation, CMV and BK viral infections didn’t harm patient and graft survival in our cohort, whereas the presence of DSA reduced survival. Further stratification showed, that the coincidence of DSA and viral infection significantly reduced patient and graft survival. This finding might impact the allocation process: Risks for viral infections- such as high-risk CMV-serostatus, should be minimized in patients with a high immunological risk.

**Figure 1**

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**P406 VIRAL INFECTION CYTOMEGALOVIRUS AND POLYOMA BK VIRUS, IMMUNIZATION AND LONG-TERM RENAL GRAFT SURVIVAL**

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**Methods:** As part of the department’s therapeutic education program (TEP), the pharmacy set up a PI for de novo kidney transplant patients, at discharge (M0), to help them manage their immunosuppressive therapy (IT). Patients are recalled at 6 months (M6) to assess their knowledge at a distance from their transplant.

**Results:** The PI takes place after the session with the TEP nurses and is designed to verify that the knowledge of IT treatments is acquired. To do this, the pharmacists fill out a questionnaire during this PI. Six months later, during a telephone call back by the pharmacy, a new questionnaire is proposed to review knowledge and discuss tolerance and daily management. The benefit of PI is evaluated by comparing the results of the two questionnaires.

**Conclusions:** Respectively 11 patients (N=23) seen since April 2022 were recontacted at M6. Of these, only 13 patients responded. Overall, the PI gained 1 point on the total response score (7.2±10 at M0 versus 8.1±10 at M6). Concerning knowledge about IT and other treatments related to the transplant, 100% of patients mastered at the notions at M6 (against 89% at M0). For the behaviour to adopt in sensitive situations, it was necessary to re-examine some notions, even at M6: in case of forgetfulness or vomiting (N=6 at M0 against N=3 at M6); self-medication (N=5 against N=3); recognition of the signs of an infection (N=4 against N=10). For the hygiene-dietary rules: 2 patients did not know how to adapt their diet at M6; 3 did not know how to identify foods to be avoided at either M0 or M6 (grapefruit, St. John’s wort, pomegranate); 10 declared that they practiced a daily physical activity at M6. Among the new concepts at M6: 9 patients had set up a method to avoid forgetting their treatment (alarm, pillbox). 6 patients declared a problem of compliance: 3 sometimes, more than twice a month. For tolerance: 3 patients had adverse effects related to ITs, mostly tingling. All knew how to warn the medical team and none of them interrupted their treatment.

**Conclusions:** The results show the benefit of PIs in providing essential assistance to patients in managing their IT treatment as well as in adherence to treatment. However, some notions need to be revisited at M6, suggesting that regular PIs should be organized throughout the patient’s journey. A link with pharmacists should therefore be developed in this context.

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**P407 EVALUATION OF THE BENEFIT OF PHARMACEUTICAL INTERVIEWS (PI) FOR DE NOVO KIDNEY TRANSPLANT PATIENTS AT 6 MONTHS**

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**Methods:** A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leukopenia, especially in CMV high-risk KTRs. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy could reduce the risk of allosensitization. Under mTOR-I CMV high-risk KTRs achieved serumconversion earlier and more frequent.

**Results:** A switch to mTOR-I was performed more often among CMV high-risk KTRs (50% vs. 21%, p=0.009). CMV primary infection (68.2% vs. 22%, p<0.001), and more severe leukopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, p=0.023). The median duration of leukopenia was comparable between the two groups (69 vs. 80 days). 9 of 67 KTRs (13%) developed de novo donor-specific antibodies (dnDSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I only (p=0.17). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m², p=0.13), and no difference in proteinuria. CMV seroconversion occurred more frequently (0.15) among CMV high-risk KTRs under mTOR-I (14/16 KTRs (88%) vs. 7/15 KTRs (47%) under reduced MPA) CMV high-risk KTRs (46.7%) under reduced MPA) and earlier (190 vs. 265 days, p=0.185).

**Conclusions:** A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leukopenia, especially in CMV high-risk KTRs. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy could reduce the risk of allosensitization. Under mTOR-I CMV high-risk KTRs achieved serumconversion earlier and more frequent.

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**P408 LEUKOPENIA AFTER KIDNEY TRANSPLANTATION: SWITCH FROM MYCOPHENOLATE TO MTOR-I IS SUPERIOR TO REDUCE ALLOSENSITIZATION AND ACHIEVE CMV SEROCONVERSION**

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**Methods:** We conducted a single-center observational cohort study analyzing 98 kidney transplant recipients (KTRs) under standard triple maintenance immunosuppression between 2020 and 2022 who developed leukopenia. We compared patient and kidney allograft outcomes between 31 KTRs who were temporarily switched from MPA to mTOR-I and 67 KTRs who underwent a reduction of MPA dose.

**Results:** A switch to mTOR-I was performed more often among CMV high-risk KTRs (50% vs. 21%, p=0.009), CMV primary infection (68.2% vs. 22%, p<0.001), and more severe leukopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, p=0.023). The median duration of leukopenia was comparable between the two groups (69 vs. 80 days). 9 of 67 KTRs (13%) developed de novo donor-specific antibodies (dnDSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I only (p=0.17). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m², p=0.13), and no difference in proteinuria. CMV seroconversion occurred more frequently (0.15) among CMV high-risk KTRs under mTOR-I (14/16 KTRs (88%) vs. 7/15 KTRs (47%) under reduced MPA) CMV high-risk KTRs (46.7%) under reduced MPA) and earlier (190 vs. 265 days, p=0.185).

**Conclusions:** A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leukopenia, especially in CMV high-risk KTRs. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy could reduce the risk of allosensitization. Under mTOR-I CMV high-risk KTRs achieved serumconversion earlier and more frequent.
P409  GLOBAL BURDEN OF IMMUNOSUPPRESSION AND ITS ASSOCIATION WITH BKV MORTALITY IN ABOi VS. PRE-TRANSPLANT DSA-POSITIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: ABO blood group-incompatible kidney transplantation (ABOi) may be associated with increased BK virus (BKV) replication. The reasons for this remain unclear, but might be attributable to more intense immunosuppression and/or use of rituximab. Global burden of immunosuppression can be estimated via measurement of Torque-Teno-Virus (TTV) in recipient blood and offer insight into this ABOi-specific phenomenon.

Methods: Longitudinal TTV-PCR was assessed in 38 ABOi and 143 pre-transplant DSA+ patients (Tx 2007-2018). TTV load was determined at baseline and at months 3, 6, 12 and 18. BKV-DNAemia was defined as at least two consecutive positive BKV-DNA detections in blood. Additionally, we recorded frequencies of presumptive (>10.000c/mL, without biopsy) or definite BKPyVAN (biopsy-confirmed).

Results: CD20 antibody rituximab was used in 83% of ABOi patients and ATG plus semi-selective immunoadsorption in 86% of DSA+ patients. TTV loads in ABOi patients were 7.6x10^3 at baseline and 1.5x10^4, 4.0x10^4, 3.5x10^5, 4.9x10^5, 9.3x10^5 and 1.1x10^6 at months of M3, M6, M12 and M18. In DSA+ patients, baseline TTV load was 5.3x10^3 and 1.1x10^4, 6.9x10^4, 9.7x10^4 and 9.4x10^4 at M3, M6, M12 and M18, respectively. BKPyVAN screening ABOi with DSA+ we found higher TTV levels in ABOi in baseline (p=0.04), with significant differences at M6 (p=0.018) but not at M12 (p=0.64) or M18 (p=0.31). Incidences of any BKPyVDNAemia did not differ between groups (ABOi 23.7% vs. 30.8% in DSA+; p=0.53). The same was true for BKPyVAN (ABOi 15.8% vs. 11.9%, p=0.18), but definite BKPyVAN were observed more frequently in ABOi patients (13.2% vs. 3.4%, p=0.03). Interestingly 17.4% of presumptive BKPyVANs occurred 18 months or later after transplantation.

Conclusions: The overall higher TTV load in ABOi recipients may reflect the use of rituximab before transplantation. As suggested by the literature BKPyVAN may be associated with increased BK virus replication. The reasons for this remain unclear, but might be attributable to more intense immunosuppression and/or use of rituximab.

P411  PROTEINURIA AND TYPE OF ALLOGRAFT INJURY IDENTIFY KIDNEY TRANSPLANT RECIPIENTS BENE- FITING MOST FROM BELATACEPT CONVERSION

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Background: Conversion to belatacept is associated with an improvement in kidney allograft function. Yet, not all kidney transplant recipients (KTRs) seem to benefit equally from this change in maintenance immunosuppression. Both type (allosensitised vs. non-allosensitised) and severity (assessed by proteinuria) of kidney allograft injury may impact the functional response.

Methods: We studied 37 KTRs from belatacept conversion to 1-year postconversion. KTRs were categorized according to allosensitisation status: 21 KTRs with low (<500mg/day), 12 with moderate (500-1000mg/day), and 4 with high proteinuria (>1000mg/day). KTRs were analyzed concerning change of kidney allograft function, change of proteinuria, and type of allograft injury.

Results: Timepoint min

Dynamic Lung Compliance

Control

Sevo-treated

5

10

15

20

40

50

60

70

80

90

100

110

120

130

140

150

160

170

180

190

200

Lung compliance

P=0.003

Conclusion: KTRs with low proteinuria and non-alloimmune injury benefit most from belatacept conversion concerning improvement of kidney allograft function. While aggravation of proteinuria post-conversion is rare, some KTRs may show improvement post-conversion. If belatacept conversion is still beneficial compared to CNI-based immunosuppression among KTRs with high proteinuria and alloimmune injury needs to be studied.
Background: Simultaneous pancreas and kidney transplantation (SPKT) is the treatment of choice for subjects with type 1 diabetes in advanced stages of diabetic nephropathy. Bone impairment in SPKT candidates is of combined etiology (diabetic osteopathy and renal bone disease) and the bone loss might be further accelerated in the early post-transplant period mainly due to the administration of high doses of corticosteroids.

Methods: The aim of our study was to compare retrospectively the development of bone mineral density (BMD) evaluated by dual energy absorptiometry (DXA) before SPKT and after the successful procedure in the same subjects. We analyzed 52 subjects (39 men, 13 women, mean age 41.9 ± 10.0 years) who entered the waiting list for their first SPKT in years 2011-16, waited more than 12 months for the surgery, were not on any antiresorptive treatment and DXA was available from their pre-transplant examination, within ± 28 days from the date of the transplantation and 2 years after SPKT.

Results: Lumbar spine (LS) BMD was stable during the pre-transplant interval but increased significantly after SPKT (1.091 ± 0.133 vs 1.170 ± 0.125 g/cm2, p < 0.001). Femoral neck (FN) BMD decreased significantly during the waiting period (0.887 ± 0.136 vs. 0.864 ± 0.122 g/cm2, p < 0.05) with insignificant post-transplant increase. Trabecular bone score (TBS) declined during the pre-transplant interval (1.258 ± 0.118 vs 1.225 ± 0.103, p < 0.001) but significant increase after SPKT was registered (1.225 ± 0.113 vs 1.280 ± 0.123, p < 0.05). The difference in BMD development between the pre-transplant and post-transplant period was significant for all sites: LS (p < 0.001), FN (p < 0.05) and TBS (p < 0.01).

Conclusions: Despite intensive corticosteroid treatment in early post-transplant period successful simultaneous pancreas and kidney transplantation has a positive impact on bone metabolism probably due to the restoration of kidney function, normoglycaemia and increased mobility of patients.

Background: Donor-specific HLA antibodies (HLA-DSA) contribute to antibody-mediated rejection (ABMR) after kidney transplantation (KT) and worst graft-survival. The role of non-HLA antibodies in the development of ABMR or microvascular inflammation (MVI) without HLA-DSA is less clear.

Methods: We evaluated 169 KT recipients (2006-2019) in our center with available serum samples preKT and at the time of biopsy. Patients had either one or two graft indication or protocol biopsies after KT with available serum samples. Biopsies corresponded to one (n=158) or three (n=146) years after KT. We analyzed the presence of 60 non-HLA antibodies in sera with a multiplex Single Non-HLA Beads kit (LIFECODES®) on a Luminex® platform. Then, we assessed the association of non-HLA antibodies at different time points with graft-survival and with ABMR/MVI at one and three years after KT. We analyzed the presence of 60 non-HLA antibodies in sera with a multiplex Single Non-HLA Beads kit (LIFECODES®) on a Luminex® platform. Then, we assessed the association of non-HLA antibodies at different time points with graft-survival and with ABMR/MVI at one and three years after KT.

Results: Altogether, non-HLA Abs were present in 94.6% before KT and 84.8 and 82.9% at one- and three-years’ post-KT. We found that 15.4% patients with 6 or more non-HLA Abs pre-KT had worse graft-survival (89.5 vs. 73.1%, p=0.012, Figure 1), being antibodies anti-thyroglobulin and PRKCBZ the most frequent ones. Regarding the 60 distinct non-HLA antibodies, pre-KT and first year antibodies against GSTT1 associated with ABMR/MVI at one- and three-year biopsies (p=0.038 and 0.048, and p=0.027 and 0.004 respectively). Anti-P2RY11 and anti-IL2 antibodies at one year serum associated with ABMR/MVI at one and three years biopsies. Anti-P2RY11 and anti-IL2 antibodies at one year also associated with ABMR at 3 years.

Conclusions: Despite intensive corticosteroid treatment in early post-transplant period successful simultaneous pancreas and kidney transplantation has a positive impact on bone metabolism probably due to the restoration of kidney function, normoglycaemia and increased mobility of patients.

Background: Left ventricular outflow tract obstruction (LVOTO) is a well described in the literature among cirrhotic patients, and is found on preoperative testing with Dobutamine stress echocardiogram (DSE) or seen intraoperative post reperfusion. LVOTO often leads to significant intraoperative hypotension. LVOTO is not known to affect overall mortality. Orthotopic liver transplantation (OLT) is curative. We present a case of resting LVOTO causing critical illness in the pre-, peri-, and post-operative setting found on preoperative transthoracic echocardiogram (TTE) which was not DES testing induced. As far as we know, this is the first case report of resting LVOTO prior to transplant.

Methods: This case report presents a 61 year old male patient with NASH cirrhosis and a MELD of 29 who was critically ill with significant resting LVOTO in the pre-operative setting. TTE measurements taken pre transplant in the ICU revealed resting LVOT gradients in excess of 140 mmHg with a mean above 50 mmHg. His cardiac dysfunction had become so profound that he was not expected to survive without OLT. The transplant team was presented with an ethical dilemma: a successful OLT would cure the patient of LVOTO but the chances of success were not clear given the severity of the patient’s illness. Electing to attempt OLT without guarantee of success had to be weighed against the alternative of forgoing OLT and allowing the allograft to be allocated to another patient.

Results: The team elected to perform OLT. Anesthesia was able to successfully manage intraoperative hypotension with alpha agonists, vasopressin, volume resuscitaation, and TEE monitoring. LVOT gradients ranged from 37 to 84 mmHg. However, he was transferred to the ICU post-op on two vasopresors with worsening LVOTO and a post-op peak gradient of 220. His condition did ultimately improve. He was weaned from pressors within 48 hours. He was discharged on post-op day 6 and continues to do well at three months.

Conclusions: We share our experience in order to help better elucidate the nuanced presentation of this well-known pathophysiology and we call for more case reports so that we may begin to develop a trend from which more informed management decisions can be made in the future for resting LVOTO.
Background: Kidney transplantation (KT) outcomes with kidney grafts from older donors are worse than with optimal donors. However, in some cases, the loss of grafts occurs prematurely with respect to their potential, the factors involved being unknown. Our objective was to determine the factors associated with premature loss of kidney grafts from older donors.

Methods: We analyzed 252 KT recipients from donors >70 years old (2011-2021). The median time from KT to death or graft loss for the cohort was 7.6 years (IQR 2.3-12.5). Age, sex, ethnicity, history of diabetes, hypertension, smoking, ischemia time, ischemia reperfusion injury, organ source, and retransplantation were analyzed in a multivariate analysis.

Results: The graft survival at 1 year was 99.4% (95% CI 99.2-99.5), and at 5 years 87.5% (95% CI 85.4-89.4). The variables that significantly influenced graft survival were recipient age (p < 0.001), ischemia time (p=0.004), and ischemia reperfusion injury (p=0.046). In the multivariate analysis, age (p=0.01), renal function (p=0.04), and higher serum cholesterol (p=0.01) were associated with graft loss. Uncertainty/Fear dimension was associated with recipient age (p=0.02) directly and osteoporosis (p=0.02) at the end of the study showed that variables significantly associated with Phys and SF-36 scores in both time-points were similar without significant differences between groups. Before KT, donor creatinine was better in longer-lasting grafts, and recipients had less cardiovascular disease and more residual diuresis. After KT, recipients with premature loss presented more DGF, cardiovascular events and worse renal function (p<0.01). In the multivariate analysis, hemodialysis [HR 4.2, CI 1.0-19.4 (p=0.041)], DGF (HR 1.5, CI 0.9-2.6), and admissions for infections (HR 2.0 CI 1.0-3.8), and increased proteinuria at 6 months (6PC IgG1g) were associated with graft loss.

Conclusions: Donor and recipient factors influence the success of KT from older donors. The main cause of graft loss is premature death of the recipient. The early identification of KTs that will have a shortened survival is essential for the correct allocation and management of the transplant and the recipient.

P420 FROM PALLIATION TO FULL-TIME OCCUPATION: CYSTIC FIBROSIS PATIENT WITH BURKHOLDERIA CAPACIA COMPLEX ON ECMO SURVIVES LUNG TRANSPLANT AND MENINGITIS

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Background: We report the evolution of a 18-year-old cystic fibrosis patient (compound heterozygote for F508del/CFTD123E). BMI 15.1kg/m² on triple CFTR-modulator therapy without adequate response with subsequent pulmonary deterioration of end-stage lung disease leading to intubation, prolonged ECMO support and for whom lung transplantation (LT) as therapeutic option was always considered to be non-viable due to the long-standing active infection with Burkholderia cenocepacia (BCC). Before activating a palliative therapy after 2 weeks on ECMO without signs of recovery, the treatment team decided to perform a LT despite the dismal prognosis based on the expected complicated course of BCC infection.

Methods: The bilateral lung transplantation was performed after 14 days on ECMO and ongoing antibiotic treatment with ceftazidime/avibactam and tetracycline, non-cooperatively following the correct allocation and management of the transplant and the recipient.

Results: The initial postoperative course was uneventful with continued combination antibiotic treatment (ceftridixime and meropenem) which were continued after discharge on day 55 for a total duration of one year (1) as outpatient and subsequently desescalated to one drug treatment and then stopped. After rehab she continued her vocational training as office clerk and finished her training 1 year later. She subsequently received a full-time employment in the company that she trained and has survived so far 2 years and 4 months to date. One major complication occurred 6 months postoperatively when despite ongoing dual antibiotic treatment, a basal meningitis occurred due to the local progression of the BCC infection with osseous defect leading to a communication between the ear and the brain cavity. Surgical revision was imminent and besides debridement of the infectious cavity antibiotic beads were locally introduced to achieve better local control of the infectious focus (Dalbert et al., doi:10.1002/ccr3.5510). After extended duration of intravenous antibiotics we reintroduced triple CFTR modulator therapy to aid with better drainage of sections in the ear nose and throat region. The subsequent course has been uneventful so far.

Conclusions: Although formally listed as a contraindication, LT in highly selected BCC positive patients could be considered. Unusual case evolution.

P421 MATERNAL LIVING DONOR LIVER TRANSPLANTATION OFFERS NO PROTECTION AGAINST GRAFT REJECTION AND GRAFT LOSS

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Background: The effect of gender on graft prognosis is a recognized entity in adult liver transplantation with male recipients of female grafts exhibiting the lowest graft and patient survival. The effect on gender mismatch in pediatric liver transplantation is less well defined. Related living donation adds the dimension of maternal antigen exposure prior to liver transplantation. The presence of non-inherited maternal antigens (NIMA) potentially induce a degree of tolerance to future maternal grafts in the child which bear the antigens shared by microchimeric cells. This study sought to determine the effect of receiving a maternal liver graft on graft rejection and survival rates relative to a non-maternal graft.

Methods: A retrospective cohort study was performed on all children below 18 years of age who underwent living donor liver transplantation at our institution between 2012 and 2020. Rates of graft loss and biopsy proven rejection were compared between patients who had received a maternal graft to those who did not. Recipient, donor and transplant characteristics were recorded as well as rates of biliary and vascular complications.

Results: A total of 87 children underwent related living donor liver transplantation. Donors were 60% maternal, 21% paternal and 19% non-parental. Median recipient age was 19 months (IQR 13 to 37 months) with equal gender distribution. Pre-transplantation liver function was chronic cholestasis in 15% of the cohort presenting in acute liver failure. Mean PELD scores at transplantation were 16.2. The majority of recipients received standard immunosuppression of steroid and calcineurin-inhibitor. Between the two groups, rates of graft loss (18%), first episode biopsy proven rejection (31%), biliary complications (38%) and vascular complications (12%) did not differ. Conclusions: Maternal living donor liver transplantation offered no protection against graft loss, rejection, biliary or vascular complications compared to other related living donors in this cohort of patients. Current evidence does not support preferentially selecting maternal donors for liver transplantation in the paediatric population is scanty. Further studies on the effects of current immunosuppression regimes on the immunotolerant arm of the immune system is warranted.
P422 REMARKABLE MORTALITY BEFORE LIVER TRANSPLANTATION IN BILIARY ATRESIA; PRELIMINARY OUTCOMES FROM A 14-YEAR COHORT STUDY

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Background: Biliary atresia (BA) is a leading etiology for liver transplantation (LT) in pediatric settings. Considering the surgical and anesthetic obstacles for LT at very young ages, Kasai portoenterostomy (KPE) performs to save naive organs till when the patient can undergo LT. In this study, we have retrospectively surveyed the long-term outcomes of BA after KPE.

Methods: 196 confirmed cases of BA who underwent KPE between 2007 and 2021 included in the study. The patients' baseline demographic, clinical, para-clinical characteristics, as well as operation information and follow-ups were collected from medical records and telephone interview.

Results: Clinical and paraclinical characteristics are demonstrated in Table 1. We could not determine the end-point outcomes of 49 (25%) cases. From the rest, 22 cases underwent LT, of which 13 were alive, and 9 died. Furthermore, 56 cases survived without undergoing LT, and 69 died before LT. Higher level of pre-KPE AST, and total bilirubin, longer hospital stays and further hospital admissions were significantly associated with poor outcomes (death or LT).

Conclusions: Many lives are being lost after KPE on the LT waitlist due to inability to undergoing LT, limited organ pool, and mismatched parental donors. Considering prognostic determinants along with PELD for organ allocation and establishing newer techniques of LT in this age group may improve the outcomes significantly.

P423 THE INFLUENCE OF ANTIBODIES AGAINST MICA ON THE OUTCOME OF KIDNEY TRANSPANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Major histocompatibility complex class I chain-related proteins A (MICA) are polymorphic antigens that induce considerable alloimmune response. The impact of anti-MICA antibodies (anti-MICA), alone or in association with HLA donor specific antibodies (HLA-DSAs), on the outcome of kidney transplantation (KTx) is investigated.

Methods: Anti-MICA and HLA-DSAs were retrospectively detected in 142 KTx recipients, 71 with biopsy proven acute or chronic active rejection (rejection group, RG) and 71 with comparable characteristics without rejection control group, CG). Among 71 patients of the RG, 51 were diagnosed with T-cell mediated rejection (TCMR) and 20 with antibody mediated rejection (ABMR). Median follow-up was 3.7 (2.9-5.2) years. Anti-MICA were determined pre- and post-KTX by Luminex method.

Results: Before KTx, 4 (5.6%) patients in the RG, all with TCMR, were found anti-MICA positive vs. 2 (2.8%) patients in the CG (p=0.681). Preformed HLA-DSA were found in 19 (26.7%) patients in RG vs. 6 (8.4%) in CG (p=0.008). Simultaneous detection of preformed anti-MICA and HLA-DSAs was found in 2 patients of the RG, all with TCMR, vs. 0 of the CG (p=0.497). At transplant biopsy, positive anti-MICA were identified in 3 patients with TCMR, preformed in all cases. In 2 TCMR cases anti-MICA and HLA-DSAs were detected simultaneously at biopsy. During follow-up, 13 (18.3%) patients in RG, 8 with ABMR and 5 with TCMR, lost their graft vs. 1 patient (1.4%) in CG (p=0.001). One (1.4%) RG patient, with TCMR, who lost the graft was found positive for anti-MICA pretransplant. Patient survival with functioning graft did not differ between anti-MICA positive and negative KTx recipients (log-rank p=0.300). Simultaneous detection of anti-MICA and HLA-DSAs did not have significant influence on patient survival with functioning graft (log-rank p=0.071). The end of follow-up was better, but not significantly, in anti-MICA negative patients vs. anti-MICA positive ones.

Conclusions: Anti-MICA detection pretransplant is not associated with an increased risk of rejection in our cohort. Their absence appears to be associated, although not significantly, with better renal function without affecting long-term graft survival. Their role in kidney transplantation requires further investigation.

P425 INFECTION, VACCINATION OR BOTH? THE SARS-CoV-2 IMMUNE FOLLOW-UP OF KIDNEY AND LIVER TRANSPLANT RECIPIENTS

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1 Clinical Center of the Warsaw Medical University, Warsaw, Poland, 2 Warsaw Medical University, Warsaw, Poland

Background: The use of vaccination against severe acute respiratory syndrome coronavirus (SARS-CoV-2) is significant to prevent COVID-19. However, it is known that over time from the vaccination, an immune response decreases in general population. The reports for immunocompromised individuals as solid-organ transplant (SOT) recipients or chronic kidney disease (CKD) patients appeared similar. Therefore, in order to prolong immunity, it was proposed to use an immune booster with the next, third or fourth vaccination dose. Knowing the importance of protection against COVID-19 for immunocompromised patients, we checked the role of SARS-CoV2 infection history during the vaccination schedules in kidney or liver transplant recipients (KTRs, LTRs) and CKD patients.

Methods: We retrospectively analyzed the data of randomly selected 78 SOT recipients (37 KTRs and 41 LTRs) and 40 patients with IgA nephropathy (IgAN) as representatives of the CKD group. They received two or three 30 μg doses of BNT162b2 vaccine. The follow up was prosecuted in five time points (TP1-5). We assessed the anti-SARS-CoV-2 spike protein IgG antibody (anti-S1 Ab) titer as well as graft function, COVID-19 history and patients’ clinical condition.

Results: Ab titer in SOT patients was lower than in IgAN group (p = 0.05). KTRs achieved lower values than LTRs. The protective level after the 3rd dose of vaccination was not observed only in 8.4% at TP4 and 5% at TPS. We demonstrated the advantage in Ab levels of a 2 doses vaccination scheme in SOT patients, we checked the role of SARS-CoV2 infection history during the vaccination schedules in kidney or liver transplant recipients (KTRs, LTRs) and CKD patients.

Conclusions: Our results showed that approach to the vaccination schedule should be individualized and should take into consideration vaccine response rate and medical history including COVID-19 history. So-called the hybrid immunization appears to be the most effective strategy to protect immunocompromised patients from SARS-CoV-2 infection.
Background: Although the importance of defining the causality of the different transplant outcomes has been identified, to date, little is known about gene expression and the intracellular interaction networks that take place in each outcome. Several studies have proposed differentially expressed genes (DEGs) and microRNAs either as outcome biomarkers or outcome regulators. However, an expression profile that allows differentiating with greater sensitivity and specificity between groups of patients is unknown. We aim to identify DEGs between blood and urine samples from kidney transplant patients with rejection and acceptance processes.

Methods: Blood and urine were collected from patients with acute (AcutePre), chronic rejection (Chronic), long term allograft survival (LTS), and acute rejection after anti-rejection treatment (AcutePost). Blood was collected from dialysis patients (HD) and non-transplanted healthy individuals (HC). RNA was isolated from all samples using Tri Reagent. A minimum of 1 µg of RNA was purified and used for generating cDNA libraries using SureSelect XT RNA Direct Human. Libraries were sequenced using Illumina Novaseq 6000 system. DEGs were those with a Log2FC smaller or greater than -2 or 2, and a FDR smaller or equal to 0.05. For functional Analysis, GO categories were obtained using ClueGO in Cytoscape.

Results: DEGs (Table 1) were used for functional analysis. Because of the amount of data, we chose only functional categories observed in urine mainly because this sample is a striking alternative for the diagnosis and following of rejection and to identify molecules associated with each outcome. Immune system enriched categories associated to up regulated genes in urine of AcutePre (Figure 1A), Chronic (Figure 1B), and AcutePost (Figure 3) are depicted.

Conclusions: According the number of regulated genes in each sample, urine seems to be more transcriptional active when compared with blood. We suggest that urine might reflect the immune response associated to the allograft outcome, and that this sample might be suitable for the identification of transcripts associated with either acute or chronic rejection.

Table 1. Number of DEGs in each comparison described.
Background: Allo- and autoimmune mechanisms are involved in kidney allograft rejection and loss. The impact of anti-angiotensin II type-1 receptor antibodies (anti-AT1R Abs), alone or in association with HLA donor specific antibodies (HLA-DSAs) on outcome of kidney transplantation (KTx) is investigated.

Methods: Anti-AT1R Abs and HLA-DSAs were retrospectively detected in 142 KTx recipients, 71 with biopsy proven rejection (rejection group, RG); 51 T-cell mediated (TCMR) and 20 antibody mediated rejection (ABMR), and 71 with comparable characteristics without rejection (control group, CG). Median follow-up was 3.7 (2.9-5.2) years. Antibodies were determined by Luminex method for HLA-DSA (positive MFI>1000) and enzyme-linked immunosorbent assay for anti-AT1R Abs (positive ≥10 U/mL).

Results: Before KTx, 23 (32.4%) patients in RG, 16 TCMR and 7 ABMR, were found anti-AT1R Abs positive vs. 11 (15.5%) in CG (p=0.031). Preformed HLA-DSAs were found in 19 (26.7%) patients in RG vs. 6 (8.4%) in CG (p=0.010). Preformed anti-AT1R Abs and HLA-DSAs was found simultaneously in 5 patients of RG, 1 ABMR and 4 TCMR vs. 2 of CG (p=0.355). At transplant biopsy, positive anti-AT1R Abs were identified in 4 patients with ABMR and 11 with TCMR, preformed (n=12) or de novo (n=3). In 3/4 ABMR and 4/11 TCMR cases anti-AT1R Abs and HLA-DSAs were detected simultaneously. During follow-up, 13 (18.3%) patients in RG, 8 ABMR and 5 TCMR, lost their graft vs. 1 patient (1.4%) in CG (p=0.001). Six out of 13 (46.2%) RG patients, 3 TCMR and 3 ABMR, who lost the graft, were found anti-AT1R Abs positive. Survival with functioning graft was better, but not significantly, in anti-AT1R Abs negative patients.

Conclusions: Anti-AT1R Abs detection characterizes KTx recipients at increased risk of rejection. Furthermore, anti-AT1R Abs pretransplant, either alone or in association with HLA-DSAs, appear to be associated with impaired graft function. The strong presence of alloimmune mechanisms may obscure our results. However, screening for anti-AT1R Abs may help identify KTx recipients at high immunological risk.

Conclusions: Our results. However, screening for anti-AT1R Abs may help identify KTx recipients at high immunological risk.

Background: Primary hyperoxaluria type 1 (PH1) is characterized by oxalate stones leading to kidney failure. In advanced stages of disease, systemic oxalate deposition may lead to heart failure. The small interfering RNA (siRNA), lumasiran, reduces the oxalate load and may improve organ impairment in systemic oxalosis.

Methods: We report a 29-year old male patient with PH1, who was referred to our center in March 2022 for evaluation for combined heart-liver-kidney-transplantation.

Results: Kidney failure was diagnosed in August 2021, a kidney biopsy revealed diffuse interstitial nephritis with massive oxalate depositions. Genetic testing confirmed two compound heterozygous Alanine-Glyoxylate Aminotransferase (AGXT) gene mutations. He was on peritoneal dialysis (PD) for 6 months. In addition, he suffered from severe heart failure (NYHA III) with a left ventricular ejection fraction (LV-EF) of 25%, marked left ventricular hypertrophy (septum of 14 mm) and NTproBNP >50,000 pg/mL. A biopsy revealed severe cardiac oxalate deposition. Hemodialysis (HD) therapy was commenced to optimize volume overload and to lower plasma oxalate (Pox) levels. The initial Pox level was 141.3 µmol/L and decreased to less than half after combined PD and intensified HD (Fig.). After the start of treatment with lumasiran s.c. and high dose pyridoxine, POx levels further decreased to 29.2 µmol/L. Subsequently, cardiac output improved with an LV-EF of 35-40%. He received a living kidney donation from his father in October 2022 using standard immunosuppression and intensified HD. Kidney function stabilized with a creatinine of 2.0 mg/dL at 3 months follow up. An allograft biopsy one month after KT showed no rejection. His recent POx level was 11 µmol/L. As a result, heart failure improved to NYHA I, LV-EF of 55%, NTproBNP <100 pg/mL and his recent POx level was 11 µmol/L.

Conclusions: To our knowledge, this is the first case demonstrating complete remission of heart failure in a patient with PH1 following lumasiran therapy and isolated KT. Our experience underscores the utility of lumasiran and the conclusion, that the cardiac dysfunction related to PH1 is potentially reversible.
Background: The introduction of potent immunosuppression (IS) such as calcineurin inhibitors (CNIs) has increased the one-year survival rates post liver transplantation (LTx) to over 90%. However, due to the deleterious side effects associated with IS such as malignancies, cardiovascular disease, recurrent infections, and chronic kidney disease, no substantial progress had been made in prolonging their long-term survival. Thus, minimization is an approach where IS is decreased to levels that do not cause clinically significant side effects, yet at the same time prevent rejection. Due to the liver’s unique ability to modulate its immunological response, it is feasible to introduce IS minimization protocols in liver transplant recipients (LTRs). In our study, IS minimization protocols were introduced to LTRs based on clinical and laboratory characteristics with the aim to establish predictive factors of successful IS minimization.

Methods: In this prospective observational study, adult LTRs were screened for eligibility and 97 LTRs were recruited after obtaining informed consent. Patients were deemed eligible if the primary cause of LTx was a non-autoimmune liver disease, they had a stable graft function for >3 years and no evidence of chronic rejection in histology was recorded. The dose of IS was minimized in 3-month intervals with laboratory tests performed at 2, 4 and 8 weeks after each dose reduction to evaluate liver function. Additional testing was performed to assess graft stability and evaluate IS related comorbidities.

Results: IS minimization was achievable in 87.6% of LTRs. After 36 months, 76 LTRs were on monotherapy with 47 of them being on subtherapeutic doses of CNI and 2 were on spacing protocols with tacrolimus (table 1). In only 12/97 LTRs were on monotherapy with 70% being overweight or obese (25.56kg/m^2 with 31% being overweight or obese vs 26.57 kg/m^2 with 70% being overweight or obese) in ALL LTRs (12.4%), an episode of acute graft failure was recorded, which resolved in 3-month intervals with laboratory tests performed at 2, 4 and 8 weeks after each dose reduction to evaluate liver function. After 36 months, 76 LTRs were on monotherapy with 47 of them being on subtherapeutic doses of CNI and 2 were on spacing protocols with tacrolimus (table 1). In only 12/97 LTRs were on monotherapy with 70% being overweight or obese (25.56kg/m^2 with 31% being overweight or obese vs 26.57 kg/m^2 with 70% being overweight or obese) in ALL LTRs (12.4%), an episode of acute graft failure was recorded, which resolved in 3-month intervals with laboratory tests performed at 2, 4 and 8 weeks after each dose reduction to evaluate liver function. Additional testing was performed to assess graft stability and evaluate IS related comorbidities.

Conclusions: Minimization of IS seems to be safe for precisely characterized LTRs and should be implemented in eligible patients to reduce IS-related comorbidities.

Table 1 Immunosuppression therapy at baseline and at 36 months

<table>
<thead>
<tr>
<th>AT BASELINE</th>
<th>AT 36 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPLETE WITHDRAWAL</td>
<td>1 (1.03%)</td>
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<tr>
<td>SPACING*</td>
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</tr>
<tr>
<td>SUBTHERAPEUTICAL MONOTHERAPY</td>
<td>24 (24.7%)</td>
</tr>
<tr>
<td>TAC</td>
<td>24 (24.7%)</td>
</tr>
<tr>
<td>CoA</td>
<td>0</td>
</tr>
<tr>
<td>MONOTHERAPY</td>
<td>55 (56.7%)</td>
</tr>
<tr>
<td>TAC</td>
<td>43 (44.3%)</td>
</tr>
<tr>
<td>CoA</td>
<td>5 (5.15%)</td>
</tr>
<tr>
<td>MMF</td>
<td>6 (6.19%)</td>
</tr>
<tr>
<td>EVE</td>
<td>1 (1.03%)</td>
</tr>
<tr>
<td>DUAL THERAPY</td>
<td>39 (40.2%)</td>
</tr>
<tr>
<td>TAC + GCS</td>
<td>17 (17.6%)</td>
</tr>
<tr>
<td>TAC + MMF</td>
<td>13 (13.4%)</td>
</tr>
<tr>
<td>TAC + EVE</td>
<td>2 (2.16%)</td>
</tr>
<tr>
<td>CoA + GCS</td>
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<tr>
<td>CoA + MMF</td>
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</tr>
<tr>
<td>MMF + GCS</td>
<td>1 (1.03%)</td>
</tr>
<tr>
<td>TRIPLE THERAPY</td>
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</tr>
<tr>
<td>TAC + GCS + MMF</td>
<td>1 (1.03%)</td>
</tr>
<tr>
<td>CoA + GCS + MMF</td>
<td>1 (1.03%)</td>
</tr>
<tr>
<td>TAC + GCS + EVE</td>
<td>0</td>
</tr>
</tbody>
</table>

* TAC ≤ 8mg/kg/8h, CoA ≤ 450ng/ml, EVE ≤ 100ng/ml; ** TAC ≤ 3mg/kg/8h, CoA ≤ 225ng/ml, EVE ≤ 50ng/ml; *** patient switched to monotherapy with TAC; **** decrease in number due to the patient being converted to monotherapy; ***** patient converted to monotherapy with MMF; **** patient converted to monotherapy with CoA, MMF, and TAC; ***** patient converted to monotherapy with CoA and TAC; ***** patient converted to monotherapy with MMF; **** addition of everolimus with the intent of withdrawing tacrolimus after consultation with oncological teams; Abbreviations used: CoA – cyclosporine A, 8OH – oromexic, GCS glucocorticosteroid, MMF mycophenolate mofetil, TAC tacrolimus.
Background: Focal Segmental Glomerulosclerosis (FSGS) can be found de novo (Dn) or as a recurrence in kidney allograft. While FSGS recurrence has been extensively described as a devastating cause of graft loss, the natural history and the prognosis of DnFSGS remain unknown.

Methods: Using a monocentric prospective database, we analyzed a cohort of DnFSGS in kidney transplant recipients (KTR). Pre- and post-transplant characteristics were recorded as well as graft outcomes. Propensity score matching was used to compare outcomes in the presence or absence of DnFSGS.

Results: From 2001 to 2019, 171 KTRs had a diagnosis of DnFSGS, half of them being at high immunological risk at transplantation. The diagnosis was made at a median time of 4.2 years post-transplant, with a proteinuria of 1.6 ± 1.6 g/g. Based on pathological characteristics, a hierarchical clustering divided the cohort into 3 clusters (K1 to K3). K1 (n=58, 34%) was diagnosed earlier post-transplant, half within the first year, and was associated with chronic vascular lesions and ischemic glomeruli. K2 (n=32, 19%) was strongly associated with a concomitant ABMR, mainly chronic active, whereas K3 (n=81, 47%) was diagnosed later (9.3 ± 6.4 years) in the context of IF/TA and chronic vascular lesions. Sixty-seven KTRs (39%) lost their graft over a follow-up of 3.3 years. Overall, the presence of DnFSGS was associated with poor outcomes in comparison to a control cohort of KTRs without FSGS (median graft survival of 57 vs 260 months, p<0.001). Among the clusters, K2 and K3 were significantly associated with an increased risk of graft failure (K2 = HR 7.1 [3.2-15.6], K3 = HR 4.8 [2.2-10.4]), whereas K1 had similar outcomes to the control, even after adjusting to the diagnostic time post-transplant.

Conclusions: The occurrence of DnFSGS lesions in KTRs can be seen in different settings. When associated with ABMR or diagnosed on a late biopsy, it is associated with a poor graft survival.

Figure: Kaplan Meier survival curve of time to graft dysfunction in de novo FSGS and matched control cohort.
AGILE DATA JOURNEY AND GOVERNANCE TO LEVERAGE DIGITAL TRANSFORMATION OF A KIDNEY TRANSPLANT CENTER IN COLOMBIA

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Background: Kidney transplantation is a complex clinical service. The decision making of the organization requires the capture of large volumes of heterogeneous clinical data (structured and non-structured). We aim to apply a data journey model to achieve the centralization of patient data across a structured clinical governance process to undergo digital transformation in a kidney transplant service in Colombia.

Methods: We performed a cross-collaborative methodology bridging health informaticians and clinical domain experts using agile methodology (Scrum and SAFe). The data journey was applied through iterative discovery sessions to build a data governance strategy involving data definitions and unified repository for those definitions. The data governance strategy leverages correct data warehousing (Integrating data from multiple operational systems) and finally, having clean, unified, and standardized data allows the organization to analyze, report and visualize resulting structured data.

Results: A total of five health informaticians, three clinicians and two clinical researchers participated in the modeling agile sessions. We identified six service data sources involved in the transplant pathway pertaining to recipients, donors, follow-ups, laboratories, outcomes and providers. Data bases were uploaded and integrated in a data warehouse using data engineering tools such as spark and an HDFS/Hive-based cloud storage. The cleaning process was iterative and took approximately one year. There is a connection to the data warehouse used by researchers who are proficient in R language for doing descriptive and predictive analysis. This allowed self-consumption of information and facilitated the use of electronic health records for research purposes.

Conclusions: Data journey has been a key solution to improve interoperability. By using data journey modelling, we were able to visualize analytics to provide a meaningful assessment of current data (decision making) and to develop two algorithms: one to predict graft survival and one to classify the status of kidney allograft. These findings would translate to other areas of the organization to improve clinical governance process as the agile frameworks helped the organization to achieve these goals the fastest and high-quality way possible.

EDUCATION ON DIGITAL TRANSFORMATION: A PRIORITY TO MAXIMIZE ITS BENEFITS AND USES. EXPERIENCE OF A SINGLE CENTER IN LATIN AMERICA

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1Colombiana de Transplantes, Department of Transplantation Surgery, Bogota, Colombia, 2Colombiana de Transplantes, Department of Transplantation Research, Bogota, Colombia, 3Colombiana de Transplantes, Department of Organ Donation Management, Bogota, Colombia, 4Colombiana de Transplantes, Department of Transplantation Nephrology, Bogota, Colombia, 5Colombiana de Transplantes, Department of Information Technology, Bogota, Colombia

Background: The digitalization of healthcare has been profound and significantly impacted current health systems. Even more, it is expected that digital transformation will become more influential and important in the future. For example, in kidney transplantation, several developments are implementing digital pathways for nephrological care and referral procedures, among others. However, to develop and apply these technologies, the education and training of the health workforce in digital competencies have to be a priority. Therefore, we aim to improve and empower the level of digital literacy among the health workforce and patients.

Methods: Since 2021, we have developed a collaborative and transdisciplinary education methodology through virtual lectures to develop digital and technology competencies in patients and the health workforce. Currently, we also have uploaded an educational platform that involves virtual lectures, knowledge assessment, and social deliberation.

Results: A total of 19 training sessions were held, 16 for the health workforce involving 299 professional attendance records and 3 for patients, including 222 renal transplant patients and families. Health workforce training topics included: digital education, digital transformation for enterprises, prediction, digital marketing, social networks, and point of care. And patient education was mainly about health systems changes, patients in the digital era, and vaccination for the transplant recipient.

Conclusions: Digital transformation of transplant care is real and rapidly evolving. Therefore, to maximize de potential benefits of digitalization, there is a need to have an equally rapid education aiming to prepare and train patients and professionals in the new technologies. Furthermore, we believe these results can be useful for other organizations to pursue the path of education in digital transformation.
Background: Simultaneous pancreas-kidney transplantation (SPKT) is the best treatment for patients with diabetes mellitus and chronic kidney disease. Technical failure (TF) is defined as graft loss within 90 days of surgery due to postoperative surgical problems. SPKT results have improved, but TF remains high: pancreas graft (PG) thrombosis is a frequent severe complication (4.7-8.6%, in recent data). Donor and recipient factors have been associated with early PG thrombosis. The aim of this study is to describe our experience in SPKT regarding TF in the first 90 days, and to identify predictors for its occurrence.

Methods: Patients who had a SPKT between 2000 and 2022 were included. Donor and recipient characteristics and complications in the post-SPKT period were analysed.

Results: 263 SPKT were performed over these 22 years. The average recipient age was 35.5 years, 52% men; 73% were on hemodialysis. Twenty-six TF (9.9%) were documented at 90 days. Patients with TF were more frequently on peritoneal dialysis (p=0.044); required prolonged hospitalization (28 (20–46) vs 16 (12–25) days, p<0.001) and needed more overall reinterventions (2.1±2.6 vs 0.3±0.8, p<0.001). They also had higher kidney graft (KG) loss (15% vs 2%, p=0.01) and higher overall 90-day mortality (19% vs 0%, p<0.001) Table 1 shows detailed data. In the multivariate analysis (excluding PG reinterventions as predictors), donor age ≥36 and previous PD were independent predictors for TF at 90 days (HR 2.513, p=0.019 and HR 2.503, p=0.021). After including PG reinterventions we identified as independent predictors of TF: reintervention for thrombosis (HR 32.751, p<0.001), or for PG leak (HR 22.655, p<0.001) and year of transplant 2000–2011 (HR 2.667, p=0.022).

Conclusions: Our population presented an incidence of TF similar to that reported by others and confirms PG loss as a severe event associated with mortality and KG loss at 90 days. Donor age ≥36 and previous PD were independent predictors of TF, an outcome strongly associated with PG reinterventions, particularly if leak or thrombosis driven.

Characterization of recipients, donors, and technical failure

<table>
<thead>
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<th>Total</th>
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<tr>
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<td>237 (90.1)</td>
<td>26 (9.9)</td>
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<td>Pancreas transplant, n (%)</td>
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<tr>
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<td>57.8 ± 8.3</td>
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<td>237 (90.1)</td>
<td>26 (9.9)</td>
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<td>263 (100)</td>
<td>237 (90.1)</td>
<td>26 (9.9)</td>
</tr>
<tr>
<td>GFR, mean ± SD</td>
<td>1.0 ± 1.3</td>
<td>1.0 ± 1.5</td>
<td>1.0 ± 1.1</td>
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<td>Donor characteristics</td>
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<td>Donor age, mean ± SD</td>
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<td>45.9 ± 8.5</td>
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<tr>
<td>Donor characteristics</td>
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</tr>
<tr>
<td>Donor age, mean ± SD</td>
<td>52.3 ± 8.8</td>
<td>52.1 ± 8.9</td>
<td>52.6 ± 8.7</td>
</tr>
</tbody>
</table>

Table 1. Characteristics of recipients, donors, and technical failure.
P440  PREDICTING INDEX FOR OUTCOMES AFTER DECEASED DONOR LIVER TRANSPLANTATION AFTER 1-YEAR POST-TRANSPLANT

Jiyoung Baik*1, Jongman Kim1
1Samsung Medical Center, Department of Surgery, Seoul, South Korea

Background: The Donor Rejected Organ Pre-transplantation (DROP) Score, and the donor risk index (DRI) have been proposed for predicting graft and overall survival. These scores are calculated based on transplant-related variables. The kidney donor profile index (KDPI), which is calculated from donor variables, is suggested for predicting prognosis after kidney transplantation. Our study aims to compare the predicted graft survival and overall survival after deceased donor liver transplantation (DDLT).

Methods: This study analyzed data from transplant recipients who underwent DDLT at Samsung Medical Center between January 1st, 2000, and December 31st, 2020. Retransplantation, pediatric DDLT, dead patients within 1 year post-transplant, or follow-up lost patients were excluded. The group of recipients was stratified into three sub-classes according to the KDPI.

Results: A total of 231 DDLT cases were included. The numbers of KDPI grade 1, 2, and 3 were 163 (70.5%), 52 (22.5%), and 16 (6.9%). The proportion of esophageal varix bleeding in the KDPI grade I was less than in the KDPI grade II and III. KDPI was correlated with the donor rejected organ pre-transplantation (DROP) (P=0.018), but was not correlated with the donor risk index (DRI). Graft failure and death occurred in 20 (8.7%) and 41 (17.7%) patients. Time to graft failure increased with increasing KDPI (P < .001). The overall survival rate was significantly higher only in the low KDPI group than in the high KDPI group (p = 0.029). The other index scores were not showed significant results in overall survival rates: DROP (p=0.517), and DRI (p=0.842). In graft survival rates, all three index scores were not significant with DROP and DRI except KDPI (p=0.029).

Conclusions: Our study suggests that KDPI also is a useful index in predicting DDLT outcomes after 1-year post-transplant.

P439  NURSING EXPERIENCE WITH TELEMEDICINE DURING THE COVID-19 PANDEMIC IN THE CARE OF PATIENTS AFTER LIVER TRANSPLANTATION

Juliana Elias1, Talita Colado1, Celia Souza1, Simone Perales1, Elaine Ataide1, Ilka Boin*1
1University of Campinas, Gastrocentro, Campinas, Brazil

Background: The concept of telemedicine is based on offering healthcare services in situations where distance is a critical factor, using telecommunications to exchange necessary information. During the pandemic period, telemedicine was used for post-liver transplant outpatient appointments.

Methods: Since liver transplant patients are immunosuppressed and social distance was compulsory, during the COVID-19 pandemic telemedicine was used to assist patients, and descriptive and quantitative research was carried out to analyse the effect of telemedical appointments on patient care. All patients were scheduled for a face-to-face appointment and were screened by the nursing and medical team, and checking their laboratory tests. Patients with laboratory alterations and/or clinical complaints were maintained in present care, while those who did not present laboratory alterations and/or clinical complaints were assisted remotely (via telephone contact), and all documentation (drug prescriptions, exams requests and return) were carried out and delivered to be collected by the patient on a scheduled period.

Results: Telemedical appointments for liver transplant patients resulted in a cost reduction of approximately US $4000 per patient for the Brazilian government since no transport or accommodation were required. Besides, it maintained the same quality as presential appointments, as no significant adverse effects were perceived: from the 4112 appointments, only one patient developed lung neoplasia and another head-neck neoplasia. Furthermore, all the 32 patients who were infected by the SARS-COV-2 virus presented no severe damage and four were hospitalized.

Conclusions: Conclusion: Through telemedicine, it was possible to maintain the same quality service without exposing already immunosuppressed patients, besides saving governmental capital. Therefore, telemedicine presented itself as a leverage and it is maintained as an outpatient care tool.
P442 DISCREPANCY BETWEEN PULMONARY ARTERY CATHETER AND CO-OXIMETRY VALUE OF MIXED VENOUS OXYGEN SATURATION DURING LIVER TRANSPLANTATION

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Background: Monitoring of tissue oxygenation is one of the most important goals in the critically-ill patients such as liver recipients. Pulmonary artery catheter (PAC) provides continuous monitoring of mixed venous oxygen saturation (SvO2) using fiberoptic reflectance spectrophotometry. Although the requirement of in-vivo calibration during liver transplantation was reported, there is no guideline about recalibration. We have observed significant drift of PAC SvO2 from reference co-oximetry value during liver transplantation. Therefore, we aimed to assess the incidence of significant discrepancy between PAC and co-oximetry values of SvO2, and the risk factors for the discrepancy.

Methods: This retrospective study included 54 recipients who underwent living donor liver transplantation at our institution between October 2021 and April 2022. PAC was inserted, and in-vivo calibration was conducted using co-oximetry value. We defined the significant discrepancy as the drift was ≥5% from the reference co-oximetry value at 1-hour after graft reperfusion. To assess the risk factors for the discrepancy, perioperative variables were compared between recipients with and without significant discrepancy. Receiver operating characteristic (ROC) curves were generated to evaluate the ability of perioperative variables to predict the occurrence of significant discrepancy.

Results: Significant discrepancy was observed in 25 of 54 recipients (46.3%). PAC SvO2 was higher than co-oximetry value in 51 of 54 total recipients, and 25 of 25 recipients of significant discrepancy. Among the perioperative variables, the changes of SvO2 in co-oximetry from the baseline to 1-hour after graft reperfusion was significantly greater in the recipients with significant discrepancy (median [IQR] -3.2 [-5.3, 0.35] vs. 2.5 [-0.45, 4.5], P = 0.001). The area under the ROC curve of the changes of SvO2 in co-oximetry from the baseline to 1-hour after graft reperfusion was 0.76 (0.63-0.87) (P = 0.001).

Conclusions: PAC SvO2 significantly drifted from reference co-oximetry value in nearly half of the recipients after graft reperfusion during liver transplantation. Therefore, in-vivo recalibration is required for reliable measurement of PAC SvO2 during liver transplantation, and further study during other operation is required.

P445 THE EFFECT OF STEROID PULSE THERAPY FOR THE REDUCTION OF ACUTE REJECTION EPISODE IN SUBCLINICAL BORDERLINE CHANGES: AN OPEN-LABEL, RANDOMIZED TRIAL

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Background: Subclinical rejection (SCR) has been correlated with subsequent chronic allograft nephropathy and allograft dysfunction. SCR is known to be effective in steroid pulse therapy (SPT) in other studies. However, there is controversy about borderline change. The purpose of this study is to investigate the effect of early SPT for the reduction of acute rejection episode during the first year after kidney transplantation in the patients who show subclinical borderline changes at 2-week protocol biopsy.

Methods: This study was a randomized clinical study in which 17 recipients with stable kidney graft function and borderline changes in the 2-week protocol biopsy were enrolled. The recipients were divided into two groups depending on SPT. We investigated changes in Banff scores through protocol biopsy after 1 year.

Results: Recipients who underwent acute cellular rejection and borderline change within 1 year were 4 recipients (50%) in the Non SPT group and 5 recipients (55.6%) in the SPT group, and there was no difference between the two groups (p > 0.999). There was no difference between the two groups in the change of the Banff score between the 2-week and 1-year protocol biopsy. And there was no difference in the rates of opportunistic infections including cytomegalovirus (p = 0.471) and BK polyomavirus (p > 0.999). Also, there was no difference between the two groups with respect to creatinine and eGFR at 2-week to 3-year after surgery.

Conclusions: There was no difference in Banff score change, infection rate, and graft function between the two groups. In conclusion, we suggest that steroid pulse therapy is not essential for subclinical borderline change which is detected at 2-week protocol biopsy.

P447 IMMUNOLOGIC RESPONSE TO SARS-COV-2 VACCINATION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Pediatric population is at a lower risk of severe SARS-CoV-2 infection compared to adults. Nevertheless, transplant-related immunosuppression in pediatric kidney recipients increases their hazard compared to the general population. This systematic review aims to evaluate the efficacy of SARS-CoV-2 vaccines and determine risk factors of no seroconversion in pediatric and adolescent kidney transplant recipients.

Methods: PubMed-MEDLINE were searched for studies reporting the efficacy of SARS-CoV-2 vaccine in pediatric and adolescent (under 18 years of age) kidney transplant recipients. Meta-analysis was also performed using fixed and random effect models.

Results: A total of 7 studies including 254 patients were included. The random effect model demonstrated a 63% seroconversion rate (95%CI 0.50-0.76) following a two-dose schedule which increased to 85% (95%CI 0.76-0.93) after 3rd dose administration. Seronegativity was 10.5-fold higher (95%CI 2.32, 47.92) in patients under mycophenolate mofetil compared to azathioprine. Rituximab administration decreased the probability for seroconversion (OR 0.12, 95%CI 0.03-0.43). Mean glomerular filtration rate (GFR) was 9.25 ±0.17 (95%CI 8.91-9.57) lower (95%CI -16.37-2.13) in patients with no seroconversion. Seroconversion rate was lower in vaccinated compared to infected patients (OR 0.13, 95% CI 0.02-0.72).

Conclusions: Vaccination against Sars-Cov-2 in pediatric and adolescent kidney transplant recipients elicits humoral response and 3rd dose is advised as response rates augment following a third immunization. Previous rituximab administration and lower GFR reduces the likelihood for seroconversion. Moreover, seroconversion rate is more frequent in patients under antimetabolite therapy with azathioprine compared to mycophenolate mofetil.
P448 IMPACT OF NONSPECIFIC ALLOGRAFT BIOPSY FINDINGS IN SYMPTOMATIC KIDNEY TRANSPLANT RECIPIENTS
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Background: An indication biopsy is indicated to diagnose the cause of allograft dysfunction. In indication biopsies, subclinical and borderline allograft findings may be fewer than in protocol biopsies. Nevertheless, we occasionally encounter ambiguous biopsy results in symptomatic kidney transplant recipients in practice. The allograft survival outcome in symptomatic recipients with nonspecific allograft biopsy findings remains unclear. The purpose of this study was to analyze the impact of nonspecific indication biopsy findings in symptomatic kidney transplant recipients.

Methods: We retrospectively collected records from 773 kidney transplant recipients between January 2008 and October 2021. The characteristics of transplant recipients with nonspecific allograft findings in the first indication biopsy were analyzed. Nonspecific allograft biopsy findings were defined as other biopsy findings excluding ABMR, TCNMC, borderline rejection, CNI toxicity, infection, glomerulonephritis, and diabetic nephropathy. The graft outcome was compared between recipients who had never had an indication biopsy and those who had a first indication biopsy with nonspecific findings.

Results: Recipients with nonspecific allograft biopsy findings (n = 81) and those with no indication biopsy findings (n = 510) were studied. The causes of the indication biopsy were increased creatinine levels (48.2%), proteinuria (11%), others (10.8%). The survival, graft survival compared to recipients who did not require the indication biopsy.

Conclusions: Nonspecific indication biopsy findings might not be a poor prognostic factor for allograft survival in recipients with nonspecific indication biopsy findings.

P449 DELAYED GRAFT FUNCTION EFFECT ON T CELL SUBPOPULATIONS FOLLOWING RENAL TRANSPLANTATION
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Background: Delayed graft function (DGF) is marked by activation of both innate and adaptive immunity and may have long-term implications in the immune response to the kidney allograft. CD28null T lymphocytes (CD28null) are terminally differentiated cells associated with cardiovascular diseases and are expanded in advanced chronic kidney disease.

Methods: In this prospective study, we included 105 patients who were transplanted and followed for up to 5 years. Those were classified in 5 groups according to the presence of DGF. Cytometric analysis was performed on the day of transplantation and then at 3, 6, 12 months posttransplantation, to estimate the phenotype of T lymphocytes. Based on this analysis, T lymphocyte subpopulations studied were: CD4, CD8, CD4/CD8null, and CD8/CD28null.

Results: DGF was recorded in 20 out of 105 patients (19%). One year after transplantation the patients remained good graft function (eGFR=64±19 ml/min/1.73m²) with no differences between the two groups. The percentage of CD28null lymphocytes was reduced in non-DGF patients at six (p=0.007) and twelve (p=0.010) months posttransplantation as compared to DGF patients. CD4/CD8null ratio was negatively associated with CD28null lymphocytes (p=0.001) at all time points and was reduced in DGF patients at 12 compared to 3 months after the transplantation (p=0.005) while in non-DGF patients it remained steady. Twelve months after transplantation, patients with non-DGF had lower CD2CD8null [15.3(16) vs 27.4(38) %, p=0.018] while DGF patients had lower CD4/CD8 ratio [1.1(1.2) vs 1.8(1.0), p=0.010].

Conclusions: One year after successful kidney transplantation, patients with DGF have a lower CD4/CD8 ratio which is comparable to that in recipients who did not require indication biopsy.

P450 HAPLOIDENTICAL HSCT WITH KIR GENOTYPE MISMATCHED: DIMINISHED RISK OF MORTALITY, DISEASE-FREE MORTALITY AND ACUTE GVHD
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Background: In allogeneic hematopoietic stem cell transplantation (HSCT), stem cells are ideally obtained from HLA-identical donors. However, it has been estimated that only 30% of patients could be transplanted with HLA-identical donors, so other alternatives such as haploidentical HSCT (hHSCT) have gained relevance. The major disadvantages with the use of haploidentical donors are an increased risk of graft rejection and graft versus host disease (GVHD). For this reason, it has been proposed to evaluate NK cell alloreactivity and its association with diverse HSCT outcomes according different KIR compatibility models.

Methods: We retrospectively analyzed 73 donor-recipient pairs with hHSCT at a single center before 2006 and 2018. Donors were first- or second-degree relatives with 3 to 5 allelic mismatches at all HLA loci. KIR typing was performed by PCR-SSO. To evaluate the KIR-gene (KIR G-G model), we defined KIR A/A genotype by the presence of activating KIR (except KIR2DS4), and KIR B/x genotypes by the presence of one or more of the following genes: KIR2DL5, 2DS1, 2DS2, 2DS3, 2DS5 or 3DS1. We evaluated the association between KIR G-G model and overall survival, disease-free survival, non-related mortality, acute and chronic GvHD, and relapse. Survival analysis was carried out by Kaplan Meier method using the log rank test. Moreover, we employed Cox regression method and Competing risk analysis.

Results: The half of the follow-up time, where 50% of the deaths occurred, was 47 months. Acute GvHD, chronic GvHD and relapse occurred in 38, 16 and 9 patients respectively. Of 73 evaluated pairs, 11 (15%) had KIR genotype mismatches (A/A donor into B/x recipient (6.8%), and B/x donor into A/A recipient (8.2%)) in patients with haploidentical donors, the recipients transplanted with KIR genotype mismatched donors had 77% less risk of mortality and 77% more likely to have disease-free survival (HR 0.27 (IC95% 0.06 – 0.82), p=0.024) also, these patients had 73% less risk of acute GvHD (HR 0.27 (IC95% 0.07 – 0.98), p=0.05).

Conclusions: These results allow us to suggest that the KIR G-G model could be an important tool to predict alloreactivity events associated with overall survival, free-disease survival and acute GvHD in patients with hHSCT. KIR genotyping could be a crucial selection criterion to choose the best donor.

Kaplan-Meier graft survival analysis

Log Rank (Mantel-Cox)
P=0.914

Overall graft survival probability

No biopsy
Nonspecific biopsy finding
No biopsy - censored
Nonspecific biopsy finding - censored

Time (month)

0 100 200
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1University Hospital of Ioannina, Department of Nephrology, IOANNINA, Greece, 2University Hospital of Ioannina, Department of Surgery and Kidney Transplant Unit, IOANNINA, Greece, 3University Hospital of Ioannina, Second Department of Cardiology, IOANNINA, Greece, 4University Hospital of Ioannina, Laboratory of Hematology - Unit of Molecular Biology, IOANNINA, Greece

Background: Kidney transplant recipients (KTRs) carry a significant cardiovascular disease (CVD) burden. The relationship between immune system responses with heart failure is intricate. The aim of our cross-sectional study was to investigate correlations between blood levels of specific immune cells subsets with conventional and novel deformation indices of left ventricular (LV) function in KTRs.

Methods: 31 stable KTRs (mean age 58 ± 9.28 years, 67% males) without CVD and 17 chronic kidney disease (CKD) stage 3 patients without CVD were enrolled. The peripheral blood immune cells, including CD14++CD16- CD14++CD16+ and CD14+CD16+ monocytes, Natural Killer (NK) cells (CD3+CD16+56+), CD3-CD19+ B cells, CD3+CD4+ T cells, CD3+CD8+ T cells and T regulatory (Tregs) cells (CD4+CD25+ FoxP3+) were measured by flow cytometry. Left atrial volume index (LAVI), LV mass index (LVMi), E/E’, global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), TWIST, UNTWIST were assessed by echocardiography.

Results: KTRs had a mean eGFR 58 ±18 ml/min/1.73 m2 (CKD-EPI) and mean 24-hour proteinuria (PER) 707 ±1185 mg/24h. B-cells, T-cells and CD8+ T cells counts correlated positively with eGFR (p<0.05). Increased non-classical CD14++CD16+ monocytes were associated with PER (p<0.01). An inverse correlation was found between classical CD14++CD16- monocytes and pro-inflammatory CD14++CD16+ monocytes counts correlated positively with LAVI and E/E’ respectively (p<0.05). Increased monocytes and pro-inflammatory CD14++CD16+ monocytes were associated with PER (p <0.01). An inverse correlation was found between classical CD14++CD16- monocytes and PER (p<0.05). Increased non-classical CD14++CD16+ monocytes were associated with PER (p<0.01). Increased monocytes and pro-inflammatory CD14++CD16+ monocytes counts correlated positively with LAVI and E/E’ respectively (p<0.05). Finally, increased NK cells levels were associated with more negative GCS values (p<0.05).

Conclusions: Alterations of immune cells subsets correlate with subclinical markers of LV dysfunction in KTRs with no established CVD and future research is required to further evaluate them as prognostic tools in KTRs.

Table 1.

<table>
<thead>
<tr>
<th>KTRs (No=31)</th>
<th>CKD (No=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (No/mm³)</td>
<td>8675±1-2852</td>
<td>7060 ±1-1671</td>
</tr>
<tr>
<td>Monocytes (No/mm³)</td>
<td>629 ±1-246</td>
<td>453 ±1-144</td>
</tr>
<tr>
<td>CD14++CD16+ (No/mm³)</td>
<td>517 ±1-223</td>
<td>356 ±1-137</td>
</tr>
<tr>
<td>CD14+ (%)</td>
<td>86 ±1-8.3</td>
<td>79 ±1-8.3</td>
</tr>
<tr>
<td>CD14+CD16+ (No/mm³)</td>
<td>22 ±1-14</td>
<td>31±1-16</td>
</tr>
<tr>
<td>T lymphocytes (%)</td>
<td>3.8 ±1-2.5</td>
<td>7.2 ±1.7</td>
</tr>
<tr>
<td>NK cells (%)</td>
<td>13.4 ±1-9</td>
<td>17.1 ±1-7.8</td>
</tr>
<tr>
<td>Tregs (No/mm³)</td>
<td>22 ±1-13</td>
<td>38 ±1-34</td>
</tr>
<tr>
<td>Tregs (%)</td>
<td>1.2 ±1-0.75</td>
<td>2 ±1-1.4</td>
</tr>
</tbody>
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Background: Diagnosis of kidney transplant (KTx) rejection is based on the pathology findings of a KTx biopsy according to the Banff Classification of Renal Allograft Pathology. Distinguishing between different types of KTx rejection when it is not a clear-cut case may be challenging due to the fact that the exact composition of the inflammatory cells can be difficult to comprehend and visualize on the same biopsy slide. Here we describe the feasibility of using a novel multiplex immunofluorescent panels on formalin fixed paraffin embedded (FFPE) KTx biopsies combined with digital image analysis to investigate the immune cell repertoire of different types of acute KTx rejection.

Methods: Two novel multiplex immunofluorescent panels were designed and performed on 76 KTx FFPE biopsies. Antibodies to panel 1: CD3 (T cells), CD8 (cytotoxic T cells) and, CD68 (macrophages) and panel 2: CD21, CD16, CD163 mononuclear phagocytes and CD56 (NK cells) were used. Three groups were compared: antibody-mediated rejection (AMR, n=25), acute T cell-mediated rejection (aTCMR, n=19), and acute tubular necrosis (ATN, n=32). Digital image analysis was performed using QuPath and data was analyzed using Graphpad Prism software.

Results: In both AMR and aTCMR, almost all immune cell subunits inflamma-
tory cells were significantly more prevalent in both glomeruli and tubulointer-
istium than in ATN cases with the exception of CD14+ and CD16+ cells in the glomeruli and CD14+CD16+ and CD16+CD56+ cells in the tubulointerstitium. The tubulointerstitial of aTCMR showed a higher abundance of T cells compared to AMR (CD3+ and CD3+CD8+, p <0.05). No differences in glomer-
ular T cells were seen. The glomeruli of AMR showed significantly more mono-
cytes and macrophages than at aTCMR (CD14+, CD16+, CD68+, CD163+ and, CD16+CD56+, p <0.05).

Conclusions: Multiplex immunofluorescent panels are a feasible method to assess T cells, monocyte and macrophage subsets in KTx FFPE biopsies. Comparing rejection cases to ATN cases, we detected a stronger expansion of T cells and mononuclear phagocytes in both glomeruli and tubulointerstitium in rejection cases. Lastly, comparing AMR to aTCMR cases revealed that AMR is characterized by expansion of mononuclear phagocytes within the glomeruli, while TCMR is characterized by interstitial T cell infiltration.

Results: First we showed that both minced parathyroids from human or pigs could be efficiently transplanted under the kidney capsule of RAG2KO mice with persistent viable tissue at day 30 post-transplantation. Then we investigated if enzymatic digestion of human parathyroids was comparable to minced tissue. After digestion, human parathyroid cells could be cultured up to 4 days and showed a response in vitro to calcium stimuli. After transplantation into mice, digested parathyroids showed similar outcomes compared to minced parathy-
roids, with an increasing secretion of parathormone from day 0 to day 30. Even though digested parathyroid graft volumes were lower than minced ones, we found a significant higher percentage of fibrosis in minced parathyroids.

Conclusions: Porcine and Human parathyroids can be transplanted success-
fully under the kidney capsule of immune-incompetent mice. Enzymatic diges-
tion of parathyroids is a reliable tool to process parathyroids before transplanta-
tion, which will be of help for future preclinical models.

Background: The intra and early postoperative ultrasound (US) evaluation of the transplanted kidneys represents the most widespread, non-invasive, reli-
able method for the assessment of the renal allograft vascular and perfusion status. US with the evaluation of the resistance index (RI) is based on blood velocity and pressure, providing an indirect perfusion measurement and it has been shown to predict short-term allograft function. We aimed at focusing on flow measurements performed after the graft reperfusion and eventual associ-
ations with clinical features.

Methods: 96 flow measurements in thirty-three consecutive transplant patients (7 from living donors, 26 from deceased of which 4 following hypothermic machine perfusion) were prospectively recruited from May to December 2022. Assessment was performed with MiraQ system which combines US and flow measurements: surgical findings can be documented through L15 High-fre-
quency US Probe that allows to assess morphology meanwhile transit time technology measures flow. This combined real-time assessment allows an early detection of vascular alterations and an immediate revision, if necessary (1 case in our series).

Results: In descriptive analysis, flow measurements distributions’ shapes changed depending on the type of donor, with their skewness suggesting better values for living donors both in the arterial and venous flow measurements (-1.7/0.2; -1.5/-0.5 respectively). A propensity score matching renal venous RI, with its regressor of impact on the vascular stiffness and resistance, patient age and weight were included in an univariate general linear model, together with BMI, warm ischemia time and the type of donor (deceased vs living) and then in a logistic model testing differences between two groups categorized by arte-
rial Renal Flow: median <249.5 (normal, n=52) and median ≥249.5 (normal, n=44) to identify peculiar and independent variables predictive impact. The preliminary results showed different significant predictive values for different types of kidney donors and independent significant values of warm ischemia times (P <0.005); the logistic model confirms, also in a categorical perspective, an impact for all the regressors, including the BMI

Conclusions: Data favor living donors flow outcomes (OR: 0.05; CI 0.06-0.8).
Liver transplant (LT) recipients have an increased risk of pulmonary diseases. This suggests excess eosinophilic airway inflammation in LT recipients, with higher odds for FeNO >25 ppb and >50 ppb compared to the general population. Adjusted odds ratio for FeNO>25 ppb was 2.99 (95% CI: 2.2-4.1, p<0.0001) and 2.61 (95% CI: 3.1-6.2, p<0.0001). No statistically significant differences in FeNO levels between LT recipients and controls. Results: We included 272 LT recipients and 2137 controls (Table 1). LT recipients were slightly younger, but proportions of current smokers, self-reported asthma and COPD were comparable between the two groups. Median FeNO was higher in LT recipients (16.0 vs. 15.4, p<0.0001) and more LT recipients had FeNO >25 ppb (27.2% vs. 12.1%, p<0.0001) and ≥50 ppb (4.0% vs. 1.7%, p=0.02). In analyses adjusted for age, sex, and current smoking, FeNO was significantly higher in LT recipients with an estimated difference of 4.7 ppb (95% CI: 3.1-6.2, p<0.0001). Simulated whole-blood tacrolimus pre-dose concentrations, with the gestational age correlated to mean haematocrit values of that period, show a clear distinction between non-pregnant state and pregnancy on CL/F (Figure 1). A rapid decrease in tacrolimus concentrations occurred during the first trimester, which decreased a bit further during the second trimester and stayed stable during the last trimester. This change rapidly disappeared postpartum. Conclusions: Gestational age and haematocrit impact the exposure to tacrolimus during pregnancy. To maintain target whole-blood tacrolimus pre-dose concentrations during pregnancy, a dose increase is suggested. This popPK model may be used in the future for tacrolimus dose adjustments in pregnant kidney transplant recipients.
**P300**

**THE PROGNOSTIC VALUE OF LYMPHOCYTE SUBSETS IN ANTIBODY RESPONSE AFTER SARS-COV2 VACCINATION IN DIALYSIS PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS**

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**Background:** The immune responses to SARS-COV-2 vaccination remain under study in hemodialysis (HD) patients and kidney transplant recipients (KTRs) in the setting of the immunosuppressed milieu. The aim of our prospective study (ClinicalTrials.gov, NCT04392876) was to determine the predictive value of lymphocyte subpopulations in the production of antibodies (Ab) against SARS-CoV-2 after the second vaccine dose.

**Methods:** The study cohort included 34 HD patients and 54 KTRs who received two doses of the BNT162b2 (Pfizer-BioNTech). Lymphocyte subsets including B cells, CD4+ and CD8+ T cells, naïve and memory T lymphocytes were analyzed by flow cytometry (FC) before vaccination (T0), before the 2nd dose (T1), 2 weeks after the 2nd dose (T2). Exclusion criteria included previous infection by SARS-CoV2 and infection by SARS-CoV2 during study follow-up. The anti-SARS-CoV2 Ab response was assessed by the ARCHITECT IgG II Quant test (Abbott). Titers >50 arbitrary units (AU/mL) were considered positive.

**Results:** The mean age of KTRs and HD patients was 58.5 and 68.5 years respectively. In KTRs, the populations of CD19+ lymphocytes, CD3+CD8+ T cells, naïve and memory T lymphocytes can predict anti-body formation (p-ANOVA<0.001) based on the multiple regression model: Ab=4869+519*CD19-226*CD3+CD16+56-139*CD4+CD45RO. In HD patients the populations of CD19+ lymphocytes, CD45RA+CD45RO lymphocytes, CD4 to CD8 ratio, CD3+CD16+56+ cells and CD4+CD45RO lymphocytes can predict Ab formation (p-ANOVA<0.001) based on the multiple regression model: Ab=20267+835.3*CD19-286*CD45RA+CD45RO-375.2*CD4+CD45RO+851*CD4+CD8-187.3*CD3+CD16+56+. The two regression models explain the variation of the dependent variable (Ab), according to the adjusted index, at a rate of 24% and 67% respectively. The 2 models were analyzed for residual autocorrelation (DW statistic >DU>DL). No multicollinearity was observed (All VIF< 1).

**Conclusions:** Quantification of lymphocyte subsets appears to have a significant prognostic value regarding development of Ab after vaccination against SARS-CoV-2, especially in KTRs. There are significant differences in lymphocyte subsets related to Ab production between HD patients and KTRs.

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**P481**

**NATURAL KILLER CELLS BEFORE KIDNEY TRANSPLANTATION INVOLVED WITH OPPORTUNISTIC INFECTION**

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**Background:** Longitudinal analysis has revealed strong links between the proportions of lymphocytes cells and acute rejection (AR), opportunistic infection (OI) or presence of DSA after kidney transplantation (KT). Lymphocytes profile at the time of KT associated with such complications have not been studied.

**Methods:** We conducted a longitudinal study to analyze lymphocytes subsets and NK cells at the time of first isolated KT before any immunosuppressive treatment from 01/2016 to 12/2018 and no exposure to anti-CD20 treatment. Within 24 months after KT, first event occurring defined groups: acute rejection (AR), opportunistic infection (OI) or DSA-free (control group). B cells subpopulations were determined as follows: B total (CD19+), naïve B cells (CD27- IgD+), switched memory (CD27+ IgD-), non switched memory (CD27-IgD+), double negative (CD27-IgD-), T B-cell (CD24 high CD38 high and plasmablast (CD24-CD38 highCD27 high). T cells subpopulations were defined by T CD3+, T CD3+CD4+, T CD3+CD8+ and NK cells as CD56+CD16+/1.

**Results:** Among 422 patients included, blood sample was not available in 139
PREVALENCE OF PERIPHERAL ARTERY DISEASE IN LIVER TRANSPLANT RECIPIENTS

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Background: Cardiovascular diseases have emerged as a leading cause of morbidity and mortality in liver transplant (LT) recipients. Peripheral artery disease (PAD) is the third leading cause of atherosclerotic cardiovascular disease following coronary heart disease and stroke. However, the prevalence of PAD and the role of traditional cardiovascular risk factors and immunosuppression in PAD pathogenesis in LT recipients is unexplored. Therefore, we investigated the prevalence of PAD in LT recipients and in sex- and age-matched controls and investigated the role of traditional risk factors and transplantation-related factors in PAD in LT recipients.

Methods: The Danish Comorbidty in Liver Transplant Recipients (DACOLT) study is an ongoing prospective, national cohort study. Controls were matched by age and sex and included from the Copenhagen General Population Study. All LT recipients underwent physical examinations including measurement of the ankle-brachial index (ABI). PAD was defined as ABI<0.9. We calculated the prevalence of PAD and investigated the association of potential risk factors using a logistic regression model adjusted for age, sex and smoking.

Results: 496 LT recipients and 2382 controls were included in the study. Median age was 55.5 years and 54.8% of the population were male. Median time since LT was 6.8 years (IQR: 2.8-13.4). There was no difference in the prevalence of PAD between the two groups (5.3% in LT recipients vs. 5.8% in controls; OR:1.01 95% CI:0.83-1.23, p=0.912). In adjusted logistic regression analyses for the whole group, hypertension and never vs. current smoking was associated with PAD (aOR 1.98 (95% CI: 1.40-2.81), p<0.001 and aOR 0.51 (95% CI: 0.31-0.82) p=0.006), respectively. Liver transplantation was not found to be associated with PAD in adjusted logistic regression analysis and no association with transplantation-related factors were identified.

Conclusions: In preliminary analyses, we found a comparable prevalence of PAD in LT recipients and in sex- and age-matched controls. Furthermore, LT was not associated with PAD in adjusted regression analysis. Further analyses are planned including analyses of the association between PAD and immunosuppressive drugs as well as other transplant-related factors. All data has been collected.

Table 1: Logistic regression analysis for Peripheral Artery Disease for the whole group

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR (95% confidence interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver transplantation</td>
<td>1.00 (0.65-1.56)</td>
<td>0.959</td>
</tr>
<tr>
<td>Age (per decade older)</td>
<td>1.02 (0.91-1.16)</td>
<td>0.717</td>
</tr>
<tr>
<td>Sex (male vs. female)</td>
<td>1.12 (1.08-1.53)</td>
<td>0.514</td>
</tr>
<tr>
<td>Hypertension (yes vs. no)</td>
<td>1.98 (1.40-2.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking (Never vs. current)</td>
<td>0.51 (0.31-0.82)</td>
<td>0.006</td>
</tr>
<tr>
<td>BMI (per 1 increase)</td>
<td>1.00 (0.69-1.43)</td>
<td>0.960</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index. Hypertension is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.
P465 AMBULATORY BLOOD PRESSURE MONITORING PRIOR TO KIDNEY DONATION

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1La Rabta Hospital, Nephrology, Tunis, Tunisia, 2a Rabta Hospital, Nephrology, Tunis, Tunisia

Background: In kidney transplantation, the requirements for organ donation has been extended to older donors or those with a history of cardiovascular disease that previously have been considered as contraindications. This study aims to determine the interest of ambulatory blood pressure monitoring (ABPM) prior to kidney donation.

Methods: It is a descriptive retrospective study of 15 living kidney donors who underwent casual clinic and ABPM.

Results: In our series of 105 living donor, in 90 among them, the hemodynamic evaluation of kidney donors was limited to clinic blood pressure levels. The remaining 15 donors underwent ABPM. Subjects were between the ages of 45 and 56, with a mean of body mass index of 26.5 kg/m² [22 - 29.5 kg/m²]. The clinic systolic blood pressure (SBP) average was 138.6 mmHg [114 – 150] (table1). For 10 cases with clinic BP the ABPM was used to diagnose high blood pressure. The diagnosis of hypertension was rejected in 5 patient aged <50 y.o with a clinic BP at 140/90 mmHg and an ABPM daytime BP <135/85 and also in 2 patients aged >50 y.o with normal BP in clinic BP measurement. The ABPM was used to check the blood pressure control in 2 patients whom were treated by calcium channel blocker associated to an angiotensin II receptor antagonists in one case and confirmed a well-controlled hypertension assessed by ABPM <130/85 mmHg under treatment but one of them had a non-dipper hypertension. They had nephrectomy for successful kidney transplantation in the recipient and simple operative follow-up for the donor.

Conclusions: ABPM reveals white coat effect hypertension and confirm well-controlled hypertension. It should be frequently used under general anesthesia and after kidney donation. The Amsterdam Forum recommend the use of an ABPM considers that, if donors whose blood pressure exceeds 140/90 mmHg should be generally challenged, some candidates over 50y.o whose hypertension is easily controlled without visceral repercussions may to be considered as donors.

Table 1: Ambulatory blood pressure monitoring prior to kidney donation in 15 patient

<table>
<thead>
<tr>
<th>Clinic SBP, mm Hg</th>
<th>140+/–13.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic DBP, mm Hg</td>
<td>90+/–8.1</td>
</tr>
<tr>
<td>Average 24-hour SBP, mm Hg</td>
<td>114+/–12.9</td>
</tr>
<tr>
<td>Average 24-hour day time SBP, mm Hg</td>
<td>109+/–9.88</td>
</tr>
<tr>
<td>Average 24-hour night time SBP, mm Hg</td>
<td>115+/–14.2</td>
</tr>
<tr>
<td>Daytime %</td>
<td>10.4+/–8.9</td>
</tr>
</tbody>
</table>

P468 LUNG FUNCTION AFTER THORACO-ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION IN A PORCINE DCD MODEL

Michiel Hu1,2, Zhang Zhang1, Niels Moeulsnd3, Pia Ryhammer3, Lars Ilkjær2, Michael Pedersen2, Steven Tsui1, Wim Timens2, Hans Elskjaer1
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Background: Thoraco-Abdominal Normothermic Regional Perfusion (TA-NRP) is a relatively new method to assess potential donor organs in vivo. This platform enables in situ reperfusion of both thoracic and abdominal donor organs with oxygenated blood in donation after circulatory death (DCD) settings. Our purpose was to investigate the lung function during and after TA-NRP in a porcine DCD model while simultaneously monitoring the effect of low and high oxygenation on donor cardiac function.

Methods: Danish landrace pigs (80 kg) underwent 15 minutes anoxic circulatory arrest after disconnecting from mechanical ventilation. Subsequently, resuscitation was initiated with TA-NRP through central cannulation. The animals received either high oxygen (FiO2 1.0, decreased to 0.6 after TA-NRP) or low oxygen (FiO2 0.21, increased to 0.40 during and after TA-NRP). Thereafter, 180 min of assessment post TA-NRP was followed. Blood gases, inflammatory cytokines and 8-isoprostane as oxidative stress marker were measured. Ventilation parameters were recorded. Tissue samples were taken from the ventral side for histological analysis and wet/dry weight ratio.

Results: In total 15/19 animals (7/9 in the low and 8/10 in the high oxygen group) were able to wean from TA-NRP. PaO2 was significantly higher during TA-NRP and after 180 min in the high oxygen group compared to baseline. In both groups the PaO2 remained acceptable and stable after TA-NRP. However, peak airway pressure was significantly increased and dynamic compliance significantly decreased during and post TA-NRP, independent of oxygen strategy. A higher trend in pro-inflammatory cytokines was seen in the high oxygen group. No differences were found in 8-isoprostane levels, histological scores and wet/dry weight ratio.

Conclusions: Lungs in both low and high oxygen groups maintained a stable and acceptable oxygenation capacity post TA-NRP. However, dynamic compliance decreased and peak airway pressure increased suggesting that TA-NRP is affecting the donor lung function which needs to be further investigated. No significant differences were observed in pro-inflammatory cytokines, oxidative stress, histological scores and oedema development. Further studies are necessary to determine lung function after transplantation.

P471 LEARNING FROM VIGILANCE – THE INSTRUCTIVE VALUE OF THE NOTIFY LIBRARY

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Background: Since 2012, the Notify Library (https://www.notifylibrary.org) collects scientific literature related to different types of adverse occurrences associated with the clinical use of blood, organs, tissues and cells (Medical Products of Human Origin, MPHO). The scope of the Library is to support the sharing of published vigilance information for educational purposes by making available the existing knowledge on serious adverse events and reactions in transfusion and transplantation. The selection and review of references for publication is performed by international experts who collaborate in 5 topic-specific editorial groups: infection transmission, malignancy transmission, living-donor reactions, process-related incidents, and other clinical complications. The aim of this communication is to provide an overview of the Notify Library and promote its use among the European Transplant community.

Results: The Notify Library contains 1848 didactic records quoting 2742 published references. Analyzing the database content by MPHO type, 44% of records (809/1848) were related to organs (kidney, 338; liver, 248; lung, 75; heart, 53; combined/multivisceral, 26; pancreas, 14; other/unspecified, 55), 20% (370/1848) to blood and blood components, 16% (301/1848) to hematopoietic progenitor cells, 14% (266/1848) to tissues and 6% (102/1848) to other MPHO. Of the 809 records that involve organs, 640 were categorized as “Harm to recipient” (infection transmission, 333; malignancy transmission, 270; immunological complications, 20; non-infectious-non malignant transmissions 13; other, 4), 101 as “Harm to donor” and 68 as “Risk of harm” (including 36 cases of donor disease without documented transmission in the recipient).

Conclusions: Notify Library is the first open-access, searchable database of systematically identified reports of disease transmission and other adverse occurrences arising from the donation and clinical application of MPHO.
P474 HISTOLOGICAL ANALYSIS OF EXPRESSION OF AT1R, ETAR AND ADHESION MOLECULES IN PEDIATRIC KIDNEY TRANSPLANT PROTOCOL BIOPSIES

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Background: Antibody-mediated rejection (AMR) is the major cause of premature kidney transplant failure. The role of alloantibodies against Human Leukocyte Antigens (HLA) in mediating AMR has been of primary interest in transplantation. However, there is evidence that non-HLA autoantibodies have a role in the involvement in AMR. Auto and allo antibodies against angiotensin II receptor 1 (AT1R) and endothelin A receptor (ETAR) have been associated with poor allograft outcomes in renal transplantation. Nevertheless, evidence for routine tests remain insufficient, especially in the pediatric field.

Methods: In our pediatric renal transplant cohort was performed ELISA assay of anti-AT1R and anti-ETAR antibodies. From these patients, we selected 12 transplant recipients with at least protocols biopsies and antibodies dosage at 6 and 24 months after transplantation. Six patients had high levels of anti-AT1R and anti-ETAR antibodies (>40 U/mL) and six were negative (<17 U/mL). Immunohistochemistry was performed on patient’s tissue biopsies to evaluate the expression of AT1R and ETAR receptors and adhesion molecules ICAM-1 and VCAM-1.

Results: Our analysis showed that there is no difference between AT1R and ETAR receptors expression in the presence or absence of circulating antibodies. In contrast, ICAM-1 and VCAM-1 expression was statistically significant in the presence of circulating antibodies at 24 months after transplant.

Conclusions: In our cohort, the presence of anti-AT1R and anti-ETAR antibodies does not seem to influence the expression of their receptors in the transplanted organ. However, anti-AT1R and anti-ETAR antibodies are associated with an increase of ICAM-1 and VCAM-1 expression in the graft. This preliminary study has some limitations, such as the low number of patients and a follow-up time which could be insufficient to observe the manifestation of a chronic change on biopsy. However, the increase in adhesion molecules could prove to be an event that anticipates the development of histological damage. Thus, increasing the cohort and extending long-term observation would help to better understand the impact of anti-AT1R and anti-ETAR antibodies after transplantation.

P475 SUCCESSFUL DESENSITIZATION WITH IMLIFIDASE AND DARATUMUMAB IN A HIGHLY IMMUNIZED, CROSS-MATCH POSITIVE LIVING-DONOR RE-TRANSPLANT RECIPIENT

Eva Schrezenmeier1, Mira Choi1, Brigitta Gloecke1, Thomas Dörner2, Alexandra Leimbach1, Katarin Amann3, Kai-Uwe Eckardt4, Klemens Budde4, Robert Ollinger5, Nils Lachmann5, Fabian Halleck1
1Department of Nephrology and Medical Intensive Care, Berlin, Germany, 2Department of Surgery, Berlin, Germany, 3Rheumatology and Clinical Immunology, Berlin, Germany, 4Department of Nephropathology, Erlangen, Germany, 5Institute for Transfusion Medicine, HLA-Laboratory, Berlin, Germany

Background: Transplantation of highly sensitized patients remains a major obstacle. Imlifidase is currently the only approved therapy for desensitization treatment of highly sensitized adult kidney transplant patients with a positive crossmatch (XM) against available deceased donors, while it is not approved for the use in living kidney transplantation.

Methods: We report as case of a successful AB0-incompatible (AB0i) living kidney transplantation in a highly sensitized, B and T cell CDC XM-positive patient with systemic lupus erythematosus (SLE) and secondary antiphospholipid syndrome (APS) with multiple thrombosis, previous kidney transplantation with graft loss 5 years ago due to venous thrombosis in the graft vein and extremely limited vascular access for dialysis.

Results: We (pre-) treated the patient with rituximab, Anti-thymocyte globulin, Intravenous immunoglobulin milifidase, and daratumumab besides standard immunosupression. From then on, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1A). Surgical procedure of living donor kidney transplantation (donor: mother, 68y) was uneventful, however, the patient remained anuric until day 28 after transplantation with subsequent increase of diuresis. Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1B). Histopathologically, the picture of acute tubular necrosis was present in biopsies on day 7 and 14 with no signs of rejection (Figure 1C). All IgG antibodies were sensitive to imlifidase treatment and, so far, remained low under daratumumab treatment and standard immunosupression. Besides donor-specific antibodies (Figure 1D) anti-dsDNA antibodies and antiphospholipid antibodies, were cleaved, too. Anti-CDS38 treatment affected mainly peripheral NK-cell numbers. Interestingly, despite anti-CD20 and anti-CD38 treatment, the patient was still able to generate peripheral plasmablasts (Figure 1F,G). Diuresis increased to 1200 ml/day (Figure 1B). Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1A). Surgical procedure of living donor kidney transplantation (donor: mother, 68y) was uneventful, however, the patient remained anuric until day 28 after transplantation with subsequent increase of diuresis. Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1B). Histopathologically, the picture of acute tubular necrosis was present in biopsies on day 7 and 14 with no signs of rejection (Figure 1C). All IgG antibodies were sensitive to imlifidase treatment and, so far, remained low under daratumumab treatment and standard immunosupression. Besides donor-specific antibodies (Figure 1D) anti-dsDNA antibodies and antiphospholipid antibodies, were cleaved, too. Anti-CDS38 treatment affected mainly peripheral NK-cell numbers. Interestingly, despite anti-CD20 and anti-CD38 treatment, the patient was still able to generate peripheral plasmablasts (Figure 1F,G). Diuresis increased to 1200 ml/day (Figure 1B). Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1A). Surgical procedure of living donor kidney transplantation (donor: mother, 68y) was uneventful, however, the patient remained anuric until day 28 after transplantation with subsequent increase of diuresis. Since then, creatinine levels declined to a baseline creatinine of 1.9 mg/dL (Figure 1B). Histopathologically, the picture of acute tubular necrosis was present in biopsies on day 7 and 14 with no signs of rejection (Figure 1C). All IgG antibodies were sensitive to imlifidase treatment and, so far, remained low under daratumumab treatment and standard immunosupression. Besides donor-specific antibodies (Figure 1D) anti-dsDNA antibodies and antiphospholipid antibodies, were cleaved, too. Anti-CDS38 treatment affected mainly peripheral NK-cell numbers. Interestingly, despite anti-CD20 and anti-CD38 treatment, the patient was still able to generate peripheral plasmablasts (Figure 1F,G).
Background: Sudden cardiac death (SCD) is the leading cause of death among ESRD and dialysis patients. Cardiovascular diseases are the leading cause of death among kidney transplant recipients (KTR). Implantation of a cardioverter defibrillator (ICD) is the first-line treatment option for prevention of SCD. Data on ICD in patients with chronic kidney disease is scarce. To the best of our knowledge there is no data in the literature on KTR with ICD and here we present our experience.

Methods: We retrospectively analysed medical records of patients receiving kidney transplant between December 1999 and December 2021. Characteristics and outcomes of patients with ICD defibrillator were investigated.

Results: Of 1689 patients who received kidney allograft 9 patients underwent ICD implantation (0.53%), 8 males. The cause of ESRD was unknown in 2 patients, ADPKD in 2 patients, 2 had tubulointerstitial nephritis while nephroan-giosclerosis, vesicoureteral reflux and Balcan endemic nephropathy were the cause of ESRD in one patient each. Mean dialysis vintage prior kidney transplantation was 3.3 years (0.7-6.5). Average age at the time of transplantation was 53 years (42-66). Indication for ICD implantation was primary prevention of SCD in 5 patients while 4 patients had ICD in secondary prevention. Mean time of ICD implantation after transplantation was 8.2 years (1.9-16.4), while female patient had ICD implanted 2.9 years prior kidney transplantation. Average age at the time of ICD implantation was 82 years (64-94). At the time of ICD implantation all patients had reduced kidney graft function with average eGFR 38 mL/min/1.73 m². During average of 4.1 years of follow up (6.7-2) graft function remained stable in all patients. One patient died 5 years after ICD implantation due to severe COVID.

Conclusions: KTR are specific category of CKD patients with increased cardiovascular risk. If there is an indication these patients should be considered candidates for ICD implantation prior or after kidney transplantation. Further studies are needed to prevent exclusion of kidney transplant recipients from this important and life-saving procedure.

Abstract: T-cells, and 2.5x10⁶ reads from the biopsy. Of these, we identified 127,310 reads from the S-protein specific T-cells, and 5.7x10⁶ reads from the biopsy. Of these, we identified 127,310 distinct clonotypes in the peripheral blood, but 0 in the kidney biopsy. This lack of T cell infiltration was confirmed by conventional histology, and exclude a T cell driven etiology. From patient 2 we obtained 9.8x10⁶ reads from the kidney transplant donor was a living relative, which enabled us to setup a mixed lymphocyte reaction to further evaluate acute rejection, as a cause of decreased kidney function.

To determine the clonotypes in the peripheral blood and kidney biopsy.

Results: From patient 1 we obtained 1.7x10⁶ reads from the bone marrow, and 2.5x10⁶ reads from the biopsy. Of these, we identified 127,310 distinct clonotypes in the peripheral blood, but 0 in the kidney biopsy. This lack of T cell infiltration was confirmed by conventional histology, and exclude a T cell driven etiology. From patient 2 we obtained 9.8x10⁶ reads from the kidney biopsy. 9.5x10⁶ reads from the bone marrow specific T-cells, and 5.7x10⁶ reads from the mixed lymphocyte reaction. This translated into 104,760, 24,743, and 5,312 distinct clonotypes, respectively. Here, 11.1% of the repertoire of the kidney infiltrating T cells were identical to S-protein specific T-cells in the periphery, and only 3.12% of the repertoire was identical to donor reactive TCRs.

Conclusions: AIRR-Seq of whole biopsies is a method to evaluate T cell infiltration and the specificity of these infiltrating T cells. We find that one patient had an infiltration of predominately SARS-CoV-2 specific T cells, indicating SARS-CoV-2 as a leading cause of the kidney function deterioration.
ENDOVASCULAR TREATMENT OF RESISTANT RENOVASCULAR HYPERTENSION IN A PATIENT WITH MIDDLE AORTIC SYNDROME (CLINICAL CASE)

Stepan Sakhovskiy*, Loudmila Bregel*, Daria Uvarova1, Igor Miloserdov1, Alla Matyunova2, Boris Mironkov1

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Background: Middle aortic syndrome (MAS) is a very rare condition generated by segmental narrowing of distal descending thoracic or the abdominal aorta. It is often associated with renal artery stenosis and resistant renovascular hypertension. We present a clinical case of surgical correction of a severe refractory renovascular hypertension in a child with middle aortic syndrome who was admitted to our clinic as a potential kidney recipient.

Methods: The patient was a 13 y.o. boy after aorto-aortic bypass grafting with recurrent of resistant vasomotor hypertension who came to Shumakov center to decide on further treatment tactics. He was considered to be a potential kidney transplant recipient. His height was 159 cm; weight was 57.4 kg. Heart rate at rest 102/min. Blood pressure measured on the right hand was 184/96, on the left hand 190/100. He had stenotic lesions of both renal arteries, a progressive decline of the left kidney function and volume. was admitted to our clinic as a potential kidney recipient. We decided on an intravascular approach instead.

We performed balloon vasodilation with stenting of the inferior pole left kidney artery, and the right renal artery. The lesions of the renal arteries and the stages of the intervention are shown in Figure 1.

Results: Control examination was performed 4 months after stenting. It showed reduction of the arterial hypertension (average blood pressure in the daytime was 142.6 mm Hg, average DBP during the daytime was 79.5 mm Hg, average blood pressure at night was 111.3/61.5 mm Hg, and LV hyper trophy (LVMI) (S) decreased from 163.8 g/m2 to 159.7 g/m2). Dopplerography of the renal arteries showed improvement of velocimetric indicators: an increased peak systolic (PSV) and diastolic (EDV) velocities and normalization of the resistance index values at all levels (Tab. 1). After the examination, we were able to reduce the antihypertensive therapy.

Conclusions: Hypoplasia of the abdominal aorta is a rare pathology with undiagnosed etiology. Surgical intervention in the form of an aorto-aortic bypass is an important stage of treatment. In case of vasorenal arterial hypertension recurrence is often associated with renal artery stenosis and resistant renovascular hypertension. We present a clinical case of surgical correction of a severe refractory renovascular hypertension in a child with middle aortic syndrome who was admitted to our clinic as a potential kidney recipient.

Figure 1

Tab. 1 a) CT angiography performed after aorto-aortic bypass surgery showing hypoplasia of the abdominal aorta and stenosis of both renal arteries. b) angiography showing renal arteries stenotic, c) renal arteries stenting, d) f) results of renal arteries angioplasty

<table>
<thead>
<tr>
<th>Peak systolic velocity (PSV) m/s</th>
<th>diastolic velocity (EDV)</th>
<th>resistance index</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td><strong>After aorto-aortic bypass grafting and implantation of the middle aortic syndrome stent</strong></td>
<td><strong>After balloon vasodilatation with stenting of the inferior pole left kidney artery, and the right renal artery</strong></td>
</tr>
<tr>
<td>Renal arteries</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
<td>0.41±0.23±97.3±5.8</td>
<td>0.26±0.20±0.52</td>
</tr>
<tr>
<td>Left</td>
<td>0.41±0.15±95.64</td>
<td>0.26±0.10±0.42</td>
</tr>
<tr>
<td>Segmental arteries</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
<td>0.41±0.09±140.8</td>
<td>0.37±0.17±0.33</td>
</tr>
<tr>
<td>Interlobar arteries</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
<td>0.41±0.06±178.6±6.8</td>
<td>0.37±0.17±0.33</td>
</tr>
<tr>
<td>Interlobar arteries</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
<td>0.41±0.06±178.6±6.8</td>
<td>0.37±0.17±0.33</td>
</tr>
</tbody>
</table>

Table 1. Intrarenal ECHO-Doppler velocimetric indices.

LONGITUDINAL ANALYSIS OF PERIPHERAL BLOOD IMMUNE CELL SUBSETS IN KIDNEY TRANSPLANT RECIPIENTS AND CLINICAL CORRELATIONS - A PROSPECTIVE STUDY

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Background: There are little data regarding the clinical value of regular monitoring of immune cells phenotypes in the peripheral blood of kidney transplant recipients (KTRs). The aim of our study was a longitudinal follow-up analysis of immune cell subtypes in the peripheral blood of KTRs and potential clinical correlations.

Methods: 48 stable KTRs were enrolled in this observational, prospective study. Patients were prospectively followed for 12 months. Exclusion criteria were history of acute rejection, cardiovascular disease (CVD), malignancy, autoimmunity and active or chronic infections before study enrollment or during follow-up. The peripheral blood immune cell subsets CD4+CD16+, CD14+CD16 and CD14+CD16+ and CD14+CD16++ absolute values and percentages out of total monocytes and NK cells (CD3-CD16+56+), CD3-CD19+ B lymphocytes, CD3+ CD4+ T cells, CD3 CD8+ T cells and Tregs (CD4+CD25+ FoxP3+) absolute values and percentages out of total lymphocytes were measured by flow cytometry at baseline (T0) and after 12 months (T1). Clinical and laboratory parameters were recorded at T0 and T1.

Results: The final cohort included 40 KTRs (mean age 58 ±9.28 years, 26 males, 17 patients on cyclosporine and 23 patients on tacrolimus). During follow up, the mean eGFR (CKD-EPI) declined from 58 ±17 to 53 ±18ml/min/1.73 m2 (p=0.004). There was a decrease in total monocytes (648±241/µL versus 537 ±194/µL, p=0.01) and total lymphocytes (2115 ±1327/µL versus 1925±742/µL, p=0.04). The classical CD14+CD16+ and CD14+CD16++ monocytes increased at T1 (S332242/µL compared to T0 (451±185/µL) (p=0.04). The rest immune cell subsets did not show any significant changes. A larger increase of the intermediate CD14+CD16+ monocytes counts from T0 to T1 correlated with a greater eGFR decline during follow-up (p = -0.339, p=0.04). No significant changes were observed in spot urine protein to creatinine ratio (UPCR), inflammatory markers (CRP, ESR) or calcineurin inhibitors blood levels between T0 and T1.

Conclusions: Our results suggest that increased yearly graft function loss might be associated with more marked augmentation of the pro-inflammatory CD14+CD16+ and CD14+CD16++ monocytes counts. Future studies with longer follow-up are required to specify the role of regular monitoring of immune cells subsets as potential prognostic biomarkers in KTRs.
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**RESULTS OF NORMOTHERMIC REGIONAL PERFUSION IN CONTROLLED DONATION AFTER CIRCULATORY DEATH PROVIDED BY A MOBILE ECMO TEAM ACROSS THE REGION OF MADRID**

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**Background:** The use of Abdominal normothermic regional perfusion (A-NRP) in controlled donation after circulatory death (dCD) is recommend in preference to in situ cooling and rapid procurement (IR-Tac). This procedure requires experience and the availability of ECMO. In order to provide support with A-NRP in centers with dCCD programs but without ECMO access, the region of Madrid created a A-NRP team. Our center, with ECMO experience, is a part of a one-week-on/one-week-off roster.

**Objective:** To describe the experience of our center as part of the Mobile ECMO team since the program begun.

**Methods:** Retrospective study (Apr 2017-Dec 2022). We included all Mobile ECMO team outcomes. We studied demographic data, ICU length of stay and the reasons for withdrawal of life-sustaining treatments (WLST) of the donors.

**Number of organs evaluated and the reasons for discard. ECMO run and complications related with ECMO cannulation.**

**Results:** During the period studied our ECMO Mobile team was mobilized 41 times to ten different hospitals. A-NRP was successfully performed in 37 cases. Of the 37 utilized donors 21 (59%) were male with mean age of 58 ± 14 years. The reasons for WLST were anoxic encephalopathy following cardiac arrest (n=20, 54%), catastrophic brain injury after ischemic/hemorrhagic cerebrovascular event or traumatic brain injury (n=16, 43%), terminal respiratory illness (n=3, 8%) and one case after euthanasia. Mean ICU length of stay was 9 ± 8 days. Cannulation problems were reported in 15 cases (40%) with 4 hemorrhagic complications during vessels cannulation and 11 events of non-progression of the aortic balloon that needed surgical cross clamp of the aorta before A-NRP. Mean warm ischemia times were 15 ± 6 minutes. Mean duration of the A-NRP was 82 ± 27 minutes. Of the 64 kidneys, 32 livers and 11 lungs evaluated, 58 kidneys, 18 livers and 7 lungs were implanted. The main reason for discard was unfavorable visual assessment and surgical complications and only in one case because of prolonged warm ischemia time.

**Conclusions:** The establishment of a Mobile ECMO team is feasible across the region of Madrid and it allows to all potential dCD donors be evaluated for A-NRP. Cannulation problems are common but in most of the cases the A-NRP is possible, that emphasized the fact that experience team is essential to achieve good results.

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**IMPACT OF CONVERSION OF TWICE-DAILY TACROLIMUS TO ONCE-DAILY EXTENDED-RELEASE MELT-DOSE TACROLIMUS ON CELLULAR IMMUNITY**

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**Background:** LCPT-LC (LCPT), a novel once-daily, extended-release formulation of tacrolimus, has reduced Cmax with comparable AUC exposure, requiring a ~30% dose reduction in contrast to immediate-release tacrolimus (IR-Tac). Once-daily LCPT in de novo kidney transplantation has a comparable efficacy and safety profile to that of IR-Tac with advantages in bioavailability and absorption. The present investigation intends to analyse the effects of conversion from IR-Tac to LCPT on phenotype and function of T-cell and B-cells.

**Methods:** 20 kidney transplant patients treated by triple standard immunosuppression with a stable graft function undergoing a switch from IR-Tac to LCPT were included in this observational prospective study. We analysed peripheral blood of the patients before and 4 and 8 weeks after IR-Tac to LCPT conversion using multi-parameter flow cytometry. We measured the main immune cell types and performed an in-depth characterization of B cell, dendritic cell (DC) and T cells including regulatory T cell (Treg). Additionally, we analysed antigenic responsivity of T cells by assessing third-party antigen (Tetanus)-reactive T cells, which could be analyzed by restimulation with tetanus vaccine (TD).

**Results:** Overall, we found no significant alterations following LCPT conversion for the most immune cell populations with a few cell populations showing quantitative increase. Thus, 4 weeks after conversion, more lymphocytes and regulatory T cells could be measured in the patients. These differences were borderline significant (p=0.051 and p=0.08 respectively). Furthermore, we found significantly more regulatory T cells with a naïve phenotype (CD45RA/CCR7+). These alterations did not change again 8 weeks after conversion.

**Conclusions:** Here, we demonstrate first insights into the immune system changes occurred under IR-Tac to LCPT conversion therapy in kidney transplant patients. While phenotypic and functional characteristics of the most T and B cell populations did not change following conversion to the Tac dose sparing regime, we could observe an increase in the number of regulatory T cells in peripheral blood following IR-Tac to LCPT conversion, which might additionally contribute to the overall immunosuppressive effect.
**P486 NOVEL ANTIBODIES TO TARGET THE MEMBRANE ATTACK COMPLEX IN TREATING KIDNEY ISCHAEMIA REPERFUSION INJURY**

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**Background:** Complement is a potent driver of inflammation in many disease processes including Ischaemia Reperfusion Injury (IRI). The cytotoxic and pro-inflammatory membrane attack complex (MAC) is the major pathological effector of the complement cascade. This direct pathological role of MAC makes it an attractive therapeutic target. Eculizumab, an anti-C5 monoclonal antibody (mAb), is one drug that has transformed patient outcome in renal diseases, but its considerable cost makes it untenable for common use. We have developed and patented a novel mAb (anti-C7) that targets MAC downstream of C5, and shown to be efficient in reducing inflammation in rodent models of myasthenia gravis. The aim of this study was to test whether this novel anti-C7 mAb could reduce injury in a rat Kidney IRI model.

**Methods:** Adult male Lewis rats were injected with anti-C7 mAb 2H2 or D1.3 isotype IgG control (n=6 each). A midline laparotomy was performed; pedicles of both kidneys were clamped for 45mins; Kidney tissue was retrieved at 48h. Paraffin sections were made and sectioned for H&E and immunohistochemistry. Blood was taken for measurement of serum creatinine and complement lytic activity pre-op and at 48h.

**Results:** Anti-C7 mAb treated kidneys showed (i) Less histological damage (reduced EGFI score; assessing the architecture of the endothelium, tubules, glomeruli and interstitium within the renal cortex); (ii) Reduced serum creatinine at 48h; (iii) Complete inhibition of complement haemolytic activity and reduced terminal complement components (TCC) in serum at 48h; and (iv) Markedly reduced TCC deposition on immunohistochemistry analysis.

**Conclusions:** MAC can be successfully targeted downstream of C5 (through inhibition of the C7/C5b-7 complex) by this novel anti-C7 mAb. Targeting MAC-intermediates has potential as an innovative therapeutic approach in treating kidney IRI and improving transplant outcomes. Moreover, this approach is potentially more cost effective than other anti-MAC therapies such as eculizumab.

**P487 STRONGEST IMMUNOGENICITY OF HETERLOGOUS COVID-19 VECTOR/MRNA VACCINATION IN COMPARISON TO HOMOLOGOUS REGIMENS IN KIDNEY AND LUNG RECIPIENTS**

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**Background:** Dual-dose mRNA vaccination proved insufficient in the induction of antiviral immunity in transplant patients. Based on our observation of increased immunogenicity after heterologous vector/mRNA vaccination in immunocompetent individuals, the impact of heterologous vaccination was analyzed after transplantation in comparison to homologous regimens. In addition, vaccine-induced immune responses were compared between renal and lung transplant recipients (RTx/LTx) and respective transplant candidates on the waiting list.

**Methods:** Blood samples of 252 transplant recipients (169 RTx, 83 LTx) and 41 transplant candidates (RTx/LTx) and respective transplant candidates on the waiting list. 14 days after heterologous vector/mRNA vaccination or after vaccination with homologous regimens.

**Results:** Overall, response rates were highest in the group of waitlist patients. Comparison of the different vaccine regimens revealed significant differences in IgG and T-cell levels in all patient groups. Despite different levels of immunosuppression, the immunogenicity profile was similar in RTx and LTx. In both groups, heterologous vaccination not only induced higher amounts of IgG (NTx p=0.027, LTx p=0.006) and T cells (CD4 NTx p=0.003, LTx p=0.017; CD8 NTx p=0.004, LTx p=0.004), but also led to significantly higher response rates than homologous regimens. Regarding antibodies, 47.8% of RTx and 70% of LTx showed vector-induced antibody activity after heterologous vaccination whereas only 24.5%-25% reacted to homologous vaccination. Similarly, heterologous vaccination induced vector-specific CD4 and CD8 T cells in 63% and 50% of RTx and 60% and 50% of LTx, respectively with only 12.3-41.7% being positive for CD4 and T 7.7-33.3% for CD8 T cells after a homologous regimen.

**Conclusions:** The heterologous vector/mRNA vaccination was superior to homologous regimens in inducing both antibodies and T cells. Additionally, the higher percentage of T-cell responders indicates that immunogenicity of the vaccines is underestimated when considering antibodies alone.

**P489 IMPACT OF IMMUNOSUPPRESSION WITHDRAWAL IN DONOR(HLA)-SPECIFIC MEMORY B CELL RESPONSES IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS**

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**Background:** To generate allograft tolerance and avoid long-term immunosuppression (IS) is key to good health and quality of life in pediatric liver transplant recipients. Despite this, IS withdrawal may activate humoral alloimmune responses that may ultimately cause rejection. Tracking donor(HLA)-specific (d-sp) memory B cells (mBCs) besides DSA may guide safe IS withdrawal by identifying early anti-donor alloimmune activation.

**Methods:** 48 pediatric liver transplant recipients participating in a complete IS withdrawal trial (IWTH, NCT01638559) with serial PBMC samples obtained during IS withdrawal were assessed for the presence of d-sp mBC frequencies and DSA. D-sp mBCs responses were characterized using a novel HLA-specific B-cell Fluorescent spot assay at baseline, prior to, during and after (months 3, 6, 9, and 12) IS withdrawal as well as at time of rejection. HLA-a mBC counts were given as means of surface spot area (mm2) per 450,000 seeded, polyclonally expanded mBC.

**Results:** At baseline, patients with DSA exhibited higher frequencies of mBCs than patients without DSA (604.5 ± 185.4 vs 129.4 ± 53.8, p=0.009, respectively) (Fig 1a). Interestingly, frequencies of d-sp mBCs increased during IS withdrawal in all patients (604.5 ± 185.4 vs 911 ±376.6, p=0.77, respectively), but most in those without detectable DSA at baseline (129.4 ± 234.7 vs 364.8 ± 442.3, p=0.05, respectively) (Fig1b). Notably, at the time of allograft rejection, high frequencies of d-sp mBCs were detected in the majority of patients, suggesting a role in driving allograft rejection in patients undergoing IS withdrawal (Fig 1c).

**Conclusions:** A wide range of donor(HLA)-specific mBC frequencies may be detected in peripheral blood in pediatric liver transplant recipients with DSA, and seem to appear over time during IS withdrawal. Thus, tracking donor(HLA)-sp mBC may identify transplant recipients not capable of maintaining a quiescent anti-donor alloimmune response as IS is reduced.
**P493 HIGH INCIDENCE AND VIRAL LOAD OF HHV-6A IN A MULTI-CENTRE KIDNEY TRANSPLANT COHORT**

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**Background:** Human herpesvirus 6 (HHV-6) is a common opportunistic pathogen in kidney transplant recipients. Two different variants of HHV-6, HHV-6A and HHV-6B, have been identified, of which the latter seems to be dominant. However, it is unclear whether they increase the likelihood of other viral reactivations.

**Methods:** We characterized a multi-centre cohort of 93 patients along nine study visits for viral load. We tested for the following viruses: HHV-6A and HHV-6B, the herpesviruses cytomegalovirus (CMV) and Epstein-Barr virus (EBV) and the polomyxovirus BK (BKV).

**Results:** We detected HHV-6A viral load in 48 (51.6%) patients, while the incidence of HHV-6B was much lower, being detected in 7 (7.5%) patients. The incidence of HHV-6A was higher than of BKV, CMV and EBV. HHV-6A also demonstrated higher viral loads than the rest of viruses. There was a strong but not significant correlation between HHV-6A and HHV-6B co-infection (P=0.112), whereas no increased incidence of other viruses among patients with HHV-6A reactivation was observed. There was no negative effect of high HHV-6A (>10,000 copies/mL) load on markers of renal graft and hepatic function or blood count twelve months post-transplant.

**Conclusions:** In contrast to previously published data, our results show a clear dominance of HHV-6A in peripheral blood when compared to HHV-6B, with higher incidence and viral load levels. Despite the high HHV-6A loads observed, we did not identify any negative effects on post-transplant outcome.

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**P494 CYCLOSPORINE STIMulates MITOCHONDRIAL RESPiration OF PORcINE PRECISION-CUT NUTRIENT-SUPPLIED KIDNEY SLICES, a PILOt STUDY**

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The optimal nutrient-rich perfusion solution for preserving mitochondria during normothermic machine perfusion (NMP) is unknown. To study prolonged normothermic preservation, we developed a precision-cut kidney slice (PCKS) model. A limitation of the model for metabolic studies is that the slices do not use their full energy-producing capacity because of the lack of renal physiological function such as reabsorption, which is present during NMP. Cyclosporine (CyA) can partly uncouple mitochondrial respiration, thus we hypothesized that the addition of CyA can challenge renal tubules by increasing their metabolic activity. In this pilot study, we aimed at finding the CyA concentration that is able to decrease spare respiratory capacity (SRC), which can make the PCKS model a better representative of NMP/Porcin kidneys (m=3) were obtained from a local slaughterhouse. After 30 minutes of warm ischemia, they were placed in oxygenated Hypothermic Machine Perfusion (HMP) for 3 hours. Next, cortical kidney slices were made in a Krumdieck slicer and then placed into an oxygenated incubator at 37°C. The basic incubation medium was Dulbecco’s Modified Eagle Medium (DMEM) without glucose and pyruvate. The Nutrients group included glucose, glutamine and fatty acids and the Control group had no nutrients. Both groups had four subgroups, one without CyA and three with different concentrations (0.01mg/ml, 0.05mg/ml, 0.1mg/ml). Every 24 hours, slices and incubation medium were sampled for O2 consumption, measured using the Oxygraph-2k, and LDH analysis. After 48 hours, the PCKS incubated in the nutrient-containing medium showed a dose-dependent response in mitochondrial respiration. The dose of 0.01mg/ml CyA resulted in higher state 3 mitochondrial respiration (Figure 1A). In line with this finding, this 0.01mg/ml CyA group had a significantly lower SRC than slices without CyA, in the nutrient group (Figure 1C). LDH, as general injury marker, was also significantly lower in PCKS incubated with the lowest dose of CyA, independent of the incubation medium (Figure 1D,E). CyA supplementation can stimulate PCKS respiration in a dose-dependent manner. The optimal concentration to achieve stimulation was 0.01mg/ml, due to its effect of higher mitochondrial respiration, lower SRC and lower toxicity compared to higher dosages.

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**Table 1**

<table>
<thead>
<tr>
<th>Contents</th>
<th>Nutrients</th>
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**Figure 1**

- A. CyA dose dependence over 48h.
- B. LDH control 48h SRC.
- C. LDH control 48h SRC.
- D. CyA mg/ml.
- E. CyA mg/ml.
TRANSEUROPEAN EDUCATIONAL INITIATIVE IN ORGAN DONATION AND TRANSPLANTATION

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Background: The shortage of organs for transplant observed in each European Union (EU) member state has been the main challenge to address in organ transplantation (OT). TransEuropean Educational Initiative in Organ Donation and Transplantation (TEODOR) is a 36-month Erasmus+ project funded by the European Commission which aims at designing an innovative training program on organ donation (OD) and OT for physicians and healthcare personnel from Latvia, Czech Republic and Lithuania. The training was designed to improve technical and non-technical competencies required for better clinical performance and patient outcome, and boost best practice exchange among countries, with the aim of enhancing OD and OT activities.

Methods: The course was addressed to Key Donation Professionals and Key Transplantation Professionals as a strategy to engage all the main stakeholders involved in the process of OD and OT. The educational intervention is student-centered and adapted to adult-learning for life-long results. This was achieved through a multilevel (from awareness to high level) and blended methodology (non-line and face-to-face). The first level comprised microlearning capsules and webinar on the most important concepts of OD and OT. The second level contained online self-guided learning modules. The third level will involve local seminars and a face-to-face trans-national seminar.

Results: A total of 75 participants were expected to be trained by the end of the course. Additionally, more than 12 trainers from the beneficiary countries would be trained to continue conducting the training after this project. We also expect to have prospective study in the three beneficiary partner countries and scientific publications.

Conclusions: The impact and potential longer-term benefits of TEODOR will be observable at different societal and professional levels, including individual, healthcare professionals, and decision makers. At European level, we expect TEODOR to create better compliance with the EU recommendations and best practice exchange among Baltic, Southern, Central and Northern European healthcare professionals to improve OD and OT practices and education. At national level, we expect it to positively impact national agencies on development of organ exchange programs.

OPPOSITE EFFECTS IN FRACTIONAL DONOR-DEIVED CELL-FREE DNA FROM URINE AND PLASMA IN KIDNEY RECIPIENTS? RESULTS FROM A PILOT STUDY

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Background: Close monitoring of kidney allograft recipients is of high relevance for a timely detection of allograft injury and rejection. Limited sensitivity and specificity of current blood and urine-based biomarkers can delay the suspicion of an allograft injury as well as the biopsy needed for diagnosis confirmation. Donor-derived cell-free DNA (dd-cfDNA) in plasma has been shown to indicate kidney allograft injury. Our aim was to perform a pilot investigation of urinary dd-cfDNA as a potential new, non-invasive biomarker for allograft monitoring in kidney recipients.

Methods: Blood and urine samples from kidney transplant recipients (n = 93) were obtained at regular clinic visits. Droplet digital PCR was performed using mismatched HLA alleles between recipient and donor, based on which the absolute (cp/mL) and relative (%dd-cfDNA) quantities of dd-cfDNA were determined. Adjusted %dd-cfDNA on dd-cfDNA in plasma was found, whereas dd-cfDNA in urine was significantly decreased (p = 0.016). Similarly, recipients of deceased donor organs showed significantly increased %dd-cfDNA values in plasma compared to living donor recipients (p = 0.049), whereas the opposite was seen in urine (p = 0.026). Additionally, higher %dd-cfDNA was observed in urine from male recipients (p = 0.003). Finally, while no correlation was found between leucocyte counts and dd-cfDNA in blood, there was a significant negative correlation between %dd-cfDNA and increased leucocyte counts in urine (p = 0.002).

Results: In samples from patients with biopsy-proven allograft injury, when compared to samples from stable recipients, significantly increased %dd-cfDNA in plasma and urine (p = 0.002) were observed. No correlation was found on dd-cfDNA in time after transplantation, correlations with clinical and biochemical parameters were assessed.

Conclusions: In conclusion, %dd-cfDNA is a potential biomarker for kidney allograft injury and rejection. It is of added value for predicting graft injury, but influencing factors like timing of measurement and clinical parameters need to be considered.

UNINARY BIOMARKERS IN A LIVING DONOR KIDNEY TRANSPLANTATION COHORT – PREDICTIVE VALUE ON EARLY AND LONG-TERM GRAFT FUNCTION

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Background: Early non-invasive detection and prediction of graft function after kidney transplantation is essential since interventions might prevent further deterioration. The aim of this study is to analyze the dynamics and predictive value of four urinary biomarkers Kidney Injury Molecule-1 (KIM-1), Heart-type Fatty Acid Binding Protein (H-FABP), N-Acetylβ-D-Glucosaminidase (NAG) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) in a living donor kidney transplantation (LDKT) cohort.

Methods: Biomarkers were measured up to 9 days after transplantation of 57 recipients participating in the VAPOR-1 trial.

Results: Dynamics of KIM-1, NAG, NGAL and H-FABP significantly changed over the course of 9 days after transplantation. KIM-1 at day 1 and NAG at day 2 after transplantation were significant predictors for estimated glomerular filtration rate (eGFR) at various timepoints after transplantation with a positive estimate (P<0.05), whereas NGAL and NAG at day 1 after transplantation were negative significant predictors (P<0.05). Multivariable analysis models for eGFR outcome improved after addition of these biomarker levels. Several donor, recipient and transplantation factors significantly affected the baseline of urinary biomarkers.

Conclusions: In conclusion, urinary biomarkers are of added value for prediction of graft outcome, but influencing factors like timing of measurement and transplantation factors need to be considered.

MULTIMODAL REMOTE HOME-MONITORING OF LUNG TRANSPLANT RECIPIENTS DURING COVID-19 VACCINATIONS: PILOT STUDY OF COVIDA DESK

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Background: Remote patient monitoring (RPM) of vital signs and symptoms for lung transplant recipients (LTRs) has become increasingly relevant in many situations. Nevertheless, RPM research integrating multisensory home-monitoring device and tested it in the context of COVID-19 vaccinations. We hypothesize that multisensory RPM and smartphone-based questionnaire feedback on signs and symptoms will be well accepted among LTRs. To assess the usability and acceptability of a remote monitoring system consisting of wearable devices including heart rate meter and a smartphone-based questionnaire application for symptom and vital sign monitoring using wearable devices, during the first and second SARS-CoV-2 vaccination.

Methods: Observational usability pilot study for 6 weeks of home-monitoring with the COVIDA Desk for LTRs. During the first week after the vaccination, intensive monitoring was performed by recording data on physical activity, spirometry, temperature, pulse-oxygen and self-reported symptoms, signs and additional measurements. During subsequent days, the number of monitoring assessments was reduced. LTRs reported on their perceptions of the usability of the monitoring device through a purpose-designed questionnaire.

Results: Ten LTRs planning to receive the first COVID-19 vaccinations were recruited. For the intensive monitoring study phase LTRs recorded symptom and vital signs data. Overall, high usability and symptom monitoring was well accepted among LTRs. To assess the usability and acceptability of a remote monitoring system consisting of wearable devices including heart rate meter and a smartphone-based questionnaire application for symptom and vital sign monitoring using wearable devices, during the first and second SARS-CoV-2 vaccination.

Conclusions: The COVIDA Desk showed favorable technical performance and was well-accepted by the LTRs during the vaccination phase of the pandemic. The feasibility of the RPM system deployment was proven by the rapid recruitment uptake, technical performance (i.e., low number of errors), favorable user experience questionnaire and detailed individual user feedback.
COVID-19: ROLE OF RESILIENCE ON THE PSYCHOLOGICAL IMPACT OF LOCKDOWN IN LIVER TRANSPLANT TRANSITIONAL CANDIDATES AND RECIPIENTS

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Background: The coronavirus disease 2019 (COVID-19) pandemic and the necessary spreading control measures implemented by the governments have induced drastic changes in daily life. The reduction in mobility and strict social contact limitations are posing a great challenge, particularly for the adolescents. The purpose of this study is to investigate the psychological and emotional impact of lockdown and their relationship with resilience, on adolescents and young adults listed for liver transplant or liver transplant recipient.

Methods: Social and demographic variables of subjects (n = 66) were collected and the analyses were based on the Depression Anxiety and Stress Scales (DASS-21), and Connor-Davidson Resilience Scale (CD-RISC 25), exploring the following pathways: assessing depression/anxiety/stress scales and resilience factors. A correlation between the measured degrees of depression/anxiety and resilience was evaluated by Pearson’s correlation coefficient and linear regression models.

Results: The results showed a significant correlation between subscales: DASS depression/anxiety (r2 = .62) depression/stress (r2 = .85) CD-RISC commitment/optimism (r2 = .71). The total score of DAAS depression/anxiety/stress scales significantly diminished and the increasing of the total score of the inverse correlation between CD-RISC and DAAS seems to refer to the subscale of the relationship between DAAS depression and CD-RISC (β = 0.33, p = 0.006).

Conclusions: Our findings suggest that resilience can be a protective factor for an adolescent liver transplant recipients and liver transplant candidates in mitigating the onset of negative psychological symptoms correlated with the pandemic.

LUNG PRESERVATION AT 4°C TO 8°C WITH A NOVEL LUNG STORAGE DEVICE: FIRST EUROPEAN EXPERIENCE

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Background: Lung preservation at 4°C to 8°C has recently been recommended as the optimal storage temperature to minimize lung injury between procurement and implantation (versus the usually accepted 0°C to 4°C). We describe herein the first European experience of lung LUNGguard cooler. LUNGguard storage details, total ischemia time, and early postoperative outcome are described. Written informed consent for reporting was obtained.

Methods: Two patients underwent a bilateral lung transplantation (Ltx) in 11/2022 and 01/2023. Donor lungs were preserved in the Paragonix LUNGguard cooler. LUNGguard storage details, total ischemia time, and early postoperative outcome are described. Written informed consent for reporting was obtained.

Results: Patient 1 is a 55-year-old male with idiopathic pulmonary fibrosis, who underwent a high-gradient bilateral Ltx (no extracorporeal life support (ECLS)) with donor lungs from a 47-year-old female (donation after circulatory death - type III). Average LUNGguard temperature was 6.9°C, and preservation and total ischemia times were 270/451 minutes (right lung) and 404/557 minutes (left lung). Primary graft dysfunction (PGD) at 0/24/48/72h was 0/0/0/0. Postoperative course was uneventful, and the patient was discharged 19 days post-transplant. Patient 2 is a 15-year-old girl with cystic fibrosis, who underwent a bilateral lobar LTx (no ECLS) with donor lungs from a 37-year-old male (donation after brain death). The lungs were stored overnight in the LUNGguard at an average temperature of 5°C, with preservation and total ischemia times of 476/686 minutes (right lung) and 680/869 minutes (left lung). PGD at 0/24/48/72h was 2/1/0/0. Similar to patient 1, postoperative course was uneventful and the patient was discharged 26 days post-transplant.

Conclusions: Despite high-risk recipient and donor profile, and long ischemia times, lung preservation at 4°C to 8°C in the LUNGguard device seems safe and feasible, and has the potential to postpone LTx to day-time. Larger cohort and longer-term outcome are needed to confirm these promising observations.
Background: Identifying HLA-specific antibodies in patients prior to kidney transplant is an established risk stratification tool toward improved outcome. The varied pathogenicity of HLA antibodies by their levels or functional characteristics is established in retrospective studies. Their use in the clinical practice of delisting is slowly evolving. As a centre with interest in HLA incompatible transplantation, we are exploring other ways to push the boundaries to improve transplantation opportunities. This study aims to show the utility of the C1q assay in improving the probability of transplant.

Methods: Current samples from 15 wait-listed highly sensitised patients (HSPs) with existing HLA IgG SAB results were selected and re-tested using the OneLambaTM C1qScreen to detect C1q-binding antibodies. We used the NHSBT matchability calculator and estimated chance of transplant tools (http://odt.nhs.uk/pdf/NHSBT_Tools.pdf) to assess the impact of delisting C1q negative specificities. Statistics were calculated using GraphPad Quickcalcs.

Results: Calculated reaction frequency (cRF) defined by IgG HLA-specific antibodies was (MF1 ≥ 2000) -100% (n=9), 99% (n=2), 98% (n=2), 96% (n=1) and 93% (n=1)). The overall change in opportunity by listing only C1q-binding HLA antibodies as unacceptable is shown in table 1. This produced drop in cRF (p=0.057) and matchability points (p=0.006). As a result, there was a predicted increase in the offer rate (p=0.053) and 1-year estimated chance of transplant (p=0.029) compared to listing total HLA antibodies. Patients that demonstrated an increased chance of transplant showed a 3 to 5 fold increase.

Conclusions: This study shows a strong potential improvement in transplant opportunities for HSPs by selectively listing preformed C1q-binding HLA antibodies instead of total IgG HLA antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor bodies instead of total IgG HLA-antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor bodies instead of total IgG HLA-antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor bodies instead of total IgG HLA-antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor bodies instead of total IgG HLA-antibodies. This approach may push the boundaries of delisting in the context of novel desensitisation on the deceased donor bodies instead of total IgG HLA-antibodies.

Table 1: Differences in output after applying C1q assay based delisting (compared with IgG SAB assay)

<table>
<thead>
<tr>
<th>Output</th>
<th>Mean (range)</th>
<th>Median (IQR)</th>
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<tbody>
<tr>
<td>cRF reduction</td>
<td>12% (0-36%)</td>
<td>4% (0-6-15%)</td>
</tr>
<tr>
<td>Matchability point reduction</td>
<td>1.07 (0-5)</td>
<td>1 (0-1.5)</td>
</tr>
<tr>
<td>Increase in offer rate (n=10000)</td>
<td>54.45 (0-3820)</td>
<td>77 (30-854)</td>
</tr>
<tr>
<td>Increase chance of transplant</td>
<td>6% (0-21%)</td>
<td>0% (0-10%)</td>
</tr>
</tbody>
</table>

Figure 1: Perfusion measurements after 10 min EVLP of human donor lungs with logistical or medical indication for EVLP.
A: Unfractioned Plasminogen Activator Receptor; B: Plasminogen Activator Inhibitor-1; C: D-dimer and D: Prothrombin Fragment 1+2.
DONOR QUALITY OF LIFE AND PSYCHOSOCIAL OUTCOMES AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: Living donor kidney transplantation (LDKT) is the treatment of choice for end-stage renal disease. Data regarding the post-donation welfare of donors is paramount to further improve and promote LDKT. This study aimed to analyse factors relating to donors' experiences and how these impact their perceived quality of life and other psychosocial outcomes.

Methods: A systematic literature search of Pubmed, EMBASE and MEDLINE was conducted using relevant keywords and MeSH terms. This was supplemented by snowballing and a grey literature search. Data was collected on discrete donor outcomes such as health-related quality of life (HRQOL), and psychosocial outcomes which encompass donor mental and physical health, financial burden, attitudes towards donation, and their relationships with the recipients.

Results: 27 studies (2017 – 2023) were analysed including 7746 donors. 60% of studies used a validated HRQOL questionnaire tool. Generally, physical utility scores in donors remained comparable to the general population. 6 studies suggested challenges to mental health post-donation influenced by several pre-disposing factors, though 4 studies demonstrated the opposite, where improvements to psychological quality of life (QOL) were seen. Most studies showed that recovery for donors had no interference with activities of daily living. A small subset of donors met criteria for chronic post-surgical pain and persistent clinical fatigue. These patients tended to show dissatisfaction with the donation, in contrast to the general donor cohort. Positive relationships between donation, in contrast to the general donor cohort. Positive relationships between donors and recipients were demonstrated. However, it was shown that a proportion of donors experienced economic losses related to donation.

Conclusions: LDKT is generally very well perceived by donors and does not affect their welfare. However, adverse effects on donor mental QOL, chronic pain, and economic status can be experienced by a minority of patients. Further research is required to identify and mitigate predictors of adverse effects on donor wellbeing post-LDKT.

POST-TRANSPLANT DIABETES MELLITUS IN KIDNEY TRANSPLANT PATIENTS – ONE CENTRE PILOT, PROSPECTIVE STUDY

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Background: Post-transplant diabetes mellitus (PTDM) is a frequent metabolic complication after organ transplantation and is associated with increased risk of graft failure, cardiovascular disease, mortality and infections. Identification of PTDM risk factors is important for prevention strategies, risk stratification and management of the immunosuppressive protocol.

Methods: We prospectively analysed risk factors and clinical consequences of PTDM in patients after kidney transplantation performed in our centre between 2018 and 2022, in the group of 129 consecutive transplant recipient without diabetes before transplantation (M79, F51), mean age 47.6 years. Diabetes was defined as the requirement of pharmacotherapy at least 3 months after transplantation or was based on the oral glucose tolerance test (OGTT). Time of observation was 3-78 months.

Results: The incidence of PTDM was 21.5% (28/130). Patients who developed PTDM were older (p=0,015), had a higher Charlson comorbidity index (p=0,038) and a higher BMI (p=0,04). None of the factors was an independent risk factor for PTDM. The mean fasting glucose level before transplantation was statistically significantly higher in the group of patients that later developed diabetes (p=0,017). No difference in sex, method and time of dialysis, number of mismatches, ischaemic time, frequency of acute rejection, delayed kidney function, reoperation and kidney graft function and also in the baseline serum level of insulin, homocysteine, uric acid, C-peptide, albumin, lipid profile, HOMA-IR, QUICKI, were found. Kaplan-Meier survival curves of patients and grafts with and without PTDM did not differ. Tacrolimus was a part of the immunosuppressive scheme in 89% of PTDM patients and in 78% of non-PTDM patients (p=0,05).

Conclusions: Risk factors for the development of PTDM after KTX are older age, higher comorbidity and BMI. General risk factors for diabetes appear to be more important for the development of PTDM than those associated with transplantation. Simple indicators such as blood glucose levels and HBA1c indicate an increased risk of PTDM.

MEASUREMENT OF THE IMMUNOSUPPRESSANT POSSESSION RATIO BY CLINICAL PHARMACISTS CAPTURES A NON-ADHERENCE ASSOCIATED WITH ANTIBODY-MEDIATED REJECTION

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Background: Transplant physicians do not yet have a quantifiable and objective method for measuring non-adherence to immunosuppressants. Our objective was to test the feasibility of calculating an immunosuppressant possession ratio (IPR) in order to quantify the level of non-adherence at the time of antibody mediated rejection (ABMR).

Methods: IPR was calculated in a non-interventional prospective cohort of 91 kidney transplant recipients (KTR) using the following formula: number of pills collected at the pharmacy / number of pills prescribed over the study period x 100. In a retrospective cohort of 451 kidney transplant biopsies, we performed a case-control study to compare the 6-month IPRs between 26 cases of ABMR and 26 matched controls, with interstitial fibrosis and tubular atrophy (IFTA).

Results: We were able to calculate a real-time IPR in the 91 patients of the prospective cohort. Patients with an IPR<90% had more frequently a tacrolimus trough level coefficient of variation >30% than patients with an IPR >100% (66.7% vs 29.4%, p=0.05). They were also more frequently non-adherent to outpatient visits (66.7% vs 23.2%, p<0.01). In the case-control study, patients with ABMR had lower 6-month IPRs than patients with IFTA (76.5% vs 99.5%, p<0.001). In the 26 KTRs with ABMR, non-adherence was more often diagnosed by a 6-months IPR<90% than by clinical suspicion (19 vs 8, p=0.02).

Conclusions: IPR is an objective and quantifiable tool which improves the diagnosis of non-adherence in KTRs with ABMR.
Hypertension is more prevalent in liver transplant (LT) recipients than in the general population. Furthermore, hypertension is an important risk factor for cardiovascular diseases, which are a leading cause of mortality in LT recipients. Therefore, in this study, we aimed to investigate the prevalence of and risk factors for hypertension in LT recipients.

Methods: LT recipients were included from the Danish Comorbidity in Liver Transplant recipients (DACOLT) study. Participants underwent a physical examination including measurements of height, weight, and blood pressure (BP), and answered a thorough questionnaire regarding lifestyle. Additionally, data on medication and LT-specific variables were obtained from reviews of medical charts. Hypertension was defined according to Joint National Committee guidelines as a systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg and/or use of antihypertensive medication. We investigated risk factors associated with hypertension using a logistic regression model adjusting for age, sex, and BMI.

Results: We included 498 LT recipients in the study, and of these, 305 (61%) had hypertension. Among the participants with hypertension, 157 (51%) had a measured blood pressure fulfilling the definition of hypertension at the physical examination, and 229 patients (75%) received antihypertensive treatment. In a model adjusted for age, sex, and BMI, hypertension was associated with age (OR 1.81 [1.56;2.10], per decade, p<0.001), male sex [OR 1.50 [1.00;2.23], p=0.049], and BMI ≥30 [OR 2.36 [1.34;4.15], p=0.003]. Table 1. Other risk factors including smoking, time since liver transplantation, and use of certain medications were also investigated.

Conclusions: We found a high prevalence of hypertension in LT recipients, and we found hypertension to be associated with age, male sex, and obesity. Furthermore, we found a high percentage of participants with measured hypertension but no antihypertensive treatment, suggesting increased attention on hypertension in LT recipients could be beneficial.

<table>
<thead>
<tr>
<th>Table 1: Risk factors associated with hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per decade</td>
</tr>
<tr>
<td>Male sex</td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>BMI 20-24.9</td>
</tr>
<tr>
<td>BMI 25-29.9</td>
</tr>
<tr>
<td>BMI≥30</td>
</tr>
<tr>
<td>Physical activity</td>
</tr>
<tr>
<td>Inactive</td>
</tr>
<tr>
<td>Moderately inactive</td>
</tr>
<tr>
<td>Moderately active</td>
</tr>
<tr>
<td>Very active</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Never smoker</td>
</tr>
<tr>
<td>Current smoker</td>
</tr>
<tr>
<td>Previous smoker</td>
</tr>
<tr>
<td>Transplant related variables</td>
</tr>
<tr>
<td>Ever rejection</td>
</tr>
<tr>
<td>Time since liver transplantation, per decade</td>
</tr>
<tr>
<td>Ciclosporin vs. Tacrolimus</td>
</tr>
<tr>
<td>Everolimus vs. Tacrolimus</td>
</tr>
<tr>
<td>Mycophenolic acid vs azathioprine</td>
</tr>
</tbody>
</table>

Tested in a logistic regression model adjusting for age, sex and BMI.
P515

THE EFFECT OF STEM CELL-DERIVED EXTRACELLULAR VESICLES ON ISCHEMIA REPERFUSION INJURY IN SOLID ORGAN TRANSPLANTATION: A SYSTEMATIC REVIEW

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1UZ KU Leuven, Abdominal Transplantation, Leuven, Belgium

Introduction: Stem cell-derived extracellular vesicles (SC-EVs) are paracrine mediators involved in tissue repair, regeneration, and immunomodulation. Protective effects of SC-EV against ischemia-reperfusion injury (IRI), still a major hurdle to the success of solid organ transplantation, have been reported. We conducted a systematic review to study the evidence of SC-EV therapy in experimental models of heart, lung, liver, kidney and intestinal IRI and transplantation.

Methods: PubMed, Embase and Web of Science were searched for studies on SC-EV therapy for cardiac, renal, hepatic, pulmonary and intestinal IRI until August 19th, 2022. Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) and the SYStematic Review Center for Laboratory animal Experiments (SYRCL) guidelines for the systematic reporting of animal studies were followed. Results: 4153 unique articles were identified, of which 96 after screening and data extraction were included (figure 1). All included studies (heart=32, lung=4, liver=21, kidney=38, intestine=1) reported improved organ injury or function. SC-EVs exerted protective effects that were observed across all organs. First, they displayed anti-inflammatory effects as shown by reduced expression of pro-inflammatory cytokines and oxidative stress. Secondly, SC-EV exerted immunomodulatory capacities by reducing leukocyte infiltration and stimulating autophagy. Third, pro-regenerative effects were observed through increased proliferation and angiogenesis, and reduced apoptosis. Overall reporting quality as assessed by SYRCL’s risk-of-bias tool was poor.

Conclusion: This systematic review shows that SC-EVs reduces IRI in heart, kidney, liver, lungs and intestine. Before translation into humans, studies on optimal dosage, timing and stem cell sources are warranted in addition to the ability to produce sufficient quantities to treat human-size organs.

Figure 1. PRISMA Flow Diagram on the results of the systematic literature search

Records identified through initial database search (up to 04-20-2020) (n = 5953) / search updated 05-01-2020 (n = 7962) -
Records after duplicates removed (n = 4335)
Records screened (n = 4335)
Records excluded after title and abstract screening (n = 3667)
Records excluded after full text screening (n = 668)
Full-text articles included for eligibility (n = 26)
Full-text articles excluded (n = 251)
No RCT (n = 196) No stem cell-derived EV therapy (n = 50)
Outcome irrelevant (n = 18) Not retrievable (n = 4)
Wrong publication type (n = 4)
Studies in cardiac ischaemia reperfusion (n = 30)
Studies on renal ischaemia-reperfusion (n = 38, 37, 36, 116, 111, 110)
Studies on pulmonary ischaemia reperfusion (n = 4, 3, 6, 1, 111)
Studies on hepatic ischaemia reperfusion (n = 21, 20, 111, 100, 55, 55, 1)
Studies on intestinal ischaemia-reperfusion (n = 1, 111, 110)

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THE IMPACT OF COORDINATION OF RENAL AND PANCREATIC ORGAN DONATION AND TRANSPLANTATION ON COLD ISCHEMIA TIME - EXPERIENCE OF THE CENTRE

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Background: The results of the analyzed publications and the research conducted in our clinic, “cold ischemia time” (CIT) ≤8h is an important predictor of good graft function and lower number complications. The study analyzed cold ischemia time depending on the type of transport, the experience of the surgical team and other important factors.

Methods: The aim of the study was to identify the factors that can shorten CIT to the greatest extent. The work analyzes the coordination of organ donations: pancreas and kidney with pancreas in the years 2015-2023. 124 coordination activities were completed with transplantation were evaluated. All organ donation coordinations were divided into those where CIT > 8h and where CIT ≤ 8h.

Variables analyzed in the thesis: 1. distance of the donor hospital from the transplantation center (>200 km<300 km<500 km)<700 km) 2. type of transportation of the procurement team (collection at the transplant center/vehicular transport/air transport) 3. transport time of the team harvesting organs for transplantation (<1h<2h<4h<5h) 4. experience of the organ harvesting surgeon (advanced/intermediate)

Results:

<table>
<thead>
<tr>
<th>Type of transport of the transplant team</th>
<th>CIT ≤8h N=42</th>
<th>CIT &gt;8h N=42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ donation at a transplant center - 51%</td>
<td>22/41</td>
<td>19/23</td>
</tr>
<tr>
<td>Wheeled transport - 44%</td>
<td>12/41</td>
<td>10/23</td>
</tr>
<tr>
<td>Air transport - 5%</td>
<td>8/41</td>
<td>3/23</td>
</tr>
</tbody>
</table>

Conclusion: The process variable that was most significant in speeding up the procurement-transplantation process was the distance of the donor hospital from the transplantation center. The organ donations made in a transplant center or at a distance of up to 200 km (up to 1.5 h of transport) or using air transport significantly shortened the cold ischemia time. Another factor affecting the CIT was the experience of harvesting the surgeon.

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EXTRACELLULAR MATRIX - KEY COMPONENT IN THE PRODUCTION OF FUNCTIONAL AND PHYSIOLOGICALLY STABLE ARTIFICIAL PANCREATIC ISLETS USING THE INKJET METHOD

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Background: There are clinical trials using stem cell-derived β cells as an innovative and future-proof solution for the treatment of T1D. These cells are expected to replace the non-functioning islets. For this it’s necessary to create their 3D conformations, which has been proven in in vitro studies. Attention should also be paid to the possibility of clinical application. The process of transplanting cluster β-cells, even from 3D culture, into the portal vein carries a high risk of damage, lack of function, as well as the risk of an undefined final location of the cells. The aim of this experiment was to assess the viability and functionality of β cells in artificial 3D bioprinted inklet pancreatic islets (PI).

Methods: INS-1E cells were used in the study. Two bioinks were used as the encapsulation carrier: 2% Methacyrloyl hyaluronic acid (HAMAX)+20% Methacrylated gelatin (GelMa) with LAP (GROUP:ECM_INS); 2% HAMAX+20% GelMa+LAP with ECM (GROUP:ECM_INS). The control group was 2D culture. Cell functionality was assessed in the GSIS test and viability by the FDA/PI test. Treatment was performed in 3D inklet pancreatic islets (PI).

Results: After 21 days, the encapsulated cells were shown to be virtually 100% viable. Dead cells were visible only in the control samples (no more than 15%). Cells suspended in the tested variants of hydrogels retained a stable structure. On day 2 of the experiment, there was no difference in cell activity. Groups of encapsulated cells showed significantly improved functionality from day 7 onwards. Both groups showed over 30% higher activity compared to the control group. On the 14th day of the experiment, cells suspended in biokin with ECM showed a definite superiority in response to the administered glucose. Compared to the control group, the increase was over 50% (p=0.0005), and with the H+G_INS over 30% (p=0.0073). Day 21 also showed a functional advantage in the ECM_INS, almost 30% higher activity compared to the control group (p=0.0047).

Conclusions: The 3D conformation is a key component for maintaining the proper functionality of β cells. In addition, the developed bioink composition and the method used enable the production of stable 3D structures that can be transplanted in a stable and safe manner without disintegrating under physiological temperature conditions.
Background: Organ transplantation has become a worldwide practice, bringing patients a more prolonged, and improving their quality of life. However, patients die due to a short number of donors; therefore, donation education and awareness represent a challenge. We aim to evaluate the perception of donation of the institutions promoting donation and life (INSPROVIDA) education program in two transplant centres.

Methods: Cross-sectional study in two hospitals through virtual surveying, a test was applied to health and administrative staff between March 2022 and April 2023. The survey included 12 questions and we evaluated donation-related myths, knowledge, religious beliefs and law. Results: Total population were 5100 workers, the sample included 1436 respondents (28.1%), mean age was 34.3 years, 74.7% were female in one of the centers, 34.9% were nursery technicians and participants worked more frequently in the Emergency department (14.3%). When asked about organ trafficking nearly 67.7% believed it existed. When asked about our country’s laws on organ donation the vast 69.1% did not know them and 56.2% were not familiar with the National Institute of Health donation registry. Also, 61.2% of the sample had not expressed their willingness to be organ donors with their family and/or friends.

Conclusions: Health and administrative staff's perception of donation in two hospitals showed the role of education programs. Our results demonstrated myths still are present and such phenomena might impact donation rates. There is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a need to promote health education focused on organ donation since there is a 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organ donation since there is a need to promote health education.
Background: Kidney transplant is the best therapy that can be offered to patients with advanced chronic kidney disease (ACKD). One of the main transplant challenges is to achieve a balance between the level of immunosuppression against the increase in complications. Assumed risks are greater in groups of patients that need desensitization in the case of living donor kidney transplantation ABO incompatible (ABOi) and HLA incompatible (HLAi). Our objective was to compare the results of Living Donor Kidney Transplantation ABOi vs HLAi.

Methods: We carried out a study of Living Donor Kidney Transplantation ABOi (n=61) and HLAi (n=27) from 2008 to 2021. Patients’ age ranged between 53 +/- 12 (ABOi) and 50 +/- 11 (HLAi). Donor waiting times for both groups were 19.4 +/- 18.8 months and 86.8 +/- 87.6 months, respectively. Incompatibility rates were 4.1 +/- 1.5 in ABOi vs 3.7 +/- 1.1 in HLAi. Follow-up, measured in months, was 66 +/- 41 (ABOi) vs 78 +/- 56 (HLAi).

Results: Sessions of plasmapheresis/immunoabsorption were 6.5 +/- 3.6 in ABOi vs 8.9 +/- 2.7 in HLAi. Incompatibility HLA was 4.2 +/- 1.6 in ABOi vs 3.7 in 1.1 HLAi (p=0.03). Immunosuppression with Basiliximab was 54% (within the ABOi group) and 45% (HLAi group); meanwhile, immunosuppression due to Thymoglobulin was 5% (ABOi) and 14% (HLAi). The incidence of acute rejection was 11.5 % for ABOi (cellular rejection 86% and 14 % mixed rejection) vs 17.2 % for HLAi (cellular rejection 60%, antibody-mediated rejection 40%) (p=0.05). Patient survival rate was 91.8% in ABOi vs 64.3% in HLAi (p=0.09). Both groups presented similar rates of CMV infection, 25% ABOi vs 29% HLAi (p=0.6), compared to 11.6% BK infection in ABOi and no cases in HLAi (p=0.06).

Conclusions: Kidney transplantation from a living donor using desensitization techniques is an effective option for patients with ACKD, resulting in high patient and allograft survival rates. Compared to the ABOi group, there are higher complications associated with patients in the HLAi group due to the greater complexity of the transplant and the degree of immunosuppression.
Background: In renal transplant recipients, compliance with medical therapy is vital. Non-adherence is considered a major risk factor for graft failure. Most literature defines adherence as self-based immunosuppression compliance but does not consider other relevant factors such as consult and procedures compliance. Therefore, this study aims to describe adherence prevalence in our patients and the factors related to non-compliance.

Methods: This cross-sectional study included 1030 renal transplant patients between January 2019 and July 2021. Sociodemographic, clinical, and adherence-related variables were obtained based on clinical records and a semi-structured interview done by the mental health group. A bivariate followed a descriptive analysis. A forward logistic regression was performed for non-compliance.

Results: Patients had a median of 47 years, and 58.1% were male. Non-adherence was presented in 30.7%, immunosuppression non-compliance in 25.9%, and low immunosuppression blood levels in 15.7% of patients. The non-adherent patients were younger, with a higher prevalence of males, single, transplanted for other transplant groups, had a longer time after transplantation, psychopathological diagnosis, and more reinforcement education by only nursing. Older age and multidisciplinary reinforcement education were protective factors. On the other hand, poor social support, psychopathology diagnosis, and longer time after transplantation presented as non-adherence risk factors.

Conclusions: Non-compliance is wider than medication non-compliance and is presented in approximately one-third of renal transplant recipients. Therefore, there is a need to consider the related factors in the health follow-up and encourage future research in modifiable factors interventions, such as social support and education reinforcement interventions, aiming to increase compliance and achieve better outcomes for renal transplant patients.
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A POLICY OF VERY SHORT PRESERVATION TIME IMPROVES THE RESULTS OF SIMULTANEOUS KIDNEY- PANCREAS TRANSPLANTATION FROM EXTENDED CRITERIA DONORS

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Background: According to the International Pancreas Transplantation Registry (IPTR), the risk of pancreas graft loss from early technical failure (TF) is significantly increased by preservation time (PT) ≥ 12 h, donor age ≥ 30 years, donor and recipient BMI ≥ 30 kg/m², cardio/cerebrovascular (CCV) death of donors and donation after circulatory death (DCD). With the current shortage of grafts, we decided from 2015 to expand the criteria of grafts regarding donor age and CCV death but aimed to achieve a very short PT (< 8 h).

Methods: We analyzed our cohort of 105 simultaneous pancreas-kidney transplantsations performed for type 1 diabetes between July 2015 and December 2022. The characteristics of recipients and donors, the rate of TF, as well as graft and patient survival were compared to the IPTR 2022 data.

Results: Median age of donors was 36 years and 65.7% of them were older than 30. The main cause of death was CCV (57%). Median donor BMI was 23 kg/m² and none had a BMI ≥ 30 kg/m². DCD donors accounted for 3.8% of cases. Recipient median age and BMI were 40 years (IQR 33-45) and 23 kg/m² (22-27). All transplantations were performed with systemic venous and enteric pancreatic drainage. Median PT was 397 min (334-455). In only 14% of cases, PT was greater than 8 but lower than 9 hours. 7 patients lost their pancreatic drainage. Median age of donors was 36 years and 65.7% of them were older than 30. In the context of shortage of pancreas grafts, a policy of very short PT (< 8 h) affords the use of expanded criteria grafts with a higher frequency of donor CCV death (Table).

Conclusions: In the context of shortage of pancreas grafts, a policy of very short preservation time (<8h) affords the use of expanded criteria grafts with similar results, compared to standard transplants. With such a policy, grafts from donors aged 30-42 years and/or deceased from cardiovascular death may provide similar results, compared to standard transplants. With such a policy, grafts from donors aged 30-42 years and/or deceased from cardiovascular death may provide similar results, compared to standard transplants.
We systematically reviewed PubMed, Embase, web of Science and Cochrane library using concepts “kidney”, “metabolism” and “perfusion” to identify preserved metabolites were used to study active metabolic pathways (mostly $13C$-glucose and $13C$-labeled fatty acids (FAG)). Kidneys are metabolically active during hypothermic perfusion, regardless of the perfusion setting. This metabolism is a complex interplay of different processes, whereby glucose, acid (AA) and FA metabolism act upon each other, citric acid cycle and overall energy metabolism. Kidney condition (control vs. ischemic), perfusate, perfusion length, and oxygen level influence this metabolism. Oxygenation seems to be a key factor in the regulation of metabolic pathways. Kidney condition (control vs. ischemic), perfusate, perfusion length, and oxygen level influence this metabolism.

Conclusions: This methodology has allowed us to reach a full consensus on important technical and interpretational topics regarding pre-implantation biopsy in the process of ECD graft assessment.
PERCEPTIONS, EMOTIONS AND SOCIAL REPRESENTATIONS RELATED TO ORGAN DONATION IN HEALTHCARE WORKERS: A QUALITATIVE RESEARCH STUDY AFTER THE COVID-19

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Background: The study aims at analyzing the perceptions, emotions and representations related to organ donation in healthcare workers of Critical Areas, with a special focus on the procurement difficulties related to the COVID-19. This scenario entailed a change for most medical procedures, that needed to be reviewed and adapted to the new situation. The COVID-19, in fact, had a strong impact on procurement activity and on the attitude of healthcare workers towards organ donation.

Methods: The study sample involves 100 healthcare professionals (doctors and nurses) from Intensive Care and Emergency Departments of 9 hospitals, distributed in 3 Italian regions (Lombardy, Lazio and Sicily). Individual anonymous open-ended interviews have been conducted, exploring the experience of organ donation during the pandemic on three facets: Emotions, Organization and Future perspectives. Interview texts were analyzed using a content analysis carried out by two independent judges.

Results: Data analysis showed specific emotions of healthcare workers related to COVID-19 experience (mainly fear and helplessness) and the use of primitive defense mechanisms, such as denial and repression, to face the emotional experience. On the other hand, organ donation brought restorative emotions (such as hope and satisfaction) which seem to represent a protective resource for the workers. For the organizational facets, COVID-19 had an impact especially on the logistic related to organ donation and on the relationships between healthcare workers and the families of potential donors. Considering the future perspectives, the need for adhoc in-the-field training emerged as well as the need to enhance social awareness toward organ donation, since an ambivalent attitude in the general population has been perceived.

Conclusions: Organ donation activities has represented a protective factor for the healthcare workers during the pandemic, since they fostered a feeling of continuity in daily work experience. However, some critical issues appeared, as the difficulty to communicate to the families due to pandemic restrictions. This work gives various hints to improve the experience of health workers in organ donation during critical times, suggesting the implementation of specific training focused on emotion management strategies.

VALIDITY OF CT DEFINED BODY COMPOSITION AS A PROGNOSTIC FACTOR FOR LONG TERM FUNCTIONAL OUTCOME IN KIDNEY TRANSPLANTATION RECIPIENTS

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Background: Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength which increases the risk of adverse postoperative outcomes. Its prevalence is markedly higher in kidney transplant candidates than in the general population.

Methods: We studied the impact of computed tomography (CT) defined preoperative sarcopenia on postoperative physical functional outcomes (grip strength, 4 meter walking test, timed up and go, sit to stand) at 6 months follow up. A total of 107 patients transplanted between 2015 and 2019 were included in this single center study.

Results: Mean age was 60.3 (±13.1) and 68.2% of patients were male. Ten patients (9.4%) were identified as sarcopenic. Sarcopenic patients were younger (20.9 (±2.7) vs. 27.4 (±3.9)), more likely to be female (60% vs. 28.9%), and had an increased dialysis vintage (19.2 (±16.3) vs. 14.0 (±20.0)) in comparison to their non-sarcopenic counterparts. In univariate analysis they had a significantly lower body mass index (BMI), skeletal muscle area (SMA) and skeletal muscle index (SMI) (P<0.001). In multivariate regression analysis SMI was significantly associated with grip strength and timed up and go performance.

Conclusions: In conclusion, we identified a significant association between low SMI (sarcopenia) and poorer physical functioning with respect to hand grip strength and timed up and go tests at six months post kidney transplantation. These results could be used to preoperatively identify patients with an increased risk of poor postoperative physical functional outcome, allowing for preparative interventions to mitigate these risks.

YOUR DEATH, MY LIFE" - A FOCUS GROUP STUDY REGARDING THE ATTITUDES OF THE GREEK POPULATION TOWARDS ORGAN DONATION AFTER CIRCULATORY DEATH

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Background: There has been growing interest in donation after circulatory death (DCD) in recent years with DCD accounting for about 20% of all deceased donor transplants worldwide. In a European survey, 26 countries reported running DCD programs and 17 countries declared no DCD activity, due to a variety of reasons from legislative to organizational obstacles, yet with half of them interested in developing DCD. Greece appeared reluctant towards DCD. The current study aims to identify and understand the attitudes of the Greek population towards DCD in order to inform future policy.

Methods: We conducted a focus group study with members of the general population across regions, age, socioeconomic and educational background about the attitudes and perceptions regarding organ donation and transplantation, and brain death vs circulatory death. Data were analysed using thematic analysis.

Results: Participants took a positive stand towards organ donation in general as part of an altruistic view of human existence. We identified factors who would favour consent to donation of a family member, as the irreversibility of the donors’ condition, a sense of wasting valuable organic material if not agreeing to donation and feelings of doing something important. Lack of adequate knowledge about the definitions of death and the donation procedure, mistrust towards the health system and hope of bringing back to life the donor, functional counterproductive towards the decision to donate. Participants made no difference between DCD and DBD in terms of supporting organ donation, but expressed that the type of death and its perception of permanence and non-reversibility would influence their decision. Brain death was perceived as more “certain” and there were some doubts regarding the finality of circulatory death. Still all agreed that DCD should be an option. Participants raised concerns as to whether the family is the right party to decide and emphasized the importance of the individual decision for or against donation during lifetime.

Conclusions: DCD would be a viable option complementary to DBD. Its specific characteristics should be taken into account in all stages of donation and transplantation process and DCD shall be implemented within a broader context that would favour organ donation and includes multidisciplinary efforts.
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**RACE-FREE VERSUS RACE-DEPENDENT ESTIMATED GLOMERULAR FILTRATION RATE AMONG KIDNEY-TRANSPLANTED PATIENTS ONE YEAR AFTER TRANSPLANTATION**

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**Background:** Glomerular filtration rate (GFR) is a measure of kidney function for use in patient diagnostics and research. In our hospital, estimated GFR (eGFR) is regularly done with the CKD-EPI formula (2009) which calculates eGFR by using serum creatinine and incorporate age, sex and race. However, race is not a known factor for the personnel at the central laboratory, so every patient is counted as non-black. We know from earlier studies that eGFR often differ from measured GFR by ±30% (1) and it is of interest to find the most reliable estimation of GFR. A new GFR formula which is not dependent on race has recently been developed (2021). In this study, we look at the best way of estimating GFR in renal transplant recipients by comparing the two formulas, using GFR measured by iohexol clearance as reference.

**Methods:** We collected data 1 year after kidney transplantation in 1274 transplant recipients. GFR was estimated with CKD-EPI 2009 (with race) and CKD-EPI 2021 (race-free), respectively, and measured GFR (reference) was assessed by iohexol-clearance. The two eGFR formulas were compared and presented as a Bland-Altman plot. P30 values of the two eGFR formulas were calculated with measured GFR (iohexol clearance) as the gold standard to assess accuracy. A chi square test was performed to evaluate the significant difference between the two tests with regards to difference in P30 values.

**Results:** As shown by a Bland-Altman plot, the difference between the two GFR estimates increases with higher eGFR levels and peaks at eGFR 70. The peak is related to a larger spread in data readings indicating discrepancy between the two eGFR estimates. CKD-EPI race-free 2021 estimation gives on average a higher GFR value. The total of eGFR values with less than 30% difference (P30) from measured GFR, was 77.4% with the CKD-EPI (2009) calculations and 69.9% with the CKD-EPI race-free (2021) calculations. The CKD-EPI (2009) estimate gives a significant higher P30 compared to the CKD-EPI race-free (2021) equation (p<0.0001).

**Conclusions:** In our population, the CKD-EPI (2009) equation is a more appropriate tool to estimate GFR compared to the new CKD-EPI (2021) race-free formula. The results are comparable with recent studies on kidney transplanted patients. Reference: LA Inker et al. N Engl J Med 2021; 385:1737-1749 DOI: 10.1056/NEJMoa2102953

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**P535**

**RECIPIENT WARM ISCHEMIA TIME AND ITS IMPACT ON GRAFT FUNCTION AND HISTOLOGY AT 3 MONTHS**

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**Background:** Previous studies showed that longer WIT is associated with an increased risk of delayed graft function and poorer graft survival. Some studies even suggest an association between anastomosis time and patient survival. In an original French transplantation cohort study including predominantly extended criteria donors (ECD), we aimed to evaluate the effect of WIT on graft function and histology at 3 months.

**Methods:** All patients admitted for a kidney transplant at a single center (Tenon Hospital, Paris) between July 2017 and December 2019 were included. We evaluated clinical, biological, radiological and histological data prospectively up to 3 months post-transplant.

**Results:** 175 cadaveric kidney transplants were performed during the study period. We only included the 147 patients in whom the anastomosis time was known. 58% had an ECD based on UNOS criteria. Median recipient age was 56 years (interquartile range 44-61). Median donor age was 61 years (49-71). Median recipient BMI was 24.0 kg/m² (21.9-27.3). Median cold ischemia time was 14.3 hours (11.9-17.9). Median WIT was 58 minutes (43-7143 (29.2%) patients had delayed graft function (DFG) or primary non-function (PNF). Median 3-month estimated glomerular filtration rate – calculated using the CKD-EPI equation – was 41.1 ml/min/1.73 m² (30.4-64.4). WIT was associated with DGF/PNF in both univariate and multivariate analyses. WIT was 71 minutes in the DGF/PNF group (n = 43) and 59 minutes in the no DGF/PNF group (n = 104) (p=0.032). In the ECD subgroup, no association between WIT and DGF/PNF nor 3-month eGFR was found. With regards to histology, no association was found between interstitial fibrosis at 3 months post-transplant and a longer anastomosis time in the general cohort (p = 0.805).

**Conclusions:** Recipient WIT was longer in our study, compared to historic cohorts. In our population, most patients received ECD kidneys, which is not associated with DGF and PNF. We found no association between recipient WIT and histology or eGFR at 3 months after transplantation in the general and ECD donor cohorts.

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**IMMEDIATE VERSUS DELAYED ABDOMINAL WALL CLOSURE AFTER PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION USING A GORE-TEX® PATCH: A SINGLE CENTER EXPERIENCE**

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**Background:** Living donor liver transplantation (LLT) is a demanding procedure that often requires a transient expansion of the abdominal wall. Delayed abdominal closure (DC) is indicated in cases with post-reperfusion swelling, an improper graftrecipient weight ratio (GRWR) and a frail portal inflow.

**Methods:** The use of a Gore-Tex® patch for a transient abdominal wall expansion was assessed in this retrospective study. Primary end-points were the occurrence of microbial contamination and abdominal wall hernias. Secondary endpoints include survival rates as well as early postoperative complications. We enrolled 66 LLTs performed in infants between 2002 and 2020 at the Medical University of Innsbruck.

**Results:** DC was performed in 34 patients (51.5%), immediate closure (IC) in the remaining 32 (48.5%). Children requiring DC were younger compared to IC (DC: 0.0 – 0.0 vs. IC: 1.0 – 7.5) p < 0.001), smaller (DC: 6.2 [5.06 – 7.06] vs. IC: 9.1 [7.04 – 22.22], p < 0.001), and had a higher GRWR (DC: 4.4 [3.33 – 5.03] vs. IC: 2.35 [1.42 – 3.18], p < 0.001). Significantly more microbial contamination was observed in the DC group compared to the IC group (DC: 4.4 [13.33 – 17.33] vs. IC: 1.0 [0 – 7.5], p = 0.001). No abdominal wall hernias were recorded in our cohort. Infants in the DC group required a median of 3 (2 – 4) operations until definite abdominal closure. Regardless, duration of hospital stay was with a median of 51 vs. 44 days (p < 0.001) in DC and IC group (p = 0.077). Similar frequencies of vascular, biliary and bleeding complications were observed. The technique of abdominal wall closure did not influence patient (PS) and graft survival (GS) (1-year PS: IC: 96.9% vs. DC: 97.1%; 1-year GS: IC: 87.5% vs. DC: 93.9%).

**Conclusions:** Primary abdominal closure can be achieved in approximately half of the cases. Smaller infants and a higher GRWR are risk factors for DC. While a higher rate of microbial contamination was seen, this did not translate into a longer hospital stay and resulted in similar survival and postoperative complication rates without added risk for hernia development.
ASYMPTOMATIC GRAFT INFECTION

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Background: Urinary Tract Infections represent the most common infection post-transplant and can have variable presentations. We describe a cohort of renal transplant recipients who had evidence of graft infection on allograft biopsy and were asymptomatic. Graft infection was defined as neutrophil cast or neutrophilic tubulitis, interstitial infiltrates with predominant neutrophils and no evidence of rejection or glomerulonephritis.

Methods: 123 kidney transplant recipients were included in the cohort. Of these, 95 were protocol biopsies, and 28 had a biopsy for elevated creatinine. We compared the above to the whole cohort to understand the risk factors for asymptomatic graft infection. We then compared it to a 1:3 matched cohort to study the impact of asymptomatic graft on graft survival.

Results: The mean age for the cohort was 55 years, 52% were females, and 78% received deceased donor transplants. The risk factors for asymptomatic graft infection on multivariate regression were recipient female sex (1.89), DM (2.48), and deceased donation (1.69). Most of the asymptomatic graft infection was identified at a 4-month biopsy (30%), 52% had positive urine cultures, 40% had negative, and 9% did not have urine cultures at the time of the biopsy. Escherichia coli was the most common bacteria on urine culture. In the culture-negative group, 14% had a positive culture in the 3 months prior to the biopsy, 39% had urinary tract infections in the next 6 months of the biopsy diagnosis, and 27% had positive urological history. The subjects with asymptomatic graft infection had inferior graft survival compared to the overall cohort. On subgroup analysis, there was an inferior graft survival in the group with recurrent pyelonephritis 2.88 (1.37-6.06), and those with renal dysfunction at the time of biopsy,2.59 (1.14-5.9). There was no difference in graft survival in patients with recurrent pyelonephritis and its association with poor graft survival, particularly in those with recurrent pyelonephritis and AKI.

Conclusions: We describe a cohort of subjects with Asymptomatic pyelonephritis and its association with poor graft survival, particularly in those with recurrent pyelonephritis and AKI.
ORTHOTOPIC ROBOT-ASSISTED KIDNEY TRANSPLANTATION: A NOVEL TECHNIQUE AND CASE SERIES

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Background: Orthotopic kidney transplant is a good alternative for patients with an end-stage renal disease non-suitable for a heterotopic kidney transplant (KT). Recently, robot-assisted kidney transplant (RAKT) has been shown to achieve excellent patient and graft outcomes, while reducing surgical morbidity. From the experience in RAKT, we developed this technique in orthotopic transplantation. The aim of this study is to describe the technique of Orthotopic robotic assisted kidney (ORAKT) and present the case series.

Methods: From 127 RAKT performed in Hospital Universitari de Bellvitge, 10 ORAKT from October 2018 to January 2023. Recipient, donor, surgical and postoperative data are analyzed. Surgical Technique: A 6Fr double J stent is prepared on the left ureter. A 10 cm laparotomy is performed on the left iliac fossa and ports are placed (Figure 1). Da Vinci Robot® is docked following renal surgery protocol and 30° camera is used. Left nephrectomy: renal vein (RV) and RA are anastomosed in end-to-end continuous fashion using a 6/0 GoreTex® CV6. At reperfusion, with insufflation maintained at 8 mmHg, doppler US is checked. A latero-lateral urinary anastomosis to native urinary tract is done with 4/0 Monocryl. 24-hour US is done, and ureteral stent is removed at 4 weeks.

Results: Median donor and recipient age were 66 (IQR 17) and 66 years old respectively. A 6Fr double J stent is prepared as RAKT protocol. When kidney is introduced insufflation is maintained at 12 mmHg. RV and RA are anastomosed in end-to-end continuous fashion using a 6/0 GoreTex® CV6. At reperfusion, with insufflation maintained at 12 mmHg, doppler US is checked. A latero-lateral urinary anastomosis to native urinary tract is done with 4/0 Monocryl. 24-hour US is done, and ureteral stent is removed at 4 weeks.

Conclusions: ORAKT is a feasible minimally invasive alternative for selected patients non-suitable for heterotopic KT in centers with RAKT experience. The potential advantages of the robotic approach are the reduction of lumbotomy morbidity, the precise vessels dissection and vascular anastomosis. Urinary tract complication is commonly present.

Figure 1

Table 1

<table>
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<th>Desensitized FC-CM negative</th>
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PROGNOSTIC VALUE OF A POSITIVE CROSSMATCH BEFORE DESENSITIZATION IN A COHORT OF HIGHLY-SENSITIZED PATIENTS

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Background: Human Leukocyte antigen (HLA) sensitization in patients is a barrier for Kidney Transplantation (KT) access, and highly-sensitized patients remain on the waiting list longer than other patients which results in a higher morbidity and mortality. Desensitization may be an option to increase their access to KT. All patients in this context have a negative Complement-Dependent Cytotoxicity crossmatch (CDC-CM) the day of KT. However, the stratification of the long-term risk of graft loss according to flow cytometry crossmatch (FC-CM) and to CDC-CM during the desensitization period remains unknown.

Methods: In this retrospective study, all highly-sensitized patients (Panel Reactive Antigen (PRA) ≥ 85) in our center were included. CDC-CM and FC-CM were performed on samples before and during the desensitization period and clinical follow-up data were retrieved. Pre-KT desensitization strategy consisted in two Rituximab infusions (375mg/m²) and a variable number of apheresis associated with a classical immunosuppression-based regimen (tacrolimus, mycophenolate and steroids).

Results: A total of 183 highly-sensitized recipients received a KT between 2014 and 2022. Of these, 23 were desensitized prior to KT and among them 18 had a positive FC-CM before KT and 5 had no positive FC-CM on all assessed serums. Mean follow-up was 5.8±4 years versus 7.5±4 years respectively. Death-censored graft survival and patient’s raw survival, using cox-survival analysis, were not statistically different between the desensitized kidney transplanted patients and the highly-sensitized patients without desensitization (p=0.77 and p=0.57 respectively). In sub-group analyses, the positivity of FC-CM did not add an additional risk of graft loss or patient mortality.

Conclusions: Desensitization allows highly-sensitized patients to access KT with an HLA-incompatible graft (with a positive CDC or FC-CM on the serum collected prior to desensitization), with the same graft survival as similarly sensitized patients transplanted with an HLA-compatible graft without desensitization. Figure: Death-censored graft survival in highly sensitized kidney transplant recipients.
EDUCATIONAL INTERVENTION AS AN APPROACH TO SUPPORT COUNTRIES IN EUROPEAN REGION TOWARDS ACHIEVING SELF-SUFFICIENCY IN TRANSPLANTATION

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Background: Training of healthcare professional is an essential component in improving quality, safety and capacity of donation and transplantation. The disruptions brought by the COVID-19 pandemic did not deter the educational interventions. A wide range of training experience on donation and transplantation in the European region was presented in this study.

Methods: A variety of programs focusing on enhancing healthcare professionals’ skills and knowledge in donation and transplantation were implemented. The programs were diversified and available at different levels to adapt to the different needs and advancements of the donation and transplant communities.

There are courses that covered the key donation processes such as identification, evaluation, and management of donors. A more specific trainings or workshops on family approach, donation after cardiac death, tissue banking and regenerative medicine were also encompassed. Three modalities of training namely face-to-face, online, or blended were used. When face-to-face could not be conducted, innovative strategies were developed and these included virtual classroom and internship, interactive gaming, immersive experience with virtual reality tool, and simulation in clinical setting.

Results: A total of 651 participants from 46 countries in the European region were involved in courses that were held between 2019 and 2022. The number participants remained relatively constant with an average of 164 trained per year. In 2019 and 2020, 80% (n= 161) and 70% (n= 95) of the participants were trained face-to-face respectively. In 2021, the participants were 100% trained online. The trend continued in 2022, with 89% of them trained in the online modality.

Conclusions: The training experience donation and transplantation among health professionals in pre- and post- covid time was shown. The training modality switched from face-to-face to online modality from 2020 onwards. The training opportunity and quality could not be compromised even in the unprecedented event, and these could be achieved through innovative adaptations.

VISIONEM AN AI PLATFORM FOR ORGAN ASSESSMENT

Concepción Gómez Gavara1, Gemma Piella1, Itxarone Bilbao1, Javier Vazquez Corral1, Nicolau Farré Saurí2, Daniel Esono Ferrer2, Miguel Angel Cordobés Aranda2, Enric Miret Alomar2, Elizabeth Pando2, Ramon Charco1

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Background: The decision to use or discard an organ is based on the surgeon’s assessment from visual (color and texture) analysis, which is fast but subjective and highly error-prone, tightly rely on the surgeon’s experience. Liver steatosis is one of the major reasons to discard livers for transplantation since it increases the risk of early allograft dysfunction and primary non-function. Currently, liver biopsy is the gold standard to evaluate hepatic steatosis, but it is invasive, costly and not always available during liver procurement. Thus, there is a need for a simple, rapid and accurate method for detecting steatosis in the donor.

Methods: To this end, we started creating an innovative co-designed method that uses image analysis and machine learning to support the medical decision process for graft liver assessment from a simple picture, referred to as LiverColor. Visionem is the AI platform where LiverColor is integrated. Visionem consists of 4 main interrelated components: 1) Mobile Application during surgical procedure; 2) the database and repository of images and clinical data; 3) the image processing and data analysis tools based on machine learning; 4) the web portal application. Various predictive models were trained and validated in an in-house dataset. Usability-related aspects of the system were also assessed both in simulated and real clinical settings. Other organs as Kidney (KidneyColor) and Pancreas (PancretIA) with different endpoints are also being trained in this platform.

Results: Surgeons appreciated the functionalities provided by the platform not only the algorithm assessment but also the dashboarding to summarise and display procurement-related data. For liver assessment, a total of 115 livers, (228 photographs and 4,560 patches) were included. The best results were obtained using the random forest classifier, achieving an AUROC=0.78, with 83.3% of accuracy, being higher than the one obtained by visual inspection by the surgeon.

Conclusions: Image analysis coupled with machine learning can help to safely identify valid livers during procurement.
E-POSTERS

P545 ENHANCED VIABILITY AND FUNCTION DURING PROLONGED CARDIAC GRAFT PRESERVATION USING THE VP'S ENCORE® OXYGENATED MACHINE PERFUSION DEVICE

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Background: Machine perfusion has become an important paradigm in the field of organ preservation; however, most machine perfusion devices are complex and expensive. We have developed a portable, simple to use, cardiac preservation device called the VP'S ENCORE® which was granted the FDA breakthrough designation status and is currently under development pending FDA approval. In this study, we show the efficacy of our device using preclinical data of testing porcine, ovine, and human hearts.

Methods: After recovery, isolated porcine (n=30), ovine (n=14) and human hearts rejected for transplantation (n=8) were placed in the VP'S ENCORE® and perfused at 4-25°C for different time points including 4h, 6h, 8h, and 24h or were kept at static cold storage (SCS). During perfusion, hourly flow, pressure, temperature, and blood gas measurements were recorded. Following either preservation method, hearts were placed in a Langendorff model to reperfusion and evaluated for cardiac function. Biopsy samples were taken for histological & gene expression analyses, and two ovine hearts underwent orthotopic heart transplantation at the Texas Heart Institute.

Results: Most perfusion experiments were conducted at hypothermia (4-8°C); while some were run at subnormothermia (25°C) by adding haemoglobin-based oxygen carrier. Venous and arterial lactate concentrations were less than 1.5mmol/L across most experiments, with no or minimal edema. Perfused porcine hearts at 4h had significantly increased contractility (p<0.05) as demonstrated by +dP/dT(mmHg/s >1000) for 4, 6, and 8 hours of perfusion. Transplant hearts indicated left ventricular contractility within the range of a healthy human heart +dP/dT(mmHg), while perfused sheep hearts had an increased contractility as shown by +dP/dT(mmHg/s >1000) for 4, 6, 8, and 24h of perfusion. In the ovine model, the VP'S ENCORE® preserved a healthy heart with normothermia at 8 hours, with minimal lactate production, and no adverse changes in ventricular function. Two ovine hearts underwent orthotopic transplantation. One had a beating cardiac rhythm at 4h post reperfusion while the other showed early signs of fibrillation within 6h. Histological analysis showed adequate myocardial viability with intact sarcomeres and no signs of fibrosis, necrosis, or edema. Gene expression analysis revealed downregulation of most cardiac and extracellular matrix proteins, supporting the viability of the transplanted hearts.

Conclusions: Our preclinical data demonstrate that the simple to use VP'S ENCORE® cardiac preservation device can serve as an alternative to the SCS and could potentially become a new paradigm to prolong organ preservation.

P546 SEARCHING NEW DONATION SCENARIOS: POTENTIAL RECEPTORS "ON THE OTHER SIDE OF THE MIRROR"

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1Hospital Clínico Universitario Virgen de La Arrixaca, Medicina Intensiva, Murcia, Spain, 2Hospital Universitario Los Arcos del Mar Menor, Murcia, Spain, 3Hospital General Universitario Santa Lucia, Cartagena, Spain

Background: Advances in the field of extracorporeal circulation have improved the prognosis and survival of patients in situations of respiratory failure or cardiovascular shock. However, due to disease progression or not considering the inclusion on the waiting list, the purpose of extracorporeal support treatment may be considered futile. These patients who were waiting for an organ can become new donation scenarios, placing a potential receptor just “on the other side of the mirror”. The descriptively study analyzed the potential receptor of a thoracic organ with extracorporeal assistance who become donors in controlled asystole.

Methods: Retrospective observational study of those donors who met the aforementioned criteria from January-2016 to September-2021 in a tertiary care hospital. Demographic, clinical, organ traceability, and donation effectiveness variables were collected.

Results: 9 real donors were collected. 77.8% were men with a median age of 56 years. 55% had some cardiovascular risk factor. The mean ICU stay was 12.1 days. 7 patients carried veno-arterial ECMO due to postinfarction cardiogenic shock (4), pulmonary thromboembolism (1), primary heart transplant failure (1), non-ischemic dilated cardiomyopathy (1). 2 patients with veno-venous ECMO due to pulmonary fibrosis pending transplantation. 19 organs were obtained (7 livers and 12 kidneys), which represents a ratio of 2.1 organs to donor and an effectiveness of 88.9%.

Conclusions: The shortage of donors forces us to broaden the search for new scenarios of donation. Although this type of “mirror” donor represents a significant change in terms of psychological impact to the families, it is a source to consider once their care team considers the adequacy of life-sustaining treatment.

P547 PERSISTENT HYPERPARATHYROIDISM AFTER PREEMPTIVE KIDNEY TRANSPLANTATION

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1Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, Nagoya, Japan

Background: Long dialysis vintage is one of the typical predictors of persistent hyperparathyroidism (HPT) after kidney transplantation. Recently, preemptive kidney transplantation (PKT) has increased. However, the incidence, predictors, and clinical implication of HPT after PKT are unknown. This retrospective cohort study attempted to clarify these questions.

Methods: Patients who underwent PKT between 2000 and 2016 were included in the study. Those who lost their graft within one year posttransplant were excluded. Hyperparathyroidism was defined as when intact parathyroid hormone (PTH) levels exceeded 80 pg/mL, or hypercalcemia unexplained by causes other than HPT. The patients were divided into two groups based on the presence of HPT one year after PKT. The primary outcome was the predictors of HPT after PKT, and secondary outcome was graft survival.

Results: Among the 340 consecutive PKT, 188 did not have HPT (HPT-free group), and 152 had HPT (HPT group). Multivariate logistic regression analysis revealed that pretransplant PTH level (P < 0.001; odds ratio [OR], 5.480; 95% confidence interval [CI]: 2.070–14.50), and preoperative donor estimated glomerular filtration rate (P = 0.033; OR, 0.978; 95% CI: 0.957–0.998) were independent predictors for HPT after PKT. Death-censored graft survival was significantly lower in the HPT-free group compared to the HPT-free group (59.4% vs 96.4% at 10 years, P = 0.009).

Conclusions: Pretransplant PTH levels and donor kidney function were the independent predictors for HPT after PKT. Additionally, HPT was associated with worse graft outcomes even after PKT.

Multivariate Logistic regression for HPT after PKT

<table>
<thead>
<tr>
<th>Factors</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (years)</td>
<td>1.010</td>
<td>0.994–1.030</td>
<td>0.210</td>
</tr>
<tr>
<td>Male recipient</td>
<td>0.855</td>
<td>0.507–1.440</td>
<td>0.557</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.769</td>
<td>0.412–1.440</td>
<td>0.410</td>
</tr>
<tr>
<td>Serum calcium before PKT (mg/dL)</td>
<td>1.090</td>
<td>0.751–1.580</td>
<td>0.655</td>
</tr>
<tr>
<td>Serum phosphorus before PKT (mg/dL)</td>
<td>0.941</td>
<td>0.770–1.150</td>
<td>0.554</td>
</tr>
<tr>
<td>Log intact PTH before PKT (pg/mL)</td>
<td>5.480</td>
<td>2.070–14.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parathyroid gland size (mm)</td>
<td>1.030</td>
<td>0.965–1.090</td>
<td>0.415</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>1.010</td>
<td>0.986–1.040</td>
<td>0.374</td>
</tr>
<tr>
<td>Male donor</td>
<td>0.720</td>
<td>0.427–2.120</td>
<td>0.217</td>
</tr>
<tr>
<td>Preoperative donor eGFR (mL/min/1.73m²)</td>
<td>0.978</td>
<td>0.957–0.998</td>
<td>0.033*</td>
</tr>
</tbody>
</table>

*P-value < 0.05
Background: Immunosuppression after kidney transplantation is mainly guided by tacrolimus (TAC) trough levels, which are not able to predict graft rejection and infection sufficiently. The plasma load of the non-pathogenic and highly prevalent Torque Teno Virus (TTV) is associated with the immunosuppression of its host. Non-interventional studies suggest that a high TTV load in recipients is at risk for graft rejection and infection. The primary objective of the current trial is to demonstrate safety, tolerability and preliminary efficacy of TTV-guided immunosuppression.

Methods: A two-arm, randomised, controlled, intervention, non-inferiority, patient and assessor-blinded, and investigator driven, phase II trial was designed: A total of 260 adult stable immunosuppression low risk recipients of a kidney graft with TAC based immunosuppression and TTV infection after month 3 post-transplant will be recruited at 13 centres in 6 European countries. At month 4 post-transplant subjects will be randomised at a 1:1 ratio to receive either a TAC dosing guided by TTV load or according to local centre standard. In the active cohort the TAC dosing is based on TTV load at month 12 post-transplantation including molecular microscope, de novo donor specific antibodies, health-related quality of life and medication adherence. Date of first recruitment was August 2022 and planned end is April 2025.

Results: Conclusions: The assessment of an individual kidney transplant recipients immune function might enable clinicians to personalise immunosuppression, thereby reducing rejection and infection. The TTVguideIT trial might act as a proof of principle for TTV-guided immunosuppression.

Table 1. Baseline characteristics of kidney transplant recipients randomized to either TAC mono or TAC-MMF, n=137 during pneumococcal and tetanus vaccinations

<table>
<thead>
<tr>
<th>TAC mono</th>
<th>TAC-MMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range in years)</td>
<td>59 (37-71)</td>
</tr>
<tr>
<td>Sex, n male (%)</td>
<td>23 (74%)</td>
</tr>
<tr>
<td>BMI, median (range in kg/m²)</td>
<td>28 (21-36)</td>
</tr>
<tr>
<td>Transplant type, n living donor transplant (%)</td>
<td>23 (68%)</td>
</tr>
<tr>
<td>CVD-EPI eGFR, median (range in ml/min/1.73 m²)</td>
<td>60 (32-105)</td>
</tr>
<tr>
<td>Proteinuria/creatinine ratio, median (range) in mg/mg creatinine</td>
<td>18.8 (6.0-84.9)</td>
</tr>
<tr>
<td>TAC trough level, median in μg/L (IQR)</td>
<td>6.4 (1.3)</td>
</tr>
<tr>
<td>MMF trough level, median in μg/L (IQR)</td>
<td>-</td>
</tr>
<tr>
<td>Daily dose MIF, median in mg (IQR)</td>
<td>-</td>
</tr>
</tbody>
</table>

*CVD-EPI: Cardiovascular risk model; eGFR: estimated glomerular filtration rate; IQR: interquartile range
Background: Many patients in need of a kidney transplant do not consider a living donor (LD). We studied the effect of having a dedicated "LD-navigator" meet with potential recipients during the evaluation to educate and provide resources for identifying a LD.

Methods: We designed an intervention to increase the number of LD kidney transplants. Pre-evaluation phone calls improved recipient knowledge of LD transplantation. Recipients were encouraged to bring potential donors or a support person to the initial evaluation. The LD navigator met with each patient and assessed their comfort with living donation. The LD navigator educated the patient and support person on living donation and dispelled myths using data. Next she focused on which methods or tools were comfortable and easy to use for that patient or their advocate: How does the patient want to tell their story? With whom do they want to share it? Examples offered: e-mail, social media, or a bulletin from organizations. If the patient expressed reluctance to speak out in their own behalf, we inquired about comfort with someone else telling their story? This is aimed at identifying advocates or a donor champion. The coordinator reviews the microsite option with the patient and offers them an invitation.

Patients leave the appointment with a written action plan and follow up dates. The LD navigator reviews the microsite option with the patient and offers them an invitation. Patients leave the appointment with a written action plan and follow up dates.

Patients leave the appointment with a written action plan and follow up dates. The LD navigator meets with potential recipients during the evaluation to educate and provide resources for identifying a LD.

Conclusions: There is benefit in utilizing a dedicated person to assess, educate, and guide patients through the LD process. Many recipients unsure of how or uncomfortable in approaching others about LD. Providing guidance and support to recipients helps increase their ability to find a living donor and shortening waiting time.

Results: Pre-intervention (11 mo), among 114 kidney transplant evaluations, only 12 (10.5%) of patients identified a potential LD. 4 received deceased donor transplants and 0 received a LD transplant in the following 12 months. Post-intervention (12 mo), 152 patients were evaluated. 53 (34.8%) identified a potential living donor. 10 received a deceased donor transplant and 8 received a LD transplant within 12 months. This number is expected to increase given its proximity to the data capture period.

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Background: Vascularized composite allograft transplantation (VCA) is the top of the reconstructive ladder for injuries or deformities of the central face or distal upper extremity. However, its success is largely compromised by high rates of graft rejection and ischemia-reperfusion injury (IRI). Pre-treatments refer to interventions applied to the donor tissue, after procurement and prior to transplantation, that aim to reduce the immunogenicity of the graft, or decrease the extent of IRI. We reviewed, categorized and delineated the most promising pre-treatments published to date.

Methods: A literature search of PubMed, Cochrane, and Embase databases was conducted, yielding 25 studies in the final analysis. Of these studies, 19 distinct pre-treatments were described. Pre-treatments were grouped into four categories: Temperature Modulation, Donor Tissue Modification, Deoxygenated Perfusate, and Oxygenation.

Results: Temperature modulation and oxygenation methods were primarily investigated to extend the timeframe in which allografts are viable ex-vivo and decrease IRI, while donor tissue modification and deoxygenated perfusate were primarily concerned with reducing rejection burden post-transplantation. Cryopreservation and oxygenation with autologous blood have been shown to markedly increase functional outcome and decrease IRI over standard storage on ice. Introduction of recipient bone marrow cells into donor tissues yielded a successful hematopoietic chimera that survived rejection-free 2.7x longer than a traditional VCA.

Conclusions: While pre-treatments aimed at extending ischemic graft survival/reducing IRI have seen moderate clinical translation, pre-treatments aimed at reducing donor immunogenicity remain largely experimental, with limited clinical adoption. The results of this study demonstrate the promise of these latter techniques and future research, in particular, multi-center clinical trials of donor tissue modification methods are warranted.

Figure 1. Timing of use (Delay), Goal of intervention (Use) as well as Pros and Cons for Pre-Treatment modalities in VCA.
ASSOCIATION BETWEEN INTRAOPERATIVE FLUID MANAGEMENT AND POSTOPERATIVE OUTCOMES IN LIVING KIDNEY DONORS

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2InVita Healthcare Technologies, Los Angeles, United States
3NYU Langone Health, New York, United States

Background: Intraoperative fluid management during living donor nephrectomy may have a significant impact on postoperative outcomes. Although aggressive fluid management (34.3 ml/kg/hour) was reported to increase the postoperative complications, the so-called standard fluid management (14.8 ml/kg/hour) might be aggressive. So, we aimed to compare the postoperative outcomes of living kidney donors according to the intraoperative fluid management of our hospital.

Methods: Medical records of living kidney donors of our hospital were reviewed. Donors were divided into three groups according to the intraoperative fluid management. Primary outcome was the postoperative maximal rise of creatinine in group 1, 2, and 3, respectively. Maximal rise of creatinine was inversely correlated with the intraoperative fluid management (Pearson correlation, R=0.23, p<0.001). Moreover, maximal rise of creatinine in group 1 was significantly higher than group 2 (0.55±0.20 vs. 0.57±0.16, p<0.001) and group 3 (0.65±0.20 vs. 0.56±0.18, p<0.001), although there was no significant difference between group 2 and 3 (p=1). Incidence of prolonged hospitalization was highest in group 1 (6.5%) and lowest in group 3 (1.2%) (p=0.036).

Results: Total 507 living kidney donors were included in final analysis. Donors were divided into tertiles according to the intraoperative crystalloid infusion rate. Mean ± standard deviation of intraoperative crystalloid administration was 3.40 ± 0.47, 4.59 ± 0.31, and 6.29 ± 1.05 ml/kg/hour for group 1, 2, and 3, respectively. Maximal rise of creatinine was inversely correlated with the intraoperative fluid management (Pearson correlation, R=0.23, p<0.001). Moreover, maximal rise of creatinine in group 1 was significantly higher than group 2 (0.55±0.20 vs. 0.57±0.16, p<0.001) and group 3 (0.65±0.20 vs. 0.56±0.18, p<0.001), although there was no significant difference between group 2 and 3 (p=1). Incidence of prolonged hospitalization was highest in group 1 (6.5%) and lowest in group 3 (1.2%) (p=0.036).

Conclusions: Too less intraoperative fluid management was associated with poor postoperative outcomes. More study about the ideal intraoperative fluid management during living donor nephrectomy is required.

RNA-SEQUENCING REVEALS A CONSERVED MECHANISM OF ACUTE REJECTION IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION ACROSS PATIENTS AND ANATOMICAL LOCATION

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Background: Despite substantial advances that make vascularized composite allotransplantation (VCA) viable for patients with devastating soft tissue injury, acute rejection remains a major morbidity. Molecular mechanisms of VCA rejection have not been fully elucidated, including potential variation across different patients and recipient anatomical sites, e.g. face and hand.

Methods: NanoString RNA sequencing (RNAseq) was performed on 18 FFPE skin biopsies (12 face, 6 hand) from 3 VCA recipients; 6 were categorized as nonrejection (NR); 12 as acute rejection (AR) by clinical status (Figure 1A, made with BioRender). Single cell RNA sequencing (scRNAseq) was performed on 10 biopsy specimens (5 face, 5 hand) post VCA recipient; 2 were NR and 8 as AR. Data analysis and visualization was performed (NanoTube, Seurat, and ggplot2 packages in R), in addition to Metascape for pathway analysis.

Results: We first investigated interpatient variation in VCA rejection, revealing 74 differentially expressed genes (DEGs) between AR face biopsies from patient #1 (n=3) and all NR face biopsies (n=6) (Figure 1B). Fold changes of these DEGs displayed strong positive correlations across all 3 patients (all r ≥ 0.6, all p < 0.05). We then investigated transcriptional variation in VCA rejection based on recipient anatomical site. Comparing all AR face biopsies (n=6) versus all AR hand biopsies (n=6) revealed 140 DEGs (Figure 1C). Similarly, fold changes of these DEGs displayed strong positive correlations with hand specimens (all r ≥ 0.6, all p < 0.05). These 140 DEGs were significantly enriched for immune response, leukocyte activation, and chemokine pathways (all p < 0.05). The top 20 most enriched DEGs from AR face biopsies localized to CD8+ T cells and NK cell clusters on scRNAseq. This strongly suggests that the immunopathogenesis of VCA rejection involves stimulation of CD8 T cells by allograft antigen, leading to cytotoxicity.

Conclusions: We demonstrate that the molecular mechanism of acute VCA rejection appears to be conserved across different patients and recipient anatomical sites. Antigen-activated T cells and NK cells mediate AR through production of cytokines and recruitment to graft tissue. Longitudinal sampling for RNA-seq will identify key genes driving the mechanism of VCA rejection and inform targeted therapies.

STREAMLINING DONATION TRANSPANTATION COMMUNICATION VIA HIPAA-COMPLIANT APP

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Background: Communication across the donation transplantation ecosystem is fractured and ineffectual, often necessitating the use of unsecured methods such as text to accomplish time-sensitive tasks. A transplant software company developed a secure, HIPAA-compliant, and fully integrated app to facilitate timely communications across diverse independent donation organizations, including Organ Procurement Organizations (OPOs), transplant hospitals, tissue banks, laboratories, transportation providers, and more.

Methods: The app provides a secure method of chat communications across multiple organizations involved in a donor case, enabling coordination of OR times, transportation, and other time-sensitive issues. Uniquely and critically, the app enables secure sharing of key and real-time donor and case information directly from the host donation organization’s EMR software within chat rooms. Host donation organizations can securely invite third-party organizations and users such as recovery and transplant partners to join their specific app domain and chat rooms. The app integrates GPS-location tracking and EMR data to allow for real-time visualization of staff locations in the field alongside current active referrals, enabling efficient dispatch of staff to referring organizations based on proximity. Additionally, the app desktop companion enables streamlin- ed communications between call centers and mobile staff on site at hospitals.

Results: Since launch over 45,000 chat messages have been sent across the platform and numerous donation organizations have formally adopted the app. Across multiple organizations there are over 2,400 app users.

Conclusions: The app has the potential to centralize and streamline communications across the complex donation-transportation ecosystem. With key integra- tion to the EMR software, the app has the capability to modernize workflows throughout the donation management process across numerous organizations.

STREAMLINING TRANSPLANTATION VIA A COMPREHENSIVE AND SECURE DIGITAL TRANSPLANT MANAGEMENT PLATFORM

John Piano1,2
1InVita Healthcare Technologies, Los Angeles, United States

Background: In the current fragmented transplantation ecosystem, costly inefficiencies exist as systems operate in silos without seamless sharing of key data. Outdated paper and manual processes lead to errors, compliance issues, time-intensive procedures, and patient safety concerns. The implementation of an integrated, real-time clinical workflow platform can alleviate workflow burdens.

Methods: A donation and transplant software company developed a comprehensive, modern, digital transplantation platform to manage the transplantation workflow, working in conjunction with a transplant hospital to design the system specifically curated to the needs of transplant centers. The platform is a modern web-based system which provides advanced patient tracking, data visualization, and communication tools and has the potential to securely interface with external systems such as Organ Procurement Organization’s (OPO) software systems.

Results: The comprehensive secure donation platform streamlines the clinical workflow by providing: 1) access to the latest chart information across multiple staff, 2) real-time and interactive data quality tools to flag potential errors, 3) reporting and compliance tools; and more.

Conclusions: Adoption of a comprehensive clinical workflow platform curated to the processes of transplant centers has the potential to streamline the transplantation workflow and enable increased compliance, patient safety, and transplants.
E-POSTERS

P557

TECHNICAL FEASIBILITY OF WHOLE-EYE VASCULAR COMPOSITE ALLOTRANSPLANTATION: A SYSTEMATIC REVIEW

Matteo Laspro1, Bachar Chaya1, Hilliard Brydges1, Nikhil Dave1, Erika Thys1, Ogechukwu Onuh1, David Tran1, Laura Kimberly1, Bruce Gelb2, Daniel Ceradini1, Eduardo Rodriguez1

1NYU Langone Health, New York, United States

Background: There are over 43 million individuals in the world who are blind. As retinal ganglion cells are incapable of regeneration, treatment modalities for this condition are limited. Since first incepted in 1885, whole-eye transplantation (WET) has been proposed as the ultimate cure for blindness. As the field evolves, different aspects of the surgery have been individually explored, including allograft viability, retinal survival, and optic nerve regeneration. Due to the paucity in the WET literature, we aim to systematically review proposed WET surgical techniques to assess surgical feasibility. Additionally, we hope to identify barriers to future clinical application and potential ethical concerns that could be raised with surgery.

Methods: We conducted a systematic review of PubMed, Embase, Cochrane Library, and Scopus from inception to June 10, 2022, to identify articles pertaining to WET. Data collection included model organisms studied, surgical techniques utilized, and postoperative functional outcomes.

Results: Our results yielded 33 articles, including 14 mammalian and 19 cold-blooded models. In studies performing microvascular anastomosis in mammals, 96% of allografts survived after surgery. With nervus coaptation, 82.9% of retinas had positive electroretinogram signals after surgery, indicating functional retinal cells after transplantation. Results on optic nerve function were inconclusive. Ocular-motor functionality was rarely addressed.

Conclusion: Regarding allograft survival, WET appears feasible with no complications to the recipient recorded in previous literature. Functional restoration is potentially achievable with a demonstrated positive retinal survival in live models. Nevertheless, the potential of optic nerve regeneration remains underdetermined.

Table 1. Mammalian Model Organisms - Surgical Techniques

<table>
<thead>
<tr>
<th>Model organisms</th>
<th>All graft structures</th>
<th>Transplant location</th>
<th>Neurons connected</th>
<th>Denervation</th>
<th>Renovascularisation</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat (Sprague-Dawley)</td>
<td>Eye, CN II</td>
<td>1</td>
<td>eye orbit</td>
<td>CN II</td>
<td>NOR</td>
<td>NOR</td>
</tr>
<tr>
<td>Mouse (C57BL/6)</td>
<td>Eye, CN II</td>
<td>24</td>
<td>eye orbit</td>
<td>CN II</td>
<td>NOR</td>
<td>NOR</td>
</tr>
<tr>
<td>Guinea pig (Cavia porcellus)</td>
<td>Eye</td>
<td>25</td>
<td>eye orbit</td>
<td>NA</td>
<td>NOR</td>
<td>NOR</td>
</tr>
<tr>
<td>Rhesus monkey (Macaca mulatta)</td>
<td>Eye, CN II, lateral rectus muscle</td>
<td>1</td>
<td>eye orbit</td>
<td>NA</td>
<td>anterior ciliary artery</td>
<td>anterior ciliary artery</td>
</tr>
<tr>
<td>Bear (Ursus arctos)</td>
<td>Eye</td>
<td>12</td>
<td>big</td>
<td>big</td>
<td>big</td>
<td>big</td>
</tr>
<tr>
<td>Sheep (Ovis aries)</td>
<td>Eye, CN II, rectus externus muscle</td>
<td>20</td>
<td>eye orbit</td>
<td>CN II, III, IV, VI</td>
<td>1</td>
<td>choroidal artery</td>
</tr>
<tr>
<td>Rabbit (Oryctolagus cuniculus)</td>
<td>Eye, CN II, rectus muscles</td>
<td>30</td>
<td>neck</td>
<td>NA</td>
<td>opticociliary artery</td>
<td>choroidal artery</td>
</tr>
<tr>
<td>Owl (Strix aluco)</td>
<td>Eye, rectus and oblique muscles, CN II, III, IV, VI</td>
<td>8</td>
<td>eye orbit</td>
<td>CN II, III, IV, VI</td>
<td>1</td>
<td>choroidal artery</td>
</tr>
<tr>
<td>Rhesus monkey (Macaca mulatta)</td>
<td>Eye, CN II, rectus muscles, CN II, III, IV, VI</td>
<td>5</td>
<td>NA</td>
<td>CN II, III, IV, VI</td>
<td>1</td>
<td>choroidal artery</td>
</tr>
</tbody>
</table>

Conclusion: Regarding allograft survival, WET appears feasible with no complications to the recipient recorded in previous literature. Functional restoration is potentially achievable with a demonstrated positive retinal survival in live models. Nevertheless, the potential of optic nerve regeneration remains underdetermined.

Table 1. Multivariate analyses: Predicting complications in pancreatectomy patients with ERSD

<table>
<thead>
<tr>
<th>Odds Ratio (OR)</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Complication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI*</td>
<td>1.037</td>
<td>[1.013, 1.062]</td>
</tr>
<tr>
<td>Female Sex</td>
<td>0.84</td>
<td>[0.76, 0.92]</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>1.31</td>
<td>[1.18, 1.45]</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>1.15</td>
<td>[1.06, 1.26]</td>
</tr>
<tr>
<td>PREDYT</td>
<td>2.5</td>
<td>[1.47, 3.3]</td>
</tr>
<tr>
<td>Female Sex</td>
<td>0.98</td>
<td>[0.77, 1.2]</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.19</td>
<td>[0.86, 1.65]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.02</td>
<td>[0.77, 1.37]</td>
</tr>
<tr>
<td>ERSD/Day(s)</td>
<td>0.93</td>
<td>[0.89, 0.97]</td>
</tr>
<tr>
<td>Therapeutic Complication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Sex</td>
<td>0.67</td>
<td>[0.44, 1.0]</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.26</td>
<td>[0.85, 1.9]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.19</td>
<td>[0.59, 2.42]</td>
</tr>
<tr>
<td>ERSD/Day(s)</td>
<td>1.94</td>
<td>[0.75, 5.28]</td>
</tr>
</tbody>
</table>

Conclusion: Panniculectomy in ERSD patients appears to be safe and may improve transplant candidacy. Pannus resection is associated with good post-transplantation outcomes with good long-term graft survival. Pancreactomy prior to transplant appears to be safe without increased comorbidity in the ERSD population.

P558

SAFETY AND UTILITY OF ADJUVANT AND CONCOMITANT PANNICULECTOMY IN RENAL TRANSPLANT CANDIDATES

Matteo Laspro1, Thor Stead2, Hilliard Brydges1, Brooke Barrow1, Ogechukwu Onuh1, Bruce Gelb2, Ernest Chiu1

1NYU Langone Health, New York, United States

Background: As the obesity crisis in the United States continues, different renal transplantation centres have loosened their BMI criteria necessary for surgery. With more individuals of larger body-habitus comorbid with End-Stage Renal Disease (ESRD) qualifying for renal transplantation, surgical modalities existing in other fields have migrated to serve this patient population. Panniculectomy has been successfully carried in ESRD patients prior to transplantation as an attempt to improve surgical field access and post-transplant outcomes.

Methods: In order to assess surgical outcomes of panniculectomy in the context of renal transplantation and ESRD, the authors performed a systematic review following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 Anticipating lack of primary studies, we also retrospectively collected data on patients with ESRD undergoing pancreactomy form the National Surgical Quality Improvement Program (NSQIP) to evaluate outcomes of body contouring in this patient population.

Results: From the systematic review, a total of 783 ESRD patients underwent panniculectomy among the studies identified. Of these, 91 patients underwent panniculectomy simultaneously to RT while 692 had their pannus resected prior to kidney transplant. The most common complication was hematoma followed by wound dehiscence. From the NSQIP analysis, 24,868 patients met the inclusion criteria for analysis. In the setting of renal transplant, patients with diabetes, hypertension requiring medication, and requiring dialysis were more likely to suffer postoperative complications (OR 1.31, 1.15, and 2.2, respectively). However, upon sub-analysis of specific types of complications, the only retained association was between diabetes and wound complication.

Conclusion: Panniculectomy in ESRD appears to be safe and may improve transplant candidacy. Pannus resection is associated with good post-transplantation outcomes with good long-term graft survival. Pancreactomy prior to transplant appears to be safe without increased comorbidity in the ESRD population.
THE ROLE OF T-LYMPHOCYTES IN ACUTE REJECTION FOLLOWING VASCULIZED COMPOSITE ALLOTRANSPLANTATION

Nikhil Dave1, Hilliard Brydges1, Ogechukwu Onuh1, Bachar Chaya1, David Tran1, Massimo Mangiola1, Bruce Gelb2,*, Catherine Lu1, Daniel Ceradini1, Eduardo Rodriguez1

1NYU Langone Health, New York, United States

Background: The mechanisms behind acute rejection (AR) following vascularized composite allotransplantation (VCA) have yet to be clearly elucidated. The role of T-lymphocytes (T-cells) in AR has implications for patient care. This systematic review endeavors to uncover how T-cells contribute to AR in VCA.

Methods: Adhering to PRISMA guidelines, Pubmed, Embase, and Cochrane databases were reviewed. After screening, data regarding study design as well as commonalities and discords of these studies were extracted, and consensus themes were derived.

Results: Twenty-one studies were included in the final analysis, Figure 1 highlights consensus themes among them. Overall, findings closely parallel the solid organ transplantation (SOT) literature, with notable exceptions. Similarly to SOT, a high graft infiltrate of CD8+ T-cells as well as pro-inflammatory cytokines (IL-2, TNF-α, and IFN-γ) were identified during AR. Distinct T-cell populations were found in blood and tissue compartments. Over time, the CD4+ : CD8+ ratio in the graft increased, as did FoxP3 expression followed by increased T-regs and IL-10 (leading to downregulation of AR). Discordantly, within the allograft T-cells clustered surrounding pilosebaceous units during AR.

Conclusions: Elucidating the biomolecular mechanisms of AR in VCA is a requisite step for safely and effectively managing this ubiquitous, devastating complication. Like SOT, we found that T-cells play a crucial role in both instigating and halting AR in VCA, a balance that must be carefully weighed when designing management approaches. Further, unique aspects of AR in VCA, including interactions with hair follicles, warrant further exploration.

Figure 1. Consensus findings regarding the role of T lymphocytes in acute rejection following vascularized composite allotransplantation.

Table 1. Consensus findings regarding B lymphocyte function in acute rejection following vascularized composite allotransplantation.

<table>
<thead>
<tr>
<th>Points of Consensus between Studies</th>
<th>B-Cell Presence in Allograft</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cells are present in the allograft.</td>
<td><strong>Kamihara</strong> 2017 Observational: B-cells same between HLA and controls.</td>
<td></td>
</tr>
<tr>
<td>No B-cells present in allograft.</td>
<td><strong>Dara</strong> 2017 Observational: B-cells absent allograft (not similar).</td>
<td></td>
</tr>
<tr>
<td>Presence of Antibody and Correlation with Rejection</td>
<td><strong>Hauer</strong> 2013 Observational: B-cells absent allograft.</td>
<td></td>
</tr>
<tr>
<td>Anti-AT1R and Anti-ETAR antibodies correlated with rejection.</td>
<td><strong>Skrzynka</strong> 2022 Observational: Patient with Positive Result of AT1R and also ETAR had highest levels of rejection.</td>
<td></td>
</tr>
<tr>
<td>Deposition of anti-body in allograft.</td>
<td><strong>Nakamura</strong> 2011 Experimental: IgG deposition present in patients with rejection &amp; not in absent.</td>
<td></td>
</tr>
<tr>
<td>No difference in non-HLA or anti-donor antibodies between VCA and SOT or controls.</td>
<td><strong>Skrzynka</strong> 2022 Observational: There were no differences in the presence of non-HLA antibodies between patients with rejection &amp; absent.</td>
<td></td>
</tr>
</tbody>
</table>
P561 MINIMALLY AND NON-INVASIVE REJECTION MONITORING MODALITIES IN VASCULARIZED COMPOSITE ALLOGRANULATION

Thor Stead1, Hilliard Brydges1, Matteo Laspro1, Ogechukwu Onuh1, Bachar Chaya1, David Tran1, Daniel Ceradini1, Bruce Geib2, Eduardo Rodriguez3
1NYU Langone Health, New York, United States

Objective: Rejection following Vascularized Composite Allograft Transplantation (VCA) is nearly ubiquitous with 85% of patients experiencing at least one episode. Current monitoring modalities aim to catch rejection before it occurs, but are highly invasive and compromise outcomes. We reviewed the most promising non- and minimally invasive techniques (NIMMs) for diagnosing and monitoring rejection in VCA.

Methods: A literature search of PubMed, Cochrane and Embase databases was conducted, yielding 28 studies that were included in the final analysis. Of these studies, 19 distinct NIMMs are described. NIMMs were grouped into five categories: Imaging, Biomarkers, Epidermal Sampling, Clinical Grading Scales, and Introduction of Additional Tissue.

Results: Imaging based NIMMs are among the most well studied. They are excellent at detecting vasculopathy, which is quite sensitive but not specific for rejection. There are several biomarkers such as MMP3 and cell-free DNA that have been shown to rise consistently before rejection episodes, which makes them extremely attractive for routine patient monitoring. Epidermal sampling is completely non-invasive and allows for accurate measurement of cytokine & enzyme levels implicated in rejection. Clinical grading scales are useful for grading rejection, but cannot preemptively identify it. Lastly, introducing additional tissue has been shown to preemptively identify rejection but must be weighed against the cost of additional trauma to the patient.

Conclusion: NIMMs have great potential to dramatically improve rejection rates in VCA, however standardization among VCA centers is needed to integrate them into the standard of care.

P563 DEVELOPMENT OF DECEASED ORGAN DONATION IN A MULTICULTURAL COUNTRY, UAE ORGAN DONATION AND TRANSPLANT SYSTEM

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1UAE Ministry of Health and Prevention, National Regulatory Center for Organ and Tissue Donation and Transplantation, Dubai, United Arab Emirates, 2SEMA, Abu Dhabi, United Arab Emirates, 3Donation and Transplantation Institute, Barcelona, Spain, 4UAE Ministry of Health and Prevention, National Transplant Committee, Dubai, United Arab Emirates

Background: 88.5% of the United Arab Emirates-UAE population is foreign with more than 200 nationalities. The country’s unique multi-ethnic, multi-religious and multi-cultural characteristics present both a challenge and an opportunity to build a deceased organ donation for transplantation system that could not only impact the UAE but also the country of origin of its habitants. Organ transplantation from brain death donors (DBD) in the UAE began in 2017 when the UAE Ministry of Health and Prevention (MOHAP) approved the regulation on the brain death declaration. Identify the actions that have led to the development of the donation system in the UAE.

Methods: Three levels of deceased donation structure where established, the National Transplant Committee at MOHAP, the Emirates Organ and Tissue Centre (Acting as the Organ Procurement Organization) at the Department of Health of Abu Dhabi, and the hospital-based organ donation units within the main hospitals. Stakeholders’ engagement, healthcare workers education on best practice in organ donation, and the application of the DBD quality key performance indicators were the foundations for the UAE donation and transplant system implementation. Education and meetings were facilitated in collaboration with a team of international subject matter experts.
Background: The quality of the deceased donor (DD)'s kidney is closely related to graft survival after kidney transplantation (KT). Vascular calcification is a highly associated with inferior patients and graft outcomes in KT. This study aimed to evaluate the predictability of vascular calcification in DDs as determined by computer tomography (CT) scan-based calcification scoring system and its correlation with kidney biopsy scoring and graft outcomes.

Methods: A review of the patients' database at Korea University Anam Hospital revealed that a total of 147 brain-death donors underwent organ procurement between 2010 and 2020. Of these patients, 52 donors were included with available pre-transplant CT scan and time-zero biopsy (TZB). The aorto-iliaic calcification score was assigned as the sum of calcification scores at the infrarenal aorta and the common iliac arteries. A calcification score >3 was regarded as moderate-to-severe (MTS) group and <3 as a non-to-mild (NTM) group. Chronicity score were reviewed based on Banff and Remuzzi scoring systems by a single pathologist. The calcification score, chronicity score of TZB, and baseline characteristics were collected and correlated with graft outcomes.

Results: In 52 patients, 30 (57.7%) were NTM and 22 (42.3%) were MTS. The mean age of MTS group was higher (49.7 ± 12.8 vs. 58.2 ± 5.2; P=0.002). Diabetes mellitus (DM) were higher in MTS group (3 (10%) vs. 11 (50%; P=0.004). MTS showed a higher KDPI score (59.4 ± 25.1 vs. 79.0 ± 15.2; P=0.001). In TZB grading, there were statistical differences in IF and TA score (14 (46.7%) vs. 18 (81.8%); P=0.022). There were no statistical differences in delayed graft function and biopsy-proven acute rejection (4 (13.3%) vs. 3 (13.6%); P=1.000, 10 (33.3%) vs. 7 (31.8%); P=1.000). Serum creatinine and estimated glomerular filtration rate of postoperative 1 year, 2 years and 3 years were no statistical differences.

Conclusions: Aorto-iliaic calcification of DDs is associated with donors' aging, DM and KDPI, which has been proven as a predictor of renal function after KT. It is also correlated with IF/TA of allograft baseline biopsies. Short-term graft outcomes according to the degree of calcification were not statistically significant, but considering the associated factors, it is thought to be related long-term outcomes after KT.

Background: Hepatitis C viremic (HCV+) donors were previously an untapped pool. Recently, with the advent of direct acting antivirals (DAA) with a >95% cure rate, the interest in HCV+ donors has increased. However, published studies have been limited to successful outcomes in candidates with lower lung allocation score (LAS). Here, we report our early experience with lung transplantation (LTx) from HCV+ donors in critically ill candidates with high LAS, defined as LAS >50, who are at high risk of waitlist mortality.

Methods: This single institution prospective study reports our experience with HCV+ donors in the period between January 2022 to December 2022. The sustained virologic response (SVR) was measured at 4 weeks and 12 weeks following an eight-week course of DAA treatment. In addition to recipient demographics, we examined postoperative course, rejection episodes, and SVR at 4 and 12 weeks.

Results: During the study period, 4 of 77 (5%) lung transplants were performed from HCV+ donors. All 4 were double lung transplant (DLTx) in male recipients (Table 1). All 4 were inpatient prior to transplant with LAS ranging from 50.59 to 94.26, with one patient requiring preoperative veno-arterial extracorporeal membrane oxygenation support as a bridge to transplant. All 4 started DAA treatment within 2-6 days following DLTx. They were successfully discharged from the hospital to home without oxygen. Following completion of the 8-week course of DAA therapy, three have SVR at 4 weeks (1 pending result) and 2 at 12 weeks (2 pending results). There were no rejection episodes.

Conclusions: Our results show a 5% increase in donor pool by successful utilization of hepatitis C viremic donors at our institution during the study period. Furthermore, our preliminary short-term outcomes support the use of HCV+ donors in the critically ill cohort with high LAS. Expanding the donor criteria to include HCV+ donors holds promise to reduce waitlist mortality.

Table 1. Recipient Demographics and Pre- and Post-Operative Course

<table>
<thead>
<tr>
<th>Patient Age (y)</th>
<th>Gender</th>
<th>LAS (y)</th>
<th>Pre-DA</th>
<th>Post-DA</th>
<th>PKa (y)</th>
<th>DAA Duration (w)</th>
<th>DAA Success (4 weeks)</th>
<th>HCV Viraemia (y)</th>
<th>SVR (4 weeks)</th>
<th>DAA Success (12 weeks)</th>
<th>SVR (12 weeks)</th>
<th>Reaction to DAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>M</td>
<td>04.26</td>
<td>Inpatient</td>
<td>34</td>
<td>8 weeks</td>
<td>YES</td>
<td>-</td>
<td>Yes</td>
<td>No</td>
<td>ABO</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>M</td>
<td>66.15</td>
<td>Inpatient</td>
<td>18</td>
<td>8 weeks</td>
<td>YES</td>
<td>50.256</td>
<td>Yes</td>
<td>No</td>
<td>ABO</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>M</td>
<td>73.71</td>
<td>Inpatient</td>
<td>14</td>
<td>8 weeks</td>
<td>YES</td>
<td>176.898</td>
<td>Yes</td>
<td>No</td>
<td>ABO</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>M</td>
<td>50.59</td>
<td>Inpatient</td>
<td>34</td>
<td>8 weeks</td>
<td>YES</td>
<td>53</td>
<td>Yes</td>
<td>No</td>
<td>ABO</td>
<td></td>
</tr>
</tbody>
</table>

LTx: Lung Transplantation, LAS: Lung Allocation Score, LOSt: Length of Stay, DAA: Direct acting Antiviral, SVR: Sustained Virologic Response (at 4 weeks and 12 weeks following completion of DAA)
UROLOGIC COMPLICATIONS IN OUR ORGAN TRANSPLANT UNIT AFFECTING RECIPIENTS FROM BRAID DEAD DONORS DURING THE LAST DECADE

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1Evangelismos General Hospital, 1st Surgical and Organ Transplant Unit, Athens, Greece

Background: Urologic complications remain the most common problem following renal transplant with a reported incidence in the range of 2.5 and 30%. Major urologic complications involve ureter obstruction, urine leak and vesicoureteral reflux (VUR) and they are associated with high readmission rates and decreased graft survival time. We aimed to study the rates and types of urologic complications in our kidney transplant unit during the last decade.

Methods: We retrospectively identified 225 kidney transplant recipients from brain dead donors from January 2013 to December 2022. All ureteroneocystostomies were performed under the care of the same lead surgeon using the Lich-Gregoir technique. PJ stent was placed intraoperatively and removed routinely 30 days post op. A negative pressure Blake drain was left in situ. Graft ultrasound and 99mTc-EC dynamic renal scan were performed routinely to identify evidence of acute kidney injury or rejection on day 1 and day 7 respectively. We attempted to associate our complications with the following factors: sex, age, viral status, and donor characteristics.

Results: In a total of 225 recipients, we identified 17 (7.6%) with urologic complications. These would involve: 4 anastomotic stenosis (23.5%), 7 ischemic ureter stenosis (41.2%), 2 ureter kinking (12%) and 4 anastomotic leaks (23.5%). 11 complications (64.7%) involved the distal ureter. The majority of the patients presented with deterioration of graft function and urosepsis. In 16 cases (94.1%) percutaneous nephrostomy under U/S guidance was performed and this was followed from JJ stent placement in 7 (43.75%) of them. 9 out of these 17 recipients (52.3%) required surgical treatment. & underwent redo of their anastomosis, 1 required psoas hitch and 1 Boari-flap procedures. 2 of these 17 recipients (52.3%) had recurrent surgery treatment. & underwent redo of their anastomosis, 1 required psoas hitch and 1 Boari-flap procedures. 2 of them died of sepsis (11.76%) and 2 of them died later during their follow up from unrelated causes.

Conclusions: Despite the fact that renal transplant is the best therapeutic option for end stage renal disease, urologic complications and ureteroneocystostomy related complications in particular remain the Achilles’ heel of the procedure leading to major complications and prolonging hospital stay for renal transplant patients.

P570 BUBBLE AND INTERMITTENT SURFACE OXYGENATION ARE AN EFFECTIVE ALTERNATIVE FOR MEMBRANE-OXYGENATED HMP-KIDNEYS TO MAINTAIN AEROBIC METABOLISM

Tom Darier1,2, Martial Vergauwen1, Louis Malfrait2,3, Robin Evrard1,4, Matteo Mueller1, Andrea Schlegel1, Christian Ludwig1, Philipp Dutkowski1, Pierre Gianello1, Michel Mourad1,2
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Background: Since 2022, brief bubble and subsequent surface oxygenation are an alternative oxygenation technique for membrane-oxygenated kidneys during hypothermic machine perfusion (HMP) in clinical practice. The aim of this study was to evaluate the metabolic effect at the end of the preservation period of the interruption of surface oxygenation (O2) for 4 hours (mimicking organ transport) during HMP as compared to continuous surface and membrane oxygenation in a pig kidney ex vivo preservation model.

Methods: A kidney of a ±40 kg pig was exposed to 30 minutes of warm ischemia and preserved according to one of the following study groups: 1) 22h HMP+intermittent surface O2 (n=12), 2) 22h HMP+continuous membrane oxygenation G1 (n=6), and 3) 22h HMP+continuous surface O2 (n=7). Brief O2 uploading of the perfusion fluid before kidney perfusion was obtained either by a hollow fiber membrane oxygenator (study group 2) or by direct bubble oxygenation (study group 1 and 3).

Results: O2 uploading of the perfusion fluid by minimum 15 minutes of direct bubble oxygenation was as efficient as membrane oxygenation to achieve pO2 levels above 450-500 mmHg (at 4°C) before connecting the kidney to the perfusion device. Metabolic tissue analysis (i.e., lactate, succinate, glutamate, ATP, NADH and Flavin Mononucleotide (FMN)) by mass spectrometry (Figure 1) and 1H-NMR (i.e., glutamate, glucose, lactate, and succinate) and perfusion analysis by 1H-NMR demonstrated a similar mitochondrial protection/preservation in all study groups after 270 minutes and at 22 hours of HMP. Perfusion FMN levels measured by spectrometry were significantly higher at the end of the preservation period in the membrane-oxygenated groups as compared by both surface-oxygenated HMP groups but comparable after 270 minutes of preservation.

Conclusions: Brief bubble and intermittent surface oxygenation of the perfusate during standard HMP at procurement site might be an effective and less expensive preservation strategy to protect mitochondria when compared with membrane-oxygenated kidneys eliminating the need for a membrane oxygenator and oxygen source during transport.

Figure 1.
**P571**

**COMPARATIVE STUDY OF PATHOGENS AFFECTING OUR KIDNEY TRANSPLANT UNIT FOLLOWING CHANGE IN ANTIBIOTIC PROPHYLAXIS PROTOCOL DURING THE PERIOD 2010-2022**

Konstantina Rekouna1, Nikolaos Dimitrokallis1, Paraskevi Trakosari1, Maria Christou1, Eugenia Karveli1, Konstantinos Pavliopoulos1, Antonia Thanasa1, Michail Papamichail1, Elena Mylona2, Stefanos Stefanakis1, Alexandra Tsriggianni1, Christalleni Christodoulou, Vasileios Vogas1

1Evangelismos General Hospital, 1st Surgical and Organ Transplant Unit, Athens, Greece, 2Evangelismos General Hospital, Athens, Greece

**Background:** Transplanted patients are more susceptible to infections. Thus, it is important that we study the pathogens responsible and prevent the course of the disease. Following a review of the most common pathogens in our Organ Transplant Unit we adjusted our antibiotic prophylaxis protocols in 2018. Our aim is to discuss the primary results of this action.

**Methods:** Kidney transplant recipient patients who presented with at least one episode of urine infection or bacteremia during the first 30 post-transplant days between 2010 and 2022 were included in this study. The patients were divided into two large groups, based on the antibiotic prophylaxis protocols used. Group A includes kidney transplant recipients from 2010 to 2017, whereas Group B includes recipients from 2018 to 2022. Group A was given cefuroxim for 7 days and ciprofloxacin for 30 days, while Group B was given one dose of vancomycin pre op and meropenem pre op and till post-transplant day 3. We analyzed the pathogens cultured during episodes of urine infection and/or bacteremia for the first 30 post-transplant days. We also analyzed the hospital stay and the effects on graft function for the same period.

**Results:** Group A with 163 patients had a total of 181 episodes of urine infection and 28 episodes of bacteremia. Most common pathogens in the urine had been E. faecium (36%), E. coli (25%), E. faecalis (20%), Kp. pneumoniae (19%), P. aeruginosa (14%), A. baumannii (7%) and Staph. epidermidis (7%). Group B with 84 patients had a total of 173 episodes of urine infection and 43 episodes of bacteremia. Most common pathogens in the urine were: E. coli (25%), Kp. pneumoniae (19%), P. mirabilis (8%), E. faecalis (1%), P. aeruginosa (1%). Blood infection pathogens: E. faecalis (11%), Kp. pneumoniae (11%), E. coli (11%), Staph. epidermidis (4%) and A. baumannii (4%).

**Conclusions:** Change in the antibiotic prophylaxis protocol in our unit resulted in a change of the most common pathogens seemingly diminishing enterococcus related and VRE infections. The flora change was associated with less in hospital stay and no major difference in graft function for the first post op period.

**P572**

**THROMBOTIC MICROANGIOPATHY AND EARLY HUMORAL REJECTION AFTER ABO INCOMPATIBLE KIDNEY TRANSPLANTATION: A CENTER MULTI-CENTER CASE-CONTROL STUDY**

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**Background:** Although long-term graft survival is comparable to that of ABO-compatible renal transplantation, the risk of humoral rejection following ABO-incompatible (ABOi) transplantation is greater and can occur as an early thrombotic microangiopathy (TMA) after kidney transplantation.

**Methods:** A multicenter study, including all patients who presented a TMA (histological and/or biological) after an ABOI transplantation (<1 month), compared to matched controls who had a favourable initial course with a normal biopsy.

**Results:** Between 2013 and 2022, 375 ABOI kidney transplants were performed and 23 patients (6.1%) developed TMA (median: 1 day; IQR: 0-3). Eleven patients (47.8%) were on dialysis. Twenty-one patients (91.3%) had biological TMA. Among 21 early graft biopsies, histological evidence of active TMA was found in 17 cases (80.9%). All patients received treatment. At least one session of plasmapheresis. At least one injection of Eculizumab. Seven early graft losses (30.4%) occurred (median: 7 days; IQR: 3-16). The control group (n=59), graft survival at 1 year was significantly higher (100% vs 69%, p<0.0001). IgG and IgM isoagglutinin levels (peak and last pre-graft assay) were significantly higher in the TMA group (peak: p=0.01 for IgG and p=0.0003 for IgM). A level 1/8 for IgG and ≥1/4 for IgM before transplantation was predictive of the occurrence of TMA with a sensitivity and specificity of 71.4% and 71.8% for IgG (AUC=0.782, p=0.0003), and 80% and 67.7% for IgM (AUC=0.786; p=0.001). No other predictive factors were found.

**Conclusions:** TMA after ABOI transplantation is a rare phenomenon but associated with a poor prognosis. Isoagglutinin titre performed by hemagglutination is an imperfect marker of the occurrence of such a phenomenon.

**P573**

**CLINICAL RELEVANCE OF THE LIVING KIDNEY DONOR PROFILE INDEX IN ASIAN KIDNEY TRANSPLANT RECIPIENTS**

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**Background:** The Living Kidney Donor Profile Index (LKDPI) was developed in the United States to predict graft outcomes based on donor characteristics. However, there are significant differences in donor demographics, access to transplantation, proportion of ABO incompatibility, and posttransplant mortality in Asian countries compared with the United States.

**Methods:** We evaluated the clinical relevance of the LKDPI score in an Asian kidney transplant cohort by analyzing 1,860 patients who underwent kidney transplantation between 2000 and 2019. Patients were divided into three groups according to their LKDPI score: <0, 1–19.9, and ≥20.

**Results:** During a median follow-up of 119 months, 232 recipients (12.5%) experienced death-censored graft loss, and 56 recipients (3.3%) died. High LKDPI scores were significantly associated with increased risk of death-censored graft loss independent of recipient characteristics (LKDPI 1–19.9: HR 1.389, 95% CI 1.036–1.863; LKDPI ≥20: HR 2.121, 95% CI 1.50–2.986) as well as increased risk of biopsy-proven acute rejection and impaired graft renal function. By contrast, overall patient survival rates were comparable among the LKDPI groups.

**Conclusions:** High LKDPI scores were associated with an increased risk of death-censored graft loss, biopsy-proven acute rejection, and impaired graft renal function among the Asian kidney transplant cohorts.
SOTROVIMAB AS PRE-EXPOSITION PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS: NEUTRALIZATION OF OMICRON BA.1 AND BA.2 VARIANTS

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Background: Pre-exposition prophylaxis (PrEP) with monoclonal antibodies (mab) is used to prevent coronavirus disease 2019 (COVID-19) in high-risk individuals. However, a significant reduction of the in-vitro neutralization capacity against the Omicron BA.1 variant (B1.1.529) was observed for most mabs. Sotrovimab (Xevudy, VIR Biotechnology GlaxoSmithKline) retained substantial in-vitro neutralization capacity against BA.1, and a half-life of 48.8 days made it a candidate for off-label use as PrEP in high-risk individuals.

Methods: We enrolled 60 kidney transplant recipients (KTR) receiving PrEP through a compassionate use indication for sotrovimab between January 4 and February 28, 2022 into a prospective cohort study. Patients received 500mg of sotrovimab intravenously and were followed at our outpatient clinic. The rate of breakthrough infections was compared to a cohort of vaccine non-responder not receiving PrEP (i.e. < 264 BAU/mL). Serum was collected at four and eight weeks after antibody infusion. Variant-specific live virus neutralization tests (NTs) were performed with BA.1 and BA.2 variants.

Results: Over a 90-day follow-up period, 15% of patients receiving sotrovimab tested positive for SARS-CoV-2 compared to 37% of patients in the control group (Figure 1, log-rank test: p=0.001). All individuals neutralized BA.1 at four weeks follow up (FU) and all but one individual retained neutralization capacity against BA.1 at eight weeks. In contrast, neutralizing capacity against BA.2 in serum was only present in 80% at four weeks and further decreased to 15% at eight weeks FU. Conclusions: PrEP with sotrovimab significantly reduced the rate of SARS-CoV-2 infection during the BA.1 wave in Austria. Activity against BA.1 was retained for eight weeks while activity against the BA.2 variant was already limited at four weeks after infusion. Our data show that sotrovimab can be used as PrEP for up to eight weeks depending on in-vitro activity against the dominant SARS-CoV-2 subvariant.

Figure 1: Kaplan-Meier curve of SARS-CoV-2 infection-free survival in KTR who received PrEP with sotrovimab and KTR who did not have protective SARS-CoV-2 humoral immunity and did not receive any form of PrEP

SPLIT RENAL FUNCTION, RENAL VASCULAR VARIATIONS AND DONOR PREFERENCES: CHALLENGE AND CROSSROADS TOWARDS RIGHT KIDNEY CHOICE

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Background: Renal vascular variations, split renal function (SRF) and potential donor’s preferences interplay on the donation decisions in living donor kidney transplantation (LDKT). This study aimed to assess the challenges in decisions for assessing the proper kidneys for donation.

Methods: Retrospective study was performed through a review of the medical history charts and national electronic database of LDKT from 2013 – 2022, in one transplantation center. Those with significant missing data, were excluded from the final analysis. Demographic characteristics, CT angiographic findings and Tc-99m DTPA renal scan for SRF and donor preferences were analysed. The bilateral presence and number of accessory renal arteries, their hilar or polar position in respect of the renal artery, early artery branching, variations of the veins number and left vein course were assessed. Significantly different SRF was defined as ≥10%.

Results: Out of 137 consecutive LDKT, 124 donors were included in the study. The mean age of donors was 50.00 ± 11.90 years, 40 (32%) were male and 14 (11%) were female. There were no blood transfusions in 88 (64%) renal arteries on the right and 69 (56%) on the left. The most common variation on both sides was an accessory hilar artery in both sides in 15%. An accessory inferior renal polar artery was observed in 15% and superior in 13% of patients. Three renal arteries or three veins on one side were observed in one patient. Variation of renal arteries on both sides was 13(10%). Early artery branching was found in 25% (8%-right and 18%-left side). Two renal veins were observed in 8(6%). The Nutcracker phenomenon was found in 6(4.8%). From the donated kidneys in 60% it was the left one and 10% were with vascular variation. In 33 (27%) of donor kidneys we found at least one vascular variation. In 41 (33%) of donors SRF was significantly different and 8 (18%) of those donated the better kidney because of donors preferences.

Conclusions: Variations in renal vascular anatomy and different SRF are very often in kidney donors. Donors preferences additionally interfere the transplantation process. The quality of the decision process relies on good institutional policy and adequate pretransplant donor evaluation.

NOVEL PROGNOSTIC MARKERS FOR LIVER CIRRHOSIS IN PATIENTS ON THE ROMANIAN WAITING LIST FOR LIVER TRANSPLANT

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Background: Chronic liver disease is a global public health problem, cirrhosis being on the top of the causes of mortality in Romania. Models that predict individual risk of disease complications are becoming more common in hepatology. The aim of our study was to assess already known and novel prognostic markers for patients with liver cirrhosis awaiting liver transplant (LT).

Methods: We analysed the following prognostic factors: Model of End-stage Liver Disease (MELD), MELD Na, MELD 3.0, albumin-bilirubin score (ALBi), occurrence of acute-on-chronic liver failure (ACLF) from grade 1 to 3, occurrence of liver cirrhosis complications, infections, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio, platelet-to-lymphocyte ratio in 108 patients included on the waiting list (WL) for LT in the last 5 years. Univariate and multivariate Cox regression analysis identified the following independent prognostic factors: presence of ACLF during follow-up (p=0.0001), refractory ascites (p=0.032), acute kidney injury (p=0.0013), hepatic encephalopathy (p=0.0257), infectious complications (p=0.0007), a higher MELD score (p=0.0137), MELD Na (p=0.0018) and MELD 3.0 score (p=0.0028) and a higher NLR (p=0.033). Multivariate Cox regression analysis identified the following independent prognostic factors: presence of ACLF during follow-up (p=0.021) and a higher NLR score (p=0.036).

Conclusions: Acute-on-chronic liver failure and neutrophil-to-lymphocyte ratio are significant prognostic markers for the WL for LT that should be included in the graft allocation system.
**P580** RECOMBINANT SARS-COV-2-ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS WITHOUT NEUTRALIZING ANTIBODIES FOLLOWING FULL VACCINATION (RESCUE-TX)

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**Background:** Pre-exposure prophylaxis (PrEP) with monoclonal antibodies (mab) is used to prevent coronavirus disease 2019 (COVID-19) in high-risk individuals. Currently, cilgavimab/tixagevimab (Evusheld) remains the only mab combination approved for PrEP.

**Methods:** We started the RESCUE-TX trial in kidney transplant recipients (KTR) not responding to at least two doses of SARS-CoV-2 vaccine. A total of n=194 patients received 300 mg of cilgavimab/tixagevimab (i.m.) between March 4 and May 3, 2022. Patients are followed at our outpatient department at 2, 4, 8, 12, 24 and 48 weeks after dosing. Serum is stored for drug level quantification (PDP diagnostics; primary endpoint) and SARS-CoV-2 neutralization testing (secondary endpoint). Additional secondary outcomes include the rate of breakthrough infections compared to a cohort of vaccine non-responders not receiving PrEP (i.e. < 264 BAU/mL). Vaccine non-responders were best matched for age and time since transplantation.

**Results:** Until end of September, 2022 (~31-week observation period), 58 patients receiving cilgavimab/tixagevimab tested positive for SARS-CoV-2 compared to 74 in the control group (infection rate 30% vs 38% for cilgavimab/tixagevimab and controls, respectively; log-rank test: p=0.04). The geometric mean of peak serum levels of cilgavimab and tixagevimab observed at 2 weeks after PrEP was 16 μg/mL and 17 μg/mL, respectively. Concentrations of both mabs declined in the following weeks and reached 9 μg/mL at 12 weeks after PrEP but was low at week 24. BA.5 neutralization activity in patient sera was severely reduced at all timepoints and at week 24 only 20% of patients showed protective NT titers.

**Conclusions:** PrEP with cilgavimab/tixagevimab significantly reduced the rate of SARS-CoV-2 infection during the BA.2 wave in Austria. In line, neutralization activity against BA.2 was strong in most KTRs for up to 12 weeks but significantly reduced against BA.5 across all time points.

**Figure 1:** SARS-CoV-2 infection free survival in vaccine non-responders with and without PrEP with Evusheld.

**P582** MORTALITY OF THE CIRRHOTIC PATIENTS ON THE LIVER TRANSPLANT WAITING LIST DURING THE COVID-19 PANDEMIC

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**Background:** Cirrhotic patients on the liver transplant waiting list may be at increased risk of severe acute respiratory syndrome and death from COVID19. Likewise, there is also a risk when transplanting a patient during the pandemic. The aim of this study was to determine the incidence of COVID-19 infection in patients on the liver transplant waiting list during the pandemic in a small-volume liver transplantation center in Romania, and to compare the mortality from COVID-19 in patients on the waiting list versus transplant patients, and the effect of vaccination on mortality.

**Methods:** In this study were included all the cirrhotic patients from the liver transplant waiting list. For the analysis of the impact of vaccination, it was considered vaccinated if the patient received at least 2 doses or had a positive SARS-CoV-2 test. Patients were compared in terms of demographic characteristics, transplant experience, and mortality. We performed a descriptive analysis and calculated proportions, means, and 95% confidence intervals. The univariate analysis was performed by means of chi-square tests, and the multivariate analysis by means of logistic regression.

**Results:** During the study period we analyzed 125 recipients on the liver transplant waiting list. Fifty-seven patients were confirmed with COVID-19. The mortality rate was 24.5% (14 patients). There were also 29 patients with liver transplant followed-up during this period. Twenty-two (75.8%) patients developed COVID-19 infection, most of them mild and moderate forms. None of these patients died during follow-up. The vaccination rate was 39.2% in the liver transplantation waiting list and 93.1% in patients with liver transplant. In the multivariate analysis, the probability of death in liver transplant waiting list patients and COVID-19 infection was associated with age over 55 years (OR=1.63, 95% CI 1.301-1.822, p=0.025), admission to intensive care unit (OR=8.81, 95% CI 2.101-34.427, p=0.015), and mechanical ventilation requirement (OR=16.7, 95% CI 5.322-36.303, p=0.002). Vaccination was a protective factor against mortality (OR=0.06, 95% CI 0.031-0.058, p<0.001).

**Conclusions:** A high mortality of COVID-19 was observed in recipients on the waiting list for liver transplant compared to liver transplant patients, and COVID-19 vaccination was efficient in preventing severe forms of COVID-19 infection.

**P583** PRETRANSPLANT EVALUATION OF LIVING KIDNEY DONORS AND RECIPIENTS: FROM THE PERSPECTIVE OF THE TRANSPLANT COORDINATORS

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**Background:** Low organ donation rates in Greece inevitably result in high waiting time for a kidney transplantation from a deceased donor. For Greek patients undergoing dialysis, a potential living donor is often the only hope. The aim of this study is to present the pairs of potential living donors and recipients evaluated at our center during a three-year period, 2020-2022, and recorded by transplant coordinators.

**Methods:** We retrospectively evaluated all potential pairs of living donors and recipients referred to our transplant center during 2020-2022. This is an ongoing study, as the pairs presented during the last semester of 2022 will hopefully be transplanted in due course.

**Results:** 300 potential pairs of living donors and recipients were recorded. Mean age of the potential donors was 45 years (range: 11-75). 99 potential recipients (29.6%) were referred for preemptive transplantation, whereas the remaining 211 (70.4%) were already on dialysis. The proportion of preemptive potential recipients significantly increased in the last two years. 33 potential recipients (11%) were pediatric. The mean age of the potential living donors was 58.14 years (range: 21-85). The distribution of potential donors regarding relation to the potential recipient was as follows: parents 49%, spouses 29%, other relatives 17%, non-related/emotional 5%. One hundred forty pairs (46.7%) have already been transplanted. Thirty-six pairs (12%) are expected to proceed within the next months. Sixty pairs (20%) were lost to follow up. The remaining 64 pairs (21.3%) were rejected due to medical conditions diagnosed during evaluation, mainly associated with donors’ comorbidities or immunological incompatibility. Mean time to the completion of pretransplant evaluation was 7.5 months (range 1-22).

**Conclusions:** Pretransplant evaluation of potential living donors and recipients is a laborious and time-consuming process. Transplant coordinators in close cooperation and collaboration with nephrologists and transplant surgeons are working hard to increase living kidney donation rates and the preliminary results of this multidisciplinary approach are encouraging giving the opportunity of kidney transplantation in significant proportion of dialysis patients.
Background: Normothermic ex vivo kidney perfusion (NEVKP) is designed to replicate physiological conditions to potentially reduce cold ischemia injury and improve graft function. However, this is still in the experimental stage. A comparison of the impact of hypothermic and normothermic organ preservation techniques on graft quality was performed by lipidomic profiling using solid-phase microextraction (SPME) chemical biopsy as minimally invasive sampling approach.

Methods: Direct kidney sampling was conducted using SPME probes coated with a mixed-mode extraction phase in a porcine autotransplantation model of the renal donor after cardiac death, comparing three preservation methods: static cold storage, normothermic and hypothermic perfusion. The lipidomic analysis was done using ultra-high-performance liquid chromatography coupled with a Q-Exactive Focus Orbitrap mass spectrometer.

Results: Chemometric analysis showed significant differences between SCS, HMP, and NEVLP renal serums in the NEVLP group was separated from the SCS and HMP groups. Further in-depth analyses were performed to identify compounds that statistically differentiate the hypothermic and normothermic preservation methods. Significantly (p<0.05, VIP>1) higher levels of Cer, PCs, ether-linked PCs, ether-linked PEs, PIs, TGs, most LPC and LPE, and longer-chain PEs were observed in the thermergic preservation group. In parallel, higher levels of Cer, PSs, and shorter-chain PEs were observed in the normothermic preservation group.

Conclusions: The NEVLP preservation method improves the renal tissue lipidome by reducing cold ischemia injury and increasing graft function. The lipidomic study supported the NEVLP method's beneficial effect on graft function.

In an unpredictable way, but not the society...
Background: Chile has historically had a low and stagnated organ donation rate (ODR) of 8 donors pmp on average, despite the efforts to improve it. This phenomenon is mainly due to the lack of detection and referral of possible organ donors (PD) at the ERs and ICUs. In fact, between 2013-17, 87% of PD were lost. What would happen if there was an intervention capable of improving and easing the PD’s referral? Could the number of patients entering procurement follow-up increase, and with it, effective donors?

Methods: We developed Kefuri, a smartphone app, which allows ER and ICU healthcare professionals to refer PDs easily and quickly to the Procurement Unit (PU). We implemented it gradually in 6 hospitals in: 5/19;12/20;12/21;3/22; 4/22; 8/22, 3 from the capital, and 3 from other cities, using change management strategies. We used descriptive statistics for analysis.

Results: During the study period (5/19 - 12/22), 337 PD referrals were made with Kefuri, 80% of total referrals, and 70% of follow-ups (including PU active search). Including 2018, PD referrals have increased at a rate of 1.16% per month, and Kefuri is responsible for 68% of that increase (p<0.001); while PU active search have increased at a rate of 0.85% per month, and Kefuri is responsible for 8% of that increase (p=0.013), and AAPDRRD ratio was 74% on average (±21%, range 45-100). During 2022, when all hospitals were active, total PD referral rate (94 pmp) was 35% larger than the average of previous years (59 pmp) (p<0.001). Effective ODR increased 11% compared to previous years (though not significantly (p=0.013), and AAPDRRD ratio was 74% on average (±21%, range 45-100). During 2022, when all hospitals were active, total PD referral rate (94 pmp) was 35% larger than the average of previous years (59 pmp) (p<0.001).

Conclusions: Kefuri has shown to significantly increase the number and rate of PD referrals in the centers where it has been implemented, albeit 3 out of 6 have not yet completed 1 year of use. We acknowledge there are gaps that must be addressed for further improving results, and implementation science tools would be a good fit for that. We recognize that ODR did not increase, maybe because next organ procurement process stages must be intervened too. We believe that Kefuri has the potential not only to increase PDs in the whole country, but also to have new functionalities to automate and standardize the rest of the process and also to be incorporated in other countries.
**P593** PREGNANCY INDUCED SENSITISATION AND HLA-ANTIBODY INCOMPATIBLE KIDNEY TRANSPLANTATION (HLA-AIT): NOT ALL IS BAD NEWS FOR LONG TERM GRAFT SURVIVAL

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**Background:** Sensitisation against HLA from pregnancy disadvantages female patients by reducing access to a compatible transplant and by the high risk considered when transplanting against a repeat, foetal HLA mismatch. We investigated the graft survival (GS) following HLA-AIT, particularly in female recipients.

**Methods:** 134 patients were transplanted against donor-HLA-specific antibodies (DSA). 43 cases were excluded due to insufficient follow-up data. We were able to obtain reliable assignment of cause of primary sensitisation in 73 patients. Post-transplant DSA dynamics were classified by unsupervised machine learning into five distinct DSA response groups (Table 1). Results: Pregnancy sensitised females had the highest rate of ER (18/24), significantly more than the combined transplant and transfusion sensitised cases (21/49; p=0.014). We saw no difference in ER between males and females overall, but males with ER had significantly poorer 10-year GS compared with females (Fig 1a). Superior GS was seen in the pregnant sensitised females (Fig 1b), with significantly better GS than the non-pregnancy sensitised females (p=0.029), with males in between. Overall, the post-transplant DSA responses are significantly different between the sexes with females having higher proportions of modulating responses (Table 1), particularly one with pregnancy sensitisation.

**Conclusions:** Our analysis challenges the notion that pregnancy is a risk factor for GS in HLA-AIT. Careful selection of cases with pregnancy induced sensitisation can reduce inequity to access in transplantation in female patients.

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**Figure 1a** Sex and impact of ER on 10-year graft survival. f=female, m=male; y=ER, n=no ER.

**Kaplan-Meier Survival by group**

Overall: p = 0.028985. m+n vs m+p: p = 0.003, m+y vs f+y: p = 0.049.

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**Figure 1b** Source of sensitisation and 10-year graft survival. f=pregnancy sensitised, n=non-pregnancy sensitised

**Kaplan-Meier Survival by group**

Overall: p-value = 0.061, f+n vs f+y: p = 0.029.

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**Table 1 Early post-transplant donor-specific antibody responses**

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**P594** ADULT KIDNEY TRANSPLANT RECIPIENTS AT RISK OF CMV INFECTION AND DISEASE: AN OBSERVATIONAL STUDY

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**Background:** Infections with Cytomegalovirus (CMV) are associated with significant morbidity and mortality in solid organ transplant recipients and a major cause of decreased graft and patient survival in kidney transplant recipients. The CMV serostatus of the donor and recipient. Currently used antiviral drugs are associated with significant adverse effects and are limited in their clinical efficacy by the increasing resistance situation. Aim of the present study was to assess the incidence of CMV disease within 52 weeks post-transplant within the context of current clinical practice for CMV prophylaxis in kidney transplant patients.

**Methods:** We performed a retrospective, multicenter cohort study in five German kidney transplant centers in which the clinical practice of valganciclovir prophylaxis in CMV-seronegative kidney transplant recipients who received an organ from a CMV-positive donor was documented. Follow-up was 52 weeks after transplantation.

**Results:** 240 patients who received a kidney transplant from 2011 – 2021 were included. Most common indication for transplantation was high blood pressure (20.8%), polycystic kidney disease (10.3%) and IgA nephropathy (10.1%). During the study period, prophylactic valganciclovir was given at an average dose of 333.67 mg/d according to kidney function. The incidence of CMV infection in recipients was 31.5%, the incidence of CMV disease was 8.8%. When disease occurred, the average CMV DNA was 14,325 copies/mL. The most common CMV disease was enterocolitis (2.9%), pneumonia (1.8%), colitis (0.8%) and hepatitis (0.8%). Side effects occurred in 20 cases during prophylaxis with valganciclovir.

**Conclusions:** Our analysis challenges the notion that pregnancy is a risk factor for GS in HLA-AIT. Careful selection of cases with pregnancy induced sensitisation can reduce inequity to access in transplantation in female patients.

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Background: A significant number of studies have demonstrated the association between target organ damage and cardiovascular events, poor renal and overall survival in kidney transplant recipients (KTRs). Obesity is an established cardiovascular risk factor in this population. The purpose of this study is to investigate a possible association of body composition with the presence of subclinical target organ damage in KTRs.

Methods: The study included 150 KTRs who underwent measurement of pulse wave velocity (PWV) with Sphygmocor device, urine protein/creatinine ratio (UPCR) and cardio intima-media thickness by ultrasound. Body mass index (BMI) was calculated, body composition was analyzed by multi-frequency bioelectrical impedance and waist circumference was measured to determine the distribution of body fat.

Results: Mean age of the study group was 51 (15±12.5) years and two thirds of patients were male (66%). From the total cohort, 39.2% of patients had normal body weight, while 43.2% were overweight and 15.5% were obese. According to this, an active group (A, 10 patients) and a sedentary group (S, 10 patients) was formed. After a comparison of means, the following results were identified: MELD (A: 12.05 ± 5.63 vs. S: 18.39 ± 3.60, P < 0.001), VO2peak (A: 29.76 ± 6.17 ml/kg/min vs. S: 18.11 ± 3.39 ml/kg/min, P < 0.001), AT (A: 16.71 ± 2.17 ml/kg/min vs. S: 13.96 ± 1.45 ml/kg/min, P < 0.001), 6MWT (A: 458.2 ± 57.5 m vs. S: 324.7 ± 55.8 m, P < 0.001), LFI (A: 49.3 vs. 0.36 vs. S: 41.3, P < 0.001). IPAQ responses allowed for a division of patients based on the presence of adequate weekly activity levels. According to this, an active group (A, 10 patients) and a sedentary group (S, 10 patients) was formed. After a comparison of means, the following results were identified: MELD (A: 12.05 ± 5.63 vs. S: 18.39 ± 3.60, P < 0.001), VO2peak (A: 29.76 ± 6.17 ml/kg/min vs. S: 18.11 ± 3.39 ml/kg/min, P < 0.001), AT (A: 16.71 ± 2.17 ml/kg/min vs. S: 13.96 ± 1.45 ml/kg/min, P < 0.001), 6MWT (A: 458.2 ± 57.5 m vs. S: 324.7 ± 55.8 m, P < 0.001), LFI (A: 49.3 vs. 0.36 vs. S: 41.3, P < 0.001).

Conclusions: A better musculoskeletal and functional capacity, as well as retention of a level of robustness, is achieved by exercise in liver transplant candidates, despite the progression of liver disease and the sarcopenia associated with it. This effect also appears to be independent of the liver disease severity. This offers a pre-transplantation treatment target to improve survival and prognosis.

EXPERIENCE OF LIVER TRANSPLANTATION IN NATIONAL SCIENTIFIC CENTER FOR SURGERY NAMED AFTER A.N. SYZGANOV

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Background: Liver transplantation (LT) is a radical treatment method for recipients with end-stage liver disease. The first LT in Kazakhstan was performed in December 2011 year. Our hospital has more than 10 years of experience in LT by December 2022. This study shows the results after LT in a leading clinic of Kazakhstan.

Methods: From December 2011 to December 2022, 233 LT were performed at the National Scientific Centre of Surgery named after A.N. Syzganov. 24 (10.3%) LT were performed from deceased donor and 169 (72.5%) from a living donor. Paediatric LT from a living donor was performed in 40 cases (17.1%). The next graft types were used: right lobe - 155, left lobe - 23, posterolateral sector-1, Dual-graft-1, left lateral sector - 29, whole liver - 24. Indications for LT were cirrhosis in the outcome: Hepatitis C - 27, Hepatitis B - 18, Hepatitis B with delta agent- 102, primary biliary cirrhosis - 30, primary sclerosing cholangitis - 15, cryptogenic cirrhosis - 8, aluminotoxic hepatitis - 3, Budd-Chiari - 1, Myofibrolastic tumor - 1, Steatohepatitis - 2, Wilson-Konovalov - 1, Biliary atresia - 23, secondary biliary cirrhosis - 2, autoimmune hepatitis - 10. Clinical results were retrospectively analyzed.

Results: The overall 5 and 10 year survival rate after LT were 75% and 72.4% correspondingly. Biliary complications after LT were observed in 32 (13.7%), vascular complications in 10 (4.2%), bleeding in 25 (10.7%), rejection crisis in 12 (5.1%) cases. The main problem at present is the need to develop organ transplantation from deceased donors.
E-POSTERS

P601
REVISED CRITERIA FOR DIASTOLIC DYSFUNCTION OF CIRRHOTIC CARDIOMYOPATHY AND MAJOR ADVERSE CARDiac EVENTS AFTER LIVER TRANSPLANT

Jeayoun Kim1, Eun Jung Oh2, Seungwon Lee1, Gaa soo Kim1
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Background: Cirrhotic cardiomyopathy (CCM) was associated with the development of Major adverse cardiac events (MACE) after liver transplant. Particularly, the diastolic dysfunction is a prominent feature of CCM. Recently, the diagnostic criteria for diastolic dysfunction of CCM has been revised. However, the association with postoperative MACE and revised diastolic dysfunction was not comprehensively evaluated.

Methods: This retrospective study included adult recipient of living donor liver transplant at a tertiary referral center, Samsung Medical Center, between May 2010 to December 2020. Patients without sufficient echocardiographic data for characterization of diastolic dysfunction by revised criteria for CCM and patient with preoperative renal replacement therapy were excluded. Diastolic dysfunction was defined as at least two of the following criteria: septal e’ < 7 cm/s, tricuspid regurgitant maximum velocity > 2.8 m/s, left atrial volume index > 34 ml/m2, or ratio of early diastolic transmitral flow to early diastolic mitral annular tissue velocity ≥ 15. The main outcomes were MACE. Multivariable logistic regression was performed to evaluate the association of CCM and MACE within 30-day after liver transplant.

Results: Of the 674 recipients included for the analysis, 117 (18.3%) patients had diastolic dysfunction of CCM and 44 (6.5%) developed MACE within 30-day. Multivariable analysis demonstrated that preoperative diastolic dysfunction defined by the revised criteria for CCM was associated with higher incidence of post-transplant MACE.

Conclusions: Preoperative diastolic dysfunction defined by the revised criteria for CCM was associated with higher incidence of post-transplant MACE.

P602
NEW NON-INVASIVE MARKERS OF PORTAL HYPERFLOW AND ITS ROLE IN CIRRHOSIS AND POST-LIVER TRANSPLANT OUTCOME

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Background: in cirrhotic patients, portal hyperflow (PH), secondary to portal hypertension, induces systemic morpho-hemodynamic changes proportional to disease severity. These changes persist in the peri-liver transplant (LT) period with an impact on post-LT outcome. The degree of PH is usually derived from morphological stigmata (e.g. porto-systemic shunts), but systemic hemodynamic alterations of PH are not considered. The aims of this study are: i) to investigate noninvasive markers of systemic PH hemodynamic changes, ii) their relationship with cirrhosis severity, and iii) their impact on post-LT outcome.

Methods: Retrospective study on LT performed for chronic liver disease from 01/2017 to 12/2019. Clinical and hemodynamic data were registered. After pre-and post-LT CTs evaluation, literature based morphologic parameters describing thoraco-abdominal vascular remodeling were considered (e.g. ratio between pulmonary artery and aorta diameter - PA/AA - and PA diameter normalized for body mass index - nPA). Data are presented as mean±SD.

Results: 133 patients were included in the study. Pulmonary hypertension secondary to PH was diagnosed in 18% of cases with a PA/AA of 1.16±0.14. Pre-LT PA/AA and nPA were positively correlated with hemodynamic parameters that describe PH (wedge pressure, p=0.012; pulmonary vascular resistance, p=0.033) and worst cirrhosis severity (MELD,p=0.003; CHILD,p=0.040; skeletal-muscle-index,p=0.048). At pre-LT CT, an increase in these parameters of hemodynamic impairment secondary to PH was associated with greater postoperative complications (Comprehensive Complication Index at hospitalization, p=0.046; rate of infections, p=0.032; acute renal failure, p=0.032; graft loss, p=0.027) and worst predictors of allograft function (EASE p=0.004; MEAF p=0.031). PH morphological parameters improved post-LT in 47% of cases. When they did not improve, the persistent PH was related to graft loss (p=0.027).

Conclusions: In this study, we identified possible noninvasive markers of PH that are related to the severity of cirrhosis and could predict worst post-LT graft function. Systemic involvement of PH should be considered, together with portal vein and morphological parameters, in the pathogenesis of PH-related graft dysfunction and small-for-flow syndrome.
SARS-CoV-2 subgenomic RNA in kidney transplant recipients. Utility in prognosis of patients who have received Remdesivir

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**Background:** COVID-19 clinical evolution in kidney transplant recipients (KTRs) is less linear and foreseeable than in general population due to immunosuppression, as well as the response to antiviral treatment. We aim to evaluate the virological response to Remdesivir in KTRs by means of longitudinal evaluation of subgenomic RNA (sgRNA) and qRT-PCR test.

**Methods:** Thirty-five KTRs who received Remdesivir for COVID-19 from November 2021 to February 2022 were included. The analysis of both sgRNA and qRT-PCR was performed at baseline and after treatment.

**Results:** Thirty-five KTRs were included in the study. Mean age was 64±15 and 57% were males. Median time since transplantation was 80[IQR 3-321]. Triple therapy with tacrolimus, mycophenolate and steroids was employed in 69% of patients, while 17% were under prednisone, tacrolimus and everolimus. In 76% of cases, a 3-dose mRNA vaccination schedule was administered. A single dose of 200mg of Remdesivir were administered followed by 2 or 4 more daily dose of 100mg. A total of 3 KTRs (8%) received 3 doses and 32 KTRs(91%) received 5 doses. Remdesivir was administered with a median time of 53-8.5)days after symptoms’ onset. Three(8%) KTRs presented asymptomatic disease, 25(71%) moderate disease and 7(20%) severe disease. At baseline, 83% KTRs had positive sgRNA. Of the total of 29 KTRs who were positive, 15 KTRs(51.7%) were negative after remdesivir treatment, while 14 (48.3%) were still positive. The qRT-PCR test was positive in all patients at baseline and after Remdesivir treatment, but a 3-dose mRNA vaccination schedule was administered. A single dose of 200mg of Remdesivir were administered followed by 2 or 4 more daily dose of 100mg.

**Conclusions:** Qualitative sgRNA may be a valuable tool to monitor the virological response to Remdesivir in KTRs and predicts prognosis.

Liver Auto-Transplantation: A Systematic Review and Meta-Analysis to Define Indications and Determine Survival

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**Background:** Liver auto-transplantation (auto-LT), which includes ex vivo and ant situ surgery, is a surgical option for the treatment of liver tumors with vascular infiltration or retrohepatic extension not eligible for conventional surgery, although its indication is not yet clearly established. Interestingly, ex situ surgery has relevant overlaps with conventional liver transplantation, both from the technical point of view and perioperative management. We present a systematic review and meta-analysis collecting all the reported cases of auto-LT. Clinical indications for surgical treatment, survival analysis and short-term prognostic factors are reported.

**Methods:** A literature search was performed on PubMed-MEDLINE, Scopus, Cochrane Library and Web of Science, including all the case reports and series published in English, with no time limit. Experimental studies were excluded. Bibliographic sources were identified using specific keywords.

**Results:** The analysis revealed 177 cases of ex vivo and 62 of ante situm. The 90-day survival was 86.5%, with better survival for ante situm compared to ex situ (94.7% vs 82.4%, p=0.027). Survival varies according to different tumors: cholangiocarcinoma (CCA) had the worst prognosis, followed by colorctal metastasis, and hepatocarcinoma (p=0.039). The most relevant prognostic factors in cox’s analysis were the year of publication, patient’s age, surgical technique and perioperative mortality. The occurrence of complications and in particular postoperative liver failure had a significant impact on auto-LT (p=0.024).

**Conclusions:** Auto-LT is a challenging technique, burdened with a high rate of morbidity and mortality. Post-operative liver failure is of major concern, and it is one of the main causes of peri-operative mortality together with sepsis. An adequate selection of candidates with careful evaluation of underlying liver conditions, anticipated liver remnant, and patient comorbidities seems to be the keys to improve results, in particular for ex vivo resections. The type of tumor is a significant prognostic factor, as well as the patient age. Auto-LT seems to be an efficient strategy in well-selected cases, and the best perspective for patients not eligible for conventional surgery, who otherwise would have a low life expectancy and a poor prognosis.
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Background: Accepting organs from donors at higher risk of viral transmission (DDKT) poses a higher immunologic risk and there is a debate surrounding its acceptance. Nucleic acid testing (NAT) can mitigate this risk as it shortens the period in which donors may be infected with BBV but serologically negative.

Methods: We gathered data retrospectively from all patients receiving kidneys from donors with an increased risk of BBV infection since 2019.

Results: 12 patients received kidneys from donors who had undergone NAT. Mean age of donors was 42 years; of recipients was 53 years. Reasons for NAT included past Hepatitis C infection (n=4), history of IV drug use (n=5), known Herpes virus type 2 infection (n=1), this organ went to an HIV positive recipient, with NAT to exclude concomitant Hepatitis B/C infection. Recipients were often highly sensitised (median peak panel reactive antibody (PRA) 29%) and 21% of recipients were waiting more than 141 days for a suitable renal graft. Donor specific antibody (DSA) was identified in 1 of 2 patients (16.7%) who had a long waiting time (median waiting time=890 days, range=405-2225). Donor cause of death included overdose (n=3), intracranial haemorrhage (n=3), hypoxic brain injury (n=3) and other (n=3). Median cold ischaemic time was 12:05 hours (range=30-208) post-transplant patient survival was 100% 2 years and 98% 5 years.

Conclusions: Patient survival was excellent, and patients were transplanted successfully from donors with a long waiting time. These results show that donor NAT may be a viable option.

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Background: The use of DCD liver grafts has significantly increased. Early allograft failure (EAF) following liver transplantation (LT) is linked to the presence of organ-specific and non-organ-specific antibodies. The risk of early allograft failure (EAF) in DCD liver transplantation (DDC-LT) is challenging and necessitates a careful consideration of the donor’s characteristics. EAF is defined as the occurrence of severe hepatic dysfunction within the first 90 days post-LT, which may result in the need for retransplantation, severe adverse events in the early post-LT period, and, in some cases, patient death.

Methods: We performed a retrospective analysis of the EAF risk in patients who underwent liver transplantation in our center between February 1995 and May 2020. The demographic characteristics, pre-transplantation parameters, and post-LT outcomes were collected. The EAF risk was assessed using the EASE score, which is a simplified version of the Olthoff EAD score. The EASE score was calculated, and its performance was compared with the Olthoff EAD score. The receiver operating characteristic (ROC) curve was used to evaluate the discriminative ability of the EASE score.

Results: A total of 203 patients received a DCD liver graft. Out of the calculated scores, the EASE score outperformed the classical Olthoff EAD in predicting 90-day graft loss in DCD liver transplantation. The EASE score showed a higher accuracy in predicting EAF compared to the Olthoff EAD score. The AUC for the EASE score was 0.72, while the AUC for the Olthoff EAD score was 0.67. The EASE score was found to be more accurate than the Olthoff EAD score in predicting 90-day graft survival (p=0.041).

Conclusions: The EASE score is superior to the Olthoff EAD score in predicting early allograft failure in DCD liver transplantation. The EASE score is a valuable tool for predicting EAF and should be considered in the selection of donor organs for DCD liver transplantation.

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E-POSTERS

P610 OUTCOME OF PATIENTS WITH C3 GLOMERULONEPHRITIS AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Background: C3 glomerulonephritis (C3GN) results from dysregulation in the alternative complement pathway and is characterized by C3 deposits with no or minimal Ig depositions in the immunofluorescence. Studies regarding the outcome of patients with C3 glomerulonephritis after kidney transplantation are limited.

Methods: We retrospectively studied patients with C3GN who underwent living donor kidney transplantation between 2016 and 2022. Demographic data, C3GN recurrence after kidney transplantation, as well as the treatment used and the graft failure rates were recorded. In all cases the diagnosis was confirmed by renal biopsy and genetic testing for disorders of the complement pathway.

Results: A total of 7 patients (57% men) with C3GN underwent living donor kidney transplantation from 2016 to 2022. The mean age was 36 years. All patients received a triple immunosuppressive regimen. Genetic mutations were found in 3 of 7 patients, while alternative complement pathway activation was established in all 7 patients (increased C3bBbp and C5b-9 in one C3NeF). C3GN recurrence was confirmed in 5 patients (71.4%). The mean time to recurrence after kidney transplantation was 18.4 months (1-31) and the diagnosis was established by renal biopsy with dominant C3 staining (3+4†). At the time of recurrence, the majority of patients had proteinuria, microscopic hematuria and low C3 levels. Three of the recurrent cases were treated with eculizumab. Graft failure occurred in 40% of the patients with recurrent C3GN. The median time to graft failure was 55 months (47-62) post-transplantation. After a median follow-up time of 52 months, the mean creatinine level of patients with a functioning graft was 1.7 mg/dl.

Conclusions: In a case series of graft recipients with C3GN, disease recurrence was frequent with a high rate of allograft loss.

P611 EPRO DIARY LIVER: A NEW WAY TO PROMOTE PATIENT COMPLIANCE AND MORE

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2Papa Giovanni XXIII Hospital, Pediatric Hepatology, Gastroenterology and Transplantation Unit, Bergamo, Italy

Background: Adolescent liver transplant recipients represent a challenging “care management” during their transition towards adulthood. Indeed, compliance is a critical issue in this population. Low executive functions and quality of life markers were found to be similar between liver transplant recipients and other chronic diseases.

Methods: In our liver transplant center we follow a large cohort of both paediatric and adult liver transplant recipients (1024 adults, 677 adolescents). 167 patients have been already enrolled in a transitional outpatient clinic once they turn 17. In the transitional outpatient, all adolescents are evaluated jointly by a dedicated psychologist and the pediatric and adult hepatologists. To improve the compliance and the relationship between adolescent patients and the physicians, a web-based APP for smart devices has been developed. It allows patients to set up reminders for drug schedules, lab and instrumental tests and medical appointments. The system is built to alert patients in case of approaching deadlines and significant test alterations. A section dedicated to Patient Reported Outcomes (PROs) and psychological testing was also developed. All data entered in the APP can be exported by the patient and the medical team. The main features of the study population are as reported: female 75 (44.9%), male 94 (53.7%), R-OLT 29 (17.4%), average time since LT 16.8 years, median time 18 years; main indication to LT is biliary atresia (49.6%). The enrollment of the transitional patients is currently ongoing.

Conclusions: ePDR Diary Liver was approved by our ethical committee. This APP can provide modern support to young patients undergoing liver transplant recipients who are transitioning from pediatric to adulthood. It allows both adolescent patients and their caregivers to manage their relationship with the health managing team with the opportunity of monitoring the clinical situation in real time. In the coming months we shall be able to show the first reports of the project.

P612 MEDICATION ADHERENCE IN KIDNEY TRANSPLANT PATIENTS: A COMPARISON BETWEEN SHORT-TERM (3 YEARS) AND PATIENTS WITH A FAILING TRANSPLANT

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Background: Non-adherence to immunosuppression is known to be a major risk factor for poor patient and graft outcomes. Rates of immunosuppression non-adherence are high within kidney transplant recipients (KTR), with estimates of between 36% and 55%. This study explored whether adherence varies between patients less than a year post-transplant, over three years post-transplant and patients with a failing graft attending Transplant Support Clinic.

Methods: This cross-sectional study conducted between 26/09/2022 - 09/01/2023 investigates adherence in three discrete cohorts of kidney transplant recipients attending Kidney Clinic: (i) patients less than a year post-transplant, (ii) long-term recipients over three years post-transplant (LTR) and (iii) patients with a failing graft attending Transplant Support Clinic (TSC). Patients completed electronic questionnaires on an iPad. Adherence was measured using the Medicines Adherence Report Scale (MARS). Patients were classified as non-adherent if they scored < 30. Results are presented in Table 1.

Results: N=92 KTR in total completed the questionnaires. Of these, there were N=20 less than one year post-transplant, N=47 LTR and N=25 TSC patients. The rate of non-adherence across all three cohorts was 56.5%. A chi-square test revealed there was no significant difference in rates of non-adherence between cohorts (p = 0.065).

Conclusions: Our comparative analysis did not identify a significant difference in adherence between patient cohorts. However, rates of non-adherence particularly within LTR and TSC recipients were high. Further interrogation of factors associated with non-adherence in each cohort is necessary. This is a preliminary analysis and ongoing data collection will allow for more thorough investigation in the coming months.

Table 1: A comparison of MARS scores between groups

<table>
<thead>
<tr>
<th></th>
<th>Less than 1 year post-transplant (n = 20)</th>
<th>More than 3 years post-transplant (n = 47)</th>
<th>Recipients with a failing graft (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherent (score of 30)</td>
<td>65.0%</td>
<td>34.0%</td>
<td>44%</td>
</tr>
<tr>
<td>Non-adherent (score &lt;30)</td>
<td>35.0%</td>
<td>66%</td>
<td>56%</td>
</tr>
</tbody>
</table>

MARS (%)

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ASSOCIATION BETWEEN PHENOTYPES OF BLOOD PRESSURE CONTROL AND BODY COMPOSITION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Hypertension is considered the most prevalent risk factor for cardiovascular disease in kidney transplant recipients (KTRs). Several studies have demonstrated that these patients achieve poor blood pressure (BP) control. Obesity is a known risk factor for cardiovascular events in this population. The aim of our study was to investigate the possible associations between different phenotypes of BP control and body composition in KTRs.

Methods: Our study included 150 KTRs, who underwent office BP measurements and 24-hr ambulatory BP measurements (ABPM) with Mobil-O-Graph device. Arterial hypertension was defined as: (1) office BP ≥140/90 mmHg or use of antihypertensive agents, (2) ambulatory BP ≥130/80 mmHg or use of antihypertensive agents. Phenotypes of BP control were defined as follows: (1) concordant control with both methods, (2) concordant lack of control with both methods, (3) white-coat hypertension, (4) masked hypertension, as defined by the European Society of Cardiology/European Society of Hypertension (ESC/ ESH) guidelines. Body mass index (BMI) was calculated. Body composition was analyzed by multi-frequency bioelectrical impedance and waist circumference was measured to determine the distribution of body fat.

Results: All patients were hypertensive. Regarding BP control, uncontrolled hypertension with either method was observed in 61.1% of patients (n = 90), concordant lack of control in 17.4% (n = 26), white-coat hypertension in 4.9% (n = 7), masked hypertension in 2.7% (n = 4), and normal BP in 17.8% (n = 26). The frequency of obesity was 62.7% (n = 94). The mean BMI was 30.4 ± 6.7 kg/m². The frequency of overweight and obesity was significantly higher among patients with uncontrolled hypertension (38.9%). Among patients with uncontrolled hypertension, 37.5% had normal body weight, overweight was observed in 40.9% and 18.2% were obese, while classification according to BMI in patients with concordant control with both methods was not significantly different. Waist circumference was significantly higher in patients with uncontrolled hypertension (Mean Difference = 2.17 ± 2.67, p = 0.019). Both masked hypertension and uncontrolled hypertension with either method was observed in 61.1% of patients (concordant control with both methods, n = 90, p = 0.033), whereas recipients with severe BK viremia were at increased risk of graft loss (HR: 3.5, CI: 1.2-10.4, p = 0.03). BK viremia was not associated with risk of death.

Conclusions: BK viremia is prevalent post-KTx and is associated with decreased graft function. Furthermore, the majority of KTx recipient with BK viremia had severe BK viremia that was associated with increased risk of graft loss. Collectively, these findings highlight the importance of close BK monitoring and clinical management post-KTx.

Figure: Cumulative incidence curves

Table: Cohort characteristics

<table>
<thead>
<tr>
<th>KT characteristics</th>
<th>All</th>
<th>BK viremia</th>
<th>Severe BK viremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>50 (42-61)</td>
<td>54 (44-69)</td>
<td>56 (45-65)</td>
</tr>
<tr>
<td>Sec. (%, (%)</td>
<td>144 (44)</td>
<td>91 (31)</td>
<td>60 (20)</td>
</tr>
<tr>
<td>Kidney number, n (%)</td>
<td>2%</td>
<td>13 (7)</td>
<td>7 (3)</td>
</tr>
<tr>
<td>2%</td>
<td>6 %</td>
<td>13 (7)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>3%</td>
<td>9 (4)</td>
<td>8 (4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>4%</td>
<td>24 (10)</td>
<td>30 (13)</td>
<td>19 (8)</td>
</tr>
<tr>
<td>5%</td>
<td>18 (6)</td>
<td>14 (6)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Dystases, n (%)</td>
<td>13 (5)</td>
<td>11 (5)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>6%</td>
<td>3 (1)</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Disease leading to KT, n (%)</td>
<td>14 (5)</td>
<td>7 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Chronic nephro</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Systemic</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>transplant</td>
<td>14 (5)</td>
<td>20 (9)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>7 (3)</td>
<td>1 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>142 (10)</td>
<td>20 (9)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Donor age at KT, median (IQR)</td>
<td>59 (44, 60)</td>
<td>67 (54, 69)</td>
<td>60 (45, 67)</td>
</tr>
<tr>
<td>ABO</td>
<td>60 (31)</td>
<td>14 (6)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Cold ischemia time, median (IQR)</td>
<td>11 (8, 15)</td>
<td>20 (12, 45)</td>
<td>21 (8, 30)</td>
</tr>
<tr>
<td>Immunoprophylaxis at KT</td>
<td>Tac+Atretomig</td>
<td>549 (99)</td>
<td>288 (59)</td>
</tr>
<tr>
<td>Tac + Tassenus, MMF</td>
<td>2 (7)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Tac + Tassenus, MMF + Mycophenolate mofetil</td>
<td>2 (7)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Tac + Tassenus, MMF + Mycophenolate mofetil + Prednisolone</td>
<td>2 (7)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Other immunosuppression regiments</td>
<td>2 (7)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Other: Other immunosuppression regiments included Ciclosporine, mTOR and Kaposirola.
**Background:** Since December 2019, kidney transplant recipients (KTRs) have experienced a great impact of coronavirus disease 2019 (COVID-19) pandemic, with a higher risk of morbidity and mortality compared to the general population. Preliminary data in KTRs suggest that the Omicron variant, which has been dominant as of December 2021, is more infectious than the previous ones but is associated with a reduced risk of severity and low lethality rates. The purpose of our study was to assess the disease course and clinical outcomes of SARS-CoV-2 infection in KTRs during the Omicron surge.

**Methods:** This single-center retrospective study included 451 KTRs who suffered from SARS-CoV-2 infection between December 1st, 2021, and September 30th, 2022. Demographic and clinical characteristics of the patients at the time of infection, vaccination data, treatment, clinical course, and outcomes were recorded. Univariate and multivariate analysis were performed to identify preoperative risk factors associated with NODAT.

**Results:** Mean age of the study population was 51.8 ± 13.7 years with a male predominance (61.2%). The majority (76.1%) were vaccinated with at least three doses of the available mRNA vaccines, although serology revealed low anti-SARS-CoV-2 antibody titers before infection (33 [1.3-1205] AU/ml). Only 6% of the patients experienced moderate and severe disease. Accordingly, there was a low prevalence of adverse outcomes related to COVID-19, such as SARS-CoV-2-related hospitalization (11.3%) and death (0.9%). Multivariate analysis revealed that only age significantly increased the risk of SARS-CoV-2-related hospitalization.

**Conclusions:** The Omicron wave, clinical course of SARS-CoV-2 infection in KTRs has drastically changed, with lower rates of moderate and severe disease and a low prevalence of adverse outcomes. Prospective clinical trials are warranted to further elucidate the evolving pathogenesis, management, and long-term outcomes of COVID-19 in such high-risk populations.

**P618**

**EARLY OUTCOMES OF LIVER TRANSPLANTS AFTER NORMOTHERMIC MACHINE PERFUSION**


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**Background:** Normothermic machine perfusion (NMP) has been increasingly used in liver transplantation. Our aim was to assess the early outcomes of liver transplants after NMP.

**Methods:** In February 2023, we retrospectively reviewed our database of liver grafts perfused on the OrganXet metra machine in a period of 39 months (April 2019 – July 2022) to allow for a follow-up period of at least 6 months. We collected data about donor and recipient characteristics, as well as primary non-function (PNF), early allograft dysfunction (EAD), hepatic artery thrombosis (HAT), biliary complications, retransplant and mortality within the first 6 months after the liver transplant.

**Results:** 136 liver grafts [75 (55.1%) from donors after brain death (DBD), 61 (44.9%) from donors after circulatory death (DCD)] underwent NMP during the aforementioned period, out of which 116 (85.3%) were transplanted [88 (58.5%) from DBD, 46 (41.4%) from DCD], whereas 20 (14.7%) were discarded [7 (55%) from DBD, 13 (65%) from DCD] due to poor function during NMP. There were 2 cases (1.7%) of PNF and 39 cases (33.6%) of EAD. HAT occurred in 2 cases (1.7%), 51 recipients (44%) had at least one form of biliary complications. In particular, anastomotic leak occurred in 8 patients (6.9%), anastomotic stricture was evident in 34 patients (29.3%), ischaemic cholangiopathy was detected in 18 patients (15.5%), while there were 5 cases (4.3%) of other biliary complications (biliary cast, leak from disconnected duct, non-anastomotic bile leak). There were 4 retransplants (3.4%) and 9 deaths (7.8%) during the first 6 months after liver transplant.

**Conclusions:** High rates of biliary complications and EAD rates are noted in marginal liver grafts after NMP. Bile duct anastomotic stricture is the predominant biliary complication. NMP enables better assessment of marginal liver grafts and decreases the risk of PNF.
Background: Native arteriovenous fistulae (AVF’s) are the gold standard haemodialysis (HD) access modality for patients in end stage renal failure. AVF failure may result in much patient morbidity and mortality as a significant proportion resort to dialysis with central venous catheters with its associated risks. Herein we present an AI-enabled approach to model prediction of AVF failure using continuous clinical measurements derived from HD machines.

Methods: We included 100 patients between Apr 2013-Aug 2019. 50 had a working AVF & 50 had a failed AVF at latest follow up. Demographic and comorbid data (e.g. diabetes, hypertension, thrombophilia) as well as machine parameters were collected. Originally 14 variables accumulated were from the HD machine, however, after feature selection process analysis only 3 were included - litres of blood processed, arterial & venous pressures. We employed feature engineering on static & temporal data, with Bayseian optimisation to train our AI model utilising random subspace methods for discrimination of AVF failure and identification of at-risk patients. We further introduced a survival-aware machine-learning-based system for the prediction of time-to-AVF failure.

Results: We found the 10-fold cross-validated discriminant subspace-based ensemble algorithms attained 79.8 ± 0.39 classification accuracy to predict the functionality of the fistula. Validation area under the receiver operating characteristic curve was 90.08 ± 0.27 which is the best performing predictive accuracy of fistula failure using routinely collected clinical data with readily available features from the dialysis machines. Using the 95% confidence interval, the sensitivity & specificity found to be 87.33 ± 0.6 and 78.67 ± 0.6, respectively. Using concordance index (c-index) as a measure of performance, our Gradient boosting machine (GBM)-based survival model achieved maximum performance values of 0.76 ± 0.07 whilst establishing a connection between the variables and the time of an AVF failure.

Conclusions: We demonstrate the potential of AI to predict fistula failure in real world example. This model can be used to trigger a specialist access review when the algorithm suggests high risk of future fistula failure leading to preemptive interventions.
E-POSTERS

P624 ASSOCIATION OF VESSEL-SPECIFIC CORONARY ARTERY STENOSIS WITH MAJOR ADVERSE CARDIOVASCULAR EVENTS IN RENAL TRANSPLANT CANDIDATE COHORT

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Background: Coronary artery stenosis is a key risk factor of major adverse cardiovascular events (MACE). Left anterior descending (LAD) artery stenosis is regarded to be the most severe vessel-specific coronary artery stenosis as depicted by its appellation “widow-maker”. We hypothesised that right coronary artery (RCA) stenoses may present poorer or similar outcomes to LAD. This study sought to understand the association of vessel-specific coronary artery stenosis using computed tomography coronary angiogram (CTCA) with MACE in a renal transplant cohort.

Methods: This was a single-centre retrospective study of all end-stage renal disease (ESRD) patients eligible for kidney transplantation who underwent CTCA between 2012 to 2014. MACE occurrences (heart failure, AMI, unstable angina, CVA, PVD and TIA) were recorded within a 9-year follow-up period. CTCA data-sets were assessed by 2 independent specialists, visually grading stenosis severity into 2 classifications (<50% or >50% coronary diameter reduction).

Results: Of 106 patients in our study, a total of 419 coronary arteries (106 RCA, 104 LAD, 104 circumflex (CX), 104 left mainstem (LM)) were graded by CTCA. 43 patients (40.6%) experienced at least one MACE within the time-frame. Statistical significance in MACE was observed when stratified by RCA stenosis severity (p=0.022) while no statistical significance in MACE observed when stratified by LAD (p=0.904), CX (p=0.472) & LM (p=0.222).

Conclusions: This challenges the conventional wisdom on individual vessel-specific coronary artery stenosis, suggesting that RCA stenoses is associated with MACE in the transplant cohort. This also offers the possibility of RCA stenosis as a prognostic tool in predicting MACE in ESRD patients.

P625 NORMOTHERMIC REGIONAL PERFUSION REDUCES APOPTOSIS MARKERS IN CONTROLLED DONATION AFTER DETERMINATION OF DEATH

Gabriel Moreno-Gonzalez *1, Eva Oliver Juan1, Elena Modrego3, Laura Anguela-Calvet1, Luis Secanella4, Laura Llado4
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Background: Normothermic regional perfusion (NRP) rescues organs for transplantation in controlled donation after circulatory determination of death (DCD), however little is known about the damage molecules that are playing a role in this recovery. Our aim is to address if there is any role of markers of apoptosis in this process.

Methods: We performed a prospective longitudinal study of a cohort of 17 controlled DCD donors with NRP from February 2020 to October 2021. Demographic characteristics was recorded. Standard protocol for DCD were performed. Serum samples were collected at theater entrance, 5 minutes after determination of death, and 60 and 120 minutes of NRP, they were processed and stored at -20ºC until analysis. Multiplex analysis of caspase-3 was performed. Biochemical and data of NRP were recorded as standard protocol. Quantitative variables were expressed as mean o median and qualitative as percentage. IBM Statistics 24 package was used.

Results: The mean age of donors was 57 years old; the main cause of death was anoxic encephalopathy in 58.8%. All the DCD was performed with pre-mortem cannulation. The total warm ischemia time (TWIT) was 18 minutes ± 4.6, and the functional warm ischemia time (FWIT) was 12 minutes ± 5 whereas the preservation time was 127 ± 25 minutes (Table 1). Lactate was 1,06mmol/L ± 0.8 previous initiation of DCD protocol, increases at 5 minutes until 6,9mmol/L ± 1.78 and then decreased progressively to 4,45 ± 1.8, 4.0 ± 1.7, 3.6 ± 1.5 and 3.53 ± 1.1 at 30, 60, 90 and 120 minutes during the NRP. The median caspase-3 levels were 833 pg/mL (277- 2494) basal, increase 4407 pg/mL (519 – 7643) at 5 minutes and then decreased progressively to 2745 (1019 – 7933) and 2355 (948 – 5483) at 60 and 120 min of NRP (Figure 1).

Conclusions: There is an increase of caspase-3 and lactate levels after determination of death, and this is reduced progressively during NRP. Further studies are needed to know the mechanisms of this reduction and to determine if this has any impact in the organ function after transplantation.
Long term effects of composite warm and cold ischaemic time in deceased donor kidney transplantation

Christopher Seet, Pankaj Chandak, Ibsam Mohamed, Muhammad Khurram*1

1The Royal London Hospital, London, United Kingdom

Background: Cold (CIT) and warm ischaemic time (WIT) are independent predictors of poor outcomes in kidney transplantation. However, their combined effect has not been studied in large cohorts. We aimed to determine if a composite measure of combined CIT and WIT is a predictor of kidney transplant outcomes.

Methods: We analysed 26,583 adult kidney transplants from 2000-2018 using the UK Transplant Registry. CIT and WIT were assessed separately, and as a combined factor. The WIT threshold was 35 minutes, and CIT threshold was 12 hours for DCD and 15 hours for DBD transplants. Univariate and multivariate analyses were performed comparing outcomes based on CIT or WIT alone and as a combined factor, adjusting for donor and recipient factors including age, sex, ethnicity, primary renal disease, dialysis modality and cRF. The main outcomes were 3, 12, and 60 month creatinine, delayed graft function (DGF), primary non-function (PNF), and graft survival.

Results: Increased CIT or WIT alone were associated with poorer early graft function. DGF or PNF rates were generally higher, although this was not consistently observed across all groups. When analysed as a composite factor, there was a more consistent effect in grafts with increased CIT and WIT compared to either factor alone, with poorer 3 and 12 month creatinine, and increased risk of DGF and PNF (Table 1). Graft survival was also poorest in grafts with both raised CIT and WIT, while low CIT and WIT grafts performed best.

Conclusions: Longer composite times have stronger effects on graft outcomes compared to CIT or WIT alone. While it may not always be possible to reduce both CIT and WIT, reducing just one of these factors can significantly improve outcomes.

Table 1: Composite WIT/CIT outcomes

<table>
<thead>
<tr>
<th></th>
<th>3m Cr*</th>
<th>P-value</th>
<th>12m Cr*</th>
<th>P-value</th>
<th>60m Cr*</th>
<th>P-value</th>
<th>DGF*</th>
<th>P-value</th>
<th>PNF*</th>
<th>P-value</th>
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<tr>
<td>DCD</td>
<td>1.05</td>
<td>&lt;0.001</td>
<td>1.03</td>
<td>&lt;0.001</td>
<td>1.07</td>
<td>0.002</td>
<td>1.87</td>
<td>&lt;0.001</td>
<td>1.80</td>
<td>&lt;0.001</td>
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<tr>
<td>Low CIT</td>
<td>1.04</td>
<td>&lt;0.001</td>
<td>1.04</td>
<td>&lt;0.001</td>
<td>1.09</td>
<td>&lt;0.001</td>
<td>1.29</td>
<td>&lt;0.001</td>
<td>1.01</td>
<td>0.31</td>
</tr>
<tr>
<td>Low WIT</td>
<td>1.51</td>
<td>0.016</td>
<td>1.00</td>
<td>0.978</td>
<td>1.04</td>
<td>0.21</td>
<td>1.18</td>
<td>0.015</td>
<td>1.50</td>
<td>0.031</td>
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<tr>
<td>DGF</td>
<td>1.07</td>
<td>&lt;0.001</td>
<td>1.07</td>
<td>&lt;0.001</td>
<td>1.03</td>
<td>0.105</td>
<td>1.48</td>
<td>&lt;0.005</td>
<td>2.01</td>
<td>0.005</td>
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<tr>
<td>Low CIT</td>
<td>1.04</td>
<td>0.002</td>
<td>1.06</td>
<td>&lt;0.001</td>
<td>1.03</td>
<td>0.096</td>
<td>1.17</td>
<td>0.052</td>
<td>2.20</td>
<td>0.002</td>
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<tr>
<td>Low WIT</td>
<td>1.51</td>
<td>0.011</td>
<td>1.02</td>
<td>0.127</td>
<td>1.03</td>
<td>0.896</td>
<td>1.21</td>
<td>0.028</td>
<td>1.54</td>
<td>0.121</td>
</tr>
</tbody>
</table>

*Regression estimate **Hazard Ratio. Baseline for comparison: Low CIT/Low WIT.
Background: Liver transplantation (LT) remains the golden standard in the treatment of end-stage liver disease, and limited graft availability remains a problem. The Split-liver technique offers a potential solution to this problem, although there is no reliable and recognized method for calculating ex-vivo graft volumes. Evaluate the use of LiDAR technology to calculate the volume of cadaveric organs (liver) and evaluate the method for application in transplantation.

Methods: A post-mortem examination was performed by the forensic team. After the hepatic graft was removed from the abdomen, it was grossly examined, including weight and volume calculation using the water immersion technique. Using a special 3D portable LiDAR camera, the graft was photographed, and a 3D digital model of the liver was created by the relevant software. Subsequently, an analysis was run to calculate the volume of the left lobe before a transplant surgeon divided the organ into two lobes. Actual left lobe weight and volume were then calculated using the same techniques as above. All relevant calculations were completed by the software.

Results: Nine liver grafts were assessed post-mortem for actual weight and estimated weight using a LiDAR camera. Due to normal distribution, the student t-test was used to compare the two sets. The mean total weight was 1647.3g, and the mean estimated weight was 1576.9g; the two groups had no statistical difference (P=0.708) with a 95% confidence interval (-86, 123).

Conclusions: Preliminary findings suggest that LiDAR photography scanning could be a potential tool for the calculation of the actual volume of liver cadaveric organs. Moreover, calculating the left lobe weight from the total graft volume using LiDAR photography and software produced a similar result compared to the actual measured weight. Validation of these findings with a larger sample is necessary.

Background: The shortage of available organ donors is a significant problem worldwide, and among the pediatric population the problem has even wider ranges, mainly because of the peculiarity of the donation scenarios and the difficulty of matching between donors and recipients. Various efforts have been carried out to increase the donor pool, such as living donation and split liver techniques; but the possibility of pediatric DCD has not been exploited in Italy yet. In order to develop a Regional network to facilitate the development of shared protocols and guidelines, to define the epidemiological context and practices and develop specific tools and guidelines for each unit, a preliminary survey was carried out to analyze the current setting of Regional pediatric DCD programs. The survey explored through 21 closed questions the number of PICU beds, the availability of WLST registry and institutional programs, the availability of an in-site NRP facility and the willingness to elaborate or collaborate to a shared educational program.

Results: 4 out of the 5 Lombardy PICUs have similar pediatric demographic characteristics, except for one PICU, which is mainly dedicated to post operative patients. Traumatic pediatric patients are centralized in one center with no exceptions. All the participants centers hospitalize together more than 2000 patients/year, ranging from 40 days to 18 years of age, with roughly 1 mortality mostly due to genetic pathology complications. In all the hospitals DCD and tissue donation programs are active. 2 of them have pediatric transplant programs. Three centers have currently no formalized institutional WLST procedure, 4 out of 5 participate to a shared National registry. The main cause of WLST is post-anoxic cerebropathy, followed by cardiocirculatory disease, chronic pathology complications in half of the patients undergoing WLST develop MOF. Educational programs focused on pediatric DCD has not started in any of the institution, yet.

Conclusions: The preliminary survey draws the picture of 5 Regional Italian PICUs that could possibly create a shared network of competences and professionals for pDCD.

Background: Current desensitization therapies have shown very poor success to decrease anti-HLA antibodies in highly sensitized patients. Besides central bone marrow-residing long-lived plasma cells (LLPC), peripheral memory B cells (mBC), peripheral memory T cells (TFH) and Central Memory B cells (CMB) contribute to antibody formation. We designed a prospective, phase-II, exploratory trial (COMBAT; NCT05145286) based on a dual-targeted approach with co-stimulation blockade with belatacept and the anti-CD38 mAb daratumumab to abrogate alloimmune compartments.

Methods: 10 patients with cPRA>99% on the deceased donor kidney transplant waiting list, without a compatible donor offer for >3 years despite being on a national prioritization program, will be included. The first phase of the strategy consists on belatacept 10mg/kg administered on days 1, 5, and end of weeks 2, 4 and 8 (T0-T1), followed by 4 sessions of apheresis (T1-T2), and subsequent 4 doses of daratumumab (8mg/kg) every two weeks until week 17 combined with belatacept (5mg/kg) (T2-T3), ending with two doses of belatacept until week 24. Changes on serum anti-HLA antibodies, frequencies of circulating IgG-producing HLA-specific mBC, TFH and Bone Marrow-residing LLPC are assessed.

Results: We describe the preliminary results of the first 3 patients included in the trial, we expect to present the full data of the study by the ESOT congress. 1 patient discontinued the trial after 3 belatacept doses because of a colitis episode. 2 other patients completed the scheduled therapy. Notably, a progressive significant reduction of serum anti-HLA antibodies has been observed over time at each time point (Figure 1A and B). This reduction is observed for both class I (mean MFI at baseline 6706 ± 8279 vs 5725 ± 7564 at T3, p<0.0001) and class II HLA antigens (mean MFI at baseline 9243 ± 9177 vs 8772 ± 8878 at T3, p<0.003). No safety concerns were observed. All cellular assays and data of the remaining patients of the study are undergoing and will be presented at the congress.
Conclusions: Dual targeting of central and peripheral humoral alloimmune compartments with daratumumab and belatacept may be an effective strategy to reduce the sensitization burden of highly sensitized patients waiting for kidney transplantation eventually facilitating access to kidney transplantation.

Results: Six (20%) patients developed acute clinical AMR, which were all implemented in all but one patient. Pre-KT plasmapheresis was performed in 13, and class II only in 9. Pre-KT DSA without positive XM in 16. Twelve patients also had ABO incompatibility. Both class I and II DSAs were detected in 1.5mg/kg. RTX dose was 100~300mg/body (median 200). CDC- and flowcytometry (FC)- crossmatch (XM) was positive in 10 patients, CDC- and flowcytometry (FC) negative in 2 patients. ABO incompatibility was associated with a worse cancer-specific survival in patients with post-transplant de novo upper tract urothelial carcinoma, which highlighted the importance of early diagnosis. Aristolochic acid exposure was independent risk factor for contralateral upper tract recurrence. The patients exposed to aristolochic acid had more multifocal tumors and higher incidence of contralateral upper tract recurrence. Thus, prophylactic contralateral resection was suggested for post-transplant upper tract urothelial carcinoma, especially for patients with aristolochic acid exposure.

Background: Long-term prognosis and risk factors of de novo upper tract urothelial carcinoma after renal transplantation were rarely studied. Thus, the aim of this study was to investigate the clinical features, risk factors, and long-term prognosis of de novo upper tract urothelial carcinoma after renal transplantation, especially the impact of aristolochic acid on tumor, using a large sample.

Methods: 106 patients were enrolled in retrospective study. The endpoints included overall survival, cancer-specific survival, bladder or contralateral upper tract recurrence-free survival. Patients were grouped according to aristolochic acid exposure. Survival analysis was performed using Kaplan-Meier curve. Log-rank test was used to compare the difference. Multivariable cox regression was conducted to evaluate the prognostic significance.

Results: Median time from transplantation to development of upper tract urothelial carcinoma was 91.5 months. Cancer-specific survival rate at 1, 5, 10 years was 89.2%, 73.2%, 61.6%. Tumor staging (T2), lymph node status (N+) were independent risk factors for cancer-specific death. Contralateral upper tract recurrence-free survival rate at 1, 3, 5 years was 80.4%, 68.5%, 50.9%. Aristolochic acid exposure was independent risk factor for contralateral upper tract recurrence. The patients exposed to aristolochic acid had more multifocal tumors and higher incidence of contralateral upper tract recurrence. Both higher tumor staging and positive lymph node status were associated with a worse cancer-specific survival in patients with post-transplant de novo upper tract urothelial carcinoma, which highlighted the importance of early diagnosis. Aristolochic acid was associated with multifocality of tumors and higher incidence of contralateral upper tract recurrence.

Conclusions: Both higher tumor staging and positive lymph node status were associated with a worse cancer-specific survival in patients with post-transplant de novo upper tract urothelial carcinoma, which highlighted the importance of early diagnosis. Aristolochic acid was associated with multifocality of tumors and higher incidence of contralateral upper tract recurrence. Thus, prophylactic contralateral resection was suggested for post-transplant upper tract urothelial carcinoma, especially for patients with aristolochic acid exposure.
VOLUMETRIC ASSESSMENT OF HEPATIC GRAFTS USING LIGHT DETECTION AND RANGING (LIDAR) TECHNOLOGY

Konstantina Elena Karakasi1, Georgios Katsanos1, Stavros Neiros1, Ion-Anastasios Karolos2, Athanasios Kofinas1, Nikolaos Antoniadis1, Styliani Vasileiadou1, Nikolaos Pagkalos1, Georgios Tsoufas1,3

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Background: Liver transplantation is the most effective treatment for end-stage liver disease. Due to continuous advances in the field, there is an increasing paucity of grafts. This means that thousands of adults and, mainly, pediatric patients are impacted by the scarcity of liver grafts. There is a need in both live donation and liver resection to be able to accurately estimate liver volume. The LIDAR 3D technology could help address this need: a study has been designed to allow us to use a LIDAR camera to estimate liver volume. The main aim of the study is to examine whether hepatic graft volume can be estimated using the LIDAR camera. The safety and accuracy of measurements were two of the main study pylons.

Methods: Hepatic grafts were used. All demographic characteristics of donors were recorded, namely age, weight and height, while body mass index was also calculated. The cause of brain (stem) death was also recorded. A biopsy of all hepatic grafts was performed. The volume of hepatic grafts suitable for transplantation was estimated. Back-table preparation was completed before weighing the graft on precision scales and then taking a picture with a special LIDAR camera. The entire process lasted 2.5-3 minutes, and in no case were grafts left outside the preservation solution for long. From 06/2021 to 12/2022, a total of 23 hepatic grafts were assessed. The graft weight, the camera-estimated graft volume, the graft volume estimated based on the Vauthey formula, the transformation of the volume measured to estimated volume, and their difference in grams and percentile deviation were all recorded on the database.

Results: Data were recorded, followed by statistical analysis, initially assessing demographic data and finding mean values for the parameters recorded. T-test of related samples followed to calculate the p-value for statistically significant differences among samples. The mean total weight was 1521.5 g, and the mean estimated weight was 1627.7 g; the two groups had no statistically significant difference (P=0.314) with a 95% confidence interval (-354, 353).

Conclusions: The results of this study indicate that a LIDAR camera to estimate total liver volume is feasible and safe. The method offers hope for estimating partial liver volume.
**P641**

**POST-TRANSPLANT DONOR SPECIFIC ANTIBODIES DYNAMICS CAN BE PREDICTED USING C3D ASSAY IN ASSESSMENT FOR HLA-INCOMPATIBLE KIDNEY TRANSPLANTATION**

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Background: HLA-incompatible kidney transplantation outcomes can be variable. Pre-transplant/ pre-desensitisation diagnostic tests can help predict behaviours of donor specific antibodies post-transplantation and associated worse outcome. This study explores value of C3d assay in prediction of post-transplant dynamics of DSA.

Methods: 134 patients were transplanted against donor-HLA-specific antibodies (DSA). 93 cases had post-transplant DSA dynamics classified by unsupervised machine learning into five distinct DSA response groups and of these 92 had C3d assay performed on samples before desensitisation.

Results: C3d positive DSA was detectable in 1 out of 20 cases that had no DSA responses following transplantation (Group 0). Modulation group (Group 1 and 2) (N=41 cases) where DSA rose rapidly and then fell within first month post-transplantation had 7 cases with C3d positive DSA whilst the Sustained dynamic group (Group 3 and 4) (N=31) where antibody levels stayed high and did not fall had 19 cases with C3d positive DSA. This was statistically significant (p =0.0002).

Conclusions: Our analysis suggests using solid phase assay on pre-desensitisation treatment for HLA-i transplant can predict post-transplant dynamics of DSA that are associated with rejection and poor graft survival long term. Thus the use of this assay for delisting and risk stratification is suggested.

**P642**

**LATE NON-CATHETER-RELATED VENOUS THROMBOTIC EVENTS IN LUNG TRANSPLANT RECIPIENTS**

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Background: Deep venous thrombosis (DVT) is a common complication in lung transplant recipients (LTRs) and is associated with higher 1-year mortality rates. Even within our population of LTRs, the majority of thrombotic events occur shortly after surgery and are generally related to the use of central venous catheter (CVC) or extracorporeal membrane oxygenation (ECMO). Instead, we hereby present a report focusing on thrombotic events that occurred at least 60 days after surgery and in sites that weren’t used for CVC or ECMO application.

Methods: This study is a retrospective analysis from a tertiary-care, university-affiliated referral centre based in Milan, Italy. Clinical records of all lung transplant recipients between January 2014 to August 2022 were reviewed for thrombotic events. Demographic information and preoperative patient characteristics including age, sex, indication for transplantation, immunosuppressive therapy at the time of the event and risk factors for thrombophilia were reported. Follow-up was obtained until Jan 15, 2023. Thrombotic events in sites of CVC or ECMO and/or occurring within 60 days were excluded.

Results: The study comprised 13 patients (see image 1), 9 of which were men (69%). Indication for transplant: 5 cystic fibrosis, 4 COPD, 4 interstitial lung disease. Median age was 56 (24, 67) years. 3 patients (23%) had a history of venous thrombosis and 2 patients (15%) had a history of pulmonary embolism; these same 2 patients were also the only ones to have genetic coagulopathy (hyperhomocysteinemia and factor V Leiden). See table 1 for other risk factors. Median time of first-time thrombotic event occurrence from transplantation was 134 days (74, 1757). Of all events in this group of patients, 7 (54%) were DVTs of lower extremities. We also recorded 3 cases of pulmonary embolism, 2 of them were concomitant with DVTs.

Conclusions: Our analysis suggests using solid phase assay on pre-desensitisation treatment for HLA-i transplant can predict post-transplant dynamics of DSA that are associated with rejection and poor graft survival long term. Thus the use of this assay for delisting and risk stratification is suggested.
DONATION AFTER CIRCULATORY DEATH IN INTESTINAL TRANSPLANTATION: THE PATH TO PROVE ITS VALIDITY IN BOTH EXPERIMENTAL AND CLINICAL MODELS

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Background: DCD (donation after circulatory death) has been precluded as a valid alternative for intestinal transplantation (IT). Our aim was double: to test the viability of the intestinal grafts using normothermic regional perfusion (NRP) in an experimental model and to assess ischemic-reperfusion injury (IRI) of the small bowel in human DCD.

Methods: We used an experimental porcine model with 6 donor-recipient pairs (25.5 ± 2.5 kg). Donors were supported using NRP. The small intestine was heterotopically transplanted into the recipients and they were followed-up for two weeks. Blood and intestinal samples were obtained throughout the procedure and 1, 2, 7, and 14 days after IT. PCS was 1.23 [0-3] and 1.65 [0-4] after 30 and 60 minutes. All grafts recovered, with no or very subtle alterations after 48h. One graft was compared with that from the native small bowel and peripheral blood function was tested at the endpoint. Glycemia from the draining veins of the graft was compared with that from the native small bowel and peripheral blood 15, 30, and 60 minutes after intra-graft glucose administration. The intestines from 26 human DCDs were sampled for histological analysis while other organs were procured with NRP after 30 and 60 minutes.

Results: All the intestines were successfully procured. One case was excluded due to venous stenosis. 6 animals (86%) reached the endpoint in good conditions. Grafts conserved architecture during NRP. The highest PCS was observed 1h after reperfusion, with PCS-4 in 3 samples (43%). All grafts recovered, with no or very subtle alterations after 48h. Four recipients (71%) did not show rejection signs at any time. Two cases (29%) expressed mild rejection 7 days after IT. At the endpoint, one of them had recovered but the other had progressed to severe acute cellular rejection (14%). Grafs' glycemia reached its maximum 30 minutes after glucose administration. All intestines from human donors appeared macroscopically normal. 80% did not show any significant IRI. PCS was 1.23 [0-3] and 1.65 [0-4] after 30 and 60 minutes.

Conclusions: This experimental model postulate DCD under NRP as an alternative source of organs for IT. Its results appear to be comparable to those of other organ procurement techniques. The analysis of the human samples suggests that this approach could be successfully translated to the clinical setting.

TRANSPLANT RENAL ARTERY STENOSIS - SURGICAL INTERVENTION: TIME IS GFR

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Background: Transplant Renal Artery Stenosis (TRAS) is a well-recognised complication following kidney transplantation. Along with clinical suspicions of rising creatinine and blood pressure, acute tubular necrosis (ATN) without rejection, the diagnosis is typically confirmed through a CTA/MRI angiograms or catheter angiography. Percutaneous Transluminal Angioplasty (PTA) is usually the initial treatment modality where possible. Surgical revascularisation is reserved for cases in which PTA is unsuccessful and/or unsuccessful. We present our experience of reimplants highlighting common pitfalls and ways to improve function by mitigating them.

Methods: A single centre retrospective study was performed on all transplants between January 2019 and June 2022. Data of donor and recipient demographics, operative findings, radiological and histological results, and biochemistry pre- and post-revascularisation was collected.

Results: Out of the 571 patients who underwent kidney transplantation during this time period, 7 were diagnosed with TRAS requiring surgical reimplantation All (3 DBD, 1 DCD and 3 LD) had rising creatinine levels, and those with serial biopsies had evidence of progressively worsening Remuzzi scores. 2/7 patients were reported to have a normal departmental ultrasound. The average time for reimplantation was 85 days post transplantation. 4/7 patients had a prior angioplasty (with the initial stent being lost) and another 2 had this outcome. 1 patient was asymptomatic and the other had an asymptomatic stenosis. One was anonymous to improve graft and patient became dialysis dependent and there was one patient death due to perioperative cardiac event. 5/7 (71%) had a functioning allograft at the last follow up (4.8 years). The patients with the longest time from diagnosis to definitive treatment (1022 days) had the worst graft outcomes (graft failed).

Conclusions: Surgical revascularisation is a complex major procedure, with significant morbidity and mortality, but if performed in the timely manner offers the greatest chance of better graft function and survival. High index of suspicion for TRAS in the face of clinical signs or prolonged ATN without obvious cause should trigger definitive investigations to prevent irreversible damage and worse outcomes.

THE IMPACT OF LIVE KIDNEY DONATION IN A KIDNEY EXCHANGE PROGRAMME ON THE HEALTH-RELATED QUALITY OF LIFE OF THE DONOR

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Background: Kidney exchange programmes (KEP) were introduced as a solution for HLA- or blood group incompatible living donor-recipient pairs. Studies have been conducted to assess the quality of life (QoL) of donors after transplantation but few focused on differences between direct and indirect donation through KEP. This is important because in KEP, a living donor donates to a different person than their intended recipient, whereas in direct donation, the donor is the recipient. In this study we analysed the difference in HRQoL between donors who donated directly or indirectly through KEP. We hypothesise that the HRQoL of donors participating in a KEP is not significantly different compared to donors who directly donated a kidney to their intended recipient.

Methods: All living kidney donors in our centre from 2014 to 2022 were included. Standardized RAND-36 questionnaires were sent at 3-, 6- and 12-months after donation to assess physical and mental health. 36 domains from these 3 domains the physical- (PCS) and mental component summaries (MCS) were calculated. Higher scores indicate higher HRQoL. Means and 95% confidence intervals were computed. Differences between groups were assessed by nonparametric statistics.

Results: 732 donors were included in the study of which 162 (22%) donated through KEP. At 3-months post-donation, we found a difference in the PCS, with a mean in KEP of 89.2 (95% CI: 86.5 - 91.9) and 84.6 (95% CI: 82.9 - 86.4, p < 0.01) in non KEP. The MCS was also higher at 3-months in KEP with a mean of 86.9 (95% CI:83.8 - 89.9) and 82.8 (95% CI: 81.8 - 84.5, p < 0.03) in non KEP. Donors who donated through KEP scored better in the domains of limitations due to physical problems, energy levels, mental health, and general health. At 6- and 12-months post-donation, we found that the PCS and MCS were not significantly different.

Conclusions: Living kidney donors who donated via KEP in general have similar quality of life compared to donors who donated directly to their intended recipient. The fact that the number to be a small but significantly higher HRQoL in the KEP donors at 3-months and no difference after 12-months is another important advantage of KEPs and takes away another level of relucance to further develop KEPs.
Background: Although laparoscopic donor nephrectomy (LDN) represents the gold-standard technique for kidney living donation, robotic donor nephrectomy (RDN) settled as another appealing minimally-invasive technique over the last decades. A comparison between LDN and RDN outcomes was carried out.

Methods: RDN and LDN outcomes were compared, focusing on operative time and perioperative risk-factors affecting surgery duration. Learning curves for both techniques were compared through spline regression and cumulative sum (CUSUM) models.

Results: The study analyzed 512 procedures (154 RDN and 358 LDN) performed from 2010 and 2021 in two different high-volume transplant centers. RDN group presented a higher prevalence of arterial variations (36.2% vs. 22.4%; p=0.001) compared to LDN cohort. No open conversions occurred; operative time (210 vs. 195 minutes; p=0.011) and warm ischemia time (230 vs. 180sec; p<0.001) were longer in RDN. Postoperative complication rate was similar (8.4% vs. 7.9%; p=0.64). Higher BMI resulted as an independent risk factor for longer operative time (210 vs. 195 minutes; p=0.011) and warm ischemia time (230 vs. 180sec; p<0.001). Spline regression models depicted a faster learning curve in RDN compared to LDN (CUSUM) models.

Conclusions: RDN grants a faster learning curve and improves multiple vessels handling. Incidence of postoperative complications was low for both techniques.

Figure. The cumulative sum (CUSUM) analysis of operative time (min) among RDN (Panel A) and LDN (Panel B)
Background: The increased numbers in living donor (LD) and extended criterion deceased donor (ECD) kidney transplants were two major developments over the last 20 years in most European countries. Post transplantation lymphoproliferative disorder (PTLD) is an aggressive malignancy which carries a lifetime development risk of up to 2.5% for kidney transplant recipients. Aim: To conduct a narrative review related to the effect of PTLD on LD and DD recipients, and ECD and SCD kidney transplant recipients.

Methods: Two searches on databases MEDLINE and EMBASE were conducted for PTLD outcomes on each of LD and ECD transplants, yielding 210 and 125 results respectively. 10 studies were included in the LD category, and 3 studies included in the ECD category following screening.

Results: Within cohort studies, the incidence of PTLD in LD and DD recipients is 0.49% and 2.50% respectively. With a median follow up period of 52 months from transplant, all-cause mortality for PTLD patients was similar at 60% for LD and 61% for DD recipients. For ECD recipients, a higher incidence of PTLD is recorded (HR 2.72, 95% CI 1.38-5.37) when compared to LD, and SCD recipients in a large Australasian analysis, but this result is not fully supported in smaller European studies. In these studies, incidence of PTLD in the ECD group range from 1.60-14.10%, while it is 0-8.20% in the SCD group. No conclusion can be made on mortality. In both study groups, EBV serological mismatch and induction using T-cell depleting agents seem to be associated with higher risk of PTLD.

Conclusions: Efforts to minimising PTLD risk should focus on applying T-cell depleting treatment in a tailored and targeted way, screening for EBV status and providing prophylaxis for CMV, while enabling shared decision-making during counselling when choosing kidney donor types and individualised risk are equally important.

Background: Cardiovascular events are a leading cause of morbidity and mortality in people with significant chronic kidney disease. Cardiac stress testing can guide risk stratification for transplantation, in addition to identifying people who may require invasive coronary intervention, although the benefit of this versus conservative strategy is contentious. We aimed to look at our practice locally, and review cardiovascular outcomes after a 3 year period.

Methods: We identified all patients we referred for a dobutamine stress echo-cardiogram (DSE) in 2019 in Nottingham University Hospitals as part of kidney transplantation work up. From this cohort, we reviewed their chronic kidney disease status, indication for referral for the DSE, results of the DSE, whether a cardiology referral was required and whether they required coronary intervention. We also looked for any cardiovascular events for at least a 3 year period since the DSE. We used online hospital patient databases and clinic letters to retrieve this information.

Results: In 2019, 54 patients had DSE performed. The majority had Chronic Kidney Disease Stage 4 or 5 (35/54) and the rest being dialysis and failing transplant patients. Diabetes was the most common reason for DSE request (48%). The average wait time between DSE request and result was 56 days. 33/54 patient had normal DSE results. 12 had inconclusive studies, but 10 of these patients did not require an angiogram or cardiology referral. 8/54 patients had evidence of inducible ischaemia – of these, all were referred to cardiology. 3 patients required diagnostic angiograms and 1 of them had a CAGB. The average wait time to see cardiology was 165 days. Of these 8 patients, 3 have died, 2 are not listed as angiogram was suggested once commenced on dialysis, 1 moved, 1 was listed as unfit and 1 was transplanted. After 3 year period, 14/54 of these patients received a kidney transplant and 10 had died. There were 4 cardiovascular events (2 myocardial infarctions, 2 had heart failure).

Conclusions: Cardiovascular events and death rates are significant in CKD population. DSE is a useful tool in predicting cardiovascular outcomes, but research on effects on transplantation listing and longer-term outcomes is needed.
Background: The diagnosis of antibody-mediated rejection (ABMR) is limited by the requirement to detect circulating anti-HLA antibodies. In the absence of anti-HLA antibodies, ABMR can be attributed to non-HLA antibodies and determining the sensitivity of current autoantibody detection assays is key to future correlation with pathological and outcome studies. We aimed to identify prevalence of non-HLA antibodies in male blood donors to determine assay testing sensitivities and thresholds, and gain insights on the pre-transplant prevalence of autoantibodies and their most common targets.

Methods: We performed this cross-sectional study using the LABScreen™ Autoantibody solid-phase assay (One Lambda, Thermo Fisher, USA) to test male blood donors (n = 92) for prevalence of 33 known non-HLA antigens.

Results: We observed significant variability between the assays performed and when comparing them to manufacturer-established cut-offs (Figures 1 and 2). The response to positive controls was significantly different between antigens, however this did not affect median MFIs based on control ratio groupings. Within assays, ratios between positive and negative controls ranged from 0.17 to >100, indicating varying degrees of antibody binding to the solid-phase assay. Further, despite being from unsensitized patients, mean fluorescence intensities (MFIs) of antigens varied by significant magnitude. There was further variability when applying manufacturer-established cut-offs to our population. 12/33 antigens had >50% of their sera samples above the manufacturer-established 95th percentile and 12/33 antigens had >25% of their sera samples above the 95th percentile and 12/33 antigens had >25% of their sera samples above the 75th percentile established by the manufacturer, while 5/33 antigens had >50% of their samples above the 95th percentile and 12/33 antigens had >25% of their sera samples above the manufacturer-established 95th percentile.

Conclusions: Autoantibody testing, in its current format, is limited by variability in the sensitivity for different antigens, with a large proportion of samples being above manufacturer-established thresholds. Caution should be exercised when interpreting results of non-HLA solid-phase assays, as demonstrated in these unsensitized male blood donors. While further refinement is required in our current outcomes of kidney allocation schemes. 

Figure 1: Ratio of Manufacturer provided positive and negative controls for multiplexing non-HLA antigens demonstrating significant variation in identification of different target antigens. Log10 Transformed

Figure 2: Response of Testing Male Blood Donors using Manufacturer’s Threshold cut-offs demonstrated a large proportion of testing being within the <75% MFI and above 95% MFI thresholds.
Background: Recipients of deceased diabetic donor kidneys (DM-D) have shown worse graft and patient survival outcomes than non-diabetic donors (N-D). However, pre-transplant information availability of diabetic donors concerning their disease with potential renal involvement is usually limited. We aimed to evaluate the availability of pre-donation clinical data of DM-D vs. N-D to improve our understanding of KT outcomes from DM-D.

Methods: Retrospective single-center study including kidney transplant (KT) patients transplanted from DM-D and N-D (2011-2020). A total of 699 recipients were included, with a mean follow-up of 41.7 (21.7-71.9) months after KT.

Results: We registered 123 (17.6%) DM-D KT and 576 (82.4%) N-D recipients. DM-D were older (67.70 vs. 48.39 years), more comorbid, and had a longer cold ischemia time than N-D (Figure 1A). Historical and pre-donation clinical data (creatinine, albuminuria, proteinuria, HbA1c, and fundoscopic examination) were only available in 16.8% of DM-D and 13.1% of N-D. DM-D were assigned to older recipients (66.8% vs. 58.83 years) with more history of cancer. DM-D recipients presented worse creatinine and higher proteinuria in all the studied periods (nadir, 6 months - 5 years). There were no differences in death-censored graft survival between groups. However, patient survival in DM-D recipients was worse (Kaplan-Meier, log rank<0.001) (Figure 1B). The multivariate analysis confirmed that an older recipient’s age (HR 1.08 [1.07-1.10], p<0.001) was predictive of mortality, regardless of age. The improvement of pre-transplant information availability from DM-D could improve characterizing the impact of these donors on our KT recipients’ outcomes.

Conclusions: Pre-transplant information availability of DM-D could improve characterizing the impact of these donors on our KT recipients’ outcomes.

(Abbreviations: Mean (SD) for continuous variables, % for categorical variables. N and Patient survival (%). N = 479 N = 505. *p<0.05 **p<0.01 ***p<0.001. Table 1. Donor characteristics. Table 2. Recipient characteristics. Table 3. Graft and patient survival by donor status. Table 4. Causes of death. Table 5. Creatinine and proteinuria in the first 3 years after KT. Figure 1A. Kaplan-Meier survival curves. Median follow-up 41.7 (21.7-71.9) months. Figure 1B. Multivariate analysis Cox proportional hazards model. Table 6. Pre-donation clinical data availability.

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E-POSTERS
Background: The universal shortage of organs has prompted the growing use of donations after circulatory death (DCDs). Nonetheless, the use of DCD as a source of intestinal grafts has been denied due to concerns regarding their ischemic susceptibility. This belief has been widely accepted for years. Now this myth is over: we present the first three DCD cases in intestinal transplantation in the world.

Methods: We reviewed the cases of intestinal transplantation after DCD performed at our center. Technical, demographic and clinical data relating donors and recipients were collected. Recipients were also studied in detail during their clinical and histological follow-up.

Results: Three DCD multivisceral transplants (MVT) were performed at our institution between June 2022 and January 2023. Donors (3M) had a mean age and weight of 3 months (1-6) and 5.3 kg (4-8). Their death was declared after their cardiac arrest and a 5-min “no-touch period”. Then, a rapid laparotomy was performed and a normothermic regional perfusion (NRP) was established. Warm-ischemia time was 25 minutes (23-29). Recipients were 3 males), with a median age of 49 years and pre-DSAs at the time of DDKT, were 31/55 patients (56%), and class II, with a median MFI 3012 [1095-24719] in 31/55 patients (56%), and class II, with a median MFI 3012 [1095-24719] in 24/55 patients (44%). Sixty-five% of pre-DSAs patients had cPRA>70%. There were no significant differences in immunosuppression regimens between the two groups, whereas 26/55 patients with pre-DSAs received the anti-CD20 monoclonal antibody Rituximab. The median follow-up period was 48 [12-145] months.

Conclusions: DCD in intestinal transplantation is feasible as demonstrated by our world-leading series. The ischemia-reperfusion injury in these grafts seems to be transient and reversible. Although experience is limited, their use could address the mismatch between the waiting list for intestinal transplantation and the scarcity of donors, especially in situations of need such as pediatric transplantation.

Background: The prognostic value of preformed HLA Donor-Specific Antibodies (pre-DSAs) detected by sensitive solid-phase assays on the long-term outcomes in Deceased-Donor (DD) Kidney Transplantation (KT) has not yet been fully elucidated. The aim of this study was to evaluate the effect of pre-DSAs on long-term patient and kidney allograft outcomes in a single-center cohort.

Methods: A retrospective, matched (1:1), cohort analysis of 110 DDKT recipients, between 1st/2011 and 12th/2021 was conducted. In total, 55 patients (21 males), with a median age of 49 years and pre-DSAs at the time of DDKT, were matched for recipients’ demographics, time on dialysis and follow-up period with 55 patients without pre-DSAs (control group-CG), at the time of DDKT. Patients’ blood samples were analyzed for IgG DSA using a SAB assay (One Lambda). Mean Fluorescence Intensity (MFI) values >1000 were considered positive for DSA. All patients were transplanted with negative CDC and T/B Flow Cross-match (FCM). There were no significant differences in immunosuppression regimens between the two groups, whereas 26/55 patients with pre-DSAs received the anti-CD20 monoclonal antibody Rituximab. The median follow-up period was 48 [12-145] months.

Results: Detected HLA-DSAs were class I, with a median MFI 1865 [1011-4305] in 31/55 patients (56%), and class II, with a median MFI 3012 [1095-24719] in 24/55 patients (44%). Sixty-five% of pre-DSAs patients had cPRA>70%. There was a significant difference in DGF occurrence between the two groups (76% vs 51% in the CG, p=0.005). Patients with pre-DSA had a higher incidence of early transplant biopsy-proven acute rejection (BPAR) (20% vs 9%, p=0.09), mainly Acute Cellular Rejection (ACR) (68.5%) and mixed ACR-Antibody Mediated Rejection (16.5%) within 30 days post-transplant. There was no significant difference in de novo DSA development between the study groups (11% vs 5.5%, p=0.49). The eGFR was comparable in both groups during the entire study period (p>0.4). Death-censored graft survival rates and patient survival rates were not significantly different between the groups.

Conclusions: DDKT recipients with circulating pre-DSA are at an increased risk of BPAR, which doesn’t seem to influence the long-term outcomes.
**P659** IMPLEMENTATION OF NEW M-HEALTH TOOL TO MONITOR IMMUNOSUPPRESSION ADHERENCE AND VITAL PARAMETERS IN KIDNEY TRANSPLANT PATIENTS

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**Background:** Current management of immunosuppression adherence is based on unreliable and ineffective tools, which do not allow any understanding of the degree of medication adherence. Also, main vital parameters such as blood pressure, glycemia or weight are key variables to understand the proper evolution of a kidney transplant patient. We developed a novel digital m-Health tool in which the medical team can perform an accurate follow-up and monitoring of transplant patients through a digital platform who receives in real-time all the feedback from patient’s behaviour through a smart mobile App (Trackyomed®; TYM).

**Methods:** From November 2021 until December 2022, 208 consecutive kidney transplants from our transplant centre, were proposed to actively use TYM, based on a novel App directly interconnected with a back-end platform used by the medical team. The aim of the study was to describe the lifespan of this new tool, both from the physician and patient’s perspectives. We recorded main reasons for not accepting its use, for stopping its use and for its active usage during the 12-month study follow-up. We analyzed main clinical and demographic variables, also degree of medication adherence and interval of times of medication in-takes.

**Results:** In 68%, TYM was given right before being discharged after receiving a kidney transplant and in 42% TYM was offered at the out-patient clinic in patients with a functioning graft for more than 2 years. Out of these 208, 64% were male and 36% female, with a mean age of 54.9 (range: 18-90). Six percent did not accept TYM because of no or lack of use of a smart phone, 28% because they already had a different tool to guide medication adherence and 66% accepted its use. At current mean time of follow-up (10±5 months), 49.5% were actively using TYM, with 54% (23/44) patients with more than 12 months of active use. Notably, the physician with the highest recruitment and active use, showed very low rates of withdrawal (25/73 [34%]). Mean optimal adherence to immunosuppression in-takes during the previous 2 months was 61%, erratic adherence (in-takes out of withdrawal) (25/73 [34%]).

**Conclusions:** Implementing m-Health technology for improving immunosuppression adherence may be an excellent option for an important percentage of transplant patients.

**P660** GENE EXPRESSION PROFILES OF PERITUBULAR CAPILLARITIS IN CHRONIC ANTIBODY-MEDIATED REJECTION

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**Background:** Chronic antibody-mediated rejection (ABMR) is a significant cause of late allograft loss. Diffuse ptc (extent >50%) was associated with worse graft survival independent from the ptc score. Nevertheless, current ptc thresholds are arbitrarily defined and may not reflect pathophysiological phenotypes accurately. We hypothesize that re-assessment of ABMR biopsies with the Nanostri ng-NCounter based gene expression analysis allows the definition of novel thresholds of ptc extent, reflecting molecular ABMR phenotypes more accurately.

**Methods:** We retrospectively analyzed 25 patients with ABMR/chronic ABMR and presence of donor specific antibodies, treated at two centers (Medical University of Vienna and Ordensklinikum – Elisabethenin Linz), PTC was re-evaluated by an experienced external nephropathologist (M.M.) and included the ptc score as well as the ptc extent (focal ptc: 10-50%, diffuse: >50%). We performed Nanostring nCounter Gene expression analysis with a customized gene set corresponding to the recommendations in Banf 2017 guidelines. Gene expressions above the first quartile (ABMR<35) were considered as positive values for ROC analysis.

**Results:** Biopsies with diffuse ptc had significantly higher gene expressions with the ABMR gene set [035/63 vs. 32/27/52; (median/IQR): p=0.012], the ABMR exhaust gene set [390/245-609 vs. 245/128-358; p=0.022], the Eculizumab gene set [180/143-339 vs. 65/57-133; p=0.0027] and the TCMR gene set [48/40-75 vs. 25/19-35; p=0.001]. Sensitivity analysis revealed improved AUCs for predicting biopsies with ABMR gene expressions over the 1st quartile with a ptc cutoff of 55% compared to ptc cutoff of 50% [ptc >35: AUC 0.76/0.61-0.90 (95% CI), p=0.013; ptc<50: AUC: 0.71/0.54-0.88, p=0.039].

**Conclusions:** With the application of gene expression-based Nanostring platform we were able to identify a new threshold of ptc extent. The newly proposed cut off >35% may reflect molecular phenotypes of ABMR more accurate than the current one and could improve early diagnosis of ABMR.

**P662** TRANSPANTATION OF EXTENDED CRITERIA DECEASED DONOR KIDNEYS TO EXTENDED CRITERIA RECIPIENTS: A CHALLENGING COHORT

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**Background:** Extended criteria deceased donor kidneys have become an accepted option in order to increase the donor pool, decrease waiting times and increase the number of transplants. The objective of the study was to compare outcomes of deceased donor kidney transplants from extended criteria donors to extended criteria recipients vs. standard criteria donors to standard criteria recipients.

**Methods:** Retrospective single-centre study of 88 recent deceased donor kidney transplants performed between 1 January 2022 and 1 July 2022. Extended criteria were defined as donors or recipients with one or more of the following: age>60, BMI>30, hypertension, diabetes, coronary artery disease, pre-retrieval donor creatinine >2.0 mg/dl.

**Results:** 46.5 % of the kidneys were retrieved from donors after circulatory death, while 53.4 % from donors after brain death. 25% of the grafts came from standard and 75% from extended criteria donors. 8% of recipients were standard and 92% of extended criteria. Of all transplants, 4.5% were of standard criteria recipients who received organs from standard criteria donors, and 69.3% of first extended criteria recipients who received organs from extended criteria donors. Graft survival rates, with a mean follow-up of 6 months, were better in the standard criteria group (p<0.05). Rates of surgical complications (bleeding, herna and surgical site infection) were higher in the extended criteria group (p<0.05). There was no significant difference in the eGFR values between the two groups at 6 months’ post-transplantation (p=0.66).

**Conclusions:** Extended criteria transplantation is “here to stay” considering the increasing prevalence of kidney failure and the aging donor and recipient populations with the relevant co-morbidity. Stratification of risk for the allocation of extended criteria kidneys to extended criteria recipients as well as mitigating modalities such as organ reconditioning are crucial for improving outcomes.
PREEMPTIVE KIDNEY TRANSPLANTATION: EXPANDING TO ALL KINDS OF DONORS AND RECEPTORS

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Background: Preemptive kidney transplantation without prior dialysis initiation improves patient and graft survival compared to remaining on dialysis or undergoing transplantation after initiation of dialysis. Despite its advantages, mainly due to cost is aimed to starting kidney replacement therapy (KRT) with a preemptive kidney transplant occurred only in 4.5% of patients in 2021 (8 ppm).

Methods: Single center descriptive study of patients who received isolated or combined preemptive kidney transplants performed and followed up in our center from the start of the program on 7/2/1979 to 7/12/2022. Clinical-demographic variables of donors/recipients/transplant as well as glomerular filtration rates (GFR) were collected.

Results: From a total of 2057 kidney or combined transplants, 105 of them (5.1%) received a preemptive kidney graft. 72.4% (N=76) were males with a mean age of 48.6±14.6 years and received a renal graft from donors of 45.2±16.1 years. The mean PRA was 15.3±16% and the mean cause of death was injury of 32, simultaneous pancreas-kidney transplant (30.5%), 13, liver-kidney transplants (12.4%), 1 heart-kidney transplant and a liver-pancreas-kidney transplant. In the isolated kidney transplant group regarding the type of donation, the majority were from living donors, 53.4% (N=31), 36.2% (N=21) were deceased donation and only 6 were circulation-dead donors. Regarding ABO blood group, 74.1% (N=20) were group A, 14.8% (N=4) group B, 2 cases were group AB, and only one transplant belonged to group 0.

Conclusions: Despite preemptive kidney transplantation is the best option for KRT, the proportion of patients in this modality remains low (5.1% of the total transplants). This modality seems to be limited to living donor and to combine pretransplant activity with other organs, however, 26% of our transplants were procured from deceased donors belonging the majority of the group A recipients receiving brain-dead donors. As organ shortage and waiting-listing times change, this modality should be expanded to a greater number of donor/recipient pairs.

DECEASED ORGAN DONATION ACTIVITY, IN THE CRITICAL CARE UNIT OF A GREEK UNIVERSITY HOSPITAL, DURING 2022

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Background: Despite the strategies to increase organ availability, the rate of organ donation in Greece remains low, especially during COVID-19 pandemic. The current study is aimed to describe deceased organ donation activity during 2022, in a medical-surgical critical care unit of a Greek University Hospital.

Methods: We retrospectively studied the deceased organ donation activity during 2022, in the 2nd Department of Critical Care of ATTIKON University Hospital of Athens. This is a 40-bed medical – surgical intensive care unit, in which ten COVID-19 and 30 non COVID-19 patients are hospitalized. Donors’ demographic characteristics, cause of death and bacterial colonization data were recorded. Days of mechanical ventilation, time of organ procurement and time of brain death and number of organs and tissues procured were also provided.

Results: During the study period, there were eleven actual deceased organ donors after brain death, 4 females and 7 males. The mean ±SD donors age was 51.3±16.0 years, 84.6% of the donors were brain-dead donors. As organ shortage and waiting-listing times change, this modality should be expanded to a greater number of donor/recipient pairs.

CONCLUSIONS TO THE NEPHROLOGY CLINIC OF THE “ATTIKON” HOSPITAL OF ATHENS DURING 2022

Methods: Single center descriptive study of patients who received isolated or combined preemptive kidney transplants performed and followed up in our center from the start of the program on 7/2/1979 to 7/12/2022. Clinical-demographic variables of donors/recipients/transplant as well as glomerular filtration rates (GFR) were collected.

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P668 EVALUATING THE BIDIRECTIONAL IMPACT OF KIDNEY TRANSPLANTATION AND HIV CONTROL

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Methods:
- A retrospective analysis of electronic health records was performed from 1998 to 2022 for key metrics correlating with HIV control in the KTRLHIV cohort (n=29). Kidney function metrics were also extracted and compared to a 1:1 matched HIV-negative KTR cohort. Patients were matched for age (55 years, range [43,74]), sex (66% male), ethnicity (72% black), and years since KT (7.4 years, range [0,7,23.8]).

Results:
- Average years since HIV diagnosis was 20.2 years (95% CI [16.6, 23.7]), with all but 1 patient having an undetectable HIV viral load (1 patient with 168 copies/ml). Comparing pre and post-transplant averages, the CD4 count reduced by 303 cells/μL (p=0.18), the total lymphocytes reduced by 144 cells/μL (p=0.12), and the CD4:CD8 ratio increased by 0.029 (p=0.32). Average eGFR in the KTRLHIV was 34 (95% CI [26.8, 41.6]) vs 43 (95% CI [35.7, 50.1]) in the matched HIV-negative KTRs (p=0.045). Significant improvements in blood pressure with anti-hypertensive medication were noted in the KTRLHIV compared to matched HIV-negative KTRs (p = 0.023). Higher rates of graft rejection were seen in the KTRLHIV (38% vs 10%, p=0.014). Majority of these cases in the KTRLHIV were T-cell mediated rejection (21%), followed by antibody mediated rejection (10%), and mixed acute rejection (7%).

Conclusions:
- There is no statistically significant difference in key HIV control metrics when comparing pre-transplant and post-transplant levels. Significantly worse overall kidney function and higher rates of acute rejection is noted in the KTRLHIV when compared to a matched HIV-negative KTR cohort.

P670 CHRONIC ALLOGRAFT NEPHROPATHY IS AGGRAVATED IN AGED DONORS BY THE EXACERBATION OF AGE-RELATED LOSS OF PROTECTIVE FACTORS

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Background:
- Kidneys are crucial for homeostasis and overall survival, and the prevalence of kidney disease increases with age. The age classification of donors and recipients is a way of expanding the group of donors. Kidneys from elderly donors have a higher risk of developing chronic allograft nephropathy (CAN). Mechanisms contributing to CAN have been linked to cellular senescence, a process implicated in regeneration failure and progression to fibrosis. However, the molecular and pathological basis of the age-related increase and its relation with iron homeostasis is not completely understood.

Methods:
- Experimental renal transplant model in rat were used. Young (3mth) and old (10mth) donors and recipients were used to perform isogenic and allogenic group without immunosuppressive treatment into 3 groups old-to-old, old-to-young and young-to-young donor/recipient groups. Tubular damage score, and proinflamatory chemokines, regulated necrosis, ferroptosis, apoptosis, senescence, age-related loss of protective factors and production of senescence-associated secretory phenotype components (SASP) were evaluated by Real Time. In parallel biochemical parameters of iron metabolism were determined on blood and tissue.

Results:
- From all processes evaluated we could not elucidate significant differences between old and young grafts independently from the recipient’s age, although a slight increase (not statistically significant) of these processes was observed in the old grafts. The analysis of the gene expression levels of SASP components Tgfβ1, Ile6, Ctgf, PAI-1, showed that Tgfβ1 were over-expressed in all grafts independently of age; IL6 and PAI1 were over-expressed in old grafts compared to the young ones, and CTGF were down-expressed in old grafts compared to the young ones. The senescent cell apoptosis resistance factor BCL-2 was evaluated. Bcl21 gene was conserved on isogenic grafts, but in all allogenic grafts independently from age was down-regulated. None of the blood parameters showed differences between groups.

Conclusions:
- In conclusion, our model did not show statistically significant results but indicates that the expression of renal protective factors are decreased in old grafts evidencing the need of further studies with older donors (20mth).
Background: Mechanical Insufflation-exsufflation (MIE) is a non-invasive device to simulate a cough and thus favoring the elimination of secretions. There is no evidence regarding its use in the maintenance/optimization of solid organ donors. We intend to assess whether the use of MIE in eligible donors is safe and improves oxygenation parameters.

Methods: This is a preliminary safety analysis of a prospective multicenter study conducted in 4 national centers. 10 eligible donors offered in 1 month have been included. After completing national maintenance oriented towards pulmonary optimization (OTP) MIE cycles were implemented. Blood gas monitoring (Pa/FIO2) (FiO2 1 and PEEP 5) was performed: initial, post MPO, 10 min and 60 min post MIE. Complications derived from the technique were recorded.

Results: Five donors were eligible lung donors (PaFi>300, ELD) and 5 did not were eligible (PaFi<300, NELD). ELD maintained PaFi>400 after the MIE. Four of 5 NELD increased 25.4% the PaFi and it was maintained 1h after (Table 1). No one had complications during or after MI-E.

Conclusions: MI-E seems to be a safe technique who use could be useful to increase the lung donor pool.

### Table 1

<table>
<thead>
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<th>Initial</th>
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<th>Post-</th>
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<td>MIE</td>
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<tr>
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<td></td>
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<td>(0.04)</td>
<td>(0.09)</td>
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<td>334.2</td>
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<td>(SD)</td>
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<tr>
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<td>(SD)</td>
<td>(2.49)</td>
<td>(2.41)</td>
<td>(1.71)</td>
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</tbody>
</table>

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Background: Laparoscopic live donor nephrectomy is a widely accepted procedure for the most transplantation centers worldwide. However, choosing the suitable donor side for kidney retrieval, is a very challenging task for the performing surgeon, which is principally affected by the donor’s vascular anatomy and complexity. As a result, CT angiography is necessarily performed in all cases. There is scarce data regarding the variations of the renal vessels and its implications to their recipients, consequently it is constantly a debatable subject.

Methods: In our center, 267 laparoscopic live donor nephrectomies were performed from October 2018 until December 2022. In all cases CT angiography was performed preoperatively. We analyzed the data, where the cases with single renal vessels were excluded. As a result, a total of 107(40%) cases were included in this research.

Results: Anatomical variations were present in 40% of the cases. Concomitant different anatomical variations were observed in 31 of 107 cases (28%). Regarding the left kidney, double artery was present in 35 out of 107 cases, 5 cases had double renal vein and 12.2% of the patients had retroaortic course of the renal vein in general. On the other hand, dual right renal artery was observed in 28 patients while 18 patients had dual right renal vein (16.8%). Rest of the vascular variations are concluded in Table 1. Operation Time and warm ischemia was slightly higher in these cases, but that fact was not clinically significant neither to the donor nor to the recipient. Blood transfusion was not needed in these patients. In addition, complication rate was very low with only 2 cases (1.87%) presenting chylous ascites postoperatively, which have been treated conservatively with dietary modification. Operation length was similar to the patients with single renal vessels.

Conclusions: Vascular anatomical variations regarding live donor nephrectomies are frequent and represent a challenge for the surgeon pre- and intraoperatively. CT angiography should not be neglected preoperatively. Through our experience, multiple renal vessels do not constitute a negative impact to the donor and the recipient. In addition, implications were rarely observed, thus we recommend harvesting kidneys with multiple vessels, but not more than 2 arteries.

### Table 1. Renal Vessels Variation

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<th>Anatomical Variation</th>
<th>Number of cases</th>
<th>Donor Implications</th>
<th>Recipient Implications</th>
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<td>DUAL LEFT ARTERY</td>
<td>11</td>
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<tr>
<td>DUAL LEFT ARTERY (LOWER POLE)</td>
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<td>-</td>
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<td>DUAL LEFT ARTERY (UPPER POLE)</td>
<td>1</td>
<td>-</td>
<td>-</td>
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<tr>
<td>DUAL LEFT VENUS</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LEFT VENUS BRANCHING</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RETROAORTIC LEFT VENUS (JOIN IVC AT 1.5 IXY)</td>
<td>18/13</td>
<td>2 (cystic sinus)</td>
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<tr>
<td>LEFT ARTERY BRANCHING</td>
<td>10</td>
<td>-</td>
<td>-</td>
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<tr>
<td>TRIPLE LEFT ARTERY</td>
<td>3</td>
<td>-</td>
<td>1 (renal artery)</td>
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<tr>
<td>DUAL RIGHT ARTERY</td>
<td>19</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DUAL RIGHT ARTERY (LOWER POLE)</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DUAL RIGHT ARTERY (UPPER POLE)</td>
<td>-</td>
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<td>DUAL RIGHT VENUS</td>
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**P674 MEDIAN ARCULATE LIGAMENT COMPRESSION-AN ACHILLES KNEE FOR HEPATIC ARTERY FLOW DURING LIVER TRANSPLANTATION**

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**Background:** Median arcuate ligament can induce the narrowing of the celiac trunk, either by the insertion of muscular fibers or by fibrous bands of the celiac nervous plexus. Significant celiac artery compression is revealed in 10-50 % in angiographic CT examination. The presence of celiac trunk compression is a risk factor for hepatic artery thrombosis after liver transplantation, and subsequently for the graft loss. Several surgical procedures have been advocated to overcome its effect in liver transplantation, but their impact is still on debate.

**Methods:** The aim of our study is retrospectively review 8 cases of celiac artery compression by median arcuate ligament, who were preoperatively identified by celiomesenteric angiography-CT and underwent orthotopic liver transplantation, between September 2016 and September 2022.

**Results:** In three cases standard hepatic artery reconstruction was performed during liver transplantation, followed by median arcuate release whereas the arterial flow didn’t recover after ligament release, an arterial aorto-hepatic jump graft was undertaken. In all the 8 cases, an excellent hepatic artery flow was restored.

**Conclusions:** Our presentation highlights the importance of early diagnosis and management of median arcuate ligament in liver transplant recipients during transplant surgery.

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**P675 PHOTOPROTECTION AND SKIN CANCER AWARENESS IN KIDNEY TRANSPLANT RECIPIENTS LIVING WITH HIV: A SINGLE-CENTRE CROSS-SECTIONAL STUDY**

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**Background:** Kidney transplant recipients (KTRs) are up to 65 times more likely to develop non-melanoma skin cancers when compared to age-matched general populations. HIV has also been associated with increased skin cancer rates. However, to date there has been no study evaluating photoprotection and skin cancer awareness in KTRs living with HIV (KTRHLH).

**Methods:** Using validated photoprotection and skin cancer awareness questionnaires we evaluated knowledge and practices in KTRHLH and an HIV-negative KTR cohort, matched for age, sex, ethnicity, and years since transplant.

**Results:** n=27 KTRHLH and n=25 matched HIV-negative KTRs completed the questionnaires. Of those n=34 (65%) were male and n=37 (71%) were Black. Average age was 56 years (43-74 years). On average patients were 7.3 years post-transplant (range years). N=22 (81%) KTRHLH had received photoprotection advice, compared with 20 (80%) of the matched KTRs (p=0.033). There were statistically significant lower rates of overall sunscreen use in KTRHLH compared to matched HIV-negative KTRs (33% vs 60%, p=0.054). Only a small proportion used sunscreen daily (22% vs 27%), of a factor >25 (78% vs 100%). A strongly positive Tetrachoric correlation coefficient of 0.77 indicated that providing photoprotection advice correlates to sunscreen use. Significantly lower rates of photoprotection behaviours were seen in the KTRHLH compared to HIV-negative KTRs, particularly never avoiding direct sunlight (59% vs 16%, p = 0.001), and never dressing to protect from the sun (52% vs 12%, p = 0.002).

**Conclusions:** We have identified statistically significant lower knowledge of photoprotection and skin cancer awareness in KTRHLH compared to matched HIV-negative KTRs. Lower rates of skin cancer protection advice may have resulted in lower rates of sunscreen use, and poorer photoprotection behaviours in KTRHLH. Dedicated skin cancer awareness education to promote patient-led skin cancer prevention alongside formal Dermatology referral is recommended.

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**P676 THE DEVELOPMENT OF REJECTION IS ASSOCIATED WITH A MORE AGGRESSIVE PATTERN OF POST-TRANSPLANT NEOPLASIA**

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1Renal Transplant Unit. Department of Nephrology and Kidney Transplant. Hospital Clinic, Barcelona, Spain. 2Institut Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

**Background:** A relation between immunosuppressive status and the development of post-transplant malignancies (PTM) is already published. Our objective is to evaluate the impact of the development of rejection and its treatments with the incidence and behavior of PTM.

**Methods:** Retrospective single-center study of adult kidney transplants recipients (KTR, 2003-2015, follow-up till December of 2020). Different statistical tests and survival analysis were used according to the type of variable used collected from the different databases of the center. The study was approved by the Ethics Committee of our Institute.

**Results:** n=169 (11.2%) of 1,505 KTR developed some type of neoplasia (60.5% men and 17% diabetics) with a mean follow-up of 62.78 +/- 158.01 months. The patients with PTM were older (p = 0.000; Exp (B) 1.042; univariable: 62.8 +/- 11.1 years vs 54.7 +/- 14.3 years, p = 0.000), with worse survival of the patient (p = 0.000; Exp (B) 2.427; K-M: 73.4% vs 88.7%, Log-rank 0.001), less incidence in patients who were CNI plus mTORi (p = 0.01; Exp (B) 0.314) and who developed rejection (p = 0.003; Exp (B) 0.521) in the multivariate analysis (binary logistic regression). Despite this unexpected lower incidence of PTM in those who developed rejection, being age (p = 0.061; Exp (B) 1.061) and the use of CNI (p = 0.016; Exp (B) 0.233) the factors in the multivariate analysis, we evaluate the aggressive pattern, and the patients who rejected and developed neoplasia, this was more aggressive with more metastases (4.8% vs 3.8%, p=0.006) and higher patient mortality associated with the tumor (5.7% vs 1.37%, p<0.002).

**Conclusions:** In long-term follow-up, patients with rejection developed a more aggressive neoplasia with higher tumor-associated mortality. Rejection types and treatments are being analyzed as potential factors associated with tumor behavior.

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**P677 BEST PRACTICES ALONG THE KIDNEY TRANSPANTATION CLINICAL JOURNEY: A QUANTITATIVE SURVEY TOOL**

Sara Machado1, Alexandre Loupy1, Gillian Divard2, Valentin Goutaudier1,3, Andreas Pascher4, Thomas Vogel4, Jacopo Romagnoli5, Sofia Zarraga6,7, Frank Dor8, Elias Mossialos1,2
1London School of Economics, London, United Kingdom, 2INSERM, Paris, France, 3Paris Institute for Transplantation and Organ Regeneration, Université Paris Cité, INSERM, U-970, AP-HP, Paris, France, 4U Muenster, Muenster, Germany, 5Policlinico Gammarelli, Rome, Italy, 6Hospital Santander, Santander, Spain, 7Hospital Bilbao, Bilbao, Spain, 8Hammersmith Hospital, London, United Kingdom

**Background:** This study designs and tests a survey tool to assess the implementation of best practices guidelines and guidelines along the kidney transplantation clinical journey, from chronic kidney disease (CKD) prevention to long-term post-transplant care.

**Methods:** Best practice recommendations and guidelines were analysed to identify the key themes and elements of the clinical journey. The most recent version of three sets of guidelines were chosen as the main source (KIDGO guidelines, European Commission’s CD-P-TO’s “Guide for Quality and Safety in Organ Transplantation”, British Transplantation Society clinical practice guidelines). Topics were identified and a comprehensive survey was created to collect data on how current practice relates to best practice. The survey was validated by a selected group of experts and stakeholders, including living organ donors, transplant patients, nephrologists, transplant coordinators, and transplant surgeons, across five countries (France, Germany, Italy, Spain, United Kingdom). Questions with divergent answers were reviewed and discussed.

**Results:** The main themes of the final version of the survey are: 1) Chronic kidney disease (definition and classification, prevention, progression, complications, referrals and models of care); 2) Kidney donation and transplantation (identification of deceased organ donors, determination of death, consent management after brain death, donor selection criteria, organ procurement, living donation, biovigilance, quality management, measuring outcomes); 3) Transplant recipients (post-operative care, prevention of infectious diseases, graft failure, long term care, quality of life); and 4) Management of donation and transplantation service (funding, governance, decision making). The final survey tool has 80 questions, and takes on average 30 minutes to complete.

**Conclusions:** This survey tool can be used to assess conformity of clinical practice with best practices. Preliminary survey responses from 56 respondents (patients, transplant surgeons, nephrologists, and transplant coordinators) from Italy and France indicate a wide range of practices and perceptions along the kidney transplantation clinical journey.
The transplantation of the pancreas is recommended in diabetes with complications. The combination of cell biology and 3D-bioprinting can create organs with vasculature which should be functional. 3D-bioprinted biomaterials showed superior functionality when bioprinted with pancreatic islets. In fully vascularized organ or macro-device, there are issues to be solved: leakage, thrombosis, enhancement against high pressure, connecting organ to the recipient.

Methods: Mathematical analysis in the designed bionic pancreas was performed. The bionic pancreas was 3D bioprinted with 2 types of bioinks. The first tests were carried out in a bioreactor then organs were subjected to magnetic resonance and ultrasound examination and radiology intervention in three animals. Histopathological organ and vascular system in MRI and X-ray examination for 5 days. No leaks or complications were observed.

Results: The tests carried out in the bioreactor showed the stability of the bionic organ and vascular system in MRI and X-ray examination for 5 days. No leaks beyond the bioprinted organ and vascular system were observed up to 400 mmHg. Animals transplantation in all 14 cases of transplantation in vivo there was stable flow throughout the organ after release of vascular clamp. DCL-VESS-Group - In all cases vascular cloth was observed.

Conclusions: It is feasible to 3D bioprint and transplant bionic organ in big animal model as a macro-device for stem-cell derived beta cells or knocked-out xeno-derived islets.

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Background: Kidney transplant recipients (KTRs) are at lifelong risk of immunosuppression-related cutaneous complications, in particular skin cancer. KTRs are up to 65 times more likely to develop non-melanoma skin cancers (NMSCs) when compared to age-matched general populations. Published evidence suggests skin disease occurs in over 90% of patients living with HIV. However, there is a paucity of published data on the prevalence and characteristics of skin disease in KTR HIV.

Methods: We performed a retrospective analysis of electronic health record data (between 1998-2022) to analyse the prevalence and characteristics of skin diseases in our KTR HIV cohort (n=29) compared to matched HIV-negative KTRs (n=29) matched for age, sex, ethnicity, and years since transplant.

Results: In each of our cohorts n=19 (66%) were male and n=21 (72%) were Black with a mean age of 55.5 years [range 43-74 years]. On average patients were 7.4 years post-transplant (range 0-23.8 years). The mean GFR in KTR HIV compared to matched HIV-negative KTRs was 31.14 (p = 0.045). Having concomitant HIV increased the risk of skin disease in KTRs 1.6 times (p = 0.027). N=27 (93%) KTRLHV experienced 120 episodes of skin disease (4.4 episodes/patient). In comparison n=21 (72%) HIV-negative KTRs experienced 26 episodes (2.6 episodes/patient). Skin infections (especially genital infections) were the most common (43% KTRLHV vs 39% HIV-negative KTRs), followed by benign lesions (17%vs22%) and inflammatory skin disease (9%vs9%). Interestingly, pre-malignant or malignant skin cancers occurred more frequently in HIV-infected KTRs (4%vs0%). Most of these were actinic keratoses (n=4) and found only in patients with fair ( Fitzpatrick Type 1) skin.

Conclusions: We have identified statistically significant higher rate of skin disease in KTRLHV compared to matched HIV-negative KTRs. Further research to evaluate the reasons underpinning this increased burden of skin disease in this cohort is necessary.
GLOBAL BURDEN OF CYTOMEgalovirus RESISTANCE TO ANTIVIRALS IN FRANCE

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Background: Refractory/resistant CMV infections are deleterious for graft survival. The global burden of resistance to anti-CMV compounds is surveyed since 2006 by the National reference Center for Herpesviruses.

Methods: Resistance genotyping indication was: viral replication persisting more than 3 weeks on treatment (NRC recommendations) and since 2018: Resistance genotyping indication was: viral replication persisting until start of treatment +180 days.

Results: Out of 2928 genotypes performed at the CNR in Limoges, 931 (31.8%) showed the presence of resistance mutations, 732 in UL97 (77.5%), 240 in UL54 (25.78%), 13/138 (9%) LT recipients (9 males/3 females, aged 57±11) were referred for subsequent inhosiptal rehabilitation. LT indications included ethyl cirrhosis (n=5), non-alcoholic steatohepatitis cirrhosis (n=2), primary sclerosing cholangitis relapse (n=1), polycystic liver disease (n=1), chronic intestinal and liver failure (n=1), post-ICU cholangiopathy (n=1) and cardiac cirrhosis (n=1). MELD score was 20±8 at moment of listing. ICU, LT centre and rehabilitation hospital admission time were 9±8, 41±31, 36±24 days, respectively. No serious adverse events were reported during the rehabilitation period. Two patients were re-admitted in the LT centre for medical reasons not related to the rehabilitation. The mean 6MWT increased from 126±88 to 362±126 meters (p<0.05). Balance/stability perception remained stable before and after rehabilitation (20±8 vs 24±8, p>0.05).

Conclusions: This study shows that referring medically stable but physically unfit LT recipients for subsequent inpatient physical rehabilitation is feasible, safe, and well-tolerated with significant functional gains. Closer collaboration between LT centres and dedicated rehabilitation hospitals to improve physical fitness, not only after but also before LT, should be encouraged and explored to further improve outcomes after LT for very frail patients.

OUTCOME OF KIDNEY TRANSPLANTATION IN PATIENTS WITH BALKAN ENdEMIC NEPHROPATHY

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Background: Balkan endemic nephropathy (EN) is a chronic tubulointerstitial aristolochic acid nephropathy with insidious presentation, slow progression to end-stage renal disease and the frequent development of urothelial cancer. Immunosuppressive treatment increases the risk for a poor outcome. To reevaluate our practice, we analyzed the incidence of urothelial cancer and treatment outcome in the group of kidney transplant recipients with EN.

Methods: We retrospectively evaluated our database, patient records and pathology results of 610 kidney transplant recipients treated at our institution during a 30-year period.

Results: From January 1993 until December 2022, 657 kidney transplants were performed in 610 adult patients at our institution. EN was diagnosed as the original kidney disease in 11 (1.8 %) of the recipients, based on medical history, clinical findings and laboratory results. All patients with EN received the first deceased donor allograft, patients' mean age at transplantation was 65 (range 36-76), 6 (54.5%) patients were male. None of the patients underwent a preventive nephroureterectomy. During the post-transplant follow-up (mean 5 years, range 1-13 years) urothelial cancer was diagnosed in 6 (54.5%) of 11 patients with EN, and resulted in the death in four patients.

Conclusions: Kidney transplant recipients with EN are at high risk for the development of urothelial cancer. Our data stress the need for careful urological evaluation and decision about pre-transplant preventive bilateral nephroureterectomy, close post-transplant follow-up and the individualization of immunosuppressive treatment.

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P670 THE STRUCTURE OF THE SYSTEM OF TRANSPLANT COORDINATORS IN POLAND

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Background: In 2010, Poltransplant started to create a structure of transplant coordinators in Poland. Over the 12 years (2010-2022), the number of organ and tissue donation coordinators in Polish hospitals was increased from 35 (2010) to 168 (2022). Over the years, the network of coordinators has been expanded to include provincial coordinators increasing donation in a given area, coordinators in transplant centers, coordinators of living kidney donors and coordinators of hematopoietic cell collection and transplantation.

Aims: The aim of the work is to present the basics of functioning, the structure of the coordinator system, and the tasks of individual groups of transplant coordinators in Poland.

Results: At the end of 2022, Poltransplant in Poland employed a total of 254 coordinators (various tasks). From the group of all coordinators, 209 (82.1%) people were responsible for organizing the coordination of organs and tissues from deceased donors and increasing the donation potential. In this group, 168 (60.1%) coordinators were donation coordinators in hospitals reporting donors, 18 (6.8%) people were transplant coordinators in transplant centers, another 15 (7.8%) people were vosivodeship coordinators, and the remaining 8 (3.8%) central (national) coordinators. A separate group of 24 people (9.5%) out of 254 coordinators is made up of coordinators responsible for coordinating the collection and transplantation of kidneys from living donors, and 21 people (8.3%) are responsible for the collection and transplantation of hematopoietic cells in hematology centers.

Conclusions: The presentation of the creation and expansion of the network of transplant coordinators is aimed at showing good practices (know-how) proven in one country, for others, like Poland, which also has a problem with too few transplant coordinators.

Key words: transplant coordinators; deceased donors; living donation coordinators; coordinators of collection and transplantation of hematopoietic cells.

P689 INTRAPATIENT VARIABILITY AND TESTS ABOVE LOWER TACROLIMUS TRESHOLD ARE ASSOCIATED WITH ACUTE REJECTION IN PANCREAS TRANSPLANTATION

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Background: The immunosuppressive maintenance regimen in solid organ transplantation with tacrolimus is currently the gold standard in clinical practice. However, this drug has a narrow therapeutic window. There are multiple studies in which the tacrolimus coefficient of variation (CV) in heart, kidney, and lung transplantation has been associated with the incidence of graft rejection. This study aims to find the association between the CV and the percentage of tests above the lower tacrolimus threshold (TALT) with the incidence of rejection in simultaneous pancreas-kidney transplantation (SPKTx).

Methods: This is a retrospective study of SPKTx performed between April 2017 and February 2021. We calculated the tacrolimus CV and the TALT of included patients. The lower target trough level was defined as 10 ng/mL during the first 3 months, 8 ng/mL from months 4 to 6, and 6 ng/mL thereafter. Bioassay-proven acute SPKTx rejections (BPAR) were registered.

Results: Thirty-four patients were analysed, 3 that were receiving mTOR inhibitors were excluded. Seventeen (46.8%) were males, 39 biopsies were performed (either protocol or for-cause). There were 9 cases of BPAR. These were significantly associated with a TALT below 70% (PPV 38.1%, NPV 94.4%, OR 10.46 (1.2 – 94.5), p = 0.023), and with a CV greater than 60% (PPV 50%, NPV 83.3%, OR 5.1 (1.1 – 27.4), p = 0.32).

Conclusions: This study suggests that CV and a new parameter, TALT, are potential tools that can help identify patients at risk of pancreatic graft rejection. Larger studies in time and number of cases are required to prove this hypothesis. Transplant physicians should be aware of their patients' tacrolimus CV and TALT and individualize the pattern and frequency of follow-up to optimize it and reduce rejections.

P690 THE IMPACT OF SURGICAL SITE INFECTIONS (SSI) ON OUTCOME AFTER DECEASED DONOR LIVER TRANSPLANT

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Background: Infections are a significant cause of morbidity and mortality after liver transplant (LT). The first period after LT is mainly characterized by the occurrence of deep and organ/space surgical site infections (SSI). Perioperative antimicrobial prophylaxis is aimed to prevent these SSIs. The objective of this study is to evaluate the incidence, etiology, timing, and outcomes of SSIs in LT.

Methods: All deceased donor LT recipients between 2016-2019 in the Erasmus Medical Center were included. All relevant donor and recipient parameters were collected. SSIs within the first 90 days after transplantation were scored according to the CDC definition.

Results: Of the 187 patients included, 43 patients (23%) experienced a total of 55 SSI events. Median time until first SSI was 9 (6-13) days after LT. The most common pathogen was Enterococcus spp. in 64% (35/55) of all SSI events and in only 8% the pathogen was multi-drug resistant. In 60% the SSI was a peritonitis. Patient survival at 1 year was 84% for SSI vs 97% for no SSI (p=0.001). Graft survival at 1 year was 80% vs 98% (p=0.001). In patients with SSI, the median units of blood products transfused was higher (14 vs 6; p=0.002), the duration of anhepatic time was longer (50 min vs 45 min; p=0.005) and the incidence of early re-laparotomy was higher (19.1% vs 6.2%, p=0.011). Patients with SSI more often had a cholecdochojejunostomy in 29.5% vs 16.1% (p=0.48). Risk factors for SSI were re-laparotomy after LT OddsRatio OR 22.535(95%CI 3.406-253.475, p=0.002) and a choledochojejunostomy OR 2.156 (95%CI 1.44-6.082, p=0.040).

Conclusions: SSIs occur frequently after LT, and result in increased morbidity and mortality. In patients with SSI, Enterococcus spp. lead to even worse survival rates. Peri-operative antibiotic prophylaxis should target Enterococcus spp., if risk factors are present.

P691 NONCODINGRNA-BASED BIOMARKERS IN AFP NORMAL HEPATOCELLULAR CARCINOMA: LNCRNA SNGH PLAYS AN IMPORTANT ROLE IN RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Alpha-fetoprotein (AFP) is most commonly used as a biomarker for the diagnosis of Hepatocellular carcinoma (HCC). Increase in AFP is considered diagnostic value and AFP> 400 ng/mL is considered good prognosis in terms of Liver Transplantation. However, the AFP threshold for the diagnosis of HCC is still controversial. The alterations of non-coding RNAs (IncRNAs and miRNAs) are related to multiple diseases including cancer. In this study, we aimed to establish a diagnostic and prognostic ncRNA signature for AFP-normal HCC recurrence after LT.

Methods: Twelve IncRNAs were chosen as candidates on the basis of the literature to evaluate the diagnostic. The candidate IncRNAs were validated by qRT-PCR arranged in the training and validation sets. Twenty-two patients with normal AFP but HCC at biopsy diagnosis and 36 patients with high AFP were evaluated (This study was supported by Gilead Grant No:220075).

Results: SNGH16 and PVT1 were significantly up-regulated in plasma samples of AFP-normal HCC patients during training set and validation set (P=0.021, P=0.0001). Receiver operating characteristic (ROC) analysis showed that plasma SNGH16 exhibited significantly increased discriminatory power for differentiating normal patients with HCC from recurrent HCC patients with normal AFP.

Conclusions: Our results suggest that plasma levels of SNGH16 achieve a fine diagnostic accuracy in diagnosing ontogenesis and recurrence of HCC patients with normal AFP and may act as novel biomarkers for AFP-normal HCC patients.
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Background: A significant proportion of kidney transplants showed a high HLA sensitization and should be considered for transplantation across the HLA barrier. The best strategy to manage these patients is still a matter of debate and the benefits of desensitization based on techniques that rituximab have not been clearly delineated.

Methods: We review all kidney transplant performed at our center between 2009 and 2021 who showed donor-specific antibodies (DSA) at the time of transplant and a negative CDC crossmatch. All patients received induction therapy with thymoglobulin and maintenance immunosuppression with tacrolimus, MMF and steroids. According to the treating physician criteria patients also received treatment with apheresis (5-7 sessions of plasma-exchange or 5 sessions of immunoadsorption) and one single dose of Rituximab 375 mg/m2.

We analyze main outcomes after transplantation in both groups.

Results: During the study period 101 out of 1525 kidney transplants performed at our unit had at least one DSA at the time of transplant. In 64 cases standard treatment was administered while in 37 cases treatment with apheresis and rituximab was added. Main donor and recipient characteristics are shown in table 1. Incidence of acute rejection (37.5% vs. 35%), renal function at 6 months and 5-year patient and death-censored graft survivals were not different between groups (table 1). The main cause of graft failure was chronic antibody mediated rejection in both groups. Infectious complications were not different between groups.

Conclusions: HLA incompatible kidney transplants are associated with a high rate of antibody-mediated rejection. Adding treatment with apheresis and rituximab during the peri-transplant period did not significantly modify main outcomes after transplantation.

<table>
<thead>
<tr>
<th>N</th>
<th>64</th>
<th>37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age</td>
<td>55 (14)</td>
<td>53 (16)</td>
</tr>
<tr>
<td>Patient age</td>
<td>56 (13)</td>
<td>47 (16)</td>
</tr>
<tr>
<td>Delay time (months)</td>
<td>76 (13)</td>
<td>77 (101)</td>
</tr>
<tr>
<td>HLA A1 incompatible</td>
<td>1.3 (0.7)</td>
<td>1.3 (1.6)</td>
</tr>
<tr>
<td>HLA B1 incompatible</td>
<td>1.5 (0.7)</td>
<td>1.4 (0.7)</td>
</tr>
<tr>
<td>HLA DR incompatible</td>
<td>1.3 (1.0)</td>
<td>1.2 (1.0)</td>
</tr>
<tr>
<td>HLA DR DR incompatible</td>
<td>95 (65-100)</td>
<td>98 (85-100)</td>
</tr>
<tr>
<td>HLA A1 / (B1 + DR)</td>
<td>21.78 / 5</td>
<td>8.26 / 3</td>
</tr>
<tr>
<td>Anti-DSA</td>
<td>4950 (4950)</td>
<td>6177 (6004)</td>
</tr>
<tr>
<td>Anti-DR (%)</td>
<td>16 (10)</td>
<td>27 (15)</td>
</tr>
<tr>
<td>Anti-DR (%)</td>
<td>8 (12.5)</td>
<td>16 (10)</td>
</tr>
<tr>
<td>Serostatus (S1 domain of spike protein, anti-N and anti-S1 IgG ratio)</td>
<td>1.7 (1.0)</td>
<td>1.4 (1.4)</td>
</tr>
<tr>
<td>6-months post transplant</td>
<td>0.62 (1.14)</td>
<td>0.62 (1.08)</td>
</tr>
<tr>
<td>5-year graft survival</td>
<td>82%</td>
<td>89%</td>
</tr>
<tr>
<td>5-year death censored survival</td>
<td>61%</td>
<td>67%</td>
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</table>
Background: Laparoscopic live donor nephrectomy, represent a milestone in the history of transplant surgery. Since 1995, this procedure provides several benefits for the live donor, reducing the constantly increased disparity between organ supply and demand. During the preoperative evaluation, various asymptomatic or symptomatic pathologies may be discovered. Live donor nephrectomy and other concomitant laparoscopic surgical procedures are rarely reported in the literature. According to our experience this kind of surgery could be performed with safety, without increased morbidity for the donor.

Methods: We prospectively collected data from 267 cases since November 2018 to December 2022 from our transplant center. Laparoscopic live donor nephrectomies with simultaneous other operations were performed in fifteen cases (5.5%). Donor demographics, art of concomitant surgery, operative time, intra- and postoperative complications and morbidity are presented in Table 1. Results: In all cases nephrectomies were preceded the other surgical procedures. Mean operative time was 164.33 minutes (median time 160 minutes, range 130-240 minutes) Changing patient’s position was done intraoperatively from lateral to supine in 13 cases, with no incidents. An extra 5mm trocar was inserted in only in 4 cholecystectomy cases below the right coastal margin. The mean hospitalization time was 3 days (range 3-4 days). The postoperative complications and morbidity are presented in Table 1. Conclusions: Laparoscopic live donor nephrectomy and simultaneous surgery for concomitant pathologies are very rare reported in the literature. Herein we report our experience with 15 cases. With is safe and feasible by an experienced surgical team. This uncommon practice is truly beneficial for the donor avoiding further anesthesia as well as surgical approach and their potential complications.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Side</th>
<th>Procedure</th>
<th>Position</th>
<th>Kidney + (Aorta)</th>
<th>Concomitant (Transplant graft)</th>
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<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>F</td>
<td>Y</td>
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<td>Supine</td>
<td>Left</td>
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<td>2</td>
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<td>F</td>
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<td>Supine</td>
<td>Right</td>
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<tr>
<td>3</td>
<td>75</td>
<td>F</td>
<td>N</td>
<td>Left Groom Hernia Repair and Cholecystectomy</td>
<td>Supine</td>
<td>Right</td>
<td>None/None</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>M</td>
<td>Y</td>
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<td>Supine</td>
<td>Right</td>
<td>None/None</td>
</tr>
<tr>
<td>5</td>
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<td>Supine</td>
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<td>Supine</td>
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</tr>
<tr>
<td>7</td>
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<td>M</td>
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<td>Umbilical Hernia Repair</td>
<td>Supine</td>
<td>Left</td>
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<tr>
<td>8</td>
<td>60</td>
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<td>Left</td>
<td>None/None</td>
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<td>9</td>
<td>59</td>
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<td>N</td>
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<tr>
<td>10</td>
<td>58</td>
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<td>N</td>
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<td>Left</td>
<td>None/None</td>
</tr>
<tr>
<td>11</td>
<td>62</td>
<td>M</td>
<td>N</td>
<td>Cholecystectomy</td>
<td>Supine</td>
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<tr>
<td>12</td>
<td>57</td>
<td>F</td>
<td>Y</td>
<td>Left Ovarian Cyst Excision</td>
<td>Lateral</td>
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<tr>
<td>13</td>
<td>58</td>
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<td>N</td>
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<td>Supine</td>
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<tr>
<td>14</td>
<td>50</td>
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<td>Supine</td>
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<tr>
<td>15</td>
<td>59</td>
<td>F</td>
<td>N</td>
<td>Uretero Cyst of Left Liver Lobe</td>
<td>Lateral</td>
<td>Left</td>
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AFTER A STEPWISE METHODOLOGY TO SHAPE A NATIONAL ALLOCATION SCORING SYSTEM FOR LIVER TRANSPLANTATION: WHICH IS THE BEST METRICS TO EVALUATE RESULTS?

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Background: A stepwise methodology to create a liver allocation system in Italy was applied through a 4-year consensus conference process leading to a new liver allocation system (ISO score) officially applied on July 1, 2019. An ideal system should regularly promote adaptive changes with the aim to equalize the risk of death/dropout while waiting among the candidates of the different etiologic groups.

Methods: as efficiency metrics of the system, we arbitrarily choose to measure the drop-out rate (defined as death on the waiting list (WL) or delisting due to clinical worsening) of the different etiologic strata of candidates to liver transplantation: liver cirrhosis (LC), hepatocellular carcinoma (HCC) and MELD-excepted (MELD-ex). We analyzed the differences between PERIOD1 (from July 1, 2018 to June 30, 2019) and PERIOD2 (from July 1, 2019 to December 31, 2020) after the introduction of ISO score. To adjust the burden of the waiting time related to previous allocation systems only incident cases in both periods were considered. To avoid the potential bias related to COVID-19 period, SARS-CoV-2 positive cases dropping out were censored. Drop-out probabilities were analyzed both as crude rates and as competing risk time dependent events.

Results: 3555 incident listings across the two periods were evaluated. They included 1185 (33.3%) LC, 1550 (43.6%) HCC and 820 (23.1%) MELD-ex. There were 727 (50.9%) LTs with 102 (7.1%) drop-outs in period1, and 1237 (58.1%) LTs with 175 (6.2%) drop-outs in period2 (p=0.000). Using HCC as reference group, competing risk drop-out in period2 was significantly higher than period1 in both LC (HR 2.54, p=0.003) and lower in MELD-ex (HR 0.50, p=0.114), in period2 the difference between HCC and LC significantly decreased (HR 1.45, p=0.027). Consistently, the advantage of MELD-ex compared to cirrhosis reduced.

Conclusions: A stepwise methodologically solid development of allocation systems is mandatory to ensure transparency and efficiency of the processes. The intrinsic complexity and diversity among the various etiological candidate categories requires regular adaptive changes. Drop-out rate homogeneity among macrogroups seems to be the first relevant metric to improve equity in the distribution of organ scarce resource.

Table 1. Crude and competing risk values of drop-out probabilities in the two study periods.

<table>
<thead>
<tr>
<th>PERIODS</th>
<th>Groups</th>
<th>LT</th>
<th>Crude (95% CI)</th>
<th>Other Causes</th>
<th>Drop-out</th>
<th>Competing-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period 1</td>
<td>LC</td>
<td>727 (50.9)</td>
<td>102 (7.1)</td>
<td>525 (37.0)</td>
<td>36 (2.5)</td>
<td>150 (10.9)</td>
</tr>
<tr>
<td></td>
<td>HCC</td>
<td>1237 (58.1)</td>
<td>175 (6.2)</td>
<td>1062 (46.4)</td>
<td>71 (2.9)</td>
<td>516 (21.5)</td>
</tr>
<tr>
<td></td>
<td>MELD-ex</td>
<td>1237 (58.1)</td>
<td>175 (6.2)</td>
<td>1062 (46.4)</td>
<td>71 (2.9)</td>
<td>516 (21.5)</td>
</tr>
<tr>
<td>Period 2</td>
<td>LC</td>
<td>727 (50.9)</td>
<td>102 (7.1)</td>
<td>525 (37.0)</td>
<td>36 (2.5)</td>
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</tbody>
</table>

*Abbreviations: HCC hepatocellular carcinoma, LC liver cirrhosis, MELD-ex excepted, LT liver transplantation, WL waiting list. *Reference: weekly.

Figure 1. Competing risk analysis of drop-out probability comparing the three patient groups (i.e. HCC vs. LC vs. MELD-ex) in the two study periods.
Table 1: patients' clinical features

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Months from KT</th>
<th>RCC size (mm)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>43</td>
<td>144</td>
<td>12x15 RFA</td>
</tr>
<tr>
<td>Patient 2</td>
<td>36</td>
<td>156</td>
<td>35x27 RFA</td>
</tr>
<tr>
<td>Patient 3</td>
<td>37</td>
<td>108</td>
<td>20x25 RFA</td>
</tr>
<tr>
<td>Patient 4</td>
<td>63</td>
<td>288</td>
<td>20x21 RFA</td>
</tr>
<tr>
<td>Patient 5</td>
<td>49</td>
<td>202</td>
<td>45x25 NSS</td>
</tr>
<tr>
<td>Patient 6</td>
<td>64</td>
<td>158</td>
<td>50x40 NSS</td>
</tr>
</tbody>
</table>

Results: No renal function loss was reported in both groups, and all patients remained with a stable renal function. Patient 5 and 6 had a complete RCC excision, PT1aG1 and PT1bG1 respectively.

Conclusions: Both RFA and NSS are valid options compared to radical nephrectomy for RCC T1 tumors allowing the preservation of the renal parenchyma and is associated with low morbidity. Considering the low grade of the RCC and the radical resection in the NSS group, the relapse risk is almost zero.

P701 Anticoagulant and Antiplatelet Use in Renal Transplantation: Is Perioperative Blood Loss and Transfusion Rates a Significant Concern?

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Background: Renal patients often have multiple pathologies which necessitate anticoagulation. Renal transplantation remains the gold standard for patients awaiting renal failure (ESRF). Major surgery poses increased risks of significant haemorrhage in the perioperative period. The role of reversal agents such as warfarin is possible, the effect of anticoagulant therapies such as aspirin, clopidogrel, new oral anticoagulants (NOACs), associated with surgical safety is less understood.

Methods: Electronic and paper records were accessed to investigate transplants occurring between 18/12/2019 and 30/11/2022. Preoperative anticoagulant/antiplatelet regimens were recorded, along with coagulation screens and haemoglobin (Hb) levels. Sequential Hb is for 72 hours perioperative were collected along with adverse outcomes.

Results: 12 transplants occurred during this period. International normalised ratios (INR) ranged from 0.9 – 2.4 preoperative. No preoperative blood products or reversal agents were administered. The average Hb drop was 16.2 g/dl at 72 hours. One patient required a 2-unit red cell transfusion (starting Hb 76 g/dl). No reversal or reoperation were administered. The average Hb drop was 16.2 g/dl at 72 hours. One patient required a 2-unit red cell transfusion (starting Hb 76 g/dl). No reversal or reoperation were administered. The average Hb drop was 16.2 g/dl at 72 hours. One patient required a 2-unit red cell transfusion (starting Hb 76 g/dl).

Conclusions: There was no difference in baseline characteristics, nor in the prevalence of peri-and postoperative complications, with a total complication rate of 59%. Despite the minor, Clavien-Dindo grade II in both groups, while a different pattern of surgical complications was noticed between them. Duration of surgery was significantly longer in the OD group (median 240 min vs. 140 min in LDN, p < 0.01), warm ischemia time was longer in the LDN group (median 4 vs. 2 min in ODN, p < 0.01) and length of hospital stay shorter in the LDN group (median 3 days vs. 7 days in ODN). Conversion rate from laparoscopic to open surgery was 1.09%. There was a drop in estimated glomerular filtration rate (eGFR) at discharge of 36 mL/min in the LDN and 32 mL/min in the ODN groups, respectively (p = 0.03). No readmission or reoperation were recorded.

One donor death has been occurred due to no surgical reasons.

Conclusions: This study provides evidence that minimally invasive surgery can be performed safely, with very good short-term outcomes, providing several benefits for the living donor kidney, thereby contributing to expanding the living donor pool, which is essential, especially in countries with deceased-donor organ shortage.

P702 When More is Not Better — Big Data and Machine Learning in Assessing the Risk of COVID-19 among Recipients and Patients on Waiting List

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1Wroclaw Medical University, Wrocław, Poland
2Wrocław University of Economics and Business, Wrocław, Poland

Background: We used big data from a single transplant center to machine learning experiments aiming to find best predictive model for COVID-19 incidence. This study’s primary objective was to determine which parameters can predict if a patient will be infected with COVID-19. Secondary objective: to determine if the addition of immunogenic data to the machine learning prediction model adds meaningful value.

Methods: Big dataset (136 features) from 565 patients (274 were SOT recipients) underwent machine learning experiments. The characteristics of patients randomly assigned to the training or testing groups. Following factors formed input parameters (134 features): a) clinical (including comorbidities) and demographic characteristics, b) genetic HLA-A, B, C, DR, DQ, TNFRSF8 (rs2297729), BSG (rs4919855), TNFA (rs1799724), IFNγ (rs7845174, rs2430561), TNFA (G-308A, rs1800629, IL-17A (G-917A, rs2275913), IL-17F (T+7488C, rs763780), ACE2 (rs1206680, rs2074192, rs420167), TMPRSS2 (rs12329761, rs2070788), rs4240157, rs12329761, rs2070788), presence of SARS-CoV-2 antibodies and vaccination status, d) inflammation related markers from peripheral blood: CRP, hemoglobin, albumin, BNP, NT-pro-BNP, sPAP, IL-6, (IFN-gamma, TNF-alpha, complement functional activity), e) blood morphology derived parameters: NLR, PLR and MFI, f) immune cell phenotypes including T cells (regulatory T cells, Tc, Th1, Th2 and Th17), B cells (naïve, memory, transi- tional, plasmablasts), NK and NKT and g) TVT viremia.
Results: Surprisingly, the best model obtained only 63% accuracy when all 134 characteristics were utilized as input data. The model using immunogenetics data without circulating biomarkers and cell phenotypes yielded the best performance (93.5%). Figure 1 depicts the neural network’s weights, which are the real values associated with each input and which represent the contribution of that feature to the final prediction.

Conclusions: Using immunogenetics data and machine learning, we were able to evaluate the risk of COVID-19 occurrence in SOT recipients with good accuracy. We have discovered that more data does not necessarily increase the accuracy of COVID-19 prediction, particularly when employing a single assessment of circulating biomarkers that are likely to change over time.

Results: We used immunogenetics data and machine learning to predict COVID-19 occurrence. We discovered that more data does not necessarily increase the accuracy of COVID-19 prediction.

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Background: The molecules released from the liver during ex situ perfusion can provide important information regarding graft function as well as the factual damage experienced by hepatocytes and cholangiocytes during the donation process. The present study investigated the use of a novel automated immunoassay platform to determine the concentration of perfusate biomarkers released by human livers subjected to Hypothermic oxygenated machine perfusion (HOPE).

Methods: The retrospective observational study includes HOPE procedures performed on DBD-ECD and DCD donor livers from 2017 to 2020 at Policlinico (Milan, Italy) and Molinette (Turin, Italy). Perfusate samples were collected hourly and stored at -80°C. Selected biomarkers relevant to inflammation, cell damage, and endogenous healing processed were assessed using the traditional approach (Enzyme-linked Immunosoropt Assay, ELISA) and the automated technology. Consistency between the 2 techniques was evaluated by Bland-Altman analysis.

Results: Eighty-nine donors were included, of whom 51 were DBD-ECD and 38 DCD. All grafts were successfully transplanted; 23 (26%) recipients developed early-allograft-dysfunction (EAD), while 52 (58%) developed acute-kidney injury (AKI). The all evaluated molecules were consistent between the two analytical protocols. The automated technology provided the results within 90 min after the beginning of the assay. Analysis of the perfusate collected at 1 h of HOPE revealed a lower concentration of Hepcidin in the EAD-yes compared to the AKI-no group (79.65±52.37ng/g vs 137.24±21.03ng/g, p<0.050, Figure, panelA), while an increased concentration of IL-33 was detected in the AKI-yes relative to the EAD-no group (190.32±69.09pg/g vs 59.11±15.23pg/g, p=0.017, Figure, panelB).

Conclusions: Molecular profiling of the perfusate collected during MP could provide important information for prediction of postoperative complications. This strategy could optimize the donorrecipient match, in line with the principles of personalized medicine.

Background: For decades the selection of potential recipients for heart transplantation (HTx) was limited to the 60 year-old as the upper age limit because of an increased risk complications and comorbidities in the older group. However, throughout the years and in experienced transplant centers, HTx in older patients can achieve acceptable results. The aim of the study was to evaluate our experience of HTx in recipients over 60 year-old.

Methods: From 2010 to 2021 HTx was performed in 177 patients, 22 (12.4%) of them were over 60 years of age. We analyzed the results of all transplant recipients grouped: early-term results, including 30-day mortality, and survival within 1 year after HTx.

Results: Recipients' mean age was 63±2 year-old (n=18 – male), Causes of heart failure (HF) were IHD (n=14), dilated cardiomyopathy (n=6), RHD (n=1) and isolated cardiac amyloidosis (n=1). LVEF was significantly decreased 23±12.3% while PASP (49.1±14.1 mm Hg) and PVR (3.1±1.5 W.U.) were elevated. Patients spent in a HTx waiting list 103±26 days (1 was bridged with an ECMO) and were classified by UNOS: 1A (n=4), 1B (n=3) and 2 (n=15). All recipients underwent HTx using the biventricular technique (369±39 minutes – duration of surgery. Results of early-term follow after HTx were: 5±2 days on respiratory support, 11±2 days – on inotrope support, 11±3 days – ICU stay. After HTx ECMO was implanted to 3 patients due to the development of right HF (RHF). During 1st month there were no episodes of allograft rejection but the following complications were diagnosed: urinary tract infection (n=6), pneumonia (n=5), acute kidney failure (n=1) and a sick sinus syndrome followed by pacemaker implantation (n=1). Early-term 3 recipients died: 1 – from stroke in 6 days and 2 – from RHF 25 and 40 days after HTx, respectively. In 9 months an allograft rejection (2R3B) was diagnosed in 1 patient which was successfully treated by pulse steroid therapy and plasma exchange sessions. In 6 months and 1 year 2 patients died from infectious complications complicated with sepsis.

Conclusions: Transplant recipients over 60 year-old were characterized by the development of RHF but only 14% of them required an ECMO implantation. In our study, 30-day mortality was 9%. Both early and long-term after HTx infectious complications prevailed in this group.

Background: Kidney transplantation is the gold-standard treatment for patients with end-stage kidney disease. Patients who receive a kidney transplant, experience an improvement in many aspects of daily life but often have poorer quality of life than the general population. Sexual functioning is a general component of health which can be affected negatively in patients with a kidney transplantation. However, the assessment of sexual functioning is not incorporated into standard practice in renal care. It is important to enhance quality of life for kidney transplant recipients, especially considering the many treatments available to successfully treat sexual dysfunction. The aim of this scoping review is to explore what is known about the management of sexual dysfunction in adult kidney transplantation to inform best practice.

Methods: A scoping review methodology was used.

Results: Results explored treatments, therapies, and interventions to treat sexual dysfunction in kidney transplantation. This included accommodative adjustment mechanisms, psychological support, medication/devices, spousal support, and healthcare professional support.

Conclusions: It is evident that sexual functioning is a complex multi-factorial, multi-faceted phenomenon. However, research is limited and there is an urgent need for high-quality evidence to inform the development of appropriate support strategies and interventions for this patient population. Healthcare professionals need to develop a better understanding of sexual dysfunction in kidney transplantation and remove challenges to the assessment and treatment in renal healthcare.
Apostolos Angelis*, Dionysios Prevezanos1, Ioannis Bokos2, Christos Nikolaidis3, Dimitrios Carousos1, Spyridon Vernadakis1

**Background:** Living kidney donor transplantation has been a significant contributor to renal transplants since its inception in 1954. Over a third of all kidney transplants in the USA are from living donors, and the procedure has been made safer since the advent of laparoscopic living donor nephrectomy in 1995. Laparoscopic renal procurement is a challenging operation. Re-interventions for the same cause are rare but may occur.

**Methods:** Our centre has performed more than 280 cases of laparoscopic living donor retrievals since October 2018, with low morbidity and mortality rates. We present a unique case in which the laparoscopic donor procedure had to be temporarily stopped due to a complication during the recipient's surgery. The left kidney of the donor and its ureter were fully dissected and almost ready to be removed. However, the donor's kidney was successfully retrieved seven months later. Patient demographics and outcomes data are presented in Table 1.

**Results:** Although this case is a one-of-a-kind occurrence, we present it for its management and findings from the second attempt. The chronic gap between the two surgeries was seven months. New Computed Tomography was performed prior to the second operation. Intraoperatively, the second surgery required again mobilization of the kidney due to adhesions in the retroperitoneum, but the renal vessels and ureter ligation was performed without any issue. The renal graft has been successfully transplanted. Hospitalization length was three days. No blood loss was occurred, while less analgesic consumption and uneventful postoperative course has been noticed. The renal graft has been successfully transplanted. Hospitalization length was three days. No blood loss was occurred, while less analgesic consumption and uneventful postoperative course has been noticed.

**Conclusions:** Laparoscopic donor nephrectomy is a challenging operation, but remains the safest procedure with low morbidity and mortality rates, offering early hospital discharge and improved post-operative quality of life to donors. Re-interventions for the same cause to the donors are rare, but may occur.

<table>
<thead>
<tr>
<th>Table 1. Patient Demographics</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
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<tr>
<td><strong>BMI</strong></td>
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<tr>
<td><strong>Laterality</strong></td>
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<tr>
<td><strong>Renal Anatomy</strong></td>
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<tr>
<td><strong>Prior surgeries</strong></td>
</tr>
</tbody>
</table>

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Background: Biliary complications, especially ischemic cholangiopathy as a result of ischemic bile duct injury, remain a major source of morbidity after liver transplantation (LT) using donation after circulatory death (DCD) grafts. Little is known about the effect of arterial reperfusion during DCD LT on the incidence of biliary complications. The objective of this study is to assess the association between the arterial reperfusion time and clinical outcomes after DCD LT.

Methods: Data for patients undergoing LT with DCD grafts between 2001-2018 were retrospectively collected from three centers, including donor and recipient characteristics, reperfusion sequence, ischemia and reperfusion times and post-operative complications. Parameter of interest was arterialization time (time between portal and arterial reperfusion). Primary endpoint was the occurrence of biliary complications, secondary endpoints were graft and patient survival, as well as re-transplantation rates.

Results: Data were available for 292 patients with a median follow-up of 4.5 years. Median arterialisation time was 34 (13-134) minutes. Overall, biliary complications occurred in 46% of patients (28% anastomotic strictures, 26% non-anastomotic strictures, 12% bile leaks), and re-transplantation in 20%. 1-year biliary complications occurred in 46% of patients (28% anastomotic strictures, 26% non-anastomotic strictures, 12% bile leaks), and re-transplantation in 20%

Conclusions: Variation in timing of arterial reperfusion during DCD liver transplantation does not seem to affect clinical outcomes of LT using DCD grafts.

Methods: For patients with preserved primary bile ducts, we compared the incidence of biliary complications after using continuous versus interrupted techniques and suture sizes (5-0 versus 6-0 pDS). In our study, the suture technique and suture size was at the discretion of the surgeon with the technique otherwise being essentially equivalent. Indication for imaging included any unexplained elevation in the liver function laboratory values, not explained with standard liver ultrasound. In general, biliary imaging was obtained primary for biopsy to evaluation of elevated enzymes, resulting in a large number of studies. Study outcomes included 1-year post transplant need for any duct imaging, presence of anastomotic strict or leak, and 90-day and 1-year graft survival.

Results: There were 1177 DDLTs included in the analysis. Overall, 37% of patients had any bile duct imaging in the first year, 44% continuous versus 36% interrupted (p=0.11), and 39% 5-0 PDS versus 31% 6-0 PDS (p=0.03). Any anastomotic stricture was seen in 28% of patients, 35% continuous versus 28% interrupted (p=0.13), and 21% 5-0 PDS versus 22% 6-0 PDS (p=0.01). Any bile duct leak was seen in 7% of patients, 6% continuous versus 7% interrupted (p=0.78), and 7% 5-0 PDS versus 6% 6-0 PDS (p=0.85). Ninety-day and 1-year graft survival were statistically equivalent for the different groups.

Conclusions: In this cohort, duct-to-duct revascularization with interrupted suturing using 6-0 PDS was equivalent to the use of 5-0 PDS with respect to the rate of biliary complications, including a lower need for imaging, a lower rate of anastomotic stricture, and with similar risk of bile duct leak. Early and late graft survival were not affected by suture technique nor by suture material.

Background: Tacrolimus remains a cornerstone of immunosuppression in kidney transplantation (KT). The common use of pharmacokinetic tools for tacrolimus prescription suggests new tools to improve graft survival and patients’ quality of life. Interindividual differences of tacrolimus metabolism pathways (TMP) suggest individualization targets. Tacrolimus concentration-to-dose ratio (Tac C/D) has been suggested as a tool for such individualization. The TIPS trial (NCT04526431). We prospectively monitored tacrolimus blood levels in incident (Tac C/D > 1.05). Trough concentrations between fast metabolizers and standard liver transplantation does not seem to affect clinical outcomes of LT using DCD grafts.

Methods: For patients with preserved primary bile ducts, we compared the incidence of biliary complications after using continuous versus interrupted techniques and suture sizes (5-0 versus 6-0 pDS). In our study, the suture technique and suture size was at the discretion of the surgeon with the technique otherwise being essentially equivalent. Indication for imaging included any unexplained elevation in the liver function laboratory values, not explained with standard liver ultrasound. In general, biliary imaging was obtained primary for biopsy to evaluation of elevated enzymes, resulting in a large number of studies. Study outcomes included 1-year post transplant need for any duct imaging, presence of anastomotic strict or leak, and 90-day and 1-year graft survival.

Results: There were 1177 DDLTs included in the analysis. Overall, 37% of patients had any bile duct imaging in the first year, 44% continuous versus 36% interrupted (p=0.11), and 39% 5-0 PDS versus 31% 6-0 PDS (p=0.03). Any anastomotic stricture was seen in 28% of patients, 35% continuous versus 28% interrupted (p=0.13), and 21% 5-0 PDS versus 22% 6-0 PDS (p=0.01). Any bile duct leak was seen in 7% of patients, 6% continuous versus 7% interrupted (p=0.78), and 7% 5-0 PDS versus 6% 6-0 PDS (p=0.85). Ninety-day and 1-year graft survival were statistically equivalent for the different groups.

Conclusions: In this cohort, duct-to-duct revascularization with interrupted suturing using 6-0 PDS was equivalent to the use of 5-0 PDS with respect to the rate of biliary complications, including a lower need for imaging, a lower rate of anastomotic stricture, and with similar risk of bile duct leak. Early and late graft survival were not affected by suture technique nor by suture material.

Methods: We compared two induction strategies with (intensive) or without plasma exchange and rituximab, with potential side effects and high cost, is not clearly established.

Background: Biliary complications, especially ischemic cholangiopathy as a result of ischemic bile duct injury, remain a major source of morbidity after liver transplantation (LT) using donation after circulatory death (DCD) grafts. Little is known about the effect of arterial reperfusion during DCD LT on the incidence of biliary complications. The objective of this study is to assess the association between the arterial reperfusion time and clinical outcomes after DCD LT.

Methods: Data for patients undergoing LT with DCD grafts between 2001-2018 were retrospectively collected from three centers, including donor and recipient characteristics, reperfusion sequence, ischemia and reperfusion times and post-operative complications. Parameter of interest was arterialization time (time between portal and arterial reperfusion). Primary endpoint was the occurrence of biliary complications, secondary endpoints were graft and patient survival, as well as re-transplantation rates.

Results: Data were available for 292 patients with a median follow-up of 4.5 years. Median arterialisation time was 34 (13-134) minutes. Overall, biliary complications occurred in 46% of patients (28% anastomotic strictures, 26% non-anastomotic strictures, 12% bile leaks), and re-transplantation in 20%. 1-year biliary complications occurred in 46% of patients (28% anastomotic strictures, 26% non-anastomotic strictures, 12% bile leaks), and re-transplantation in 20%.

Conclusions: Variation in timing of arterial reperfusion during DCD liver transplantation does not seem to affect clinical outcomes of LT using DCD grafts.

Methods: For patients with preserved primary bile ducts, we compared the incidence of biliary complications after using continuous versus interrupted techniques and suture sizes (5-0 versus 6-0 pDS). In our study, the suture technique and suture size was at the discretion of the surgeon with the technique otherwise being essentially equivalent. Indication for imaging included any unexplained elevation in the liver function laboratory values, not explained with standard liver ultrasound. In general, biliary imaging was obtained primary for biopsy to evaluation of elevated enzymes, resulting in a large number of studies. Study outcomes included 1-year post transplant need for any duct imaging, presence of anastomotic strict or leak, and 90-day and 1-year graft survival.

Results: There were 1177 DDLTs included in the analysis. Overall, 37% of patients had any bile duct imaging in the first year, 44% continuous versus 36% interrupted (p=0.11), and 39% 5-0 PDS versus 31% 6-0 PDS (p=0.03). Any anastomotic stricture was seen in 28% of patients, 35% continuous versus 28% interrupted (p=0.13), and 21% 5-0 PDS versus 22% 6-0 PDS (p=0.01). Any bile duct leak was seen in 7% of patients, 6% continuous versus 7% interrupted (p=0.78), and 7% 5-0 PDS versus 6% 6-0 PDS (p=0.85). Ninety-day and 1-year graft survival were statistically equivalent for the different groups.

Conclusions: In this cohort, duct-to-duct revascularization with interrupted suturing using 6-0 PDS was equivalent to the use of 5-0 PDS with respect to the rate of biliary complications, including a lower need for imaging, a lower rate of anastomotic stricture, and with similar risk of bile duct leak. Early and late graft survival were not affected by suture technique nor by suture material.
Background: Although the national shortage of deceased donor kidneys, around 55% standard criteria (SCD) DBD and 63% SCD DCD are declined at least once before being utilised elsewhere. Based on the data from National Health System, Blood and Transplant (NHSBT), The Winton Centre for Risk and Evidence Communication has developed a Kidney Transplant Tool (KTT) that provides a predictive graft and patient survival. We wanted to see if the predictive scores of the declined kidneys in terms of graft and patient survival were significantly worse leading to offer rejection.

Methods: In this single centre, retrospective pilot study, we used KTT to compare the predicted outcomes for the accepted and declined kidneys in our centre during 2022. Recipient’s age, ethnicity, primary kidney disease, waiting time, previous transplant and HLA mismatch, with donor’s age, history of hypertension and body mass index were collected to be used on the online KTT to calculate the allograft and patient survival figures of 1, 3 and 5 years. We included all accepted kidneys and kidneys declined by our centre but used elsewhere.

Results: The predicted outcomes of 112 accepted offers showed expected patient survival of 94.47±4.02, 90.88±6.47 and 86.69%±7.73 at 1, 3 and 5 years respectively. Of the 101 declined deceased kidney offers that were transplanted elsewhere, the expected kidney survival was 86.21±4.42, 83.19±6.14 and 78.76%±7.43, and patient survival was 93.14%±4.03, 88.72%±6.22 and 86.26%±7.41 at 1, 3 and 5 years respectively. Comparing the means of both groups showed no significant difference with p-value >0.05.

Conclusions: This analysis does not look into the reasons of decline (patient decline, unwell recipient, positive crossmatch or low risk apatite), hence it is not possible to draw direct conclusions, but it highlights the subjective nature of decision making when accepting organs. With no significant difference between accepted and declined offers predicted survival estimates in this study, we wonder if a more granular look at the causes of organ refusal will identify areas of focus to improve organ utilisation. This analysis also highlights the benefits of prompt re-offering of organs after first decline to improve utilisation.

Background: Hepatitis B virus (HBV) reactivation in kidney transplant recipients may be associated with liver failure and graft loss, especially in anti-Hbc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients. Belatacept, a selective costimulation blocker, has been used in kidney transplantation for some time and has been associated with reactivation of other viruses as BK or CMV. However, there are few data on HBV reactivation among kidney recipients treated with belatacept.

Methods: We performed a retrospective study in two French kidney transplantation centres including all transplant recipients receiving belatacept. Among HBcAb-positive patients, we analyzed HBV reactivation rate, outcomes and risks factors.

Results: 135 patients treated with belatacept were included, and 32 were HBcAb-positive. Seven patients reactivation HBV (21.9% of HBcAb-positive patients), including 5 HBsAg-negative patients (16.7%); reactivation occurred 54.8 (± 70.9) months after transplantation. There was no significant difference in survival between patients that reactivated HBV and patients that did not: 5-year patient survival of 100% (28.6; 100) and 83.4% (67.6; 100), respectively (p=0.363) and 5-year graft survival of 100% (28.6; 100) and 79.8% (61.7; 100), respectively (p=0.335). No factor, including HBsAb positivity and antiviral prophylaxis, was statistically associated with the risk of HBV reactivation.

Conclusions: Compared to the few studies that exist in this area, the HBV reactivation rate was high in patients treated with belatacept in our study. Our findings suggest that systematic antiviral prophylaxis for anti-Hbc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients should be considered and that there should be close monitoring of HBV serology and viral load in these patients to detect early HBV reactivation.

Background: Pancreas transplantation is an established method of treatment of diabetes mellitus patients. Advances in as well as surgical techniques as immunosuppressive treatment have led to improving results in pancreas transplantation recipients.

Methods: We reviewed 254 consecutive pancreas transplants performed in our Centre since 2004 until February 2023. Among these patients we performed 218 SPK, 28 PTA and 8 PAK. In years 2004-February 2018 we performed systemic venous anastomosis with the donor’s iliac vein (n=196). Since February 2018 until February 2023 we performed 57 venous anastomosis with the donor’s inferior vena cava (IVC).

Results: We statistically analysed the two groups of patients – one with the systemic venous anastomosis with iliac vein and one with the anastomosis with the IVC. There were no significant differences in patient, kidney, or pancreas allograft survival rates. The statistical significance was found in pancreas graft thrombosis incidence.

Conclusions: Systemic venous drainage is the most common type of the venous anastomosis. The results show that pancreas graft thrombosis was less common in the IVC group. Systemic anastomosis with IVC seems to be more beneficial for the pancreas graft recipients.
Background: Kidney transplantation (KT) is increasingly offered to older and more co-morbid patients: ‘high risk recipients’ (HRR). The UK kidney allocation scheme preferentially allocates kidneys from expanded criteria donors to these patients, with associated increased risk of graft failure and poor graft function. The aim of this study is to understand outcomes of HRRs and their predictors in a contemporary dataset to quantify the potential risks and benefits of KT for this cohort.

Methods: This single-centre cohort study of patients receiving deceased donor KT between 01/10/2014-31/12/2019. Data about previous co-morbidity, biochemical and haematological markers of frailty were used in multivariate models of graft and patient outcome.

Results: 645 patients were included of which 111 were HRR. HRR were older (60 yrs vs 51.5 yrs, p<0.001), predominantly male (69.4% vs 61.6%, p=0.12) with a higher incidence of diabetes (32.4% vs 8.3%, p<0.001), ischaemic heart disease (27.9% vs 3.9%, p<0.0001) and peripheral vascular disease (8.1% vs 0.5%, p<0.001). There were no significant differences in donor demographics, cold ischaemia time, or brain/circulatory death donors. HRR had higher rate of abnormal red-cell distribution width (RDW) pre-operatively (57.7% vs 39.7%, p=0.002). EGFR at 3 (47.5 vs 49, p=0.36) and cold ischaemia time, or brain/circulatory death donors. HRR had higher rate of disease (27.9% vs 3.9%, p=0.0001) and peripheral vascular disease (8.1% vs 0.5%, p=0.001). Cox proportional hazards survival analysis showed recipient age (1.74, 95% CI 1.4-2.3, p=0.0001), RDW (1.8, 95% CI 1.06-3.07, p=0.03) and previous stroke (6.7, 95% CI 1.6-29.9, p=0.01) to be independent predictors of survival post-transplant.

Conclusions: HRR are older and more co-morbid than standard risk recipients. Whilst there is no difference in eGFR or graft survival in this cohort, they suffer a survival disadvantage post-transplant. It is likely that KT offers significant advantages over dialysis for HRR, but careful consent is critical.
P728  PRE-TRANSPLANT MITOCHONDRIAL RESPIRATION IN HUMAN KIDNEY ALLOGRAFTS PREDICTS CLINICAL OUTCOME UPON TRANSPLANTATION

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Background: With the increasing use of extended criteria donors for kidney transplantation biomarkers with robust predictive capacity are necessary. The renal cortex has low ischemia tolerance as proximal tubuli have the second highest mitochondrial density in the human body and oxidative phosphorylation (OXPHOS) is essential for ATP synthesis. Furthermore, post-reperfusion mitochondrial respiration is associated with delayed graft function (DFG). Therefore, we evaluated the predictive value of pre-transplant mitochondrial respiration towards graft function after transplantation.

Methods: In a prospective study, cortex biopsies were taken in 45 human kidneys at the end of static cold storage (SCS) and/or hypothermic machine perfusion (HMP). Mitochondrial respiration was assessed by high-resolution respirometry. OXPHOS capacity, maximal mitochondrial respiration and ATP production efficiency with the respiratory substrate succinate were evaluated.

Results: We found significantly lower OXPHOS capacity (53.4 ± 17.6 vs. 74.2 ± 23.0 pmol·s⁻¹·mg wet mass⁻¹ [mean ± SD, p = 0.0083]), maximal respiration (60.9 ± 22.9 vs. 91.1 ± 29.0 pmol·s⁻¹·mg wet mass⁻¹, p = 0.0029), and ATP production under succinate stimulation (74.2 ± 0.12 vs. 0.012 pmol·s⁻¹·mg wet mass⁻¹) in biopsies of kidneys developing delayed graft function as compared to those with normal post-transplant function. These values also correlated significantly with the 7-day creatinine and glomerular filtration rate (GFR) values. The OXPHOS capacity in the biopsy after HMP inversely correlated with the 3-month creatinine values (Pearson r = -0.41, p = 0.039). In contrast, the Remuzzi score did not correlate with DGF, 7-day or 3-month creatinine and GFR values.

Conclusions: In kidney grafts eventually developing DGF, mitochondrial respiration is associated with delayed graft function. These findings support the need for further research to identify mitochondrial respiration as a new biomarker for kidney transplantation.

P729  EX-SITU SPLIT LIVER TRANSPLANTATION: A SAFE PARACHUTE PROCEDURE WHEN IN-SITU SPLITTING IS NOT POSSIBLE

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Background: Split liver (SL) transplantation is an established technique which enables to procure two liver grafts from the same deceased donor: the left-lateral section (LLS) for a pediatric recipient and the extended right lobe (ERL) for an adult. Despite the splitting is generally performed in-situ during multi-organ retrieval, sometimes either for donor hemodynamic instability or for logistic reasons it may be necessary to perform ex-situ SL. Thanks to this technique, surgeons can expand the number of grafts suitable for pediatric liver transplant recipients. Hereby, we present results from our centre’s experience.

Methods: From January 2016 to December 2022, we performed 195 liver transplants: 56 whole-livers, 131 in-situ SL and 8 ex-situ SL. 1 out of 8 was a re-transplant.

Results: According to UNOS criteria, 6 (75 %) patients were Status 1 and 2 (25 %) were Status 3, thus confirming the high waitlist priority of these recipients. The recipients’ median age and body weight were 4 months and 6.5 Kg, respectively. Three grafts were procured from ex-situ SL during Dual Hypothermic Oxygenated Perfusion (D-HOPE). Two of them were from the same donor, one standard LLS and one ERL. Mean total ischemia time was 633 min. As for the practise at our centre, we applied a synthetic biodegradable glue on the resection site for further anastomosis. Mean Intensive Care Unit (ICU) stay was 29.5 days while mean length of stay was 123 days. One (12.5 %) patient underwent retransplantation because of Primary Non-Function (PNF). However, also the second transplant was an ex-situ SL but unfortunately the patient died because of Multi-Organ Failure (MOF). On the other hand, only one out of four adult recipients who got the extended right lobe after ex-situ SL transplantation died because of PNF.

Conclusions: Ex-situ SL is a safe procedure that may contribute to rescuing pediatric grafts even in hemodynamically instable donors. However, considering the high proportion of severely ill recipients, it is burdened with a relatively high risk of immediate post-transplant death and complication rate. D-HOPE should be systematically introduced in order to improve post liver transplant results.
Background: Diabetic kidney transplant recipients (KTR) have a high cardiovascular mortality. GLP-1 agonists have proven to reduce CV morbidity and mortality in diabetics, and its subcutaneous presentation has at least proven to be safely administered in KTR. The aim of this study is to determine the safety of oral semaglutide in the KTR population.

Methods: This is a retrospective observational study of a KTR population who were prescribed oral semaglutide. Medical data were taken from electronic health records. Proper maintenance of tacrolimus levels was measured by calculating the coefficient of variation (CV). Oral semaglutide was taken at least 2 hours before lunch or dinner, as preferred by the patient.

Results: 12 patients were analysed. Their mean age was 63, 58% of them were men. 10 had type 2 diabetes before transplantation (Tx), while 2 presented new-onset diabetes after transplant. 7 were on oral antidiabetics and became insulin dependent after Tx. 9 patients were started on oral semaglutide at discharge after Tx. 2 abandoned treatment, one due to nausea and the other due to lack of appetite. From the remaining 10, one patient’s dose was not increased from 3mg daily due to unknown reasons, 2 reached the 14mg dose with good tolerability, and 7 were maintained on 7mg according to their physician’s advice, though none reported drug intolerance. The mean BMI reduction with the 3mg dose was 1.6 kg/m² during the 1st month, 3.65 kg/m² with 7mg in the 2nd month, and was maintained at 2.6 kg/m² in the 3rd month. The 2 patients that took 14mg, had a BMI reduction of 3.5 kg/m² by the 6th month. Their insulin dose was reduced by 3 U at 3 months, and 12 U at 6 months after initiating treatment. We did not find an HbA1C reduction. Total cholesterol reduced by 2.3 mg/dL, LDL by 19.4 mg/dL, and triglycerides by 28.8 mg/dL, while HDL increased by 21 mg/dL, 3 months after oral semaglutide introduction. The mean tacrolimus CV was 27.8%. There were no rejections since the beginning of the medication.

Conclusions: We did not find an HbA1C reduction. Total cholesterol reduced by 2.3 mg/dL, LDL by 19.4 mg/dL, and triglycerides by 28.8 mg/dL, while HDL increased by 21 mg/dL, 3 months after oral semaglutide introduction. The mean tacrolimus CV was 27.8%. There were no rejections since the beginning of the medication.
**Background:** Normothermic machine perfusion (NMP) enables assessment of donor liver viability pre-transplantation. However, objective tests for measuring integrated liver function during NMP are lacking. We assessed the clinically validated indocyanine green (ICG) elimination test to objectively evaluate liver function during ex-vivo machine perfusion.

**Methods:** A combination of dual-hypothermic machine perfusion (DHOPE) and NMP was performed on extended criteria donor livers in an optimization phase (n=10) and clinical phase (n=22). In the optimization phase, the ICG test was performed during DHOPE and NMP (Figure), with optimization for use during NMP. In the clinical phase, the ICG clearance was correlated to clinical perfusion parameters and post-transplantation outcomes.

**Results:** During DHOPE no ICG perfusate elimination was seen. During NMP, significant ICG plasma elimination was demonstrated. The ICG plasma disappearance rate (PDR) was dependent on perfusion blood flow and plasma volume. After correcting for these factors, this corrected NMP-PDR was closely correlated to the hepatic extraction rate (R=0.923; P<0.001) and also to ATP content in liver biopsies (R=0.692; P=0.027). The NMP-PDR was also to ATP content in liver biopsies (R=0.692; P=0.027). The NMP-PDR was not correlated to liver damage (ALT, AST, LDH, and TUNEL). In the clinical phase, 22 liver grafts were evaluated for transplantation, being blind for outcome of ICG testing. Eleven livers were transplanted. The NMP-PDR was higher in the transplanted cohort than in the non-transplanted cohort (16.7 [12.9-23.3] vs 10.3 [8.5-12.1] %/L·Kg; P<0.0001). Both the overall hepatocellular and cholangiocellular acceptance criteria were correlated to the NMP-PDR.

**Conclusions:** We demonstrated that ICG elimination is not present during DHOPE, but the test is feasible during NMP. A NMP-PDR ≥13.3 %/L·Kg is indicative for absence of post-transplant hepatocellular or biliary failure in extended criteria donor livers. The ICG plasma elimination test has the potential to increase the donor liver utilization rate, while at the same time preventing extended criteria donor livers. The ICG plasma elimination test has the potential to increase the donor liver utilization rate, while at the same time preventing extended criteria donor livers.

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**Background:** Both T-cell depletion by alemtuzumab (ALEM) as well as IL-2 receptor blocking by basiliximab (IL2R) are used as induction for simultaneous pancreas-kidney (SPK) transplantsations. Multiple studies have reported higher rates of infections with ALEM versus IL2R. Due to the COVID-19 pandemic we adapted our standard induction from ALEM to IL2R for low immunological risk SPK transplantsations. We compared 180 days transplantation outcomes between ALEM and IL2R induction.

**Methods:** Patients with low immunological risk who underwent SPK between September 2015 and June 2022 at our center were analyzed. Induction was either ALEM (30 mg, until February 2020) or IL2R (2x 20 mg, from February 2020 onwards) and triple maintenance therapy (prednisolone, tacrolimus, mycophenolate mofetil). All pancreas allograft transplants were performed using enteric drainage. Standard prophylaxis included antibacterial, antifungal and antiviral therapies. Valganciclovir prophylaxis for cytomegalovirus (CMV) infection was risk stratified. All patients routinely went to the intensive care unit postoperatively.

**Results:** Thirty-five SPK transplant recipients were included (67% males, mean age 42±10 yr). Fifty-four percent of patients were transplanted pre-emptively, 37% received organs from a DBD donor and mean donor age was 31±11 yr. Twenty-one recipients received ALEM and 14 recipients IL2R induction therapy, see Table. Two pancreatic grafts were lost in the ALEM group and one kidney graft was lost in the IL2R group. No patient deaths occurred. No differences between ALEM and IL2R groups in kidney and pancreas graft function or rejection incidence were observed. More recipients in the ALEM group suffered from bacterial (81% vs. 50%, p=0.05) and viral infections (57% vs. 38%, p=0.21) compared to the IL2R group. The duration of initial hospitalization was longer for the ALEM group compared to the IL2R group (28 [20-39] vs. 12 [10-16] days, p<0.001). The percentage of recipients with hospital readmission was equal (57%) for both groups.

**Conclusions:** Our experience, although limited, with IL2R induction for SPK transplants with low immunological risk has shown encouraging results with equivalent short-term graft function and decreased post-operative infection rates and hospital admission duration compared to ALEM induction.
**P737** STABLE RECOVERY AFTER A MYOCARDITIS TREATED WITH CENTRAL ECMO AND IMPELLA: SHOULD WE DESIGN DIFFERENT ALLOCATION RULES FOR MYOCARDITIS?

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**Background:** Cardiogenic shock (CS) carries a high mortality risk; ECMO is becoming the standard treatment for CS as a bridge to recovery (BTR) or decision. The impella system (IS) is easy and effective for left ventricular (LV) support. It has been shown that IS can unload LV while ECMO provides good perfusion in overt cardiogenic shock due to biventricular failure.

**Methods:** In November 2012, a 20-year-old girl experiencing sudden dyspnea was referred to a local hospital for pericardial effusion. After a successful pericardiocentesis, LV contractility rapidly worsened despite increased inotropic support. A 2.5 L IS was implanted to maintain circulation but precipitated toward right ventricular failure; the patient was referred to our hospital with an indication for ECMO implantation and transplantation. Due to technical issues with the femoral vessels, ECMO was implanted via median sternotomy to ensure optimal perfusion.

**Results:** The IS was maintained to ensure myocardial unloading and low chances of myocardial recovery. A fine-needle biopsy of the LV showed minimal necrosis with a high probability of myocarditis and encouraged the feasibility of BTR. ECMO implantation was complicated by severe coagulopathy that required massive administration of blood products and re-exploration by tamponade. SNP dosage decreased rapidly during the first postoperative week, a suboptimal donor was discarded, and ECMO was removed on day 6. On day 7, IS was removed percutaneously.

**Conclusions:** This report further supports the synergistic effect of IS and ECMO when dealing with potentially reversible diseases. Imaging and functional tests performed after ten years showed complete recovery. Echocardiographic diagnosis through biopsy should be performed whenever possible to avoid wasting organs for patients whose recovery may be full and whose postoperative outcome is suboptimal.

**P738** KIDNEYS FROM UDCD WITH NRP SUPPORT VS KIDNEYS FROM BRAIN DEAD DONORS: A COMPARATIVE ANALYSIS OF TRANSPLANTATION OUTCOMES

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**Background:** Normothermic regional perfusion (nRP) is a preservation strategy that re-establishes the flow of oxygenated blood following cardiac arrest and can reverse warm ischemic injury in donation after uncontrolled circulatory death (DCD) especially.

**Methods:** In this study, we compared the transplantation outcomes of kidneys from uDCD with nRP support, with the results attained using kidneys from brain-dead donors. The analysis entailed a single-Centre, prospective cohort of 294 consecutive kidney transplantations performed from January 2016 to December 2020. 117 transplants were from brain-dead donors defined as standard criteria (SD) (39.8%), 93 from expanded criteria (ECD) (31.6%) and 84 from cardiocir (59.2%). After adjusted analysis, uDCD is associated with a 2.84 risk higher for PNF and 6.44 for DGF. Inde-

**Results:** For uDCD, warm ischemic time (WIT) pre-ECMO correlated with PNF along the years (2017, PNF 0% median WIT 60min (45-100); 2018 PNF 23.48%, median WIT 100min (86.3-62.5); 2019 PNF 15.4%, median WIT 90min (86.3-62.5); 2020 PNF 0%, median WIT 45min (45-45); 2020 PNF 0%, median WIT 45min (45-45); 2020 PNF 0%, median WIT 45min (45-45); 2020 PNF 0%, median WIT 45min (45-45). Since the 18 months, eGFR is higher for uDCD than ECD (difference mean 9,623ml/min/1.73m2; p=0.002). At 5 years the mean difference of uDCD-eGFR is higher at 26.87ml/min/1.73m2 than ECD (p<0.001). In recipients from SCD and uDCD, eGFR increased in 1.31ml/min/1.72m2 (p=0.039) and 2.62 1.31ml/min/1.72m2 (p<0.007) per annum respectively, independently of age and sex. Although, the eGFR of those from ECD declined to -2.21ml/min/1.73m2 per annum (p=0.026).

**Conclusions:** At 5 years, uDCD kidney transplantation outcomes are similar to brain-dead donors in all major transplantation criteria supporting the use of uDCD kidneys as a successful mean to address organ scarcity.
**P739**  A RETROSPECTIVE OBSERVATIONAL STUDY ON THE DECLINING LIVER TRANSPLANT ASSESSMENT RATES AT EDINBURGH TRANSPLANT CENTRE

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**Background:** Despite the increasing prevalence of liver disease, there has been a significant reduction in the number of liver transplant assessments as well as a corresponding decrease in liver transplants at Edinburgh Transplant Centre (ETC) since 2018. Given that this predates the COVID-19 pandemic, we sought to explore the other potential reasons for this decline through a retrospective analysis of the ETC database.

**Methods:** Data were collected for all adult patients assessed for primary elective liver-only transplantation at ETC between 2017-2021. Patients assessed for multi-organ transplants, for Variant or Super-Urgent indications, <18 years old and repeated assessments were excluded. Variables including patient demographics, transplant indication, referring healthboard and Scottish Index of Multiple Deprivation (SIMD) were examined by year. Kruskal-Wallis and Chi-square tests were used to assess for significant differences in variables over time.

**Results:** A total of 733 patients fit the study criteria. There was no statistically significant change in sex, age, bilirubin, creatinine, INR, sodium, UKELD, height, BMI, indication, or SIMD over the study time period (p>0.05). Patient demographics, transplant indication, referring healthboard and SIMD over time.

**Conclusions:** While there has been a significant reduction in the number of liver transplant assessments at ETC since 2018, this appears to be driven by other factors rather than a decrease in the prevalence of liver disease. Further research is needed to understand the underlying causes and potential implications on resource allocation and transplantation.

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**P740**  LIVER STIFFNESS MEASUREMENT IS ASSOCIATED WITH THE DEVELOPMENT OF PERSISTENT ASCITES AND POSTOPERATIVE COMPLICATIONS AT 90 DAYS AFTER LIVER TRANSPLANTATION

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**Background:** Liver transplantation (LT) is associated with high morbidity and mortality. Persistent ascites (PA) develops in 5-7% of the cases and its management is still very challenging. The diagnostic and prognostic role of transient elastography (TE) in cirrhotic patients has already been established, however, its impact in patients undergoing LT remain unclear.

**Methods:** Prospective observational study in patients undergoing liver stiffness measurement (SSM) at 30 days after LT between August 2020 and December 2022 at Bologna Transplantation Unit. IRCSS. Spleen stiffness measurement (SSM) was also collected when available. Postoperative complications were categorized according to the Clavien-Dindo Classification (CDC) and Comprehensive Complications Index (CCI).

**Results:** A total of 109 patients were included in this study. Median LSM and SSM were 8.8 kPa (IQR 6.5 – 13.1) and 30.0 kPa (22.1 – 44.7) respectively. The development of persistent ascites was observed in 16 patients (14.7%). Medical therapy was the main treatment for PA, while splenic artery embolization was performed in two cases. Thirteen patients with PA underwent hepatic vein pressure gradient (HVPG) measurement (median 13 mmHg, IQR 9 – 15). LSM and SSM were both associated with the development of PA (OR 1.159, 95% CI 1.069 – 1.255, p=0.000) and (OR 1.018, 95% CI 1.011 – 1.086, p=0.010). LSM also correlated strongly with HVPG (Pearson coefficient 0.632, p=0.015). Severe complications (grade 3 or higher) occurred in 37 patients (34%). LSM was significantly associated with CCI at 90 days (Pearson coefficient 0.195, p=0.046).

**Conclusions:** LSM is associated with the development of medical and surgical complications at 90 days after LT. Transient elastography can play an important role in the diagnosis and management of persistent ascites after transplantation.

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Table 1 Predictive role of LSM for complications at 90 days after LT

<table>
<thead>
<tr>
<th>Complication</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Allograft Dysfunction</td>
<td>1.02 (0.99 – 1.05)</td>
<td>0.2</td>
</tr>
<tr>
<td>Persistent ascites</td>
<td>1.16 (1.07 – 1.26)</td>
<td>0.000</td>
</tr>
<tr>
<td>Biliary Complication</td>
<td>1.03 (0.99 – 1.07)</td>
<td>0.1</td>
</tr>
<tr>
<td>Vascular Complications</td>
<td>1.05 (1.01 – 1.08)</td>
<td>0.008</td>
</tr>
<tr>
<td>Severe complication</td>
<td>1.02 (0.99 – 1.05)</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Background: Liver transplantation is the established standard procedure for the treatment of chronic and acute end-stage liver disease. However, limitations remain, such as the limited number of donor organs and the high incidence of early allograft dysfunction (EAD) due to the compensatory increase in the number of expanded criteria donors (ECD). The aim of this work was to investigate the short- and long-term outcome in liver transplant recipients with and without EAD.

Methods: A retrospective analysis of adult patients who underwent deceased donor liver transplantation between January 2007 and December 2017 was performed. EAD was defined by one or more of the following criteria: (i) bilirubin ≥10 mg/dL on postoperative day 7; (ii) international normalized ratio ≥1.6 on postoperative day 7, and (iii) alanine aminotransferase or aspartate aminotransferase >2000 IU/L within the first seven days after transplantation.

Results: A total of 631 patients were studied and 53.6% of recipients developed EAD. Recipient criteria such as age (49.19 vs. 49.64 years; p=0.652), dialysis requirement (18.9% vs. 16.6%; p=0.451), invasive ventilation before transplantation (5.9% vs. 5.3%; p=0.740) as well as cold ischemia time (595.53 vs. 578.44 minutes; p=0.081) showed no significant differences between the EAD and non-EAD groups. However, donor ventilation time (5.2 vs. 4.5 days; p=0.013), graft weight (1834.39 vs. 1589.73g; p<0.001), donor BMI (27.38 vs. 25.83; p=0.001) and number of donors with ECD criteria (59.2% vs. 49.5%, p=0.018) differed significantly between the two groups. Compared to the non-EAD group, patients with EAD had a higher likelihood of needing dialysis post-transplant (38.2% vs. 23.0%; p<0.001) or re-transplant (16.0% vs. 4.6%; p<0.001). They also had higher mortality during ICU stay (16.8% vs. 5.7%; p<0.001) and significantly lower graft survival (98.0 vs. 116.0 months; p=0.005), but without a significant difference in patient survival (111.0 vs. 120.0 months; p=0.177).

Conclusions: EAD and non-EAD recipients differ primarily in donor rather than recipient criteria. EAD has a significant impact on graft survival and postoperative mortality on the ICU.

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Conclusions: EAD and non-EAD recipients differ primarily in donor rather than recipient criteria. EAD has a significant impact on graft survival and postoperative mortality on the ICU.
Background: Urolithiasis is an infrequent complication in kidney transplanted patients, although its diagnosis and management is challenging and its consequences potentially serious. Our aim is to analyze the management of renal transplant recipients with de novo urinary lithiasis in a series of more than 1500 transplanted patients.

Methods: A total of 1543 transplant patients were included in a and single-center study from 2013 to present. The inclusion criteria were patients who developed de novo allograft lithiasis. Demographic data, graft survival, diagnoses, treatment, stone free rate (SFR) and complications were described.

Results: Nineteen patients developed urinary stones in the study period. The prevalence observed in our sample was 1.22 cases per 100 transplanted patients. The median time to the appearance of lithiasis was 85 months (IQR = 222 months). In nine patients (47.36%) were multiple stones and the most frequent localization was the renal pelvis (12 patients (62%). The median of the largest diameter of lithiasis was 10mm (IQR = 11mm). In nine cases (47.36%) were obstructive stones (being the main indication for surgical treatment). Three patients (15.7%) were treated by URS, three patients (15.7%) by standard percutaneous surgery, one patient (5.2%) by laparoscopy surgery and one patient a nephrectomy was performed due to graft failure. One patient (5.2%) had a spontaneous expulsion. In the remaining 10 cases medical treatment or observation was performed, observing the stability of the lithiasis or its resolu-

Conclusions: The prevalence of lithiasis in the kidney graft is low but can be potentially severe. Its diagnosis, due to the graft denervation, is usually incidental and delayed. Surgery in cases of obstruction is the main indication, but it requires a multimodal treatment tailored according to stone and graft characteristics. In non-obstructive lithiasis cases, active surveillance and medical treatment is a good option.
Conclusions: Sputnik V vaccination is well tolerated in most heart transplant recipients. Vaccinated patients have reduced the incidence and severity of COVID-19, as well as the incidence of post-COVID complications. There was no allograft complications associated with vaccination against COVID-19.

Background: In February of 2020, a novel virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cause the coronavirus disease 2019 (COVID-19) pandemic. The physician ignored the disease course and different treatments have been proven. Kidney transplantation recipients (KTRs) had increased risk of development serious complications or deaths, and the withdrawn or decrease immunosuppression treatments was widespread. Nowadays, we find the consequences of these decisions.

Objectives: We aim to assess long term effects of decrease or withdrawing immunosuppression treatments in kidney function, develop a rejection or novo donor specific antibodies (nDSA), allograft’s survival and patient’s survival.

Methods: Retrospective observational study that included all KTRs who were infected by SARS-CoV-2 during first and second pandemic waves from January 2020 to December 2020. KTR were followed since the COVID-19 to February 2023 or death or graft lost. We included demographic variables, renal function measure as estimate glomerular filtration rate (eGFR), renal biopsy performed after COVID-19, nDSA, renal and patient survival and their causes of lost.

Results: Our study included 73 KTR. The table shown the demographics and the outcomes of the patients. After two years of COVID-19 pandemia, the global graft survival was 62,9%, graft survival death censored 82,6% and patient survival 82,6%. The majority of patient death in the first year, but the graft lost occurred after two year of SARS-CoV-2 infection.

Conclusion: COVID-19 had and has a high impact in KTR both in patient’s survival in the first year after infection and nowadays in the renal function and graft survival. We need more time to understand the grave complication derivate of the pandemia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male), n (%)</td>
<td>44 (60,3%)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>11 (15,1%)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>14 (19,2%)</td>
</tr>
<tr>
<td>Intestinal nephropathy</td>
<td>9 (12,3%)</td>
</tr>
<tr>
<td>Polycystic renal disease</td>
<td>13 (17,8%)</td>
</tr>
<tr>
<td>Others</td>
<td>17 (23,3%)</td>
</tr>
<tr>
<td>Baseline immunological risk, n (%)</td>
<td>58 (79,5%)</td>
</tr>
<tr>
<td>Induction therapy, n (%)</td>
<td>15 (20,5%)</td>
</tr>
<tr>
<td>Antithymocyte globulin</td>
<td>47 (64,4%)</td>
</tr>
<tr>
<td>Immunosuppressive regimen COVID diagnosis, n (%)</td>
<td>15 (20,5%)</td>
</tr>
<tr>
<td>Discontinue Immunosuppressive regimens at COVID-19 diagnosis, n (%)</td>
<td>STOP tacrolimus 5 (6,8%)  STOP mycophenolate 7 (9,6%)  STOP both 40 (54,8%)</td>
</tr>
</tbody>
</table>

*Compared with preCOVID levels
ROLE OF CORONARY CALCIUM SCORE IN RULING OUT CORONARY ARTERY DISEASE AND IN WAITLIST PATIENTS' SELECTION FOR LIVER TRANSPLANT CANDIDATES

Luigina Cocchiarelli1, Chiara Marcelli2, Antonio Russo1, Enrico Prosperi2, Alessio Aloisi3, Stefania Manno3, Mario Sabatino1, Paola Prestinenzi4, Laura Borgese1, Francesca Aversano1, Federica Mirici1, Maria Cristina Morelli1, Matteo Ravioli1, Matteo Cescon1, Luciano Pervunina

1IRCt Azienda Ospedaliero-Universitaria di Bologna, Heart Failure and Transplant Unit, Bologna, Italy. 2IRCt Azienda Ospedaliero-Universitaria di Bologna, General Surgery and Transplantation Unit, Bologna, Italy. 3IRCt Azienda Ospedaliero-Universitaria di Bologna, Internal Medicine Unit for the treatment of Severe Organ Failure, Bologna, Italy.

Background: Cardiovascular (CV) events are a major cause of morbidity and mortality after liver transplantation (LT). Consensus is lacking about the optimal CV screening in LT candidates. In addition, incidence and predictors of CV events in the early postoperative phase are unclear. Coronary artery calcium (CAC) score is a widely available and reproducible test based on chest CT scan without contrast media, to assess risk of coronary artery disease (CAD) and CV events in general population. Herein we evaluate if in LT candidates CAC may help to rule out significant CAD and early CV events reducing the need for invasive or more expensive tests.

Methods: We included all LT candidates who received CV risk assessment in our center between 2019 and 2021. CAC score was required in case of at least 1 CV risk factor or pathological ECG/echocardogram. Coronary CT was performed when technically feasible and in patients with high CV risk, per choice of consultant cardiologist. Study endpoint was occurrence of in-hospital post-LT CV events (acute myocardial infarction, stroke, acute heart failure, atrial fibrillation, CV death).

Results: 314 pts received CV risk evaluation, and 184 (59%) were listed. CV risk factors were highly prevalent, with 65% of patients bearing at least 2 CV risk factors. CAC score was assessed in 190 patients. CT coronary angiography was performed in 89 (28,3%) patients, with evidence of critical stenosis in 18 (20%) of whom 17 had CAC score >35 (negative predictive value of 97%; P<0.01). CV risk profile including CAC score was significantly lower in listed patients vs those not listed (Table). Of note only 7 patients with coronary lesions at CT scan were listed, two of them after coronary stenting. 182 patients underwent LT of whom 12 (7%) died, 1 for CV cause. Additional 16 patients experienced non-fatal CV events, only one of them had coronary lesions. Low CAC score showed higher than CV events than those without (43 vs 7). Conclusion: CAC score showed very high negative predictive value for significant CAD and may help to reduce the need for additional testing in LT candidates. CAC score guided screening allowed to list patients with lower CV risk profile resulting in a very low occurrence of posttransplant CV events.

A SINGLE CENTRE FIRST EXPERIENCE OF PAEDIATRIC HEART TRANSPLANTATION FROM ADULT DONORS

Maria Simonenko1, Petr Fedotov4, Tatiana Veshchinska2, Maria Sitnikova1, German Nikolaev1, Mikhail Gordeev1, Mikhail Karpenko1, Tatiana Pervunina1

1Aamazov National Medical Research Centre, Heart transplantation Clinical Department, CPET Research Department, St. Petersburg, Russian Federation. 2Aamazov National Medical Research Centre, Heart failure Research Department, St. Petersburg, Russian Federation. 3Aamazov National Medical Research Centre, Thoracic surgery research department, St. Petersburg, Russian Federation. 4Aamazov National Medical Research Centre, Cardiothoracic surgery research department, St. Petersburg, Russian Federation. 5Aamazov National Medical Research Centre, Scientific and Clinical Council, First Deputy General Director, St. Petersburg, Russian Federation. 6Aamazov National Medical Research Centre, Director of the Institute of Perinatology and Pediatrics, St. Petersburg, Russian Federation.

Purpose: To estimate early and long-term outcomes in recipients under 18 year-old who have been heart transplanted from adult donors.

Methods: From April 2011 to January 2023 we performed 12 heart transplantations (HTx) in paediatric recipients (7 – female) from adult donors (37; 27; 41 years old). The median of age was 15 (range 10-17) year-old, LVEF prior HTx - 22% (10-65 %). Causes of heart failure (HF) were dilated cardiomyopathy (n=7), non-compacted myocardium (n=1), arrhythmogenic ventricular dysplasia (n=2) restrictive cardiomyopathy (n=1) and Ebstein’s anomaly (n=1). They spent in HT waiting list 155 (12-884) days. Two patients were bridged to transplant by ECMO followed with Berlin Heart EXCOR implantation (n=1; days on support – 250) and LVAD implantation (n=1; days on support – 355). Due to coronary angiography (CAG) results patient underwent HTx and CABG simultaneously. All recipients managed with triple-drug therapy (steroids, calcineurin inhibitors, mycophenolate mofetil), induction (thymoglobulin - n=4, basiliximab - n=8). We analyzed retrospectively outcomes of paediatric HTxs.

Results: Eleven recipients are alive, 7 of them (currently from 18 to 26 year-old) already became adults and were transitioned to the adultcare transplant follow-up. In a year 1 died from early-term developed neurological complications without being discharged after HTx. Patients spent in ICU 10 (range 4-18) days: 1 of them spent 18 days due to posterior reversible encephalopathy syndrome (PRES), tacrolimus was switched to cyclosporine. They required inotrope support during 4 (3-8) days. In 1 year after HTx TTE results got to normal values, the same as VO2max value of life estimated by SF-36 significantly improved. During 1 year episodes of rejection (R2, AMR2) were diagnosed in 16% cases: 1 case of AMR3 in 9 months due to non-compliance and discontinuation of immunosuppression for 3 weeks. In long-term follow-up there were no significant transplant complications and co-morbidities.

Conclusions: Paediatric HTxs is an successful treatment of end-stage HF and there are successful. Adult donors are acceptable to transplant children if they are matched. All patients recovered and went back to normal life. Physical capacity improved in all recipients.
**Background:** to estimate the frequency and outcomes of COVID-19 in patients after heart transplantation (HTx).

**Methods:** Between January 2010 and January 2023 it was performed 207 HTx, 18 of them were infected with COVID-19 and recovered from it prior to surgery. All recipients were included in the dispensary follow-up group that is leaded by one transplant cardiologist. We analyzed retrospectively results of 165 patients excluding those who died before the COVID-19 era.

**Results:** From February 2020 to January 2023 68% (n=112; 46±13 year-old, n=73- male) of heart transplant patients were diagnosed with COVID-19: 37 – were re-infected in more than 1 month after the first recovery, 10 – were infected 3 times. Pneumonia was developed in 69% (n=110) of cases; swabs were positive in 60% cases. From the 1st day of the onset of clinical symptoms, MMF 1 mmol/L was temporarily discontinued (< 14 days). Outpatient treatment included the appointment of oselatamiv, bromhexine, levofloxacil, antiocoagulants and vitamins C and D. In 52 cases steroids were prescribed or the initial dose was increased. In 32 cases patients were admitted to the hospital and 13 of them had oxygen inhalation through nasal cannula; none required invasive ventilation. In 2 weeks after the onset of fever 3 recipients with pneumonia (COVID-19 plus bacterial) developed heart transplant dysfunction that was successfully treated by pulse steroid therapy and resumption of MMF in high doses. Since the beginning of the pandemic the mortality rate from COVID-19 is 3.7%. There were 3 patients who reported about their condition days after the onset of symptoms died from gastrointestinal bleed, thrombosis and acute kidney injury, respectively. In 6 months after the recovery from COVID-19 Epstein-Barr virus antibody tests were positive in 63% recipients and Cytomegalovirus – in 10%.

**Conclusions:** The remote consultations of heart recipients lead to the on-time diagnosis of COVID-19 and treatment initiation from the 1st day of the onset of clinical symptoms what allowed to decrease the number of hospital admissions and to increase the survival. Temporal reduction of immunosuppression is a key to manage COVID-19.

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**Background:** Pre-exposure prophylaxis with Tixagevimab/Cilgavimab (TIXA/CILGA) is a promising new drug for the prophylaxis and treatment of COVID-19 disease in immunocompromised patients. The aim of our study was to evaluate the efficacy and safety profile of TIXA/CILGA in a Slovenian national cohort of kidney transplant recipients (KTRs) as pre-exposure prophylaxis in the Omicron era.

**Methods:** All KTRs who received TIXA/CILGA (150 mg TIXA and 150 mg CILGA - prophylaxis dose) from May 1 to October 31, 2022, were included in the historical cohort study. Demographic, clinical, laboratory, and therapeutic data were collected from electronic and paper medical records.

**Results:** 106 patients with a transplanted kidney received preexposure prophylaxis with TIXA/CILGA; 72 men, 34 women, mean age 60 years (range 20 to 82 years), mean time since transplantation 9 years (range 1 month to 25 years). 45% were not infected with Sars-CoV-2 before treatment with TIXA/CILGA. 45% had recovered once from COVID-19, and 8% had been infected twice. Only one patient had COVID-19 twice before treatment with TIXA/CILGA. Almost all patients had been vaccinated against COVID-19; only one patient had not been vaccinated due to severe adverse reactions to influenza vaccination in the past. Six patients (5.7%) acquired Sars-CoV-2 infection after receiving TIXA/CILGA. The incidence of Sars-CoV-2 infection was only slightly lower than in patients who did not receive TIXA/CILGA (7.0%). All patients who received TIXA/CILGA had a mild disease course, whereas 20% of patients who did not receive TIXA/CILGA required hospitalization and two died. Adverse effects most likely related to TIXA/CILGA occurred in 12% of patients, one of whom experienced deep vein thrombosis. None of the patients suffered acute myocardial infarction or cerebrovascular insult.

**Conclusions:** In the Slovenian KTRs population the benefits of using TIXA/CILGA appear to outweigh the potential risk of adverse events and provide additional protection against severe COVID-19 progression.
Background: Live kidney donation significantly reduces waiting times and offers recipients significant long-term benefits. Multiple minimally invasive nephrectomy techniques are now available. We aimed to define and compare the benefits and harms between these techniques for live kidney donors.

Methods: A systematic review and meta-analysis, using Cochrane methodology, of randomised control trials (RCTs) comparing outcomes between open donor nephrectomy (ODN), laparoscopic donor nephrectomy (LDN), and robotic donor nephrectomy (HALDN) for live kidney donation. Mixed-effects meta-regression was also conducted to investigate trends of change in outcomes over time.

Results: Twelve RCTs were included, randomising 1230 live kidney donors. Seven RCTs randomised 815 donors between LDN and ODN. LDN was associated with a reduced length of stay, shorter procedure duration and longer warm ischaemia time (Mean difference in ODN vs LDN 2.13 min, 95% CI 1.50 to 2.76 min). One RCT randomised 45 donors between LDN and RDN and found RDN to have a longer warm ischaemia time. Conversion rates to ODN were 6/135 (4.42%) in LDN, 1/135 (0.74%) in HALDN, and 0/15 in RDN. In meta-regression analysis between LDN and ODN, procedure duration changed in favour of LDN significantly over time (yearly reduction = 0.107, 95% CI 0.022 to 0.192; P = 0.014).

Conclusions: LDN is associated with less pain compared to open surgery and has comparable pain to HALDN and RDN. HALDN is comparable to LDN and has comparable pain to HALDN and RDN. Both HALDN and LDN are associated with reduced analgesia use, shorter hospital stays, longer procedure duration and longer warm ischaemia time compared to ODN.

Table 1. Summary of findings comparing open vs laparoscopic vs robotic live donor nephrectomy

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Comparison</th>
<th>Intervention favoured</th>
<th>No. of participants (RCTs)</th>
<th>Effect size (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaesthesia requirements</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>596 (6)</td>
<td>0.45 (0.10, 0.80)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (3)</td>
<td>-0.40 (0.55)</td>
<td>0.76</td>
</tr>
<tr>
<td>Duration of procedure (min)</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>815 (7)</td>
<td>4.85 (10.86, 66.25)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (6)</td>
<td>10.00 (-24.13, 44.13)</td>
<td>0.57</td>
</tr>
<tr>
<td>Warm ischaemia time (min)</td>
<td>ODN vs HALDN</td>
<td>LDN</td>
<td>815 (2)</td>
<td>2.92 (2.09, 4.74)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>270 (2)</td>
<td>2.05 (0.72, 3.37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>775 (6)</td>
<td>0.88 (0.27, 1.49)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (6)</td>
<td>0.18 (0.05, 0.42)</td>
<td>0.13</td>
</tr>
<tr>
<td>Blood loss</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>775 (6)</td>
<td>0.06 (-0.19, 0.33)</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (6)</td>
<td>-0.16 (-0.64, 0.33)</td>
<td>0.50</td>
</tr>
<tr>
<td>Perioperative complications</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>775 (6)</td>
<td>1.06 (0.59, 1.90)</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (6)</td>
<td>1.32 (0.79, 2.22)</td>
<td>0.29</td>
</tr>
<tr>
<td>Reoperations</td>
<td>ODN vs LDN</td>
<td>LDN</td>
<td>596 (6)</td>
<td>0.57 (0.09, 3.64)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>HALDN vs LDN</td>
<td>LDN</td>
<td>270 (6)</td>
<td>2.61 (0.62, 12.81)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

CI - confidence interval; HALDN - hand-assisted laparoscopic donor nephrectomy; LDN - laparoscopic donor nephrectomy; ODN - open donor nephrectomy; RCT - randomised control trial
Background: Post-transplant diabetes mellitus (PTDM) is a serious complication following solid organ transplantation, which significantly increases cardiovascular events and mortality. PTDM has also been associated with decreased graft survival. In contrast to PTDM the evidence linking impaired glucose tolerance (IGT) to these complications is scarce. The aim of this study was to evaluate the incidence of IGT and PTDM and the risk of acute rejection and graft loss in pediatric kidney transplant recipients.

Methods: The study cohort included patients aged <18 years who underwent a kidney transplant in a tertiary transplant center, from 2005 to 2020. Primary outcome was acute rejection and secondary outcome included graft loss and mortality. Survival analysis using Kaplan Meier curve was used to compare outcomes by PTDM/IGT group. Cumulative incidence of acute rejection and graft loss was estimated considering death as a competing risk. The proportional subdistribution hazard model of Fine and Gray was used to analyze the effect of PTDM/IGT status on the event. Follow up was defined as the period from transplantation until the occurrence of the outcome or otherwise censored at death, lost to follow up or end of the study.

Results: A total of 73 pediatric kidney transplant recipients were included. Average age was 13.4 years. IGT was presented in 12 (16.4%) patients and 9 (12.3%) PTDM. Acute graft rejection occurred in 5 (55.6%) of PTDM, 7 (58.3%) of IGT and 11 (21.2%) of non-PTDM/IGT patients. Comparing to non-PTDM/IGT patients, kidney graft recipients with PTDM and IGT had a higher risk of acute rejection (PTDM: HR = 1.12 95% CI 1.12-8.44, p-value 0.029, and IGT: HR = 1.35, 95% CI 1.54-9.57 p=0.004). Regarding graft loss, a total of 3 (33.3%) patients in PTDM group, 6 patients (50%) in IGT group and 7 patients (13.5%) in non-PTDM/IGT group had graft loss during the follow up. PTDM and IGT were found to have a higher risk of graft loss when compared with non-PTDM/IGT patients (IGT: HR 1.69 95% CI 1.47-19.9, p=0.011, and PTDM: HR 4.99, 95% CI 1.15-21.7, p=0.032).

Conclusions: PTDM and IGT patients had a higher risk of acute rejection and graft loss in pediatric kidney transplant recipients. Which justify a close follow up with these patients also in pediatric population.

Figure 1: Kaplan Meier curve stratified by IGT/PTDM status
THE MOLECULAR MICROSCOPE (MMDx) IN THE PROGNOSTIC STRATIFICATION OF HEART TRANSPLANTED PATIENTS: JUST A RESEARCH TOOL OR A USEFUL GUY?

Marco Masetti1, Gianmarco Spinozzi1, Laura Borgese1, Laura Giovannini1, Letizia Marcantoni1, Barbara Corti1, Chiara Baldovini1, Mario Sabatino1, Alessio Aloisio1, Sofia Martin-Suarez1, Davide Pacini1, Philip F. Halloran1, Luciano Potena1
1Heart Failure and Transplant Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 2School of medicine and surgery, University of Bologna, Bologna, Italy, 3Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 4Cardiac Surgery Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 5Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 6Cardiac Surgery Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 7Cardiac Surgery Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 8DMEC, University of Bologna, Bologna, Italy, 9Department of Medicine, Division of Nephrology and Transplant Immunology, University of Alberta, Edmonton, Alberta, Canada, 10DMEC, University of Alberta, Edmonton, Alberta, Canada, 11Department of Medicine, Division of Nephrology and Transplant Immunology, University of Alberta, Edmonton, Alberta, Canada, 12Department of Medicine, Division of Nephrology and Transplant Immunology, University of Alberta, Edmonton, Alberta, Canada

Background: The microarray analysis of mRNA transcripts on endomyocardial biopsies (molecular microscope, MMDx), has been recently studied in heart transplantation (HT) as a potential tool to assess the probability of rejection. However, its use is actually limited to the research field and its prognostic ability has never been investigated in the clinical practice. We sought to study the prognostic role of MMDx when integrated with the information derived from histology (H), donor-specific antibodies (DSA), right heart catheterization (RHC) and echocardiography in heart transplanted patients.

Methods: In our monocentric retrospective study we included all patients undergoing to MMDx analysis between 2016-19. We report the prevalence of cellular (ACR) and antibody mediated rejection (AMR) according to H and MMDx and their relationship with hemodynamic and echocardiographic data. The primary endpoint was the freedom from major cardiovascular events (MACE) at 7 years after the first MMDx analysis.

Results: 243 biopsies with MMDx analysis were performed in 110 patients (3.7±3.1 years from HT). 40.3% and 29.6% were ACR+ and AMR+ according to H, 5.5% e 14% for MMDx respectively; 25% of histologically detected ACR were labeled as AMR by MMDx. LVEF was not different according to the histological diagnosis, whereas it was lower in patients with a pathologic MMDx (MMDx+); diastolic dysfunction was more frequent in patients with AMR at H and in those with MMDx+ (p<0.01). Patients with AMR at either H or MMDx had an higher pulmonary capillary wedge pressure, those with ACR at MMDx had a lower cardiac index (p<0.01 all). At univariate analysis, the predictors of MACE were: H+, MMDx+, an impaired RHC, DSA (OR: 6.7, 4.0, 5.3, 3.3 respectively, p<0.01 all). Patients with H+/MMDx- or H-/MMDx+ were in an intermediate risk of 12.6 vs 11.4%, p=NS). Biopsies revealed rejection (TCMR or ABMR) in 28% of 12.6 vs 11.4%, p=NS). Biopsies revealed rejection (TCMR or ABMR) in 28% overall, 32 in the Predigraft and 29 in the SOC groups respectively (incidence 4.4±5.7 yrs. Mean recipient and donor age were 52±14 and 52±15 yrs respectively. Other baseline characteristics were similar between groups. The mean follow-up time after randomization was 9.6±3.6 months. In the Predigraft group, 38 iBox alerts were recorded among which 232 (58%) were deemed clinically relevant by physicians and 133 (33%) were followed by a change in clinical management and/or therapeutics. A total of 61 biopies were performed overall, 32 in the Predigraft and 29 in the SOC groups respectively (incidence of 12.6 vs 11.4%, p=NS). The primary endpoint was the number of allograft biopsies amenable to therapeutic changes. This study presents the interim period results at 9 months after randomization (NCT05112315)

Results: A total of 507 subjects were recruited, among which 252 in the Predigraft group and 255 in the SOC group. The mean time from transplant to induction was 4.4±5.7 yrs. Mean recipient and donor age were 52±14 and 52±15 yrs respectively. Other baseline characteristics were similar between groups. The mean follow-up time after randomization was 9.6±3.6 months. In the Predigraft group, 38 iBox alerts were recorded among which 232 (58%) were deemed clinically relevant by physicians and 133 (33%) were followed by a change in clinical management and/or therapeutics. A total of 61 biopies were performed overall, 32 in the Predigraft and 29 in the SOC groups respectively (incidence of 12.6 vs 11.4%, p=NS). The primary endpoint was the number of allograft biopsies amenable to therapeutic changes. This study presents the interim period results at 9 months after randomization (NCT05112315)

Conclusions: Our study shows a good correlation between MMDx and hemodynamics and a prognostic role of this tool, thus suggesting its integrated use with histology hemodynamic in the every day clinical practice.

CLINICAL IMPACT OF THE PREDIGRAFT/IBOX SYSTEM AS A CLINICAL DECISION SUPPORT FOR KIDNEY TRANSPLANT PATIENTS MANAGEMENT: RESULTS OF A PROSPECTIVE RCT

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1Paris Institute For Transplantation and Organ Regeneration (PITOR), Paris, France, 2Predict 4 Health, Paris, France, 3University Medical Center Hamburg, Hamburg, Germany, 4Transplant Department Toulouse Rangueil, Toulouse, France, 5University Medical Center Düsseldorf, Düsseldorf, Germany, 6King’s College Hospital London, London, United Kingdom, 7Transplant Center, Oxford, United Kingdom, 8Guy’s and Saint Thomas’ Hospital London, London, United Kingdom, 9Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom, 10Hospital Del Mar, Barcelona, Spain, 11Fundacion Puigvert Barcelona, Barcelona, Spain, 12Hospital La Fe, Valencia, Spain, 13Sourasky Medical Center Ichilov, Tel Aviv, Israel, 14University Medical Center Innsbruck, Innsbruck, Austria, 15Leeds Teaching Hospital NHS trust, Leeds, United Kingdom

Background: Computer based decision support systems are emerging tools for decision-making optimization, but their clinical benefit for patient care has not been demonstrated.

Methods: We designed a European multicenter RCT involving 16 centers from Europe (France, UK, Spain, Germany, Austria and Israel). Kidney recipients were randomly (1:1) assigned from 3 months up to 10 years after transplant to receive either SOC or management guided by a companion software Predigraft (CE mark FRMF 601) that provides automatic iBox patient risk assessment and prognostic trajectories. The primary endpoint was the number of telemonitoring biopsies (molecular microscope, MMDx), has been recently studied in heart transplantation (HT) as a potential tool to assess the probability of rejection.
LONGITUDINAL DD-CFDNA MONITORING REDUCES TIME TO ABMR DIAGNOSIS IN DNSSA POSITIVE KIDNEY TRANSPLANT RECIPIENTS: A DIAGNOSTIC RANDOMIZED CLINICAL TRIAL

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1Charité - Universitätsmedizin Berlin, Department of Nephrology and Medical Intensive Care, Berlin, Germany, 2University Medical Center Göttingen, Department of Clinical Pharmacology, Göttingen, Germany, 3Charité Biomedical GmbH, Göttingen, Germany

Background: Donor-derived cell-free DNA (dd-cfDNA) is a valid biomarker for the detection of antibody-mediated rejection (ABMR) in kidney transplant recipients (KTR) with dnDSA. However, the clinical benefits of dd-cfDNA monitoring still need to be established.

Methods: In this diagnostic, single-center, open label, randomized clinical trial, we randomly assigned 40 DSA+ KTR with eGFR > 20 mL/min/1.73m², but without biopsy after DSA occurrence into dd-cfDNA-guided biopsy (intervention group) or clinician-guided biopsy (standard of care) over a period of 12 months. Dd-cfDNA monitoring was performed at study inclusion and after 1, 3, 6, 9, and 12 months, and values above 50 cp/mL indicated a biopsy in the intervention group. Additionally, treating physicians could indicate a biopsy at any point during the study period, and 12 months after study inclusion, a biopsy was scheduled per protocol for patients without previous biopsy. The primary endpoint was time from study inclusion to diagnosis of active or chronic active ABMR. Secondary endpoints included diagnostic test metrics among others.

Results: From 40 patients, one patient died in the control group unrelated to ABMR. Secondary endpoints included diagnostic test metrics among others. From the remaining 39 patients, all had a functioning graft at the end of the observation period. In total, 26 patients underwent biopsy, 13 in each group. In the intervention group, 7/13 (54%) had ABMR and in the control group 5/13 (38%) patients had ABMR. Time to study inclusion to ABMR diagnosis was significantly shorter in the intervention group than in the control group (3.6 +/- 3.0 vs. 14.1 +/- 1.9 months, p<0.001) among patients with ABMR diagnosis. Longitudinal dd-cfDNA monitoring in this cohort of KTR with dnDSA had a positive predictive value (PPV) of 0.77 and negative predictive value (NPV) of 0.85 for the diagnosis of ABMR.

Conclusions: Dd-cfDNA-guided kidney allograft biopsy in DSA+ KTR can reduce time to ABMR diagnosis and hereby expedite therapy initiation.

Table 1. Diagnostic test metrics of longitudinal dd-cfDNA monitoring for ABMR in DSA+ KTR

<table>
<thead>
<tr>
<th>dd-cfDNA</th>
<th>ABMR</th>
<th>No ABMR</th>
<th>Total</th>
<th>Prev 0.46</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 cp/mL</td>
<td>10</td>
<td>3</td>
<td>13</td>
<td>PPV 0.77</td>
</tr>
<tr>
<td>≤ 50 cp/mL</td>
<td>2</td>
<td>11</td>
<td>13</td>
<td>NPV 0.85</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc 0.81</td>
<td>Sens 0.83</td>
<td>Spec 0.79</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Study Outline.

cfDNA-DSA Trial (NCT04897438)

Primary Endpoint m12: Time from Study Inclusion to ABMR diagnosis

Secondary Endpoints: Diagnostic test metrics (Sensitivity, Specificity, Positive predictive value, negative predictive value) of longitudinal dd-cfDNA monitoring for ABMR detection

Clinical Outcomes at m12 and m24
LOS1_5
IDENTIFICATION OF PROTEIN SIGNATURES THAT PREDICT KIDNEY TRANSPLANT OUTCOME

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Background: Kidney transplantation is a life-saving treatment for end stage kidney disease, but every year hundreds of patients with kidney failure die while waiting for a transplant. Donor organ acceptance criteria have been expanded in an effort to decrease organ shortage; however, current acceptance criteria depend heavily on immune matching and donor age and lack granularity. This study aimed to identify donor circulating protein signatures to improve granularity of assessing donor kidneys, predicting kidney transplant outcomes.

Methods: We analysed deceased donor plasma samples that were linked to complete donor and recipient metadata obtained from the QUOD biobank. A selection of 49 analytes were measured at three timepoints in the plasma of 132 brain death donors (DBD) and at two timepoints in the plasma of 119 circulatory death (DCD) donors. These measurements, along with donor age, height, and sex, were used to construct separate DBD and DCD 10-fold cross-validated lasso regression models using 12-nm recipient averaged eGFR as outcome end point. Models were compared using root mean squared error (RMSE) which is a measure of prediction accuracy.

Results: Lasso regression identified unique protein signatures in both DBD and DCD donors consisting of 20 and 22 proteins respectively with 8 proteins common to both models. The DBD model achieved a RMSE of 18.7 mL/min/1.73 m² while the DCD model RMSE was 19.0 mL/min/1.73 m². Both models performed considerably better than models containing clinical variables alone which had RMSES of 21.7 mL/min/1.73 m² and 22.7 mL/min/1.73 m² for DBD and DCD respectively.

Conclusions: This study identified protein signatures in DBD and DCD kidney donor plasma that could improve prediction of posttransplant outcome compared to using clinical variables alone. Identified protein signatures will be validated in a follow-up study on 1000 donors to develop a predictive score which could be used to improve transplant outcome prediction.

LOS1_6
URINARY CELL-CYCLE ARREST BIOMARKERS FOR PREDICTION OF ACUTE KIDNEY INJURY FOLLOWING LUNG TRANSPLANT

Valentina Vago1, Marco Bosone1, Gloria Turconi1, Nicola Palmieri1, Matteo Chiarle2, Lorenzo Rosso3,4, Giacomo Grasselli5, Vittorio Scaravilli4
1University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, 2Fondazione IRCCS Ca’ Granda - Ospedale Maggiore Policlinico, Thoracic Surgery and Lung Transplant Unit, MILAN, 3Fondazione IRCCS Ca’Granda - Ospedale Maggiore Policlinico, Department of Anesthesia Critical Care and Emergency, Milan, Italy, 4University of Milan, Department of Biomedical Surgical and Dental Sciences, Milan, Italy

Background: Lung transplant (LUTX) is a feasible option for end-stage respiratory failure. Acute kidney injury (AKI) is a common and impactful complication of LUTX. Urinary cell cycle arrest proteins as early indicators of AKI are not yet tested in LUTX recipients.

Methods: In a single-center prospective observational study, we assessed the capabilities of early urinary Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) and Insulin-Like Growth Factor Binding Protein 7 (IGFBP7) (i.e., [IGFBP7]x[TIMP-2]) Astute Medical, Paris, FRA) in predicting AKI and acute kidney disease (AKD) following KIDGO criteria, in adult patients undergone primary double LUTX. Exclusion criteria were preoperative chronic kidney disease (stage > 3) and emergent enlistment. AKI score was measured at 6 and 36 hours from graft reperfusion.

Results: Thirty consecutive adult LUTX patients were included (12 (40%) females, 51.5 (43.8-60.0) years old, Lung Allocation Score 40.5 (36.6-46.6)). Restrictive (14 (46%)) and suppurative (7 (23%)) diseases were the most frequent indications. Enlistment creatinine and estimated glomerular filtration rate were 0.78 (0.68-0.9) mg/dL and 91.0 (74.5-106.0) mL/min/1.73 m² (see Table 1, respectively). Creatinine peaked 2-5 days after LUTX, at a median 0.98 (0.52–1.17) mg/dL with 4 (13%), 7 (2%), and 4 (13%) patients having postoperative AKI stages 1, 2, and 3 (1%) needing renal replacement therapy during ICU stay, 6 (21%), 3 (10%), and 9 (31%) developed AKD stage 1, stage 2, and 3, respectively. AKI score was > 0.3 at 6 and 36 hours detected in 10 (33%) patients and 16 (53%) patients, respectively. 6-hours AKI score > 0.3 was associated with increased risk of AKI > 0 (p=0.036, OR 6.0 (1.2-31)) with AUC 0.66 (0.49-0.82 CI 95%) with sensitivity of 0.6 (0.31-0.83 CI 95%) and specificity 0.8 (0.58-0.91 CI 95%), 36-hours AKI score > 0.3 was associated with increased risk of AKI > 0 (p=0.049, OR 5.9 (1.0-35)) with AUC 0.65 (0.47-0.82 CI 95%), with sensitivity of 0.8 (0.49-0.94 CI 95%) and specificity 0.6 (0.38-0.78 CI 95%) (see Fig 1). AKI score > 0.3 was not associated with increased risk of AKD.

Conclusions: Patients undergone LUTX have high risk of AKI and AKD. Measurement of urinary cell cycle arrest proteins was predictive of AKI and may be used to guide AKI preventive measures in LUTX recipients.
**LOS1_7**

**TNF-α PATHWAY ACTIVATION ON DECEASED KIDNEY DONORS: A CRITICAL MEDIATOR OF UNFAVORABLE POST-TRANSPLANT OUTCOMES**

*Ioannis Michaelakis¹*, *Sarah Fawaz¹*, *Ivan Hartling¹*, *Rebecca Vaughan¹*, *Smaragdi Marinaki²*, *Philip Charles³*, *John Boletis¹*, *Rutger Ploeg¹*, *Maria Katsi¹*

¹University of Oxford, Nuffield Department of Surgical Sciences, Oxford, United Kingdom, ²Medical School, National and Kapodistrian University, Athens, Greece, ³University of Oxford, Big Data Institute, Oxford, United Kingdom

**Background:** Elevated levels of TNF-α pathway related proteins have been linked with kidney function decline and injury; yet the mechanisms have not been fully elucidated neither evaluated on deceased donors. The aim of this study was to evaluate the circulating levels of TNF-α, TNFRSF1A, TNFRSF1B and TNFRSF17 in donors after brain (DBD) and circulatory death (DCD) and investigate whether high levels of these mediators may impact graft function posttransplant.

**Methods:** Plasma samples from 284 deceased donors (158 DBD, 126 DCD) were obtained from the Quality in Organ Donor (QUOD) biobank. Using Luminex assays, longitudinal levels of the analytes were quantified in plasma samples collected during donor management (prior to cross clamp in DBDs and withdrawal of support in DCDs). Statistical associations were performed of donor analyte levels and posttransplant events of primary non-function (PNF), delayed graft function (DGF), acute rejection (AR), 12-month posttransplant graft function (eGFR<30, 30-59, >60 ml/min) and graft loss (GL), within 60 months of follow up.

**Results:** Among 556 paired recipients of 284 donors, 11 (2%) recipients developed PNF, and 74 (13%) donors had a GL during follow-up. High donor levels of TNFRSF17 were significantly elevated (p<0.05) in donors who offered concordant grafts with suboptimal 12-month post-transplant function (eGFR<30, Fig 1). GL associated with significantly higher levels of TNFRSF1A and TNFRSF17 pre-transplant (p<0.05, Fig 2). Grafts developed PNF were obtained from donors with higher levels of TNFRSF1A, TNFRSF2A, TNFRSF17 compared to donors who offered kidneys with immediate function (TNFRSF17, p=0.04). Donor TNF-α, TNFRSF1A, TNFRSF17 levels were significantly elevated (p<0.05) in donors who offered concordant grafts with suboptimal 12-month post-transplant function (eGFR<30, Fig 1). GL associated with significantly higher levels of TNFRSF1A and TNFRSF17 compared to donors who offered kidneys with immediate function (TNFRSF17, p=0.04). Finally, in AR, higher levels of the markers were observed, but were not of significance.

**Conclusions:** We demonstrated that increased circulating inflammatory levels are associated with poorer prognosis. In an era of donor shortage crisis, our study sheds light on a critical pathway of donor kidney injury in “high-risk” and of uncertain quality donors and offer the opportunity for more granular assessment of transplants.

![Fig 1](image1)

![Fig 2](image2)

**LOS1_8**

**SINGLE-CELL RNA SEQUENCING REVEALS ACTIVATION OF IMMUNE CELLS IN STABLE HUMAN KIDNEY AFTER TRANSPLANTATION**

*Gang Huang¹*, *Hui Zhang¹*, *Xutao Chen¹*, *Guodong Zhao¹*, *Jinquan Luo¹*, *Shicong Yang¹*, *Jiang Qiu¹*

¹The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

**Background:** Our objective was to determine differences between native kidney and stable transplanted kidney (STK) using single cell RNA sequencing (scRNA-seq).

**Methods:** Single cell transcriptome profiles were generated from two STK samples and merged with data of six native kidneys from the Gene Expression Omnibus (GEO) database. The cell types were determined according to reported marker genes by scRNA-seq analysis. Cell cell communication analysis, trajectory analysis, and gene-set variation analysis (GSVA) were used to explore differences of natural killer T (NKT) cells, macrophages, and proximal tubule cells (PTcs) between native kidney and STK.

**Results:** Nine main cell types were identified: endothelial cells (ECs), granulocytes, intercalated cells, PTcs, loop of Henle and distal tubule (DT) cells, NKT cells, mononuclear cells and macrophages, smooth muscle cells, and podocytes. Intercellular and molecular interactions were elevated in STK. The number of NKT cells was increased in STK, and NK cells accounted for the largest proportion, with the expression of some rejection-related genes. The WNT signaling pathway, Jak-STAT signaling pathway, and pattern-recognition receptor (PRR) signals were activated in macrophages of STK. PTcs in STK exhibited elevated metabolism.

**Conclusions:** There are differences in cell communication and gene enrichment between STK and native kidney. These differences may be helpful in the research of kidney transplant complications.

**Table Information of two patients with stable transplanted kidneys.**

<table>
<thead>
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<th>Patient</th>
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<tr>
<td>Sex</td>
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<tr>
<td>Time after surgery</td>
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<tr>
<td>Immunosuppressive regimen</td>
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<tr>
<td>eGFR (mL/min/1.73m²)</td>
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</tr>
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<td>Creatinine (µmol/L)</td>
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<td>SV40-T</td>
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</table>

(a) UMAP showing the identified cell types. (b) The number and proportion of the assigned cell types in the different groups. (c) Heat map showing the enhanced Gene Ontology biological process terms in NKT cells by GSVA analysis. (d)Box plot showing the GSVA score of KEGG pathway in macrophage of different groups.
**Background:** Natural Killer (NK) cells are an heterogeneous population of lymphocytes that, in addition to anti-viral and anti-tumoral activities, regulates several aspects of the alloimmune response in solid organ transplantation. The early activation of NK cells upon transplantation depends on the repertoire of ligands exposed by the allogeneic target cells. In the last years, MHC-I null stem-cell-derived β cells have been proposed as alternative source for treatment of Type 1 Diabetes (T1D). However, despite their use prevents T cell response, it could trigger NK cells via missing-self recognition leading to graft loss. As we described that stem-cell derived β cells express high levels of the NK activating ligands CD276 and CD155, we focused on their engineering to escape NK recognition after transplantation.

**Methods:** We generated luciferase-expressing wild type (WT) (negative control of rejection), MHC-I-/- MHC-I-/-/CD155-/- (TKO) human induced pluripotent stem cells (iPSCs). Gene-edited iPSCs were differentiated into β cells (iBeta) following 35-days in vitro protocol. We transplanted 200 islet equivalent in the lower limb muscles of hIL-15 NOG mice humanized with donor-derived NK cells, then assessed iBeta engraftment up to 30 days through in vivo imaging system.

**Results:** Gene-edited iPSCs differentiated into iBeta with high efficiency (>50% of NK6.1+ and >40% of INS+ cells) and viability (>90%). Strikingly, once transplanted into mice reconstituted with human NK cells, T-KO iBeta successfully escaped NK recognition and killing. Indeed, we observed only a once transplanted into mice reconstituted with human NK cells, T-KO iBeta long-term persisted for MHC-I-/- and properly maintained their functionality as confirmed by measuring of plasma human c-peptide levels.

**Conclusions:** We proposed genetic manipulation of the NK activating ligands as next-generation strategy to make grafts invisible to NK cells, offering new perspectives for using clinical-grade stem cell pancreatic derivatives as cell therapy for T1D treatment.
LATE BREAKING ORALS

LOS2.4 OXYGENATED HYPOTHERMIC MACHINE PERFUSION OF OLDER DCD KIDNEYS REDUCES MITOCHONDRIAL DAMAGE-ASSOCIATED MOLECULAR PATTERNS RELEASE IN PERFUSATE

Maria Letizia Lo Faro1,2, Sadr Shaheed1, Cees van Kooten1, Henri Lorenzen3, Ina Jochmans4, Maria Kaiser5, Rutger Ploeg6
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Background: Oxygenation during hypothermic machine perfusion (HMP) of the kidney can reduce mitochondrial damage during organ preservation and consequently limit ischaemia reperfusion injury at time of transplant. The COPE COMPARE trial showed that HMP of older (>50) kidneys donated after circulatory death (DCD) is safe, reduces severe post-transplant complications and improves graft survival compared to non-oxygenated hypothermic machine perfusion (HMP) (Jochmans et al., 2020). Using perfusate samples collected in the COMPARE trial, the present study aims to assess whether HMP reduces the release of mitochondrial damage-associated molecular patterns (mitoDAMPs) into the perfusate compared to standard HMP.

Methods: Perfusate samples from the COMPARE trial collected at the beginning (P1) and end (P3) of the cold perfusion were selected from paired kidneys (i.e., one kidney of a pair received HMP and the other HMPo 2 (n=20 donors). Perfusate levels of typical mitoDAMPs, including cardiolipin, succinate and TFAM (mitochondrial transcription factor A) were measured by fluorimetric, colorimetric and untargeted proteomics analysis, respectively. Perfusate levels of cell-free DNA and cell-free mitochondrial DNA are currently analysed by PCR.

Results: Perfusate cardiolipin levels were significantly lower in the HMPo 2 group (p=0.0426, linear regression analysis, Figure 1) and tended to increase in both groups, with longer preservation times. Similarly, succinate levels were lower in the HMPo 2 group compared to the end of HMP (p=0.005, Kruskal-Wallis with Dunn’s multiple comparisons test). No TFAM could be detected in the perfusate samples.

Conclusions: Our results suggest that the release of mitoDAMPs is reduced in HMPo 2, confirming findings from previous animal studies that the addition of oxygen during HMP may protect mitochondria, which is essential for tissue recovery from IRI. Accumulating clinical evidence suggest that increased DAMPs levels in perfusate associate with poorer outcomes post-transplant. The reduced levels of mitoDAMPs observed in this study underpin the clinical benefit observed of HMPo 2 preserved kidneys in clinical transplantation and make markers of mitochondrial health a useful tool in assessing organ injury and recovery.

LOS2.5 COST-EFFECTIVENESS OF DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION VERSUS STATIC COLD STORAGE IN DCD LIVER TRANSPLANTATION

Chikako Endo1, Christian van der Hilst1, Rianne van Rijn1, Ivo Schurik1, Aad P. van den Berg1, Sarwa Darwish Murad2, Bart van Hoek3, Volkert Huysman4, Vincent E. de Meijer5, Joerem de Jonge6, Robert J. Porte1
1University Medical Center Groningen, Groningen, Netherlands, 2Erasmus MC Transplant Institute, Rotterdam, Netherlands, 3Leiden University Medical Center, Leiden, Netherlands

Background: End-ischemic dual hypothermic oxygenated machine perfusion (DHOPE) of donor livers protects against ischemia-reperfusion related complications, such as post-transplant cholangiopathy, post-reperfusion syndrome, and early allograft dysfunction. Data on cost-effectiveness, however, are lacking. We performed an economic evaluation of DHOPE versus static cold storage (SCS) alone, based on a multicenter randomized controlled trial in donation after circulatory death (DCD) liver transplantation (DHOPE-DCD trial).

Methods: Data of patients enrolled in the Netherlands were included in this study. Direct medical costs of the transplant procedure, hospital stay, diagnostics, and interventions, including all out-patients treatments up to one year post-transplant, were included in the analysis. Deceased patients and patients requiring re-transplantation were included in the mean cost per year of graft survival. The total cost for machine perfusion was calculated for three different scenarios: 1) costs for machine perfusion, including machine, disposables, and fluids; 2) costs for machine perfusion plus costs for personnel; 3) scenario 2 plus depreciation expenses for a dedicated organ perfusion room.

Results: A total of 118 patients were included; 58 received a liver after SCS and 60 received a liver after DHOPE. Mean total cost per patient up to one year post-transplant was €121,930 for the SCS group and €110,794 in the DHOPE group (including costs for DHOPE). When costs were separated in domains, a cost reduction was noted in each domain, but was most pronounced for intensive care treatment (-26.4%), non-surgical interventions (-22.2%), hospital stay (-17.1%), and out-patient treatments (-16.7%). In cost scenario 1, DHOPE was cost-effective after only one procedure. In cost scenarios 2 and 3, DHOPE was cost-effective after 38 and 45 procedures/year, respectively.

Conclusions: DHOPE in DCD liver transplantation is cost-effective and reduces total medical costs up to one year post-transplant, compared to SCS.

Figure 1. Linear regression analysis of perfusate cardiolipin levels (µM) vs perfusion time (h).

LOS2.6 SINGLE LOBE LUNG TRANSPLANTATION AFTER STEM CELL TRANSPLANTATION FROM THE SAME LIVING DONOR: A RISK WORTH TAKING

Stefania Camagni1, Fabiano Di Marco1, Lorenzo D’antiga1, Lorenzo Grazio1, Ezio Bonanomi1, Domenico Pinelli1, Maria Beretta2, Michela Bravi2, Alessandro Lucianetti1, Michela Guizzetti1, Michele Colledan1
1ASST Papa Giovanni XXIII, Department of Organ Failure and Transplantation, Bergamo, Italy, 2ASST Papa Giovanni XXIII, Respiratory Unit, Bergamo, Italy, 3Università degli Studi di Milano, Milano, Italy, 4ASST Papa Giovanni XXIII, Pediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy, 5ASST Papa Giovanni XXIII, Department of Anesthesia and Intensive Care, Bergamo, Italy, 6ASST Papa Giovanni XXIII, Thoracic Surgery, Bergamo, Italy, 7Università degli Studi di Milano-Bicocca, Milano, Italy

Background: Currently, living donor (LD) lung transplantation (LT) represents an extraordinary procedure in Western countries, where the access to deceased donor LT is safely improving. Irreversible pulmonary complications of hematopoietic stem cell transplantation (HSTC) may be an indication for LT. The availability of a lung graft from the same LD as for HSTC may provide immunological advantages, which may justify the risks of living donation.

Methods: We report a successful single lobe LT from the same LD as for HSTC. This is the first LD LT in our country and, to our knowledge, an almost unique case in Europe.

Results: A 42-year-old boy underwent haploidentical HSCT from his father due to thalassemia major, and consequently developed end-stage bronchiolitis obliterans syndrome, requiring LT. For the purpose of transplant tolerance, as a possible effect of full donor chimerism, single lobe LT from the patient’s father appeared an appropriate and acceptable option. In January 2023, at age 5.8, the child underwent right LT with his father’s right lower lobe. The estimated forced vital capacity (FVC) of the graft (1.17 l) was 192% of the predicted FVC of the recipient (0.61 l). Graft volume (922 cm³) was 74% of the recipient’s hemithorax (845 cm³). Intraoperative veno-arterial-venous extracorporeal membrane oxygenation support was used. The graft pedicles were the result of a donor-friendly cutting line (figure). 8-shaped bronchial and venous stumps were Anastomosed to the recipient’s main bronchus and upper vein, respectively; the arterial stump was anastomosed to the recipient’s right artery. The patient was extubated on postoperative day (POD) 9, and discharged on POD 35. Immunosuppression with low-dose tacrolimus and steroids was tapered till suspension. The child’s lung function progressively improved, his FVC (0.99 l, 83% of predicted) now approaching the estimated graft FVC. No complications were observed in the donor.
Conclusions: The postulated immunological benefit, conferred by full donor chimerism, was deemed to exceed the risks for the LD, the high complexity of complement regulatory proteins. We aimed to investigate whether hypoxia and reoxygenation alter complement regulatory protein expression (CD46, CD59 and CD55) in kidney tissues.

Methods: 5 formalin-fixed, paraffin embedded samples from unaffected poles of tumour nephrectomy were cut into 5-μm sections, then processed for immunofluorescence (IF) staining were used as a control group. 8 specimens after cold ischemic time (11-27h) and 5 post-perfusion samples (4-7h) were examined to determine CD46, CD59 and CD55 proteins in tubules. The signal intensity was quantified by ImageJ.

Results: Decreased IF staining of CD46 was observed in tubules of post-perfusion samples (p=0.0249). There was basal and cytoplasmic staining for CD46 in normal kidney samples, whereas there was weaker staining of CD46 protein on basolateral membrane during hypoxia and reoxygenation. A significant reduction of the IF signal of CD59 was seen in hypoxic and post-perfusion tissues (p=0.033, p=0.0134 respectively). A decrease of CD55 protein staining was observed in tubules in both conditions (p<0.0035, p<0.0001 respectively).

Conclusion: This finding suggests that hypoxia and reoxygenation significantly decrease expression of CD59 and CD55, and reoxygenation causes a significant decrease of IF signals of CD46 in tubules. This data may explain the high susceptibility of proximal tubular cells to ischemia-reperfusion injury during kidney transplantation. Altered expression of complement regulators within tubular epithelium may be a crucial factor permitting complement activation.

Background: Lung transplantation (LTx) is the primary treatment for end-stage pulmonary disease but faces challenges due to donor lung scarcity and low survival rates. Lung injury from aspiration often leads to primary graft dysfunction (PGD), contributing to early mortality. This prompts an urgent need to restore donor lungs and reduce post-LTx mortality. We hypothesized that early passage mesenchymal stromal cells (MSCs) administered during ex vivo lung perfusion (EVLP) and after LTx could regenerate damaged lungs and reduce PGD incidence.

Methods: Pigs (mean weight 45 kg) were randomized into three treatment groups (n=6): Single EVLP dose, repeated dose (during EVLP and after LTx), and placebo (no MSC treatment). Acidic gastric contents were instilled in donor animals to induce lung injury over 6 hours. Lungs were harvested and subjected to 4-hour EVLP with respective treatments. The left lung was then transplanted into a recipient pig which was followed and closely monitored over 3 days. A right pneumonectomy was performed to evaluate the transplanted lung in isolation for the last four hours and PGD grades were determined in all recipients based on chest x-rays together with blood gases at 72 hours.

Results: Donor lung injury met the Berlin definition of ARDS with significantly decreased lung function. Histopathological assessment confirmed alveolar wall thickening, immune infiltration, and edema. The individuals treated with repeated doses of MSCs showed improved lung function together with improved histopathology assessed through lung injury scoring, which was also reflected in the incidence of PGD. At the 72-hour mark after LTx, most animals in the single dose and placebo groups exhibited PGD grade 2-3, whereas the repeated dose animals showed no signs of PGD.

Conclusions: A repeated dosage of early passage MSCs offers a promising therapeutic option to restore lung function in rejected aspiration-injured donor lungs and reduce PGD incidence post-transplantation.
**LATE BREAKING ORALS**

**RESULTS OF THE NEW ALLOCATION RULES IN ITALY: THE ROAD TOWARD A MORE EQUITABLE ALLOCATION**

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**Background:** Following a progressive increase in the requests for exemption in the access to the High Urgency (HU) Program for heart transplantation (HT), National Transplant Center found necessary to revise the criteria to apply for HU. Based on the new rules, active since 9 March 2020, two tiers of urgency are defined: national (1) and macro-area (2). Herein we compare the competing outcomes in patients listed before and after adopting the new criteria.

**Methods:** This analysis includes patients listed during the two years preceding the adoption of the new protocol (9 March 2018–8 March 2020) and the two years after (9 March 2020 to 8 March 2022). The probability of transplant, death, improvement, and delisting were assessed on the newly listed patients. Pathophysiologic phenotypes and blood group impact on the waiting time were also analyzed.

**Results:** During the second period, the number of patients listed in High Urgency decreased from 26.6% to 15.2%, with a growing number of Urgent listings (19.1%). The probability of transplants at 180d and d365 at competing outcome analysis differed significantly during the second period (29.6% vs 35.4% p<0.001 and 41.3 vs 46% p=0.002). The number of listings with an elective urgency remained similar (65.7 vs 67.3%). Despite the COVID pandemic, the number of transplants during the second period was higher without a significant increase in waitlist mortality (8.5% vs 6%), with fewer patients remaining listed and fewer delisting due to worsening.

**Conclusions:** The new allocation system achieved an increased number of timely transplants, reducing some of the inequalities of the allocation (i.e., Group 0). Despite the improvements achieved, the allocation system must be reviewed and extended to address inequalities and warranting an equitable timely transplant.

### Outcome Analysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Num</th>
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<tbody>
<tr>
<td>TRANSPLANT</td>
<td>256</td>
<td>46.0%</td>
</tr>
<tr>
<td>DEATH</td>
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<td>8.5%</td>
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<td>0.7%</td>
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<td>IN LIST</td>
<td>243</td>
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Background: The IMPROVEMENT project (ClinicalTrial.gov NCT05289609) was designed to develop predictive models of 90-day/1-yr allograft failure after liver transplant (LT). The study was draw up by a steering committee from the 5 continents. Yet, the study collects 3,882 adult LTs. There are a retrospective cohort (at least 40 centers) and a prospective one (40 centers).

Methods: The study design includes 3 LT categories (living donors; DCDs and high-risk DBDs; standard DBDs). Since the prospective collection is ongoing, we focused on the retrospective data (3,051 LT; 2017-2020). Each Center was committed to enroll a fixed number of LT to minimize Center-volume bias. The study design includes 3 LT categories (living donors; DCDs and high-risk DBDs; standard DBDs). Since the prospective collection is ongoing, we focused on the retrospective data (3,051 LT; 2017-2020). Each Center was committed to enroll a fixed number of LT to minimize Center-volume bias.

Results: Results were summarized (Fig. B, panels 1-20). Italy and Asia presented the larger adoption of perfusion machines (MP), while in Europe and in the North America there were fewer. DCDs were prevalent in Asia and in Europe. Living donors were mainly performed in Asia, while were less in the Western areas and even lower in Italy. Italy showed the highest prevalence of hepatocellular carcinoma (HCC); in the rest of the world, there was a dichotomic distribution (higher even lower in Italy.

Conclusions: The epidemiological analysis of IMPROVEMENT data depicts a screenshot of global liver transplant activity, never done before. Differences are due to cultural and logistic issues. The prospective data (ongoing) will provide more accurate information.
Simon Knight1*, Achille Salama1, Laura Wingfield1, Tingting Zhu1
1University of Oxford, Nuffield Department of Surgical Sciences, Oxford, United Kingdom, 2University of Oxford, Computational Health Informatics Lab, Oxford, United Kingdom

Background: The decision to accept an organ offer for transplant, or wait for something potentially better in the future, can be challenging. Clinical decision support tools predicting transplant outcomes from the time of offer are not readily available but might help in clinical decision making.

Methods: Using 20 years of recipient, donor, and transplant data available at the time of organ offer, along with associated outcomes from the UK Transplant Registry, we trained and validated single- and multiple-risk machine learning models to predict graft and patient survival following renal transplantation. Feature selection identified factors more important than random noise. We used post-hoc interpretability techniques to add clinical explainability to these models.

Results: In a single risk setting, neural networks provide comparable performance to the Cox proportional hazards model, with AUROC of 0.71 and 0.81 for prediction of 10-year graft and patient survival respectively. Predictive performance improves with the time post-transplant, with the most accurate predictions seen at 10 years (table 1). Using SHAP as a post-hoc interpretability method, we found that recipient and donor age, calculated reaction frequency (CRF), cause of primary renal disease, donor eGFR, donor type and the number of HLA DR mismatches were the most important predictors for transplant outcome prediction, in keeping with the published literature (figure 1). We also extended the neural network approach to multiple competing outcome predictions, maintaining consistent performance and interpretability.

Conclusions: Neural networks perform well for the prediction of long-term outcomes following renal transplantation, and the use of SHAP values allows assessment of the most prominent predictive features for the model as a whole and for individual predictions. Use of interpretable models will improve clinician’s trust over more traditional “black-box” methods, meaning that such predictions may be useful in offer decision-making and informed consent.

Table 1 – Performance of single-risk models for graft and patient survival at years 1, 5 and 10 post-transplant.

<table>
<thead>
<tr>
<th>Model</th>
<th>Graft Survival</th>
<th>Patient Survival</th>
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<tbody>
<tr>
<td></td>
<td>AUROC</td>
<td>F1-Score</td>
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<tr>
<td>Random forest</td>
<td>0.61</td>
<td>0.14</td>
</tr>
<tr>
<td>Cox PH model</td>
<td>0.60</td>
<td>0.35</td>
</tr>
<tr>
<td>Neural network</td>
<td>0.68</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Figure 1 – SHAP-based feature importance for 10-year graft survival using a neural network model.

Anil Chandraker1*, Anil Regmi2, Reginald Gohi3, Akhil Sharma4, E. Steve Woodle5, Mohammed Ansari6, Vinay Nair7, Ling-Xin Chen8, Tarek Alhamad9, Silas Norman10, Francesca Cardarelli11, Julie MA11, Sarah Gilmore11, Sspridvala Vasileiou12, David Wojciechowski13
1Brigham and Women’s Hospital, Boston, United States, 2Inova Transplant Center, Falls Church, United States, 3Rhode Island Hospital, Providence, United States, 4University of Pittsburgh Medical Center, Pittsburgh, United States, 5University of Cincinnati College of Medicine, Cincinnati, United States, 6Northwestern University, Chicago, United States, 7Northwell Health, New Hyde Park, United States, 8University of California, Davis, Transplant Center, Davis, United States, 9Washington University School of Medicine, St Louis, United States, 10University of Michigan, Ann Arbor, United States, 11AlloVir, Wattham, United States, 12Baylor College of Medicine, Houston, United States, 13UT Southwestern Medical Center, Dallas, United States

Background: Kidney transplant (KT) recipients with BK virus infection are at risk of nephroptathy and graft loss and are without treatment options. Posoleucel (PSL) is an off-the-shelf multi-virus-specific T cell therapy targeting BKV.

Methods: In this phase 2 double-blind study (NCT04605484), KT patients with BK viremia were randomized 1:1:1 to receive PSL cells wky for 3 wks then every 14 (PSL1) or 28 days (PSL2), or placebo (PBO) for 12 wks. Primary objective was safety; secondary was plasma BK viral load (VL) reduction. Functional BKV immune responses (infused and endogenous) were evaluated by IFNγ ELISpot analyses and the contribution of PSL to antiviral immunity was evaluated by T cell receptor (TCR) β immunosequencing. TCR sequences unique to PSL were identified computationally and used to track persistence.

Results: Baseline (BL) characteristics among 81 patients were similar across groups. No deaths, GVHD, or cytokine release syndrome were observed. Three PSL patients had graft rejection, but none related to treatment. Patient had a prior history of rejection, 1 had renal TB, and 1 had rejection 68 days after last PSL dose. Median eGFR was stable in all groups. The table shows VL changes in 52 patients with stable immunosuppression (IS) in the 30 days before randomization who completed the study demonstrating superior antiviral effects in both PSL groups vs PBO. At 64 weeks the majority of patients with high BL VL did not have pre-existing BK-specific T cell immunity. Recipients of PSL vs PBO had increases in BKV IFNγ+ T cells against PSL-target antigens at wks 14 and 24. Upregulation of endogenous BK-directed T cell activity against non-PSL-target antigens was seen following PSL infusion. In PSL1 patients, the frequency of functional cells was greater and their overall BKV IFNγ+ T cell responses increased over 6-month study period, coincident with VL reduction. The presence and persistence of PSL was confirmed by TCRβ deep sequencing out to 12 wks post dosing, with higher frequencies of PSL clones in patients with high VLs.

Conclusions: PSL was generally safe and well tolerated. Clinically meaningful BK VL reductions and increases in BK-reactive T cells occurred in PSL patients. PSL was detected during dosing and for up to 12 wks after infusion period, which is the first demonstration of PSL persistence in KT patients.

Table 1 – Performance of single-risk models for graft and patient survival at years 1, 5 and 10 post-transplant.

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</table>

Results at week 24 in patients with stable IS before randomization.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>PSL1</th>
<th>PSL2</th>
<th>PBO</th>
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<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>N=18</td>
<td>N=17</td>
</tr>
<tr>
<td>PSL vs BK VL decreased by ≥1 log, BKV DNA copies/mL vs baseline, n (%)</td>
<td>10 (50)</td>
<td>5 (28)</td>
<td>2 (14)</td>
</tr>
<tr>
<td>BK VL reduction from baseline, median log, BKV DNA copies/mL (min, max)</td>
<td>-0.9 (-2.1, 1.0)</td>
<td>-0.45 (-1.8, 0.5)</td>
<td>-0.15 (-2.1, 0.3)</td>
</tr>
<tr>
<td>BK VL ≤50% reduction, n (%)</td>
<td>17 (85%)</td>
<td>10 (56)</td>
<td>6 (43)</td>
</tr>
<tr>
<td>Change in GFR, median mL/min/1.73 m² (min, max)</td>
<td>-2.5 (-11, 7)</td>
<td>0 (16, 20)</td>
<td>0 (21, 9)</td>
</tr>
</tbody>
</table>

*0% reduction in CNI, mTOR, MMF/MPA, or azathioprine within 30 (or 21) days of randomization.
| characteristics | were lost to follow-up or 2 had pre-randomization IS rejection. The patient was lost to follow-up or had pre-randomization IS rejection. P<0.05 vs PBO. | B|
**Background:** Measuring health system performance across countries may help to identify areas for improvement and guide national reform efforts. Here we present a set of expert validated indicators intended to form the basis of a scorecard for measuring the performance of national organ donation and transplant systems.

**Methods:** The indicators were collected and validated in five steps: (1) We extracted a total of 104 possible quality indicators from the websites and reports of national transplant organizations and other key documents (such as the Global Observatory on Donation and Transplantation). (2) We divided these according to the categories of prevention, donation, transplantation, follow-up, responsiveness, equity, and efficiency; based on a recently published framework on a scale from 0 (not important) to 10 (very important). (3) We convened a multinational, multiprofessional expert group consisting of a total of 10 experts including a patient representative. This group were initially asked to rank each indicator on a scale from 0 (not important) to 10 (very important). (4) We held a series of virtual meetings with the group of experts to discuss the outcomes of the ranking exercise and the virtual meetings were synthesized into a general lessons for building a national transplant system scorecard and b.) a shortlist of indicators that can be used to build a national transplant system scorecard.

**Results:** A transplant system scorecard needs to reflect different organ systems, be multidimensional, clear in its definitions and appropriately adjusted for demographic differences to make fair comparisons. We present a total of 11 possible indicators with strengths, limitations, and alternatives (Table 1).

**Conclusions:** To build a scorecard assessing national organ donation and transplant system performance in Europe, we present a set of validated indicators that will be used to create a scorecard for measuring the performance of national organ donation and transplant systems.

**Table 1: Indicators and Alternatives to build a National Scorecard for Transplant System Performance**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Strengths</th>
<th>Limitations</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waiting list time</td>
<td>Time on the waiting list</td>
<td>Measures the time a patient spends waiting for a transplant</td>
<td>Can be influenced by various factors such as organ availability and policy changes</td>
<td>Median time to transplant, waiting list turnover rates</td>
</tr>
<tr>
<td>Time to transplant</td>
<td>Median time from listing to transplant</td>
<td>Measures the timeliness of the transplant process</td>
<td>Can be affected by organ matching and availability</td>
<td>Waiting list duration, time to first offer of a suitable organ</td>
</tr>
<tr>
<td>Transplant survival</td>
<td>Long-term survival post-transplant</td>
<td>Evaluates the effectiveness of the transplant procedure</td>
<td>Data collection can be challenging</td>
<td>Three-year survival, five-year survival</td>
</tr>
<tr>
<td>Rejection rate</td>
<td>Percentage of patients experiencing rejection</td>
<td>Monitors the success of the immune suppression therapy</td>
<td>Requires careful monitoring</td>
<td>Rejection-free survival, graft survival</td>
</tr>
<tr>
<td>Graft failure</td>
<td>Percentage of grafts that fail</td>
<td>Measures the durability of the transplant</td>
<td>Limited to graft survival data</td>
<td>Rejection-free survival, graft survival</td>
</tr>
<tr>
<td>Patient survival</td>
<td>Overall survival of transplant recipients</td>
<td>Evaluates the overall health outcomes</td>
<td>Data collection can be complex</td>
<td>Cause-specific mortality, cause-specific survival</td>
</tr>
<tr>
<td>Resource utilization</td>
<td>Costs associated with the transplant process</td>
<td>Measures the efficiency of resource use</td>
<td>Data collection can be resource-intensive</td>
<td>Resource allocation, cost-effectiveness analysis</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>Patient-reported satisfaction with the transplant experience</td>
<td>Assesses patient-reported outcomes</td>
<td>Requires subjective reporting</td>
<td>Health-related quality of life measures</td>
</tr>
<tr>
<td>Compliance</td>
<td>Percentage of patients adhering to post-transplant medication</td>
<td>Measures the success of post-transplant management</td>
<td>Data collection can be challenging</td>
<td>Adherence to immunosuppression, medication possession rate</td>
</tr>
<tr>
<td>Mortality risk</td>
<td>Risk of death post-transplant</td>
<td>Evaluates the overall survival risk</td>
<td>Requires long-term follow-up data</td>
<td>Cause-specific mortality, overall survival</td>
</tr>
</tbody>
</table>

**Table 2: Indicators and Alternatives for Measuring Transplant System Performance**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Strengths</th>
<th>Limitations</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Age of the patient at the time of transplant</td>
<td>Evaluates the age-related factors affecting transplantation outcomes</td>
<td>Data collection can be challenging</td>
<td>Age-specific survival, adjusted survival rates</td>
</tr>
<tr>
<td>Gender</td>
<td>Sex of the patient</td>
<td>Measures the impact of gender on transplant outcomes</td>
<td>Limited to sex differences</td>
<td>Sex-specific survival, gender-adjusted survival rates</td>
</tr>
<tr>
<td>Blood group</td>
<td>Blood type of the patient</td>
<td>Evaluates the compatibility of blood types</td>
<td>Limited to blood typing data</td>
<td>Blood group matching, crossmatching</td>
</tr>
</tbody>
</table>

**Results:** The indicators were collected and validated in five steps: (1) We extracted a total of 104 possible quality indicators from the websites and reports of national transplant organizations and other key documents (such as the Global Observatory on Donation and Transplantation). (2) We divided these according to the categories of prevention, donation, transplantation, follow-up, responsiveness, equity, and efficiency; based on a recently published framework on a scale from 0 (not important) to 10 (very important). (3) We convened a multinational, multiprofessional expert group consisting of a total of 10 experts including a patient representative. This group were initially asked to rank each indicator on a scale from 0 (not important) to 10 (very important). (4) We held a series of virtual meetings with the group of experts to discuss the outcomes of the ranking exercise and the virtual meetings were synthesized into a general lessons for building a national transplant system scorecard and b.) a shortlist of indicators that can be used to build a national transplant system scorecard.

**Conclusions:** To build a scorecard assessing national organ donation and transplant system performance in Europe, we present a set of validated indicators that will be used to create a scorecard for measuring the performance of national organ donation and transplant systems.
Background: Organ shortage has always been one of the most important issues to be addressed in organ transplantation. The denial consent to organ donation remains one of the key factors affecting the number of available organs. Numerous studies have identified targeted information campaigns as a way to increase willingness to donate by both individuals and family members. Those campaigns must be addressed and targeted according to the socio-economic environment to achieve the expected results. Despite this, in literature, studies describing the socio-economic and demographic characteristics of those who decline the consent for donation in Italy are lacking.

Methods: A retrospective study based on the North Italian Transplant Program (NITp) donation registry was performed. Age, state of origin, and residence were analyzed. Census section-level deprivation index was considered as an indicator of socioeconomic hardship and disadvantage to assess the possible association between socioeconomic status and opposition. Results: From January 2007 to December 2022, there were 2510 oppositions in the NIT area (represented 25.6% of the reports). 73% were in hospitals not housing a transplant center. The average age is 63 years. 503 of these (20%) were born in foreign countries, of which 65 (2.6%) were resident abroad at the time of death, of which 26 (1%) in EU countries. 1054 people (42%) resided in areas at the 4th quartile of the Italian deprivation index. Conclusions: The study describes the characteristics of those who expressed opposition to donation in the NIT area over the past 15 years. Although upon preliminary analysis, the prevalence of opposition in areas with high socioeconomic deprivation and in hospitals not home to a transplant centre seems prominent. This stratification may enable policymakers to assess opportunities to promote and support organ donation and anticipate possible challenges to confidence in donation policies.

### RESULTS FROM TWICE-DAILY TO ONCE-DAILY TACROLIMUS

**Results:** The full analysis set (FAS) included 4028 KTRs (1060 ECs; 2968 LCs). Most patients (60.5%) were male, with a mean age of 50.9 years and a mean eGFR of 56.05 mL/min/1.73m² at conversion. Most KTRs were converted to PRT in <3 months post-transplant, and LCs >24 months post-transplant. eGFR remained stable post-conversion in the overall FAS group, with improvement in ECs (Figure). At 5 years post-conversion, the mean dose of PRT was 3.95 mg/day (Table). At study end, 66.7% of KTRs had tacrolimus trough levels ≥5 ng/mL and >80% of KTRs had trough level coefficient of variation <35%; both were consistent throughout the study. At 5 years post-transplant, Kaplan-Meier estimate of patient survival was 92.9% for ECs and 98.5% for LCs; graft survival was 88.1% for ECs and 97.5% for LCs. Overall, 4.9% of patients who were DSA negative prior to or at conversion had DSA occurrence post-conversion. At study end, 70.8% of patients remained on PRT. Adverse events (AEs) were reported in 72.4% of enrolled patients; 19.3% had ≥1 PRT-related AE. Serious AEs (SAEs) were reported in 50.6% of patients; 10.4% had ≥1 PRT-related SAE. The discontinuation rate due to AEs was 11.8% and PRT-related AEs was 5.5%.

### CONCLUSIONS

Conclusions: Results from this large cohort of KTRs showed renal function remained stable overall. Patient and graft survival were high at 5 years post-transplant with no unexpected safety findings, supporting the long-term use of PRT.

Figure: Mean change from baseline in renal function (eGFR)
LONG-TERM MORTALITY OF LIVING LIVER DONORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Although the outcome of LDLT recipients has been developed, concerns remain about donor safety and moral issues. The safety of the living donor is the top priority when performing a living liver transplant. Several studies reported donor complications and mortality rate, but the results were short-term, mostly related the operation. Although liver donation is considered safe for healthy people, the donation has lifelong effects. Due to the short history of living liver transplantation, studies of the long-term survival of donors after living donor are lacking. At this point, the justification for living liver transplantation will be established only when there is a long-term result from donors after organ donation. This is a meta-analysis of long-term survival of LDLT donors.

Methods: We searched PubMed, EMBASE, and The Cochrane Library database for studies comparing Living liver transplantation donor with control group published between the date of database creation and June 2021. Statistical analysis was performed using Revman 5.3. We included all data from recent studies and assessed methodological quality using the risk of bias from the Non-Randomized Study of Intervention (ROBINS-I) assessment tool.

Results: Three studies met the eligibility criteria. In the included clinical study, 24,371 patients received living donor surgery. In this paper, we compiled all the data on donors’ reported deaths from subsequent published papers on cause of death, including short-lived deaths that may be related to surgery performed within 90 days of donors. In a worldwide survey long-term deaths were reported, with suicide being the most common cause of death. Living donor group have been shown to have reduced long-term mortality rates than healthy group.

Conclusions: This meta-analysis suggests that liver donation is safe and feasible for living donor liver transplantation compared to non-donation people. It is also worth mentioning that regular psychological evaluations of donors by a psychologist before and after donation were mandated. To maintain the LDLT program, careful selection and surgical technique of living liver donors are important for the safety of living liver donors.
PROGNOSTIC VALUE IN KIDNEY TRANSPLANTATION OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING

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Background: Kidney transplantation is the best therapeutic option in advanced chronic kidney disease. For this reason, it is important to have markers that help to predict its evolution, in order to establish measures that prolong its survival. Multiparametric Magnetic Resonance Imaging (MRI) could safely provide these markers, as it does not require the administration of exogenous contrast. Objective: to study the prognostic utility of the parameters provided by MRI in the assessment of allograft function in a population of kidney transplant recipients.

Methods: Thirty-two kidney transplant recipients who underwent an MRI in the first week post-transplant, including perfusion (RBF), diffusion (f, D*, D, ∆D, ADC, ∆ADC) and T1 mapping (T1, ∆T1) sequences, were included. Patients were divided into 2 groups according to estimated glomerular filtration rate (eGFR) measured at 3 months: inferior graft function (eGFR<45 ml/min/1.73 m2, n=10) and superior graft function (eGFR>45 ml/min/1.73 m2, n=22). Two models were created with the cortical MRI parameters (RBF, f, D*, D, ADC and T1) and cortico-medullary differences (∆D, ∆ADC and ∆T1) and their predictive capacity for eGFR at 3 months was compared with that of the eGFR at the time the MRI was performed. Receiver-operator characteristic (ROC) curves were calculated for univariate models and multivariate models.

Results: In this study, eGFR showed the highest AUC while similar results were found for RBF. The prognostic utility of the model 1 demonstrated in the analysis of ROC curves with an area under the curve (AUC) of 0.9747 (CI: 0.92-1.00), specificity =100% and sensitivity =86%), was better than using only the eGFR (Figure 1).

Conclusions: MRI is a safe diagnostic tool with higher prognostic efficiency than eGFR for determining allograft function in the 3-month period. The use of MRI opens up as a useful tool, which might help to optimize the decision-making in the care of kidney transplant recipients and probably improve graft survival rates.
LATE BREAKING ORALS

LBOS_12 REDUCTION OF RENAL GRAFT FIBROSIS WITH VALGANCICLOVIR PROPHYLAXIS FOR CYTOMEGALOVIRUS INFECTION COMPARING TO PREEMPTIVE THERAPY: A RANDOMIZED CONTROLLED TRIAL

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Background: Prevention of cytomegalovirus (CMV) infection including CMV indirect effects is essential in kidney transplantation. The 12-month results of OVERT Study showed less subclinical rejection and a trend toward lower incidence of acute rejection in recipients receiving valganciclovir prophylaxis compared to preemptive therapy. Here we report long-term results of OVERT Study.

Methods: This was an open-label, single-center, randomized clinical trial of valganciclovir prophylaxis vs preemptive therapy in 140 kidney transplant recipients recruited between June 2013 and May 2016. CMV-seronegative recipients with negative donors (D-R-) were excluded. Patients were randomized 1:1 to receive either valganciclovir prophylaxis for 3 months (or 6 months in D+R-) (n=70) or preemptive valganciclovir for significant CMV DNAemia detected in predefined assessments through month 24 (n=70). The primary outcome was the incidence of moderate to severe interstitial fibrosis and tubular atrophy (IFTA) in protocol biopsy at 3 years. Key secondary outcomes included acute rejection, CMV disease and DNAemia, patient and graft survival.

Results: Among the 127 patients who had a protocol biopsy specimen available at 3 years, 5 (8%) of 66 patients in the prophylaxis group and 14 (23%) of 61 patients in the preemptive group had moderate to severe IFTA (P=0.015). At 3 years the incidence of acute rejection was lower with valganciclovir prophylaxis (13% vs 36%, P=0.052). In spite of 5 (7%) additional patients with CMV DNAemia after month 12 in the prophylaxis group in contrast to none in the preemptive group (P=0.025) the cumulative incidence at 2 years remained lower with prophylaxis (51% vs 75%, P<0.001). Both regimens prevented CMV disease (6% vs 4%, P=0.733). While the 4-year graft survival was comparable between the 2 groups (99% vs 95%, P=0.414) the cumulative incidence of CMV DNAemia 12 months after transplantation was significantly lower in the prophylaxis group (10% vs 12%, P=0.042).

Conclusions: Among kidney transplant recipients, the use of valganciclovir prophylaxis, compared with preemptive therapy, led to less severe IFTA at 3 years after transplantation.

LBOS_13 ORGAN UTILIZATION RATE (OUR): A NEW APPROACH TO IMPROVE ORGAN ACCEPTANCE RATE?

Franz Immert1, AnniKa Ballmer1, Michel Tsimaratos2, Massimo Cardillo3, Beatriz Dominguez-Gil4, Beatriz Mahillo4, Marina Alvarez4, Derek Manas5, Ali Rahmel6, Serge Vogelaar7
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Background: Availability of organs from deceased donors is the most important limitation for organ transplantation. Many studies focused on the number of deceased donors per million inhabitants (pmp). The issue of organ acceptance by background individuals and transplant professionals involved in decision making for the acceptance of organs for transplantation is another crucial aspect. Organs offered for transplantation may be rejected in one center and being successfully transplanted in another or even exported in a foreign country. The aim of the study is to compare the organ utilization rate (OUR) for heart, lungs, liver and kidney in selected European countries (FRA, GER, AUT, ITA, ESP, POR, NL, UK, CH).

Methods: Data from 2018 to 2021 have been extracted from the Newsletter Transplant, published from the EDQM/Council of Europe and the GODT 2021. The numbers of utilized donors (UTI) were extracted for DBD, DCD and overall. The percentages of 60 and 6 years old reported in 2021 in the GODT has been extracted. Transplantation activity pmp for heart, lungs, liver and kidney in selected European countries (FRA, GER, AUT, ITA, ESP, POR, NL, UK, CH). The percentage of donors of 60 years and older was the lowest OUR. For lungs average OUR was 24.5% with 37% in Germany in comparison to 9.3% in Italy and 9.5% in UK. Similar variations can be found by analyzing DBD- and DCD-donors only.

Conclusions: OUR between 2018 and 2021 shows important variations in all organs. Donor characteristics may vary in terms of the enrolment of older donors and the percentage of DCD- and DCD-donors between the different countries, which has an additional effect on the interpretation of the OUR. Considering that posttransplant outcome are quite similar in these countries one may assume that potentially transplantable organs could be rejected and lost due to restrictive national and/or center acceptance criteria.

LBOS_14 HEALTH-RELATED QUALITY OF LIFE AFTER LIVING KIDNEY DONATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Living donor kidney transplantation (LDKT) is the most effective treatment for end-stage kidney disease, offering superior outcomes compared to deceased donor kidney transplantation or dialysis. The assessment of health-related quality of life (HR QoL) following living kidney donation (LKD) is crucial given that a healthy individual willingly undergoes this procedure. Compensation rates of LKD are low, however, there is conflicting evidence regarding the post-donation HR QoL. It is unclear whether post-donation physical- and physiological functioning levels (including fatigue and chronic pain) return to pre-donation levels. Furthermore, we compared the HR QoL of LKD to other relevant populations, such as the general population and healthy controls. Comprehensive searches were conducted in Embase, MEDLINE, CENTRAL, Web of Science, and Google Scholar up to the 16th of June 2023. Our primary outcome measures included the SF-36 and composites mental- (MCS) and physical component summary (PCS), comparing post-donation HR QoL to baseline or other relevant populations. A total of 69 studies encompassing 12,523 donors were included in this study. The MICS was not significantly different at 3, 6, and 12 months post-donation compared to baseline (Figure 1), with a standard mean difference (SMD) of -0.04 (95% CI: -0.14 - 0.06, p = 0.75). However, the PCS was significantly lower at 3 months post-donation (Figure 2). Nonetheless, no difference was observed at 6 and 12 months post-donation, with an SMD of -0.07 (95% CI: -0.20 - 0.05, p = 0.09). Both PCS and MCS were significantly higher compared to the general population. Furthermore, the separate domains of the SF-36 were significantly decreased at 3 months post-donation. However, these domains were significantly increased at 12 months post-donation, with an SMD of 0.63 (95% CI: 0.60 - 0.66, p < 0.001). Compared to the general population, SF-36 domains were significantly higher at 3, 6, and 12 months post-donation, with an SMD of 0.14 (95% CI: 0.10 - 0.18, p < 0.001). Based on the available evidence, HRQoL appears to be diminished shortly after LKD but does not exhibit a significantly decrease after 6 months or longer post-donation. Furthermore, LKD have significantly higher HRQoL compared to the general population, which is encouraging to expand LDKT programmes.
IMPACT OF DONOR-DERIVED CELL-FREE DNA ASSESSMENT IN MONITORING KIDNEY TRANSPLANT RECIPIENTS: INTERIM REPORT OF A PROSPECTIVE LONGITUDINAL STUDY

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Background: Donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for monitoring kidney transplant (KT) recipients. We aim to evaluate its clinical utility in a prospective cohort of 500 cases.

Methods: Since July 2022, we prospectively collect plasma from each KT recipient immediately prior to renal biopsy, to measure dd-cfDNA, using a locally implemented standardized assay (AlloSeq cfDNA, CareDx, CA), and correlate %dd-cfDNA with allograft and recipient status.

Results: Of the 292/500 samples collected so far, dd-cfDNA has been already measured in 229, with 92.1% of samples passing quality control. The %dd-cfDNA <14 days post-TX (0.71% [0.53-0.85]) was significantly higher than >14 days post-TX (0.21% [0.12-0.32]; p=3.3x10^{-7}, Fig.1A). Dd-cfDNA was increased in deceased donor (DD) kidneys, both DBD (0.24% [0.16-0.38]; p=0.004) and DCD (0.24% [0.12-0.4]; p=0.03), compared to living donation (LD) (0.13% [0.1-0.25], Fig.1B), but not different between DBD and DCD kidneys. The difference between DD and LD kidneys persisted >14 days post-TX (DBD 0.21% [0.15-0.31]; DCD 0.22% [0.11-0.32]; LD 0.13% [0.10-0.25]). Dd-cfDNA was significantly higher at the time of indication biopsies (0.41% [0.26-0.85]) than at surveillance biopsies (0.18% [0.11-0.30]; p=2.8x10^{-10}). 13.3% of cases had (borderline) allograft rejection (AR). Dd-cfDNA was higher in AR (0.80% [0.47-1.64]) versus no rejection (0.31% [0.25-0.70]; p=0.016, Fig.1C) in indication biopsies only, which also showed more cases of full-blown AR than surveillance biopsies (17% vs 3%, respectively). Within 14 days post-TX, the inherently higher %dd-cfDNA masked the association between dd-cfDNA and AR. In indication biopsies performed >14 days post-TX, AR was associated with higher %dd-cfDNA (1.19% [0.32-2.00] vs 0.28% [0.23-0.44] in AR vs no rejection, Fig.1D).

Conclusions: Awaiting study completion by end-2023, this interim analysis indicates that, when measured >14 days post-TX, dd-cfDNA could guide whether to perform an indication biopsy. However, within <14 days post-TX, the injury/healing process occurring after TX masks the ability of dd-cfDNA to uncover ongoing AR. The impact of donor type on %dd-cfDNA persists >14 days post-TX. The clinical utility of dd-cfDNA for subclinical AR will be addressed upon study completion.

Figure 1: A. Box and whisker plot showing %dd-cfDNA median levels within and after 14 days post-transplantation. B. Box and whisker plot showing %dd-cfDNA median levels in kidney transplant recipients from deceased (DBD and DCD) and living (LD) donation. C. Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection (AR) at the time of indication and surveillance biopsies. D. Box and whisker plot showing %dd-cfDNA median levels in patients with and without allograft rejection at the time of indication biopsies performed within and after 14 days post-transplantation. DBD=donor after brain death; DCD=donor after cardiac death.
Background: While the number of CKD patients requiring dialysis treatment is significantly increasing, current dialysis patients face the demanding schedule of thrice-weekly, four-hour-long dialysis sessions, high/low blood pressure before/during the treatment, and strict restriction of water intake. Our group proposed "hybrid" renal replacement therapy, where an implantable artificial kidney, or a nano-filtering device, "i-Azinzo", continuously removes adequate amount of fluid during the treatment, and strict restriction of water intake. Our group proposed “hybrid” renal replacement therapy, where an implantable artificial kidney, or a nano-filtering device, “i-Azinzo”, continuously removes adequate amount of fluid from blood while the excessive waste products are removed by the conventional dialysis treatment. Consequently, this hybrid therapy reduces the dialysis treatment frequency down to once a week or less (depending on the residual kidney function) and maintains the body fluid amount while allowing the patients to drink 1.5 L of water per day. Since i-Azinzo is used in the implanted manner, the long-term dialysis and antithrombotic performance needs to be investigated.

Methods: i-Azinzo is a layered filter comprised of a polyethersulfone (PES) dialysis membrane and micro-sized blood flow and filtrate flow channels arranged alternately. It is equipped with two artificial blood vessels connected to the artery and vein and works at blood pressure without an external pump. In this study, we designed i-Azinzo tailored for miniature pigs weighing between 20 to 25 kg (n=3) (Figure 1). They were then connected to the pigs’ neck arteries and veins using medical-grade tubing. 6-hour ex vivo experiments were conducted to evaluate the filtration performance and antithrombotic properties of the device.

Results: Throughout the 6-hour experiments, the filtrate volume remained consistent without any decline (Table 1). After the experiment, the device was disassembled to observe the internal blood flow channels, and there were no blood clots present. This verified the device’s high antithrombotic properties.

Conclusions: We have successfully conducted 6-hour ex vivo experiments to validate the performance of i-Azinzo. Currently, our focus is on achieving the target implantation period of 6 months for i-Azinzo. Up to this point, evaluations have been conducted for a period of 96 hours.

Table 1. Filtrate volume in 6-hour ex vivo experiments.

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<th>Time(hour)</th>
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<th>3</th>
<th>3.5</th>
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<th>4.5</th>
<th>5</th>
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<td>5.4</td>
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<td>7.6</td>
<td>7.7</td>
<td>6.2</td>
<td>6.6</td>
<td>5.8</td>
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Norihisa Miki1, Takashi Ota2, Yoshihiko Kanno1
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Background: The current maximum cold ischemic time for donor lung transplant is around 8 hours. Six hours is the commonly accepted limit of cold ischemic time at most transplant centers in United States. Now Paragonix LUNGguard™ system brings a new technology to donor lung transportation and extends the cold ischemia time to even longer than 8 hours without compromising the quality of the donor lungs. We review our experience of LUNGguard at our institute. Methods: A total of 45 donor lungs were procured and stored in LUNGguard at our institution between April 2022 and July 2023. Recipient’s demographic, clinical diagnoses, and morbidity are analyzed. 30-day survival is reviewed. Results: The demographics of the recipients is in table 1. 45 donor lungs (15 single lung, 30 double lungs) were flushed with Perfadex solution and stored in LUNGguard. Among 45 cases, 42 donors were DBD, 3 donors were DCD. Total cold ischemic times were grouped as follows: 26 cases <8 hours, 7 cases between 8-10 hours, 12 cases between 10-12 hours, 4 cases had no significant PGD in first 72 hours, only 4 recipients developed PGD 3, but none was on ECMO support. Five recipients received tracheostomy after the transplants (2 patients secondary to reflex and aspiration. 2 patients had right ventricular failure. 1 patient had multi organ failure). Average ICU stay is 10.5 days (range from 3 days to 39 days). There was one death in 30 days due to heart failure (cold ischemic time 410 minutes). Conclusions: The analysis of this cohort showed that the Paragonix LUNGguard is an advanced organ preservation device, extends cold ischemic time beyond 8 hours and has a good outcome at short-term.

Table 1. Recipient’s demographic

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Race</th>
<th>BMI</th>
<th>CAS</th>
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<tbody>
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<td>Mean 58 years (range 32-76)</td>
<td>Male 30</td>
<td>Caucasian 32 (71%)</td>
<td>29 cases</td>
<td>Mean LAS 49.1 (before 4/1/2023) Mean CAS 23.5</td>
</tr>
<tr>
<td>Female 15</td>
<td>Black 7 (16%)</td>
<td>&lt;25 9 cases</td>
<td>&lt;35</td>
<td></td>
</tr>
<tr>
<td>Other 6 (13%)</td>
<td>&lt;30 7 cases</td>
<td>&lt;35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. A 54-year-old female receive double lungs transplant with lung ischemic time 11 hours 28 min. left lung ischemic time 12 hours 43 min. Left chest X-ray was took right after the transplant. Right one shows she discharged home after 18 days.
TTV GUIDED BELATACEPT CONVERSION AFTER LUNG TRANSPLANTATION: REPORT OF 7 CASES

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1Medical University of Vienna, Wien, Austria, 2Medical University Vienna, Vienna, Austria

Background: Calcineurin inhibitor (CNI) based protocols are still the standard immunosuppressive regimen (IS) after lung transplantation (LuTx), although CNI-related toxic effects may occur. Lung transplantation (LuTx), although CNI-related toxic effects may occur. Belatacept, a novel immunosuppressant that blocks a T-cell co-stimulation pathway, is a non-nephrotoxic drug indicated as an alternative to CNI-based protocols. It showed an improved IS regimen for patients treated with Belatacept IS. In this study, we investigated the use of TTV-guided Belatacept dosing to overcome this problem.

Methods: We reviewed a series of 7 LuTx recipients with conversion to a CNI-sparing Belatacept IS regimen within the first 3 years post-LuTx (n = 7). Belatacept dosing was started according to the protocol used in kidney Tx recipients and adapted thereafter based on TTV PCR values (therapeutic range log7 – log9 TTV – PCR copies).

Results: Use of Belatacept was triggered by severe renal failure in all patients. Time to Belatacept after LuTx was 44±30 days (mean 401 days). Mean estimated glomerular filtration rate after starting Belatacept had significantly improved 6 months after initiation (GFR ml/min/1.73m² before start was 29.5±1.1 and GFR after 6mo 41.0±4.7, p = 0.039). Tacrolimus dosing was reduced in all patients but not stopped (reduction of target trough level from 1.5–3 ng/ml). There were no episodes of acute cellular (ACR) or humoral rejection (AMR) and none of the patients developed CVD. One patient died due to pulmonary embolism 101 days after Belatacept start. In 3 patients Belatacept dose had to be adapted according to TTV levels (in 2 cases dose had to be increased, in 1 case dose had to be reduced).

Conclusions: Conversion to CNI-reduced Belatacept-based IS with TTV-guided Belatacept dosing improved renal function without increasing risk of ACR, AMR or CVA. Further studies are needed to prove the safety and efficacy of this therapeutic regimen.

INTEGRATED COGNITIVE ERGONOMICS OF THE REMOTE EVALUATION OF THE GRAFTS WITH ROBOTICS AND MACHINE PERFUSION TECHNOLOGY IN SOLID ORGAN TRANSPLANTATION

Constantinos S Mammas1,2, Adamantia S Mamma1
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Background: Big data collected on a real time mode from ESOT’s records on 07.11.2017 have the potential to compute crucial risks, sourcing from the damaged organs interrelated with the human-system design of the remote evaluation of the grafts and decision making in the procurement phase of Organ Transplantation (OT) enhanced by Robotic framework and machine perfusion technology and method.

Methods: In a prospective real time experimentation using the Prometheus digital medical device (pn:2003016) applying AI and the Robotic framework "Stamoulis" for the remote evaluation of the grafts and the robotic based computational analysis for 189,721 transplants in Europe from 2011 to 2016, computed the expected damaged organs and compared with the expected impact of the applied machine perfusion technology and method for trauma, cancer, infection and injury pathologies.

Results: Robotic cognitive ergonomics integration and simulation of the remote evaluation of the grafts in the procurement phase of OT showed and accuracy for liver, renal, pancreas, uterus, heart and lung grafts that ranged from: 90.93–97.6%

Conclusions: Results that showed that Robotic cognitive ergonomics integration simulation of the remote evaluation of the grafts in the procurement phase of OT enhanced significantly operational maneuverability and inter-operability to remotely and instantly: a. Minimize damaged or diseased, with infection, trauma and cancer, grafts applying AI and Big Data analytics and computing, for evidenced real time computations and interventions, b. Develop an international clinical surveillance system integrated with cognitive ergonomics of the remote evaluation of the grafts integrated with robotics and machine perfusion technology. Source: GoST 2011-16.

<table>
<thead>
<tr>
<th>Organ</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>Total</th>
<th>Expected damaged organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>1980</td>
<td>1960</td>
<td>2037</td>
<td>2146</td>
<td>2235</td>
<td>2254</td>
<td>12612</td>
<td>1.261</td>
</tr>
<tr>
<td>Lung</td>
<td>1677</td>
<td>1756</td>
<td>1825</td>
<td>1822</td>
<td>1818</td>
<td>1916</td>
<td>10814</td>
<td>1.081</td>
</tr>
<tr>
<td>Liver</td>
<td>7006</td>
<td>6845</td>
<td>7173</td>
<td>7390</td>
<td>7894</td>
<td>7762</td>
<td>43870</td>
<td>3.510</td>
</tr>
<tr>
<td>Kidney</td>
<td>18712</td>
<td>18684</td>
<td>19227</td>
<td>19670</td>
<td>20102</td>
<td>20638</td>
<td>117203</td>
<td>12.892</td>
</tr>
<tr>
<td>Pancreas</td>
<td>559</td>
<td>525</td>
<td>865</td>
<td>818</td>
<td>821</td>
<td>750</td>
<td>49685</td>
<td>0.96</td>
</tr>
</tbody>
</table>
Background: Gold standard for measuring glomerular filtration rate (mGFR) is the iohexol clearance test. Simple non-invasive estimation of GFR by computed tomography (CT) may hence be achievable when iohexol is used as contrast medium. This study therefore aimed to develop a simple and precise technique to quantify GFR from clinical renal CT by segmentation of the renal pelvis and bladder. Methods: Medical records of adult living kidney donors operated 2013-2022 and patients considered for neoadjuvant cisplatin prior to cystectomy 2019-2022 were reviewed. Inclusion criteria were renal CT obtained before and 7-13 minutes after administration of contrast medium and an iohexol clearance test within three months from the imaging. Estimated GFR (eGFR, mL/min) derived from cystatine C (eGFRcystatin C) and creatinine using both the Cockroft-Gault formula (eGFR-Cockroft-Gault) and the Revised Lund-Malmö formula (eGFRLM18) within 3 months of the CT scan was additionally obtained. To determine GFR from renal CT scans (eGFRCT), renal pelvis and bladder were segmented on CT images. eGFRCT was calculated by: renal volume (ml) * ∆ radiodensity (HU) * contrast medium (grams) / time (minutes). A multivariate linear regression analysis comparing mGFRiohexol to calculated by: renal volume (ml) * ∆ radiodensity (HU) * contrast medium (grams) / time (minutes). A multivariate linear regression analysis comparing mGFRiohexol to

Conclusions: Renal function can be estimated with high precision using standard renal CT. This method might be of special relevance in the assessment of both living and deceased kidney donors as well as in the planning of urologic therapies. However, eGFRCT could potentially be used in any clinical setting where a precise estimate of kidney function and multiphase contrast-enhanced abdominal CT is required. A prospective study is underway.

Results: Out of 339 screened patients, 104 were included in the analysis (mean age: 50 ± 13 years; 61% women). Main reason for exclusion (n=99) was a CT at different voltage than 120 kV. Multivariate linear regression analysis combining GFRCT with body surface area and age gave an adjusted R-square correlation of 0.56 to GFRiohexol (p <0.001). GFRCT had the strongest relationship to GFRiohexol with a mean absolute error (MAE) of 9.8 mL/min, while eGFRLM18 had an MAE of 12.1 mL/min. Figure 1. Conclusions: Renal function can be estimated with high precision using standard renal CT. This method might be of special relevance in the assessment of both living and deceased kidney donors as well as in the planning of urologic therapies. However, eGFRCT could potentially be used in any clinical setting where a precise estimate of kidney function and multiphase contrast-enhanced abdominal CT is required. A prospective study is underway.
Faecal microbiota transplantation for recurrent urinary tract infections in kidney transplant recipients: promising results with research implications

Changliang Cao*, Yongguang Liu’, Jianmin Hu’, Ming Zhao’
‘Zhujiang hospital, Organ transplantation department, Guangzhou, China

Background: Kidney transplant recipients (KTRs) are highly susceptible to infections due to immunosuppressive therapy, with urinary tract infection (UTI) being the most prevalent. The rising antibiotic resistance rates among urinary isolates in KTRs pose significant treatment challenges. According to reports, over 70% of UTIs in kidney transplants are caused by Gram-negative bacilli, predominantly Escherichia coli. Additionally, early post-transplantation, extended-spectrum β-lactamase (ESBL)-producing Enterobacter cloacae is prevalent, whereas ESBL-producing Escherichia coli and Klebsiella pneumoniae dominate after the third month. In response to the escalating antibiotic resistance challenge, faecal microbiota transplantation (FMT) emerges as a potential treatment.

Methods: Eight KTRs with diagnosed recurrent UTIs and associated symptoms underwent FMT treatment. The procedure involved administering frozen capsulized microbiota obtained from healthy donors. Urine culture and urinalysis were performed both before and after the FMT intervention. Additionally, one patient with a complex condition underwent metagenomic next-generation sequencing (mNGS) before and after the FMT intervention to gain deeper insights.

Results: Prior to FMT, seven KTRs were affected by ESBL-producing E. coli, and one by ESBL-producing K. pneumoniae. During the 15 to 31-month follow-up after FMT, all patients displayed a positive response to the treatment, with six out of eight showing no symptoms of UTIs. Two patients experienced symptoms, including one patient with infrequent urination once during the 27-month follow-up and another with fever once during the 20-month follow-up. Both of these symptoms were effectively resolved with sulperazone treatment.

Conclusions: FMT holds promise as an intervention for recurrent UTIs in kidney transplant recipients with ESBL-producing E. coli and K. pneumoniae infections. However, further research is indispensable to comprehend its underlying mechanisms and optimize therapeutic efficacy in this vulnerable patient population.
Background: Kidney transplantation is often seen as the optimal form of kidney replacement therapy for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD-5). Psychosocial factors have been cited to delay their access to a kidney transplant, however it is unclear what these factors are. We undertook a multi-centre qualitative study that explored the range of psychosocial and social factors that CYP, their carers and their paediatric nephrology multi-disciplinary team (MDT) perceived to influence how soon a CYP with CKD-5 accesses a kidney transplant. This included factors that were perceived to influence kidney transplantation outcomes or deemed important to patients and their families in terms of their quality of life (QoL).

Methods: Across 8 paediatric nephrology units in the United Kingdom, semi-structured interviews were conducted with CYP, their carers and their paediatric nephrology MDT. These interviews were reviewed for pertinent themes using thematic analysis following the approach of Braun and Clarke.

Results: A total of 37 interviews were conducted with 13 families and 17 members of the paediatric nephrology MDT. The majority of participating families identified as White (57.1%), followed by Black (21.4%) or Asian (21.4%). The following themes were perceived as important to accessing kidney transplantation and post-transplant outcomes: health beliefs; relationship with and trust in healthcare; support networks; family relationships; socioeconomic circumstances; cultural and religious; and mental health and coping strategies. Specific challenges from living with CKD-5 and living through the COVID-19 pandemic were also discussed due to their impact on QoL and accessing a kidney transplant.

Conclusions: There are a wide range of psychosocial factors that are perceived to influence a CYP’s access to kidney transplantation. Longitudinal and prospective studies are needed to fully assess the relationship between these psychosocial factors and a CYP’s access to, and outcomes of, kidney transplantation.

Background: Ex situ machine perfusion is increasingly used to preserve and assess donor livers prior to transplantation. Compared to traditional static cold storage (SCS), machine perfusion exposes livers to an additional risk of microbial contamination. However, information on the risk of microbial transmission after liver transplantation following either hypothermic oxygenated machine perfusion (HOPE) or normothermic machine perfusion (NMP) is limited.

Methods: A retrospective observational study of patients who underwent liver transplantation after HOPE or NMP preservation between 2014-2022. We examined the microbial transmission from SCS preservation fluid to the machine perfusion fluid and the subsequent recipients.

Results: A total of 155 patients were included, of which 102 patients received a liver after HOPE, and 53 patients after NMP. Although SCS preservation fluid cultures prior to HOPE and NMP were positive for at least one microorganism in 54% and 58%, respectively, machine perfusion fluid cultures were positive in only two cases after either HOPE or NMP. One case of de novo contamination occurred during HOPE. In one recipient of a NMP liver (1.9%), the same E. coli strain was grown from abdominal drain fluid, as was grown from SCS preservation fluid prior to NMP. This patient was otherwise asymptomatic but treated with antibiotics for 14 days. No other cases of microbial transmission after HOPE or NMP were found.

Conclusions: The risk of microbial transmission after machine perfusion is generally very low (1.9% after NMP); however, it is not entirely absent. We observed no difference in the risk of microbial contamination and transmission during and after either HOPE or NMP, despite the fact that NMP inherently carries a higher risk due to the perfusate composition (e.g., red blood cells) and the applied temperature of 35-37ºC. We recommend implementation of routine sampling of machine perfusion fluid at the end of the procedure for microbiological analysis to enable prompt initiation of antibiotics in recipients if indicated.

Table 1. List of microorganisms identified in the cold storage preservation fluid

<table>
<thead>
<tr>
<th>Organism</th>
<th>Origin</th>
<th>Pathogenic*</th>
<th>Frequency n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>Skin</td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Atopobium frenatum</td>
<td>Gut</td>
<td>1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>Gut/Oral</td>
<td>1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Bacillus subtilis</td>
<td>Gut (coli)</td>
<td>1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Bacillus cereus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacillus coagulans</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BacteroidesLoviae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bifidobacterium sp.</td>
<td>Gut</td>
<td></td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Candida sp.</td>
<td>Skin/Gut/Oral</td>
<td>Yes* 7 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>Gut</td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Cylindrocarpon sp.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus sp.</td>
<td></td>
<td></td>
<td>6 (4.5)</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td></td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus gallinarum</td>
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<td></td>
<td></td>
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<tr>
<td>Enterococcus hirae</td>
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</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td>Yes</td>
<td>8 (6.0)</td>
</tr>
<tr>
<td>Faecalibacterium praeputii</td>
<td>Gut</td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus parainfluenza</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kocuria sp.</td>
<td>Skin/Gut/Oral</td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Lactobacillus sp.</td>
<td></td>
<td></td>
<td>6 (4.5)</td>
</tr>
<tr>
<td>Other CNS</td>
<td></td>
<td></td>
<td>22 (16.6)</td>
</tr>
<tr>
<td>Pedicoccus pentosaceus</td>
<td></td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td></td>
<td></td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Prevotella salivae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td></td>
<td></td>
<td>33 (24.8)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td></td>
<td>23 (17.3)</td>
</tr>
<tr>
<td>Streptococcus sp.</td>
<td>Skin/Gut/Oral</td>
<td></td>
<td>6 (4.5)</td>
</tr>
<tr>
<td>Veillonella parvula</td>
<td></td>
<td></td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

*Pathogenic in immunocompromised patients

Figure 1. Graphic overview of all samples available for microbiological analysis during HOPE (Panel A) or NMP (Panel B) procedures.

A. Cultures taken during and after HOPE (n=102)

B. Cultures taken during and after NMP (n=53)
**LATE BREAKING E-POSTERS**

**LBP03**

**PERFUSION PRESSURES, INTRAHEPATIC PERIVASCULAR EDEMA, AND PARADOXICAL WEIGHT LOSS DURING NORMOTHERMIC MACHINE PERFUSION OF HUMAN DONOR LIVERS**

Blanca Lascari1, Sille Bodewes1, Adam M. Thorne1, Marius van den Heuvel1, Robert J. de Haas1, Maarten W.N. Nijsen1, Vincent E. de Meijer1, Robert J. Porte2

1University Medical Center Groningen, Groningen, Netherlands, 2Erasmus MC, Rotterdam, Netherlands

**Background:** Normothermic machine perfusion (NMP) is increasingly used to preserve and assess donor livers prior to transplantation. NMP, however, may also cause adverse effects. We investigated the effect of perfusion pressures during NMP on the development of infrahepatic peri-portal edema (IPE) after transplantation.

**Methods:** All donor livers transplanted after a NMP procedure (Liver Assist; XIVIVO, the Netherlands) between March 2019 and March 2022 were included. Data on perfusion settings, perfusate composition, and clinical outcome were collected. Livers were weighed before and after NMP. CT scans performed in the first week post-transplantation were reviewed for the presence of IPE defined as increased fluid around the Glisson’s capsule.

**Results:** A total of 36 livers were transplanted after NMP. Initially, post-transplant CT scans frequently showed increased IPE. This prompted us to lower perfusion pressures with a median (IQR) of 47 mmHg (42-54 mmHg) for the hepatic artery (HA) and 8 mmHg (7-10 mmHg) for the portal vein (PV). In group T2 we mainly decreased the HA pressure to 44 mmHg (35-50 mmHg), and in group T3 we decreased both pressures to 34 mmHg (30-39 mmHg) for the HA and 7 mmHg (6-8 mmHg) for the PV (Table 1). This change led to a reduction of IPE noted on CT scans but did not negatively affect the venous saturation, lactate clearance, or hepatocellular injury markers during NMP. Instead of developing IPE, most livers lost weight during NMP. Paradoxically, weight loss increased with decreasing perfusion pressures and subsequent reduction of IPE (Table 1). The rate of reduction in liver weight was inversely correlated with the applied PV pressure during NMP (r = -0.52, p = 0.005) and the HA flow (r = -0.38, p = 0.045).

**Conclusions:** NMP of human donor livers is associated with IPE development. Despite this, livers lose weight during NMP, which is more pronounced when a low PV pressure is applied. To avoid IPE, we advocate to apply the lowest perfusion pressures possible to achieve adequate flows and oxygen delivery during liver NMP. The precise mechanisms leading to liver weight loss during NMP require further research.

**LBP04**

**QUALITY OF LIFE OF LIVING KIDNEY DONORS AT CHO RAY HOSPITAL: THE SHORT-FORM 36-ITEM HEALTH QUESTIONNAIRE SURVEY**

Chuan Hoang*, Thang Diep†, Sam Thai†

1Cho Ray Hospital, Department Of Urology, Ho Chi Minh City, Vietnam, 2Pham Ngoc Thach University Of Medicine, Ho Chi Minh City, Vietnam

**Background:** This study aimed to identify the psychological and social effects of kidney donors after kidney donation by using the short-form 36-item health survey (SF-36) as the quality-of-life questionnaire.

**Methods:** A cross-sectional study was conducted on living kidney donors in the Cho Ray hospital’s outpatient department. The donors were assessed their quality of life based on the SF-36 from May 2022 to November 2022. The follow-up ranged from 12 to 264 months after donor nephrectomy (10.7% of kidney donors over 10 years). Most kidney donors had a good quality of life, and 87.5% of the donors would make the same choice again. 10.7% of donors experienced financial hardship, and 8.9% reported negative occupational consequences.

**Conclusions:** The quality of life for kidney donors was not affected by nephrectomy for donation. Living kidney transplantation is safe and suitable for the rescue of patients with end-stage renal disease.

**LBP05**

**HEPATIC ARTERY COMPLICATIONS AFTER LIVER TRANSPLANTATION IN CHILDREN**

Arianna Trizzino*, Domenico Pinelli*, Naire Sansotta†, Paolo Pizzini†, Paolo Marra*a, Lorenzo D’Antiga†, Michele Colledan‡,4

1ASST Papa Giovanni XXIII Hospital, Department of Organ Failure and Transplantation, Bergamo, Italy, 2ASST Papa Giovanni XXIII Hospital, Department of Pediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy, 3ASST Papa Giovanni XXIII Hospital, Department of Radiology, Bergamo, Italy, 4University of Milan-Bicocca, School of Medicine and Surgery, Milano, Italy

**Background:** Hepatic artery complications (HAC) are the most frequent vascular complications and the main cause of graft disfunction and loss after liver transplantation in pediatric population. Its management is still matter of debate.

**Methods:** We retrospectively analysed all the pediatric liver transplantsations performed at Our Institution from January 2006 to December 2022. The aim of this study is to evaluate incidence, risk factors, treatment and outcomes after HAC in children transplanted with different type of grafts. Diagnosis was based on ultrasound, clinical and biochemical variations.

**Results:** 470 patients have been studied. HAC occurred in 58 cases (12.3%): 37/50 left lateral segments (LLS), 10/28 right extended grafts (R-Ext) and 11/52 whole liver (WL) grafts. Intraoperative HA thrombosis occurred in 10 LLS grafts, successfully treated by Redo-anastomosis, Fogarty embolectomy and RPTA in 8 cases. 2 of them were re-transplanted after thrombosis recurrence. The arterial flow was not restored in 2 cases and the patients were retransplanted. We observed 48 postoperative HAC: 23 thrombosis (17 with early onset, < 14 days), 24 stenosis and 1 HA anastomosis damage. Interventional radiological approach was preferred in 40 HAC (83%). It was effective in 6 of 16 thrombosis (0 grafts lost) and in 22 of 24 stenosis (4 grafts lost) but failed in 10 thrombosis (7 grafts lost) and in 2 stenosis (0 grafts lost). HAC risk was associated with retransplantation (p=0.004) and R-Ext grafts (p=0.004) and was closely statistically significant for WL grafts (p=0.05). Neither vascular anomaly of donor and recipient nor the number of anastomoses influenced the HAC incidence (p>0.20). Concomitant biliary complications occurred in 17 cases (29.3%). 22 of the 58 patients with HAC were re-transplanted (37.9%). Graft failure was directly related to HAC in 17 cases. At the multivariable analysis, HAC was confirmed to be an independent risk factor for graft loss (p=0.0002), with graft survival of 54.81±8.79% at 12-24-36 months respectively, but not for patients’ overall survival (p=0.19).

**Conclusions:** The occurrence of HAC was associated with retransplantation and right extended grafts. Radiological treatment is safe and effective in most cases. HAC impact significantly on graft survival but didn’t affect patients’ survival.

**LBP06**

**REVERSIBILITY OF DECEASED DONOR KIDNEY INJURY FOLLOWING DONATION AFTER CARDIOPULMONARY RESUSCITATION: A NATION-WIDE POPULATION-BASED COHORT STUDY**

Dimitra Limnatitou*, Angeliki Kosti*, Ffion Dewi†, Christine Biela†, Kamlesh Patel†, Adnan Shari†, James Hodson†, Vasileios Mavroeidis*, Jay Nath†

1Southmead Hospital, North Bristol NHS Trust, Department of Transplant Surgery, Bristol, United Kingdom, 2Southmead Hospital, North Bristol NHS Trust, Department of Vascular Surgery, Bristol, United Kingdom, 3University Hospitals Birmingham NHS Foundation Trust, Department of Renal Transplantation, Birmingham, United Kingdom, 4Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

**Background:** Donors that had received cardiopulmonary resuscitation (CPR) are frequently used for transplantation. Duration of cardiac arrest and quality of CPR are likely to contribute to the degree of organ ischaemia, and these factors are often difficult to determine at the time of organ offer. The aim was to compare the outcomes for kidney grafts from cardiac arrest donors to those from non-cardiac arrest donors, stratified by the degree of renal dysfunction at the time of donation.

**Methods:** A nation-wide population-based cohort study was performed using prospectively collected data from the National Health Service Blood and Transplant service in the United Kingdom between January 2016 and December 2020 for all deceased donor renal transplants. Kidneys were stratified into three groups depending on terminal creatinine of the donor (normal = <100 µmol/L, raised= 100-200µmol/L and high = >200 µmol/L). Analyses were performed using general linear models. Creatinine levels were log10-transformed when results are summarised using percentage differences or geometric means.

**Results:** A total of N=6,239 kidney donors were included, of whom 43.6% (N=2,718) suffered cardiac arrest, with median CPR duration of 25 minutes. Donor terminal creatinine was found to increase progressively with duration of CPR (p<0.001) by an average of 6.0% (95% CI 5.3%-6.8%) per 10 minutes
of CPR (approximately equivalent to 4.5 µmol/L per 10 minutes). However, for the N=11,375 recipients, there was no significant association between donor CPR duration and 12 month creatinine levels (gradient: -0.6% per 10 minutes of CPR, 95% CI: -1.3%, +0.2%, p=0.131). Recipients from cardiac arrest donors had significantly better 12 month creatinine in all three subgroups of donor terminal creatinine, with this being most pronounced in the high terminal creatinine subgroup (geometric mean: 113 vs. 126 µmol/L, p=0.002).

Conclusions: Our study demonstrates that, whilst duration of CPR correlates with the degree of acute donor renal dysfunction, there is no such association with functional outcomes for recipients. This provides reassurance that raised donor creatinine after cardiac arrest is reversible and appears more favourable than raised donor creatinine due to other causes.

LBP07 ISCHEMIC PRECONDITIONING AMELIORATES MOUSE RENAL ISCHEMIA-REPERFUSION INJURY THROUGH ACTIVATING THE NRF2/HO-1 PATHWAY ENHANCED AUTOPHAGY

Eun Sil Koh1
1The Catholic University of Korea Yeouido St.Mary’s Hospital, Seoul, South Korea

Background: Ischemic preconditioning (IPC), which is a brief and nonlethal episode of ischemia, confers protection against subsequent ischemia-reperfusion (IR) through the up-regulation of endogenous protective mechanisms. Recent studies have reported that the activation of autophagy is associated with IPC. However, there is not fully unveiled the underlying mechanisms involving in giving rise to this IPC. In this study, we investigated the role of IPC in renal IR injury and demonstrated that IPC could ameliorate renal IR injury by activating the Nrf2/Keap1/HO-1 pathway and induction of autophagy.

Methods: In order to gain insights into IPC-induced alterations at the cellular level, an in vitro model for IPC was designed using the human proximal tubule 293 epithelial cell line HK-2. IPC was performed by a 10 min period of incubation of cells under mineral oil followed by a 30 min recovery period prior to the 120 min ischemic insult and reperfusion, along with the treatment of 3-Methyladenine (3-MA) for inhibit autophagy. In a renal IR injury model, mice were subjected to 30 min of renal ischemia followed by 24 h of reperfusion. IPC was produced by a 10 min of ischemia followed by 10 min of reperfusion prior to sustained ischemia.

Results: IPC markedly improve renal IR injury by attenuating renal apoptosis, and tolerable anti-CMV therapies on patients’ perspectives of symptoms and emotional, physical and social well-being.

Conclusions: In conclusion, the results of the present study indicate that IPC protects against renal injury induced by IR through activation of autophagy and Nrf2/Keap1/HO-1 pathway.

Table. Most frequently reported, most important to improve and most bothersome concepts describing signs and symptoms and impact of difficult-to-treat post-transplant CMV, as reported during semi-structured interviews.

<table>
<thead>
<tr>
<th>Number (%) of participants reporting concepts</th>
<th>N=28*</th>
<th>N=28*</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms</td>
<td></td>
<td></td>
<td>(90 concepts across 7 domains)</td>
</tr>
<tr>
<td>Most frequently reported concepts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>37(100)</td>
<td>LACK OF PHYSICAL ENERGY</td>
<td>28 (54.3)</td>
</tr>
<tr>
<td>Fever</td>
<td>35(100)</td>
<td>UNABLE TO COMPLETE HOUSEHOLD Chores</td>
<td>33 (54.4)</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>30(100)</td>
<td>ANXIETY</td>
<td>22 (42.9)</td>
</tr>
<tr>
<td>Most important to improve concepts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>4 (14.3)</td>
<td>ANXIETY</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>Fever</td>
<td>3 (10.7)</td>
<td>NEED TO TAKE PRECAUTIONS</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>3 (10.7)</td>
<td>LACK OF PHYSICAL ENERGY</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>Most bothersome concepts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>11 (44.7)</td>
<td>UNABLE TO COMPLETE HOUSEHOLD chores</td>
<td>5 (35.6)</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>9 (35.7)</td>
<td>ANXIETY</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>Fingertips</td>
<td>4 (14.3)</td>
<td>LACK OF PHYSICAL ENERGY</td>
<td>3 (21.4)</td>
</tr>
</tbody>
</table>

* The denominator for Most bothersome differs between concepts, as only participants who received post-transplant CMV infection were also asked about impacts on the bothersome concepts. A total of 28 participants provided at least 1 concept to the most bothersome concepts.

Figure. Number of participants (out of 28 total) reporting impact of difficult-to-treat post-transplant CMV by domain.

LBP09 EXPERIENCE AND BURDEN OF POST-TRANSPLANT CYTOMEGALOVIRUS INFECTION AND TREATMENT FROM THE PATIENT’S PERSPECTIVE

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Background: Patient-reported data on how cytomegalovirus (CMV) infection in transplant recipients impacts patients’ health, well-being, and daily activities are limited. This study based on qualitative interviews is the first, to our knowledge, to examine signs/symptoms and impact of post-transplant CMV from a patient perspective.

Methods: Participants were adults (≥18 years) with a past or current clinician-confirmed difficult-to-treat CMV infection (eg, intolerance to treatment, resistant, refractory, and/or recurrent infection; or presence of co-morbidities) following solid organ or allogeneic hematopoietic stem cell transplant (SOT or HSC/T, within the last 5 years prior to recruitment; 2015–2022). Participants were recruited via outreach to recruitment agencies, clinical sites, advocacy groups, and patient organizations. Participant informed consent and ethics approval were obtained. Semi-structured, qualitative, virtual, 60-minute, 1:1 interviews with participants were conducted by trained interviewers to describe signs/symptoms, impact, and disease/treatment burden of post-transplant CMV. Transcribed audio-recordings were anonymized, coded, and analyzed using qualitative data analytic methods, including concept frequency, clarification (eg, symptom severity and related impacts), and bothersome analyses. Concepts were organized into a patient-centric CMV conceptual model.

Results: 28 participants from the US (n=16), Germany (n=5), France (n=4) and the UK (n=3) were interviewed between May 2021 and September 2022. Participants had a mean±SD age of 51.8±13.1 years; 60.7% (n=17) male. The majority (78.6%; n=22) were SOT recipients. Refractory CMV was the most common type of difficult-to-treat CMV (n=11; 39.3%). CMV infection was reported as moderate to very severe by 17 (60.7%) participants. Of 26 CMV-related signs and symptoms (table and figure) concepts, 26 participants reported tiredness (60.7%), fever (53.6%), lack of physical energy (64.3%), and anxiety (42.9%). A further 23 and 20 concepts were related to disease or treatment burden, respectively.

Conclusions: Further research is needed on the impact of more effective and tolerable anti-CMV therapies on patients’ perspectives of symptoms and emotional, physical and social well-being.
CAN CT ANGIOGRAPHY REPLACE RENAL SCINTIGRAPHY FOR PREDICTION OF SPLIT RENAL FUNCTION IN PREOPERATIVE LIVING KIDNEY DONOR ASSESSMENT?

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1University Hospital CHUV, Department of Visceral Surgery, Lausanne, Switzerland, 2University Hospital CHUV, Department of Nuclear Medicine, Lausanne, Switzerland, 3University Hospital CHUV, Transplantation Center, Lausanne, Switzerland, 4University Hospital CHUV, Department of Diagnostic and Interventional Radiology, Lausanne, Switzerland

Background: In living donor kidney transplantation, the decision regarding which donor kidney to retrieve is based on anatomy and split renal function (SRF). The study aim was to compare split renal volume (SRV) and SRF measured on CT angiograms (CTA) and that of SRF of renal scintigraphy to predict donor residual single kidney function.

Methods: Retrospective monocentric study including all consecutive patients considered and assessed for living donor nephrectomy between 01/2005 and 05/2022. To determine SRV on CT, regions of interest (ROI) were drawn over kidneys using a semi-automatic interactive algorithm, and SRF was expressed as percentage (%). For each kidney, renal enhancement (E) was calculated as the difference between CT numbers of all ROIs from enhanced and unenhanced series to obtain the SRF (%). SRF was also measured with Tc-99m-MAG scintigraphy. Correlations between these measures were evaluated by linear regression analysis (Pearson correlation coefficient).

Results: A total of 393 patients were included. Mean age was 53 years (SD 12), mean BMI was 25.0 kg/m2 (SD 3.6), and 130 (39.2%) were male. The right kidney was chosen in 185 (47%) cases for donation, because of better functional or vascular anatomy. The correlations between CT-SRV/CT-SRF and scinti-SRF of the preserved kidney were low (respectively r=-0.089 and r=0.032). The mean absolute difference of predonation SRF between preserved and scinti-SRF of the preserved kidney were low (respectively r=-0.089 and r=0.032). The mean absolute difference of predonation SRF between preserved and donated kidney was lower for CTA than renal scintigraphy (2.4 vs 6.8%, p<0.001).

Conclusions: Morphology (SRV) and function (SRF) derived from CTA alone should not replace functional data (SRF) provided by renal scintigraphy in order to determine which donor kidney to retrieve. These results suggest that kidney volume does not necessarily correlate with kidney function, and each potential donor should benefit from both investigations for anatomy and relative function.

OPTIMIZATION OF HLA MATCHING IN KIDNEY ALLOCATIONS, WITH MINIMAL EFFECT ON QUEUE

Sapir Israeli1*, Ronit Pasovsky Gutman2, Maya Mor Cohen1, Ron Loewenthal3, Eytan Mor2, Benaya Rosen Zvi3, Moshe Israeli1, Yoram Louzoun3
1Bar Ilan University, Ramat Gan, Israel, 2Sheba Medical Center, Ramat Gan, Israel, 3Rabin Medical Center, Petah Tikva, Israel

Background: HLA matching between the donor and the recipient can extend the lifespan of the transplanted kidney, and prevent the emergence of donor-sensitized antibodies. In Israel, kidney donations have three origins: altruistic or paired living donations and deceased donors. In all three, the HLA match is only considered as a minor contribution to the allocation score.

Methods: We analyzed recent altruistic, deceased, and paired living donations from two hospitals, with a total of 172, 35, and 28 pairs, respectively. Sensitive recipients were not studied. We computed the match assuming optimal pairing, considering the blood type and age of the donor and recipient, and using a linear programming solution. Such a match requires extensive changes to the order. To maximize the match, with a minimal effect on the kidney allocation queue (Top-K method), we tested the optimal match allowing only a choice between the K top candidates of the queue, (K=2-10), ensuring blood type and age matching. A patient that waited more than K-1 positions automatically receives the next blood type and age matched transplant. We further tested whether it is possible to improve the HLA matching for related donor-patient pairs, by allowing crossover in chain transplants.

Results: In altruistic and disease donors, the optimal matching level is 3-4 times higher when testing either HLA-B&DRB1, or only class II or all 5 loci (Optimal vs Current in table), and keeping into consideration blood type and age limitation. Even when we limit the perturbation, and ensure no one is moved more than 10 positions in the queue, the match level is twice higher, with practically no change to the queue (Top10 in table). The same occurs for related pairs.

Conclusions: Minimal modifications of the kidney allocation queue can improve the HLA match. This method can accommodate any HLA alleles combination that is desired to maximize their match.

<table>
<thead>
<tr>
<th>HLA Matching</th>
<th>5 loci Class II</th>
<th>B&amp;DRB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altruistic</td>
<td>Current</td>
<td>1.76</td>
</tr>
<tr>
<td></td>
<td>Optimal</td>
<td>4.68</td>
</tr>
<tr>
<td></td>
<td>Top10</td>
<td>2.51</td>
</tr>
<tr>
<td>Deceased</td>
<td>Current</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Optimal</td>
<td>3.56</td>
</tr>
<tr>
<td></td>
<td>Top10</td>
<td>2.74</td>
</tr>
<tr>
<td>Paired</td>
<td>Current</td>
<td>3.96</td>
</tr>
<tr>
<td></td>
<td>Optimal</td>
<td>4.57</td>
</tr>
<tr>
<td></td>
<td>Maximal</td>
<td>10</td>
</tr>
</tbody>
</table>

Current allocation: Average HLA match - 1.6

The options to choose from top 3

Best from top 3: Average HLA match - 3

Top K method (K = 3). ID is the position in the current queue (1 is top current queue in first row). Middle row – Current donors and their HLA match to each patient. Bottom row rearranged queue by Top3 method.
**LATE BREAKING E-POSTERS**

**LBP12**

**ARTIFICIAL INTELLIGENCE IN PREDICTING PATIENT AND GRAFT SURVIVAL FOLLOWING DECEASED DONOR LIVER TRANSPLANTATION**

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1Korea University College of Medicine, Surgery, Seoul
2Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, University Hospital RWTH-Aachen, Aachen, Germany

**Background:** Although the Model for End-stage Liver Disease (MELD) score is commonly used to prioritize patients awaiting liver transplantation, previous studies have indicated that MELD score may fail to predict well for the postoperative patients. Similarly, other scores (D-MELD score, balance of risk score) that have been developed to predict transplant outcome have not gained widespread use. These scores are typically derived from linear statistical models. The aim of this study was to compare the performance traditional statistical models with machine learning approaches in predicting survival following liver transplantation using multi-center data.

**Methods:** Data came from 785 deceased donor liver transplant recipients enrolled in the Korean Organ Transplant Registry (KOTRY, 2014–2019). Five machine learning methods and 4 traditional statistical models were compared for the prediction of survival.

**Results:** Of the machine learning methods, random forest (RF) yielded the highest area under the receiver operating characteristic curve (AUC-ROC) values (1 month = 0.94, 3 month =0.97, 12 month = 0.92) for predicting survival. The AUC-ROC values of Cox regression analysis was 0.80, 0.89 and 0.84 for 1month, 3month and 12 month posttransplant survival, respectively. However, the AUC-ROC values of the MELD, D-MELD and BAR score were all below 0.70.

**Conclusions:** Machine learning algorithms such as random forest was superior than conventional cox regression and previously reported survival scores in predicting 1 month, 3month and 12 month survival following liver transplantation. Therefore, artificial intelligence may have significant potential in providing assistance with clinical decision making during liver transplantation including matching donors and recipients.

**LBP13**

**PANCREATIC CYSTIC LESIONS IN IMMUNOSUPRESSED PATIENTS WITH SOLID ORGAN TRANSPLANTATION**

Young-dong Yu1*,2, Hye-Sung Jo1, Dong-Sik Kim1
1Korea University College of Medicine, Surgery, Seoul
2Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, University Hospital RWTH-Aachen, Aachen, Germany

**Background:** Solid organ transplant recipients have an increased risk of cancer due to immunosuppressive therapy. Pancreatic cystic lesions (PCLs) are increasingly being detected, some with malignant potential. We aimed to determine the prevalence of these lesions and describe their clinical course in these patients.

**Methods:** We identified the presence of pancreatic cystic lesions in a retrospective cohort of 804 consecutive solid organ transplant recipients from 2009 to 2019 and compared lesion characteristics at initial and follow-up imaging, when available. We also compared these features with an immunocompetent control group encompassing patients under surveillance for greater than 12 months.

**Results:** There were 7 and 60 patients in the study group and 60 patients in the control group. There were no significantly different features including the rate of size increase or the development of worrisome features between the study and control group. Similarly, other scores (D-MELD score, balance of risk score) that have been developed to predict transplant outcome have not gained widespread use. These scores are typically derived from linear statistical models. The aim of this study was to compare the performance traditional statistical models with machine learning approaches in predicting survival following liver transplantation using multi-center data.

**Conclusions:** Pancreatic cystic lesions are somewhat common in solid organ transplant recipients. In lesions without high-risk features, the development of features worrisome for cancer is rare. These lesions can be managed conservatively, and their presence should not affect transplant eligibility.

**LBP14**

**IMPROVED PRESERVATION BY OMNISOL COMPARED TO RED BLOOD CELL PERFUSATE FOR 6 HOUR NMP OF WARM ISCHEMIA-DAMAGED PORCINE KIDNEYS**

Laura Zarnitz*, Benedict Doorschodt1,2*, Lisa Ernst1, Tamara Fechter1, Alexander Theissen1, René Tolba1, Christian Bleilevens1
1Department of Anesthesiology, Faculty of Medicine, University Hospital RWTH-Aachen, Aachen, Germany
2Institute for Laboratory Animal Science and Experimental Surgery, Faculty of Medicine, University Hospital RWTH-Aachen, Aachen, Germany

**Background:** Normothermic machine perfusion (NMP) is increasingly applied in clinical practice since it holds the potential of increasing the viability of marginal grafts. NMP offers the possibility of real-time viability assessment and therapeutic intervention prior to transplantation, in contrast to hypothermic preservation methods. A readily available cell-, albumin- and oxygen carrier-free solution could enhance employment of NMP and potentially prevent adverse effects, such as inflammation transfusion reactions and hemolysis, associated with packed red blood cell (pRBC)-based perfusates.

**Methods:** In this study, the novel cell- and oxygen carrier-free organ preservation solution Omnisol for cold storage and hypothermic machine perfusion was compared to a clinically established pRBC-based perfusate (pRBC) protocols. In the Omnisol group, porcine kidneys were cold stored in Omnisol for 24 h, followed by NMP using the same solution and compared to NMP using pRBC, directly after transplantation. All kidneys sustained 20 min of warm ischemic damage and NMP was applied at 75 mmHg using 1L/min oxygenation at 37°C.

**Results:** In the Omnisol group, renal blood was over 3-fold higher after 1 h of NMP compared to NMP using pRBC, directly after transplantation. All kidneys sustained 20 min of warm ischemic damage and NMP was applied at 75 mmHg using 1L/min oxygenation at 37°C.

**Conclusions:** Omnisol solution demonstrated improved preservation quality for cold storage followed by NMP compared to direct NMP using a pRBC-based perfusate during 6 h NMP of warm ischemia-damaged porcine kidneys.

**Graph:**

- **Arterial Flow (mL/min)**
- **Time (min)**

- 0
- 200
- 400
- 600
- 800

- LEVEL ONE
- LEVEL TWO
- LEVEL THREE
- LEVEL FOUR
- LEVEL FIVE

- *P<0.05
- **P<0.01
- ***P<0.001
Background: Despite requiring opposite treatments, BKV and T cell-mediated rejection (TCMR) can exhibit overlapping clinical and histological features, presenting a diagnostic dilemma with significant implications for patient management. Novel tools are thus needed to help confirm the diagnosis and predict response to treatment. Then, we aimed to distinguish the BKPyVN and TCMR from microenvironment by single-cell RNA sequencing (scRNA-seq).

Methods: Single-cell RNA seq was performed on 2 stable grafts (STA), 5 BKPyVN, and 2 TCMR (Fig. A).

Results: 41,565 single cells were clustered into fourteen major clusters. With marker-based annotations, seven major cell types were identified in STA, BKPyVN and TCMR microenvironments had a similar cellular composition (Fig. D). However, there were slight variations in the percentage of cells in each microenvironment. Moreover, we found the PT exhibited the highest contribution score among all subsets, indicating that it was crucial for aggravating disease progression in both BKPyVN (Fig. E) and TCMR (Fig. F). Specifically, in BKPyVN, we noticed subsets, indicating that it was crucial for aggravating disease progression in both BKPyVN and TCMR from heterogeneity of microenvironment.

Conclusions: The microenvironment heterogeneity bears significant implications for distinguishing BKPyVN and TCMR, despite the clinical convergence of their phenotypes. These findings present a substantial advancement in diagnostic tools, ultimately facilitating the precise identification and management of these intricate kidney transplant-related disorders.

LATE BREAKING E-POSTERS

LBP15 SINGLE-CELL RNA-SEQ REVEALS THE HETEROGENEITY OF MICROENVIRONMENT BETWEEN BKPYVN AND TCMR

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1Sun Yat-sen University, The First Affiliated Hospital, Guang Zhou, China, 2Sun Yat-sen University, Guang Zhou, China

LBP16 OUTCOMES FOR DECEASED DONOR KIDNEY TRANSPLANTATION FOLLOWING DONOR CARDIAC ARREST: A NATION-WIDE POPULATION-BASED COHORT STUDY

Dimitris Limnatiotis1, Angeliki Kosti1, Ffion Dew1, Christine Biela1, Kamilesh Patel1, Adnan Shafii1, James Hodson2, Jay Nath3, Vasileios Mavroeldis1
1Southmead Hospital, North Bristol NHS Trust, Department of Transplant Surgery, Bristol, United Kingdom, 2Southmead Hospital, North Bristol NHS Trust, Department of Vascular Surgery, Bristol, United Kingdom, 3University Hospitals Birmingham NHS Foundation Trust, Department of Renal Transplantation, Birmingham, United Kingdom, 4Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

LBP17 SURVIVAL BENEFIT OF KIDNEY TRANSPLANTATION IN PATIENTS WITH END-STAGE KIDNEY DISEASE AND PRIOR ACUTE MYOCARDIAL INFARCTION

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Background: Patients with end stage kidney disease (ESKD) and a previous acute myocardial infarction (AMI) have less access to KT.

Methods: Data on ESKD patients with an AMI history who underwent first KT or dialysis between January 2007 and December 2018 were extracted from the Korean National Health Insurance Service. Patients who underwent KT (n=423) were chronologically matched in a 1:3 ratio with those maintained on dialysis (n=1,269) at the corresponding dates, based on time-conditional propensity scores.

Results: The 1-, 5-, and 10-year cumulative incidences for all-cause mortality were 12.6%, 39.1%, and 60.1% in the dialysis group and 3.1%, 7.2%, and 14.5% in the KT group. Adjusted hazard ratios (HRs) of KT versus dialysis were 0.17 (95% confidence interval [CI], 0.12–0.24; P<0.001) for mortality and 0.38 (95% CI, 0.23–0.51; P<0.001) for major adverse cardiovascular events (MACE). Of the MACE components, KT was most protective against cardiovascular death (HR, 0.23; 95% CI, 0.12–0.42; P<0.001). Protective effects of KT for all-cause mortality and MACE were consistent across various subgroups, including patients at higher risk (e.g., age >65 years, recent AMI [≥6 months], congestive heart failure).

Conclusions: KT is more beneficial than maintenance dialysis in reducing all-cause mortality and MACE in ESKD patients with a prior AMI.
Results: Of the full analysis set (FAS, N=4028 patients), 887 were from Asian countries (92 ECs; 795 LCs). Most patients (59.0%) were male, with a mean age of 49.5 years and a mean eGFR of 66.8 mL/min/1.73m² at conversion. There was a decreasing trend in eGFR post-conversion in the Asian cohort (Figure). At 5 years post-conversion, the mean change in eGFR from baseline was -3.35 vs -1.36 in FAS. The median PRT dose remained stable at 3.0 mg/day throughout the study. The median tacrolimus trough level was 4.9 ng/mL at 5 years post-conversion (Table). At 5 years post-transplant Kaplan-Meier estimate of patient survival was 98.9% and graft survival was 97.8%. Overall, 1.4% of patients who were negative prior to or at conversion had DSA occurrence post-conversion. At study end, 78.2% of patients remained on PRT. Adverse events (AEs) were reported in 58.1% of enrolled Asian patients; 9.1% had ≥1 PRT-related AE.

Conclusions: There was a decreasing trend in renal function in the Asian cohort. Patient and graft survival estimates in the Asian cohort were similar to the overall study group.

Background: Organ transplantation criteria and capabilities may differ in Asia compared to Europe and North America. Conversion from twice-daily (BID), immediate-release tacrolimus (IRT) to once-daily (OD), prolonged-release tacrolimus (PRT; Advagraf®, Astellas Pharma Europe, Ltd.) is associated with improved short-term outcomes in kidney transplant recipients (KTRs). This subgroup analysis of a prospective, global, non-interventional CHORUS study (NCT02555787) assessed 5-year long-term clinical outcomes in KTRs enrolled in Asian countries who converted from BID IRT to OD PRT.

Methods: The study enrolled KTRs (≥18 years, N=4389) converting to PRT according to the treating physician’s judgment. KTRs were grouped by time of conversion post-transplant to early (≤6 months) converters (ECs) and late (>6 months) converters (LCs). The primary endpoint was the change in renal function (measured by estimated glomerular filtration rate, eGFR) from conversion up to 5 years. Secondary endpoints included graft and patient survival, tacrolimus dose and trough levels, emergence of donor-specific antibodies (DSA) and safety.

Table. PRT dose and tacrolimus trough levels (FAS, Asian cohort)

<table>
<thead>
<tr>
<th>Time after conversion (months)</th>
<th>Early converters</th>
<th>Late converters</th>
<th>Total (FAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
</tr>
<tr>
<td>6</td>
<td>3.9 (3.7-4.1)</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
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<tr>
<td>12</td>
<td>3.9 (3.7-4.1)</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
</tr>
<tr>
<td>24</td>
<td>3.9 (3.7-4.1)</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
</tr>
<tr>
<td>36</td>
<td>3.9 (3.7-4.1)</td>
<td>4.0 (3.9-4.1)</td>
<td>4.0 (3.9-4.1)</td>
</tr>
</tbody>
</table>

Adverse events were reported in 58.1% of enrolled Asian patients; 9.1% had ≥1 PRT-related AE.

Conclusions: There was a decreasing trend in renal function in the Asian cohort. Patient and graft survival estimates in the Asian cohort were similar to the overall study group.
Background: During the initial phase of the persisting COVID-19 pandemic mortality was very high in kidney transplant recipients (KTR). In the general population, vaccines were the most important efforts in stopping the pandemic. In KTR a low humoral response to primary vaccination against SARS-CoV-2 was soon detected and additional booster-doses were recommended. However, a significant proportion of KTR remain vaccine unresponsive or with very low measurable antibody (AB) levels even after receiving up to five previous doses. Should we continue vaccinating KTR with additional doses? We here demonstrate the impact of a sixth vaccine dose on humoral vaccine response in KTR.

Methods: We included KTR (>18 years) who had previously received five doses of the mRNA-based vaccines Spikevax® (Moderna) or Comirnaty® (Pfizer) with no physician- or self-reported infection with SARS-CoV-2. The level of SARS-CoV-2 IgG anti-S AB were quantified by an in-house flow cytometry method 4-6 weeks after vaccination. The measured AB response after dose 5 was used as a baseline for evaluating the effect of dose 6. All patients were on a triple immunosuppressive regimen consisting of calcineurin-inhibitors, myco-phenolate, and prednisolone.

Results: Of the 1168 KTR with measured vaccine response after dose 5, we included 167 whom so far have received dose 6 and measured response after 5 [4, 6] weeks. This cohort had a median [IQR] age of 70 [63, 75] years, 59% male, and were 6 [4, 15] years post-transplantation (66% with deceased donor). Following the sixth dose, median AB concentration increased from 261 [1, 3733] to 2288 [2, 12039] binding antibody units per millilitre (BAU/mL), and the proportion of individuals with no previous vaccine response (<5 BAU/mL) was reduced from 32% to 25% (Figure 1). Additionally, there was a substantial increase in the proportion of individuals with high response (>5000 BAU/mL) from 22% to 40%. The level of poor responders. This is in line with previous observations following dose 3, 4, and 5, and as such we recommend continued vaccination in non- to low-responders.

Conclusions: Our study reveals that a sixth dose of the mRNA-based COVID-19 vaccines may ultimately be used as biomarkers of disease progression in clinical trials. Furthermore, links were found between protein expression and clinical measurements (bilirubin, prothrombin time, platelet count), suggesting potential as early diagnostic markers.

Figure 1. A volcano plot based on fold change (Log2) and P value (Log10) of all proteins identified.
Background: Experimental lung injury and transplantation models in large mammals are an important translational tool for exploring novel lung therapies. However, understanding the complex spatial and morphological changes that arise in injury, after transplantation, and after a given treatment, is a challenge. Current imaging readouts lack the sensitivity, resolution and multiplex capacity to explore lung spatial biology, particularly in human and large animal models.

Methods: Lung tissue biopsies were taken from porcine lung tissue after acute lung injury with gastric aspiration, ex vivo lung perfusion and transplantation to a recipient. These tissues were used to develop an advanced light imaging pipeline to generate more advanced morphological readouts and build on our understanding of the pulmonary environment after each of these processes.

Results: Through high resolution imaging of the bronchoalveolar scaffold we have developed a novel alveolar morphology readout capable of extrapolating the precise changes that occur in alveolar wall thickness and circularity after injury and transplantation. Furthermore, we have developed the first multiplex advanced imaging pipeline compatible with porcine tissue which reveals discordant quantitative architectural changes across several proteins.

Conclusions: These data represent the inception of a more detailed means to study the molecular mechanisms of acute lung injury and transplantation. Application of this pipeline to broader human and large mammalian transplant research will serve to better understand how our exploratory therapies improve graft survival and guide the development of future therapies.

Background: This presentation focuses on the results of our Lung Transplantation Program from its beginning and what innovations we performed to rebuild our Program after the coronavirus pandemic, when we have centralised recipient evaluation and have simplified the referral process. We also implemented personal visits to the pulmonology clinics and wards as a new feature.

Methods: We made retrospective data analysis of all transplanted patients and all donors between 12.12.2015-27.04.2023. We extracted data from healthcare software, Eurotransplant Statistics Library, DonorData and our transplantation (Tx) databases. We also used data from the National Blood Transfusion Service.

Results: After an uneventful beginning, the Program was still relatively young when a pandemic coronavirus disease spread all around the World. There was a dramatic shortage of donors, and the recipients’ condition worsened. The recipients’ evaluation process stopped. After the end of the COVID-19 pandemic, it was necessary to reorganise both the recipient and donor sides. The recipients’ evaluation process stopped. After the end of the COVID-19 pandemic, it was necessary to reorganise both the recipient and donor sides. The recipients’ evaluation process stopped. After the end of the COVID-19 pandemic, it was necessary to reorganise both the recipient and donor sides.

Conclusions: We suggest that the use of HBsAg positive donors is safe and should be considered, particularly in moderate risk recipients. Due to the severe shortage of the donor pool, the use of hepatitis B surface antigen-positive donors is a possible strategy to increase the donor pool, but there are few data about the outcomes in liver recipients with hepato-cellular carcinoma (HCC) and their recurrence rate.

Methods: Patients undergoing liver transplantation (LT) between January, 2004, and November 2022, were retrospectively evaluated. 17 patients (1.5%) with HCC, received the graft from hepatitis B surface antigen positive (HBsAg)-positive deceased donors

Results: All patients were male and Milan. Median time of follow up was 63±5 months. Median MELD was 16. Seven (41%) recipients had not an HBV-related liver disease. Only one patient before LT had hepatitis B surface antibodies. Three patients had an HBV/HDV cirrhosis. In all recipients HBV DNA was suppressed at the time of LT. Eight (47%) patients did a prophylaxis with HBV-specific immunoglobulins after LT. At 1 – 3 and 5 year in all the recipients hepatitis B surface antigen positivity was recorded. Only one patient developed hepatitis B surface antibodies but was immunized before LT. HBV DNA was detected in one patient at 1 and 3 years, but they were responsive to antiviral treatment. Only one patient had HCC recurrence. Overall survival at 1-3 and 5 year was 76.5%.

Conclusions: We suggest that the use of HBsAg positive donors is safe and is in our cohort of HCC transplanted patients, only one experienced HCC recurrence. Moreover, it would be fundamental to immunize all patients before LT.
LATE BREAKING E-POSTERS

LBP31
ACTIVE PARTICIPATION DURING THE EDUCATIONAL PROCESS OF DONATION AFTER CIRCULATORY DEATH AT EXTRA CORPOREAL MEMBRANE OXYGENATION INTENSIVE CARE UNITS

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Background: Participatory Action Research (PAR) is a theoretical approach offering experimentation with evidence-based and people-based inquiry and are promoting the grounding of knowledge in human agency and social history. Intervention research examines the effects of an intervention with an outcome of interest, in this case how active participation from ICU nurses can frame a feeling of participation, secureness and curiosity for the caring team in the complex caring situation of Donation after Circulatory Death (DCD) at Extra Corporal Membrane Oxygenation (ECMO) - ICU's.

Methods: Aim: Evaluate active participation during the educational process of DCD, and if active participation can frame a feeling of comfortability and secureness for the ICU nurses in the caring situation of a potential DCD donor patient with on-going ECMO-treatment. • Can active participation from the ICU nurse during educational process lead to an experience of comfortability and secureness in the complicated process of DCD and ECMO-treated patients? • Can a specific made education plan lead to a feeling of participation, secureness and curiosity for the complex process of DCD and ECMO-treated patients. A quasi-experimental, nonequivalent two group design. One experimental group and one active control group. A quantitative non-standardized questionaries will collect data before and after the intervention.

Results: Caring of a potential organ donor patient is described as a complex and multidimensional situation. ICU nurses care for the patient as a patient with an extreme need of intensive treatment. When treatment goes from lifesaving for the patient himself to a situation with focus on medical treatment for the organs for someone else, the dimension of caring changes, and a deeper level with a need for reflection and contemplation for the ICU nurse is illuminated.

Conclusions: The DCD-process and ECMO-treatment is an un-explored area, which leads to a huge need for further dissemination of this type of studies worldwide. By create an education plan managed by ICU nurses, for ICU nurses by using their active participation, the process hopefully manage a new way to avoid ethical challenges and dilemmas during implementation of complicated processes at ECMO-ICU's worldwide in the future.

LBP32
CHANGES IN ENDOGENOUS PEPTIDES IN DCD KIDNEY BIOPSIES ASSOCIATE WITH PROLONGED WARM ISCHAEMIA

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Background: Warm ischaemia (WI) is an inherent part of the donation after circulatory death (DCD) pathway. Functional WI (fWI) starts when donor blood pressure drops below 50 mmHg until in-situ cold perfusion, and associates with organ hypoperfusion, and a switch to anaerobic glycolytic metabolism. DCD kidneys have increased incidence of delayed graft function and early graft loss posttransplant, however the molecular implications of WI on kidney quality remains under-explored. Here, we investigate protein degradation and biological dysregulation in pretransplant kidney biopsies from DCDs with prolonged fWI.

Methods: Pretransplant kidney biopsies (n=42) from DCDs were selected from the Quality in Organ Donation (QUOD) biobank. Two experimental groups were defined as short (<25 minutes; n=15) and long (30-120 minutes; n=27) fWI. Biopsies were analysed using High-efficiency Undecanal-based N-TERmini enrichment (HUNTER) degradomics. Endogenous peptide sequences were used to identify probable degraded proteins and cleaving proteases, using MaxQuant, Uniprot and the MEROPS database. Reactome pathway analysis was used to compare degradome data between long and short fWI groups.

Results: Degradomics mass spectrometry analysis identified 2,563 peptides matched to 1,053 proteins. Peptide cleavage sites linked to 63 proteases, likely catalytic activity, and degradation of cytoskeletal and extracellular matrix (ECM). Correlation analysis of peptidomes against the continuum of fWIT suggest that 78 proteins were differentially degraded and signposts to the activity of 7 key proteases. Differences in protein cleavage patterns and protease activity between long vs short fWI groups indicate that 78 proteins were differentially degraded and signposts to the activity of 7 key proteases. Differences in protein cleavage patterns and protease activity indicate that dysregulated pathways include metabolism and oxygen transport, catalytic activity, and degradation of cytoskeletal and extracellular matrix (ECM).

Conclusions: Our results provide evidence that prolonged fWI associates with protein degradation that may alter the kidney ECM and cytoskeleton. Further mapping of tissue protein degradation will provide novel insights into the impact of hypoxic injury on donor kidneys.

Figure 1

EnhancedVolcano

-Log10 p-value from Linear Model

Log2 fold Change from Grouped Comparison (Long/Short)

total = 534 variables
**LATE BREAKING E-POSTERS**

**LBP34** 440 CONSECUTIVE HAND-ASSISTED-RETROPERITONEOSCOPIC DONOR-NEPHRECTOMIES (HARP): A COMPREHENSIVE ANALYSIS OF THE INTRAOPERATIVE CHALLENGES

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**Background:** This analysis highlights the various pitfalls and challenges encountered in living kidney transplantation. This study aims to evaluate the outcomes and trends within an established living kidney program, providing valuable insights into the effectiveness and advancements in this area of transplantation.

**Methods:** A retrospective analysis was conducted on a cohort of living kidney transplant recipients who underwent transplantation at a specialized German transplant center between 06/2010 and 06/2023. Relevant data, recipient demographics, surgical data, post-transplant outcomes, and long-term follow-up, were extracted from a prospective database. Statistical analyses were performed to assess graft survival, patient survival, complications were categorized in vascular, urinary tract associated, device- and donor associated pit falls.

**Results:** A total of 440 living kidney transplant procedures were included in the study. The mean age of the recipients was 52.8 ± 11 years, with a slight female predominance 55.5% female. All kidney grafts were taken out with hand assisted total retroperitoneal nephrectomy (HARP). 65% (286) were left kidneys. No conversion surgery had to be performed. Time of kidney explantation was 108.4 ± 27.9 min, time of the whole donation surgery 130 ± 27.5 min, warm ischemic time during kidney harvest was 122 sec ± 57, blood loss of the recipients was 49.2 ± 42 ml, 64 donors 16.4% had multiple arteries and veins.

**Conclusions:** The importance of blood loss, warm ischemia time, and operative time. By addressing these pitfalls, we can strive to improve the overall success and long-term outcomes of living donor renal transplantation and enhance the quality of life for transplant recipients. The importance of blood loss, warm ischemia time, and operative time.

**LBP36** INCREASED PERCENTAGES OF CD8+DR+ T-CELLS IN PATIENTS WITH DIFFICULT TO CONTROL CMV INFECTION IN SOLID ORGAN RECIPIENTS: A NEW BIOMARKER?

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**Background:** CMV infection is a barrier to long-term survival after solid organ transplantation (SOT). Although most cases are adequately controlled with antivirals (ganciclovir, valganciclovir, itemovir, maribavir), control of infection is sometimes difficult. The identification of potential immune mechanisms of difficulties to control CMV infection (DC-CMV) is of the greatest interest since it can be used to assess biomarkers to detect patients at special risk to evaluate specific therapeutic interventions.

**Methods:** In a prospective observational study, the immunophenotype of CD4+, CD8+ CD19+, and NK T cells was evaluated in patients diagnosed with CMV infection (n=20, heart n=9, liver n=8, kidney n=4, lung n=1). The polyfunctional activity of CD4+, CD8+ and NK+ T cells producing IFN-gamma and TNF-alpha was evaluated after stimulation with CMV peptides. The immunophenotypic study included the evaluation of CD8+ T cell activation markers and the maturation status of B lymphocytes. Multiparametric flow cytometry was used. The DC-CMV definition included one or more of the following: Persistent CMV infection, recurrent CMV infection, CMV infection with neutropenia secondary to antivirals, refractory CMV disease or resistant CMV disease. As controls, 14 patients with SOT who were free of any type of infection in the first 3 months after transplantation were included. Study time was at the time of diagnosis of DC-CMV after SOT or similar time in controls.

**Results:** Patients with DC-CMV showed a tendency to a lower percentage of CD8+ IFN-gamma+ T cells to CMV IE1 vs controls (0.0 vs 0.53%, p=0.10). The percentage of CD8+ DR+ T cells was significantly higher in these patients (60.2 vs 35.9%, p=0.0002). The level of naive B cells was similar in both groups (52 vs 57, p=0.577). In logistic regression CD8+ DR+ >50% was associated with high risk of DC-CMV.

**Conclusions:** The level of CD8+DR+ cells in peripheral blood could serve as a biomarker of risk for development of DC-CMV post-SOT. Future studies are warranted to validate the potential role of this biomarker in multicentre studies.
LATE BREAKING E-POSTERS

LBP37 IMPACT OF DONOR-DERIVED CELL-FREE DNA ASSESSMENT IN MONITORING KIDNEY TRANSPLANT RECIPIENTS: INTERIM REPORT OF A PROSPECTIVE LONGITUDINAL STUDY

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Background: Donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for monitoring kidney transplant (KT) recipients. We aim to evaluate its clinical utility in a prospective cohort of 500 cases.

Methods: Since July 2022, we prospectively collect plasma from each KT recipient immediately prior to renal biopsy, to measure dd-cfDNA, using a locally implemented standardized assay (AlloSeq cfDNA, CareDx, CA), and correlate %dd-cfDNA with allograft and recipient status.

Results: Of the 292/500 samples collected so far, dd-cfDNA has been already measured in 229, with 92.1% of samples passing quality control. The %dd-cfDNA <14 days post-TX (0.71% [0.53-0.85]) was significantly higher than >14 days post-TX (0.21% [0.12-0.32]; p=5.3x10^{-7}). Dd-cfDNA was increased in deceased donor (DD) kidneys, both DBD (0.24% [0.16-0.38]; p=0.004) and DCD (0.24% [0.12-0.4]; p=0.03), compared to living donation (LD) (0.13% [0.1-0.25], Fig.1B), but not different between DBD and DCD kidneys.

Conclusions: Awaiting study completion by end-2023, this interim analysis indicates that, when measured >14 days post-TX, dd-cfDNA could guide whether to perform an indication biopsy. However, within <14 days post-TX, the injury/healing process occurring after TX masks the ability of dd-cfDNA to uncover ongoing AR. The impact of donor type on %dd-cfDNA persists >14 days post-TX, AR was associated with higher %dd-cfDNA (1.19% [0.32-2.00]) than at surveillance biopsies (0.21% [0.15-0.31]; DCD 0.22% [0.11-0.32]; LD 0.13% [0.10-0.25]). Dd-cfDNA was significantly higher at the time of indication biopsies (0.41% [0.26-0.85]) than at surveillance biopsies (0.18% [0.11-0.30]; p=2.8x10^{-10}). 13.3% of cases had (borderline) allograft rejection (AR). Dd-cfDNA was higher in AR (0.80% [0.47-1.64] versus no rejection (0.31% [0.25-0.70]; p=0.016, Fig.1C) in indication biopsies only, which also showed more cases of full-blown AR than surveillance biopsies (17% vs 3%, respectively).

LBP38 JOIN T ALLOTRANSPLANTATION: A SYSTEMATIC LITERATURE REVIEW AND EXPERIMENTAL EXAMINATION OF IMMUNE REJECTION OF CARTILAGE

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Background: Joint allograft transplantation (JA) offers substantial promise for the functional and non-prosthetic reconstruction. However, the clinical application of JA is restricted due to immune rejection commonly associated with all forms of allotransplantation. This study aims to offer a comprehensive understanding of the current JA landscape through a systematic review. Additionally, considering cartilage as a critical component of JA, the immune rejection of cartilage was specifically analysed in a porcine VCA model.

Methods: We executed a systematic literature review in line with the PRISMA guidelines, sourcing relevant articles from PubMed. The results were thoroughly analyzed and potential prospects were discussed in-depth. Within the swine heterotopic VCA model, cartilage, including the articular cartilage and meniscus, was collected. Immune rejection of cartilage, in the rejected cartilage.

Conclusions: Joint allotransplantation(JA) offers substantial promise for the functional and non-prosthetic reconstruction. However, the clinical application of JA is restricted due to immune rejection commonly associated with all forms of allotransplantation. This study aims to offer a comprehensive understanding of the current JA landscape through a systematic review. Additionally, considering cartilage as a critical component of JA, the immune rejection of cartilage was specifically analysed in a porcine VCA model.

Methods: We executed a systematic literature review in line with the PRISMA guidelines, sourcing relevant articles from PubMed. The results were thoroughly analyzed and potential prospects were discussed in-depth. Within the swine heterotopic VCA model, cartilage, including the articular cartilage and meniscus, was collected. Immune rejection of cartilage was analysed.

Results: Our systematic review included 14 articles detailing pertinent developments in JA. At present, most JA research utilizes small animal models, showcasing graft survival and functional restoration with short-term immunosuppression. In human patients, only six knee allotransplantations have been carried out to date, all of which ultimately failed. In our experimental study, histologic examination of cartilage samples showed infiltration of inflammatory cells and tissue destruction, particularly in the meniscus. However, tissue damage was less severe compared to the rejected skin and muscle. Transmission electron microscopy confirmed tissue damage and necrosis in cartilage, skin, and muscle. Immunofluorescent staining highlighted the activation of both innate and adaptive immune systems, with an up-regulation of cell death biomarkers in the rejected cartilage.

Conclusions: Over the past 20 years, research on joint allotransplantation has rarely been pursued due to the scarcity of clinical applications, the complexity of surgical procedures, and the unpredictable outcomes resulting from immune rejection. Our experimental results suggest that cartilage does not possess immunological privilege and undergoes immune rejection alongside skin and muscle in the VCA model, albeit with less severe inflammation, particularly in articular cartilage.
LATE BREAKING E-POSTERS

**LBP39**  
**ACCESS TO AND RESULTS OF TRANSPLANTS IN CATALONIA; REVIEW FROM THE STANDPOINT OF GENDER**  
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**Background:** Different studies have described the existence of inequality based on sex and gender at each stage of the transplant process. Access to the transplant waiting list, access to transplant once the patient is on the waiting list, and the result of the transplant. Our objective is to review the tendencies in access to and results of transplants in Catalonia, by sex and type of solid organ.

**Methods:** We evaluated the tendencies in access to solid organ transplant through the correlation between the proportion of recipients and the proportion of active patients on the waiting list for men and women in 4 periods (2014-2015; 2016-2017; 2018-2019; 2021-2022). The results of solid organ transplants were calculated on the basis of survival models; time elapsed from transplant until graft loss, death or end of study (31st of December 2021). The hazard ratios for women were obtained (in comparison with those for men) for each solid organ using the Cox model adjusted for potential confounding factors: donor age, transplant indication, period, urgency and recipient age.

**Results:** Slight disparities were found in the access to women to transplant among the candidates on waiting list and these were substantially greater among women awaiting a lung transplant in the first period (2014-2015). Patient survival among recipients of solid organ transplants is higher, in general, for women. In contrast, in the study of graft survival in renal transplant was not associated with worse recipients or graft survival compared to rATG.

**Conclusions:** In Catalonia there exists a slight disparity in access to lung transplant between men and women, as with the transplant results. We consider it a priority to continue working on the analysis of the activity and results of donation and transplantation, from a gender perspective.

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**LBP40**  
**GRAFT FAILURE AND DEATH AMONG OLDER PRIMARY DECEASED DONOR KIDNEY RECIPIENTS IN THE UNITED STATES**  
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**Background:** Induction choice varies widely in older transplant recipients, especially with the challenging senescent immune system. Herein, we report on the association between different types of induction and outcomes of older deceased donor recipients in the United States.

**Methods:** Between 2000-2022, we analyzed the Scientific Registry of Transplant Recipients Database. Primary deceased kidney recipients 55 years of age or older. We excluded those who received an unusual induction regimen or were discharged on a regimen other than tacrolimus and mycophenolate mofetil with or without steroids. All transplants were HLA and ABO compatible and received one of the following induction: rabbit anti-thymocyte globulin (rATG (n=43097), alemtuzumab (n=20948) or interleukin-2 receptor antagonist IL-2RA (n=16106). Kaplan-Meier curves were generated for death-censored graft failure and recipient survival through ten years from transplantation. The association between induction and outcomes of interest were examined in multivariable Cox Proportional hazard models. Models were adjusted for clinically pertinent donor and recipient factors, while the center was included as a random effect.

**Results:** Induction with rATG increased while IL-2RA and alemtuzumab use declined (Figure 1). In the univariable Kaplan-Meier analyses (Figure 2), alemtuzumab was associated with the lowest probabilities of death-censored graft survival (log-rank p < 0.0001) and recipient survival (log-rank p=0.008). In the multivariable models, compared to rATG, alemtuzumab was associated with 20% increased risk of graft loss [HR 1.20, 95% C.I. (1.12, 1.29), p<0.001] and 7% increased risk of mortality [HR 1.07, 95% C.I. (1.02, 1.12), p<0.001]. IL-2RA was not associated with worse recipients or graft survival compared to rATG.

**Conclusion:** In this large cohort of older deceased donor kidney recipients, compared to rATG induction, alemtuzumab but not IL-2RA was associated with worse long-term recipients and graft survival.
Background: Acute-on-chronic liver failure (ACLF) is a global epidemic in hospitalised patients with high short-term mortality. This study was performed to assess the transplant benefit of ischemia-free liver transplantation (IFLT) in patients with ACLF compared to standard liver transplantation (SLT).

Methods: In this retrospective study, 20 patients received IFLT and 92 patients received SLT were chosen for the entire cohort between July 2017 through October 2022. A 1:2 propensity score matching was performed, 20 IFLT recipients and 37 matched SLT patients were enrolled in propensity-matched cohorts. Donor and recipient characteristics, intraoperative and postoperative outcome between two groups were assessed.

Results: Both in the entire cohort and propensity-matched cohort, patient in the IFLT group had lower incidence of post-reperfusion syndrome, faster recovery of hemodynamics, less remote organ injury and acceptable survival benefits. In the entire cohort, the patients in the IFLT group had lower incidence of acute kidney injury grade 3 and less application of renal replacement therapy within 14 days. No primary non-function occurred in patients in the IFLT group. In the Kaplan–Meier analysis, the 6-month and 3-year graft survival in the IFLT group were significantly higher than those in the SLT group (P=0.038).

Conclusions: IFLT largely prevent IRI of liver grafts when performed in patients with ACLF, resulting in good transplant outcome with intraoperative stable hemodynamics, less remote organ injury and acceptable survival benefits.

Abbreviations: AKI, acute kidney injury; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EAD, early allograft dysfunction; GGT, γ-glutamyl transpeptidase; ICU, intensive care unit; IFLT, ischemia-free liver transplantation; IRI, ischemia-reperfusion injury; INR, international normalized ratio; NT-pro BNP, N-terminal fragment of the pro brain natriuretic peptide PNF, primary non-function; POD, postoperative day; SLT, standard liver transplantation; TnT, troponin T

The graft survival by Kaplan Meier survival analysis for patients transplanted for ACLF between the IFLT and SLT groups for a 2-year follow-up in the propensity-matched cohort.
**LATE BREAKING E-POSTERS**

**LBP44**  
**EX VIVO CHARACTERIZATION OF KIDNEY TRANSPLANT TUBULAR EPITHELIAL CELL CO-STIMULATORY AND IMMUNOMODULATORY MOLECULE EXPRESSION DURING INFLAMMATION**


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**Background:** Direct allorecognition is generally regarded as a result of antigen presentation and activation of recipient T cells by donor professional antigen presenting cells. However, tubular epithelial cells contribute the vast majority of cells in the kidney transplant, and their contribution to allorecognition despite being targets of cytotoxic T cells is not well understood.

**Methods:** We collected urine samples of healthy donors, kidney transplant patients, and living donors of kidney transplants and isolated and cultured urine-derived kidney tubular epithelial cells. To ensure transplant origin, we characterized blood and epithelial cells of living donors and the respective recipients by chimerism analysis. After treatment with cytokines (IFNγ, TNFα, IL-17, IL-6, IL-17A, and IL-22), as well as with 1% oxygen hypoxia, we performed a flow cytometric characterization of over 20 markers.

**Results:** Chimerism analysis of living donor and recipient pairs revealed a near total transplant origin of the cultivated tubular epithelial cells (median 100% donor origin, minimum 96%, n=6 living donor-recipient pairs). Inflammatory treatment with IFNγ, TNFα, and IL-17 resulted in an upregulation of MHC-I and -II, costimulatory molecules CD40, CD70, ICAM-1, and ICOS-ligand, the immunomodulatory molecule HVEM and/or PD-L1. Other molecules, such as CD80/CD86, 4-1BBL, CD48, and CD58, only showed little expression and/or modulation by inflammatory treatment. Treatment with IL-6, IL-17A, IL-22, and hypoxia only caused minimal modulation of immunomodulatory molecule expression.

**Conclusions:** Taken together, human kidney transplant tubular epithelial cells can be isolated ex vivo and studied without invasive procedures. We used this tool to characterize the immunomodulatory potential of tubular epithelial cells under inflammatory conditions, which are present during ischemia-reperfusion injury and rejection episodes. Tubular epithelial cells express not only MHC-I, but also MHC-II and a multitude of important immunomodulating molecules. Thus, they can significantly contribute to the activation and modulation of alloreactive CD4+ and CD8+ T cells.

**LBP45**  
**SURFACE MOLECULE EXPRESSION OF KIDNEY TUBULAR EPITHELIAL CELL DERIVED EXTRACELLULAR VESICLES – A NEW PERSPECTIVE ON THE MODULATION OF ALLOIMMUNITY?**

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**Background:** Alloimmunity is one of the leading causes of a limited short- and long-term graft survival. Extracellular vesicles (EVs) have recently been recognized to hold a key role in immune processes in many conditions. They could therefore also impact alloimmunity, for example through the expression of surface proteins that in- or decrease adaptive immune cell reactivity after inflammatory or hypoxic episodes. Kidney parenchymal cells are an important source of EVs in kidney transplantation. Thus, we aimed to shed light on the immunomodulatory molecule expression of renal tubular epithelial cells (iTECs) derived EVs in the pathophysiology of alloreactivity.

**Methods:** To evaluate whether EVs released by iTECs could directly modulate the activation and presentation of allogeneic recipient T cells, we performed in vitro experiments. In particular, we examined the property of EVs to stimulate CD4+ and CD8+ T cells in a co-culture setting. We performed several EV isolation experiments, with IL1β stimulation enhancing vesicle production strongly. Surprisingly, IFNγ and TNFα only moderately increased the quantity of EVs, despite their regular use as EV-production stimulants. Furthermore, we could show that iTEC-EVs potentially influence T cell activation via immunomodulatory surface molecules. This was further tested in functional analysis of T cell activation after co-culture with EVs by flow cytometry.

**Results:** EV production capacity of cells varies between probands and conditions, with IL1β stimulation enhancing vesicle production strongly. Surprisingly, IFNγ and TNFα only moderately increased the quantity of EVs, despite their regular use as EV-production stimulants. Furthermore, we could show that iTEC-EVs potentially influence T cell activation via immunomodulatory surface molecules. This was further tested in functional analysis of T cell activation after co-culture with EVs by flow cytometry.

**Conclusions:** Taken together, we showed that iTECs can have immunomodulatory effects via the production of EVs, leading to new insights into alloimmunity after ischemia-reperfusion injury and intragraft inflammation.

**LBP46**  
**UNSUPERVISED ANALYSIS OF KIDNEY BIOPSY TRANSCRIPTOMES FROM DONORS AFTER BRAINSTEM OR CARDIAC DEATH**

**Rachel Thomas**, Tobias Bohnepoli, Ricardo Castro, Maria Kaisar, Maria Letizia Lo Faro, Georg Ebeling, Sadr Shaheed, Lente Lerink, Nelly Mostajo Berrospi, Royan Daou, Tim Blokker, Olivier Radresa, Uwe Andagi, Gabriel Oniscu, Rutger Ploeg

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**Background:** Brainstem and cardiac death result in profound cellular and molecular changes in donor kidneys, that adversely impact graft function and clinical outcome. Here unsupervised methods were used to characterise biopsy transcriptomes from different donor types with aim to improve mechanistic understanding of organ quality, injury and repair.

**Methods:** Kidney biopsies from live donors (n = 20), donors after brainstem death (DBD, n = 801) or standard cardiac death (nDCD, n = 133) or normothermic regional perfusion (nRDP-DCD, n = 13) were obtained from a biobank and processed for RNA sequencing. Transcriptomes were clustered by similarity via self-organizing maps (oposSOM) and further explored via dimension reduction (PHATE) to integrate technical, clinical and molecular data.

**Results:** Unsupervised clustering of biopsy transcriptomes revealed three molecularly distinct groups of different sizes (Fig. 1A), labelled blue (n = 724), red (n = 170) and green (n = 75). Interestingly, molecular clustering did not separate DBD from nDCD, highlighting molecular similarities largely independent of donor type (Fig. 1B). Integration of clinical and technical variables using a decision tree approach suggested that red and green clusters could be explained by RNA quality and biopsy type (core needle vs. punch), respectively. RNA concentration showed a gradient separating the red cluster from high-quality samples (Fig. 1C). Variability in sampling procedures affected biopsy composition, with the green cluster enriched for needle biopsies and characterized by a stronger medullary signal (Fig. 1D). Importantly, initial exploration of high-quality transcriptomes with comparable tissue composition (cluster blue) revealed gradients of tubular damage and metabolic adaptation, and stromal and immune activation, underlining the potential of the dataset to study mechanisms of kidney injury and repair.
Conclusions: Unsupervised analysis of biopsy transcriptomes revealed technical variability in RNA quality and tissue composition, potentially confounding biological signals. Data-driven selection of high-quality transcriptomes with comparable tissue composition will enable the study of kidney injury-repair mechanisms across major transplant conditions.

Fig 1: Unsupervised analysis of biopsy transcriptomes. (A) Transcriptomes clustered into three molecular groups (PHAET dimension reduction). (B) Distribution of donor types across molecular groups. (C) Embedding RNA concentration in PHATE space. (D) Embedding medullary gene expression signature in PHATE space.
Conclusions: Roxadustat – as a new treatment option of anaemia for patients with chronic kidney diseases. Our first analysis confirmed that roxadustat is very effective not only in patients with CKD, but also in patients with anaemia after kidney transplantation.

LBP52 THE DETRIMENTAL EFFECTS OF A BK POLYOMA-VIRUS INFECTION IN KIDNEY TRANSPLANT PATIENTS

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Background: BK polyomavirus-associated nephropathy (BKPyVAN) preceded by BKPyV viremia is a well-known complication of kidney transplantation, which can lead to significant allograft damage and graft loss. The mainstay of prevention and treatment of BKPyVAN is reduction of immune suppression upon detection of viremia, which subsequently carries a risk of allograft rejection. In this single center, retrospective cohort study we assessed the impact of BK PyV viremia detection on kidney allograft outcomes.

Methods: All patients with a kidney transplantation between 2011 and 2021, transplanted at Leiden University Medical Center (LUMC) were included. Data on the incidence, management and course of BKPyV viremia were collected whereverupon we studied the association between incidence and load of BKPyV viremia and kidney function and episodes of rejection using logistic regression analysis.

Results: In total, 1158 kidney transplant recipients were included of which 273 patients (23.6%) developed BKPyV viremia and 36 (3.1%) were diagnosed with BKPyVAN. On average onset of BKPyV was 7.4 months after transplantation. At 5 years after transplantation, patients that had developed BKPyV viremia had a lower eGFR (45 ml/min/1.73m², p <0.001). Development of de novo donor-human leukocyte antigen specific antibodies (dnDSA) was more common in kidney transplant patients with viremia, compared to patients without (OR 2.0, 95% CI 1.0 to 4.1, p=0.043). Rejection was not significantly different between groups.

Conclusions: Kidney transplant patients who develop a BKPyV viremia are more at risk for the development of dnDSAs and have worse kidney allograft outcomes. Risk for developing rejection is similar between the two groups. This might implicate that the reduction of immunosuppression when a BKPyV viremia arises should be less aggressive.

Conclusions: Roxadustat – as a new treatment option of anaemia for patients with chronic kidney diseases. Our first analysis confirmed that roxadustat is very effective not only in patients with CKD, but also in patients with anaemia after kidney transplantation.

LBP53 ASSOCIATION OF HEMOGLOBIN LEVELS WITH RENAL FUNCTION DURING NORMOTHERMIC MACHINE PERFUSION OF PORCINE KIDNEYS: A RETROSPECTIVE COHORT STUDY

L. Annick van Furth*1, Tobias Huijink1, Leonie van Leeuwen1, Hanno Maassen1, Veerle A. Lantinga1, Baran Ogurolu1, Tim L. Hameink1, Merel Pool1, Rianne Schutter1, Cyril Moers1, Stefan Berger1, Henri Leuvenink1, Rene Posma1, Leonie Venema1

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Background: Ex vivo normothermic machine perfusion (NMP) is used to assess and recondition an isolated marginal kidney before transplantation. However, there is no consensus on the optimal conditions such as the oxygen-carrying capacity of the perfusate to support renal function. To investigate the association of hemoglobin levels with renal function, a retrospective analysis of porcine kidneys being perfused at our laboratory was performed.

Methods: In total, 228 kidneys underwent 4 hours of NMP with a hemoglobin-containing perfusate between 2015 and 2021. A generalized linear model was used to determine the association of hemoglobin levels with time-weighted means of renal function markers, such as fractional sodium excretion (FENa) and creatinine clearance. These outcomes over time stratified by baseline hemoglobin level (<4.5, 4.5-6, or >6 mmol/L) were modeled with a generalized linear mixed-effects model as well.

Results: Increasing hemoglobin levels were associated with improved FENa and creatinine clearance, with the nadir of FENa and peak creatinine clearance, respectively, both at about 5 mmol/L. A baseline hemoglobin level <4.5 mmol/L was associated with higher FENa rates and lower creatinine clearance (p<0.001 and p<0.05). Hemoglobin was not significantly associated with proteinuria during NMP, or ATP levels at the end of NMP. Hemoglobin levels exceeding 6 mmol/L do not provide additional benefits in terms of renal function and may even contribute to increased injury.

Conclusions: In conclusion, this study revealed a correlation between baseline hemoglobin levels with parameters of renal function, but not injury, during NMP of marginal kidneys.

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Conclusions: In conclusion, this study revealed a correlation between baseline hemoglobin levels with parameters of renal function, but not injury, during NMP of marginal kidneys.

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**LATE BREAKING E-POSTERS**

**LBP55**  
**GROUND BREAKING DECISIONAL ROLE OF TRANSIT TIME DURING A LIVING DONOR TRANSPLANTATION EVALUATED BY A FAST AND FRUGAL TREE**

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**Background:** Acute thrombosis of the iliac artery is an extremely rare event during a kidney transplantation and may occur as a complication of traumatic injuries or systemic disorders. We assessed the decision making during a case report of acute and unexpected iliac thrombosis in a living donor transplant for a PKD recipient evaluated by constructing a fast frugal tree (FFT). FFTs are simple algorithms that facilitate accurate decisions based on limited information. FFTs have been successfully exploited to describe decisions and to provide prescriptive guides for effective real-world resolutions, but despite their effectiveness, they are still not widely used.

**Methods:** We split the three principal phases where iliac thrombosis may occur (organ procurement, vessel isolation, graft reperfusion) according to diagnostic and intervention procedures, weighted for decisional impact and Grade degree of evidence; then we compared the fitting between the occurred decisional steps and the best possible decision making

**Results:** From observational data, the performed revascularization and removal and reallocation of graft resulted as mandatory interventions in order to preserve the graft when thrombosis occurs unexpected from previous ultrasound assessments. The used transit time evaluation emerged also with a discriminant decisional power, measuring the degree of thrombosis (flow reduction 220 to 80 ml/min in < 30 min) and further unsuccessful first try revascularization by resistance index (>3), strengthening fastness in graft removal and reallocation from right to left.

**Conclusions:** FFTs help the goal of a decision maker to accurately prioritize each step during the transplant critical milieu and at actionable turning points to maximize correct decisions (hits and correct rejections), while minimizing errors (misses and false-alarms) and noise: as learning algorithm used to solve binary classification tasks, they may unlock the full potential of transit time intraoperative measurements.

**LBP56**  
**35 YEARS OF PAEDIATRIC HEART TRANSPLANTATION: OUTCOMES AT A VERY LONG TERM FOLLOW-UP**

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**Background:** Thirty-five years after the first successful paediatric heart transplantation (pHTx), the long-term outcome of this population is still unknown. The aim of this study is to analyse clinical results in this population in a single centre experience.

**Methods:** A retrospective analysis of all the patients who underwent Htx in paediatric age was performed. Clinical, laboratory, and instrumental follow-up was completed. Outcomes were survival, severe coronary allograft vasculopathy (CAV), severe chronic kidney disease (CKD). Kaplan-Meier analysis was performed for survival, cumulative incidence functions were applied for incidence of CAV and CKD.

**Results:** Between 1987 and 2022, 86 paediatric patients underwent Htx. Median age at Htx was 11.9 years. Postoperative mortality was 13% (11 patients). Median follow-up period was 13.7 years, with a cumulative experience of 35 years. Twenty patients died at follow-up (27%), of whom 11 for cardiovascular causes. At 1, 5, 10, 20 and 30-year follow-up survival was 98%, 92%, 84%, 74%, and 60%, respectively. Cumulative incidence of severe CAV at 1, 5, 10, 20, and 30-years follow-up was 4.9%, 12.9%, 40%, 51.2%, 67%, respectively. Cumulative incidence of severe CKD at 1, 5, 10, 20, and 30-year follow-up was 0%, 2%, 5%, 18.75%, and 35%, respectively. At a multivariable analysis, donor age is related with CAV (p=0.004).

**Conclusions:** Paediatric Htx has good survival and functional outcomes, with a growing cohort of patients approaching their second and third decades. Main causes of death at follow-up were cardiovascular diseases and donor age resulted related with CAV.
Background: The average life expectancy is continuously increasing in developed countries. Simultaneously, the incidence of heart failure is rising with age. In cases of end-stage heart failure, heart transplantation is the treatment method of choice. Therefore, we investigated the outcomes of the elderly patients (over 65 years old) with end-stage heart failure who were treated with orthotopic heart transplantation.

Methods: We investigated the entire group of patients treated with heart transplantation at the age ≥65y. In that group the median age at the time of transplantation was 66.3y, IQR 65-67 and 4(15%) pts were women. Among these patients, the heart failure was of ischemic origin in 50% of cases, two pts were bridged with ECMO, 4 with LVAD and 4 with IABP. 21 pts had diabetes, median eGFR was 53ml/min/1.73m², IQR: 39-61ml/min/1.73m². Median observation period was 23, IQR: 1.75-63months. Baseline immuno-suppressive regimen consisted of steroids and: cyclosporine-A with azathioprine (6.7%), cyclosporine-A with mycophenolate (6.7%) and tacrolimus with mycophenolate (8.1%).

Results: Among 1488 patients treated with Htx between November 1985 and June 2023, 60pts (4%) were transplanted at the age ≥65y. In that group the one-year survival (conditional on one-month survival) was 85.1%. 25 pts survived to 1 h. Liver parameters AST and ALT were numerically, and LDH significantly elevated in the CytoSorb® group. During the one-year survival, kidney function worsened significantly. Baseline cytokine levels were comparable in all groups. Levels of pro-inflammatory cytokines IL-1 alpha, IL-1 beta, IL-6, IL-18 and TNF-alpha increased throughout perfusion in the CytoSorb® group. Ex vivo machine perfusion methods have emerged as promising tools for organ preservation, reconditioning and repair. However, the underlying process triggers inflammatory processes. Especially ECD grafts are more vulnerable and therefore cytokines as additional biomarkers may be promising for graft assessment.

Methods: Porcine steatotic (n = 7) and healthy (n = 4) livers were subject to 24 h static cold storage and subsequently perfused for 24 h in a subnormothermic oxygenated perfusion circuit. Throughout perfusion perfusate was collected for analyzing perfusion parameters (pH, glucose, lactate) and snap frozen for post hoc assessment of liver function and cytokine levels. Tissue biopsies were taken every 3 h. The effect of cytokine adsorption was assessed in a follow-up experiment by connecting the CytoSorb® adsorber to the circuit and perfusing additional livers either with (n = 5) or without (n = 3) this adsorber.

Results: Baseline cytokine levels were comparable in all groups. Levels of pro-inflammatory cytokines IL-1 alpha, IL-1 beta, IL-6, IL-18 and TNF-alpha increased throughout perfusion. Ex vivo machine perfusion methods have emerged as promising tools for organ preservation, reconditioning and repair. However, the underlying process triggers inflammatory processes. Especially ECD grafts are more vulnerable and therefore cytokines as additional biomarkers may be promising for graft assessment.

Background: In kidney transplantation normothermic machine perfusion can be used to reduce exposure to cold ischaemic injury. This may improve outcomes and allow the technology to extend preservation times and repair marginal kidneys. Subnormothermic acellular perfusion (SNAP) is a new approach proposed to achieve a balance between the cytoprotective effects of reduced cellular metabolism under hypothermia while having sufficient metabolism to allow potential organ repair. Kidneys can be perfused without red blood cells to simplify the procedure, reduce cost and prevent potential harmful effects of hemolysis. The aim of this study was to assess the effects of different durations of SNAP after bridge to a human kidney program in our center (1985) and searching for the subpopulation of patients aged 65 years and older.

Methods: Twelve kidneys declined for transplantation were perfused ex vivo using SNAP. Kidneys were perfused with a human serum albumin-based solution at 32°C for either 6, 12 or 24 h (n = 4 per group). After the preservation phase, kidneys were reperfused ex vivo at 37°C for 4 hours using a blood-based perfusate.

Results: The mean donor age was 70±6y, 63±9y and 61±15y in the 6h, 12h and 24h groups, respectively (P=0.530). There was no significant difference in the cold ischaemic time prior to SNAP (6h 892±155; 12h 1203±327; 24h 1042±368 minutes, P=0.523). Throughout SNAP the perfusate flow, mean arterial pressure and acid-base balance remained stable in all kidneys. Kidneys in the 24h group had a significantly lower mean perfusate flow rate compared to the 6h and 12h kidneys (24h 184±5; 12h 260±5; 6h 214±36 ml/min/100g, P=0.008). During reperfusion, kidneys in the 24h group had a numerically lower urine output (24h 27±3; 12h 63±7; 6h 198±176ml/h; P=0.074) and lower level of creatinine fall (24h 38±11; 12h 61±23; 6h 59±22%, P=0.266) but this did not reach statistical significance. Renal blood flow was similar in all groups (6h 119±32; 12h 187±55; 24h 146±36ml/min/100g, P=0.243). Histological evaluation showed preserved renal morphology but an increase in ischaemic damage in the 24h group.
LATE BREAKING E-POSTERS

LBP63

DONATION AFTER CIRCULATORY DEATH INCREASES OVERALL ORGAN DONATION AND TRANSPLANTATION IN SWEDEN, BUT NOT WITHOUT NEW CHALLENGES

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Background: Donation after Circulatory Death (DCD) was introduced in Sweden in 2019, aimed to increase organ transplantation. Focus of DCD implementations impact on transplantation in Sweden, and the Intensive Care Units (ICUs) perception as well as number of donors and accomplished transplantations will be presented.

Methods: A survey was sent to all (n = 84) Swedish ICUs in January 2023, aimed to follow up on the implementation of DCD. Non-responder units, n = 22 (26%), are not included in the result. The number of donors and transplant statistic were retrieved from the Swedish Intensive Care Registry (SIR) and Scandiatransplant.

Results: Overall, 61% of the respondent ICUs declared implementation of DCD at their unit. In 2023, DCD implementation differs depending on national localisation; university hospitals (81%), county hospitals (57%) and local hospitals (46%). Implementation of DCD in Sweden was successful. An increase of deceased donations was seen in Sweden during this period, but the number of DCD donors and transplantations of liver, heart and lungs decreased.

Conclusions: Due to the decrease in DBD, are needed to increase access to transplantation for all heart transplants. Additional efforts, such as considering an ethical framework to follow the development.

LBP64

HEART TRANSPLANTATION FROM ANTIB-HBCORE POSITIVE DONORS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Organ transplantation is constrained by the scarcity of available organs, necessitating efforts to increase organ availability while preserving positive recipient outcomes. Extended criteria donors, including HBs(−) and anti-HBcore(+) donors, have emerged as a promising option for individuals on the organ transplant waiting list. This study aimed to assess the long-term safety of heart transplantation (HTx) from anti-HBcore(+) donors.

Methods: Retrospective analysis of heart transplant recipients operated in a single high-volume transplant center between January 2013 and June 2023. In further analyses, HBs(−) recipients with HTx from both HBs(−) and anti-HBcore(+) donors were identified.

Results: Among the 583 transplanted patients during the analysed period, a total of 29 cases (including 6 females) received HTx from anti-HBcore (+) and HBs(−) donors. The mean recipient age at the time of transplant was 53.7±12 years. The median observation period equaled 11.25, IQR: 0.9-34.5 months. All except for one recipient declared complete hepatitis B vaccination. Prior to HTx, the anti-HBs antibody level was assessed in three patients, with only one patient showing an antibody level<12 mIU/mL. Among HTx recipients, none received Anti-HBs global at the time of HTx. As there are no unequivocal guidelines, the decision to use prophylaxis against hepatitis B was at the discretion of the attending physician. One-year prophylaxis with lamivudine was used in four cases. Additionally, up to 3 months, 65.5% of the patients received valganciclovir. In the whole group of recipients, frequent transaminase and HBs controls (every month in the first three months and every three months up to one year and then every 6 months) were performed. In the whole observation period, none of the patients developed HBs antigen. Mean INR, APAT, ALAT, bilirubin, and GGT levels were at the one year: 26(12) U/L, 28(24) U/L, 10(4) umol/L, 103(234) U/L. Mean LVEF at one year, 2, and 5 years was 60(13)% 58(3)% and 58(4)% accordingly.

Conclusions: HTx from anti-HBcore (+) donors in patients vaccinated against hepatitis B seems to be viable and a safer option even without the application of additional antiviral prophylaxis.

LBP65

THE IMPACT OF DECEASED DONOR ORGAN PROCUREMENT WORKSHOP ON SURGICAL TRANSPLANT FELLOWS’ CONFIDENCE AND COMPETENCE

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Background: Deceased donor organ procurement entails complex techniques and meticulous anatomical dissection, and is vital to the success of organ transplantation. In our institution, this surgery is often performed by a surgical transplant fellow. Thus, training transplant fellows in these intricate surgical techniques is imperative, but such opportunities are currently limited in Canada. To address this, we organized a two-day hands-on deceased donor workshop for the abdominal transplant fellows at our institution. The objective of this study is to assess the workshop’s impact on fellows’ confidence and competence to gauge its overall benefit and to identify areas of improvement.

Methods: The abdominal transplant fellows who attended the workshop were invited to participate in the study. At the beginning of the workshop, the participants were asked to report their exposure to and confidence on various aspects of the organ procurement surgery. The fellows’ knowledge on organ procurement were also assessed using multiple choice questions. Participants were asked to complete the questionnaires immediately post-workshop, and at one month and six months following the workshop. Descriptive statistics and t-test or Wilcoxon test were used, as appropriate, to compare the responses of participants pre and post workshop.

Results: Seven transplant fellows participated in the study. The fellows’ confidence improved at the end of the workshop (6(6)-4.05, p<0.006), at 1 month (6(6)-3.68, p=0.01) and six months post-workshop (6(6)-3.31, p=0.016). Participants’ confidence also increased at the end of the workshop (72.4% vs. 81.6%, p=0.46), at one month (72.4% vs. 85.7%, p=0.06) and six months post-workshop (72.4% vs. 86.7%, p=0.1). All of the participants reported that the course was useful and that they would like to see this course offered in future.

Conclusions: The workshop led to a significant improvement in post-workshop trainee confidence, which remained evident even after six months. Although competence levels did not increase significantly, the results indicate a positive impact on trainees. Future studies will explore alternative measures of technical competence and the impact of regular deceased donor workshops on surgical trainees.
**Distinct Cytokine Signatures According to Model for End-stage Liver Disease Scores After Living Donor Liver Transplantation**

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**Background:** The model for end-stage liver disease (MELD) score is widely acknowledged for prognosis in patients with end-stage liver disease (ESLD) because it represents the severity of liver dysfunction. The score does not consider systemic inflammation and septic complications. We compared the MELD scores to the levels of serum cytokines as immune mediators, which represents the systemic inflammation, and then investigated the usefulness of serum cytokines as representing the functions of the grafted liver in patients who underwent living donor liver transplantation (LDLT).

**Methods:** We enrolled 232 patients in a retrospective study at our institute between March 2011 and December 2021. Demographic, and biochemical data were obtained using electric medical records system. The levels of seven serum cytokines were collected at the preoperative and immediate post-transplant period: interferon (IFN)-γ, interleukin (IL)-10, IL-12, IL-17, IL-2, IL-6 and tumor necrosis factor (TNF)-α. The MELD scores were calculated on 1 day (D), 2 D, 3 D, 7 D, 10 D, 15 D, and 30 D after post-transplantation. We identified the influences of serum cytokines on the MELD scores based on Pearson correlation coefficient using correlation analysis, and investigated the cut-off value of serum cytokines identifying high MELD scores using area under the receiver operating curve (AUROC).

**Results:** Four cytokines, viz., IFN-γ, IL-10, IL-6, and TNF-α were significantly correlated with post-transplant MELD scores (P < 0.05). The others, viz., IL-12, IL-17, and IL-2 were not correlated with the MELD scores. IL-6 and IFN-γ showed a statistically significant correlation with the MELD scores from 1 D to 30 D after LT. The cut-off value of IL-6 and IFN-γ in predicting high MELD scores after LDLT (> 23) were 7.3 and 14.6 pg/ml, respectively (AUROC = 0.619 and 0.641; sensitivity, 66.7% and 44.4%; and specificity, 62.8% and 83.2%, respectively).

**Conclusions:** The levels of serum cytokines, viz., IL-6 and TNF-α, which are pro-inflammatory cytokines, are strongly correlated with post-transplant MELD scores. Therefore, IL-6 and TNF-α could be useful predictors of the dysfunction of grafted liver in patients undergone LDLT, and 7.3 and 14.6 pg/ml, respectively, were the cutoff values in predicting high MELD scores (> 23) after LDLT.

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**Surgical Treatment of the Papillary Renal Cell Carcinoma in the Transplanted Kidney. Case Report**

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**Background:** Kidney transplant recipients (KTRs) are at increased risk of developing renal cell carcinoma (RCC). After transplantation, 90% of RCCs are detected in the native kidneys, particularly if acquired cystic kidney disease has developed during prolonged dialysis. The incidence of donor transmitted RCC is unknown. A systematic review on solid masses in kidney allografts found 175 tumors reported in 163 patients, mostly clear-cell RCC (46%) or papillary RCC (42%). The majority were treated with partial nephrectomy (68%), fewer with allograft nephrectomy (19%), radiofrequency ablation (10%), and cryoablation (2%). Cancer recurrence after partial nephrectomy was 3.6% after 3.1 y, which is similar to nontransplanted patients. (Transplantation 2022;106: e52–e63).

**Methods:** We report a case of a 48 y.o. patient, almost 12 y. after primary kidney transplantation (KTx) from a brain-dead donor with a permanent nephrostomy as a definitive option after recurrent pyelonephritis of the transplanted kidney with destruction of a graft ureter after three unsuccessful uretero-vesical reimplantations. The patient with otherwise functional graft was referred for a surgery due to incidental ultrasound finding of a tumour mass in the upper pole of the transplanted kidney, confirmed by 3-D CT scan with a high risk for a malignancy, and graftectomy was primarily planned.

**Results:** Per-operative finding of a very well localised tumour sized up to 4cm in the upper pole of the graft with dominant extrarenal grow was considered by a transplant surgeon as suitable for nephron sparing resection with per operative histological confirmation of negative resection margin. R0 resection of the papillary renal cell carcinoma pT1bNxMx, WHO/ISUP grade 1, was confirmed on definitive histology exam. Clinical oncologist did not recommend adjuvant oncological treatment. Maintenance immunosuppression was switched to mTOR inhibitors. Patient was discharged on POD 12 with maintained graft function – KDIGO G3b.

**Conclusions:** There are no randomized controlled studies to guide recommendations. Our report is only another one successful case of preferred treatment option for papillary renal cell carcinoma in the transplanted kidney graft. Prospectively collected data and randomized trials are urgently needed.
FACTORS INFLUENCING KIDNEY FUNCTION AFTER LIVING DONOR NEPHRECTOMY

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Background: Long-term graft survival is superior when living donors are used for kidney transplantation. As following of increase in the number of live-donor kidney transplantation, many studies have aimed at evaluating risk to the donors and revealed that kidney donation is a relatively safe procedure with minimal adverse effects. But some reports have described the development of proteinuria and hypertension and decrease kidney function after donation. There are number of reports about safety and good quality of life after living donor kidney transplantation but not enough reports have been published in domestic studies. This study was evaluated factors influence kidney function after kidney donation.

Methods: Between January 2005 and June 2021, we retrospectively reviewed 152 cases of living kidney donor with at least 12months of outpatient clinical follow up with latest follow up laboratory studies. Mean age of kidney donor was 42.2 years (range 17-71). The donors were predominantly male (51.2%). We measured glomerular filtration rate (GFR), preoperatively relative renal uptake ratios, blood pressure, body mass index, hemoglobin, creatine, cholesterol and assessed prevalence of hypertension, proteinuria.

Results: The average time after donation was 78.6 months (range, 12-460), the left kidney was used in 67 patients (65.6%). There was a total complication rate of 8% but serious complication was absent. Proteinuria was found in 8 patients (5.3%), hypertension in 11 patients (11%). Glomerular filtration rate decrease from 106.8±23.6 ml/min/m² to 67.6±15.18 ml/min/m²(p<0.001). 23% of the patients (25/67) developed a postoperative GFR that was below 60 ml/min/1.73 m². Thirty-nine patients (25.6%) developed a postoperative decrease GFR between 30 and 60 ml/min (35 patients, CKD grade 3) and one patient (0.7%) between 15 and 30 ml/min (CKD grade 4) and two patients (1.3%) developed below 15 ml/min (CKD grade 5). Factors affected eGFR after nephrectomy are age at nephrectomy(p<0.001) and pre-nephrectomy eGFR(p<0.001), other factors such as BMI, underlying disease, sex, laboratory findings did not (p>0.05). male have higher serum creatinine after nephrectomy (p<0.001)

Conclusions: Living kidney donation resulted in a reduced GFR in the donor long term follow up of living donor recipients. Males are at risk for having higher creatinine following donor nephrectomy.

DIGITAL DONOR EVALUATION TOOL: A NEW TECHNOLOGY IMPROVES DONOR ENROLLMENT ON INTENSIVE CARE UNIT

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Background: Due to the shortage of organs, contraindications for organ donation are extensively reviewed and in transition. Most of the ICU-doctors are not involved in these discussions and exclude therefore potential donors for medical reasons, which are no longer applicable. In critical urgent patients transplant centers take a higher risk in accepting marginal organs. Swisstransplant implemented a digital donor evaluation tool (DET), which allows the coordinators on the ICU to send a request to the medical advisor (MA) from Swisstransplant before excluding potential donors. Based on the medical condition of the potential donor and the situation on the National Waiting List the MA gives a written feedback to the coordinator of the requesting center.

Methods: All requests in 2022, which have been entered in the DET by coordinators have been analyzed. Patient characteristics, co-morbidities, decision by the MA and final enrollment as potential donor have been analyzed.

Results: 156 requests have been entered in the DET. This is approximately 20% of the expected potential of DBD- and DCD-donors per year in Switzerland. 117 patients (75%) have been accepted by the MA, out of which 60 patients (51%) have been enrolled as organ donor. In the remaining 57 patients missing consent in 69% was the main cause for not enrolling these patients. Main reasons for using the DET were malignancies (22%), infectious diseases (23%) and age/co-morbidities (22%). Average age of the enrolled donor was with 65.3 years significantly higher compared to the regular enrolled donors with 56.8 years (p<0.001). In average 1.9 organs have been transplanted in the DET-collective, compared to 3.2 organs in the remaining donors.

Conclusions: The DET is a new technology which allows ICU-doctors in the situation of a discontinuation of therapy to have easy and fast access to a medical expert in the field of organ donation, providing recommendations on the medical suitability for organ donation. Additional examinations can be requested by the MA and the organs, which may qualify for organ donation are defined at an early stage. This allows to reduce the number of examinations and gives the option to have a tailored approach in the discussion with the family, if the number of organs which will be evaluated is limited.
LATE BREAKING E-POSTERS

LBP71

ATTACHMENT AND PARENTAL BOND: IMPACT ON PSYCHOPATHOLOGY, MENTAL HEALTH AND QUALITY OF LIFE OF KIDNEY TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL STUDY

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Background: Attachment theory represents a reference model for understanding better how pre-existing personality factors can contribute to the development of some chronic conditions. The onset of a chronic disease can represent a “threat” to the relationships between the subject and parental figures according to the type of bond that already exists. The aim of our study was to investigate, in a sample of kidney transplant recipients, attachment style and parental bond, to evaluate the impact on any psychological symptoms and perceived quality of life.

Methods: Fifty transplant kidney recipients were given the following tests: Attachment Style Questionnaire (ASQ) to assess attachment styles, Parental Bonding Instrument (PBI) to assess parental bonding, Short Form Health Survey-36 (SF-36) for perceived quality of life and Middlesex Hospital Questionnaire (MHQ) to detect key psychological symptoms and relevant traits.

Results: The results showed that secure attachment is significantly associated with adequate general health (B= .926; P= .021) and mental health (B= 1.104; p=.002) of the SF-36. Maternal care was also significantly associated with a good SF-36 mental health index (B=.528; p=.021).

Conclusions: The results confirmed the positive role of a secure attachment style and a good parental bond for adequate psychological health. Early identification of patients with dysfunctional attachment styles will make it possible to offer them targeted interventions to improve their ability to accept, adapt and manage the disease and to maintain adequate psychological well-being.
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