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Ten-Year Follow-Up Of The Multicenter ALLEGRO Trial Comparing Early Steroid Withdrawal And Tacrolimus Minimization To Standard Quadruple Maintenance Therapy In Kidney Transplantation

Background

In the multicenter ALLEGRO study early steroid withdrawal by post-transplant day 3 (ESW) and tacrolimus minimization (tac-min; 3-5 ng/ml) from 6 months post-transplant was compared with the standard immunosuppressive regimen (basiliximab induction, prednisolone, tacrolimus; 5-7 ng/ml, mycophenolate) in kidney transplant recipients (KTR). Here, we report the 10-year post-transplant follow-up outcomes.

Methods

The primary objective was to assess, on an intention-to-treat basis, 10-year mean differences in estimated glomerular filtration rate (eGFR), rejection, death-censored graft failure (DCGF), all-cause graft failure, and death. The secondary objective was to assess the per-protocol effect of sustained steroid withdrawal on rejection. eGFR was measured at discharge, 3 months, and annually thereafter. Data on rejection, graft loss, and death were obtained from the Dutch National Transplant Registry (NOTR). eGFR trajectories were modeled using joint models, and 10-year cumulative incidences of graft loss and death were estimated using the Kaplan–Meier method. Rejection and DCGF were estimated using the Aalen–Johansen method to account for competing risks. Per-protocol effects were estimated using a dynamic marginal structural model with inverse probability of censoring weights.

Results

A total of 298 KTR participated in the trial and were 1:1:1 randomized over the three treatment arms. Participants were followed for a median of 9.9 years (IQR: 5.3–10 years). The kidney function in participants on the standard regimen showed a decline of -1.78 mL/min/1.73 m^2/y (95%CI: -1.82 to -0.43) to an eGFR of 20.2 mL/min/1.73 m^2, in the ESW arm kidney function declined with -1.13 mL/min/1.73 m^2/y (95%CI: -1.64 to -0.61), reaching 24.8 mL/min/1.73 m^2, and in the tac-min study arm kidney function declined with -1.95 mL/min/1.73 m^2/y, reaching 18.6 mL/min/1.73 m^2 at 10 years. At 10 years, DCGF and death occurred in 10% and 44% of standard therapy recipients, 11% and 35% of ESW, and 13% and 39% of tac-min. The intention-to-treat, per-protocol, and sensitivity analyses all yielded statistically non-significant results.

Conclusion

The 10-year decline in eGFR, rates of rejection, graft loss, and death were comparable across all treatment arms. These findings confirm the long-term safety of early immunosuppression minimization strategies in selected low- to moderate-risk KTR.

Daratumumab Reduces Microvascular Inflammation And Stabilizes Graft Function In Chronic Active Antibody-Mediated Rejection: A Target Trial Emulation

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Background

Antibody-mediated rejection (AMR) remains a major cause of late renal allograft loss, yet no targeted therapy has achieved regulatory approval. CD38 has emerged as a promising target due to its expression on plasma cells and NK-cells, key mediators of AMR. Daratumumab, a CD38-directed monoclonal antibody approved for multiple myeloma, may therefore provide dual immunomodulatory benefit. After early termination of the IMAGINE trial investigating clazakizumab for AMR due to futility, daratumumab became available under compassionate use at our center.

Methods

We emulated a target trial comparing daratumumab with placebo in kidney transplant recipients with biopsy-proven chronic active AMR. Placebo recipients from IMAGINE (2021−2023; n=7) were compared with patients treated with daratumumab (post-2023; n=8). All daratumumab-treated patients met identical IMAGINE eligibility criteria. Treatment allocation was determined solely by calendar time. Patients with AMR before 2024 were enrolled in IMAGINE, those after received daratumumab, minimizing confounding by indication. Patients without follow-up biopsy due to trial termination (placebo, n=2) or limited follow-up (daratumumab, n=2) were excluded from histologic analyses. Longitudinal eGFR and urine protein-to-creatinine ratio (UPCR) were modeled using Gamma mixed-effects models; donor-specific antibody (DSA) mean fluorescence intensity (MFI) and Banff activity, chronicity, and microvascular inflammation (MVI) scores were compared using paired and between-group Wilcoxon-tests.

Results

Baseline MVI and activity scores were comparable between groups (Daratumumab vs. placebo: MVI 5.0 [4.2−5.8] vs 5.0 [5.0−6.0]; activity 10.5 [7.8−11.8] vs 10.0 [5.5−11.0]). Daratumumab significantly reduced MVI (Δ−1.5 [−2.0 to −1.0], p=0.03) versus no change with placebo (Δ0 [0−0], p=1.0; between-group p=0.05). A strong trend toward reduced rejection activity was seen with daratumumab (Δ−2.5 [−3.8 to −2.0], p=0.06) but not placebo (Δ0.0 [0.0 to +2.0], p=1.0). A trend toward attenuated chronicity progression was observed with daratumumab (Δ−1.0 [−2.0 to −0.8]) compared with placebo (Δ+3.0 [0.0 to +6.0]; p=0.08). Daratumumab stabilized kidney function (eGFR slope +0.8 vs. −1.2 mL/min/1.73 m^2/month; p=0.01) and improved proteinuria (UPCR −0.92 vs +0.87 mg/mmol/month; p=0.05). DSA MFI changes were nonsignificant.

Conclusions

In this placebo-controlled target trial emulation, daratumumab reduced microvascular inflammation and stabilized graft function in chronic active AMR, supporting CD38-targeted therapy as a promising treatment strategy.

Additive Effect Of APOL1 Risk Variants On Creatinine In A Multi-Ethnic Amsterdam Cohort

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Background

The apolipoprotein L1 gene (APOL1) has two variants that are associated with an increased risk of kidney disease. These risk variants are only found in people of West African descent. Initially, two risk variants and a second-hit were thought to be necessary for increased risk of kidney disease, but recent studies from Africa and the USA suggest an additive effect. This study aimed to assess whether an additive hereditary pattern is present in our large multi-ethnic cohort.

Methods

A cross-sectional analysis was performed with Dutch, African Surinamese, Moroccan or Ghanaian participants from the Healthy Life in an Urban Setting (HELIUS). The APOL1 variants were determined by PCR or a TaqMan Assay. Primary outcome was the prevalence of APOL1 risk variants. Secondary outcome was the association between APOL1 risk variants and creatinine, evaluated by ethnicity-stratified multiple linear regression adjusted for age, sex, BMI, hypertension, and diabetes. Box-Cox transformation corrected for non-normality.

Results

A total of 12 624 participants were included. 0.6% of Dutch and 2% of Moroccan participants carried one or more APOL1 risk variants. Of the African-Surinamese participants, 9.4% had two risk variants and 39.5% had one. In the Ghanaian group, 30.4% had two and 45.6% had one. Linear regression for creatinine showed a positive association with not only two but also a single APOL1 risk variant in the African-Surinamese (1vs0 risk alleles: p<0.01; 2vs0: p<0.01; 2vs1: p=0.01). This difference was also apparent in the Ghanaians (1vs0: p= 0.03; 2vs0: p<0.01; 2vs1: p= 0.2).

Conclusions

In conclusion, APOL1 risk variants are highly prevalent in the African-Surinamese and Ghanaian population in Amsterdam. We found evidence for an additive effect of APOL1 risk variants on creatinine levels, supporting the recent paradigm shift. Future efforts will focus on confirming the results longitudinally.

Impact Of Cold Ischemia Time On 5-Year Kidney Graft Survival After Brain- And Circulatory-Death Donation In The Era Of Hypothermic Machine Perfusion

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Background

Cold ischemia time (CIT) has historically been a key determinant of kidney graft survival, particularly in donation after circulatory death (DCD) kidneys. Since 2016, the Netherlands has implemented routine hypothermic machine perfusion (HMP) for all deceased donor kidneys. A development that may mitigate ischemic injury. It remains uncertain whether CIT continues to influence death-censored graft survival (DCGS) in this modern preservation era. This study evaluated the association between CIT and 5-year DCGS in brain-death (DBD) and DCD donor kidneys preserved by HMP.

Methods

We analyzed all adult first-time, kidney-only transplants performed in the Netherlands between 2016 and 2024 using data from the national Dutch Organ Transplant Registry. The cohort comprised 3,560 transplantations, including 1,371 from DBD and 2,189 from DCD donors. Multiple imputation was applied to address missing covariate data. CIT was modeled using restricted cubic splines and tested for interactions with donor type and, within DCD grafts, with warm ischemic time. Cause-specific Cox proportional hazards models were adjusted for donor-, recipient-, and transplant-related characteristics. An arbitrary cut-off was chosen for 10 & 18 hours CIT to calculate the hazard ratio.

Results

The median CIT was 12.9 hours (interquartile range 9.4−17.3; range 0.1−34.5) for DBD grafts and 11.3 hours (IQR 8.6−14.4; range 0.8−32.0) for DCD grafts. Across all models, CIT showed no significant association with 5-year DCGS, either overall or by donor type. Within DBD grafts, the adjusted hazard ratio (HR) for 18 versus 10 hours of CIT was 0.79 (95% CI 0.46−1.38; p = 0.42). Within DCD grafts, the HR was 1.01 (95% CI 0.62−1.63; p = 0.98). When further stratifying DCD transplants by Eurotransplant Senior Program (ESP) participation, the adjusted HR for 18 versus 10 hours of CIT was 1.19 (95% CI 0.67−2.10) in non-ESP pairs and 0.80 (95% CI 0.32−1.96) in ESP pairs, indicating no evidence that the effect of CIT differed by donor−recipient age matching.

Conclusions

In the Dutch era of universal HMP, CIT was not associated with 5-year DCGS after either DBD or DCD kidney transplantation, suggesting that its impact on graft outcomes has diminished with current preservation and transplant practices.

Kidney Transplantation Is Associated With Improved Survival In Heart And Lung Transplant Recipients With Kidney Failure: A Retrospective Cohort Study

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Pre-Transplant Donor-Specific Anti-HLA Antibodies (DSAs) And Their Relationship with Kidney Graft Survival: Results From The PROCARE 2.0 Cohort Study

Background

Ten to fifteen percent of heart or lung transplant recipients develop kidney failure due to nephrotoxic immunosuppression and pre-existing comorbidities. It is unknown whether kidney transplantation after thoracic transplantation (K-TTx), regardless of whether it is pre-emptive or after a period of dialyses, improves patient and graft survival compared to dialysis alone. In this study, we compared outcomes of kidney transplantation after TTx to dialysis after TTx.

Methods

In this longitudinal cohort study using data from the TransplantLines biobank and cohort study, we analyzed patients with a history of heart or lung transplantation who developed kidney failure, requiring dialysis (D-TTx) or underwent kidney transplantation (K-TTx). A group of propensity-matched kidney-only transplant patients (KTx) was included for comparison. Kaplan-Meier and Cox regression analyses were performed to assess kidney allograft and patient survival.

Results

Twenty-three K-TTx patients (age 62.9 years ± 14.1 year, 48% female, BMI 23.3 ± 3.1 yearkg/m2) were included, comprising 6 heart and 17 lung transplant recipients. These patients were compared with 23 propensity-matched KTx patients and 26 D-TTx patients. K-TTx patients were matched to KTx recipients based on age, sex, BMI and type of kidney donor (living vs. deceased). The D-TTx group was not matched and represents an independent cohort. Five-year patient survival was 72.0% in K-TTx, 23.1% in D-TTx and 91.3% in KTx. Multivariable Cox regression, with adjustment for sex, age at transplant, donor type (living or deceased), and dialysis before transplantation, showed that D-TTx was associated with significantly higher mortality risk compared to K-TTx (HR 3.98, 95% CI 1.66-9.53, p=0.002).

Conclusions

Kidney transplantation after heart or lung transplantation is associated with significantly better overall survival compared to those who remained on dialysis.

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Background

A risk factor for long-term kidney graft survival identified in previous studies, including PROCARE 1.0 (1995−2005), is the presence of pre-transplant donor-specific anti-HLA antibodies (DSAs). Building on these findings, PROCARE 2.0 established a national retrospective cohort of all kidney transplantations in the Netherlands from 2006 to 2016 to reassess the impact of pre-transplant DSAs in a modern population.

Methods

All kidney transplantations in the Netherlands between 2006 and 2016 were included, with a median follow-up of 5 years. Clinical data were obtained from the national organ transplant registry (NOTR) and linked to donor and recipient HLA typing and Luminex Single Antigen Bead (SAB) data (One-Lambda and Immucor) from all Dutch HLA laboratories. Pre-transplant DSAs were classified as positive as described by Wisse et al. (2019). Baseline characteristics and graft survival were compared with PROCARE 1.0, and the relationship between pre-transplant DSAs and death-censored graft survival was assessed.

Results

Clinical data were available for 9,674 kidney transplantations; after excluding cases without follow-up or HLA data, 9,659 were analyzed. Preliminary analyses demonstrated shifts in baseline characteristics between PROCARE 1.0 and 2.0, including a higher proportion of living donors, increased donor and recipient age, more frequent use of IL-2 receptor blocker induction, and wider adoption of tacrolimus-based maintenance immunosuppression.

Pre-transplant DSAs were present in 369 of 9,659 transplantations (~3.8%). Despite a significant improvement in 10-year death-censored graft survival from 73% in PROCARE 1.0 to 82% in PROCARE 2.0 (p < 0.001), pre-transplant DSAs remained strongly linked to inferior outcomes.

This effect was seen in both living and deceased donors, with DSA-positive deceased-donor recipients showing the lowest graft survival (70% in living vs. 48% in deceased, p = 0.001). In contrast, DSA-negative recipients had better outcomes (85% living, 78% deceased). Combined HLA class I and II DSAs conferred the poorest survival (30%), while DSAs restricted to class I or II resulted in intermediate outcomes (~70%).

Conclusions

The PROCARE 2.0 cohort represents a national dataset on kidney transplantation. While overall graft survival improved from 1995 to 2016, this preliminary analysis shows that pre-transplant DSAs are an important determinant of poorer outcomes after both living and deceased donation.

Reference

Wisse et al. Transplantation. 2019 Apr;103(4):789-797. doi:10.1097/TP.0000000000002357.PMID: 30106794

Validating The Impact Of HLA-DQα05 Heterodimer And HLA-DQ Evolutionary Divergent Mismatches In Kidney Transplant Recipients: A Multinational Cohort

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Background

De novo donor-specific HLA antibodies (dnDSA) most often target HLA-DQ mismatches in kidney transplantation, yet not all DQ mismatches are equally immunogenic. HLA-DQ forms a heterodimer of polymorphic α- and β-chains, and prior work showed that specific qualitative properties of these chains drive dnDSA formation. Evolutionary analyses classify HLA-DQ heterodimers into two major clades: clade 1, comprising DQα01-heterodimers, and clade 2, encompassing all non-DQα01 heterodimers. Prior single-center research demonstrated that in patients with two DQ mismatches but one dnDSA (2MM1DSA), most dnDSA targeted heterodimers belonging to the opposite evolutionary clade as the recipient or heterodimers carrying the DQα05 chain. This unique model allowed direct comparison of mismatch immunogenicity within a controlled recipient milieu. Here, we validated these findings in a multicenter cohort spanning two continents and three allocation systems.

Methods

We analyzed 3,841 consecutive kidney transplant recipients with second-field HLA-DQ typing from five centers. Patients fully matched at HLA-DQ or with preformed DSA (any locus) or early posttransplant DQ-DSA (<6 weeks) were excluded, yielding 3,003 analyzable recipients. Ninety-four were classified as 2MM1DSA. Within each patient, mismatches were categorized as dnDSA-generating or non-dnDSA-generating and classified as evolutionary clade mismatch, DQα05 heterodimer mismatch, or neither.

Results

Among 2MM1DSA patients, dnDSA-inducing alleles were significantly enriched for DQα05 heterodimer mismatches and for evolutionary clade mismatches in clade-homozygous recipients (Combined 71.3% vs. 14.8%, $p<0.001$ compared to non-dnDSA inducing mismatches). These associations persisted in the full cohort. After multivariable adjustment, DQα05 heterodimer mismatches conferred higher dnDSA risk than all other DQ mismatches (HR 2.08, 95%CI 1.60−2.71, $p<0.001$). Evolutionary clade analyses demonstrated directional effects: clade 1 homozygous recipients (DQα01-heterodimers) mismatched with a clade 2 donor allele showed the highest risk (HR 12.35, 95%CI 4.56−33.41, $p<0.001$), whereas

the reverse direction (clade 2→clade 1) had a smaller but still significant effect (HR 1.82, 95%CI 1.29−2.58, $p=0.001$).

Conclusions

This multicenter study confirms the strong immunogenicity of DQα05 heterodimer and evolutionarily divergent clade mismatches, both within the 2MM1DSA model and in full-cohort analyses. These findings challenge the β-chain-centric view of DQ immunogenicity and support evaluating HLA-DQ as a heterodimer to refine risk stratification and guide tailored immunosuppression.

Steadfast Study Update: A Phase 1/2 Clinical Trial Of Regulatory T Cells Expressing A Chimeric Antigen Receptor Directed Towards HLA-A2 In Renal Transplantation

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Background

The goal of treatment with TX200-TR101 (TX200), autologous naïve regulatory T cells expressing a chimeric antigen receptor directed to HLA-A2, was safe reduction of standard-of-care immunosuppression in transplant recipients by induction of immunological tolerance.

Methods

STEADFAST is a Bayesian Optimal Interval Design, first-in-human, phase I/IIa, multicenter, open-label, ascending single dose-ranging study to assess the safety, tolerability and proof of mechanism of TX200 in living-donor kidney transplant recipients. The study recruited subjects aged 18-70 years, HLA-A2 negative, receiving a renal allograft from an HLA-A2 positive donor. Subjects received one infusion of escalating dose levels (DL) of TX200 11-23 weeks post-transplant with follow-up for 72 weeks post-dose. Control subjects had similar enrolment criteria. The primary endpoint was safety and tolerability 28 days post-treatment. Secondary endpoints were long-term safety, acute graft related outcomes, reduction of immunosuppression, and localization of TX200 in the graft.

Results

The study is ongoing; data cut made 11July2024. Eight transplant recipients received TX200 compared with 3 control transplant recipients. Three subjects were recruited to DL1, 1 to DL2, 1 to DL3 and 3 to DL4. The study demonstrated excellent safety of TX200 with similar proportions of treatment-emergent adverse events (AEs) and serious AEs for TX200 treated vs. control subjects, none was considered related to TX200, and the majority (96%) were of grade 1 or 2 in severity. TX200 cells were detected by ddPCR in blood up to 8 months post-treatment and observed in the graft, along with tolerogenic structures indicating engraftment. By end Jan 2025, 3 of 5 subjects in DL2 or above achieved complete tapering of mycophenolate mofetil (MMF) to tacrolimus monotherapy compared to none of the control subjects; it is too early to assess the success of the other 2 subjects. No subjects experienced graft loss and kidney function remained stable with no signals of proteinuria, despite complete tapering of MMF in some subjects.

Conclusions

These data demonstrate that TX200 has a favourable safety profile, with preliminary biomarker data consistent with the proof of mechanism and establishment of tolerance in the renal graft. The study completes 4Q2025.

Intensive Care Unit-Specific Virtual Reality (ICU-VR) Impact On ICU Preparation And Anxiety Levels In Lung Transplant Patients

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Background

Aim

Undergoing Lung transplantation (LTx) surgery can lead to a prolonged Intensive Care Unit (ICU) admission. Often, ICU survivors develop psychological distress, including anxiety, depression, and post-traumatic stress syndrome (PTSS) (Vlake et al., 2020). ICU-VR is designed to provide patients with a virtual, immersive experience of the ICU environment, aiming to improve their understanding of the ICU and reduce pre-admission anxiety. This study evaluated the effect of ICU-VR on comprehension of ICU workflows and treatments and anxiety reduction in LTx patients.

Methods

A monocentric randomized controlled trial was conducted in which LTx patients on the waiting list were assigned to standard care (control group) or standard care supplemented with ICU-VR (intervention group). All participants completed a questionnaire assessing information provision, while ICU-VR participants answered additional questions regarding their ICU-VR experience.

Results

Forty-nine LTx patients were included, (median age: 60 years; range: 41–68 years), of whom 67% were female. The ICU-VR group reported significantly better provision of ICU-related information (p-values ranging from 0.029 to <0.001) and a reduced perceived disease burden. No significant difference was found in perceived anxiety (p = 0.99). Most participants found ICU-VR to be accessible, understandable, realistic, and would recommend the intervention. The study is ongoing, and additional results are pending.

Conclusions

ICU-VR appears to be an effective and accessible tool to enhance ICU preparation in LTx patients on the waiting list by improving information provision and reducing the perceived burden of illness. Although no significant effect on anxiety was observed, participants acknowledged its added value. Further studies are warranted to optimize ICU-VR, evaluate long-term effects, and explore its use in other transplant populations.

Reference

Vlake JH, van Genderen ME, Schut A, Verkade M, Wils EJ, Gommers D, van Bommel J.J Intensive Care. 2020 Jan 9;8:6. doi: 10.1186/s40560-019-0422-0. eCollection 2020.PMID: 31938546

Grasp On Fatigue: A Behavioral And Educational Intervention To Reduce Post-Lung Transplant Fatigue

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Background
Introduction

Over a 100 lung transplants surgeries occur annually in the Netherlands. Although transplantations significantly improve quality of life, many patients experience persistent fatigue. The problem analysis identified key determinants. Positive determinants on fatigue are higher muscle mass, adequate- self-management and expectation management. Negative determinants on fatigue are low lung function, medicinal side effects and inadequate coping. Influencing the behavior of lung transplant patients can help reduce fatigue. This study aims to develop a theoretically grounded and feasible intervention to reduce fatigue after lung transplantation.

Methods

An intervention ("Grasp on Fatigue") was developed using the Precede-Proceed model, Intervention Mapping and a Logic Model of Change, supported by literature and stakeholder research. Implementation feasibility was assessed through literature research and the Innovation Contingency Model. Financial feasibility was assessed through the Indicative Social Cost-Benefit Analysis.

Results

"Grasp on Fatigue" intervenes through modules on expectation management, self-management and coping. The expectation management module supports patients through educational- and psychological guidance, emphasizing goal setting and adaptive coping strategies. The online self-management module is based on educational sessions with interactive training in decision-making and action planning. The coping module focuses on digital cognitive behavioral therapy and psychoeducational support.

Implementation could be feasible if co-creation and autonomy of caregivers is guaranteed. The Indicative Social Cost-Benefit Analysis suggests that Grasp on Fatigue could be economically, strategically and socially viable, if structural financing is realized. This could result in potential health cost savings and better care outcomes.

Conclusions
Discussion

"Grasp on Fatigue" fills a gap in fatigue interventions for lung transplant patients. Tailoring educational needs and improved operationalization of the concept of fatigue and fatiguability is required for optimal effect monitoring of the intervention. Furthermore, if the intervention is proven effective, strategies to ensure a sustainable implementation should be developed and monitored.

Conclusion

"Grasp on Fatigue" offers a promising, feasible approach to reducing fatigue after lung transplantation, with potential to improve quality of life and reduce healthcare costs.

A Structural Impetus For Lifestyle Care Within Transplantation

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Background

Transplant recipients frequently experience lifestyle-related problems and complications as a result of immunosuppressive medication. Cardiovascular disease is the leading cause of mortality within this population. Despite the proven importance of lifestyle factors for long-term transplant success, current care is fragmented and insufficiently aligned with these needs. Lifestyle counselling is currently in part the responsibility of nurse consultants/specialists within organ-specific teams, who are already heavily burdened. Moreover, within primary care there is often undertraining and limited expertise in the management of this complex patient group.

Methods

The Transplant Institute is committed to integrating lifestyle in patient care by appointing a master's degree professional (nurse practitioner/physician assistant) who provides lifestyle counselling, is authorised to prescribe anti-obesity medication, establishes links with primary care, and contributes to knowledge sharing through training, consultation, and regional collaboration. To support the proposed appointment, the current BMI and diabetes distribution was assessed among post-transplant patients.

Results

At present, 4,613 transplant recipients (lung, (mechanical support) heart, liver, kidney) are in outpatient follow-up at the Transplant Institute. Among heart (including mechanical support), liver, and kidney transplant recipients for whom up-to-date weight data are available (n = 3,496), 27% of patients have a BMI > 25 (n = 936), and 18% have a BMI > 30 (n = 629). In addition, diabetes is present in 31% of heart, 25% of liver, and 35% of kidney transplant recipients.

Conclusions

These figures underscore the urgency of structural lifestyle interventions. We expect that this investment will contribute to a reduction in complications, including cardiovascular disease and readmissions, and to improvements in quality of life and patient satisfaction. These outcomes will be systematically evaluated during outpatient consultations.

Life After Kidney Donation: Exploring The Experiences And Care Needs Of Kidney Donors In The First Year After Donation

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Background

About half of the kidney transplantations in the Netherlands are performed using a kidney of a living donor. Although the vast majority of LKDs are satisfied with (after)care, dissatisfaction is sometimes reported. It is not clear to care professionals why these donors are unsatisfied. The aim of this study was to gain insight into donation experiences and potential unmet care needs among living kidney donors in the first year after donation, in order to improve quality of care and aligning the development of interventions with donors' needs.

Methods

We conducted a qualitative research, based on semi structured interviews with male and female LKD between the age of 18 and 80 years old. Participants received pre-operative screening, surgery and aftercare at Erasmus MC. The findings were categorized according to the overarching themes identified after a previous literature

review: donor experiences, unmet care needs, and the use of a conversational intervention.

Results

A total of nine kidney donors (five female, ages 34-75 years) were interviewed. Participants were included when there were signs of psychological distress, complications or a changed donor-recipient relationship.

Negative experiences were primarily related to uncertainty regarding physical recovery or renal function, as well as perceived discrepancies between pre-donation information and the actual post-donation trajectory.

Unmet care needs included a desire for more frequent follow-up contact with healthcare professionals and improved access to psychosocial support, such as social work. The need for psychological support post-donation was greater among donors who presented with psychosocial or psychological risk factors prior to donation.

Participants did not express a need for donor gratifications or meetings with fellow donors. However, they were open to the use of a conversational intervention as part of post-donation care.

Conclusions

While participants generally reported positive experiences with post-donation care, there appears to be a need for improvements in psychosocial support and adjustments to information and patient education regarding physical recovery and nutritional advice. Although data on whether interventions will help improve satisfaction in donors with psychological risk factors are lacking, there is a need for improvement of postdonation (conversational) interventions.

Living Kidney Donation In The Presence Of Asymptomatic Microscopic Hematuria

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Background

AMH can be challenging to interpret during the evaluation of a potential living kidney donor. The aim of this study is to investigate whether AMH identified during donor screening (after common causes have been ruled out) is associated with post-donation outcomes, such as (severe) loss of kidney function.

Methods

A quantitative retrospective study was conducted on living kidney donors who donated a kidney at our center between 1981 and 2012. All donor needed to have at least two separate pre-donation urine tests available. The cohort was divided into a group without microscopic hematuria (control group) and a group with AMH. All donors underwent urological and gynaecological evaluation; no pre- donation biopsy was performed. The main outcomes were kidney function and albuminuria over time, rate of kidney failure, and onset of hypertension.

Results

71 kidney donors with AMH and 1096 donors without AMH were identified. The average age at the time of donation was 50 ($\pm$ 12.8) years. The AMH-group consisted of more women (78%). There was no difference between the groups in pre-donation kidney function and blood pressure. In the AMH group, the ACR pre- donation was numerically higher than in the control group (1.3 vs 0.7 mg/mmol, p <0.001). The median follow-up time was 15 [IQR 11-18] years. There was no significant difference in eGFR between the two groups during the follow-up period, even 25 years after donation (50 ml/min vs 60 ml/min, p=0.675). In the AMH group, four donors had kidney failure (5.6%) versus seven donors (0.6%) in the control group (p=0.003 odds ratio = 9.29). The median time from donation to kidney failure was 18 [range 12-30] years. The last measured albumine-creatinine ratio was severely increased (>30 mg/mmol) in 18.3% in the AMH-group vs 6.4% control group (p=0.001). Fifteen years after donation, 23.9% donors from the AMH-group have high blood pressure compared to 160 donors from the control group (14.6%, p=0.03).

Conclusions

Kidney donation in donors with pre-donation AMH was associated with an increased risk of kidney failure, severely increased albuminuria, and hypertension after a median follow-up time of 15 years.

National Study On Improving Care For Living Kidney Donors

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Background

Within LONT, a proposal was developed to improve the care of living kidney donors. Following this proposal, a project group was able to conduct an improvement project from September 2024 to July 2025, supported by a grant from the Dutch Kidney Foundation. The focus was on improving the following components: (After)care for kidney donors; acceptance criteria for kidney donors; establishment of a national consultation framework; uniform informed consent; and reimbursement by health insurers.

Methods

(After)care for kidney donors: A structured questionnaire was distributed to 1,509 donors who donated in the period 2022–2024 (response rate: 686 donors; 44.1%) and to donors who discontinued the donor trajectory (response: 358 donors). Consultation took place with social workers from all Dutch university medical centres (UMCs) to develop a uniform psychosocial screening, using the Dutch version of EPAT as the reference framework.

Acceptance criteria for kidney donors: An inventory was made of similarities and differences in donor acceptance criteria across all UMCs in the Netherlands.

Establishment of national consultation: A foundational document was drafted, submitted to LONT, and subsequently approved.

Uniform informed consent: An inventory was made of similarities and differences in informed consent documents.

Reimbursement by health insurers: A national consultation of healthcare administration staff was established to identify bottlenecks. Meetings were held with Zorgverzekeraars Nederland and the Ministry of Health, Welfare and Sport (VWS) to raise and discuss these bottlenecks.

Results

Ad 1: A research report with recommendations for improving kidney donor care was produced and distributed to all stakeholders involved in living donation. A nationally uniform psychosocial screening for living kidney donors was established.

Ad 2: A proposal for uniform acceptance criteria for kidney donors was submitted to the National Working Group for Living Kidney Donation (LWLN).

Ad 3: The National Working Group for Living Kidney Donation (LWLN) was established, with multidisciplinary participants from the UMCs.

Ad 4: A proposal for a uniform informed consent was submitted to the LWLN.

Ad 5: The Ministry of Health, Welfare and Sport (VWS) is exploring the possibility of declaring costs to the donor's health insurer, while retaining the option of declaring costs to the recipient's health insurer in specific situations. Specific hurdles were brought to the attention of health insurers.

Conclusions

The questionnaire study resulted in recommendations addressing the following aspects: duration of the donor trajectory, patient information, modes of communication, communication when discontinuing the donor trajectory, hospital admission, post-donation recovery period, interpersonal approach, periodic follow-up, and peer support.

The Importance Of Nutrition Advice In Immunosuppressed Solid Organ Transplant Recipients For The Prevention Of Foodborne Bacterial Infections

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Background
Successful solid organ transplantation (SOT) requires a balance between minimizing graft rejection and maintaining immune function to prevent infections. To reduce the risk of foodborne infections, SOT recipients are generally advised to avoid raw animal products and unpasteurized dairy products. However, strictness and recommended duration of these dietary restrictions vary between transplant centres, leading to confusion and nonadherence. To support a uniform evidence-based advice, this analysis provides an overview of current literature on the incidence and consequences of foodborne infections in SOT, taking patient adherence into account.

Methods
A systematic search was conducted in PubMed for articles published in the past ten years, using terms such as "organ transplant" AND ("food" OR "nutrition") AND "infection". Studies focusing solely on non-bacterial or non-foodborne infections were excluded. After screening titles and abstracts, relevant articles were selected for full-text review and subsequently evaluated and compared.

Results
Of 62 articles initially identified as applicable, 16 articles were used in this review. The percentages of cases in the different study populations were consistently around 3.0%. Standardized incidence ratios (SIRs) showed that infections occurred 7.4 times more often in SOT recipients compared to the general population, and Salmonella infections showed SIRs ranging from 2.8 to 4.6. Common symptoms included diarrhea (93.5%), abdominal pain (39.6%), fever (36.7%), nausea (24.5%). Hospital admission was required in 47.7% of cases, ICU admission in 4.1%. Severe infections typically occurred 1.5 to 2.4 years post-transplantation.

Although only 17.7% of patients fully adhered to all food safety recommendations, most reported partial adherence, with higher adherence the first year post-transplant.

Dietary advice was largely consistent across centres, but the recommended duration varied from 3 months to lifelong.

Conclusions
The number of studies investigating the actual impact of foodborne infections in SOT recipients is limited. Foodborne infections occur more frequently in SOT recipients and consequences are more severe compared to the general population. This burden is likely even underestimated due to underreporting of mild cases. Notably, severe infections tend to occur later than one year post-transplantation, possibly due to declining adherence and short recommended duration for dietary restrictions. These findings underscore the importance of sustained adherence.

Quality Of Life In The First Year After Kidney Transplantation

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Background

Quality of life is an important outcome for patients after kidney transplantation. Patient-reported outcome measures (PROMs) allow systematic assessment of quality of life in kidney transplant recipients. Insight into both physical and mental quality of life is essential for optimal patient care.

Methods

In the Patient-Reported Outcomes in Kidney Transplant Recipients, i.e. Input of Valuable Endpoints (POSITIVE) study, 101 men (57 years, $\pm$13) and 47 women (52 years, $\pm$16) in the first year after kidney transplantation were included at Maastricht UMC+ and LUMC. From January 2021 onwards, patients completed the SF-12 questionnaire before transplantation and at 6 weeks, 6 months, and 12 months after kidney transplantation. The SF-12 provides scores for physical (PCS) and mental (MCS) health. Analyses were performed for the total cohort, with additional tests examining whether donor type (living vs deceased) and timing of transplantation (pre-emptive vs non-pre-emptive) influenced PCS and MCS.

Results

For the total cohort, the PCS at the time of kidney transplantation was 41 (SD = 9.31). This decreased to 38 (SD = 9.28) after 6 weeks and recovered to 45 (SD = 8.80) after 6 months and 47 (SD = 8.72) after 12 months. The MCS gradually increased from 47 (SD = 10.49) at transplantation to 50 (SD = 10.39) after 6 weeks, 52 (SD = 9.92) after 6 months, and 53 (SD = 8.38) after 12 months.

Recipients of a living donor had a significantly higher MCS at 6 weeks compared with recipients of a deceased donor (p = 0.001), while PCS remained comparable between the two groups. Pre-emptive transplantation was associated with a higher PCS at 12 months (p = 0.030), with no difference in MCS at any time point.

Conclusions

Physical quality of life temporarily declines at 6 weeks after kidney transplantation but improves over the first year. Within this recovery, patients who underwent pre-emptive transplantation had better physical health at 12 months, without differences in mental quality of life. Mental quality of life improves gradually, with recipients of a living donor showing an advantage as early as 6 weeks after transplantation, while physical quality of life remains comparable.

Advancing Glycosylation Profiling Of Donor HLA-Specific Antibodies To Elucidate Their Pathogenic Potential

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Background

Antibody-mediated rejection is a major reason for graft failure after kidney transplantation. Antibody glycosylation has been recognized as an important determinant for antibody pathogenicity. Here, we describe the development of a mass spectrometry-based method to specifically determine the glycosylation pattern of donor HLA-specific antibodies (DSA) from serum.

Methods

Anti-HLA-specific antibodies were isolated from 10 µL human serum using ELISA-plates coated with streptavidin and biotinylated HLA-A2, HLA-B7, HLA-DQ2 or HLA-DQ6 (12.5-30 ng/well; HLA Protein Technologies Inc). Captured antibodies were eluted under acidic conditions, trypsinized, and glycopeptides were measured by liquid chromatography-mass spectrometry (LC-MS). The method was validated using serum negative for anti-HLA antibodies, as determined by Luminex, and negative serum spiked with 1 µg/mL of monoclonal antibodies (MoAb) against the HLA of interest. As proof of concept, five sera of pregnant women with known anti-HLA specificities were used. DSA glycosylation profiles were

compared to profiles of total IgG from the same donor, which was isolated from serum using Protein G.

Results

For HLA-DQ2 and HLA-DQ6, the efficiency of MoAb capturing from spiked serum was relatively low (5.5%±5.6% and 14%±2.2% respectively) and some non-specific IgG signal was present (55%±19% and 20%±2.5% of the spiked serum signal respectively). For HLA-A2 and HLA-B7, the MoAb capturing efficiency was higher (48%±8.7% and 33%±0.028% respectively) and minimal capturing of non-specific IgG was observed (0% and 3.1%±1.9% of the spiked serum signal respectively). The glycosylation profile of the captured anti-HLA-A2 and anti-HLA-B7 MoAbs from spiked serum overlapped with the profile of the pure MoAb, indicating an unbiased isolation of the HLA-specific antibodies.

The methods for these four HLAs were successfully applied to profile total and HLA-specific IgG from donor sera, revealing distinct glycosylation of HLA-specific IgG. Fucosylation, galactosylation, sialylation and bisection were assessed. Differences were particularly apparent for IgG1 fucosylation, with a median of 83.5% (IQR 82.6%-91.5%) and 94.4% (IQR 91.6%-96.1%) for specific and total IgG1, respectively.

Conclusions

With this ELISA- and LC-MS-based method, the glycosylation pattern of anti-HLA-specific antibodies could be determined, although optimization for HLA class II is still possible. It can be applied to study DSA pathogenicity in the context of kidney transplantation.

A Human Organoid-On-Chip System To Study Liver-Kidney Communication In Transplantation

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Background

Liver and kidney communication holds a crucial role in maintaining homeostasis. Pathological conditions that primarily affect either the liver or the kidney can lead to reciprocal organ dysfunction. Lack of representative *in vitro* models hinder the elucidation of mechanisms underlying liver-kidney connection in the context of organ transplantation. The aim of the present study is to develop a robust organ-on-chip (OOC) system to model human liver-kidney crosstalk *in vitro*.

Methods

Human induced pluripotent stem cell-derived kidney organoids and adult liver-derived hepatocyte-differentiated organoids were generated and transferred to separate chambers of the TissUse HUMIMIC OOC system connected through a unidirectional, pulsatile flow. To validate the system, three culture setups were compared; static mono-culture, static co-culture, and fluidic co-culture. Kidney and hepatocyte-differentiated organoid phenotypes were characterized by gene expression and immunohistochemical analyses of key differentiation markers. To test the robustness of the model, 3 different kidney-liver line combinations were tested. To examine protein transfer between the kidney and hepatocyte-differentiated organoid compartments upon fluidic co-culture SILAC mass spectrometry was performed.

Results

The organ-on-chip system supported the expression of key kidney (WT1, PODXL, CDH1, VIL1) and hepatocyte (*ALB*, *CYP3A4*) differentiation markers of kidney and hepatocyte-differentiated organoids, respectively. Notably, hepatocyte markers were significantly upregulated during fluidic co-culture in comparison to both mono-culture and static co-culture conditions. Consistent results were obtained for different liver-kidney line combinations, indicating a strongly robust system. SILAC MS data revealed that proteins derived from hepatocyte-differentiated organoids are transported through

the system and taken up by the kidney organoids. Interestingly, the observed proteins are mainly involved in detoxification processes and amino acid metabolism which are key pathways involved in liver-kidney physiological crosstalk. Collectively, our results demonstrate that co-culturing kidney and hepatocyte-differentiated organoids in an OOC system enables their active and beneficial communication in a physiologically mimicking manner.

Conclusions

Our study demonstrates the development of a novel and robust liver-kidney OOC system which holds great promise as an *in vitro* model to study liver-kidney communication in physiology and disease. Further research steps will be focused on the application of the system to study organ injury and crosstalk in the transplantation setting.

HLA-DQ Chimeric HLA Antibody Receptor (CHAR) T Cells Target HLA-Specific B Cells To Treat HLA Sensitisation In Solid Organ Transplantation

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Background

An increasing number of patients on the kidney transplant waiting list is HLA-sensitised. These patients face difficulties finding a suitable donor organ due to the presence of HLA-specific antibodies and B cells. Current desensitisation approaches are aimed at eliminating circulating antibodies and/or B cells without distinguishing between antigen-specificity. Chimeric HLA Antibody Receptor (CHAR) T cells are a promising therapy for specific desensitisation. Previous research demonstrated that CHAR T cells can eliminate HLA class I-specific B cells with high precision. Given that many highly sensitised patients have antibodies directed against HLA-DQ, we aimed to develop HLA-DQ CHAR T cells to target HLA-DQ-specific B cells.

Methods

We designed lentiviral vectors encoding HLA-DQ CHAR constructs composed of HLA-DQA1*05:01 with either HLA-DQB1*02:01 (DQ2) or HLA-DQB1*03:01 (DQ7) and the CLIP peptide combined with intracellular 4-1BB costimulatory and CD3ζ signalling domains. We transduced primary CD8+ T cells to express CHAR molecules and enriched when necessary. Furthermore, we generated B cell lines expressing HLA-DQ2 and HLA-DQ7-specific human recombinant B cell receptors (BCRs). We established a mouse model using B cells expressing LALAPG-mutated HLA-DQ2 and HLA-DQ7-specific BCRs to investigate the efficacy of HLA-DQ CHAR T cells *in vivo*.

Results

We successfully generated CD8+ T cells expressing HLA-DQ2 and HLA-DQ7 CHAR molecules that specifically produced IFNγ upon overnight incubation with their respective HLA-DQ2-specific or HLA-DQ7-specific target cells. Moreover, HLA-DQ2 and HLA-DQ7 CHAR T cells exclusively eliminated either HLA-DQ2-specific or HLA-DQ7-specific B cells, respectively. Importantly, HLA-DQ2 and HLA-DQ7 CHAR T cells eradicated their respective HLA-DQ-specific B cells in an *in vivo* model.

Conclusions

To conclude, HLA-DQ CHAR T cells can be efficiently generated and eliminate HLA-DQ-specific B cells *in vitro* and *in vivo* with exquisite specificity. This therapy has the potential to desensitise sensitised renal transplant patients and treat antibody-mediated rejection after solid organ transplantation.

Genome Wide Association Study Identifies Donor Genetic Risk Loci Linked To Non-Anastomotic Biliary Strictures After Liver Transplantation

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Background

Biliary complications affect up to 30% of liver transplant recipients, with a threefold higher incidence in livers from donation after circulatory death (DCD) compared to donation after brain death (DBD). Non-anastomotic biliary strictures (NAS), a treatment-resistant complication, is hypothesized to result from ischemia-reperfusion injury, immune processes and bile salt toxicity. We hypothesized that genetic variants in bile salt transporter genes of the donor liver may predispose to increased risk of NAS after liver transplantation.

Methods

We conducted genome-wide analyses (GWAS) to identify loci associated with NAS, analyzing recipients of DBD and DCD livers separately. We applied logistic regression models adjusted for donor age, sex and principal components 1 to 3. Risk loci (p<1x10-5) were prioritized using Functional Mapping and Annotation, incorporating gene expression data from the Genotype-Tissue Expression project. We then performed targeted gene analyses focusing on bile salt transporter genes and SNPs previously associated with disorders of the biliary tract.

Results

We analyzed data from 776 liver transplant recipients (84% DBD) with a threefold higher incidence of NAS in the DCD group (28%) compared to the DBD group (9%). While bile salt transporter and other targeted gene analyses revealed no significant associations with NAS, the GWAS and subsequent prioritization identified novel risk loci with eQTL effects. After adjusting for confounders (donor age, transplantation indication, warm ischemia time, and transplant era), SNPs in *G Protein-Coupled Receptor 180* (*GPR180*) (Hazard Ratio (HR) 3.10 [95%CI 1.82-5.30], $p=3.5\times10^{-5}$) and *Lipolysis Stimulated Lipoprotein Receptor* (*LSR*) (HR 3.42 [95%CI 1.99-5.88], $p=9.0\times10^{-6}$) showed significance. These genetic variants were relatively common (20% and 8% minor allele frequency, respectively), and conferred a significant synergistic risk for NAS when both loci were present (HR 9.70 [95%CI 4.68-20.12], $p=6.4\times10^{-14}$).

Conclusions

This study links genes *GPR180* and *LSR* to NAS, highlighting systemic processes like vascular remodelling and fibrosis (GPR180), and lipid metabolism (LSR), rather than genes related to bile salt transport. Integrating genetic and clinical data will be essential for refining NAS risk prediction and personalizing management strategies.

Cellular Respiration Of The Liver During Hypothermic And Oxygenated Machine Perfusion: The Relation Between CO_2 And Mitochondrial Injury

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Background

Dual Hypothermic and Oxygenated Machine Perfusion (DHOPE) has been established as a safe and viable strategy for resuscitating donation after circulatory death (DCD) grafts prior to transplantation. During DHOPE, the liver enters a hypometabolic state and receives high, non-physiological levels of oxygen. Upon re-oxygenation of the ischemic graft, flavin mononucleotide (FMN) is released from mitochondrial complex-I due to electron overflow. The extent of mitochondrial damage dictates the rate of electron overflow, and consequently, the production of reactive oxygen species, leading to cellular damage and graft failure. FMN has been validated as a marker for assessing viability during DHOPE. This study investigates cellular respiration in DCD grafts during DHOPE based on CO_2 levels in the perfusate and their correlation with mitochondrial injury.

Methods

In this study, 28 DCD grafts underwent DHOPE prior to transplantation. Perfusate FMN levels after 60 minutes of perfusion were measured using light spectroscopy. Based on the median FMN concentration, two groups were formed: low-FMN (n=14) and high-FMN (n=14) for comparison of the CO_2 production rate. During perfusion, the CO_2 concentration in the exhaled air from the oxygenators was continuously measured. Based on the flow rate (L/min), liver weight (kg), and the molar masses of $^{13}CO_2$ and $^{12}CO_2$, the peak and total CO_2 production could be calculated for each specific liver.

Results

In all livers, concentration FMN ranged from 0.01 to 0.09 μg/mL, with a median of 0.03 μg/mL. The calculated total CO_2 production rate ranged from 11.7 to 41.9 mmol/kg/h, with significantly higher CO_2 production in high-FMN livers (27.3 [23.4–33.3] mmol/kg/h) compared to low-FMN livers (18.1 [12.5–23.1] mmol/kg/h), p=0.006. The peak CO_2 production rate was also significantly higher in the high-FMN group: 0.010 (0.009–0.012) mmol/kg/s vs. 0.007 (0.005–0.008) mmol/kg/s, p=0.011.

Conclusions

Mitochondrial damage, as indicated by high FMN release into the perfusate during DHOPE, was coupled with increased peak and total CO_2 production during the first hour of hypothermic perfusion. This is the first study to assess cellular respiration by considering the individual CO_2 profiles of each liver. This simple, real-time measurement during DHOPE could serve as a surrogate marker for mitochondrial oxidative stress and aid in selecting transplantable grafts.

Everolimus-Based Immunosuppression Induces Donor-Specific Regulatory CD4+ T Cells With Potent Suppressive Capacity

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Background

Everolimus is known for its potential to expand regulatory T cells (Tregs) both in vitro and in vivo. In the OPTIMIZE trial, everolimus−low-dose tacrolimus−prednisolone immunosuppression (EVR-IS) was compared with mycophenolate mofetil−standard-dose tacrolimus−prednisolone immunosuppression (MMF-IS) in elderly recipients of a kidney transplant. We previously observed that EVR-IS, but not MMF-IS, increased circulating CD4^{+} Tregs. This study aimed to assess the donor specificity and suppressive capacity of Tregs under both regimens.

Methods

Donor-specific Tregs were quantified by activation-induced marker (CD137) expression following stimulation with donor cells from kidney transplant recipients on EVR-IS (n=10) or MMF-IS (n=10) before and 12 and 24 months (M) after transplantation. Tregs were sorted from peripheral blood mononuclear cells (PBMCs) at M12 (5 recipients per treatment arm) and expanded for 11 days with either irradiated donor cells or αCD3/αCD28-coated beads in the presence of IL-2 and IL-15. Expanded Tregs were labeled with PKH26 and co-cultured at graded ratios with CFSE-labeled recipient PBMCs stimulated with irradiated donor or fully mismatched third-party cells (3rdP). After 6 days, inhibition of T-cell proliferation was assessed by CFSE dilution via flow cytometry.

Results

In EVR-IS recipients, donor-specific CD137^{+} Tregs increased from 3.9% pre-transplant to 5.8% at M24, while declining under MMF-IS from 3.7% to 0.8% (P<0.01). Tregs had phenotypic characteristics of central- and effector-memory T cells. Tregs from both groups expanded equally well to donor-antigen or polyclonal stimulation, with an average 26-fold expansion. Expanded Tregs induced a dose-dependent inhibition of T-cell proliferation even at ratios<1:100. The suppressive potency did not differ between the Tregs derived from participants treated with either of the two treatment regimens. Interestingly, donor-specific Tregs possessed a superior capacity of suppressing donor-antigen-induced T-cell proliferation compared to suppression of 3P-induced proliferation. At a ratio of 1:64, donor-antigen-induced proliferation was inhibited by 36% whereas 3rdP-induced proliferation was not inhibited (P<0.01).

Conclusions

EVR-IS promotes the expansion of donor-specific Tregs with potent suppressive capacity. These findings imply that EVR-based immunosuppression helps control alloreactive T-cell responses in kidney transplant recipients through Treg-mediated mechanisms.

Ex Vivo Optimization Of Donor Lungs With Inhaled Sevoflurane During Normothermic Ex Vivo Lung Perfusion (VITALISE): A Randomized Dose-Response Study In Sheep Lungs

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Background

Volatile anaesthetics modulate ischemia–reperfusion injury (IRI) through mitochondrial protection, endothelial preservation, and anti-inflammatory effects. Ex vivo lung perfusion (EVLP) enables evaluation and reconditioning of donor lungs within a therapeutic window. We hypothesized that ventilation with sevoflurane during EVLP reduces injury and improves graft function.

Methods

Thirty-two sheep lungs were randomized to four groups (n = 8/group) ventilated with sevoflurane at 0%, 2%, 4%, or 6% end-tidal concentration (Cet) during 4 h of normothermic EVLP after 3 h of cold storage. Dynamic compliance (Cdyn) was the primary outcome. Secondary outcomes included oxygenation (PaO$_2$), edema indices, perfusate biochemistry, and tissue mRNA of inflammatory and endothelial markers.

Results

Target Cet values were reached within 10 min. Sevo 4% and Sevo 6% improved compliance versus Sevo 0% (p = 0.04, p < 0.0001). Normalized ΔCdyn was higher in all sevoflurane groups (p < 0.0001). Oxygenation improved in Sevo 6% versus Sevo 0% (p = 0.05). Wet-to-dry ratio and total lung weight were similar between groups. Lactate production was lowest in Sevo 2%, whereas AST was reduced in Sevo 6% versus Sevo 0% (p = 0.04). Perfusate calcium was consistently lower in all sevoflurane groups. IL-6 expression decreased in Sevo 2% and Sevo 6%, and Sevo 2% showed the strongest preservation of glycocalyx-related transcripts.

Conclusions

Ventilation with sevoflurane during EVLP enhanced compliance and oxygenation, reduced biochemical and inflammatory injury, and preserved endothelial integrity. Effects were concentration-dependent, with functional improvement at 6% and endothelial protection at 2%, suggesting a dual mechanism of sevoflurane-mediated organ protection.

Decreased CD8+ T Cell Receptor Affinity For Allogeneic HLA Associates With Older Age And A Lower Risk For Acute T Cell-Mediated Rejection

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Background

The age-associated decrease in CD8^{+} T cell alloreactivity is poorly understood but may contribute to a decreased risk for acute T-cell mediated rejection (aTCMR) after kidney transplantation.

Methods

Broad assessment of human peripheral blood-derived CD8^{+} T cell function was performed in relation to age using multi-parameter flow cytometry. This included cytotoxicity, proportions of cytokine producing T cells and proliferation of CD8^{+} T cell subsets in response to polyclonal, allogeneic HLA and virus peptide stimulation. Expression of interferon regulatory factor 4 (IRF4) is a measure of T cell receptor (TcR) affinity and related to the degree of T-cell proliferation. Induction of IRF4 was measured under different conditions of T-cell stimulation and blocked on the protein level. Antigen-reactive T cells were identified by expression of the activation-induced marker CD137 upon short-term stimulation.

Results

CD8^{+} T cell function assessed after polyclonal stimulation with anti-CD3/anti-CD28-coated beads was not affected by age. Allogeneic HLA stimulation of CD8^{+} T cells of older kidney transplant recipients yielded higher frequencies of alloreactive T cells, similar proportions of cytokine producing cells but paradoxical lower proportions of proliferating cells. The expression of IRF4 was

directly related to the degree of CD8^{+} T cell proliferation. Blocking of IRF4 abolished CD8^{+} T cell proliferation with a simultaneous increase in T-cell apoptosis. An age-related increased expression of IRF4 was observed in more differentiated CD8^{+} T cell subsets upon stimulation with virus peptides while the reversed was observed for the alloreactive CD8^{+} T cell response. Expression of IRF4 in alloreactive CD8^{+} T cells was significantly higher in recipients experiencing aTCMR within the first year after transplantation.

Conclusions
Older age is associated with an increase in virus-specific CD8^{+} but decreased alloreactive TcR affinity with subsequent less CD8^{+} T cell proliferation and lower risk for aTCMR.

Plasma Symmetric Dimethylarginine As A Novel Biomarker Of Kidney Function In Living Donors

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Background
Accurate evaluation of kidney function in living donors prior to donation is essential. Measured glomerular filtration rate (mGFR) remains the gold standard for assessing kidney function; however, its clinical use is limited by its invasive nature, time requirements, and high costs. Symmetric dimethylarginine (SDMA) has recently emerged as a promising biomarker for the diagnosis and screening of kidney disease in small animal practice. To date, however, the relationship between SDMA and mGFR in humans has rarely been investigated. This study aims to evaluate the association between baseline plasma SDMA level and mGFR both at baseline and three months after donation in living kidney donors.

Methods
Living donor data were obtained from the prospective TransplantLines study. Assessments of mGFR were performed using I[125]-iothalamate at baseline and three months after donation in living kidney donors. Pre-donation and post-donation plasma SDMA and cystatin C concentrations were determined using an automated IDEXX SDMA® immunoassay and a turbidimetric assay, respectively. Univariable and multivariable linear regression analyses were performed to examine the associations between baseline kidney function indices and mGFR. Differences between regression coefficients were assessed using Steiger's Z-test.

Results
Plasma SDMA and mGFR data were available for 46 living donors. Mean SDMA and cystatin C before donation were 11.2 ± 1.6 ug/dL and 0.87 ± 0.18 mg/L, respectively. Values of mGFR before donation and at 3 months after donation were 95.4 ± 13.2 ml/min/1.73m^2 and 60.8 ± 8.9 ml/min/1.73m^2. Pre-donation plasma SDMA was significantly associated with both pre- and post-donation mGFR (st. β: -0.51 ,95%CI [-0.76,-0.26], p<0.001 and st. β: -0.49, [-0.75,-0.23], p<0.001, respectively). Associations remained materially unchanged after multivariable adjustment for donor age, sex, BMI, smoking status, hypertension, and diabetes. Moreover, we found that the strength of the association of plasma SDMA with both pre- and post-donation mGFR was comparable to that of plasma cystatin C (both p>0.05).

Conclusions
These findings indicate that pre-donation plasma SDMA exhibits an association with kidney function comparable to that of cystatin C, both before and after kidney donation in living donors. SDMA may serve as a novel biomarker for assessing kidney function in living donors.

Center-Level Variation In Deceased Donor Kidney Offer Acceptance And Its Impact On Transplant Waiting Time In The Netherlands

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Background

In the Netherlands, the decision to accept a deceased donor kidney offer depends on the judgement of the transplant clinician on call. A prior survey among transplant clinicians demonstrated that this decision varied strongly between centers. Aim of this study was to quantify the variability in kidney offer acceptance behavior among Dutch transplant centers.

Methods

A population-wide cohort study was performed, including all deceased-donor kidney offers to waitlisted patients in the Netherlands between January 1st, 2014 and December 31st, 2024. Only offers within Eurotransplant Kidney Allocation System (ETKAS) and Eurotransplant Senior Program (ESP) were included for analyses. Behavior of transplant centers was modelled at two levels: (i) the patient level, which models the decision to decline the decision to accept the kidney offer for a specific patient, and (ii) the center level, which models the decision to decline the kidney for all patients in a center. Differences between centers were quantified using mixed-effect logistic regression, estimating the adjusted odds ratios (AORs) for acceptance and compared to the median-effect reference center. All models were adjusted for donor-, recipient (e.g. age, sex) and match factors (e.g. HLA, cross-match) and performed separately by allocation program. Subsequently, difference in expected dialysis vintage was assessed using linear regression analyses, with adjustment for recipients covariates and time period.

Results

A total of 13,114 deceased kidney donor offers, of which 8,004 in ETKAS and 5,100 in ESP, were analyzed. For ETKAS, patient-level AORs for acceptance ranged from 0.44 [0.34−0.57] to 1.46 [1.16−1.84], with center-level AORs ranging from 0.87 [0.67 − 1.13] to 1.27 [0.96 - 1.69]. For ESP, larger differences were observed with patient-level AORs ranging from 0.39 [0.27−0.56] to 2.16 [1.57−2.97], and center-level AORs from 0.45 [0.33−0.60] to 1.66 [1.18−2.34]. Centers with higher AORs compared to the reference center, had significantly shorter expected dialysis vintage at transplant: adjusted center effects ranged from -9 to +3 months in ETKAS, and -4 to +4 months in ESP.

Conclusions

Kidney offer acceptance behavior differs markedly between the Dutch transplant centers, and this is associated with clinically meaningful differences in dialysis vintage.

Outcomes Of Kidney Transplantation After Solid Organ Transplantation Are Comparable To First And Second Kidney Transplants Patients

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Background

For patients with kidney failure after non-renal solid organ transplantation (SOT), kidney transplantation (KTx) is a viable treatment option.

Methods

In this single-center, retrospective study, we included all patients who underwent KTx between 2010 and 2024 after SOT. Patient survival was compared to SOT patients who had developed kidney failure in the study period but did not proceed to transplantation. Additionally, patient and death-censored kidney allograft survival were compared across SOT organ types, as well as to patients who received a first or second KTx. Hospital readmissions within 1-year were recorded.

Results

74 patients received a KTx after SOT (heart=16, lung=18, liver=40 of which 15 combined liver/kidney). 260 SOT patients with kidney failure (heart=28, lung=47, liver=185) did not proceed to KTx, while 2379 patients received a first KTx and 349 patients a second KTx. Age was lower for KTx after SOT, compared to first KTx (median 54 vs 60, p=0.003), but not to second KTx (median 54 vs 52, p=0.39). BMI for KTx after SOT was lower compared to first (median 24 vs 27, p <0.001) and second KTx (median 24 vs 25, p=0.03).

When comparing KTx after SOT to controls who did not proceed to transplantation, 1-year patient survival for heart was 93% vs 41% (p<0.001), lung 91% vs 60% (p=0.001) and liver 91% vs 71% (p <0.001).

5-year patient survival for KTx after SOT was comparable to both first (82% vs 78%, p=0.55) and second KTx (86% vs 78%, p=0.24). 5-year death-censored kidney allograft survival after SOT was comparable to both first KTx (84% vs 88%, p=0.13) and second KTx (84% vs 86%, p=0.64).

5-year death-censored kidney allograft survival was not significantly different between SOT (80% for heart vs 68% for lung vs 86% for liver, p=0.51) Hospital readmissions within one year were comparable for the different KTx after SOT groups (median 1.5 for heart, 2.0 for lung, and 1.0 liver, p=0.72).

Conclusions

Kidney transplantation after SOT, in selected patients, has excellent outcomes, with patient and death-censored graft survival comparable to a first or second KTx. Data on immunosuppressive drug use and rejection rates will follow.

The Urethral Catheter Can Be Removed Safely Three Days After Kidney Transplantation Instead Of Five Days

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Background

Kidney transplantation is currently the optimal treatment for end-stage kidney disease. After surgery, a urethral catheter (CAD) is left in place, but the optimal duration for this is still unknown. CAD's are usually left in place between 4-10 days. It is thought that catheterization decreases the incidence of urological complication, such as urine leakage, by decreasing pressure on the new cysto-ureteric anastomosis. However, prolonged catheterization might also increase the risk of urinary tract infections (UTI). The currently available studies indicate that earlier removal of the CAD might be safe and possibly beneficial. In the current analysis safety and risks of a reduction of CAD duration from postoperative day 5 to 3 is evaluated.

Methods

This analysis was a single centre non-randomized retrospective analysis comparing CAD removal at five days to removal at three days after kidney transplantation. The 3-day cohort transplanted in 2023 and 2024, the 5-day cohort was transplanted in 2022 and 2023. No other protocol changes or studies were implemented in this period. Primary outcomes were UTIs and urological complications. Secondary outcomes were catheter reinsertion, readmissions, kidney function, delayed graft function and hospitalization duration.

Results

The 3-day and 5-day cohort consisted both of 70 patients, of which 33% vs 43% was female, and 34% vs 46% had known urological issues, respectively. Mean age of the patients was 53.2 ± 13.2 years, mean donor age was 55.2 ± 13.8 years. Median (IQR) CAD duration in the 3-day cohort was 3 (3-3) and 5 (5-5) in 5-day cohort. No relevant associations were found for the CAD duration with UTIs (adjusted OR: 0.60, p=0.46), urological complications (adjusted OR: 0.61, p=0.39), catheter reinsertion (adjusted OR 0.59, p=0.39), readmissions (adjusted OR: 1.77, p=0.21), hospitalization duration (adjusted B: -0.76, p=0.10), delayed graft function (adjusted OR: 1.23, p=0.75) and kidney function (adjusted B= -3.20 (p=0.21).

Conclusions

This analysis indicates that changing the CAD duration from five days to three days postoperatively can be done safely. There was a trend to a shorter admission duration.

Longitudinal Plasma Proteomic Landscape Of Early Allograft Dysfunction In Kidney Transplant Patients

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Background

Early after kidney transplantation, allograft function is unstable due to immune and non-immune injury. Here, longitudinal plasma proteomics characterized allograft dysfunction in the first two weeks after transplantation.

Methods

Plasma proteins from the Olink immuno-oncology and organ-damage panels were measured at protocol days 3 and 7, month 6 (post-recovery baseline), and at for-cause biopsy in well-phenotyped kidney transplant patients from an unselected prospective cohort. Proteins' ability to detect allograft dysfunction and their trajectories in the first two post-transplant weeks were evaluated.

Results

Among 126 patients, 67 (53.2%) presented early allograft dysfunction and thus underwent a for-cause biopsy. Antibody- and T cell-mediated rejection were diagnosed in 5 (4.0%) and 20 (15.9%) patients, respectively. Regression analysis defined an allograft dysfunction signature mainly reflecting hypoxia (CAIX, CA12), tissue injury-repair (VEGFA, PGF), and TNF-signaling (TNFRSF9, TNFRSF12A, CD40). Longitudinal assessment showed dynamic trajectories for these proteins.

A rejection-specific signature was not identified through regression. In contrast, unbiased bootstrap clustering identified coordinated modules reflecting both immune and non-immune injury mechanisms, including [CXCL9-11, GZMA/B/H] and [BAMBI, CD27, CD83, NCR1, PDL1, PGF, TNFRSF9].

Conclusions

Comprehensive plasma proteome profiling revealed distinct mechanisms underlying early kidney allograft dysfunction, demonstrating potential to decipher its immune and non-immune causes.

Trajectories Of Physical Performance After Solid Organ Transplantation: Results Of The TransplantLines Biobank And Cohort Study

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Background

Physical functioning varies after organ transplantation and recovery may differ by type of transplanted organ. Longitudinal data on objective measures of physical performance are lacking. We assessed changes in physical performance up to 24 months after kidney, lung and liver transplantation.

Methods

We analyzed repeated pre- and post-transplant assessments in kidney (KTR), lung (LuTR) and liver (LiTR) recipients from the TransplantLines cohort. Physical performance was evaluated using 4-meter walking test (4MWT), sit-to-stand test (STS), and dominant handgrip strength at pre-transplant baseline and 3, 6, 12, and 24-months post-transplant. Linear mixed-effect models were used within each group. Participants unable to perform tests received conservative values ($95^{th}/5^{th}$ percentile). Model estimates (β) represent the change from baseline. Negative β-values indicate improvement for time-based tests, positive β-values for strength.

Results

We included 2125 recipients (1214 kidney, 452 liver, 326 lung; 39.5% female; mean age 56.7 $\pm$ 13.4 years). Baseline 4MWT data were available for 94.6% of KTR, 74.5% of LuTR, and 88.7% of LiTR, with respective values of 3.99$\pm$1.16s, 4.80$\pm$1.23s, and 4.09$\pm$4.54s. KTR showed modest improvements peaking at 6 months (β=-5.05s; p<0.01), followed by a decrease to baseline values, while LuTR improved at all moments through 24 months (β=-3.40s; p<0.01). LiTR remained stable from baseline through 24 months. Baseline STS data were available for 95.2% of KTR, 75.2% of LuTR, and 88.4% of LiTR, with respective values of 13.62$\pm$4.02s, 18.94$\pm$5.20s and 14.48$\pm$4.54s. KTR improved at 6 months (β=-4.26s; p<0.01), and 12 months (β=-3.68s; p<0.01). LuTR progressively improved, peaking at 24 months (β=-6.10s; p<0.01), while LiTR only improved at 24 months (β=-2.74s; p=0.02). Baseline handgrip strength data were available for 96.5% of KTR, 83.0% of LuTR, and 91.1% of LiTR, with respective values of 33.38$\pm$12.42kg, 35.63$\pm$12.98kg and 33.99$\pm$10.57kg. KTR showed consistent gains from 3 through 24 months (β=10.55kg; p<0.01), LuTR showed minimal change, while LiTR exceeded baseline values only at 24 months (β=2.59kg; p=0.04).

Conclusions

Physical function recovery follows organ-specific trajectories. LuTR showed greatest improvements in 4MWT and STS, while handgrip gains were minimal. KTR and LiTR demonstrated sustained handgrip improvements, with modest 4MWT and STS improvements, highlighting the need for organ-specific rehabilitation strategies.

Virtual Crossmatch In Living Donor Kidney Transplantations: Two Pilot Studies

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Background

'Wet' crossmatches (wXM) have been introduced to detect pre-formed donor-specific antibodies (DSA), to prevent hyperacute rejection. Virtual crossmatches (vXM) detect pre-formed DSA by comparing recipient's HLA antibody screening to donor's HLA typing. The benefits of vXM over wXM are multiple: the most sensitive HLA antibody screening technique is used (Luminex single antigen, LSA), no recipient and donor cells are needed (saving blood draws and amount of blood), and the result can be obtained faster.

Methods

We performed a retrospective analysis of 2284 wXM (CDC and/or flow cytometric wXM) of non-immunized recipients (vPRA 0%), tested for two transplant centers over the period 2016-2023. In 2024, we performed a first prospective pilot study for the same two transplant centers. In this study, the vXM (n=150) was performed for non-immunized recipients, excluding female recipients with children or partner as candidate-donor. As of July 2025, a second prospective pilot study was started to perform the vXM for all recipient-donor combinations, including immunized recipients.

Results

All 2284 wXM of non-immunized recipients between 2016-2023 were negative. In the first prospective study, 2 out of 150 vXM were positive, based on the most recent LSA with previously unknown pre-formed DSA. An additional 4 vXM were followed by a wXM, based on a positive LSA (without DSA). Besides the 150 vXM, still 200 flow cytometric wXM were performed for 344 recipient-donor combinations. The ongoing second prospective study resulted in 78 vXM between July and October 2025, of which 3 were positive. These 3 positive vXM resulted in exploring alternative donor options.

Conclusions

Our results demonstrate the feasibility of vXM in the setting of living kidney transplantation — like it has been demonstrated for both stem cell transplantation and postmortal organ transplantations. The vXM results in faster and safer testing, a lower burden for recipients and donors, and with omission of unnecessary additional laboratory tests. Further research will be required to determine the long-term clinical implications of this strategy for transplant outcomes.

Risk Of Deficient Mismatch Repair Colorectal Cancer And Precursors After Kidney Transplantation: A Nationwide Study

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Background

Colorectal cancer (CRC) incidence rises post-transplant, though the mechanism remains unclear. We hypothesize that impaired immunosurveillance of kidney transplant recipients (KTRs) allows progression along the serrated pathway, increasing only immunogenic deficient mismatch repair (dMMR) CRC incidence and not proficient mismatch repair (pMMR) CRC.

Methods

The nationwide transplant, pathology, and cancer registries were linked by probabilistic matching to retrieve data of all KTRs in the Netherlands. Standardized incidence ratios (SIRs) were calculated. Premalignant lesions were identified within the Dutch CRC screening program, and KTRs were matched to controls.

Results

Among 15,013 KTRs, 109 CRCs were observed between 2015-2021, resulting in a SIR of 1.22 (95% confidence interval [CI]:0.99-1.47). The median time from transplantation to CRC was 7.9 years (interquartile range:4.2-13.6). dMMR CRC occurred in 31% of KTRs, significantly higher than the general CRC population's 13%, with a SIR of 3.09 (95%CI:2.23-4.30). Incidence of pMMR CRC was not increased, SIR of 0.94 (95%CI:0.75-1.18). Sessile serrated lesions (SSL) with dysplasia occurred 2.9-fold more often in KTRs than matched controls (95%CI:1.7-5.1).

Conclusions

This nationwide population-based study demonstrates the increased risk of neoantigen-containing SSL-D and dMMR CRC after kidney transplantation compared to the general population. These findings emphasize the need to consider a colonoscopy-based surveillance program for KTRs to detect and resect relevant precursor lesions in a timely manner, aiming to reduce CRC incidence and improve survival.

Mitochondria Transferred During Normothermic Machine Perfusion Of Porcine DCD Kidneys Are Taken Up By Cortical Cells

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Background

Donor kidneys are prone to ischemia-reperfusion injury (IRI) due to extended oxygen deprivation, which can complicate transplant outcomes. To mitigate this risk, Normothermic Machine Perfusion (NMP) has emerged as an advanced *ex vivo* preservation modality that enables both functional assessment and therapeutic intervention prior to transplantation. Mitochondrial transplantation, the targeted delivery of isolated respiration-competent mitochondria into diseased organs, has shown promise in counteracting IRI effects. However, its application during *ex vivo* kidney preservation remains unexplored. Therefore, this study aims to evaluate uptake of mitochondria delivered during NMP in a porcine model of donation after cardiac death (DCD).

Methods

Porcine kidneys (n=5) were obtained from a local abattoir. Following 30 min of warm ischemia, kidneys were flushed and placed in oxygenated Hypothermic Machine Perfusion (HMP). Autologous mitochondria were isolated from skeletal muscle via differential centrifugation, stained with Mitotracker Deep Red, and functionally assessed using high-resolution respirometry (Oroboros Oxygraph 2K). After 4 h of HMP the kidneys were transitioned to NMP, gradually rewarmed for one hour and upon reaching 37°C received an arterial bolus of

labeled mitochondria. Perfusion continued for an additional hour. Tissue uptake was assessed by fluorescence microscopy of DAPI-stained cortical, medullary, and arterial biopsies collected before and after mitochondrial administration.

Results

Fluorescence microscopy confirmed successful delivery, revealing labeled mitochondria selectively taken up by tubular and glomerular cells in the cortex. ATP content of kidney biopsies significantly increased one hour after mitochondrial transfer (p=0.0087) as did oxygen consumption, measured in perfusate samples, (p=0.033). Comparative studies between treated and untreated kidneys are ongoing to assess the functional impact of mitochondrial transplantation.

Conclusions

Mitochondria transferred during NMP in a porcine DCD model successfully enter cortical cells.

Metabolic Alterations During Normothermic Machine Perfusion Of Discarded Human Kidneys

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Background

Although normothermic machine perfusion (NMP) is being explored as a promising method to assess the pre-transplant viability of deceased-donor kidneys and potentially enhance their quality, it remains unclear which metabolic processes are active during NMP. To realize NMP's full potential, a deeper understanding of renal metabolism under *ex vivo* NMP conditions is essential. This study aimed to characterize metabolic alterations in human kidneys throughout NMP.

Methods

Discarded human donor kidneys (n = 25) underwent 4 hours of oxygenated hypothermic machine perfusion, followed by 6 hours of NMP. Cortical tissue samples were collected before and after NMP for metabolomics and transcriptomics analyses. Differences between post- and pre-NMP samples were examined to identify metabolic changes that occur during NMP.

Results

Metabolomics analysis revealed marked increases in eicosanoids and lactoyl amino acids, alongside pronounced decreases in fatty acid and glycosyl-PE metabolism over the course of 6 hours of NMP. When examining broader pathways with substantial changes, strong elevations in gamma-glutamyl amino acids and marked reductions in glutathione metabolism were observed, with decreased cysteine levels as a common denominator. Additional analyses demonstrated that the metabolic alterations were not associated with functional changes during NMP and showed only minimal associations with donor characteristics. Moreover, the metabolic alterations were linked to transcriptional pathways related to immune responses and cell survival.

Conclusions

These findings reveal distinct metabolic patterns during NMP that appear largely independent of functional changes and donor characteristics, providing novel insights into the metabolic state of kidneys under *ex vivo* conditions and suggesting a link between metabolic alterations and cellular processes.

Comparative Analysis Of Blood Collection Tubes On Serum And Plasma Proteomes For Biomarker Identification Of Liver Viability During Normothermic Machine Perfusion

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Background

Extended criteria donor (ECD) livers have an increased risk for post-transplantation complications and require thorough viability assessment through Normothermic Machine Perfusion (NMP). However, current viability criteria show limited predictive value for post-transplant outcomes, highlighting the need for novel biomarkers. Proteomic analysis is a powerful tool for biomarker discovery, but the choice of blood collection tube matrix can significantly influence proteomic profiles. To assess how blood collection matrices influence proteomic signatures, this study compared the proteomic profiles of serum, EDTA plasma, and citrate plasma during liver machine perfusion.

Methods

Perfusate-derived blood samples were collected from transplanted (N=4) and non-transplanted (N=4) livers subjected to 150 minutes of NMP. Samples were drawn using serum separator tubes (SST, serum), EDTA tubes (plasma), and citrate tubes (plasma). Proteins were extracted and processed via automated filter-aided sample preparation on a liquid handling station. Peptides were analysed using high-performance liquid chromatography (HPLC) cou-pled to tandem mass spectrometry (MS/MS). Proteomic differences among tube types were assessed by ANOVA ($p < 0.05$), and differences between transplanted and non-transplanted livers were evaluated using the Mann–Whitney U test ($p < 0.05$) for each tube type.

Results

Across all tube types, 509 proteins (66.9%) were shared, while 40, 60, and 60 unique proteins were identified in serum, EDTA plasma, and citrate plasma, respectively. Average protein abundance in serum was 24% and 5% higher than in citrate and EDTA plasma, respectively, though only two proteins showed significant differences. When analysing transplanted and non-transplanted livers separately, principal component analysis (PCA) revealed clustering primarily by individual donor liver rather than by tube type, indicating minimal matrix-related bias in overall protein profiles. However, when differentiating transplanted from non-transplanted livers, the PCA of serum samples demonstrated the clearest separation. Consistently, 134 significantly differentially abundant proteins were identified in serum, compared with 24 in EDTA plasma and 35 in citrate plasma, and only three proteins overlapping across all tube types.

Conclusions

Serum collection tubes provide the most informative matrix for distinguishing transplanted from non-transplanted livers and are therefore preferred for biomarker discovery in liver perfusion studies. These findings emphasize the critical importance of selecting the appropriate blood collection tube for reliable proteomic analysis.

Prolonged Hypothermic Machine Perfusion Enables Daytime Liver Transplantation And Improves Sleepyield Of On-Call Staff

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Background

Prolonged dual hypothermic oxygenated perfusion (DHOPE-PRO) combines the graft-preserving benefits of short-duration DHOPE with the logistical advantage of enabling liver transplantation to be performed during daytime hours. By decoupling organ retrieval from implantation timing, DHOPE-PRO may improve not only clinical logistics but also the working conditions of transplant teams. This study assessed the effect of DHOPE-PRO on night-time workload and calculated sleepyield as an indicator of rest opportunity among on-call transplant staff, hypothesizing improved sleepyield with daytime liver transplantation enabled by DHOPE-PRO.

Methods

This analysis was based on patient-level time-registration data from the prospective DHOPE-PRO trial (NL8740), which included adult recipients of livers donated after brain death. Time records for perfusion and surgery were translated into working-hour intervals for on-call perfusion and surgical staff. To quantify the effect of transformation to daytime scheduling, the DHOPE-PRO group was remodelled into a hypothetical night-time scenario reflecting pre−DHOPE-PRO conditions, in which short-duration DHOPE (1−2 h) was initiated after donor hepatectomy and transplantation surgery proceeded during the night instead of using prolonged DHOPE with scheduled daytime implantation. Sleepyield was defined as the ratio of actual to optimal sleep duration (0−10 scale), with optimal sleep set at eight hours between 22:00 and 06:00.

Results

Twenty-four recipients were included (12 DHOPE and 12 DHOPE-PRO). Night-time working hours for the perfusion team were lowest with DHOPE (0.28 h [IQR 0.00−0.04]), followed by remodelled DHOPE-PRO (4.18 h [3.18−5.51]) and highest with DHOPE-PRO (8.11 h [6.85−9.78]; all adjusted p<0.001). The surgical team showed the opposite pattern, with markedly reduced night-time hours for DHOPE-PRO (0.29 h [IQR 0.00−0.00]) compared with DHOPE (13.1 h [IQR 6.7−17.9]) and remod-

elled DHOPE-PRO (25.5 h [IQR 21.3−30.7]; all adjusted p < 0.001). Corresponding overall sleepyield scores were 2.6 for remodelled DHOPE-PRO, 6.6 for DHOPE, and 8.2 for DHOPE-PRO.

Conclusions

By enabling liver transplantation to be performed during daytime hours, DHOPE-PRO substantially reduces night-time workload and improves rest opportunity for on-call transplant staff. Beyond its established benefits for graft preservation, DHOPE-PRO represents a meaningful advancement in operational efficiency, workforce sustainability, and patient safety in liver transplantation.

Commercially Available Bile Collections Lines Affect Measured Bile pH During Normothermic Liver Machine Perfusion

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Background

As favorable donor characteristics become increasingly scarce in the Netherlands and indications for liver transplantation remain high, more donated livers are tested for functionality using normothermic machine perfusion (NMP). Various criteria for assessing liver viability have been proposed, most of which consider cholangiocyte function. A key indicator of cholangiocyte viability is bile pH. After our institution switched from the bile tubing supplied by the NMP set manufacturer to an alternative tubing, a markedly lower bile pH was observed. This study investigates how bile pH fluctuates depending on the materials used from bile duct cannulation to bile collection.

Methods

A total of 150 mL of bile was collected and pooled from five NMP procedures, then placed in a gas-permeable cell culture bag at 37°C and 5% CO_2. From this homogeneous bile, 50 mL syringes were filled with 20 mL and capped. An infusion pump in an insulated container mimicked NMP temperature conditions. A 20 cm tubing line connected the pump to a 50 mL tube without plunger, filled with 2 mL mineral oil. Eight tubing types—including commercial NMP bile lines, pressure lines, IV extensions, and feeding lines—were tested at 3, 10, and 25 mL/hour. Blood gas measurements of the pumped bile and bile in the syringe pump were taken in immediate succession.

Results

Sodium bicarbonate concentration in the homogenous bile was 20.6 mmol/l, and therefore not supplemented. Bile pH increased after pumping in all conditions, with slower flow rates showing the largest ΔpH. At 3 mL/hour, the highest ΔpH (0.48) occurred with OrganOx bile tubing, while a pressure line extension (Edwards) showed a ΔpH of 0.05. The XVIVO bile drainage line produced a ΔpH of 0.17.

Conclusions

During NMP, particularly in prolonged (>6 hours) perfusions, bile production rates vary. Quality of bile is regarded as vitally important for viability assessment and is associated with a venous blood-like pCO_2. Rapid CO_2 diffusion alters the bicarbonate buffer equilibrium, raising pH. While mineral oil in the collection reservoir helps limit diffusion, our findings highlight that tubing materials leading to this reservoir also require careful consideration.

Warming Up For Success: Controlled Oxygenated Rewarming Prior To Normothermic Machine Perfusion For The Liver

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Background

To alleviate the donor organ shortage, the use of extended criteria donor (ECD) livers has increased. These grafts carry an increased risk of post-transplantation outcomes, including post-transplant cholangiopathy (PTC). Dual Hypothermic Oxygenated Perfusion (DHOPE) has shown to reduce the incidence of PTC, whereas Normothermic Machine Perfusion (NMP) enables viability assessment of the liver graft. To prevent abrupt temperature shifts and mitigate ischemia-reperfusion injury, Controlled Oxygenated Rewarming (COR) is performed between DHOPE and NMP. During COR, the liver is gradually rewarmed in 1 hour from 20°C to 37°C, with increasing pressure sets on the hepatic artery (HA) and portal vein (PV). COR is a complex and dynamic phase of DHOPE-COR-NMP, requiring continuous monitoring and timely intervention.

Methods

DHOPE-COR-NMP with hepatobiliary assessment was performed for ECD livers. Perfusion flows and perfusate blood gasses were recorded and gas composition and flow were adjusted based on HA oxygen (O_2) and carbon dioxide (CO_2) levels. Sodium bicarbonate was supplemented when the base excess dropped below -13 mmol/L, preventing excessive acidosis. To preserve Na^+/K^+-ATPase function, potassium chloride was administered when potassium levels fell below 3.5 mmol/L. Dynamic changes during COR and differences between transplanted and non-transplanted livers were analyzed using linear-mixed models.

Results

35 livers underwent DHOPE-COR-NMP, of which 22 passed all viability criteria and were transplanted (63% utilization). As livers became more metabolically active, indicated by rising CO_2 and decreasing O_2, increased gas flow and higher O_2 concentration were required to maintain adequate levels. Sodium bicarbonate suppletion was required in all cases, but hypernatremia should be avoided, as activation of Na^+/K^+-ATPase will contribute to increased sodium levels. A decreasing potassium trend was observed, and suppletion at 4-5

mmol/L is recommended to prevent hypokalemia. Differences in evolution over time between transplanted and non-transplanted livers were observed for potassium, chloride and lactate. Overall, transplanted livers demonstrated higher PV flows, lower O_2 levels, higher base excess and higher chloride levels. Higher sodium and lower potassium levels in transplanted livers indicate earlier metabolic recovery, combined with earlier lactate metabolization.

Conclusions
Active perfusion management during COR is required and continuous monitoring of perfusate parameters provides valuable insights into metabolic recovery of the liver.

Optimizing Colloid Composition Improves Perfusion Dynamics And Hepatic Metabolism During Clinical Normothermic Machine Perfusion

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Background
Normothermic machine perfusion (NMP) provides a platform for preservation and viability testing of donor livers. Colloid choice in the perfusate may influence endothelial and glycocalyx integrity, potentially affecting hepatocellular injury. However, translational data comparing colloids during NMP are limited and clinical data are lacking.

Methods
Donation after circulatory death liver grafts were subjected to sequential dual hypothermic oxygenated perfusion followed by NMP using either gelatin-based (n=9) or albumin-based (n=9) perfusates. Perfusion dynamics and biochemical markers of metabolism and injury were compared between groups.

Results
Albumin-based perfusates resulted in lower arterial pressure while maintaining comparable arterial flow at the end of perfusion. Portal flow was higher at equal portal pressures at the end of perfusion, reflecting reduced portal resistance. Metabolic function was improved with albumin, shown through lower gluconeogenesis and superior lactate clearance up to 6 hours of NMP. Livers that gained weight during perfusion had a 2.2 fold higher increase in weight using gelatin-based perfusate. Although transaminase release during perfusion was higher with albumin, it remained below thresholds for viability assessment criteria. Post-transplant transaminases in recipients were lower in the albumin group compared to the gelatin group.

Conclusions
Albumin-based perfusates enhance perfusion dynamics and metabolism during NMP resulting in improved biochemical outcomes after transplantation. This suggests that albumin-based perfusates are preferred over gelatin based perfusates during NMP of the liver. Future studies will focus on endothelial and glycocalyx injury to further elucidate protective mechanisms.

Hepatocyte Isolations Using The PancReatic Islet Separation Method (PRISM) Machine – A Novel Approach

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Background

While orthotopic liver transplantation (OLT) remains the only treatment for acute liver failure, a suitable donor liver is often not available in time. Hepatocyte transplantations could offer a potential bridge to either recovery or OLT.

The hepatocyte isolation protocol varies strongly across centers, is manual and arduous. We recently developed PRISM (PancReatic Islet Separation Method), a novel, standardized and automated method to isolate pancreatic islets, and adapted it for hepatocyte isolation (HI). Here we report on our initial experiences and analyses of PRISM-based HI.

Methods

Five non-use liver lobes were used for PRISM HI. The HI's were performed on a PRISM machine with a custom, closed, continuous tubing set. The liver lobes were placed in an organ chamber and connected to the set, rinsed, and perfused with digestive enzymes. Harnessing differential sedimentation rates of cell types, a purified cell pellet was created and washed to a cryo-preservation solution within the continuous flow centrifuge bowl. Cell number and viability of hepatocytes, freshly isolated, and stored in liquid nitrogen for up to 12 months, were determined via trypan blue exclusion. Four luminescence-based CYP enzyme assays (1A1, 1A2, 2C9 and 3A4) were performed to assess hepatocytes functionality.

Results

Five HIs were performed using the PRISM system. Hepatocyte viability after isolation was 60.7%, 49.0% after three months and declined to 37.0% over 12 months, figure 1. All isolations preparations had two or more CYP positive assays and were thus identified to have functional hepatocytes.

Conclusions

The use of the PRISM isolation method during HIs has been shown to successfully isolate viable hepatocytes from non-use livers. The hepatocyte preparations con-

tinue to exhibit viability after having been cryo-preserved for 12 months. Further refinements of PRISM HI will facilitate the creation of a clinical hepatocyte transplantation program.

Organ Temperature Course During Deceased-Donor Organ Procurement – A Prospective Cohort Study

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Background

During deceased-donor kidney procurement, a cold flush is applied to reduce kidney temperature as much as possible and thus slow down the accumulation of ischemic injury. However, real-time data on intra-abdominal organ temperature dynamics and their relationship with delayed graft function (DGF) remain limited. This prospective study aimed to identify donor- and procurement specific factors associated with kidney temperatures >15°C after procurement.

Methods

Kidney surface temperature was measured at predefined time points using an infrared thermometer. Multivariable logistic mixed-effects models were used to identify risk factors associated with elevated kidney temperature (>15 ºC) and to assess the relationship between temperature and post-transplant DGF.

Results

Temperature data were collected from 237 deceased donors (47% female, mean age 53.5±15.8 years; 55% donation after circulatory death (DCD)), encompassing 460 kidneys. After procurement, 255 (52%) kidneys had a temperature >15ºC. Independent risk factors associated with temperature >15ºC included male donor sex (odds ratio (OR): 4.89; 95% confidence interval (CI) [2.20 to 10.90]; p<0.001), longer kidney extraction time (OR: 1.05; [1.02 to 1.08]; p=0.001) and higher perfusion solution temperature (OR: 1.24; [1.04 to 1.47]; p=0.01). Notably, kidney temperature >15ºC was not significantly associated with DGF (p=0.40).

Conclusions

Over half of deceased-donor kidneys experienced suboptimal cooling during procurement, underscoring opportunities for procedural optimization. These findings highlight that improving control of perfusion solution temperature and minimizing extraction time can enhance procurement quality.

Cytokines Released By Human Kidneys During NMP Do Not Predict Early Post-Transplant Outcomes

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Background

The pathophysiologic effects from deceased organ donation trigger a systemic inflammatory response, i.e. a cytokine storm, that can impair graft quality at transplantation. Endothelial cells are directly exposed to these mediators and are therefore especially vulnerable to transplantation-associated injury, further damaging the allograft. Normothermic machine perfusion (NMP) offers the opportunity to evaluate kidney quality pretransplant, providing valuable insight into graft immunogenicity and injury. Cytokines are released by the kidney during NMP, yet their effect on graft quality and post-transplant kidney function remains largely unknown. We examined perfusate cytokines and chemokines, including mediators associated with vascular inflammation, released by human kidneys during NMP and investigated their correlation with early post-transplant outcomes.

Methods

Kidney perfusate samples (n = 41) from a randomized controlled trial were collected at 0, 1, and 2 hours of NMP. Cytokines were quantified with a human vascular inflammation panel kit (Biolegend) and analysed by flow cytometry. Results were expressed in pg/mL. Endpoints included immediate graft function, delayed graft function (need for dialysis in the first week after transplantation), primary non-function, and acute rejection in the first two weeks after transplantation.

Results

All perfusate cytokine levels significantly increased during the first hour of NMP. In the second hour, only CCL2, IL-10, IL-6, sCD40L, sST2, TIE2, and TNF showed a significant rise - while sFlt1 stayed the dominant cytokine at every timepoint. Contrary to a previous study in a porcine

model, we did not observe an inflammatory milieu during perfusion. Instead, anti-inflammatory cytokine concentrations increased 1.2-fold (p = 0.059) and 2.2-fold (p = 0.018) more than pro-inflammatory cytokines during the first and second hour, respectively, suggesting a more anti-inflammatory perfusion environment. Nevertheless, cytokine profiles at 1- and 2 hours NMP were not associated with categorical post-transplant graft outcomes.

Conclusions

We characterized cytokine release during NMP of human kidneys and investigated their association with early clinical outcomes. Kidneys released a broad range of pro- and anti-inflammatory cytokines during NMP, possibly reflecting graft injury responses. However, these levels did not correlate with early post-transplantation outcomes and therefore the clinical relevance of perfusate cytokines released by the kidney during NMP appears limited.

Factors Influencing Number Of Organ Donors In The Netherlands; What Is Happening In 2025?

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Background

After the implementation of the opt-out consent system in 2021 an increase in the number of organ donors is observed. However, there are lower numbers of donors in 2025 compared to 2024. This study identifies factors of influence.

Methods

National data on deceased patients in intensive care units, collected by the Dutch Transplant Foundation (NTS) via NovaNORD, are used to analyse the organ donor numbers. The study period is from January to October for the years 2021 – 2025.

Results

The annual number of organ donors increased between 2021 and 2024, rising from 271 to 285, 292, and 360, respectively. The current 2025 trend (249 donors as of October) appears comparable to that of 2023. There are several possible explanations for the lower number of donors this year compared to 2024. During the study period (January - October 2021 - 2025), the number of deaths initially declined from 6300 in 2021 to 5621 in 2021, but stabilized in the following years reaching 5,491 in 2025. However, the number of potential organ donors rose steadily from 819 to 937, 1,002 and 1,085, returning to a level comparable to that of 2023 in 2025 (1,000).

The overall family consent rate fluctuated from 67% in 2021 to 62% in 2022, 64% in both 2023 and 2024, and declined to 61% in 2025. When families were approached in cases where the Donor Register indicated consent ('Yes' registration), the approval rate remained stable at approximately 86%. In contrast, when families were approached in cases of 'No objection' registration, the approval rate declined from 48% in 2021 to 41% in 2025. For registrations indicating 'Decision by next of kin/specific person,' the consent rate decreased from 39% in 2021 to 27% in 2025.

Conclusions

The number of organ donors in 2025 is lower compared to 2024 and more resembles the numbers of 2023. The main factors of influence appears to be a lower number of potential organ donors in 2025, as well as a decline in the family consent rate for organ donation in cases of a 'No objection' and 'Decision by next of kin/specific person' registrations.

Research Plan To Investigate Medication Adherence After Kidney Transplantation: Part Of The PERSIMMON Project

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Background

Adherence to the immunosuppressive regimen is one of the biggest challenges for kidney transplant recipients (KTRs) and professionals struggle to identify, monitor and support for non-adherence. Prevalence of non-adherence to the immunosuppressive regimen ranges between 30- 50%. In the 'PERSonalized IMMunosuppression for ONe kidney for life' (PERSIMMON) project we aim to conceptualize, describe, and understand the multiple influences on adherence and develop patient-approved adherence-promoting strategies.

Methods

The Context and Implementation of Complex Interventions (CICI)-framework will be used for a context analysis. We will use an explanatory mixed-methods design using quantitative and qualitative methods to assess (1) prevalence rates, evolution, and profiles of non-adherence and (2) geographical, epidemiological, sociocultural and socioeconomic factors and current practice patterns influencing the development and implementation of an adherence-promoting program. Retrospective data (n>1,200) will be used to gain insight into the prevalence and evolution of non-adherence among KTRs and explore profiles of non-adherence based on demographic, clinical, and personal factors. A multicenter, prospective cohort study will further investigate predictors of adherence. Interviews with stakeholders will help identify potential barriers and facilitators for implementation of an adherence management toolbox in daily practice.

Results

In the Collaborative Living-Lab for Adherence Support (CLAS) we will develop, together with stakeholders, an adherence toolbox comprised of measures to identify, monitor, and manage adherence in KTRs that can be tailored to individual needs and preferences.

Conclusions

The PERSIMMON project aims to realize personalized immunosuppression and patient-centered strategies to support adherence therefore improving survival and quality of life.

Reasons For Non-Participation In A Prehabilitation Study Of Kidney Transplant Candidates

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Background

For kidney transplant candidates (KTCs) it is important to be physically and mentally fit for transplant surgery. Although over 90% of KTCs experience modifiable problems regarding physical functioning, nutritional status, or mental well-being, only 28% agreed to participate in the PreCareTx prehabilitation trial. The aim of the Non-ResponseTx-study was to explore reasons for non-participation and to gain insight into the health status of KTCs who did not respond to the invitation of the PreCareTx-study.

Methods

All eligible KTCs on our transplant center's waiting list who declined participation in the PreCareTx-study or did not respond to the invitation received a survey. The survey included demographic and clinical variables, reasons for non-participation, and questions regarding physical functioning, nutritional status, and mental wellbeing. Descriptive and comparative statistics were used for analysis.

Results

Out of 242 KTCs who were sent the questionnaire, 108 KTC (45%) responded. Mean age was 62.4 years (SD 11.0), 64% was male, and 42% was on dialysis. Main reasons for non-participation included: working on fitness independently (33%); travel distance to the transplant center (25.5%), and lack of time (16%). Being too fatigued was mentioned as an additional reason by 19.8%. Educational level differed significantly between groups, with PreCareTx participants being more highly educated (p = .006). PreCareTx participants also reported a higher level of anxiety symptoms than non-participants (41% vs. 27%,

p = .04). No significant differences were found in clinical variables.

Conclusions

Since health status was comparable between participants and non-participants, many non-participants may still be suitable for prehabilitation—even if they are already working on their fitness. Therefore, assessing health status during transplant screening is recommended to identify candidates who could benefit. In addition, future programs should consider offering prehabilitation and progress measurements in the patient's living environment and develop strategies to engage underrepresented groups to ensure equitable access.

The MONKEY Challenge: Machine-Learning For Optimal Detection Of Inflammatory Cells In The KidneY

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Background

Because Banff classification of kidney transplant biopsies suffers from subjectivity and is time consuming, development of automated biopsy assessment is potentially useful to increase scoring consistency. We organized the MONKEY challenge, in which participants developed AI algorithms to detect individual inflammatory cells in Periodic acid-Schiff (PAS) stained kidney transplant biopsies.

Methods

A multicenter dataset of 116 whole slide images (WSIs) was collected, in which 31.101 monocytes and 60.629 lymphocytes were annotated within 174 ROIs. Annotations were guided by immunohistochemical (IHC) re-staining to create a robust ground truth. The publicly released training data contained 81 WSIs, scanned with three different scan profiles and a corresponding IHC restained WSI. For independent validation, 26 WSI from two centers were held back. Submissions were ranked using Free Response Operating Characteristic (FROC) analysis.

Results

MONKEY was conducted from September 2024 to February 2025. For the model with the highest FROC score, an overall inflammatory cell detection performance of 76.7%, 71.6% and 74.1% was achieved for precision, recall and F1, respectively. Visual inspection of the results of the three top-performing teams look promising to be further established in a diagnostic tool.

Conclusions

The MONKEY challenge demonstrated how a wisdom-of-the-crowd approach resulted in very promising AI applications. As eight of the 17 Banff lesion scores rely on the presence and distribution of inflammatory cells in specific renal compartments, this work marks a meaningful step toward automated Banff scoring. The final best performing algorithm will be combined with structural segmentation to mimic full Banff scoring and is currently being evaluated in an ongoing reader study.

Integrating Evolutionary And Functional Divergence Of HLA-DQ Alleles Improves Prediction Of Humoral Immunogenicity In Kidney Transplantation: A Multinational Cohort

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Background

De novo donor-specific HLA antibodies (dnDSA) most often target HLA-DQ mismatches in kidney transplantation, yet not all DQ mismatches are equally immunogenic. HLA-DQ forms a heterodimer of polymorphic α- and β-chains, and qualitative properties of these heterodimers strongly influence dnDSA formation. Donor heterodimers from an evolutionarily distinct clade or carrying the DQα05 chain exhibit heightened immunogenicity. We hypothesized that evolutionary divergence between DQ heterodimer families contributes to functional differences in immunogenicity and developed an integrated risk model incorporating evolutionary and structural features to improve upon existing quantitative approaches.

Methods

We analyzed 3,841 kidney transplant recipients with second-field HLA-DQ typing across five centers. Patients fully matched at HLA-DQ or with preformed DSA or early posttransplant DQ-DSA (<6 weeks) were excluded, yielding 3,003 recipients with 4,173 HLA-DQ mismatches. All HLA-DQ alleles were classified by evolutionary clade and DQα05 status. Because the risk of DQα05 heterodimer mismatches was reduced when the recipient shared the β-chain, six functional HLA-DQ subcategories were defined: DQα01-heterodimers, DQα05/DQβ02, DQα05/DQβ03, non-DQα05/DQβ02, non-DQα05/DQβ03, and DQβ04-heterodimers. Mismatches were categorized as low-risk when donor and recipient belonged to the same subcategory (n=1,554), high-risk for DQα05-positive donor mismatches with a different β-chain or cross-clade mismatches in clade 1 homozygotes (n=803), and moderate-risk for all others (n=1,816). Model performance was evaluated using multivariable Cox and time-dependent ROC-AUC analyses, benchmarked against established molecular metrics.

Results

Low-risk mismatches showed excellent dnDSA-free survival (97.7% at 5 years) compared with 89.7% for moderate (HR 3.98, 95%CI 2.78–5.70, p<0.001) and 83.1% for high-risk mismatches (HR 6.58, 95%CI 4.52–9.58, p<0.001). The model significantly outperformed eplet and amino acid mismatch load (ΔAUC 0.031 and 0.022, both p<0.05). Recipients with moderate- or high-risk mismatches had higher risk of antibody-mediated rejection (HR 1.84, 95%CI 1.24–2.72; HR 2.32, 95%CI 1.52–3.54, respectively) and dnDSA development to moderate- or high-risk mismatches predicted graft failure (HR 2.54, 95%CI 1.73–3.72, p<0.001), whereas dnDSA development to low-risk mismatches did not.

Conclusions

Integrating evolutionary divergence and structural dissimilarity enables accurate risk stratification of HLA-DQ mismatches. This biologically grounded model improves prediction of alloimmunity beyond conventional molecular metrics, supporting individualized immunologic risk assessment and donor selection.

Studying Health-Related Harms And Needs Of Kidney Sellers In A Migration Context: A Scoping Review And Conceptual Framework

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Background
Reports indicate that migrants are solicited to sell their kidney. While some research has examined the health effects of kidney sales (KS), and migration is recognized as a social determinant of health, little research explores the intersection of both. This scoping review aims to answer two research questions (RQ): (1) what are the physical, psychological, and socio-economic harms and needs reported by kidney sellers; (2) what those harms and needs experienced by migrants.

Methods
Searches were conducted on January 25th, 2023, across 5 databases. Eligible studies were English-language publications published after January 1st, 2003. Two investigators independently screened the records. Subsequently, they coded the data and merged findings into a shared coding framework.

Results
3,577 and 224 articles were screened for RQ1 and RQ2 respectively, from which 38 and 61 articles were respectively included. Literature emphasizes harms rather than needs of kidney sellers and migrants.

Kidney sellers are harmed before, during, and after their nephrectomy. Physical harms are reported as a result of inadequate screening and insufficient care. Psychological harms include depression, anxiety, and poor self-esteem. Socio-economically, kidney sellers are coerced by brokers who exploited their vulnerability through fraudulent deals, leaving many unpaid and trapped in debt. Additionally, they face limited job opportunities due to their inability to perform labor-intensive work and the heightened social discrimination they encounter.

Migrants are harmed before, during, and after migrating. Physical harm includes chronic conditions, infectious diseases, and poor reproductive health. Depression and post-traumatic stress disorder are common psychological harms. Socio-economically, migrants experience restricted access to healthcare due to their precarious socio-legal status. Overlall, harms are reinforced by exposure to violence and discrimination, poor socio-economic and socio-demographic settings, and absence of social support.

Migrants and kidney sellers' needs are often inferred from accounts of harm and externally framed in ways that overlook their own perspectives.

Conclusions
Kidney sellers and migrants endure physical, psychological, and socio-economic harms before, during, and after nephrectomy or migration. These harms are shaped and perpetuated by structural inequalities and social exclusion. The limited attention to their expressed needs highlights the importance of future research that centers the personal perspective of migrant kidney sellers.

Navigating CUSUM Design In Surgery: A Systematic Review Of Applications And Methodological Trade-Offs

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Background

Cumulative sum (CUSUM) charts have become an important tool for monitoring surgical outcomes, offering a way to detect deviations in performance more rapidly than traditional periodic audits. However, the methodological variation in CUSUM design creates uncertainty about how best to implement these charts in clinical settings. This review aims to provide an overview of the current applications of CUSUM in surgical monitoring, compare the advantages and disadvantages of commonly used methods, and offer practical guidance to support future development in clinical quality assurance for both researchers and clinicians.

Methods

A systematic review was completed using PubMed, for studies published between Jan 1, 2015 to Jan 1, 2025. The search focused on the application of CUSUM charts for monitoring usage, excluding learning curve studies. Data extraction covered seven domains: surgical domain, outcome monitored, CUSUM type, CUSUM calculation method, control limit, risk-adjustment, and risk model.

Results

Of the 21 included studies, most were focused on abdominal surgery, and primarily monitored post-operative complications, surgical quality, and mortality. CUSUM charts were mostly used to monitor binary outcomes, with the log-likelihood ratio (LLR) and observed minus expected (O-E) methods used equally. Over half of the studies were risk-adjusted, typically using logistic regression. Risk-adjustment was common in studies monitoring mortality and surgical quality, but less common in those focused on complications. The use of control limits was highly variable, with many studies using no control limits.

Conclusions

O-E CUSUMs provide a simple and intuitive approach that is easy to construct, while LLR CUSUMs offer improved sensitivity, albeit at the cost of being statistically more complex. While risk-adjusted CUSUMs are more ideal, the added complexity as well as data requirements may present a barrier for clinics with lower patient volumes or less developed data infrastructure. In the end, the effective use of CUSUM in surgery depends less on universal standardization and more on contextual alignment, ensuring that methodological choices correspond to the clinical purpose, data availability, and reporting strategy of the monitoring system.

Pioneering Donor Reported Outcome Measures (DROMs) In Living Kidney Donation

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Background

Living kidney donors represent a unique population, since they undergo surgery without direct medical benefit to themselves. It is not part of usual care to collect donor reported outcomes (DROMs) throughout the donation process. Our transplant center is the first to aim for integration of DROMs during lifelong follow-up of living kidney donors. In this study, donor response rate to DROMs as well as the use of DROMs by healthcare professionals (HCP) was assessed.

Methods

DROMs (PROMIS-27, Visual Analogue Scale, Multidimensional Fatigue Index, Brief Symptom Inventory) were implemented in October 2024, with data extraction conducted in October 2025. HCP use of DROMs was defined by opening the valued based healthcare dashboard with the DROMs results on the day or before consultation of the donor. An open box was included for donors to indicate topics they wanted to discuss with their HCP during consultation. For analyses, donors were stratified into

subgroups: pre-donation, < 1 year post-donation, 1-5 years post-donation and > five years post-donation.

Results

Questionnaires were administered to 121 donors prior to donation, 117 donors within the first year post-donation, 127 donors from 1-5 year post-donation and 417 donors > 5 year post-donation. Overall response rate from donors pre-donation was 83% and post-donation 64%. The response rate of donors who donated 1-5 years ago was significantly higher than donors who donated > 5 years ago (75 vs 58%, p<0.001). HCPs opened the DROMs dashboard in 41% of consultations pre-donation and in 79% of consultations post-donation. Early post-donation topics donors wanted to discuss with their HCP focused on recovery, whereas long-term topics addressed general health concerns.

Conclusions

DROMs were actively utilized by both donors and HCP, although response rates tended to be lower among those who donated longer ago. A return to pre-donation levels of functioning is an important short-term outcome for donors. DROMs allow more personalized monitoring of donors and help to identify if and when support, education or interventions are needed.

Transmission And Persistence Of Donor-Derived Anellovirus In Pediatric Kidney Transplant Recipients

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Background

One of the most abundant viruses in the human blood virome are anelloviruses. Kidney transplantation is the preferred treatment for children with end-stage renal disease. Previous studies performed in adult kidney transplant recipients have shown that plasma levels of *Alphatorquevirus*, including Torque teno virus (TTV), hold promise as immune activity marker, where high TTV loads indicate a reduced immune activity. TTV is part of the *Anelloviridae*. The human "anellome" contains not only TTV but also *Betatorquevirus*, and *Gammatorquevirus*. It is unclear if anelloviruses are transmitted through kidney transplantation in pediatric patients and persist in their new host. This study aims to assess how the anellome changes in children post-transplantation, hypothesizing (1) that anelloviruses will be introduced with the donor kidney and (2) that donor anelloviruses may colonize and persist in the recipient.

Methods

Six donor-recipient pairs were analysed, including three living-unrelated (LUR) and three living-related (LR) pairs. Recipients were monitored from before transplantation and up to two years post-transplantation (median age = 15.1 years (2.93 – 17.5), median number of samples = 6.5 (2 - 11)), donors were measured one time before transplantation. DNA from serum or plasma was analysed using quantitative Polymerase Chain Reaction (qPCR) and Rolling Circle Amplifications, Illumina library preparation, and SCANellome V2 to study the anellome.

Results

Three out of six donors (LUR) tested positive for anelloviruses, allowing comparison with the composition and development of the anellome in recipients. One recipient, who was on immunosuppressive therapy before transplantation, showed high anelloviral DNA (>10^{10} copies/mL) from start. One donor-derived anellovirus lineage was identified in one recipient. No donor lineages were detected in the other recipients. However, additional lineages became detectable in recipients over time.

Conclusions

Donor-derived anellovirus was identified in one pediatric recipient, possibly due to transmission or reactivation of a pre-existing lineage, suggesting a more compromised immune status. No donor-derived lineages were detected in the other recipients. However, additional lineages became detectable in all recipients, making it uncertain whether these originated from the donor or were already pre-existing but undetectable in the recipient. These findings indicate that TTV transmission is seen in a minority of pediatric kidney transplant recipients.

TTV-Loads In Pediatric Kidney Transplantation: Association With Immunosuppression, HLA Mismatch, Age And Sex

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Background

Kidney transplantation (KTx) is the treatment of choice for children with end-stage renal disease. These patients need lifelong immunosuppressive therapy to prevent graft rejection, however achieving an optimal balance is challenging. Reliance on plasma drug levels for dosing strategies does not accurately reflect a patient's immune status, risking immunosuppressive imbalance. To improve personalized treatment, better immune function biomarkers are needed. In adult KTx recipients, plasma levels of Torque Teno virus (TTV) have shown potential as markers for immune activity. Higher TTV loads reflect reduced immunity. Therefore, we aim to investigate the relation between post-transplant TTV load and immunosuppressive drug regimens in pediatric KTx recipients. We hypothesize that TTV load increases after transplantation, and is associated with patient age, sex, immunosuppressive regimen, and HLA-mismatch.

Methods

In this cohort study, 92 children who underwent kidney transplantation (KTx median age=10.5) were included. DNA extracted from serum or plasma samples were analyzed with qPCR for the presence of viral DNA. Samples were collected just before transplantation and up to two years after transplantation (1styear, every 2 months and 2ndyear, every 4 months). Results were analyzed with R-studio.

Results

All patients tested positive for TTV. Before KTx, the median TTV load was 3.39 Log_{10}. A peak was observed at 4 months post KTx (median:7.72 Log_{10} copies/mL;IQR:7.20-8.15 Log_{10} copies/mL). After 14 months, the median TVV load stabilized to 5.90 Log_{10} (IQR= 4.51-7.19 Log_{10}). No correlations were observed between age, sex, and TTV load (p=0.638; p=0.35). A significant decrease in TTV load over time post-KTx was found (p=0.0017). No significant effect of immunosuppression regimen (early vs. non-early steroid withdrawal) on TTV load was found (p=0.44575). Significant differences were observed between HLA-mismatch groups (p<0.05).

Conclusions

Post-KTx, TTV loads increased, peaking at 4 months and stabilizing by 14 months, with an overall decline over time. No associations were found with age, sex, or immunosuppressive regimen. TTV load differed significantly by HLA mismatch, being higher with more mismatches. These findings support TTV as a potential biomarker for immune monitoring after pediatric kidney transplantation. Future analyses will assess correlations with immunosuppressive drug levels and aim to define clinically relevant cut-off levels.

HLA Class I Leader Peptides Shared With CMV And The Risk Of Acute Rejection In Lung Transplantation

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Background

Certain cytomegalovirus (CMV) strains produce a protein (UL40) of which a peptide sequence is identical to peptide sequences found in the leader of specific HLA-A and HLA-C alleles. Of this UL40 that overlaps with HLA leader peptides, 3 variants exist: VMAPRTLIL, VMAPRTLLL and VMAPRTLVL. In CMV seropositive kidney transplant recipients, transplantation of an organ with a mismatched HLA-leader peptide was associated with early T cell mediated rejection. The aim of this study was to determine whether CMV seropositive lung transplant (LTx) recipients who receive lungs from donors with mismatched HLA class I leader peptides shared with CMV, are at increased risk of early acute rejection (AR).

Methods

A total of 293 lung transplantations were analyzed for donor and recipient characteristics, HLA profiles, HLA class I leader peptide mismatches and CMV serostatus. Primary outcome was AR during the initial post-transplant hospitalization. Patients were censored at discharge or after 6 weeks. Time-to-event analyses were performed using Cox regression models.

Results

Among the 154 CMV seropositive recipients, AR rates differed depending on the type of mismatched leader peptides, with a particular strong association for the LVL mismatch (p=0.0028). This association was absent in CMV- recipients (p=0.14). In univariable analysis of CMV+ recipients, reperfusion time, pulmonary hypertension and VMAPRTLVL mismatch were significantly associated with AR. In multivariable analysis of CMV+ recipients, reperfusion time (HR0.98, p=0.006) and pulmonary hypertension (HR12.5, p=0.004) remained significant predictors, whereas the LVL mismatch (HR2.3, p=0.073) did not reach significance, likely due to the limited number of LVL-mismatched cases in this cohort (n=14).

Conclusions

In CMV seropositive lung transplant recipients, mismatches between HLA leader peptides shared with CMV are associated with an increased risk of early acute rejection in univariable analysis. However, this association was not confirmed in multivariable analysis.

3DCT-Based Body Composition As Marker Of Functional Capacity In LTx

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Background

Estimation of the recovery potential after lung transplantation (LTx) in candidates relies on a comprehensive assessment of functional capacity (FC). Guidelines on how to structure this assessment are lacking, resulting in many different approaches that are currently used for this. An alternative or addition to this heterogeneous approach may be 3D CT-based body composition analysis to assess muscle and fat-mass and distribution as markers of FC. Hence, we explored the association of 3D CT-based body composition with different FC tests as a first step towards more structured FC assessment.

Methods

Muscle volume (MV) was automatically segmented from CT scans with Data Analysis Facilitation Suite. FC tests included in this analysis were six-minute walk distance (6MWD), 1 minute sit to stand (1MSTS), handgrip strength (HGS), maximal inspiratory and expiratory pressures (MIP and MEP) 24hour urinary creatinine excretion (24hCER), albumin, BMI and estimates of body composition using DEXA or bio-impedance analysis (BIA). Correlation-coefficients of FC tests with CT-based body composition were calculated and multivariable linear regression was conducted, whilst adjusting for age, sex, indication, and length.

Results

113 LTx candidates were included in the study. Strong correlations were found between MV and fat volume on CT and fat-(free) mass on DEXA and BIA. Multivariable analyses showed that higher MV (per 1-SD) was associated with higher HGS (β = 7.16 95% CI 4.81-9.51), 24hCER (β = 1.57 95% CI 0.86-2.27), MIP (β = 0.90 95% CI 0.31-1.50) and MEP (β = 1.30 95% CI 0.47-2.13). 6MWD and 1MSTS were not significantly associated with MV.

Conclusions

3D CT-based MV strongly reflects body composition obtained by DEXA and BIA, confirming validity of automated 3D-CT analysis. Our other findings indicate that FC muscle-measures can be closely linked to MV on the CT scan, in contrast to tests that also rely on cardiorespiratory status. Future research will target prognostic and added value of 3D-CT parameters in relation to outcomes.

Temperature Dynamics Of Porcine Lungs During Preservation: Conventional Ice Storage Versus A Commercially Available Thermoelectric Cooler

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Background

Donor lungs for transplantation are traditionally preserved on ice, but this can induce cold-related injury. Controlled hypothermic storage better preserves mitochondrial integrity and cellular homeostasis. Recently, several transplant centers have implemented this strategy by using commercially available thermoelectric coolers as a lower-cost alternative to Paragonix's LUNGguard. This study aims to provide the first insights into temperature trajectories in porcine lungs preserved using a thermoelectric cooler compared with lungs preserved on ice.

Methods

Porcine lungs obtained from a local slaughterhouse were retrieved by rapid sternotomy, inflated, and flushed with cold solution. Lungs were stored for 6 hours either on ice (n=4) or in a thermoelectric cooler (Makita, Japan) set at 5°C (Makita5; n=5) or 10°C (Makita10; n=3). Core temperature (CT) was measured continuously by a probe inserted into the pulmonary artery. Surface temperature (ST) of the lateral aspect of the lung was measured using

a thermographic camera at the end of the preservation period. Data are reported as median (IQR) or mean ± SD.

Results

CT for lungs preserved on ice decreased progressively from 11.5°C (9.4-15.7) at baseline, to 8.3°C (5.2-9.9) after 60 min, 3.8°C (2.4-4.6) after 120 min, 2.0°C (1.1-2.5) after 180 min, 1.2°C (0.5-1.6) after 240 min, 0.8°C (0.3-1.2) after 300 min, and 0.5°C (0.2-0.9) at 360 min.

In contrast, CT in Makita5 remained relatively stable, measuring 10.3°C (9.5-12.9) initially, 9.4°C (7-10.5) after 60 min, 9.1°C (5.1-9.5) after 120 min, 8.3°C (5.0-9.0) after 180 minutes, 8.4°C (4.9-8.6) after 240 min, 8.3°C (5.2-8.5) after 300 min, and 8.2°C (5.4-8.2) at 360 min.

Similarly, CT in Makita10 remained stable throughout preservation, with 12.8°C (10.2-14.4) at baseline, 10.8°C (10.8-12.3) after 60 min, 11.2°C (10.9-12.1) after 120 min, 11.3°C (11.2-12.1) after 180 minutes, 11.6°C (11.5-12.1) after 240 min, 11.9°C (11.6-12.1) after 300 min, and 12.1°C (11.6-12.2) at 360 min.

ST of lungs stored on ice was 3.2°C ± 2.1°C, while those preserved in Makita5 and Makita10 were 6.2°C ± 1.7°C and 12.1°C ± 1.0°C, respectively.

Conclusions

Compared with storage on ice, which maintains temperatures near 0°C, thermoelectric cooling may offer greater temperature stability and homogeneity, although slightly above the target setpoint.

Should Baseline Lung Allograft Dysfunction Be Defined According To Donor Rather Than Recipient Lung Function Values?

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Background

Baseline Lung Allograft Dysfunction (BLAD) is currently defined as post-lung transplant (LTx) baseline lung function (FEV1 and/or FVC) ≤ 80% of predicted recipient reference values. This definition does not account for donor-recipient lung size mismatch. Wealso use donor reference values to determine the definition of BLAD that best predicts clinical outcome and provides the most appropriate definition for analyzing potential preventable risk factors.

Methods

All adult bilateral LTx recipients transplanted until June 1st 2024 in our center were included. BLAD-r uses recipient-predicted lung function values, BLAD-d uses donor-predicted values calculated both using the Global Lung Initiative (GLI) calculator. Baseline characteristics, survival and risk factors for BLAD were compared.

Results

In total 641 patients were included. Of those 287 (45 %) met the criteria of BLAD-r and 306 (48%) of BLAD-d. Both BLAD-r as BLAD-d were associated with reduced survival. Donor-recipient lung mismatch was -11,1% for patients with restrictive lung disease (Fib) and +4,53% in COPD. Fib received in 26% more than 20% undersized donor lungs while almost 10 % of the COPD recipients received lungs more than 20% oversized. In 163 out of the 641 recipients (25%) were different classified by BLAD-r (n=72) and BLAD-d (n=91). This led to a difference in risk factors for BLAD. For example, diagnosis of pulmonary fibrosis was not a risk factor for BLAD anymore.

Conclusions

Given the influence of lung size mismatch on BLAD-r and BLAD-d we suggest that donor normal lung function might be better suited to evaluating donor-related- and peri-operative risk factors for BLAD.

Between Lung And Kidney: How Patients Experience Collaboration Within Psychosocial Care During A New Transplant Process

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Background

In the Transplant Centre, patients who are undergoing both lung and (possible) kidney transplants are increasing. This dual process requires intensive medical and psychosocial support. Psychosocial support usually involves several medical social workers, each with their own specialism in pulmonary medicine or nephrology. Although both disciplines work within the same centre, cooperation and the division of roles are not always sufficiently coordinated. Patients sometimes experience overlap, uncertainty or, conversely, gaps in support.

At the same time, effective collaboration offers the opportunity for greater continuity in care, trust and patient autonomy - factors that are essential for recovery and improving quality of life. However, limited research has been done on how patients experience and perceive this collaboration. We aim to answer this question through our study.

Methods

For this study, a qualitative descriptive study was conducted within a single transplant centre. Semi-structured interviews were held with nine patients who had previously undergone a lung transplant and were now in the process of undergoing a possible kidney transplant. The interviews focused on the patient experience of the collaboration between social workers in the pulmonary medicine and nephrology departments.

The interviews were not recorded, but were paraphrased based on extensive notes. The data obtained were then analysed thematically, identifying recurring topics and patterns related to collaboration, division of tasks, continuity, important phases and potential hurdles. The research group consisted of five women and four men, four of whom had undergone both a lung and kidney transplant. Their ages ranged from 30 to 65 years.

Results

The results show that cooperation between social workers in pulmonology and nephrology has a direct impact on the perceived quality of psychosocial care for patients with combined lung and kidney problems within the (pre)transplant process. Most patients are satisfied with the current support; however, patients emphasise the importance of having a single point of contact for continuity and trust, combined with good coordination between the disciplines involved. Clear communication, joint initial consultations and unambiguous information provision reinforce the feeling of calm and control during the process. When coordination is lacking, gaps in support arise.

Conclusions

Structural cooperation between social workers appears to be essential for achieving integrated, value-driven care within complex transplant care.

Organ And Tissue Donation Discussion Board

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Background

One recommendation from the evaluation of the amended donor law (2024) was to provide better communication support to donation professionals and families during the donation process in hospitals. This is because a lot depends on the patient's family during a

donation procedure. During an emotional period, a lot of information is provided and many arrangements have to be made. From studies, it is known that relatives are in shock during these conversations and remember little afterwards.

Methods

In collaboration with intensive care specialists, organ donation coordinators (ODCs) and next of kin, a communication diagram about organ and tissue donation has been developed. This communication diagram supports the family during and after the donation procedure and provides guidance to the doctor/ODC during the conversation.

Results

The communication diagram has a front and back. The doctor uses the front to support the donation discussion. The ODC uses the back. The communication diagram is printed on tear-off notebooks. The front page of the notebooks contains an explanation and brief instructions on how to use the communication diagram. The communication diagram has been distributed to all ICUs and ODCs.

Conclusions

A communication diagram has been developed with the aim of providing better support to families during and after a donation procedure.

Depletion Of Complement-Binding Donor-Specific HLA Antibodies During Plasmafiltration In Antibody-Mediated Rejection Following Lung And Heart Transplantation

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Background

Donor-specific HLA antibodies (DSA) play a central role in antibody-mediated rejection (AMR) and can significantly compromise transplant outcome after solid organ transplantation. The main goal in managing AMR is therefore diminishing the level of DSA and preventing the formation of new DSA. Reduction of DSA levels can be achieved via several methods, such as plasmafiltration or antibody adsorption, immunosuppressive therapy, intravenous immunoglobulin, and depletion of B-cells.

Methods

In this study we characterized DSA profiles before, during, and after plasmafiltration in three recipients with AMR after heart transplantation (n=2) and lung transplantation (n=1). DSA presence and Mean Fluorescence Intensity (MFI) where monitored at multiple timepoints using Luminex single antigen bead assays. In addition, solid-phase C1q binding assays were performed to identify DSA capable of binding complement factor C1q.

Results

AMR occurred in all three patients within one month after transplantation. At the time of AMR diagnosis, serum DSA against both HLA class I and class II were detected. In two patients, no DSA were detected pretransplant. In those patients the serum DSA levels decreased significantly (< 5000 MFI) after six rounds of plasmafiltration.

In one patient DSA were detected pretransplant. These pretransplant DSA were not able to bind complement C1q. At AMR diagnosis, however, the detected DSA were able to bind complement factor C1q. After 21 rounds of plasmafiltration, some DSA showed a reduced serum level (<5000 MFI) whereas other DSA remained high (>13000 MFI). Interestingly, despite persistently high MFI values during and after plasmafiltration, complement fixing DSA became undetectable after five rounds of plasmafiltration.

Conclusions

Serum DSA levels can significantly decrease during plasmafiltration in patients with AMR. Although observed in a single case, our results suggest that, despite the loss of complement-fixing DSA after plasmafiltration, non-complement-fixing DSA can persist. Importantly,

the assessment of complement-fixing DSA might offer a more accurate measure of the therapeutic effect of plasmafiltration compared to a regular DSA MFI profile. These observations warrant further investigation in larger patient cohorts to better understand the mechanisms and clinical relevance of this differential DSA response in relation to plasmafiltration.

The Impact Of Donor Lung Size On Lung Transplant Waiting Time

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Background

In lung transplantation (LTx), donor-recipient size matching is crucial, yet candidates requiring smaller lungs may experience prolonged waiting times. This study aimed to evaluate the association between recipient total lung capacity (TLC) and wait time for LTx. We hypothesized that a smaller requested minimal TLC is independently associated with longer wait times.

Methods

We performed a retrospective observational study including all adult LTx recipients from our Center transplanted between May 2012 and January 2025. For these patients, baseline characteristics, Lung Allocation Score (LAS) score, blood group, and the minimum and maximum requested TLCs were recorded for analysis. Wait time was $\log_{10}$-transformed, because it was not normally distributed. The association between requested minimal TLC and wait time was examined using univariate and multivariate linear regression models. Multivariate analyses were adjusted for LAS score and blood group, as potential confounders.

Results

In total 417 LTx candidates were included. The median waiting time was 428.57 days. Requested minimal TLC demonstrated a significant negative association with waiting time. In univariate analysis, a lower minimal TLC correlated with longer wait time (β = -0.09; p = 0.003). This relationship persisted after adjustment for LAS and blood group in the multivariate model (β = -0.121; p = <0.001).

Conclusions

Smaller requested TLC is independently associated with prolonged wait times for LTx in the Netherlands, even after adjusting for LAS and blood group. These findings suggest that candidates requiring smaller donor lungs face an inherent disadvantage within the current allocation system. Future research should explore policy modifications and surgical strategies to mitigate this inequity.

Inspiratory Muscle Strength In Lung Transplant Candidates

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Background

The number of lung transplantations is increasing worldwide and outcomes are improving. Lung transplant candidates suffer from a lack of exercise capacity resulting in loss of (respiratory) muscle strength. A low respiratory muscle strength may result in a reduced Maximal Inspiratory Pressure (MIP) and correlates with dyspnea, exercise capacity and health-related quality of life. Inspiratory muscle strength might also be important to prevention of early postoperative pulmonary complications and to reduce

hospital length of stay. Optimization of respiratory muscle function might also be important to improve perioperative outcomes. We here study if a MIP<70% predicted in lung transplant candidates is related to diagnosis, lung function, strength of other muscle groups and body composition to determine possible intervention options.

Methods

We included 89 lung transplant candidates, evaluated between April 2024 and October 2025. Two groups were formed based on MIP<70% versus MIP>70% predicted. Lung function (FEV1, FVC, TLC), body composition (BMI, Fat Free Mass Index (FFMI, Man<16, Woman<15)), peripheral muscle function (grip strength and m. Quadriceps strength) and exercise capacity (6MWT) were analyzed.

Results

A low MIP (MIP<70 pred.) was found in 40,4% of lung transplant candidates. Diagnosis, Age, Gender, FEV1, TLC, BMI, peripheral muscle function and 6MWT did not differ between the low and normal MIP group. However, FFMI and FVC were lower in the group MIP <70%predicted ($p \leq 0,05$).

Conclusions

Low inspiratory muscle strength is common in lung transplant candidates, independent of diagnosis and peripheral muscle strength. Low Fat Free Mass Index and low FVC are suggestive for low MIP. Both FFMI and FVC are known health indicators and associated with vulnerability. We currently study if a low MIP results in a prolonged early postoperative outcome and thereafter plan to see if training of respiratory muscles is effective preventing early post-operative complications.

Serum Sickness Caused By Rabbit Anti-Thymocyte Globulin In A Lung Transplant Patient: A Case Report

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Background

Serum sickness is a type 3 hypersensitivity reaction and a rare, but known complication of rabbit anti-thymocyte globulin (rATG) treatment. The classical symptoms are fever, polyarthralgia, and skin rash, seven to fourteen days after the first dose. We describe an atypical case of serum sickness after lung transplantation.

Methods

na

Results
Case Presentation

A 54-year-old lung transplant recipient, eight months post-transplant because of a pulmonary silicosis, was admitted eleven days after his first rATG treatment because of acute cellular rejection (A1B1) (total of three doses in six days (1.5mg/kg)). He presented with groin, joint, and a pronounced jaw pain. He was febrile (39.7°C) without skin abnormalities. Laboratory results showed an elevated C-reactive protein (722mg/L) with normal complement 3 and 4 levels. The pain progressed within hours to a headache and abdominal pain. The joint pain escalated rapidly rendering him immobile. Analgesics including opioids and ketamine were started. Extensive bacterial cultures of blood, urine and joint fluid were negative. No replication of Epstein Barr-Virus and Cytomegalovirus were detected. Computed Tomography (CT) ruled out intra-abdominal pathology, and joint fluid aspiration ruled out septic arthritis. Two days after presentation, acute kidney injury developed (CKD-EPI-eGFR declined from 70 ml/min to 27 ml/min), without abnormalities in urine analysis. As a diagnosis per exclusionem, serum sickness was considered and 80mg prednisolone (1mg/kg) was initiated. Within two days, all pain disappeared and a day later, kidney function was restored. He fully recovered on a quick prednisolone tapering scheme. Additional history taking revealed a rabbit bite in his youth and serum rabbit antibodies at the moment of presentation were strongly positive (341 IU/ml).

Conclusions

This case underscores the importance of including serum sickness in the differential diagnosis in patients presenting with severe (joint) pain and inflammation after rATG treatment, despite atypical features like the absence of skin abnormalities, normal complement levels and with extremely high CRP. Early recognition is important and steroid treatment should be considered if infections are ruled out. Additionally, a history of rabbit exposure should prompt clinicians to assess sensitization before administering rATG.

Patient-Reported Outcomes Among Heart Liver, Kidney And Lung Transplant Recipients: Changes In Quality Of Life Over Time And Between Organs

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Background

Patient-reported outcomes measures (PROMs) can help identify patients who need additional support after transplantation as well as improve quality of care. In our center we collaborated across all organs to implement PROMs and fully integrate these into the electronic patient records and daily clinical practice from 2023. This extensive multi-organ dataset has not previously been analyzed and can offer valuable insights into patient-reported outcomes. This study aims to investigate changes in the domains of health-related quality of life (HR-QoL) over time and differences between recipients types.

Methods

All adult transplant recipients are invited to complete online PROMs. HR-QoL was measured using the validated PROMIS-27 questionnaires for the following domains: global health, global QoL, physical functioning, social functioning, depression, anxiety, fatigue, and a pain intensity rating (0-10). Measurements were at baseline (pre-transplant), 3, 12 and 24 months post-transplant. Average T-scores are presented.

Results

In total since implementation, 503 liver recipients (61% male), 1037 kidney recipients (61% male), 241 lung recipients (54% male) and 235 heart recipients (63% male) completed at least one PROMs measurement. Average age at transplant was 52.6 years (55 were transplanted as children). At pre-transplant, lung recipients scored significantly lower than kidney recipients on physical functioning (T=29 vs T=39) and social functioning (T=37 vs T=44). Liver recipients (T=48) reported significantly lower social functioning than heart (T=56) and lung recipients (T=55) at 1-2 years. Similarly, liver recipients reported significantly higher depression at 1-2 years (T=52) than the other organs but the average levels remained within the normal range (T<55). Lung recipients had significantly lower physical functioning (T=42 vs T=45-46) and higher pain intensity (Mean=3 vs Mean=2) than all other organs at 2 or more years post-transplant. There were no significant differences between organ recipients on fatigue or anxiety levels at the various timepoints.

Conclusions

While transplantation affords quality of life advantages for all recipients, there are differences in the course per organ over time. This initial analysis of the currently available data demonstrates the potential of measuring patient-reported outcomes in transplantation. Future directions include multivariate analyses assessing trajectories over time, differences between subgroups and variables that influence this change.

Outcome Of Dual Hypothermic Oxygenated Machine Perfusion Versus Abdominal Normothermic Regional Perfusion In Donation After Circulatory Death Liver Transplantation

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Background

Donation after circulatory death (DCD) has expanded the liver donor pool but remains constrained by ischemia-related injury affecting graft and biliary outcomes. In-situ abdominal normothermic regional perfusion (aNRP) and ex-situ dual hypothermic oxygenated perfusion (DHOPE) aim to mitigate these risks, yet direct comparative data are limited.

Methods

This international, multicenter retrospective observational cohort study included adult recipients of a first whole-organ DCD liver transplant from donors <60 years, preserved with DHOPE (The Netherlands) or aNRP (Spain) between 2016-2022. The primary endpoint was one-year graft survival. Secondary endpoints included patient survival, biliary complications, primary non-function (PNF), and hepatic artery thrombosis (HAT). Overlap-weighted propensity score adjustment was applied to balance donor, preservation, and recipient characteristics.

Results

A total of 113 DHOPE and 370 aNRP and liver transplants were included. After adjustment, 72 DHOPE and 97 aNRP transplants remained with balanced baseline variables. Adjusted one-year graft survival was lower with DHOPE compared with aNRP (85% vs 94%; p=0.003), whereas patient survival was similar (89% vs 94%; p=0.069). One-year cumulative incidence of biliary complications was significantly higher after DHOPE (51% vs 19%; p<0.001 after adjustment), including post-transplant cholangiopathy (23% vs 0%; p<0.001) and anastomotic strictures (41% vs 11%; p<0.001). Rates of PNF (2.9% vs 1.0%; p=0.576), HAT (1.4% vs 3.1%; p=0.637), and acute rejection (9.7% vs 11.3%; p=0.736) did not differ significantly between groups.

Conclusions

aNRP and DHOPE enable successful use of DCD grafts for liver transplantation with equal patient survival. The choice between techniques could be guided by local expertise, logistics, and resource availability, but aNRP is associated with higher graft survival and lower biliary complication rates compared to DHOPE.

Persistent Dysregulation Of Bile Acid Metabolism After Liver Transplantation: A Longitudinal Metabolomic Analysis

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Background

Liver transplantation profoundly affects bile acid metabolism. Bile acid composition can reflect liver function and may contribute to post-transplant health outcomes, potentially including cardiovascular disease. However, literature on specific patterns of bile acid changes after transplantation remains scarce. We characterized bile acid profiles in liver transplant recipients throughout the transplantation trajectory, using kidney donors as a reference population.

Methods

We performed a longitudinal analysis of EDTA plasma bile acids quantified by mass spectrometry. Nineteen bile acids (CA, CDCA, DCA, LCA, HDCA, HCA, GLCA3S, LCA3S, TLCA3S, GCA, GCDCA, GDCA, GLCA, GHDCA, TCA, TCDCA, TDCA, THDCA, TLCA) were measured. Total bile acid (TBA) concentration was calculated as the sum of all individual bile acids. Data from patients with re-transplantations and combined transplantations were excluded.

Results

We included 540 liver transplant recipients (43% female, age 55 ± 14 years at ≥12 months post-transplantation) with samples available at pre-transplant (n=145), 3 months (n=95), 6 months (n=101), and ≥12 months post-transplant (n=412), and 93 kidney donors pre-donation. Concentrations of all bile acids, except GHDCA, changed significantly over time (p<0.05). TBA concentrations decreased from 41.19 [IQR 10.04-86.32]μmol/L pre-transplant to 4.61 [2.92-8.13]μmol/L at ≥12 months post-transplant (p<0.001), but remained higher than in kidney donors, 2.91 [2.06-4.08]μmol/L (p<0.001), while the secondary:primary bile acid ratio increased from 0.05 [0.01-0.23]μmol/L pre-transplant to 0.54 [0.15-1.02] μmol/L at ≥12 months post-transplant (p<0.001). Principal Component Analysis of bile acid composition demonstrated significant differences between all time points during the liver transplant trajectory (p<0.001), and between recipients ≥12 months post liver transplantation vs. controls (p<0.001). Shannon diversity of bile acids increased from 1.5 [1.3-1.8] pre-transplant to 1.9 [1.7-2.1] at ≥12 months post-transplant (p<0.001) but remained lower than in controls (2.2 [2.1-2.3];p<0.001).

Conclusions

Bile acid homeostasis only partially normalized at ≥12 months after liver transplantation, with persistent differences when compared with kidney donors, potentially influenced by shifts in gut microbiota composition. These findings suggest bile acid profiles may provide insight into post-transplant metabolic health and cardiovascular risk. Further studies should assess relationships between gut microbiota, bile acids and cardiovascular endpoints to elucidate underlying mechanisms and evaluate the potential of bile acid profiles as biomarkers for risk stratification and targeted interventions.

Prolonged Liver Preservation Using Dual Hypothermic Oxygenated Machine Perfusion May Not Be Safe In Circulatory Death Donors: Initial Experience

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Background

Recent studies suggest that prolonged (≥4 hours) dual hypothermic oxygenated machine perfusion (DHOPE) can be safely used in livers donated after brain death, as well as in donation after circulatory death (DCD) livers following normothermic regional perfusion to extend preservation time overnight and allow day-time transplantation. The objective of this study was to evaluate the outcomes after adoption of the strategy of prolonged DHOPE in DCD livers without additional perfusion.

Methods

We conducted a retrospective, single-centre cohort study, analysing the graft-related complications of prolonged (≥4 hours) DHOPE in DCD livers, and compared them to the outcomes of control (<4 hours) DCD-DHOPE. Outcomes included the core outcome set for liver transplantation, with key complications reported such as primary non-function, new renal replacement therapy and post-transplant cholangiopathy. Additional parameters recorded were intensive care unit and hospital stay, operation duration, intraoperative red blood cell transfusion, and postoperative intra-abdominal bleeding (IAB). Post-transplant cholangiopathy-free graft survival and overall patient survival were also assessed at one year.

Results

In the study period, 207 DCD livers were included in the DHOPE cohort, of which 85 met the inclusion criteria. Prolonged DHOPE was performed on 30 livers, whereas the control group consisted of 55 livers. The median prolonged DHOPE duration was 7.2 (5.1-12.9) hours and 3.0 (2.7-3.6) hours in the controls (p<0.001). The duration of the transplantation was significantly longer in the prolonged DHOPE group (7.4 hours vs. 5.8 hours, p<0.001). The incidence of IAB was significantly higher in the prolonged DHOPE group (30% vs. 11%, p=0.038). Post-transplant cholangiopathy-free graft survival was significantly lower in the prolonged DHOPE group at 71%, compared to 96% in the control group (p=0.010). Additionally, overall patient survival was reduced in the prolonged group, with 85% survival versus 98% in the control group (p=0.022).

Conclusions

This study confirms our impression that prolonging preservation time of DCD livers using DHOPE is associated with an increased risk of complications. Currently, the use of prolonged DHOPE solely to facilitate daytime transplantation is not justified, given its association with a longer operation duration, a significantly higher incidence of IAB, lower post-transplant cholangiopathy free graft, and overall patient survival.

The Impact Of Extended Hypothermic Machine Perfusion Prior To Normothermic Machine Perfusion On Viability Assessment And Outcomes

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Background

Liver machine perfusion is increasingly used to test and select extended criteria donor (ECD)-livers to counter decreasing quality of available organs. Combining sequential oxygenated hypothermic and normothermic machine perfusion, linked by one hour of controlled oxygenated rewarming (DHOPE-COR-NMP) can be used to resuscitate donor livers and subsequently perform viability assessment. To optimize transplant logistics and enable daytime transplantation, prolongation of the DHOPE

phase has been proposed to extend preservation time. This study aimed to evaluate the impact of prolonged DHOPE on donor liver utilization and outcomes, compared with historical standard DHOPE−COR−NMP.

Methods

All donation after circulatory death (DCD)-ECD-livers treated with DHOPE-COR-NMP were included until September 2025. DCD livers were classified as ECD based on elevated laboratory values, age $\geq$61 years, or fWIT>30 mins. Prolonged DHOPE was defined as perfusion time $\geq$4 hours. The main outcome was acceptance rate after hepatobiliary viability assessment. Secondary outcomes included death-censored graft survival, overall patient survival, as well as post-transplant complications, such as post-transplant cholangiopathy.

Results

In total, 74 DHOPE-COR-NMP procedures were included, of which 16 had a prolonged DHOPE, and 58 were in the standard group. There were no relevant statistically significant differences in donor and recipient characteristics of both groups. In the prolonged group, 8 of the livers passed acceptance criteria (50%), whereas this was 44 in the standard group (76%) (p=0.064). Death-censored graft survival was 75% at one year in the prolonged group vs. 88% in the control group (p=0.184). Patient survival at one year was 100% for the prolonged group, whereas this was 85% in the control group (p=0.442). No differences in post-transplant complications were observed, except for 2 cases of hepatic artery thrombosis in the prolonged group, which did not occur in the control group. During transplantation, more red blood cell transfusions were required in the prolonged group (p=0.015).

Conclusions

This study illustrates that prolonged DHOPE prior to viability assessment through COR-NMP allows for safe transplantation for ECD-DCD livers, with similar results to our historical standard cohort. However, prolonging DHOPE was associated with a lower acceptance rate, which is clinically relevant and needs to be closely monitored to optimize organ utilization.

The Role Of Liver Transplantation In Multicentre Real-World Treatment Practices For Hepatocellular Carcinoma In The Netherlands

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Background

Real-world data on treatment patterns of newly diagnosed hepatocellular carcinoma (HCC) in the Netherlands are scarce. This study aimed to analyze real-world treatment practice and assess the role of liver transplantation (LT) within current treatment strategies.

Methods

Prospective, multicenter cohort study. Treatment-naïve patients ($\geq$18 years) with HCC were enrolled from 2019 to 2024, across six Dutch tertiary referral centers. Staging was in accordance with the Barcelona Clinic Liver Cancer (BCLC) classification system. Data were collected during routine visits every 3−4 months, and all treatments during the observation period were recorded.

Results

A total of 619 patients were included, BCLC stage distribution at diagnosis was: 11% (n = 70) BCLC-0, 53% (n = 325) BCLC-A, 14% (n = 85) BCLC-B, 18% (n = 114) BCLC-C, 2.9% (n = 18) BCLC-D, and 1.1% (n = 7) missed data for classification. Median follow-up was 365 days (IQR 235-365 days). 514 (83%) patients received a total of 814 oncological treatments, 28% received more than one treatment. Thirty-six patients (6%) underwent liver transplantation. Their BCLC stage at initial diagnosis was BCLC-0 17% (n = 6), BCLC-A 75% (n = 27), BCLC-C 6% (n = 2), and BCLC-D 3% (n = 1). 72% (n = 26) of patients fulfilled Milan criteria, 6% (n = 2) were beyond them, and data were missing for 22% (n = 8). Their median age was 65 years (IQR 6.5); 83% had cirrhosis, with alcoholic liver disease as the main etiology. LT was performed as first-line therapy in 10 patients (28%). In all other cases (n = 26, 72%) neoadjuvant locoregional therapy was performed prior to transplantation. Treatments included thermal ablation (n = 16, 61%), transarterial chemoembolization (n = 5, 19%), transarterial radioembolization (n = 3, 12%), and stereotactic body radiotherapy (n = 2, 8%).

Conclusions

In this 5-year multicenter real-world cohort, only 6% of newly diagnosed HCC patients underwent LT within 12 months after diagnosis. Given that 64% patients presented with very early or early stage disease in tertiary referral centers, these findings highlight the importance of early consideration and awareness of liver transplantation in potentially eligible patients.

Redefining Futility In The Machine Perfusion Era: Insights Based On The UK-DCD Risk Score In 362 DCD Liver Transplantations

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Background

The scarcity of suitable donor grafts and the increased risks associated with donation after circulatory death liver transplantation (DCD-LT) highlights the importance of donor–recipient matching to optimize outcomes and graft utility. The UK-DCD risk score categorizes DCD-LTs as low-risk, high-risk, or futile based on donor and recipient characteristics. In the era of machine perfusion, DCD grafts undergo additional hypothermic or normothermic machine perfusion to resuscitate and evaluate the graft before transplantation. This study compares graft survival in DCD-LT after static cold storage (SCS), hypothermic machine perfusion (HMP), and normothermic machine perfusion (NMP), stratified by UK-DCD risk categories.

Methods

In this single-center, retrospective cohort study, 362 DCD-LTs (November 2002-July 2024) were grouped by preservation method: SCS (n=176), HMP (n=105), and NMP (n=81). Baseline donor and recipient characteristics were collected for the UK-DCD risk score. The primary outcome was 2-year graft survival, censored for patient death with a functional graft. Graft loss due to primary non-function (PNF) and post-transplant cholangiopathy (PTC) were also compared.

Results

Low-risk DCD-LTs were highest after SCS (64%), followed by HMP (43%) and NMP (30%). In contrast, futile DCD-LTs occurred in 5% of the SCS group, 8% of the HMP group, and 27% of the NMP group. Graft loss due to PNF occurred in 4 cases (2%) in SCS, 2 cases (2%) in HMP, and none in NMP (p=0.404). Graft loss due to PTC was observed in 14 cases (8%) in SCS, none in HMP, and 2 cases (2%) in NMP (p=0.005). Two-year graft survival was significantly higher in HMP and NMP compared to SCS, with survival rates of 93% and 90%, respectively, versus 81% (p=0.015). This improvement was most pronounced in the high-risk group, where survival rates were 83% in SCS, compared to 100% and 97% in HMP and NMP, respectively (p=0.002).

Conclusions

Despite more high-risk and futile transplantations, hypothermic and normothermic machine perfusion significantly reduced graft loss due to PTC, improving 2-year graft survival rate in DCD-LT up to 93%. This solidifies the role of machine perfusion in DCD-LT and highlights the need for a new risk model to better predict graft utility and long-term outcomes.

Thiopental Is Metabolized In DCD-V Livers That Are Perfused At Normothermic Temperature

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Background

Euthanasia is typically performed with the coma-inducing drug thiopental, and a muscle relaxant drug rocuronium. Thiopental is a lipophilic drug which is metabolized in the liver to (among others) pentobarbital and is eliminated via the kidneys. Due to its lipophilic properties it is thought that thiopental and its metabolites accumulate in liver cells, particularly in steatotic livers, thereby potentially causing hepatotoxicity which can reduce organ quality for liver transplantation. As the effects of thiopental on outcome after donation after circulatory death (DCD-V) transplantation are unknown, in this study we determined thiopental concentrations in the perfusate of machine perfused DCD-V livers and correlated these with donor parameters and organ viability criteria.

Methods

DCD-V donor livers were included between 2021 and 2025. All livers underwent dual hypothermic oxygenated perfusion followed by subsequent controlled oxygenated rewarming and normothermic machine perfusion (DHOPE-COR-NMP) to allow viability assessment according to standard clinical protocol. We determined thiopental and pentobarbital concentrations in the perfusate during the DHOPE phase at 5 and 60 min, as well as during the COR-NMP phase at 60 and 180 minutes of perfusion. Thiopental and pentobarbital concentrations we determined by using LC-MS according to standard clinical procedure.

Results

A total of 16 livers were included in the study, of which 11 (69%) met the viability criteria for transplantation after 2.5 hours of NMP. During DHOPE, median thiopental concentration increased from 1.7 mg/L to 4.15 mg/L ($p<0.05$) while pentobarbital concentration remained below the lower limit of detection (LLOD). During the first 3 hours of COR-NMP, median thiopental concentration of accepted livers decreased from 6.16 mg/L to 1.47 mg/L ($p<0.05$) while in declined livers median thiopental concentration did not decrease significantly (5.93 vs 5.01 mg/L, $p>0.10$). In accepted livers the metabolite Pentobarbital appeared in 4/11 of cases (36%) during NMP, increasing to a median concentration of 0.64 mg/L.

Conclusions

These results indicate that thiopental is actively metabolized during NMP of DCD-V donor livers. Higher initial concentration of thiopental during NMP and lower clearance rate during the first 3 hours of NMP was associated with decreased likelihood of acceptance for subsequent transplantation.

Immortalized Microvascular Renal Endothelial Cells As Target Cells For Antibody Mediated Rejection Risk Assessment In Kidney Transplant Recipients

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Background

Antibody-mediated rejection (ABMR) in kidney transplantation, driven by donor-specific antibodies (DSA), involves complement-dependent (CDC) and antibody-dependent cellular cytotoxicity (ADCC). Current models lack kidney-specific endothelial cell (EC) targets and donor diversity. This study developed immortalized microvascular renal ECs (iMPRECs) from donor perfusion fluid for use in EC flow cytometry-based crossmatch (ECFXM) and *in vitro* NK cell-mediated ADCC assays.

Methods

ECs were isolated via CD31 magnetic beads and immortalized using a lentiviral vector containing the SV40T antigen and mCherry reporter gene. Endothelial identity was confirmed through flow cytometry (expression of CD31, CD34, VEGFR-2, ET-1, and vWF) and single-cell RNA sequencing. Functionality was tested via a tube formation assay. The iMPRECs were evaluated in ECFXM and NK cell−mediated ADCC assays using sera containing anti-HLA antibodies and complement for the ECFXM, and CD16^{+} oNK-1 cells for the ADCC.

Results

Seven iMPREC lines were generated and confirmed to have retained their endothelial markers and function. In the pilot tests, ECFXM demonstrated significant IgM, IgG, and C3b binding post−anti-HLA exposure (P<0.05), while the ADCC assays showed elevated cytotoxicity against HLA class I−sensitized iMPRECs compared to controls (P=0.01). The ECFXM assay was also used in cases of atypical ABMR (i.e., ABMR in KTRs with negative single antigen tests and pretransplant lymphocyte crossmatching) in detecting complement deposition, suggesting a potential use as a screening tool for non-HLA DSA.

Conclusions

We showed that iMPRECs provide organ-specific targets for assessing DSA-mediated cytotoxicity. ECFXM and ADCC assays capture complement- and NK cell−driven damage, revealing different cytotoxic potential among anti-HLA sera. This model addresses limitations of current assay systems to potentially improve understanding and predicting allograft rejection. Future directions include expanding the iMPRECs bank and exploring HLA gene silencing to model non-HLA-mediated rejection.

Quantitative Spatial Lipidomics Identifies Phospholipid Signature Of Acute Injury In Human Donor Kidneys

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Background

Ex vivo kidney perfusion has emerged as a promising technique for organ quality assessment prior to transplantation, with the ultimate goal to reduce donor organ discard rates. However, reliable, tissue-based parameters that reflect the degree of injury in this context are lacking.

Methods

We used matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI) combined with multiplex immunofluorescence (IF) to spatially characterize the lipidome, reflecting cellular identity and disease state, in human deceased donor kidneys with and without clinically diagnosed acute kidney injury (AKI). Next, we compared these findings to the spatial lipid fingerprints emerging during human kidney normothermic machine perfusion (NMP), and explored to which extent these dynamic, injury-associated tissue lipid signatures are reflected in the perfusate during warm perfusion.

Results

High-resolution spatial MALDI-MSI in both negative and positive ion mode combined with IF on consecutive tissue slides allowed for lipidome-based identification of detailed proximal and distal tubular, and stromal cell clusters. With the use of lipid class internal standards, we were able to perform relative quantification of lipid features within the proximal tubule clusters, which revealed specific epithelial injury signatures that distinguished between healthy and injured cells in both control and AKI samples. These signatures were characterized by a decrease of predominantly phosphatidylethanolamine (PE) and phosphatidylinositol lipid features. Similar epithelial injury signatures were observed within longitudinal NMP tissue biopsies, suggesting organ quality deterioration over the course of prolonged (24h) kidney NMP. Lastly, we demonstrate that these epithelial PE fingerprints can be traced back in the perfusate during both subnormothermic and normothermic machine perfusion.

Conclusions

Our work reveals an injury-associated phospholipid fingerprint in human deceased donor kidneys and highlights the potential use of such dynamic lipid remodelling processes for tubular integrity assessment based on liquid perfusate biopsies during machine perfusion.

Studying Liver Transplantation-Associated Acute Kidney Injury In A Human Organoid-Based Model

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Background

Acute Kidney Injury (AKI) is a common complication following liver transplantation (LTx), affecting up to 50% of patients. It is strongly associated with the development of chronic kidney disease, higher risk of graft failure and increased mortality rates. Recent evidence highlights the key role of hepatic ischemia reperfusion injury (IRI) in post-

LTx AKI development. However, the exact mechanisms involved remain unknown and relevant human models do not exist. The aim of the present study is to develop a human *in vitro* model to further study post-LTx AKI.

Methods

Induced pluripotent stem cell-derived kidney organoids and adult liver-derived hepatocyte-differentiated organoids were generated and co-cultured to simulate kidney-liver crosstalk. To mimic key aspects of hepatic IRI, hepatocyte-differentiated organoids were subjected to either hypoxic conditions for 48h or IL1b exposure for 24h prior to co-culture with kidney organoids. Phenotypic changes were assessed based on bulk RNA sequencing, immunohistochemical analyses and LDH cytotoxicity assay. To assess AKI-like phenotype induction in kidney organoids, gene expression and immunohistochemical analysis of nephron and AKI-related markers were performed following 24h, 48h, and 7 days of co-culture. Cisplatin treatment of kidney organoids was performed as a positive control for AKI phenotype induction.

Results

Hypoxic and IL1b exposure conditions induced cell death-indicative morphological changes in hepatocyte-differentiated organoids and increased LDH release. Transcriptomic analysis revealed enrichment of hypoxia- and inflammation-induced genes in hepatocyte-differentiated organoids under hypoxic and IL1b exposure conditions respectively, indicating a stimulus-specific response. Kidney organoid phenotype did not show major changes after co-culture with hepatocyte-differentiated organoids subjected to hypoxia. In contrast, co-culture with IL1b-exposed hepatocyte-differentiated organoids led to upregulation of pro-inflammatory markers (*TNF-a*, *IL-6*, *CCL2*) and induction of AKI biomarkers NGAL and KIM-1 in kidney organoids. Notably, this effect was observed after 24-48h of co-culture and was resolved by day 7, indicating an acute response of kidney organoids reflecting clinical AKI. This response was also similar to the one induced following cisplatin treatment of kidney organoids.

Conclusions

Our study demonstrates that the present model holds great potential for modelling post LTx-AKI *in vitro*. Further research steps will focus on mechanistic studies including identification of soluble factors driving post-LTx AKI and intervention methods.

Molecular Responses Of Human Donor Kidneys During Normothermic Machine Perfusion Are Independent Of Conventional Donor Characteristics

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Background

Conventional donor characteristics poorly predict kidney transplant outcomes, emphasizing the need for other approaches to evaluate graft quality. Normothermic machine perfusion (NMP) offers a platform to study kidney biology ex vivo before transplantation, but it remains unclear to what extent molecular changes during perfusion reflect donor characteristics. This study examined whether donor characteristics explain transcriptomic and proteomic variability during human kidney NMP.

Methods

Twenty-four discarded human donor kidneys available for research in the United States, in accordance with the national Uniform Anatomical Gift Act, were included.

Cortical tissue was analyzed by bulk RNA sequencing and LC–MS/MS at five time points: after cold preservation (preNMP) and after 1, 2, 3, and 6 hours of NMP. Temporal changes in gene expression were assessed by comparing each time point to preNMP values. Associations between donor variables (e.g., age, sex, BMI, serum creatinine, cold and warm ischemia times, DCD/DBD) and molecular profiles were tested using linear modelling with empirical Bayes moderation (using limma in R). Continuous variables were dichotomized at the median, and analyses were repeated after subtraction of preNMP values to isolate NMP-induced changes.

Results

Unsupervised clustering (UMAP) revealed that gene expression profiles clustered by time point, indicating that the temporal effect of NMP outweighed interindividual variability, whereas protein profiles grouped by individual, reflecting heterogeneity in protein abundance between kidneys. Comparing preNMP to NMP time points showed a pronounced molecular shift, with 73% of transcripts and 10% of proteins differentially expressed at 6 hours of NMP (FDR<0.05). Despite this extensive response, there were no associations between molecular profiles and donor characteristics across time points; most comparisons yielded no differentially expressed genes or proteins. Only kidneys from donors with elevated peak serum creatinine or urea, indicating acute kidney injury, showed altered transcripts and proteins, which disappeared after adjustment for preNMP values. This suggests they reflect pre-existing molecular differences rather than NMP-induced effects.

Conclusions

Donor characteristics do not explain the extensive molecular changes occurring during ex vivo kidney NMP. The molecular response to perfusion appears driven by other intrinsic factors, highlighting the potential of NMP-specific molecular profiles as a new source of biomarkers for kidney transplant outcomes.

Four-Day Subnormothermic Perfusion At 25°C Allows For AAV Vector-Based Genetic Modification Of Human Donor Kidneys Ex Vivo

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Background

The ability to preserve kidneys on subnormothermia for multiple days has created a potential window for genetic modification of donor organs prior to transplantation. In this context, the use of adeno-associated viral (AAV) vectors includes a promising strategy for delivery of target genes. Ultimately, therapeutic AAV vectors can be used *ex vivo* to modulate ischemic reperfusion injury and reduce immunogenicity in a pre-transplantation setting while overcoming current limitations of AAV dosage restrictions and toxicity *in vivo.* In this study, we aimed to explore the feasibility of AAV vector-based gene delivery within our four-day cell-free human kidney subnormothermic machine perfusion (sNMP) platform.

Methods

We conducted two different kidney sNMP (25°C) experiments, during which we intra-arterially injected an AAV vector mix after three hours of perfusion. In the first experiment, we injected 25 different AAV capsids that contained individually barcoded constructs encoding green fluorescent protein (GFP) into the renal artery within the first hours of perfusion. Perfusate and tissue samples were harvested throughout four-day sNMP and processed for gDNA, cDNA and protein analysis. In a second experiment, we selected two kidney-trophic AAV capsids from the first experiment, containing either GFP or mCherry encoding constructs, and repeated the aforementioned perfusion and readout workflow.

Results

The intra-arterial delivery of AAV capsids in the first experiment led to cellular uptake of AAV vector genomes, mRNA transcription and protein translation within our four-day sNMP window. Importantly, GFP protein expression could be visualized in human tissue biopsies obtained at the end of perfusion (T92), thereby proving feasibility of AAV vector-based delivery at 25°C. Quantification of AAV capsid-specific mRNA barcode transcripts led to detailed tropism profiles of various cells of interest (i.e. proximal tubule cells, endothelial cells). Regarding the second experiment, selective delivery of two kidney-trophic AAV capsids led to strong fluorescent protein expression within tissue biopsies, showing potential for widespread transduction of target cells within the sNMP platform.

Conclusions

Overall, these experiments provide an important proof of concept for AAV vector-based genetic modification of donor kidneys *ex vivo* at 25°C, while offering detailed insights into AAV capsid tropism in the human kidney.

Radiomics Analysis Of Kidney Grafts During Ex Vivo Normothermic Perfusion: A Novel MRI-Based Approach To Pre-Transplant Viability Assessment

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Background

The growing shortage of donor kidneys necessitates the use of marginal grafts, emphasizing the need for objective viability assessment methods. Normothermic machine perfusion (NMP) could enable real-time kidney evaluation under near-physiological conditions before transplantation. While biochemical markers have been explored, imaging-based assessment offers non-invasive monitoring capabilities. This study investigated whether radiomics features extracted from multi-sequence MRI can distinguish between different ischemic and perfusion states, potentially providing a novel tool for graft viability assessment.

Methods

Thirty pigs underwent bilateral nephrectomy with paired randomization, where one kidney received 75 minutes of warm ischemia (WI) while the contralateral kidney served as control (no WI). Kidneys were subsequently subjected to NMP. Multi-sequence MRI data were acquired at multiple time points: in vivo (baseline), pre-NMP, and at 1, 2, 3, and 6 hours during NMP. The renal cortex was delineated as the region of interest for radiomics feature extraction. Comprehensive features including texture, shape, and intensity-based parameters were extracted from different MRI sequences. Statistical analysis evaluated the discriminative capacity between in vivo versus ex vivo states, and between WI versus no WI conditions.

Results

Depending on sequence type, a total of 107 - 1316 radiomics features could be extracted from MRI scans. Radiomics analysis revealed distinct feature patterns across different MRI sequences and time points. Several sequences demonstrated significant discriminative capacity between in vivo and ex vivo conditions, reflecting physiological changes during transition from in situ to machine perfusion. Specific radiomics features successfully differentiated between WI and no WI kidneys, while conventional image analysis could not always pick up such differences. The multi-parametric nature of radiomics features provided information similar to biological multi-omics approaches, where different feature categories captured distinct aspects of tissue characteristics and perfusion dynamics. Temporal analysis showed progressive changes in radiomics signatures throughout NMP.

Conclusions

MRI-based radiomics could distinguish between different ischemic and perfusion conditions in kidney grafts during NMP. The ability of radiomics analysis to differentiate in vivo from ex vivo states and WI from no WI suggests potential clinical utility for rapid non-invasive pre-transplant graft viability assessment, as an adjunct to biochemical markers and clinical parameters.

The Profile Of Senescence Marker Expression On CD8+ T Cells Is Associated With Clinical Parameters Of Frailty In Elderly Recipients Of A Kidney Transplant

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Background

Elderly kidney transplant recipients often exhibit increased frailty, which is associated with higher morbidity and mortality. Their T cell compartment typically shows premature aging, characterized by a shift from naïve to differentiated memory cells expressing markers of senescence and exhaustion. It remains unclear whether clinical frailty scores correlate with immunosenescence or represent distinct risk factors for adverse outcomes such as mortality.

Methods

In the multicenter OPTIMIZE study (EudraCT 2018-003194-10), blood samples were collected before and at 12 and 24 months after kidney transplantation. Recipients aged $\geq$65 years were randomized to either MMF-based

or EVR-based immunosuppression (MMF-IS or EVR-IS). Circulating CD4^{+} and CD8^{+} T cells (N=169; 86 EVR-IS, 83 MMF-IS) were analyzed by multiparameter flow cytometry for expression of senescence and exhaustion markers. Data were assessed using unbiased FlowSOM clustering (Omiq platform) and correlated with frailty scores (Clinical Frailty Scale (CFS) and Fried Frailty Index (FFI)) and mortality.

Results
FlowSOM identified 18 distinct T cell clusters differing in senescence/exhaustion marker expression. Before transplantation, these markers did not correlate with frailty scores. At month 12, 19.8% and 38.5% of older recipients were classified as frail by CFS (>3) and FFI (>1), respectively. Only one T cell cluster was significantly increased in the most frail (5%) of recipients, showing a two-fold rise (on average 22% of viable T cells, P=0.03) compared to non-frail recipients (on average 11% of viable T cells). The cluster identified CD8^{+} T cells characterized by high expression of TIM3 and LAG3, dim expression of CD160, CD244, PD1, and CTLA4, and absence of TIGIT. The proportion of this subset correlated with CFS (r=0.357, P<0.001) and FFI (r=0.275, P=0.008). No differences were observed between the two treatment arms. An exploratory analysis revealed this cluster to be elevated approximately two-fold in recipients who died (4.3% of the kidney transplant recipients), representing 24% of viable T cells (P<0.05) compared with 11% in surviving elderly kidney transplant recipients.

Conclusions
Clinical frailty scores in elderly kidney transplant recipients are associated with expansion of a CD8^{+} T cell subset expressing multiple senescence and exhaustion markers, suggesting that clinical frailty and immune senescence are intertwined.

Development Of An In Vitro Kidney Allograft Model Using Kidney Organoids To Study Renal Graft Fibrosis

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Background
Renal graft fibrosis is common among transplant recipients with graft function exceeding 10 years and commonly measured together with tubular atrophy. However, the underlying mechanisms remain incompletely understood. The pathogenesis of renal graft fibrosis involves a cascade of events, in which macrophages play an important role, such as promoting inflammation and secreting pro-fibrotic cytokines. Reliable in vitro models are essential to elucidate these mechanisms and test potential therapeutic strategies. Here, we present a novel in vitro kidney allograft model utilizing human-induced pluripotent stem cell (iPSC)-derived kidney organoids and macrophages to study kidney allograft fibrosis.

Methods
Four iPSC clones were used to generate macrophages and kidney organoids. These kidney organoids, co-cultured with and without allogeneic macrophages, were subjected to various injuries mimicking transplantation-related conditions, including inflammation (IL-1β), ischemia-reperfusion injury (hypoxia), and calcineurin-induced cytotoxicity (tacrolimus). Gene and protein expression levels in these experimental groups were assessed using quantitative PCR, single cell RNA sequencing and immunohistochemistry.

Results
Gene- and protein expression analyses demonstrated significantly elevated levels of fibrosis markers, including fibronectin and collagen 1, in kidney organoids subjected to hypoxia, IL-1β, and tacrolimus. While all transplant-related injuries individually resulted in fibrosis, their combination led to significantly more pronounced fibrosis. The incorporation of macrophages further amplified the fibrotic responses and the expression of pro-inflammatory cytokine markers upon injury, compared to organoids without macrophages.

Conclusions
We are here providing a new model to study allograft fibrosis in organoids with the presence of macrophages. This platform can help to dissect mechanisms of allograft fibrosis and test novel interventional strategies. Our findings pave the way for future research into therapeutic interventions to mitigate fibrosis and improve kidney allograft outcomes.

40 Years Of Paediatric Heart Transplantation In The Netherlands: Medical And Psychosocial Outcomes, As Well As Challenges Ahead

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Background

In 1986, the first paediatric heart transplantation (HTx) in the Netherlands was performed at our institution, where the national programme for paediatric HTx started in 1998. Here, we present the survival, follow-up data, and medical complications of the 97 paediatric HTx recipients. Moreover, psychosocial wellbeing of the paediatric HTx recipients was evaluated for the first time.

Methods

Data from all paediatric HTx recipients transplanted between 1986 and November 2025 were collected from the electronic patient database, including baseline characteristics, survival, and post-operative complications. Psychosocial wellbeing is evaluated prospectively since 2023, using established PROMIS questionnaires.

Results

In total, 97 paediatric patients underwent HTx. Median recipient age was 12 years [IQR 10-15]; 53 (55%) were female. The most frequent indications were dilating (59%), restrictive (11%), and chemotherapy-induced (8%) cardiomyopathies. Since 2013, an increasing number of recipients with congenital heart diseases (6%) were transplanted. Twenty-one patients (22%) required mechanical circulatory support before HTx. Induction therapy with anti-thymocyte globulin was administered to 96% of recipients. Four (4%) recipients, transplanted between 1986 and 1987, did not receive induction therapy. The most common maintenance immunosuppression regimens were tacrolimus/mycophenolate mofetil (MMF) (31%), tacrolimus/prednisone/MMF (21%), and tacrolimus/prednisone (20%). One-, five-, ten-, and twenty-year survival post-HTx was 96%, 93%, 89%, and 55%, respectively. The main transplant-related complications during follow-up included rejection (46%), Epstein-Barr and cytomegalovirus infections, lymphoproliferative disease, and cardiac allograft vasculopathy. The median quality-of-life score (1-10) during follow-up was 7 [IQR 6-8], compared to a mean quality-of-life score (1-100) of 75.72 ± 15.22 in paediatric patients with chronic health conditions (CHC) such as juvenile arthritis or IBD. The median self-rated health score (1-10) was 7 [IQR 6-8], compared to a mean self-rated health score (1-100) of 73.62 ± 22.89 in paediatric patients with CHC.

Conclusions

Children undergoing HTx in the Netherlands since 1986 show excellent survival, with survival rates exceeding those reported globally. Quality of life and self-rated health during follow-up were favourable and comparable to those of CHC patients, underscoring the value of the paediatric heart transplantation programme. Challenges ahead include the increase in congenital heart disease patients undergoing HTx, which coincides with specific challenges in surgical and post-operative management.

Maximizing Organ Utilization And Patient Safety Of Combined Thoracic-Liver Transplantations With Ex Situ Machine Perfusion: A Single-Center Case Series

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Background
Combined Heart-Liver Transplantations (CHLT) and Combined Lung-Liver Transplantations (CLLT) are rarely performed. In the Netherlands, only 13 combined thoracic-liver transplantations have been performed between 1999-2025. These combined procedures necessitate specific donor characteristics, logistical challenges, team effect, and optimal preparation. We questioned whether *ex situ* machine perfusion (ESMP) may aid in these challenges by safely extending preservation time, allow patient stabilization, multidisciplinary consultations, and potentially expanding the available donor pool.

Methods
In this single-center observational cohort study, all CHLT and CLLT were included. Organs were either preserved using Static Cold Storage (SCS), or machine preservation. Machine preserved livers were perfused using Dual Hypothermic Oxygenated Perfusion (DHOPE), hearts were perfused with Ex Situ Normothermic Heart Perfusion (ESHP), and lungs were perfused with Ex Vivo Lung Perfusion (EVLP).

Results
A total of 13 combined thoracic-liver transplantations were included, of which in six transplants (all CLLT) both organs were preserved using SCS, and in seven cases (four CHLT and three CLLT) at least one organ underwent *ex situ* machine perfusion. Median *ex situ* liver preservation times in the SCS group were 11h46, whilst ESMP livers had a cold ischemia time of 4h52 (n=7), ESMP time of 4h43 (n=4), and ESMP time of 12h17 (n=3) for patients that went to the ICU between transplantations to stabilize (n=2) or to re-allocate the liver because the patient was no longer transplantable (n=1). In one case, EVLP was used to increase lung preservation times from a maximum of 12h with only SCS to a maximum of 16 hours with a combination of SCS and ESMP to bridge the liver transplantation and allow a liver-first CLLT. Due to the introduction of ESHP and the subsequent increase in DCD heart donors in the Netherlands, two patients received a CHLT faster. One-year graft and patient survival were similar with 66.7% and 85.7% for the SCS and ESMP groups respectively.

Conclusions
This case series shows that ESMP can both maximize organ utilization by being able to accept a wider range of organs, especially DCD organs, and increase patient safety by providing a time window for multidisciplinary consultation and stabilizing patients on the ICU.

Pancreas Transplantation After Euthanasia: Comparative Analysis Of DCD-V, DCD-III And DBD Donors

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Background

Pancreas transplantation remains a rare but important treatment option for patients with complicated diabetes. Given the shortage of viable donor organs, Donation after Circulatory Death (DCD) donors have shown to be a viable source. This study provides the first comparative analysis of pancreas transplantation between DCD Type III (controlled cardiac arrest), DCD Type V (euthanasia) and Donation after Brain Death (DBD).

Methods

We conducted a retrospective cohort study using data from the Dutch Transplant Registry, including all pancreas transplantations from DCD-V, DCD-III and DBD donors between 2002 and 2024. Evaluated outcomes included organ allocation and utilization, transplant type, graft and patient survival, surgical complications, and metabolic function.

Results

Over a 22-year period in the Netherlands, 4,755 pancreases were offered, of which 517 were transplanted (DCD-III: 98; DCD-V: 19; DBD: 398). Donor age and BMI differed between groups (p<0.01). The utilization rate was higher for DBD (20.7%), and DCD-V donors (18.4%) compared with DCD-III donors (4.0%) (p<0.01). No significant differences were observed in 5-year graft or patient survival (p=0.11 and p=0.52, respectively). The first warm ischemia time was comparable between the DCD-III and DCD-V cohorts (p=0.09), whereas the second warm ischemia time differed (p<0.01). In simultaneous pancreas−kidney (SPK) transplants, dialysis post transplantation occurred more often in de DCD-III cohort, but no differences in creatinine levels, rejection rates, chronic transplant glomerulopathy, or chronic damage were observed. Interestingly, thrombosis occurred most frequently among DBD donors (p<0.01). HbA1c levels at 3-, 12-, and 36-months post-transplantation did not differ significantly between groups.

Conclusions

Pancreas transplants from DCD-V donors demonstrate comparable utilization and outcome to those from DCD-III and DBD donors. Further studies with larger cohorts are needed to confirm these findings.

Allogeneic Islet Transplantation In The Netherlands: 15-Year Outcomes In Patients With Severe Beta Cell Deficiency

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Background

Allogeneic islet transplantation (ITx) is performed in patients with severe beta-cell deficiency with or without a previous organ transplantation. ITx aims to stabilise glycaemic control by restoring endogenous insulin secretion. Here we report the long-term outcomes of this single-centre cohort.

Methods

This retrospective cohort study included islet-after-kidney (IAK), islet-transplantation-alone (ITA), and islet-after-lung (IAL) recipients who underwent 1−3 intraportal islet infusions at Leiden University Medical Center between October 2007 and September 2025. Outcomes included patient and graft survival (stimulated C-peptide >0.1 nmol/L), graft function (peak C-peptide during mixed-meal testing), insulin independence, glycaemic control, severe hypoglycaemic events (SHEs), rejection and procedure-related complications. Assessments were performed pre-transplant, at 3 months, and annually thereafter.

Results

We included 108 allogeneic ITx performed in 71 recipients (38% female; BMI 24.0±3.2 kg/m²; age 53.0±9.2 years; HbA1c 63.7±17.4 mmol/mol Hb; diabetes duration 36.6±11.1 years). Overall, 59 (83.1%) patients received IAK or IAL, and 12 (16.9%) received ITA. 34 (50.7%), 29 (43.3%), and 4 (6%) recipients received 1, 2 and 3 islet infusions,

respectively. Median patient survival time was 12.2 years, and graft survival was 75.6% after a median follow-up of 7.5 years. ITx resulted in a significant increase in mean peak C-peptide compared to baseline, sustained for 8 years post-ITx ($p<0.02$). HbA1c and the number of SHE were significantly lower compared to baseline (HbA1c up to 2 years post-ITx ($p<0.01$) and SHE throughout follow-up ($p<0.05$)). Insulin independence was achieved in 24 patients (32.1%) at a median of 6.2 months post-ITx. Insulin independence lasted for a median duration of 6.7 months. Graft failure occurred in 18.7% and rejection occurred in 23.9 % of recipients (total of 20 rejection episodes, median onset 7.1 months). Bleeding from the liver occurred in 9.8% of infusions (no CTCAE grade 4 and 5 bleeding), and no cases of portal vein thrombosis were observed.

Conclusions

ITx is a minimally invasive procedure that effectively prevents SHEs and improves long-term glycaemic control. While insulin independence can be achieved, the duration is often limited.

The Dutch Experience With Organ Donation After Euthanasia: Comparing DCD-V And DCD-III Lung Transplantation Outcomes

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Background

The procedure that combines medical assistance in dying (MAiD) with donation after circulatory determination of death (DCD) is referred to as organ donation after euthanasia (ODE) or DCD-V. Currently, DCD-V is allowed and performed in six countries, with the first documented case in the Netherlands in 2012. DCD-V has emerged as a significant and expanding source of donor lungs in the Netherlands, comprising up to 40% of all DCD lung donations in 2024. Although early small-cohort data suggested comparable short-term outcomes between DCD-V and DCD-III, larger series and long-term outcome data lack. We report our experience with lung transplantation (LTx) after ODE and compare outcomes to DCD-III donors.

Methods

All LTx recipients (LTR) receiving DCD-III or DCD-V grafts between 2012 and 2024 were retrospectively analyzed. Outcomes included rates of ICU and hospital discharge, as well as length of stay (LOS) and these were compared between DCD-III and DCD-V using Fishers exact and Mann-Whitney U-tests. Survival was compared using Kaplan-Meier analysis.

Results

In total, 471 LTR were included. 389 (83%) received DCD-III and 82 (17%) DCD-V grafts. 42% were female and median age was 59[IQR 52−63] years. Wait time (DCD-III: 241[67-672] days; DCD-V: 82[42 − 451] days) and LAS (DCD-III 34.5[32.1 − 39.0]; DCD-V: 35.8[33.4 − 40.3]) differed significantly between groups ($p = 0.01$ and $p = 0.02$ respectively). In the DCD-III group, 91% survived until ICU discharge (LOS 5[3-16.5] days), compared to 93% in the DCD-V group (LOS 6[4-11]; $p = 0.74$). For hospital discharge, 90% survived in the DCD-III group (LOS 31 [23−49] days), compared to 94% in the DCD-V group (LOS 32 [22−45] days; $p = 0.70$). Recipients from DCD-III lungs had a 5-year survival of 69%(95%-CI 64 − 75%). Recipients from DCD-V lungs had a 5-year survival of 75% (95%-CI 75 − 87%). There was no statistically

significant difference in survival between both groups. There was no significant difference in long-term survival between both groups (*p* = 0.66).

Conclusions
LTx from DCD-V procedures demonstrates comparable short- and long-term outcomes to DCD-III procedures. These findings support DCD-V as a safe, viable donor source that helps expand the lung donor pool.

Chronic Kidney Disease After Lung Transplantation: Impact Of Tacrolimus Exposure And Clinical Complications Post-Transplantation

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Background
Lung transplant recipients (LTR) frequently develop chronic kidney disease (CKD). Risk factors for CKD after lung transplantation have been identified (e.g. Acute kidney injury, hypertension and diabetes), but these are often non-modifiable. A high tacrolimus metabolizing phenotype defined by a low pre-dose concentration-to-dose ratio ([C0/D]), has been shown to negatively impact kidney function after heart, liver, and kidney transplantation. Our aim was to investigate the determinants of CKD in the lung transplant population and the [C0/D] ratio in particular.

Methods
This was a retrospective study which included all LTR transplanted between 2001 and 2023 at Erasmus MC Rotterdam. Patients who received immediate-release tacrolimus and were alive at 3 months were followed up to 60 months. Variables on kidney function, known risk factors post-transplant, tacrolimus C0 and dose were collected at 3, 6, 12, 36 and 60 months. LTRs were categorized as fast, slow or intermediate metabolizers according to their median [C0/D] ratio.

Results
A total of 302 LTRs were included in the analysis. Median age was 57.9 years and 157 were male (52%). The most common transplant indications were ILD (42.7%), COPD (35.8%). Median follow-up was 57.5 months. Sixty-eight LTR (22.5%) died during follow-up. AKI occurred in 130 LTR (43%), with 34 LTR (11.3%) requiring renal replacement therapy. Median baseline eGFR decreased from 95 ml/min/1,73m^2 to 44 ml/min/1.73m^2 during follow-up. 49/302 LTR (16%) progressed to CKD stage 5, of which 29 started dialysis (59%), while 13/49 were treated conservatively. 17/49 (34.6%) of the CKD patients received a kidney transplant. Median time to CKD stage 5 was 50 months. Metabolizers were categorized slow with a [C0/D] ratio <1.16 ng/ml/mg, intermediate between 1.16-1.83 ng/ml/mg and fast >1.83 ng/ml/mg. Fast and intermediate metabolizers had a significantly lower eGFR at 36 months (46.3 and 45ml/min/1.73m^2, respectively) compared to slow metabolizers (55.2 ml/min/1.73m^2) (p=0.003) and 60 months (44.8 and 43.5 ml/min/1.73m^2, respectively vs. 53.4 ml/min/1.73m^2, p=0.02).

Conclusions
CKD frequently complicates lung transplantation. This study demonstrates that LTRs with a higher tacrolimus metabolizing phenotype have a higher degree of CKD in the long-term. Faster metabolizers may benefit from dose reduction or switching tacrolimus formulation.

40 Years Of Heart Transplantation In The Netherlands

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Background
Over the past four decades, donor and recipient profiles and management after heart transplantation (HT) have changed markedly, driven by shifts in immunosuppressive therapy, donor legislation, the introduction of left ventricular assist devices (LVAD) and adoption of donation after circulatory death (DCD). We studied the impact of these changes on patient characteristics, post-HT malignancies and survival.

Methods
We prospectively collected data in December 2024 from all consecutive adult HT recipients from all Dutch transplant centers, categorized into two cohorts: A (1984-1999, n=615) and B (2000-2024, n=1022). Cohorts were defined by changes around 2000, including availability of donor hearts, early post-HT statin use and newer immunosuppressive drugs.

Results
The most common etiology of heart failure shifted from coronary artery disease in cohort A (55%) to cardiomyopathy in cohort B (64%), with more female recipients (19% vs. 34%, p<0.001); pre-transplant BMI increased (23[21-25] vs. 24[22-27] kg/m^2, p<0.001) and serum creatinine improved (75[62-93] vs. 68[53-85] μmol/L, p=<0.001). Bridge-to-transplant LVAD use and DCD transplantation were newly introduced (all p<0.001).

Donor age (30 [21-40] vs. 45 [34-52] years) and waiting list duration (148 [43-263] vs. 399 [143-839] days) increased in cohort B (both p<0.001) with more female donors (39% vs. 51%, p<0.001).

Donor cause of death shifted from mostly head trauma in cohort A (50%) to cerebral events in cohort B (64%), with the addition of euthanasia (4%).

With increased induction therapy (24% vs. 42%) and a shift from cyclosporine-based immunosuppression in cohort A (90% cyclosporine, 8% tacrolimus) to tacrolimus-based immunosuppression in cohort B (18% cyclosporine, 82% tacrolimus) at year one (all p<0.001), post-HT skin and solid organ malignancies decreased (18% vs. 9% and 16% vs. 7%, both p<0.001).

Compared with cohort A, one-year survival was lower in cohort B (87% vs. 82%, p=0.009), while five-year survival was similar (77% vs. 76%, p=0.703) and ten-year survival improved significantly (58% vs 67%, p=0.001).

Conclusions
Over the past four decades, HT recipients have faced longer waiting times with more co-morbidities, while receiving hearts from older donors. These changes might attribute to slightly lower short-term survival. Nonetheless, advancements in immunosuppressive therapy and clinical practice have improved long-term survival.

Lung Transplantation After Normothermic Abdominal Regional Perfusion (LUNAR) — The Dutch Experience

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Background

Abdominal normothermic regional perfusion (aNRP) is a technique used during organ donation after circulatory death (DCD) to restore blood flow to abdominal organs and allows for assessing their viability for transplantation. However, aNRP involves selective perfusion of the abdominal region, which may complicate or compromise the procurement and outcomes of lungs from the same donor. Given the anticipated increase in aNRP procedures, we analyzed aNRP parameters in relation to lung procurement and the Dutch LuTx outcomes after aNRP. This will help reach consensus on safety and the optimal strategy for lung procurement in the context of aNRP.

Methods

We conducted a retrospective multicenter cohort study from January 2018 to February 2025, including cases in which both aNRP and lung procurement were performed in the same donor in the Netherlands. Donor, procedural, and recipient characteristics were collected and analyzed to assess aNRP performance, lung utilization, and transplant outcomes.

Results

Of 78 aNRP procedures, 25 (32%) lungs were offered to Dutch centers; 19 (76%) lungs were accepted, of which 15 (82%) lungs were transplanted. Two accepted lungs were excluded for insufficient onsite quality; in two others, the role of aNRP remains uncertain. Of the 15 aNRP with lung procurement, 4 (27%) aNRPs could not be completed due to technical failure with thoracic blood loss.

The incidence of primary graft dysfunction grade 3 at 72 hours after LuTx was 3/14 (21%), compared to 8% in a historic DCD control cohort in the Netherlands. The median ICU and hospital stay were 3 and 27 days, respectively. The survival rate 1-year after transplantation was 79%, compared to 84% in the DCD LuTx population in the Netherlands. Acute cellular rejection occurred in 6/11 (55%) recipients and chronic allograft dysfunction in 1/11 (9%) within the first year after LuTx.

Conclusions

This study presents the preliminary results of LuTx outcomes after aNRP procedures, showing numerically higher PDG3 rates and lower 1-year survival rates compared to historical Dutch DCD cohorts. ANRP learning curve may play a role in these outcomes. Further analysis will compare other lung procurements from the same period to guide clinical practice.

Tacrolimus Exposure During Pregnancy In Kidney And Liver Transplantation Recipients: A Comparison Between Whole Blood And Plasma Concentration-To Dose Ratios

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Background

Tacrolimus monitoring is generally performed in whole blood (WB). Most (>85%) of circulating tacrolimus is bound to red blood cells. During pregnancy, WB monitoring might be suboptimal due to physiological changes including increased plasma volume and decreased hematocrit.

Therefore, plasma tacrolimus monitoring might better indicate potential dosage needs in pregnant women.

Methods

This prospective single-center cohort study aimed to assess and compare tacrolimus WB and plasma concentration-to-dose (C/D) ratios before, during, and after pregnancy in kidney or liver transplant recipients. Linear mixed model analysis was used.

Results

Nine women with ten pregnancies were included. Based on WB tacrolimus concentrations, the median prescribed dosage significantly increased from 3 pre-pregnancy to 7.5 mg/day (+150%) in the third trimester (p<0.001). The correlation between plasma and WB tacrolimus concentrations decreased throughout pregnancy with a correlation coefficient of 0.70 in the first trimester, 0.41 in the second and 0.30 in the third trimester of pregnancy. Median WB tacrolimus C/D ratios significantly decreased from 1.48 pre-pregnancy to 0.58 in the second and third trimester (-61%) (overall time effect p<0.001). The effect of time became non-significant after adjusting for hematocrit (p=0.40). Median plasma tacrolimus C/D ratios decreased from 0.03 pre-pregnancy to 0.02 in the first trimester (-33%) and remained stable afterward (overall time effect p=0.33) and was not affected by hematocrit.

Conclusions

Our findings suggest that increasing dosages targeting WB tacrolimus concentrations, may not be necessary during pregnancy based on plasma tacrolimus concentrations. However, larger studies are needed to confirm the findings.

Damage-Associated Molecular Patterns In Porcine Donation After Circulatory Death Heart Transplantation

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Background

Donation after circulatory death (DCD) has expanded the donor pool for heart transplantation (HTx), but ischemia−reperfusion injury (IRI) remains a major barrier. Reliable methods to assess graft injury before implantation are lacking. Damage-associated molecular patterns (DAMPs) are promising biomarkers that reflect cellular stress and injury. This study investigated DAMP behaviour during hypothermic oxygenated perfusion (HOPE) in a porcine DCD transplantation model, comparing direct procurement and perfusion (DPP) with normothermic regional perfusion (NRP).

Methods

Hearts from porcine DCD donors were retrieved using either direct procurement and perfusion (DPP, n = 5) or normothermic regional perfusion (NRP, n = 7). All were preserved with hypothermic oxygenated perfusion (HOPE) before orthotopic transplantation. Perfusate was analyzed for high-mobility group box 1 (HMGB-1), tumor necrosis factor-α (TNF-α), intercellular adhesion molecule 1 (ICAM-1), and cytochrome c and correlated with mitochondrial respiration and cardiac performance.

Results

DAMP concentrations remained low and stable during HOPE, increasing mainly after reperfusion. Functional and mitochondrial correlations differed: In DPP, cytochrome c correlated inversely with left-ventricular end-systolic pressure−volume relationship (ρ = −0.900, p = 0.037; 95% BCa CI [−1.000, −0.111]). Whereas in NRP, during HOPE, HMGB-1 also correlated positively with mitochondrial coupling efficiency in NRP (ρ = 0.812, p < 0.050; 95% BCa CI [0.000, 1.000]). After transplantation, in NRP, ICAM-1 correlated with left-ventricular pressure−volume area in NRP (ρ = 0.886, p = 0.019; 95% BCa CI [0.515, 1.000].

Conclusions

In conclusion, DAMP release during and after HOPE in DCD heart transplantation showed modest differences between NRP- and DPP-preserved grafts but did not clearly determine mitochondrial or cardiac performance. Rather than actively driving recovery, DAMPs may reflect the graft's inflammatory and/ormetabolic state. Monitoring DAMPs during perfusion could enhance mechanistic insights and graft assessment, although larger, mechanistic studies are needed to clarify whether these molecules act as active mediators or passive indicators of cardiac resilience.

Prevalence Of Medication-Related Issues Post Discharge After Lung- And Kidney Transplantation: Identification Using Pharmacy-Based Evaluation Interviews

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Background

Following solid organ transplantation, patients are confronted with numerous challenges, including management of an extensive medication regimen. Therefore, the outpatient pharmacy provides medication counselling regarding patients' medication use at discharge and evaluates this after one week.

We aimed to identify medication-related issues faced by transplant patients.

Methods

Data of the first series of discharge interviews of lung transplantation (LTx) and kidney transplantation (KTx) patients were analysed. Outcomes assessed included patients' medication knowledge (scale: 1-10), patient-reported adherence, adverse effects, medication management strategies used and difficulties encountered.

Results

LTx (n=17) and KTx (n = 43) patients graded their medication knowledge at 7.7 and 6.9, respectively. All patients used tacrolimus and mycophenolate, except for two KTx patients who used tacrolimus with everolimus. All LTx patients reported full adherence and taking dosages at the right time, while six KTx patients (14%) reported taking incorrect doses of immunosuppressants. Adverse effects were reported in 14 (82%) and 23 (54%) LTx and KTx patients, respectively. In LTx patients, the most common adverse events were hand tremor (13, 76%), gastrointestinal side-effects (9, 53%) and headache (4, 23%). KTx patients reported similar adverse events albeit to a lesser degree, with hand tremor in 13 patients (30%), gastrointestinal side-effects (7, 16%), insomnia, and headache, both reported by two patients (5%). Both LTx and KTx patients used several methods to remember taking their Tx medications e.g.: alarm or phone, medication box, fixed intake times, social support and/or a Baxter roll. Occurrence of these methods were similar between groups. Reported issues in LTx and KTx patients included difficulty managing the medication schedule (24% and 14% respectively) and swallowing pills (18% and 5%), while the majority of patients (65% and 88%) experienced no issues within a week of hospital discharge.

Conclusions

While self-reported medication adherence is high in both groups after Tx, dosing errors, practical issues and adverse events are common and remain areas of improvement. By evaluating medication usage through follow-up calls with patients, the pharmacy proactively identifies and may solve medication-related issues as part of the multidisciplinary transplant team.

Empowerment Or Confrontation: A Qualitative Investigation Of Kidney Transplant Recipients' Perspectives On Self-Monitoring

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Background

Self-monitoring systems are increasingly being used to improve post-transplant monitoring, however, little is known about users experiences, needs and preferences. The objective of this study was to investigate perspectives of kidney transplant recipients (KTR) with regard to self-monitoring and compare perspectives of those who use or do not use this system.

Methods

Semi-structured interviews were held with KTRs (users and non-users). Non-users were defined as having never performed self-monitoring or stopped briefly after transplantation. Users were defined as those who actively self-monitored at the time of interview. An interview guide was developed to explore their opinions on the use, their experience of barriers and facilitators and possible improvements to self-monitoring. Interviews were audio-recorded and transcribed verbatim. Inductive qualitative analyses were conducted in NVivo.

Results

To self-monitoring after kidney transplantation. Non-users who had previously performed self-monitoring were more inclined to view the concept of self-monitoring negatively. All KTRs endorsed advantages/benefits of self-monitoring. These included early detection and management of post-transplant problems, hospital provision of self-monitoring equipment after transplantation, the opportunity to 'self-check' vital signs on demand, and ease of use. Willingness to maintain self-monitoring differed between groups; users perceived self-monitoring as a necessity to manage their health. Self-monitoring helped them build confidence in the body through reassurance. Non-users perceived more negative themes such as: self-monitoring being a reminder of being a patient, leading to increased stress instead of empowerment; burden of measuring; lack of personal contact; lack of tailoring measurements; and hassle of registration. Problems during the introduction contributed to cessation of self-monitoring.

Conclusions

The combination of necessity and benefits of self-monitoring were the most important factors mentioned by users, making them feel reassured. For non-users, the necessity of using self-monitoring did not outweigh the barriers or negative perceptions. To increase the use of self-monitoring, it is important to focus on a smooth introduction and the emotional impact, whilst still respecting the autonomy of the patient.

The Risks And Benefits Of Immune Checkpoint Inhibitors In Kidney Transplant Recipients: A Systematic Review

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Background

Immune checkpoint inhibitors (ICI) in solid organ transplantation (SOT) recipients pose a therapeutic dilemma. While immune checkpoint inhibitors have proven to be effective for malignancies in the general population, by activating the immune response against cancer cells, they could trigger allograft rejection in SOT patients. This systematic review aimed to evaluate the clinical efficacy and safety of immune checkpoint inhibitors in solid organ transplantation recipients with post-transplantation malignancies.

Methods

The systematic search was conducted using the PubMed database, including studies published until October 16, 2025. The search string consisted of terms as 'kidney transplantation', 'malignancy' and 'immune checkpoint inhibitors' to find relevant studies. Eligible studies included adult SOT recipients with any type of malignancy who received at least one dose of ICI following transplantation. We extracted data on tumour response, allograft rejection and allograft loss, patient survival and immune related adverse events (irAEs). All articles were assessed for quality using the Newcastle-Ottawa scale or the Before-After Studies With No Control Group tool.

Results

Three studies, with a total of 98 kidney transplant recipient, were included. Quality assessment of these studies ranked two as good and one as fair. The most common reported malignancies were cutaneous squamous cell carcinoma (42.9%) and melanoma (23.5%). Nivolumab was the most used ICI (26.5%). The reported tumour response ranged from 28.9% to 53%. Allograft rejection

occurred in 31.6% (range 0% - 42%) of all the patients, resulting in allograft loss in over half (20.4%) of these rejections. Median overall survival ranged from 3.2 to 22.5 months. Of interest, one study with cemiplimab, mTORi conversion and pulse dose steroids during ICI-therapy showed no allograft rejection in 12 recipients. Mild forms of irAEs were experienced in 40.8% of patients, while 30.6% experienced a severe or life-threatening irAEs.

Conclusions

Despite relative positive tumour responses, ICIs are still associated with a high rate of allograft rejection and immune-mediated toxicity. Optimal type and dosing of ICIs, and optimal immunosuppressive regimens remain to be defined.

and belatacept. We discuss a kidney allograft recipient with cTTP having repeated episodes of T-cell- mediated rejection with systemic TMA. Changes to his immunosuppressive regimen and intensification of plasma exchange therapy terminated TMA temporarily but failed to prevent its recurrence. Ultimately, he was treated with recombinant a disintegrin and metalloproteinase with a thrombospondin type one motif, member 13 (ADAMTS13) infusions, halting TMA and preventing future episodes. This is the first case of prophylaxis with recombinant ADAMTS13 in a kidney allograft recipient, illustrating its potential benefit over plasma exchange by assuring therapeutic immunosuppressants' concentrations and preventing both rejection and TMA- induced graft injury.

Kidney Transplantation In Congenital Thrombotic Thrombocytopaenic Purpura: Using Recombinant ADAMTS13 To Balance Relapse And Rejection

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Background

Congenital thrombotic thrombocytopaenic purpura (cTTP) is an extremely rare disease, and kidney transplantation in this population is even rarer. Finding an appropriate immunosuppressive regimen in cTTP transplant recipients can be challenging, as calcineurin inhibitors are associated with an increased risk of thrombotic microangiopathy (TMA), whereas prophylactic plasma exchange reduces the blood concentrations of mycophenolic acid

Professional Perspectives On Self-Monitoring After Kidney Transplantation

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Background

Telemedicine is increasingly being developed and implemented in transplant medicine. However, the perspectives of professionals as stakeholders have been neglected. Self-monitoring after transplantation has become standard of care, but has not been evaluated with regard to professionals' experienced barriers and facilitators, needs, and preferences. These provide valuable insight on how their perspectives influence the implementation. Our objective was to investigate these perspectives of professionals with regard to self-monitoring.

Methods

Semi-structured interviews were held with regional and academic nephrologists to maximize generalizability of findings. An interview guide was developed to explore their experience with self-monitoring in clinic, their opinions on the system, perceived barriers and facilitators for patients and professionals, and suggestions

for improvement. Interviews were audio-recorded and transcribed verbatim. Inductive qualitative analyses were conducted in NVivo.

Results

26 professionals were interviewed of whom 12 worked in an academic hospital. Professionals saw benefits but also obstacles to self-monitoring after kidney transplantation. Positive aspects of self-monitoring included: Visualization over time; improved knowledge and engagement of patients in their own health; patient empowerment; efficient teamwork in managing patients' health; enhanced safety through alerts; positive societal impact.

Negative aspects included: the lack of physical checkups; perceived patient burden (including monitoring avoidance); technical inabilities of patients; uncertainty regarding boundaries of responsibility; administrative burden; financial compensation.

Professionals had ambivalent perspectives on the integration of self-monitoring in electronic patient records (EPR), wherein the load times, data ownership and security were common themes.

Conclusions

In conclusion, professionals were generally positive about implementing self-monitoring into their daily practice as this enables better care from a distance with patients being more involved in their own health. The need for better integration of self-monitoring within the EPR was commonly endorsed as an area for improvement. Involvement of IT experts, policymakers, health-insurance companies is required to take on these challenges. Moreover, burdens need to be minimized for users in order to maximize engagement. If these challenges are overcome, self-monitoring could become the standard for transplant recipient care.

Estimated Glomerular Filtration Rate Trajectories, Graft Failure, And Mortality In Kidney Transplant Recipients

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Background

No previous studies have compared the longitudinal trajectories of estimated glomerular filtration rate (eGFR) derived from different formulas to predict adverse outcomes after kidney transplantation. This study aimed to investigate the relationship between eGFR based on serum creatinine (eGFRcr), cystatin C (eGFRcys), and muscle mass trajectories with graft failure and mortality in kidney transplant recipients (KTRs).

Methods

Data were obtained from the TransplantLines Biobank and Cohort Study. Participants with ≥2 post-transplant measurements of eGFRcr, eGFRcys, and 24hUCr were included. Longitudinal trajectories of renal function were identified using latent class mixed models (LCMMs). Joint models integrating linear mixed-effects models (LMM) with Cox proportional hazards regression were applied to assess associations between biomarker trajectories and outcomes. Two combined models were compared: one incorporating eGFRcr and eGFRcys, and another integrating eGFRcr with 24hUCr. Model performance was evaluated using time-dependent area under the curve (AUC) and C-index.

Results

Among 1,029 KTRs (median age 59.1 years), 169 experienced graft failure and 154 died during a median follow-up of 57 months (interquartile range, 32−82). LCMM

identified three distinct trajectory classes for each bio-marker, representing improving, stable, and declining kidney function (p < 0.001). Survival analyses revealed significant differences in both graft and overall survival across trajectory groups (p<0.001). LMM further revealed divergent eGFR trajectories between survivors and non-survivors, as well as between graft survivors and non-survivors. Joint models combing eGFRcr and eGFRcys trajectories showed stronger predictive power for graft failure (β =-0.409, p < 0.001) and mortality (β = −0.379, p < 0.001) compared to those including 24UCr. The eGFRcr + eGFRcys model demonstrated superior predictive accuracy for graft failure (average C-index = 0.80 vs 0.76) and mortality (average C-index = 0.78 vs 0.72). Additionally, dynamic individualized predictions illustrated that patients exhibiting faster declines in eGFRcys showed more rapid decreases in graft and overall survival probability.

Conclusions

Trajectories of eGFRcr, eGFRcys, and 24hUCr are independently associated with graft failure and mortality. Integrating cystatin C with creatinine-based eGFR provides a more robust and better-fitting joint model, enhancing long-term prognostic precision and supporting its use for individualized post-transplant risk monitoring.

The Impact Of Modifiable Physical And Psychological Problems On Frailty And Quality Of Life In Kidney Transplant Candidates: Preliminary Results Of The PreCareTx-study

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Background

For kidney transplant candidates (KTCs) it is important to be in an optimal physical and psychological condition to be able to handle the stress of transplant surgery and to enhance post-transplant recovery. However, the overall fitness of KTCs is often compromised due to their chronic kidney disease, comorbidities, and adverse effects of dialysis. This study aimed to assess the prevalence of modifiable physical and psychological problems among KTCs and their impact on frailty and quality of life.

Methods

We analysed the findings at screening for participants of the PreCareTx-study, an ongoing study into the feasibility and effects of prehabilitation in kidney transplant candidates. Participants completed questionnaires and physical tests assessing physical functioning, nutritional status, mental wellbeing, quality of life, and frailty. Descriptive and comparative statistics were used for analysis.

Results

Data from 110 participants (mean age 61.5 years; 75% male; 41% on dialysis) were included. Physical functioning was comprised in 55.5%: 40% experienced poor physical functioning, 41% reduced strength, and 19% reduced mobility. Nutritional status was comprised in 85.5%: 53% had an unhealthy Body Mass Index, 78% high fat percentage, and 31% were at high risk of malnutrition. Mental wellbeing was comprised in 82%: 79% reported fatigue, 46% depressive symptoms, and 41% anxiety symptoms. Of the 110 participants, only four (3.6%) experienced no problems, 15.5% had problems on one domain, 35.4% on two domains, and 45.5% on all domains. The median number of problems per participant was four (range 0-9). Comparing groups based on number of problems (0-2/3-5/>6) revealed significant differences (p<.001) between the groups in frailty score (respectively, 1.4 vs. 3.2 vs. 6.1) and both physical (respectively, 71.2 vs. 58.8 vs. 37.7) and mental (respectively, 77.9 vs. 64.5 vs.48.8) quality of life scores, with participants with >6 problems showing the worst scores on all outcomes.

Conclusions

Nearly all KTCs (96%) experienced physical, nutritional status, or mental problems, negatively affecting frailty status and quality of life. Addressing these modifiable problems by prehabilitation, the process of improving the overall fitness before surgery through lifestyle interventions, may not only enhance transplant readiness, but also reduce frailty and improve quality of life of KTCs.

Predictive Modelling For Kidney Transplantation: Incorporating Hypothermic Machine Perfusion Data

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Background

Hypothermic machine perfusion (HMP) has been established as a standard preservation method for deceased-donor kidneys, providing measurable perfusion parameters. Many centers rely on these parameters, such as renal resistance, to guide decisions on organ acceptance. As current predictive models for kidney transplant outcome have limited accuracy, this study aimed to evaluate whether incorporating HMP variables improves such models.

Methods

Data were collected retrospectively from the Dutch Organ Transplant Registry (2015-2024). The primary endpoint was adverse outcome within 1 year (graft failure, death or chronic kidney disease stage 4). HMP-related variables, including oxygen, duration, flow, pressure, and vascular resistance parameters, were screened for correlation with outcomes. Variables showing univariate significant associations with the primary outcome were then incorporated into prediction models constructed using logistic regression analysis with donor, recipient and HMP factors. Model performance was assessed in training (n=991) and validation (n=487) cohorts using C-statistic and calibration plots.

Results

The model without HMP characteristics achieved a C-statistic of 0.715 (training) and 0.633 (validation). Incorporating relative change in vascular resistance at 60 and 120 minutes of HMP reached a C-statistic of 0.724 (training) and 0.655 (validation). The difference in C-statistic between the models with and without HMP parameters was not statistically significant (DeLong's test).

Conclusions

Adding HMP parameters did not result in a statistically significant improvement of a typical prediction model for transplant outcome, suggesting that these parameters should not be relied upon when considering an organ offer. Although relative changes in vascular resistance were associated with post-transplant outcomes, their addition to existing models did not enhance predictive performance. These findings indicate that HMP-associated variables have limited value for outcome prediction.

Explainable Machine Learning For Cardiovascular Risk Prediction In Kidney Transplant Recipients

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Background

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in kidney transplant recipients (KTR). Current population-based CVD risk assessment modules have not proven useful in this specific population.

The aim of the present study was to develop an explainable machine learning (ML) model to predict individualized CVD risk in KTR over time, providing interpretable survival curves as output to support clinical decision making.

Methods

Our prospective cohort included 523 KTR from The Netherlands, with a functioning graft >1 year post-transplantation, recruited between August 2001 and July 2003. The primary outcome was a composite of CVD events: cardiovascular death, non-fatal myocardial infarction and revascularization procedures (percutaneous transluminal coronary angioplasty or coronary artery bypass grafting). A random survival forest (RSF) model was trained to predict CVD event risk. Features were selected through forward selection and backward elimination. Model performance was evaluated using a 5-fold cross-validation procedure, with hyper-parameter tuning and feature selection to mitigate bias. The final results were measured by the time-dependent area under the receiver operating characteristic curve (td-AUROC) and Shapley additive explanations (SHAP) visualizations were included in the analyses for explainability.

Results

During a mean ($\pm$ standard deviation) follow-up of 4.8 $\pm$ 1.3 years, 12.8% of KTR had a first CVD event. At baseline, mean age was 50.5 $\pm$ 12.2 years and 54% were males. Mean kidney function (CKD-EPI 2009 eGFR) was 47.0 $\pm$ 15.8 mL/min/1.73 m^2. Donors had a mean age of 37.2 $\pm$ 15.4 years and 53% were male. The RSF model achieved an average td-AUROC of 0.76 using features selected by backward elimination. SHAP analysis identified high sensitivity troponin T, N-terminal pro-brain natriuretic peptide, and hemoglobin A1c as the most important predictors of CVD event risk.

Conclusions

The newly developed explainable machine learning model accurately predicts CVD risk in KTR over 5 years from baseline. Individualized risk stratification, using models such as the one proposed, could help to guide and support early preventive interventions in KTR follow-up.

Effect Of Tacrolimus And Mycophenolic Acid Exposure On Torque Teno Virus Load In The First Year After Kidney Transplantation; A Cohort Study

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Background

Kidney transplant recipients (KTR) are subject to a precarious balance between over- and underimmunosuppression. Torque teno virus (TTV) has been proposed as a marker of immune function, but little is known on how tacrolimus (Tac) and mycophenolic acid (MPA), the most frequently prescribed immunosuppressants, affect TTV dynamics. We aimed to investigate the effect of Tac through levels (C_0) and MPA concentration (AUC) on TTV blood loads in the first year after transplantation.

Methods

This observational cohort study contains 255 KTR transplanted between 2005-2012 with a living donor, receiving triple maintenance immunosuppressive therapy (Tac, MPA, and prednisolone). We conducted linear regression analyses to assess the association between Tac-C_0, MPA-AUC and TTV load at different time points post-transplant (months 1.5, 3, 6, and 12).

Results

The observed median TTV load was 3.6 log at baseline, peaked at month 3 (7.9 log) and decreased to 5.5 log at months 12. Every unit (μg/L) increase in $Tac-C_0$ lead to an increase in TTV load at month 3, 6 and 12. (Month 3: 0.11 [CI 0.02;0.21]; Month 6: 0.15 [CI 0.03;0.28]; Month 12: 0.17 [CI 0.03;0.31] per μg/L C_0). MPA-AUC had no effect on the TTV load on any timepoint. TTV load dynamics were not affected by $Tac-C_0$ nor MPA-AUC.

Conclusions

A significant but small effect of Tac exposure on TTV load was observed, suggesting that the high variation in TTV loads after kidney transplantation is only partially explained by drug exposure.

Secretin-Induced Biliary Bicarbonate Secretion In Donor Livers: A Novel Viability Marker During Ex-Situ Normothermic Machine Perfusion

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Background

Ex-situ normothermic machine perfusion (NMP) is increasingly used for preservation and assessment of donor livers prior to transplantation. Cholangiocytes actively modify bile composition by secretion of bicarbonate (HCO_3^-), creating alkalotic bile that protects against bile salt toxicity, named the "bicarbonate umbrella". Low biliary HCO_3^- during NMP indicates cholangiocellular injury and contributes to additional bile salt injury and is used as biliary viability criterium. Secretin is a hormone that stimulates biliary HCO_3^- secretion in-vivo. We hypothesized that adding secretin in NMP may stimulate biliary physiology, enhance the protective bicarbonate umbrella, and could be a novel test for biliary viability.

Methods

First, human synthetic secretin was tested in-vitro on intrahepatic cholangiocyte organoids (ICO). Next, a preclinical study using human livers on NMP was performed to assess whether secretin increases biliary HCO_3^- in non-viable livers. Last, secretin was administered during our clinical protocol of sequential hypo- to normothermic perfusion with controlled oxygenated rewarming (DHOPE-COR-NMP). Secretin was added at the beginning of the rewarming phase and after hepatobiliary viability assessment at 2.5 hours of NMP. The primary outcome was the response in biliary HCO_3^- secretion. Secondary outcomes focused on early clinical outcomes in comparison with a historical cohort.

Results

ICO increased in size in a swelling assay and showed an increased signal in Ussing chamber experiments, indicating increased ion and water transport. In our preclinical study, non-viable livers did not respond to secretin and therefore viability testing was not camouflaged. Subsequently, we performed 15 DHOPE-COR-NMP procedures, resulting in 10 liver transplants. Viable livers, treated with secretin excreted more HCO_3^- in bile throughout the perfusion in comparison with historical viable livers without secretin treatment. Increased biliary HCO_3^- after administration was observed in viable compared to non-viable grafts (10.1 mmol/L vs. 2.2 mmol/L; p = 0.03). Recipient outcomes in the first 90 days were similar to historical controls.

Conclusions

Administration of secretin during ex-situ NMP of human donor livers increases biliary secretion of HCO_3^- in livers with viable bile ducts. Secretin is a physiological relevant hormone that stimulates restoration of biliary physiology during liver NMP, and may serve as novel biomarker of preserved cholangiocellular viability.

Kidney Exchange For Compatible Pairs: Improved HLA Antigen Mismatch Does Not Necessarily Predict A Molecular Matching Benefit

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Background
Compatible pairs may benefit from kidney exchange (KEP) via improved donor-recipient Human Leukocyte Antigen (HLA) matching. Compared to current A-B-DR antigen matching, molecular matching tools provide more granular information on the immunogenic potential of HLA mismatches. In this study, we simulate the potential, molecular matching improvement for compatible pairs in KEPs with antigen matching.

Methods
Dutch KEP (Cross-over+) was simulated over four years. Fictive pairs were generated from a database of KEP participants between 2018-2023, supplemented with directed compatible donors and recipients. We generated 112 compatible pairs to participate maximum one KEP run. The kidney exchange requirement for compatible pairs was ≥1 reduction in total A-B-DR antigen mismatches, or ≥1 reduction in DR with unchanged total. High resolution typing was unavailable for the majority of participants and imputed. HLA A-B-C-DR-DQ solvent accessible (SA) amino acid, total eplet, and antibody verified (AbV) eplet mismatches were calculated with HLA-EMMA software (Version 1.06).

Results
Of compatible pairs, 68 (61%) were transplanted via KEP in simulation (n=9 with reduced DR and unchanged total antigen mismatches). Mean molecular mismatch difference between the KEP versus intended donor was -9.2 for SA amino acids, -10.2 for eplets and -1.9 for AbV eplets. Patients with higher antigen mismatch reduction had higher SA amino acid mismatch difference (-19.2 for -2 and +3.7 for -0 antigen mismatches, p=0.002).

Importantly, of 68 patients, 21 (31%) had increased SA amino acid mismatches (mean +8.2). Increased molecular mismatches were found more often in patients with reduced DR and unchanged total antigen mismatches (56% for -0, 38% for -1 and 0% for -2 antigen mismatches, p=0.002). The chance of increased molecular mismatches did not correlate with the number of antigen mismatches with the intended donor (18% for 4 and 31% for 6 antigen mismatches, p=0.54). Trends were confirmed for eplets.

Conclusions
The HLA antigen mismatch of compatible pairs can be reduced via KEP. However, one-third of patients with reduced antigen mismatches had increased molecular mismatches. With accumulating evidence on the impact of class I and II molecular mismatches, future studies could test molecular matching in KEP algorithms.

Is PCEA Or Plexus Catheter More Effective For Postoperative Pain Relief And Reduction Of Nausea Symptoms In Living Liver Donors?

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Ureteral Stent Types And Surgical Outcomes After Kidney Transplantation: A Retrospective Cohort Study

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Background

Living liver donation is a major procedure in which optimal postoperative pain management is essential for recovery, mobilisation and patient satisfaction. Commonly used techniques are patient-controlled epidural analgesia (PCEA) and the plexus catheter. Although both methods are effective, they differ in terms of analgesic quality, side effects and comfort. Nausea is a common post-operative complaint that can affect recovery and may be related to the type of analgesia used. To date, it remains unclear which method — PCEA or plexus catheter — offers the best balance between effective pain relief and minimal side effects in living liver donors.

Methods

PubMed was searched for publications from the period 2014−2024. In addition, the snowball method was applied to relevant articles. A total of nine studies were identified, of which one systematic review with meta-analysis and one retrospective cohort study were included for further analysis. The selection and assessment of the articles was carried out using the UMCG assessment forms.

Results

Two studies were included: a systematic review with meta-analysis and a retrospective cohort study. In the meta-analysis, based on three RCTs, living liver donors with a plexus catheter recovered faster than those with PCEA. Pain scores were comparable on the first postoperative day, but higher with the plexus catheter on the second day, while opioid use was lower. The cohort study of 340 donors also found higher pain scores with the plexus catheter. There was no difference in nausea symptoms, although prophylactic dexamethasone was administered more often in this group. Donors with a plexus catheter resumed a normal diet faster and had a shorter hospital stay, but this difference remained insignificant after correction.

Conclusions

Living liver donors experience less postoperative pain when using PCEA than when using a plexus catheter. Although the plexus catheter may contribute to a faster recovery, it is associated with higher pain scores. No significant differences were found in nausea or vomiting symptoms. The results should be interpreted with caution, as the more frequent administration of dexamethasone in the plexus group may have influenced this. Further prospective studies are needed to determine the optimal analgesia method for living liver donors.

Background

Ureteral stents are routinely placed in recipients of kidney transplantation to prevent complications such as ureteral stenosis and urine leakage. Various stent types exist, including splints, non-magnetic JJ stents, and magnetic JJ stents, but their comparative effectiveness and safety remain unclear.

Methods

A retrospective cohort study was conducted including 1219 adult kidney transplant recipients treated between 2018 and 2024 at a tertiary transplant center. Patients were grouped per stent type: splint (n = 277), non-magnetic JJ stent (n = 319), and magnetic JJ stent (n = 623). The choice between splint and JJ stent was surgeon preference and surgical protocol change during the study period. Primary outcomes were ureteral stenosis and urine leakage within 3 months post-transplantation. Secondary outcomes included urinary tract infection (UTI), estimated glomerular filtration rate (eGFR) at 3 months, length of hospital stay, and allograft rejection. Statistical tests included Fisher's Exact Test for binary outcomes and Kruskal-Wallis tests for non-normally distributed variables. Pairwise comparisons were performed with Bonferroni correction.

Results

There were no significant differences in urologic complications such as ureteral stenosis (Splint: 7 cases, JJ: 5 cases, Magnetic JJ: 19 cases; p=0.42) or urine leakage (Splint: 4 cases, JJ: 13 cases, Magnetic JJ: 18 cases; p=0.15) across stent types. UTIs occurred significantly more often in patients with JJ and Magnetic JJ stents compared to Splints (p<0.001). Post-hoc analyses showed a higher proportion of UTIs in the JJ and Magnetic JJ groups (27.2% and 29.3%, respectively) compared to the Splint group (15.5%). Splint recipients had a significantly higher median eGFR at 3 months compared to both JJ and Magnetic JJ stent groups (p=0.002). This difference may be explained by a higher proportion of living donor kidney transplants in the splint group. No significant differences were found in hospital stay duration (p=0.10) or in rejection within 3 months post-transplantation (p=0.49).

Conclusions

There were no significant differences in ureteral stenosis or urine leakage among the three stent types. However, JJ and Magnetic JJ stents were associated with a higher incidence of urinary tract infections compared to splints. These findings suggest that stent selection may influence postoperative infectious outcomes in kidney transplant recipients.

Evaluation Of Direct Post-Operative Removal Of The Urinary Catheter (UC) Following Donor Nephrectomy

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Background

In the past years we were used to leaving the UC in for one day post operative after donor nephrectomy. In October 2024 we introduced a protocol to remove UC immediately post operatively. This study was conducted to evaluate the safety of the protocol.

Research Question

Can an UC be removed immediately post-operatively without adverse consequences for the patient?

Methods

We performed a retrospective study on 68 patients that underwent a donor nephrectomy, Between October 2024 and September 2025. In 56 of these patients, the UC was removed immediately post-operatively. In 12 patients, the UC was not removed immediately by not following the new protocol, with seven of these patients having the catheter removed after several hours. The five patients where the UC was removed the following day were excluded from analysis.

Results

The cohort consisted of 30 men and 33 women, with a mean age of 54 years. A total of 50 left and 13 right kidneys were donated. The surgical technique included 44 robot-assisted donor nephrectomies, 17 laparoscopic donor nephrectomies, and two hand-assisted laparoscopic donor nephrectomies. The mean post-operative hospital stay was 2.2 days. A new UC was inserted in 1 of the 63 patients due to postoperative urinary retention.

Conclusions

Immediate post-operatively removal of the UC after donor nephrectomy is safe and feasible, probably without an increased risk of urinary retention. This approach results in reduced discomfort for kidney donors, thereby improving their post-operative experience.

Torque Teno Virus, Granulocytes And Lactate Dehydrogenase After Solid Organ Transplantation

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Background

Torque Teno Virus (TTV) is considered a non-pathogenic virus. TTV load increases after initiation of immunosuppression, and is currently being investigated as a marker of overall immune function to guide immunosuppressive therapy after solid organ transplantation. A recent study has shown a positive association between TTV load and immature granulocytes and a negative association with mature granulocytes, raising the question whether TTV exerts a lytic effect on granulocytes following replication in immature granulocytes. This study aimed to investigate whether TTV load is associated with lactate dehydrogenase (LDH) as a marker of cell lysis, and whether this association is mediated through the mature-to-immature granulocyte ratio.

Methods

TTV load was quantified by real-time PCR assay (TTV R-GENE®, bioMérieux). Granulocytes were counted using a Sysmex XN hematology analyzer and LDH was quantified using a kinetic assay. Associations were tested using univariable linear regression. Mediation analysis was performed with 95% confidence intervals (CI) estimated by 1,000 bootstrap resamples. The mature-to-immature granulocyte ratio was $\log_{10}$-transformed in all analyses.

Results

A total of 509 kidney transplant recipients (KTR; mean age 56.9 $\pm$ 14.3 years, 36.7% female) and 72 lung transplant recipients (LuTR; mean age 56.1 $\pm$ 10.6, 41.7% female) were included at 6 months post-transplantation. Mean TTV loads were 5.2 $\pm$ 2.1 $\log_{10}$ copies/mL in KTR and 7.0 $\pm$ 1.4 $\log_{10}$ copies/mL LuTR, mean LDH concentrations were 237 $\pm$ 64 and 294 $\pm$ 105 U/L respectively. In KTR, TTV load was positively associated with LDH (st. β=0.40, 95% CI (0.32; 0.48), p<0.001) and negatively associated with the mature-to-immature granulocyte ratio (st.β=-0.56, 95% CI (-0.63; -0.49), p<0.001) and this ratio was negatively associated with LDH (st.β=-0.41, 95% CI (-0.49; -0.33), p<0.001). Similar associations were

observed in LuTR. In KTR and LuTR respectively, 38% (95% CI 25−54%) and 35% (95% CI 13−59%) of the association between TTV load and LDH was mediated by the mature-to-immature granulocyte ratio.

Conclusions

These findings support the theory that TTV exerts a lytic effect on granulocytes. Whether this potential effect increases susceptibility to bacterial or fungal infections in transplant recipients with high TTV loads remains to be determined.

Extended-Release-Tacrolimus Versus LCP-Tacrolimus: A Cross-Over Study

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Background

Tacrolimus is a first-line immunosuppressant in kidney transplantation. Its use is complicated by a narrow therapeutic window and variable exposure. Extended-release formulations, ER-tacrolimus (Advagraf) and LCP-tacrolimus (Envarsus®), improve adherence, with LCP-tacrolimus also improving bioavailability. However, direct comparisons are limited. This study evaluates the safety and benefits of switching from ER-tacrolimus to LCP-tacrolimus, focusing on dose requirements, adverse effects, pill burden, and pharmacokinetics.

Methods

In this prospective, open-label cross-over study, adult first kidney transplant recipients with stable transplant function, therapeutic ER-tacrolimus levels, and high metabolizer status (CDR <1.05 ng/mlx1/mg) were switched from ER-tacrolimus to LCP-tacrolimus with a 30% dose reduction, monitored for three weeks, then switched back to ER-tacrolimus. Trough and peak tacrolimus levels, Area Under the Curve (AUC), adverse effects, pill burden and patient preference were assessed. The primary outcome was the difference in tacrolimus dose needed for therapeutic trough concentrations. Secondary outcomes included adverse effects and pharmacokinetic parameters.

Results

Twelve kidney transplant recipients (median age 54.5, 25% female, median BMI 27.7, median time post-transplant 12.5 months) were included. The dose to achieve therapeutic trough levels (5-8 ug/L) was significantly lower with LCP-tacrolimus compared to ER-tacrolimus (6.0 mg vs. 8.5 mg, p=0.004), with similar pill burden and adverse effects. No significant differences were found in AUC, peak levels (LCP-Tac: 14.75 [11.68-16.27]; ER-Tac: 17.15 [13.53-20.93]), renal function, or blood pressure. For CYP3A5 expressors (n=7; 58%), LCP-tacrolimus showed a stronger correlation between trough levels and AUC than ER-tacrolimus (0.85, p=0.016; 0.43, p=0.34). No serious adverse events occurred. Patient preference was divided: 42% preferred ER-tacrolimus, 33% LCP-tacrolimus, and 25% had no preference.

Conclusions

The dose required to reach therapeutic trough levels was lower with LCP-tacrolimus compared to ER-tacrolimus, without a change in pill burden or exposure. Our results suggest that, in CYP3A5 expressors, LCP-tacrolimus trough levels correlate better with exposure than with ER-tacrolimus, suggesting that trough monitoring with LCP-tacrolimus may be more reliable for this subgroup. The crossover design allowed patients to serve as their own controls, but the small sample size, short follow-up and selection bias limited analyses. Larger, randomized controlled trials are needed to identify patient groups that may benefit most from each formulation.

Incidence And Disease Burden Of Non-SARS-CoV-2 Respiratory Viral Infections In Kidney Transplant Recipients Between 2021 And 2024 In A Single Centre In The Netherlands

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Background

The COVID-19 pandemic highlighted the impact of respiratory viral infections on solid organ transplant recipients. However, respiratory viral infections other than SARS-CoV-2 and influenza virus are understudied. Better insight into the disease burden of these viruses is needed, particularly as new vaccines are developed. This study set out to assess the incidence and disease burden of respiratory viral infections in adult kidney transplant recipients (KTR).

Methods

We retrospectively studied our centre's adult KTR with an in-hospital positive test for a respiratory virus between January 2021 and May 2024. Positive tests for SARS-CoV-2 were excluded. The primary endpoint was the incidence of respiratory viral infections. Additionally, we obtained patient data from hospital charts including baseline characteristics, disease severity, clinical outcomes and co-infections.

Results

From January 2021 to May 2024, 742 KTR were tested for respiratory viruses during clinical or ER visits, out of a total of 2,658 KTR in follow-up at our centre. We identified 85 disease episodes in 77 KTR, 9.1% of whom had a history of COPD or asthma. The most frequently detected respiratory viruses were influenza A or B virus (n=31), rhinovirus (n=25) and respiratory syncytial virus (RSV) (n=13). Among these, two influenza virus and ten rhinovirus detections were considered incidental findings, as they did not explain the clinical presentation. Influenza virus infections resulted in 11 hospital admissions of which two ICU (hospital stay 8 [2-35] days), rhinovirus in ten, two ICU (3.5 [1-46] days) and RSV in six, two ICU (14 [4-37] days). Coinfections were observed in five, six and two hospitalisations associated with influenza virus, rhinovirus and RSV, respectively. Within 30 days, graft failure occurred during one rhinovirus and one rhinovirus and RSV co-infection, while mortality was observed in one RSV and one RSV and rhinovirus co-infection.

Conclusions

RSV-related hospitalisations were twice as long in duration as those related to influenza virus. Notably, over half of the hospital admissions with rhinovirus were coinfections, suggesting that rhinovirus can lead to severe secondary infections. Collectively, these findings underscore the considerable burden of respiratory viral infections in KTR and support prioritising vaccination strategies in this population.

Transplantation Of Pancreatic Islets Isolated Using The Pancreatic Islet Separation Method (PRISM) Machine – A Case Report

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Background

For a select group of patients suffering from complicated type 1 Diabetes Mellitus, pancreatic islet transplantation may be considered as a treatment option. Vital to this treatment is isolating as many islets from donor pancreases as possible. The standard isolation technique is an open method, involving many types of machinery, and varies strongly among centers.

To refine and standardize the islet isolation procedure, we developed a novel and automated method (PancReatic Islet Separation Method, PRISM) and integrated this into a machine. We report on the first clinical transplantation using PRISM-isolated islets.

Methods

A donation after brain death pancreas was procured from a 22-year-old female with a BMI of 32. The isolation was performed using the PRISM machine in our cGMP facility.

After purification, density fractions were pooled based on purity and aspect, total IEQ was determined, a dynamic Glucose Stimulated Insulin Secretion (dGSIS) test performed, and islets were cultured for 2 days.

After our standard release criteria were met, the islets were transplanted in a 54-year-old female (BMI 21 kg/m^2) with T1D complicated by recurrent hypoglycemia and kidney failure for which she had received a kidney transplantation. Using a continuous glucose monitor, glycemic control was used as a marker for islet function after transplantation.

Results

The islet isolation using PRISM yielded a total IEQ of 1,018,913. Functionality was confirmed via dGSIS with a peak stimulation index of 21.5. The patient received 945,652 IEQ in a pellet volume of 3,625 µL and with 60% islet purity.

At 20 months the patient became insulin independent. The glucose time in range had improved from 52% to 90%, time above range decreased from 37% to 7%, and the glucose management indicator improved from 7.5% to 6.1%.

Conclusions

Islets isolated using the PRISM machine can exhibit proper functional secretory capacity after transplantation.

Simultaneous Kidney Pancreas Transplant Recipients Require Higher Tacrolimus Trough Targets For Prevention Of First-Year Rejection Compared To Solitary Kidney Transplantation: A Cohort Study

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Background

Tacrolimus (Tac) targets in simultaneous pancreas-kidney transplant recipients (SPK) are often extrapolated from kidney transplant recipients (KT) as evidence is scarce. Instead of extrapolating from KT, tailoring the maintenance regimens to SPK, by accounting for their distinct immunological and pharmacokinetic characteristics, may further improve post-transplant outcomes.

We aimed to assess how pharmacokinetic differences between SPK and KT recipients alter Tac-exposure (AUC) for a given trough level (C_0), and how these, alongside SPK-specific immunological challenges, shape Tac-C_0 targets needed to prevent first-year rejection.

Methods

We included 183 SPK and 1239 KT transplanted between 2011-2023 starting on oral Tac, mycophenolic acid (MPA), and prednisone triple therapy directly post-transplant. First, differences in 12-hour Area-Under-the-concentration-time-Curve (AUC_{0-12h}) to C_0 ratio measured at one week, six weeks, six months, and one year after transplantation were assessed between SPK and KT using linear mixed effects models, independent of CYP3A5-status, BMI, age, and sex. Potential mechanisms behind the difference in AUC_{0-12h}/C_0 were explored by investigating effect modification by diabetes, hematocrit, and serum albumin. Second, the SPK-specific dose-response relationship between the longitudinal Tac-C_0 trajectory and rejection was estimated with joint models. The lower Tac-C_0 limit for SPK was established using logistic regression plots.

Results

SPK obtained an adjusted -8.39% (-11.80 to -4.97%) lower Tac-AUC_{0-12h} for similar C_0 as KT during the first 6 weeks post-transplant. This difference decreased during the first-year post-transplant to -2.27% (-6.90 to 2.15%) and was not impacted by loss-to-follow-up. The lower Tac-AUC_{0-12h}/C_0 could be explained by diabetes status as well as differences in albumin and hematocrit. The adjusted hazard ratio for every 1 ng/ml increase in Tac-C_0 on diagnosed rejection was 0.81 (95%CI:0.67−0.93, P=0.009). A lower Tac-C_0 limit between 6−8 ng/ml was found to be most optimal to prevent rejection during the first-year post-transplant.

Conclusions

While prior studies recommend a Tac-C_0 target of 5−7 ng/mL for KT, our findings suggest SPK may require 6−8 ng/mL during the first-year post-transplant, reflecting their distinct pharmacokinetics and immunological challenges to better prevent rejection.

Fluorescence-Based Measurement Of The Indocyanine Green Elimination Test During Normothermic Machine Perfusion – Overcoming Practical Limitations For Clinical Application

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Background

The indocyanine green (ICG) plasma disappearance rate (PDR) during normothermic machine perfusion (NMP) has been proposed as a functional viability assay for extended-criteria donation after circulatory death (ECD-DCD) livers. The NMP-PDR correlates with liver function during NMP and short-term post-transplantation outcomes. Currently, ICG elimination is determined using ICG absorbance in NMP plasma, requiring pre-processing of blood-collection tubes. Alternatively, fluorescence-based detection methods could enable NMP-PDR as a point-of-care test by eliminating sample pre-processing. Therefore, we aimed to assess the performance of different fluorescence−based detection methods, compared to the current standard.

Methods

An ICG bolus was administered at 60 minutes of NMP (n=18). Perfusate samples were collected in EDTA blood-collection tubes and processed. A plate reader was used to quantify the ICG elimination rate using fluorescence in red blood cell (RBC) containing perfusate and plasma. Alternatively, an experimental spectroscopy setup was used to determine the NMP-PDR using fluorescence in plasma. The NMP-PDR is expressed in %/L·Kg (median and interquartile range).

Results

A comparison between ICG concentrations measured in standard curves using absorbance and fluorescence revealed a linear correlation between certain ICG concentrations. We did notice lower NMP-PDR scores using fluorescent-based methods compared to the absorbance-based NMP-PDR. However, the fluorescent-based NMP-PDR retained significant differences between transplanted livers (11.7 (9.9-18.3), n=11) and non-transplanted livers (7.8 (5.8-8.9), n=7) with a P-value of 0.027. Next, the NMP-PDR was determined directly in RBC containing NMP perfusate without sample processing. A significant difference (P=0.037) was observed between transplanted livers (13.4 (10.7-18.4), n=11) and non-transplanted livers (7.8 (6.1-9.9), n=6). Linear correlations were observed between measurements using an experimental spectrometry setup and a plate reader in plasma (R2 $\geq$ 0.98, n=10) and RBC containing perfusate (R2 $\geq$ 0.98, n=9).

Conclusions

Fluorescence-based ICG quantification for the determination of the NMP-PDR is a promising method for assessing graft viability of ECD-DCD livers during NMP. ICG can be measured in plasma and perfusate samples using fluorescence. Excellent correlations between the experimental spectrometry setup and fluorescence measurements were observed. These findings represent important steps towards clinical implementation of point-of-care assessment of liver viability using the NMP-PDR.

Cost-Effectiveness Of Prolonged Hypothermic Oxygenated Machine Perfusion Enabling Daytime Liver Transplantation

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Background

Short-duration (1–2 h) dual hypothermic oxygenated perfusion (DHOPE) reduces ischemia−reperfusion injury and improves post-transplant outcomes compared with static cold storage. Prolonged DHOPE preservation (DHOPE-PRO) may facilitate logistics and allows livers to be preserved overnight, enabling transplantation during regular hours. This study evaluated the economic impact of DHOPE-PRO compared with conventional short-duration DHOPE, hypothesizing cost-neutrality at one year.

Methods

This post-hoc economic evaluation of the prospective DHOPE-PRO trial (NL8740) included adult recipients of livers donated after brain death. All transplantation-related medical expenses up to one-year post-transplant were collected. Cost of resource use was calculated using 2022 full hospital prices indexed to 2024. Time-driven variable costing was applied to perfusion, surgery, and intensive care costs. The primary endpoint was total one-year transplantation-related cost per patient.

Results

Twenty-four patients were analyzed (12 DHOPE, 12 DHOPE-PRO). Median total one-year costs were €83,583 [IQR 78,400−104,158] for DHOPE and €78,582 [IQR 73,123−92,855] for DHOPE-PRO (p=0.347). Perfusion costs were higher for DHOPE-PRO (€23,926 [IQR 22,711−24,697] versus €17,306 [IQR 16,928−17,594]; p<0.001), whereas surgery costs were lower (€18,560 [IQR 17,806−20,747] vs €21,303 [IQR 19,535−25,418]; p=0.033). ICU and other postoperative costs did not differ between groups.

Conclusions

DHOPE-PRO enables scheduled daytime liver transplantation without increasing total one-year costs. Higher perfusion expenses are balanced by lower surgical costs due to improved logistics and reduced night-time activity. These findings support DHOPE-PRO as a cost-neutral strategy that enhances patient and staff safety, optimizes resource use, and may facilitate broader clinical implementation of machine perfusion in liver transplantation.

Nitazoxanide For Enterocytozoon Bieneusi Infection Treatment In Renal Transplant Recipients: Case Series

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Background

Microsporidiosis caused by *Enterocytozoon bieneusi* is an opportunistic infection in solid organ transplant recipients. The mainstay management involves tapering immunosuppressive therapy to aid the immune system in clearing the microsporidia. However, immunosuppressant reduction will not always result in pathogen clearance and might be unfeasible due to the risk of transplant rejection. In this report, we present clinical case series of nitazoxanide treatment for refractory *E. bieneusi* infection and summarize the evidence regarding existing antimicrobial therapeutic options.

Methods

We retrospectively analyzed three cases involving renal transplant recipients treated with nitazoxanide for chronic relapsing-remitting diarrhea caused by *E. bieneusi* accompanied by either wasting, hospital admissions, and/or acute kidney injury. In addition, we performed a literature review focusing on two most frequently investigated antimicrobial therapies for *E. bieneusi* infection, namely fumagillin (an antibiotic derived from the fungus *Aspergillus fumigatus)* and nitazoxanide (a thiazolide discovered for the treatment of tapeworm infections).

Results

Limited evidence exists for the efficacy of fumagillin and nitazoxanide as treatment options for *E. bieneusi* infection in immunocompromised patients. The effectiveness of fumagillin has been described in a small (*n* = 12) randomized controlled trial and several case reports.

Fumagillin is not widely available and has been linked to serious adverse reactions, such as hepatotoxicity, bone marrow suppression, and aseptic meningitis. In agreement with the existing literature, we describe the clinical course of *E. bieneusi* infection in three renal transplant recipients with persistent symptoms despite aggressive immunosuppressive therapy tapering. The patients were treated with nitazoxanide (500–1000 mg b.i.d. per os), leading to rapid symptom cessation in all cases and proven definitive pathogen eradication in two cases. No significant side effects were observed.

Conclusions

Solid organ transplant patients can suffer from chronic relapsing-remitting *E. bieneusi* infection despite optimal immunosuppressive regimen tapering. We propose nitazoxanide as a first-line antimicrobial therapy for *E. bieneusi* infection with high efficacy and a favorable side effect profile.

Distinct FMN Release Patterns During DHOPE In DCD V vs DCD III Donor Livers Despite Comparable Biliary Outcomes

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Background

In an attempt to decrease donor organ shortage, some countries allow transplantation of organs donated after euthanasia (Donation After Circulatory Death [DCD] Type-V, DCD-V). Similar to grafts from DCD Type-III (DCD-III), DCD-V organs experience a period of warm ischemia, which can lead to post-transplant complications. Donor warm ischemia time is significantly shorter in DCD-V donors, potentially resulting in improved outcomes. Flavin mononucleotide (FMN), a marker of mitochondrial complex I injury, provides insight into graft mitochondrial integrity.

Methods

In this retrospective study we analyzed perfusate samples during DHOPE at multiple timepoints of DCD-III and DCD-V liver transplantations between 2018 and 2024. FMN concentrations were quantified by fluorescence spectrometry and analyzed over time. Minimal follow-up was 12 months. FMN concentrations were correlated to DCD type and post-operative complications, including biliary complications at 1 year.

Results

A total of n=100 DCD-III and n=28 DCD-V liver transplantations were analyzed. Donor BMI was similar in DCD-V and DCD-III donors 22.5 (21.0-26.0) vs 24.0 (21.0-25.0), however DCD-V donors were significantly younger than DCD-III donors (36 years (30-53) vs 50 years (36-56) p=0.021). Also, last ALT levels were significantly lower in DCD-V donors (22IU/L (13-26) vs 49 IU/L (13-96) p<0.001). Recipient characteristics including age and LabMELD similar in both groups. FMN release was significantly lower in DCD-V grafts compared with DCD-III at 60 min of DHOPE (0.023 µg/ml (IQR 0.020-0.0349) vs 0.032 µg/ml (IQR 0.024-0.043), p < 0.036), indicating reduced mitochondrial injury. The incidence of biliary complications at 1 year post transplant were similar in both groups, 50% (14/28) in DCD-V vs 35% (35/100) in DCD-III, p=0.171. The incidence of post-transplant cholangiopathy was 11% in DCD-V (3/28) vs 9% in DCD-III (9/100), p=0.808.

Conclusions

DCD-V grafts exhibit lower mitochondrial injury during DHOPE compared with DCD-III, yet have similar incidences of biliary complications after transplantation compared to DCD-III. These findings suggest that biliary complications in DCD-V are less likely to result from ischemia−reperfusion−induced mitochondrial dysfunction and may instead be influenced by donor-related or pharmacological factors.

Two-Stage Liver Transplantation, CVVHDF And Plasmapheresis With Normothermic Machine-Perfused Graft In Acute Liver Failure: A Case Report

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Background

Liver transplantation in critically ill patients with acute liver failure (ALF) is challenging, especially when profound hemodynamic instability and multiorgan failure exist, often rendering transplantation futile. Emerging technologies such as normothermic machine perfusion (NMP) and extracorporeal detoxification therapies may extend stabilization time during the anhepatic phase while maintaining graft viability.

Methods

A 27-year-old female presented with ALF due to idiosyncratic drug-induced liver injury. Despite N-acetylcysteine therapy, she progressed to renal, respiratory, and circulatory failure requiring continuous renal replacement therapy (CVVHDF), mechanical ventilation, and high-dose vasopressors (0.94 µg/kg/min Noradrenaline, 1.77 µg/kg/min Terlipressin). She was urgently listed for liver transplantation on day seven after fulfilling the King's College criteria, but her condition continued to deteriorate, with rapid progression to severe coagulopathy, tense ascites, and marked lactic acidosis (peak lactate 14.5 mmol/L). Plasmapheresis was added to ongoing CVVHDF.

An 83-year-old donation-after-brain-death (DBD) liver graft was accepted and maintained on NMP (OrganOx Metra®). Due to the recipient's instability, a one-stage liver transplantation was considered futile, and a two-stage transplantation strategy was adopted. In the first stage, hepatectomy and a temporary portocaval shunt were performed, while the donor liver remained viable on NMP. The patient returned to ICU for hemodynamic optimization with only CVVHDF. Over a ten-hour anhepatic period, vasopressor requirements halved, acidosis improved, and neurological function remained intact. The second stage—artery-first reperfusion and definitive graft implantation—was subsequently completed.

Results

Estimated blood loss was 500 mL and 1,800 mL during the first and second stages, respectively. Two units of packed red cells and two units of fresh frozen plasma were transfused during the second operation. Postoperatively, the patient developed pneumonia, which resolved with antibiotics. Renal function fully regained, and she was discharged on postoperative days 7 and 15 from the ICU and hospital, respectively, without major complications and with full recovery.

Conclusions

This case demonstrates that in ALF with severe multiorgan failure and circulatory collapse, the combined use of plasmapheresis, CVVHDF, staged liver transplantation, and graft preservation via NMP could enable successful recovery. Maintaining the graft on NMP permits prolonged patient stabilization during the anhepatic phase and preserves the option of graft reallocation if transplantation becomes unfeasible.

Validating The Igls Criteria 2.0 For Graft Outcomes In Patients With Islet Transplantation

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Background

Reliable assessment of β-cell replacement functional outcomes is imperative for clinical follow-up, decision making, comparing and benchmarking different transplantation (Tx) options. Currently, multiple scoring methods are available to define graft outcomes. Igls criteria 1.0 (Igls 1.0) were the first standardised approach, recently updated to a proposed Igls criteria 2.0 (Igls 2.0). In this study, we validated Igls 2.0 in islet transplant (ITx) recipients.

Methods

We included data from all first ITx recipients (2007-2023) in our centre. Islet graft function was scored at 6 months post-Tx using Igls 1.0 and Igls 2.0. Both criteria categorize outcome as Optimal, Good, Marginal or Failure. Igls 1.0 is based on HbA1c, severe hypoglycaemic episodes (SHE), insulin requirements and C-peptide. Igls 2.0 distinguishes treatment outcome (Igls 2.0 T) based on HbA1c and SHE or CGM time-in-range and time-in-hypo, and graft outcome (Igls 2.0 G) based on C-peptide and insulin requirements.

Results

We analyzed 56 islet transplant alone (17.2%), islet-after-kidney (75.9%) or islet-after-lung (3.4%) recipients (age 60.2±10.2 years; 33.9% female). According to Igls 1.0, outcome was Optimal in 9.6%, Good in 63.5%, Marginal in 19.2%, and Failure in 7.7%. According to Igls 2.0, treatment outcome T was Optimal in 50.0%, Good in 28.8%, Marginal in 21.2%, and Failure in 0.0%, and graft outcome G was 11.8%, 80.4%, 2.0%, and 5.9%, respectively. In 66.0% of cases, Igls 2.0 were different to Igls 1.0. In all (35/35) of these cases, the Igls 2.0 domains of treatment and graft outcome differed from each other (T Optimal with G Good in 60.0%, T Marginal with G Good in 25.7%), and Igls 1.0 scored similar to the lowest of these two domains, underestimating either treatment or function. When Igls 1.0 scored Marginal (n=9), Igls 2.0 further distinguished this to Marginal treatmegraftnt outcome T with Good graft function G in 88.8%. Using CGM yielded similar treatment outcome as using HbA1c in 77.8%. When different, CGM-based treatment outcome was more similar to the corresponding graft outcome.

Conclusions

Igls 2.0 provide a finer distinction between clinical treatment outcome and graft function. Using CGM in Igls 2.0 compared to only HbA1c seems to correspond better to graft outcome.

Similar Islet Graft Function With Fewer And Less Severe Side-Effects In Basiliximab Compared To Alemtuzumab Induction Immunosuppression For Islet Transplantation

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Background

T-cell depletion as induction immunosuppression (iIS) is often used in islet transplantation (ITx) but comparisons with other iIS regimens on efficacy and safety are lacking. At the Leiden University Medical Centre we switched from mainly using the T-cell depleting agent alemtuzumab to basiliximab as iIS during the COVID-19 pandemic. This allowed for comparison of different outcome measures between the two regimens.

Methods

This is a single-center, retrospective study comparing basiliximab to alemtuzumab as iIS for all first ITx recipients with at least 3 months of post-ITx data between 2007–2024. Islet graft function was assessed using the area-under-the-curve (AUC) of C-peptide during a mixed meal tolerance test (MMTT). Igls criteria 2.0 were used as clinical outcome parameter. Reported infections and side-effects were extracted from patients' electronic health records. Data were analysed at baseline and 3 months post-ITx.

Results

Data of 63 first ITx recipients were analysed, of which 28 (44.4%) received basiliximab and 35 (55.6%) alemtuzumab. At 3 months post-ITx, patients receiving basiliximab showed similar islet graft function compared to recipients receiving alemtuzumab (AUC C-peptide 120.8 [76.6–235.1] *vs* 120.0 [83.7–193.2; p=0.581]). There was no difference in Igls 2.0 Treatment outcome in basiliximab *vs* alemtuzumab (Optimal 57.1% *vs* 67.6%, Good 32.1% *vs* 8.8%, Marginal 10.7% *vs* 17.6%, Failure 0.0% *vs* 5.9%, respectively; p=0.081). CD3+ T-cells were higher (p<0.001) and infections less often reported in the basiliximab group (28.6% vs 55.9%; p=0.031). There was no kidney function decline in the basiliximab group (eGFR 59.9 ± 20.4 to 59.2 ± 21.9 mL/min/1.73m^2 [p=0.411] but a significant reduction in the alemtuzumab group (56.2 ± 18.5 to 48.4 ± 15.8 mL/min/1.73m^2 [p<0.001]). Severe side-effects (CTCAE grade 3 or 4) were only present in the alemtuzumab group.

Conclusions

Basiliximab results in similar islet graft function as alemtuzumab, but with fewer and less severe side-effects at 3 months post-transplantation.

Attitudes And Acceptance Among Liver Transplant Recipients For Self-Measuring With Home-Monitoring (LASER-Study)

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Background

Self-monitoring offers the potential for liver transplant recipients (LTRs) to monitor outcomes which are integrated into the patient records for improved patient-professional collaboration and aftercare. This study aimed to assess the relationship between attitudes, expectations and experiences with the self-monitoring system in the first year post-transplant.

Methods

This prospective cohort study included LTRs between 1-6-2023 until 31-05-2024. The questionnaire was based on Unified Theory of acceptance and Use of Technology (UTAUT-32) which measured the subscales of expected load, facilitating conditions, social influence, fear, data security, self-efficacy and intention to use. Engagement in health was measured using the Patient Activation Measure - 13. All measures used a 5-point Likert scale. Subsequent measurements were during admission (prior to start of self-monitoring), 3, 6, 9 and 12 months. Correlation analysis was performed between outcomes.

Results

A total of 58 participants were included, of whom 28 (49%) were female, median age was 57 (IQR 21). Inclusion and retention is shown in Figure 1. At baseline participants showed Intention to use (M= 3.14 $\pm$ .47), confidence

using new technology (Self-Efficacy M= 3.38 ± .49), feeling Informed & engaged (M= 2.75 ± .52), expected good Facilitating conditions (M= 3.08 ± .49), and did not expect more burden (Expected load (M= .71 ± .45) or negative social influence (Social influence M= 3.00 ± .51). They also reported low Fears (M = 1.21 ± .49) and concerns about Data Security (M= 3.0 ± .47). At baseline engagement in health was positively correlated with feeling Informed & engaged (r=.52 p<.001), Facilitating conditions (r = .55 p< .001), Intention to use (r= .56 p< .001) and, and Social influence (r= .47 p=.001). Furthermore, negatively correlated with Expected load (r= -.58 p< .001) and Fear (r=-.42 p= .004). Fear (Δ= .59 p=.005) and Self-Efficacy (Δ= .74 p<.001) significantly decreased between baseline and 6 months.

Conclusions

Before initiating self-monitoring, attitude and expectations were generally positive. During the first 6 months support may be required to promote use to reduce burdens and fears. These findings can help improvement of the self-monitoring use and thus post-transplant care.

Longitudinal Trends In Proton-Pump Inhibitor Use And Indication Validity Among Solid Organ Transplant Recipients

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Background

Proton-pump inhibitors (PPIs) are frequently prescribed to solid organ transplant recipients (SOTRs). Prolonged PPI therapy has been associated with adverse outcomes such as micronutrient deficiencies, fractures, and infections in kidney transplant recipients. Longitudinal data describing PPI use across the broader transplant population are limited. We aimed to characterize longitudinal trends in PPI utilization and indication validity among SOTRs, and to examine the association of long term PPI use with micronutrient deficiencies during the post-transplant course.

Methods

Longitudinal data from SOTRs were collected pre-transplantation, and at 0, 3, 6, 12, 24, and 60 months post-transplantation. PPI use was extracted from electronic health records, and valid indications were determined based on Dutch national guidelines for prevention of medication-induced gastric complications and local transplantation protocols. Long-term PPI use was defined as continuous PPI use ≥12 months. Micronutrient deficiencies in magnesium, calcium, phosphate, and vitamin B12 were investigated. Group differences were assessed using ANOVA, Kruskal–Wallis or Chi-square test. Associations were assessed using logistic regression analyses.

Results

We included 2100 SOTRs (kidney, liver, lung and heart transplant recipients), mean age 56±14 years and 39% females at 12 months post-transplantation. PPI use increased from 56% pre-transplant to 90% at 3 months post-transplant, declining to 68% at 60 months. Throughout the transplantation trajectory, the proportion of patients without a valid indication ranged between 66% and 76%, excluding the 3-month post-transplantation timepoint. Among 1747 patients with data on multiple timepoints, 993 (57%) showed prolonged PPI use, 648 (37%) short-term use, whereas 106 (6%) SOTRs did not use a PPI during the transplant trajectory. Hypomagnesemia occurred more frequently in short- and long-term PPI users than in non-users (53.3% and 44.0% vs. 15.1% resp.; p<0.05). Similar patterns were seen for hypophosphatemia (32.9% and 28.5% vs. 5.1% resp.; p<0.05). Frequency of hypocalcemia and vitamin B12 deficiency did not differ between groups.

Conclusions

PPI use remains high in SOTRs, often without a valid indication. Our study shows an association with hypomagnesemia and hypophosphatemia, regardless of treatment duration. These findings emphasize the importance of periodic reassessment of ongoing PPI therapy to prevent unnecessary exposure and potential adverse effects.

Ureteral Reconstruction After Renal Transplantation: 10-Year Overview From A Tertiary Academic Center

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Background
Although kidney transplantation outcomes have improved over time, urological complications still account for a considerable proportion of postoperative morbidity, with incidences reported between 2.5% and 30%. In a cohort from our center between 1995 and 2009, Alberts et al. (2011) reported that 5.2% of recipients required surgical ureteral reconstruction and identified ureteral stenting during transplantation as a protective factor, which has since become standard practice. Since then, surgical techniques have evolved, and robot-assisted approaches have been introduced with promising results in both transplant surgery and ureteral reconstruction. This study provides a 10-year update from our tertiary academic center, assessing current incidence, management, and outcomes of ureteral reconstruction after kidney transplantation.

Methods
Between January 2015 and September 2025, 2,000 kidney transplants were performed, including 73 robot-assisted kidney transplants (RAKT). Patient charts and operative reports were reviewed retrospectively.

Results
Surgical ureteral reconstruction was required in thirty-five patients (1.8%). Fifteen patients (42.9%) received neoureterocystostomy, 17 (48.6%) ureteropyelostomy reconstruction, and three (8.6%) other techniques. Two neoureterocystostomies and one ureteropyelostomy were performed robotically. Reoperation was required in two ureteropyelostomy cases and one case who received a pyelovesicostomy; none of the robotic ureteral reconstructions required reintervention. Among 73 robotic kidney transplants, two patients (2.7%) required ureteral revision.

Conclusions
Over the past decade, the incidence of ureteral reconstruction decreased to 1.8%, compared with 5.2% in the earlier cohort from our center. Regarding urological complications robot-assisted techniques were successfully applied in both primary transplantation and selected ureteral reconstructions, suggesting a safe and effective role for robotic surgery in modern kidney transplantation.

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Kidneys From Older Donors After Circulatory Death Plus Normothermic Regional Perfusion Or Standard Rapid Retrieval Have Comparable Function In The Context Of Ex-Situ Hypothermic Machine Perfusion

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Background

With growing transplant waiting lists, optimizing donor organs is necessary to increase utilization. Normothermic regional perfusion (aNRP) benefits the outcomes of transplanted livers and pancreatic islets, but its effects on donor kidneys subsequently preserved on hypothermic machine perfusion (HMP) remain to be determined. This study examines function and survival of aNRP-perserved donation after circulatory death (DCD) kidneys followed by HMP.

Methods

From October 2018 until June 2023, we evaluated all kidneys from DCD donors, aged ≥ 50 years, with impaired liver function and declined livers, retrieved using aNRP in a pilot implementation project in the Netherlands and compared them to comparable DCD kidneys retrieved by standard rapid retrieval (SRR) during the same period. All kidneys were subsequently preserved with HMP or oxygenated HMP. Data was used from the Dutch Organ Transplantation Registry. This study primarily compared eGFR (CKD-EPI), one year graft and recipient survival. Secondary outcomes were primary non-function, delayed graft function and long-term graft and recipient survival.

Results

Data of 85 aNRP-preserved kidneys were compared to a control group of 178 kidneys. One year eGFR was comparable between groups (40.7 [28.9-52.4] vs. 40.1 [29.8-48.2]; p=0.5), as well as graft and recipient survival at one year, (HR=1.3, 95%CI 0.7-2.3, p=0.4 and HR=1.2, 95%CI 0.5-2.7, p=0.7, respectively). Delayed graft function occurred more frequently in the aNRP kidneys (OR=1.8, 95%CI 1.0-3.2, p=0.03), but not if oxygenated HMP was used.

Conclusions

This study shows that aNRP-preserved kidneys from DCD donors ≥ 50 years have comparable outcomes to kidneys retrieved with SRR, in the context of HMP as standard ex-situ preservation technique. This is different from earlier results showing improved results of aNRP in the context of cold storage. Delayed graft function was slightly more common in aNRP kidneys, without consequences for survival or graft function at one year.

Insights Into The Relatives' Experiences With The Procedure Of Organ Donation After Euthanasia; A Preliminary Analysis

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Background

Organ donation after euthanasia (ODE) has been increasingly performed since the first case in Belgium in 2005. Limited information is available on the experiences of patients and their relatives. Insights from these individuals are essential for refining existing guidelines, addressing ethically sensitive aspects and supporting countries developing new ODE frameworks. Because directly studying patients at the end of life poses ethical and emotional challenges, the perspectives of relatives provide valuable indirect insight into patient experiences and the overall ODE process.

Methods

This is a retrospective multicenter questionnaire study. Relatives of patients who donated organs after euthanasia within the past seven years were invited via their organ donation coordinator (ODC). Participation was voluntary. The online questionnaire covered four domains: experiences before, during, after the ODE procedure, and demographic information.

Results

Fifteen relatives were approached, all expressed interest and completed the online questionnaire, with twelve relatives completing it in full (80%). The key findings were that 83% of patients found information on ODE online,

while only 17% were informed by their treating physicians. All patients independently made the request, and 33% of physicians reported limited or no knowledge of ODE.

All relatives found the information from the ODC clear and comprehensive, though 33% noted unexpected situations during the procedure. None felt pressured by physicians or the ODC to donate organs, postpone, or cancel the timing of euthanasia.

All relatives believed the patients would have made the same choice again, and 10 out of 12 reported that ODE helped in their mourning process. All relatives expressed a positive view of the procedure.

Conclusions

This study shows that the ODE procedure is well-executed in the Netherlands and viewed positively by relatives. While the information from the ODC is generally clear, more education on ODE is needed for treating physicians.

Living Kidney Donation Prior To Euthanasia: Lessons Learned From A Dutch Case Series

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Background

While deceased donation *after* euthanasia has been previously been conducted, living donation (LD) *prior to* euthanasia has never been reported and is absent from current clinical guidelines. This study aims to (1) share a case series of living donation prior to euthanasia and (2) discuss the unique medical, procedural, psychological and ethical considerations.

Methods

At our centre, 3 donor candidates with a euthanasia wish due to untreatable psychiatric illness were evaluated. All were female, aged between 20-60 years. Donor-recipient relationships were specified (1 genetically related, 1 unrelated) and unspecified. Of the 3 candidates, 2 donated; one was declined for medical reasons. In both cases, donation was experienced as positive by both donor and multidisciplinary team. As part of standard evaluation we assessed the likelihood of any pre-existing physical or psychological conditions worsening as a result of donation, and did not observe any detrimental effects after donation. In two cases, to date, euthanasia has been performed and in one case the request for euthanasia was retracted after donation.

Results

We identified possible challenges and lessons for similar cases in the future. Medically, kidney function should be assessed under the presumption that remaining kidney function will need to sustain long-term health as subsequent euthanasia remains uncertain. Procedurally, timing may be difficult: if euthanasia is scheduled before transplant need arises, requests to postpone euthanasia may feel coercive or harmful. Psychologically, donation could exacerbate mental health symptoms, but being declined for donation may also cause psychological harm. Ethically, capacity to consent must be rigorously assessed, especially given the degree of mental suffering. Strategies to overcome these challenges include discussions with the multidisciplinary team, the candidates themselves, their informal support networks, General Practitioners and mental health teams.

Conclusions

We conclude that living donation and euthanasia should be seen as separate and independent processes and that a euthanasia request should not be considered an absolute contra-indication for living donation. Our initial experiences underscore the need for dialogue and policy on living kidney donation prior to euthanasia.

Cardiopulmonary Outcomes And Exercise Capacity In DCD And DBD Heart Transplant Recipients

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Background
Heart transplantation (HTx) using donation after circulatory death (DCD) has become an increasingly important strategy, contributing to a rise in HTx-procedures. While survival is comparable between DCD and donation after brain death (DBD), little is known about potential differences in post-HTx exercise capacity between recipients of these donor types.

Methods
This single-center retrospective study included all patients who underwent HTx between January 2022 and September 2024 and completed a cardiopulmonary exercise test (CPET) at 1-year follow-up. Peak oxygen consumption (pVO2) and other exercise capacity measures, as well as echocardiographic parameters and laboratory values were compared between recipients of DCD and DBD donor hearts.

Results
In total 45 DCD and 30 DBD recipients were analyzed. No significant differences were found between groups regarding recipient age (49 ± 10 vs.52 ± 12 years, respectively; p=0.99), sex (24 vs. 33% female, p=0.56), primary cause of heart failure (dilated cardiomyopathy: 76% vs. 63%; p=0.12), donor age (36 ± 11 vs. 39 ± 15 years; p=0.28) or primary graft dysfunction (7 vs 7%; p=1.0). Allograft ischemic time was shorter in DCD than DBD (133 [120-155] vs 179 [162-196] min; p<0.001), while the time on organ care system (DCD) was 274 ± 74 min.

Time from HTx to CPET was similar (361 ± 18 vs. 366 ± 32 days, p=0.46). There were no differences in peak VO_2 (19.3 ± 5 vs. 19.3 ± 7 ml/min/kg; p=0.93), % predicted VO_2 (62 ± 19 vs. 65 ± 21%; p=0.55), VE/VCO_2 slope (35 ± 5 vs. 36 ± 4; p=0.52), respiratory exchange ratio (1.15 ± 0.09 vs. 1.17 ± 0.08; p=0.56), or heart rate response ($+39\pm20$ vs. $+43\pm24$ bpm; p=0.43). LV ejection fraction (55 ± 5 vs. 57 ± 4%; p=0.23), TAPSE (15 ± 3 vs. 15 ± 4 mm; p=0.99), hemoglobin (8.1 ± 0.9 vs. 7.9 ± 1.0 mmol/L; p=0.30) and NT-proBNP levels (389 [184-729] vs. 516 [327-899] ng/L; p=0.43) were also comparable.

Conclusions
Recipients of DCD and DBD donor hearts showed comparable exercise capacity 1-year after HTx. These findings support the use of DCD HTx without compromising functional outcomes.

BLAD-r-d-, BLAD-r+d-, BLAD-d+r- Or BLAD-d+r+, Variations In A Theme!

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Background
Baseline Lung Allograft Dysfunction (BLAD) is currently defined as post-lung transplant (LTx) baseline lung function (FEV1 and/or FVC) $\leq$ 80% predicted recipient reference values. This definition does not account for donor-recipient lung size mismatch. The aim of this study was to identify the definition of BLAD that best correlates with clinical outcomes.

Methods

All adult bilateral LTx recipients transplanted until June 1st 2024 in our center were included. Recipient predicted lung function values and donor predicted values calculated using the Global Lung Initiative calculator were used. Patients with BLAD-r+d- fulfilled criteria for BLAD only according to recipient normal values but not for donor normal values. BLAD-d+r- fulfilled criteria for BLAD only according to donor normal values but not for recipient values. BLAD-dr had BLAD by both definitions and BLAD-r-d- did not have BLAD.

Results

641 patients were included. 263 (41%) had no BLAD (BLAD-r-d-), 72(11,2%) had BLAD-r+d-, 91(14,2%) had BLAD-d+r- and 215(33,5%) BLAD-dr. Donor-recipient lung mismatch was -11,1% for patients with restrictive lung disease (Fib) and +4,53% in COPD. Fib received in 26% more than 20% undersized donor lungs while almost 10 % of the COPD recipients received lungs more than 20% oversized.

Median survival of BLAD-d-r- was 14,25 yrs, for BLAD-r+d- 16,25 yrs (p=NS), for BLAD-d+r- 11.05 yrs (p=NS) while only patients with BLAD-d+r+ had a significantly shorter survival of 6.7 yrs (p<0,001).

Conclusions

Donor-recipient lung mismatch leads to different grading of BLAD. Strikingly only pts with BLAD according to both definitions (BLAD-d+r+) had a worse survival and might be best to analyze risk factors for BLAD.

Donor Anti-Cytomegalovirus IgG Titer And Risk Of Cytomegalovirus Infection After D+R- Kidney Transplantation

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Background

Primary cytomegalovirus (CMV) infection is an undesirable complication after kidney transplantation and is associated with adverse graft and patient outcomes. Despite prophylactic treatment, nearly half of CMV-seronegative recipients that receive a kidney from a CMV-seropositive donor (D+R-) experience primary CMV infection. We hypothesized that high anti-CMV immunoglobulin G (IgG) titers of CMV seropositive donors are a risk factor for primary CMV infection in D+R- kidney transplantations, since high titers may reflect more intense prior CMV viremia, with more extensive CMV dissemination, and an impaired cell-mediated CMV response.

Methods

Anti-CMV IgG titers were measured using enzyme immunoassay. CMV infection episodes were identified from medical records. CMV infection was defined as the presence of a positive CMV polymerase chain reaction (PCR) and/or seroconversion to positive anti-CMV IgG in a previously seronegative recipient. Cox regression analyses were performed to evaluate determinants of the risk of CMV infection. Multivariable Cox regression analysis was performed with adjustment for recipient age, recipient sex and donor age as potential confounders.

Results

A total of 99 D+R- kidney transplant recipients (KTR) with a living kidney donor were included and assessed at 6 months post-transplantation. The mean age was 50.1 ± 14.6 years and 26 (26.3%) were female. Overall, 37 (37.4%) developed CMV infection in the year after the study visit. KTR with donors who had an anti-CMV IgG titer above 250 AU/mL (n = 17; 17.2%) had a significantly increased risk of CMV infection compared to those with lower donor titers (hazard ratio = 3.54, 95% confidence interval = 1.69−7.40; p<0.001). This association remained independent of adjustment for recipient age, sex, and donor age (hazard ratio = 5.09, 95% confidence interval = 2.26−11.47; p<0.001).

Conclusions

High donor anti-CMV IgG titer is associated with an increased risk of CMV infection in CMV-seronegative KTR. These findings support the theory that a high anti-CMV IgG titer reflects more extensive CMV dissemination, a poorer cell-mediated CMV response, or both. Donor anti-CMV IgG titer might be a valuable parameter to identify KTR at higher risk of CMV infection and to potentially optimize or extend antiviral prophylaxis and post-transplant monitoring strategies.

Human CD4+ T Cell Engraftment In A Human Kidney Organoid Mouse Model Requires Support From T Cell-Depleted PBMCs

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Background

Fibrosis is a major cause of kidney allograft failure. The angiotensin II type 1 receptor (AT1R)-reactive CD4+ T cells are enriched in transplanted kidneys, correlate with fibrosis severity, and exhibit a pro-fibrotic cytokine profile. To investigate their role in inducing fibrosis, we are developing an in vivo model using human pluripotent stem cell-derived kidney organoids implanted in immunodeficient mice. This system provides a physiologically relevant platform to study human immune responses via adoptive transfer. Peripheral blood mononuclear cells (PBMCs) allow reliable T cell engraftment in this model, but it is unknown whether isolated CD4+ T cells can successfully engraft.

Methods

CD4+ T cells were isolated from PBMCs and used either unstimulated or after two-week expansion. Expansion was performed polyclonally (anti-CD3/anti-CD28-coated beads) or antigen-specifically (AT1R protein), both in the presence of IL-2 and IL-15. CD4+ T cell engraftment efficiency was evaluated with or without T cell-depleted PBMCs. Immunodeficient mice received intraperitoneal injections of either 5 million unstimulated or expanded CD4+ T cells alone, or combined with 2.5 million T cell-depleted PBMCs. PBS and PBMCs were administered as negative and positive controls, respectively. After four weeks, human T cell populations in blood and spleen were analyzed by flow cytometry.

Results

Engraftment of CD4+ T cells alone was poor for unstimulated cells and virtually absent for expanded cells. Co-transfer with T cell-depleted PBMCs markedly enlarged spleens and increased T cell numbers by 148-fold in spleen and 51-fold in blood compared to expanded CD4+ T cells alone. Similarly, co-transfer led to larger spleens and 4-fold and 100-fold increases in spleen and blood T cell numbers, respectively, compared to unstimulated CD4+ T cells alone. Notably, mice receiving unstimulated CD4+ T cells, either alone or with T cell-depleted PBMCs, exhibited larger spleens and higher T cell numbers than those receiving the corresponding expanded cells. Human leukocytes isolated from the spleens were identified as CD4+ T cells and B cells with few monocytes. These cells were reused successfully for engrafting other mice.

Conclusions

Successful engraftment of human CD4+ T cells in immunodeficient mice requires support from non-T cells, most likely B cells, with the option to reuse engrafted spleen cells.

Introduction Of Robot-Assisted Living Donor Right Hepatectomy In The Netherlands: A Video Case Report

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Background

Living donor liver transplantation (LDLT) helps reduce waitlist mortality, even in regions where deceased organ donation predominates. Donor safety is paramount, and robotic liver surgery has shown potential for faster recovery and fewer complications. We report our first experience performing a fully robotic right hepatectomy in a living donor, outlining the key technical steps and perioperative outcomes.

Methods

The donor was positioned supine with both arms tucked and placed in a 22° reverse Trendelenburg position. Four robotic trocars were inserted along the umbilical line, with an additional assistant port at the umbilicus. The right liver was mobilized by sequential division of the falciform, right triangular, and coronary ligaments. The right−middle hepatic vein boundary was identified on the liver surface, and the caudate lobe was detached from the inferior vena cava (IVC) to create a tunnel between the hepatic veins.

After retrograde cholecystectomy, the right portal vein and hepatic artery were dissected. Temporary clamping and indocyanine green (ICG) fluorescence delineated the Cantlie line, guiding parenchymal transection. Using the hanging maneuver, the transaction was completed. ICG fluorescence identified the right hepatic duct before division, ensuring an adequate stump for closure.

When the recipient team was ready, the vascular structures were divided, and the graft was extracted through a 12-cm Pfannenstiel incision. Hemostasis and biliostasis were confirmed before closure. The donor was transferred to the intensive care unit for monitoring.

Results

Intraoperative blood loss was 1,000 mL, and operative time was 744 minutes. Postoperatively, a rectus hematoma was diagnosed which was managed conservatively. US and CT scan showed patent vessels and no other complications. The donor was discharged on postoperative day 7. At six weeks, he showed complete recovery with normal liver function, satisfactory remnant hypertrophy, and no complications.

Conclusions

This case demonstrates the feasibility and safety of a fully robotic right hepatectomy in a living donor program without prior open experience. The robotic platform allows precise dissection, potential lower blood loss, and rapid recovery, supporting its role as a safe and reproducible approach for developing living donor liver transplantation programs.

Robot-Assisted Kidney Transplantation Compared To Open Kidney Transplantation In Living Donor Recipients: A Propensity-Score Matched Cohort Study Of Initial Outcomes

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Background

Kidney transplantation is the definitive treatment for end-stage renal disease. While conventional open kidney transplantation (OKT) is the traditional standard, robot-assisted kidney transplantation (RAKT) offers a minimally invasive alternative, potentially mitigating challenges and complications associated with the invasiveness of open surgery.

Objective

To assess the perioperative and clinical outcomes of RAKT compared to OKT in living donor recipients.

Methods

This single-center, retrospective cohort study analyzed all consecutive RAKT procedures against 1:1 propensity score-matched OKT procedures from January 2021 until November 2024 in living donors. The main outcomes were intraoperative results, postoperative results, and postoperative graft function.

Results

From 304 living donor transplantations (254 OKT and 50 RAKT), 50 RAKT and 50 propensity-score matched OKT patients were included, with comparable baseline characteristics. The RAKT group had a significantly lower incidence of postoperative complications (24% vs. 52%, P=.004) and severe complications (Clavien-Dindo grade $\geq$IIIa) (4% vs. 18%, P=.025). This translated to a shorter median hospital stay (7 vs. 8 days, P=.045) and lower 24-hour median pain scores (3 vs. 4 VAS, P=.011) in favor of RAKT. Intraoperative times were longer for RAKT, including mean operative time (241 vs. 158 min, P<.001), mean anastomosis time (44 vs. 28 min, P<.001), and mean cold ischemia times (227 vs. 187 min, P=.004). RAKT demonstrated significantly less median estimated blood loss (75 vs. 150 mL, P <.001). Intraoperative complications were similar (2 vs 3, P=.646), with 4 conversions in the RAKT group. No significant differences were observed in the 3-month mortality rate (P=.495), incidence of rejections (P=.488) or graft function at one week (P=.583), one month (P=.708), and three months (P=.470) post-transplantation.

Conclusions

This initial experience indicates RAKT is a safe and feasible alternative to OKT, offering reduced complications, shorter hospital stay, less pain and blood loss, without compromising early graft function. Despite longer operative times, these findings support RAKT's potential patient recovery benefits. Longer-term follow-up is necessary.

Comparison Of Four MELD-Based Scores And Assessment Of Gender Equity In Waiting List Outcomes In Patients Awaiting Liver Transplantation In The Netherlands

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Background

The Model for End-Stage Liver Disease (MELD) score has been the cornerstone of organ allocation for liver transplantation in many organ sharing societies worldwide. Over time, several refinements have been implemented to enhance equity and predictive accuracy, leading from the original MELD to MELD-Na, refitted MELD-Na (reMELD-Na), and MELD 3.0. This study aims to (1) compare the predictive performance of MELD, MELD-Na, reMELD-Na, and MELD 3.0 in adult patients actively listed for liver transplantation in two transplant centers in the Netherlands, and (2) to evaluate potential gender disparities in waiting list mortality and transplantation rates.

Methods

Consecutive adult patients who were ever assigned an active transplantable status ("T-status") on the liver transplantation waiting list between 2007 and 2024 in two Dutch transplant centers were included. Patients listed for acute liver failure or polycystic liver disease and patients in whom one of the scores could not be calculated due to missing data were excluded. Cause-specific hazard ratio models for death were estimated using a competing risks framework. Competing events were liver transplantation, removal from the waiting list for other reasons than transplantation, transition to non-transplantable status, or assignment of exception points. Each model had two risk factors: MELD-based score and gender.

Results

1867 unique patients were included. The 1-year predictive ability for death on the waiting list of the four scoring systems was comparable for all MELD-based scores: MELD HR_{CS} 1.13 (95%CI 1.12-1.14) and gender HR_{CS} 1.25 (95%CI 0.98-1.59); MELD-Na HR_{CS} 1.13 (95%CI 1.12-1.15) and gender HR_{CS} 1.24 (95%CI 0.98-1.58); reMELD-Na HR_{CS} 1.16 (95%CI 1.14-1.18) and gender HR_{CS} 1.15 (95%CI 0.90-1.46); MELD 3.0 HR_{CS} 1.13 (95%CI 1.12-1.15) and gender HR_{CS} 1.43 (95%CI 1.12-1.81). No significant gender differences were observed in the cumulative incidence of death on the waiting list (p = 0.55) or transplantation (p = 0.79).

Conclusions

In this multicenter Dutch cohort, the predictive performance for death on the waiting list of MELD, MELD-Na, reMELD-Na, and MELD 3.0 was comparable. Moreover, the absence of significant gender-related differences in mortality and transplantation rates supports the fairness of currently used MELD-based scores for organ prioritization and allocation between men and women.

The Value Of Predicted Heart Mass For Donor-Recipient Matching In Heart Transplantation: A Review Of Current Evidence

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Background

Accurate donor-recipient size matching is critical in heart transplantation to minimize complications and improve survival. While there currently is no consensus on the best method for determining size matching, PHM (Predicted Heart Mass) is gaining popularity compared to traditional metrics (weight, height, BMI, BSA). Here, we evaluate the evidence supporting PHM as a metric for donor-recipient size matching in heart transplantation compared to traditional metrics across different patient populations.

Methods

A structured narrative review was conducted using PubMed, Embase, and Scopus. Twenty-three studies were included based on predefined criteria. The analysis focused on PHM versus traditional metrics, optimal PHM ratio thresholds, subgroup outcomes (obesity, pulmonary hypertension, different types of structural heart disease in recipients), the impact of sex mismatch, and the effects of PHM oversizing.

Results

PHM consistently outperformed traditional size metrics in predicting 1-year post-transplant survival. Undersizing, defined as a donor-to-recipient PHM ratio below 0.86, was associated with increased mortality, particularly in non-obese recipients and those with pulmonary hypertension. The association between PHM and outcomes in different types of structural heart disease in recipients was inconsistent. PHM-based matching eliminated the increased risk of female-to-male transplants, suggesting sex mismatch may no longer be clinically relevant. The impact of PHM oversizing remains inconclusive.

Conclusions

PHM provides a more reliable and equitable approach to donor-recipient size matching in heart transplantation than traditional metrics. Undersizing below a PHM ratio of 0.85–0.86 increases 1-year mortality, especially in non-obese and pulmonary hypertension recipients. Importantly, PHM matching neutralizes the risk of sex mismatch, potentially simplifying allocation strategies. Prospective, multicenter studies are needed to refine PHM thresholds for diverse populations and to validate PHM-based matching into allocation algorithms to optimize transplant outcomes.

Inequity In Kidney Transplant Allocation Within Eurotransplant: The Netherlands And The Dutch Caribbean

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Background

The Dutch Caribbean islands, part of the Kingdom of the Netherlands, have a highly diverse population due to historical migration and the transatlantic slave trade. Since 1998, residents with kidney failure can join the Eurotransplant waiting list for a deceased kidney transplantation. However, the predominantly European donor pool may reduce the likelihood of finding a suitable Human Leucocyte Antigen (HLA)-matched donor kidney for Caribbean patients. This study aimed to investigate whether current transplantation practices disadvantage patients residing in the Dutch Caribbean.

Methods

Waiting times to kidney transplant and contributing factors were compared for patients living in the Dutch Caribbean or the Netherlands, using two cohorts. The first, a retrospective cohort, included adult first-time deceased donor kidney transplant recipients (2021–2023), excluding immunized patients and those with high urgency status, and examined differences in waiting time, blood type, donor frequency and HLA mismatches. The second, a cross-sectional cohort, comprised all patients on the deceased donor kidney transplant waiting list in March 2024 residing in the Dutch Caribbean or the Netherlands. The prevalence of broad HLA antigens in these groups was compared to all deceased donors typed between 2021 and 2024.

Results

Sixty-six patients were included. Dutch Caribbean patients experienced longer waiting times compared to patients living in the Netherlands, both from dialysis initiation (2170.00 [1679.00-2742.00]; 813.00 [640.50-1056.50], p<0.001) and waiting list registration (385.00 [149.50-1075.00]; 112.00 [49.50-270.50], p<0.001). No significant differences were found in HLA mismatches, but none of the Caribbean patients received a kidney with ≤1 HLA mismatches, unlike some patients living in the Netherlands. Blood type distribution contributed to the disparity. Analysis of HLA-A allele prevalence revealed greater differences between Caribbean patients

and donors than between patients living in the Netherlands and donors.

Conclusions

Dutch Caribbean patients wait more than twice as long to receive a deceased donor kidney transplant compared to patients residing in the Netherlands. This is partly due to their restriction to donation after brain death kidneys only, a higher prevalence of blood type O, and less overlap in HLA antigens with the Eurotransplant donors. These findings highlight the need for further research into equitable allocation affecting underrepresented ethnic groups.

Public Opinions On Removing Disincentives And Introducing Incentives For Organ Donation: A Randomized Survey And Choice Experiment In Germany, Spain, And The Netherlands

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Background

Removing financial disincentives (FD) and introducing financial incentives (FI) for organ donation are potential solutions to the widespread, chronic, and costly organ shortage. A US study found that 70% of citizens would favour payments to donors if these payments were to eliminate the organ transplant waitlist. We collected the opinions of German, Dutch, and Spanish citizens on removing FD and introducing FI for deceased organ donation (DOD) as well as living kidney donation (LKD). We also examined whether support varies with potential organ supply gains and aligns with moral values.

Methods

In September 2025, we fielded an online survey to nationally representative samples (N = 6000 adult respondents; ~2000 in each country). We randomly assigned respondents to eight alternative reward systems, varying by payment amount, reward type, and payer identity. For each assigned system, respondents indicated support at three hypothetical organ supply levels (corresponding to 0%, 50% and 100% of the waiting list) and to rate each scenario on eight moral dimensions (e.g. voluntariness, autonomy, fairness).

Results

Across the three countries, we found between 50% and 90% support for the proposed schemes, with most respondents favoring the removal of FD for LKD. Up to 70% supports FI for both DOD and LKD, with Spanish and Dutch citizens largely favoring FI for DOD and German citizens largely favoring FI for both DOD and LKD. We further found high levels of polarization across the three countries, with many respondents being either very much in favor or very much against FI, regardless of possible supply gains.

Conclusions

Majorities in Spain, Germany, and The Netherlands support a range of FD-removal and FI policies for DOD and LKD., but attitudes are highly polarized on FI. Policy makers should be aware that although public support for FD and FI seems strong, rewarding donors might also generate opposition. Pilots on FI for DOD may generate the most support. Pilots on FI for LDK should evaluate whether paying organ donors violates ethical principles.

The Diagnostic Accuracy Of CT Derived Measurements Compared With Renogram In Living Kidney Donors

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Background

Kidney transplantation from living donors is the preferred treatment for patients with severe kidney failure, but it requires a thorough preoperative evaluation to ensure donor safety. Current workup of living donors in many transplant centres consists primarily of CT imaging and split renal function (measured with renogram) is only performed when a notable difference in kidney length or volume is observed on the CT scan. This study investigates whether CT-derived anatomical measurements correlate with split renal function.

Methods

A retrospective cohort study was conducted, including 96 living kidney donors between May 2019 and June 2025, all of whom underwent both CT imaging and renogram analysis. A $\geq 10\%$ difference in split renal function was considered clinically significant. CT scans were evaluated for sagittal length difference (≥ 10 mm), double oblique length difference (≥ 10 mm), and volume difference ($\geq 10\%$), calculated using the ellipsoid formula. These anatomical parameters were compared with functional asymmetry to assess diagnostic performance.

Results

The median age of donors was 61 years, and 62.5% were female. The median difference in split renal function (between the left and right kidney) was 6%, with 28 donors showing a difference of $\geq 10\%$. CT-derived measurements demonstrated low sensitivity (33–44%) and moderate specificity (77%) in detecting functional asymmetry. Predictive values were all below 64%, except for the negative predictive value of the double oblique measurement, which reached 77%.

Conclusions

CT-derived anatomical measurements show limited diagnostic accuracy in identifying significant differences in split renal function in our centre. Future studies are necessary to investigate the role of CT-derived measurements in predicting renal function after donation and transplantation.

Accelerating Viability Assessment Of Extended Criteria Donor Livers During Dual Hypothermic Oxygenated Perfusion Using Raman Spectroscopy

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Background

Extended criteria donor (ECD) organs are increasingly used to address the ongoing shortage of donor livers. Advances in machine perfusion technology have enabled safe use of these higher-risk grafts. Dual Hypothermic Oxygenated Machine Perfusion (DHOPE) plays a critical role by restoring mitochondrial function and increasing intrahepatic ATP levels. Currently, ECD grafts are fur-

ther evaluated during Normothermic Machine Perfusion (NMP), a resource-intensive procedure, as only one viability marker has been established for the DHOPE phase. This study investigates the use of Raman spectroscopy combined with chemometric analysis as a rapid, non-invasive process analytical tool to classify ECD livers as suitable or unsuitable for transplantation during DHOPE.

Methods
Perfusate samples from 100 ECD livers undergoing DHOPE followed by NMP were analysed using Raman spectroscopy after 60 minutes and 120 minutes of DHOPE. Fifteen baseline samples collected prior to DHOPE were included as reference. Spectra were collected using an integration time of 60 seconds, with three accumulations for a total acquisition time of 3 minutes per spectra. Of the 100 livers, 70 (70%) were transplanted, and 30 (30%) were deemed unsuitable based on standard NMP viability criteria. Classification models were developed using Partial Least Squares Discriminant Analysis (PLS-DA) and Support Vector Machines (SVM). Seventy percent of the data were used for model training, with the remaining 30% for cross-validation to identify early indicators of graft viability.

Results
In a pilot experiment involving 10 ECD livers, of which 50% were transplanted, PLS-DA achieved a classification accuracy of 72.9%. Analysis of the full dataset (N=100) is ongoing at the time of submittance. Preliminary findings suggest that Raman-based chemometric modelling can distinguish between ECD livers deemed suitable and unsuitable for transplantations during the DHOPE phase. Based on strict classification thresholds, the finalized model is expected to achieve >90% accuracy in predicting transplantation suitability while advising unclassified samples for further evaluation using NMP.

Conclusions
These findings aim to prove ECD liver viability can be classified early in the DHOPE phase using Raman spectroscopy. This is a promising approach to accelerate the viability assessment of ECD livers, and reduce the need for NMP.

Vasoreactivity As A Measure Of Kidney Viability During Ex Vivo Normothermic Machine Perfusion

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Background
Normothermic machine perfusion (NMP) could serve as a platform to assess deceased-donor kidney viability before transplantation, yet it remains unclear which parameters during NMP indicate renal viability. As vascular integrity is important for adequate renal function after transplantation, this study aimed to investigate the influence of warm ischemic injury on vascular smooth muscle cell (VSMC) responsiveness to vasoactive drugs during NMP.

Methods
Fourteen porcine kidneys (n = 7 per group) were exposed to either 30 or 60 min of warm ischemia (WI), followed by 3.5 h of cold machine perfusion. After cold perfusion, kidneys underwent 4 h of NMP (37°C). During NMP, boluses of vasoactive drugs were sequentially infused into the renal artery at 30-min intervals, starting with epoprostenol (10 μg), followed by dopamine (1 mg), sodium nitroprusside (2 mg), acetylcholine (1 mg), norepinephrine (10 μg), and finally verapamil (2.5 mg).

Results
Renal blood flow (RBF) during NMP changed significantly in both groups after administration of dopamine, acetylcholine, norepinephrine, and verapamil, but not following epoprostenol and sodium nitroprusside bolus infusion. In kidneys subjected to 30 min of WI, the reduction in RBF in response to dopamine (30.4% $\pm$ 11.6%) was more pronounced compared to kidneys that sustained

60 minutes of WI (17.6% $\pm$ 10.2%, p<0.05), and this was similar in response to norepinephrine (64.9%$\pm$10.3% versus 51.3%$\pm$12.5% resp., p<0.05). Additionally, the arterial pH was higher in kidneys with 30 minutes of WI (7.44$\pm$0.03) compared to kidneys with 60 minutes of WI (7.38$\pm$0.03, *p*<0.05), and oxygen consumption during NMP was higher as well (2.7$\pm$0.3 mLO$_2$/min/100g versus 2.3$\pm$0.4 mLO$_2$/min/100g resp., p<0.05).

Conclusions

This study indicates that prolonged warm ischemic damage diminishes the contractility of VSMCs through the α-adrenergic receptors. Our findings suggest that the renal vascular responses to dopamine and norepinephrine, as well as decreased oxygen consumption and blood pH, could serve as objective indicators to quantify warm ischemic injury during renal NMP, thus potentially serving as pre-transplant organ assessment biomarkers.

The Effect Of Semaglutide On Kidney Function And Outcomes In Kidney Transplantation Recipients

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Background

Semaglutide is a long-acting glucagon-like peptide-1 receptor agonist (GLP-1RA) indicated for the treatment of type 2 diabetes and obesity. Clinical trials have shown GLP-1RAs improve glucose regulation, reduce cardiovascular events, improve kidney function, lower blood pressure, decrease albuminuria and promote weight loss in non-transplanted patients with type 2 diabetes. Kidney-transplant recipients (KTRs), frequently develop metabolic complications. However data on the effectiveness and renal safety of semaglutide in this population remains limited. The aim of this study is to evaluate the effect of semaglutide in kidney transplant recipients.

Methods

A retrospective cohort study was conducted among 21 adult kidney transplant recipients who were subsequently prescribed semaglutide. Baseline was defined as the closest measurement within 6 months before or on the date of semaglutide initiation. Outcomes assessed included eGFR, creatinine, albuminuria, HbA1c, weight, BMI, and blood pressure. Linear mixed-effects models, with a random intercept for each patient and time as a continuous predictor were used to analyze the data. Subsequently, the linear mixed-effects models were corrected for time since transplantation.

Results

A total of 21 kidney transplant recipients (median age 65 years, 47.6% female, median BMI 33.0 kg/m^2, median HbA1c 59 mmol/mol) were included. During the treatment period with semaglutide, eGFR increased significantly by 0.73 mL/min/1.73 m^2 per month (p=0.0096). There were no significant changes in creatinine or HbA1c. Albuminuria showed a non-significant downward trend. Both weight ($-$0.356 kg per month, p = 0.00021) and BMI ($-$0.122 kg/m^2 per month, p = 0.00039) decreased significantly. Systolic blood pressure also showed a significant decrease ($-$0.594 mmHg per month, p = 0.0438), while diastolic blood pressure remained unchanged.

Conclusions

It can be concluded that the use of semaglutide is safe in kidney transplant recipients. Limitations of this study include its retrospective design, the small sample size, and the lack of a control group. Future efforts should focus on prospective studies with larger sample sizes and control groups to confirm these findings.

Sexual Complaints After Kidney Transplantation: An Overview Of The Prevalence, Associated Sexual Distress And Need For Care

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Background

Sexual complaints (SC), such as reduced sexual desire and erectile dysfunction, are common after kidney transplantation. These complaints can cause anxiety, depression, and a reduced quality of life. Despite this, SC are not routinely discussed by healthcare providers. The aim of this study was to assess the prevalence of SC and the associated distress and care needs among kidney transplant patients, and possible differences based on gender and age.

Methods

A cross-sectional study was conducted among adult kidney transplant patients received a questionnaire developed for this study, including the Sexual Distress Scale (SDS), to assess the presence of SC and the associated distress and care needs. The score range of the SDS is 0 to 48, with clinically relevant distress defined as a score of $\geq$15.

Results

Of the 285 patients approached, 78 participated in the study (response rate: 25%), with a mean age of 55 (SD 14); 56 men (72%) and 20 women (28%). SC were reported by 71% of the men and 73% of the women (p=0.900), and by 61% of the younger patients and 83% of the older patients (p=0.031). The mean SDS score for patients with SC was 21 (SD 12), with no relevant difference based on gender (p=1.000) or age(p=0.266). Among the 56 patients with SC, 59% experienced clinically relevant distress, with no differences between gender (p=0.659) or age (p=0.936). A care need was expressed by 59% of patients with SC, significantly more often by men (69%) than women (38%; p=0.029) and more often by older (73%) than younger patients (41%; p=0.018). Patients with a care need had a higher SDS score (25 (SD 11)) than those without a care need (14(SD 11); p<0.001).

Conclusions

This study shows that the majority of kidney transplant patients experience SC, and the distress caused by these complaints can be clinically relevant. More than half of the patients with SC express a care need. Despite some limitations, the findings highlight the need for more structured attention to sexuality in the post-transplant care of kidney transplant patients. Training healthcare providers in the routine and systematic discussion of SC is recommended.

HLA-B-21M Leader Variant Is Associated With Increased Risk Of Early Acute Rejection In CMV Seropositive Lung Transplant Recipients

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Background

HLA class I leader peptides may influence transplant outcomes. At position −21 of HLA-B leader peptide, two variants occur: methionine (21M) or threonine (21T). In kidney transplant recipients, carrying ≥1 HLA-B -21M allele has been associated with a higher risk of early T-cell-mediated rejection. This study aimed to determine whether lung transplant (LTx) recipients with at least one HLA-B 21M variant have an increased risk of early acute rejection (AR) risk.

Methods

A total of 293 lung transplantations were analyzed for donor and recipient characteristics, HLA profiles, HLA-B leader peptide and CMV serostatus in a time to event analysis and using Cox regression models. Primary outcome was AR during the initial post-transplant hospitalization. Patients were censored at discharge or 6 weeks after LTx.

Results

HLA-B leader genotype distribution was 12% -21MM, 47% -21T-MT and 41% -21TT. Among CMV positive recipients, AR rates differed significantly between genotypes (-21MM, -21MT and -21TT) in univariate analysis (p = 0.0026). This effect was absent in CMV negative patients (p=0.79). In univariable cox analysis for CMV positive recipients, -21MM, -21MT, reperfusion time, and pulmonary hypertension were significantly associated with AR.

In a multivariable analysis, -21MM in CMV positive recipients was independently associated with an increased AR risk (HR 6.6 95% CI 1.59-27.4, p=0.0092). Other predictors were reperfusion time (HR 0.98, CI 0.989-0.997, p=0.0060) and pulmonary hypertension (HR 12.5, CI 1.12-139.0, p=0.040). The increased hazard ratio for recipients with HLA-21MT was not significant in the multivariable model (HR 2.6, CI 0.966-6.79, p=0.059), yet the trend may be indicative for a gene dosage effect of -21M.

Conclusions

CMV seropositive lung transplant recipients carrying HLA-B-21MM genotype are at increased risk for early acute rejection. These findings support a role for HLA leader peptides in shaping early alloimmune responses following transplantation.

How To Recognize Anxiety After A Lung Transplant And Discuss This

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Background

Anxiety symptoms are common in patients after lung transplantation (LOTX). In the problem analysis that preceded this design-oriented research, various determinants of these anxiety symptoms were identified, including the risk of rejection and infections, an uncertain future with reduced life expectancy, physical complaints, compliance with lifestyle rules, medication use, repeated hospital admissions and post-operative complications. In the current situation, patients do not always discuss their anxiety symptoms with healthcare providers, and there is a lack of structural attention towards anxiety symptoms. The aim of this research is to develop an appropriate innovation to improve the care for anxiety in LOTX patients.

Methods

The study consists of a systematic literature review and qualitative interviews. Sixteen scientific articles were analysed. Semi-structured interviews were conducted with seven LOTX patients and four healthcare providers from LOTX centres.

Results

The sub-studies show that healthcare providers play an essential role in recognising and discussing anxiety. The use of a specific screening tool, followed by a discussion with the patient, is recommended. Respondents and the literature identify nurse practitioners (NPs) as the appropriate professionals to take on this task. Both patients and healthcare providers advocate for standardising the discussion of anxiety symptoms within the care process in order to normalise the topic of anxiety symptoms. In the event of abnormal findings, this can be discussed in a

multidisciplinary consultation and, if necessary, a referral can be made for follow-up care. In addition, the provision of a transplant buddy is mentioned as valuable support by both healthcare providers and patients.

The innovation developed comprises a combination of interventions: six-monthly screening with the Thermo-TX – a screening tool focused on transplant issues – discussing screening results with the patient, referral to appropriate care if necessary, discussing abnormal screening results in multidisciplinary consultations, structural attention to anxiety symptoms during each check-up consultation with the nurse practitioner, and the use of a transplant buddy.

Conclusions

The innovation offers a structural approach for the systematic and accessible recognition and discussion of anxiety symptoms after LOTX. The NP plays a coordinating role in this. Implementation of this innovation can contribute to increased patient satisfaction, reduced anxiety symptoms and improved quality of life.

Pharmacokinetics Of Sufentanil Clearance In Pediatric Kidney Transplantation With Adult Donor

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Background

Transplantation of a relatively large, adult, donor kidney in a young child results in a suddenly and significantly increased cardiac output. This can lead to unpredictable clearance of hepatically cleared drugs in the direct postoperative period. Data on pharmacokinetics shortly after transplantation are scarce but needed to construct adequate dosing regimens.

The aim of this study is to assess the pharmacokinetic effects of adult-kidney transplantation in young children for a hepatically cleared drug.

Methods

Observational, single center study (CHILD-KiTC) in children for living-donor kidney transplantation between December 2017 and April 2021. Sufentanil was given during anesthesia and the first postoperative day. Blood samples were taken at 2 timepoints before kidney reperfusion and two-times-daily up to day 3 postoperatively. Samples were stored at -80 until analysis. Sufentanil levels were measured using a validated liquid chromatography tandem mass spectrometry assay. In total, 75 plasma samples from 15 participants were available for analysis. A non-linear mixed-effects model was adapted from a previously developed sufentanil pharmacokinetic model. Typical Pk parameters were estimated. Reperfusion was tested as a covariate. Plasma concentrations were corrected for dosage and bodyweight.

Results

Fifteen patients were included with mean [IQR] age 7 [4.7-8.5] years, weight 21 [16-25] kg. All patients had diuresis within one hour after kidney reperfusion and good renal function at discharge. Cardiac output increased with 35% [15-74] after kidney transplantation. Estimated sufentanil clearance was 55.8 L/h and central volume of distribution (Vd) 24.6L. Peripheral Vd after transplantation increased by 50.0% (p=0.006) (95% CI: 7.9% - 115%).

Conclusions

The significant increased Vd in small children receiving an adult-size donor kidney can be explained by increased liver flow-dependent clearance of sufentanil resulting from an increased cardiac output, but also by peroperative fluid loading. This finding suggests that dosing adjustments might also be needed for hepatically cleared medication.

Bridge To INSPIRE – A National Training Program To Ensure Standardized Implementation Of aNRP

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Background

In 2026, a randomized controlled trial (RCT), "INSPIRE", in the Netherlands will be initiated comparing outcomes of donation after circulatory death (DCD) liver transplantation using two retrieval strategies: in-situ abdominal normothermic regional perfusion (aNRP) followed by static cold storage, versus super rapid retrieval followed by ex-situ machine perfusion. A national training program was started to ensure standardized implementation prior to RCT initiation. In this study we evaluate the implementation phase across all participating retrieval teams.

Methods

In this observational cohort study, all DCD procedures in the Netherlands between June and November 2025 will be included. Combined thoracic-abdominal DCD procedures were ineligible during the implementation phase. For each DCD procedure in which the liver was accepted by a Dutch center, the feasibility of performing aNRP was evaluated. If aNRP was not performed, logistical and operational barriers were documented. Donor characteristics and procedural parameters were collected.

Results

Among 91 DCD livers accepted for transplantation, 43 involved combined thoracic retrieval, leaving 48 eligible for aNRP. In 52% of these cases (n=25), the aNRP team was not alerted, as retrieval teams were not yet aligned on the implementation timeline. In eight additional cases, aNRP could not be performed due to lack of perfusionist availability (n=4), or absence of a proctor surgeon (n=4), resulting in 15 planned aNRP procedures. Of these, five were aborted because of a prolonged agonal phase (n=3), donor sepsis (n=1), or technical malfunction (n=1). Three liver grafts were declined due to elevated transaminases during assessment and one due to arterial injury. Of the 10 initiated procedures, six livers were successfully transplanted following aNRP. Median donor age was 61.5 years and median aNRP duration was 126 minutes. Median arterial flow and pressure were 2.0 L/min and 84 mmHg, respectively. A median of one fluid bolus was required to maintain perfusion targets.

Conclusions

During the initial implementation phase of aNRP in the Netherlands, coordination and logistical barriers were the predominant limitations to feasibility. When aNRP was initiated, procedural performance was stable with satisfactory flows and minimal fluid supplementation. Continued efforts to streamline coordination are expected to facilitate aNRP implementation ahead of the planned RCT.

RSV-Specific Humoral And Cellular Immune Responses In Kidney Transplant Recipients

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Background

Due to intensive immunosuppressive regimens, kidney transplant recipients (KTR) are particularly vulnerable to developing severe disease after respiratory virus infection. Additionally, inducing *de novo* virus-specific immune responses in KTR is challenging, as demonstrated by the need for multiple COVID-19 vaccinations. However, pre-existing immunity against respiratory viruses typically encountered first during infancy, such as respiratory syncytial virus (RSV), is not well-characterised in KTR. RSV has two major surface glycoproteins, the attachment (G) and fusion (F) protein. To better understand RSV-specific immune responses in KTR, humoral and cellular immune responses were measured in a cross-sectional manner in samples obtained in March and October 2021 (during and after COVID-19 lockdown).

Methods

RSV-specific antibody levels were measured in serum from KTR (n=64) and controls (n=37) collected in March and October 2021 in the context of the RECO-VAC study. Levels of F- or G-specific binding antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Neutralising antibody levels were measured by virus neutralisation assay. To assess cellular responses, peripheral blood mononuclear cells (PBMC) from KTR (n=15) and controls (n=14) were stimulated with a range of RSV-derived peptide pools and virus-specific T cells were detected in an activation-induced marker (AIM) flow cytometry assay. Peptide pools contained immuno-dominant epitopes of RSV (Select), or spanned a single protein in an overlapping manner (F, G, M or N). Concurrently, we performed phenotypic analysis of RSV-responding CD4$^+$ and CD8$^+$ T cells.

Results

Binding IgG antibody levels and neutralising antibody levels were comparable between KTR and controls, and stable between March and October 2021. Additionally, RSV-specific CD4$^+$ memory T cell levels were comparable between KTR and controls. Both KTR and controls demonstrated a variable T cell repertoire, which differed per person. RSV-specific CD8$^+$ memory T cells were scarcely detected.

Conclusions

Our results indicate that humoral and cellular RSV-specific immune responses in KTR are comparable to those found in controls. Although a precise correlate of protection for RSV remains to be determined, these results indicate that despite the immunosuppressive regimens that KTR are using, pre-existing immunity towards viruses encountered in childhood is maintained.

Reappraisal Of Risk Factors For And Long-Term Cumulative Incidence Of T cell-Mediated Kidney Rejection With A Basiliximab Induction And Tacrolimus-Based Maintenance Regime

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Background

The risk factors for and impact of T cell-mediated rejection (TCMR) in the long-term after kidney transplantation in recipients who received anti-CD25 induction, followed by tacrolimus/mycophenolate mofetil/prednisone maintenance is unknown. The importance of pre-transplant donor-specific anti-HLA antibodies (preDSA) as a risk factor for TCMR is uncertain.

Methods

A single center cohort of 2024 kidney transplant recipients between 2010-2020 with follow up until June 2025 was analyzed retrospectively for frequency and type of TCMR, impact on kidney function and graft loss. Known risk factors for TCMR were evaluated including the significance of preDSA.

Results

The cumulative incidence of TCMR was 15.9% (4.2% borderline TCMR, 4.1% TCMR type 1 and 7.6% TCMR type 2-3) after a median follow-up of 7 years, TCMR frequency was associated with recipient and donor age and in particular with the presence of preDSA (HR 1.85 (1.41-2.17), p<0.001). In the group without preDSA (N=1731), TCMR was associated with a lower eGFR at 1 year (43 ml/min vs 52 ml/min, p <0.001) and TCMR-related graft loss at 10-year FU was 2.8% of total number of graft loss. The total number of MM (per MM; aHR 1.09 (1.01-1.18), p=0.035) and type of donor organ (DD vs LD; aHR 1.34 (1.01-1.70), p=0.038) showed a statistically weak association with TCMR.

In the group with preDSA (N=293), the frequency of TCMR (at 1 year 20% vs 11% in the no preDSA group, P<0.001) and TCMR-related graft loss (at 1 year 3.4% vs 0.6%, p<0.001) was substantially higher than in the group without preDSA. This effect was driven by the subgroup of recipients with preDSA against HLA class II. Within the group of TCMR 2-3 treated with T cell depleting therapy, the risk of infection-related death was increased in those aged 45 years and above (aHR 2.15 (1.16-3.56), p=0.008).

Conclusions

An immune suppressive regime of anti-CD25 induction and tacrolimus/mycophenolate mofetil/prednisone maintenance is associated with a low risk of TCMR-related graft loss and modest impact of traditional risk factors. The presence of DSA against HLA class II before transplantation constitutes a major risk factor for TCMR-mediated graft loss.

Non-Invasive Ultrasound Localization Microscopy (ULM) Enables High Resolution Functional Imaging Of The Renal Vasculature Ex Vivo

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Background

The renal vasculature consists of an intrinsically complex network of blood vessels that play an essential role in the physiological functionality of the kidney. Non-invasive high-resolution ultrasound localization microscopy (ULM) represents a promising approach for functional evaluation of this specialized cortical vasculature. Current *in vivo* ULM applications, however, have not yet shown the capability to distinguish the smallest functional vascular units within the renal cortex.

Methods

We incorporated ULM into our 25°C cell-free subnormothermic machine perfusion (sNMP) platform and obtained high-resolution images within both a human

deceased donor (n=1) and abattoir-derived porcine (n=3) 6-hour kidney perfusion model. Localization and tracking of individual microbubbles as a contrast agent allowed for reconstruction of detailed images of the vascular tree and its hemodynamics, which were used for segmentation of vascular compartments and subsequent evaluation of functional parameters within the cortical vessels.

Results

By applying ULM within our human *ex vivo* sNMP platform, we were able to create a super-resolution image of the renal vasculature which enabled segmentation, and subsequent functional measurements of individual small vessels, glomeruli and capillaries. We demonstrate flow velocity measurements within a single glomerulus and its connecting afferent and efferent arterioles. Similarly, we show the ability to perform functional measurements within the cortical capillaries while providing detailed anatomical information on the intactness of the capillary network itself. Repeated experiments on porcine kidneys *ex vivo* demonstrate low inter-variability between measurements and consistent feasibility of functional parameter evaluation within a 15-minute acquisition window.

Conclusions

We have visualized the human renal vasculature at the glomerular and peritubular capillary level during *ex vivo* preservation. We believe that application of ULM within a kidney perfusion setup offers a promising, high-resolution, non-invasive approach for functional evaluation of donor organs *ex vivo*.

Outcomes Of Second-Opinion Kidney Transplants: A Retrospective Cohort Study

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Background

Referral for kidney transplantation, generally considered to be the best option for end-stage kidney disease, can be impeded by comorbidities. This study compared the outcomes of patients referred from outside versus from within the referral area.

Methods

This retrospective, single-center cohort study included adult kidney transplant recipients who underwent transplantation between January 2010 and January 2020, with follow-up until October 20, 2025. The primary outcome was patient and death-censored graft survival. Secondary outcomes included hospital readmissions within the first year and kidney function (eGFR) 1-year post-transplant. Data were obtained from the electronic health records and the Dutch Organ Transplant Registry. Survival was analyzed by using Kaplan-Meier curves and compared with the log-rank test. Additionally, a subgroup analysis will be performed for different risk profiles.

Results

On average, 40 patients per year were referred for second opinion, of whom 10-15 patients per year were declined and not listed for transplantation. During the study period, 255 patients referred from outside the referral area were transplanted and 1864 patients referred from within the area. Referrals from outside the referral area included obesity, ABO-or HLA incompatibility, cardiovascular comorbidities, prior malignancies, and poor general condition. Transplanted patients from outside the referral area had a higher BMI (median 27.2 versus 26.1, p=0.007), with fewer pre-emptive transplants (23% vs. 35%, p<0.001) and longer dialysis vintage (median 632 versus 349 days, p<0.001). In both groups, 61% were living donor kidney transplants.

Cumulative 5-year death-censored graft survival was 86% for patients from outside the referral area versus 88% for patients from within the referral area (p=0.86). Cumulative 5-year patient survival was 85% for both groups (p=0.95). eGFR at 1-year post-transplant was median 50 ml/min for both groups (p=0.60). We are

currently analyzing transplant outcomes and surgical complications according to different risk profiles ("second-opinions"), irrespective of the referral area. Additionally, we will analyze the survival of patients who were declined for transplantation.

Conclusions
Despite unfavorable baseline characteristics, patients referred from outside the referral area had comparable outcomes to patients referred from within the area. We are awaiting the results of the subgroup analyses for specific risk profiles.

Unveiling Donor-Derived BKPyV DNAemia Through Analysis Of Contralateral Kidney Transplant Recipients

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Background
BK Polyomavirus(BKPyV) infection is of notable concern in kidney transplant recipients, as it can cause BKPyV-associated nephropathy (BKPyVAN). Currently, there is no effective treatment for BKPyV infection, underscoring the need for preventive strategies. There is emerging evidence that donor-derived BKPyV plays a role in the development of BKPyV DNAemia. To further explore this hypothesis, we conducted a retrospective, multi-center cohort study to evaluate the risk of developing BKPyV DNAemia in kidney recipient pairs sharing the same donor.

Methods
At the Leiden University Medical Center, we identified recipients of deceased donor kidneys (2011−2021) with and without BKPyV DNAemia within the first year post-transplant. Contralateral kidney recipients were identified through national registries. Cox regression assessed the risk of BKPyV DNAemia when the contralateral recipient was affected.

Results
Among 117 recipient pairs, BKPyV DNAemia was more frequent when the contralateral recipient was affected (28.8%[15/52]), compared with pairs in which the contralateral recipient remained unaffected (10.8%[7/65],p=0.013). Multivariate analysis confirmed this increased risk (HR4.2,95%CI:1.5−11.9;p=0.007).

Conclusions
This study shows a significantly increased risk of BKPyV DNAemia in recipients of deceased donor kidneys when the contralateral kidney recipient develops BKPyV DNAemia. These findings highlight the influence of donor-derived factors in BKPyV transmission in kidney transplantation.

The OPTIMIZE Study, A Randomized Clinical Trial In Elderly Kidney Transplant Recipients, Comparing Everolimus And Reduced-Dose Tacrolimus With Mycophenolate And Tacrolimus Immunosuppression

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Background

We hypothesized that older kidney transplant recipients receiving corticosteroids, everolimus (EVR) and reduced-dose tacrolimus have better outcomes than patients receiving corticosteroids, mycophenolate mofetil (MMF) and tacrolimus.

Methods

The OPTIMIZE study was a randomized controlled clinical trial in kidney transplant recipients over 65 years in The Netherlands and Belgium. Patients (65+) receiving a kidney from a deceased donor over 65 years (stratum A), or a kidney from a deceased donor younger than 65 years or a living donor (Stratum B) were included.

At transplantation, patients were randomized to EVR or MMF groups. Tacrolimus target trough levels in the EVR group were 5-7 µg/L until 3 months, 2-4 from 3 to 6 months, and 1.5-4 from 6 months onwards. Tacrolimus target trough levels in the MMF group were 8-12 µg/L, 6-10, and 5-8. Everolimus target trough levels were 3-8 µg/L.

The primary endpoint of successful transplantation was defined as being alive with a functioning graft with an eGFR above a predefined threshold at 2 years after transplantation. Predefined eGFR thresholds were 30 ml/min*1.73m^2 (stratum A) or 45 ml/min*1.73m^2 (stratum B).

Results

379 patients were randomized of whom 197 in stratum A and 182 in stratum B. The mean trough levels for everolimus and tacrolimus were within the target range throughout the study. There was no statistically significant difference in the frequency of successful transplantation at 2 years between the EVR and MMF groups (EVR 94 (50.3 %), MMF 110 (57.3%); p = 0.17). Regarding the predefined secondary outcomes, patient survival (EVR 167 (89.3%), MMF 171 (89.1%); p = 0.94) and graft survival (EVR 155 (82.9%), MMF 162 (84.4%); p = 0.70) did not differ significantly at 2 years. There was no significant difference in the frequency of treated rejection (EVR 39 (20.6%), MMF 34 (17.4%); p = 0.42). Within strata A and B there were no significant differences in the endpoints.

Conclusions

Everolimus and reduced-dose tacrolimus did not result in a higher rate of successful transplantation in older transplant recipients compared to MMF and tacrolimus immunosuppression.

Spatial Quantitative Metabolomics Reveals Modality-Dependent Metabolic Signatures During Clinical Liver Perfusion

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Background

Machine perfusion enables functional reconditioning and assessment of marginal donor livers. While normothermic machine perfusion (NMP) restores near-physiological conditions to facilitate viability assessment, ischemia-reperfusion injury occurs ex situ on the machine. Dual hypothermic oxygenated perfusion (DHOPE) has shown promise in mitigating this injury by restoring cellular energy reserves. However, the impact of perfusion modality on the hepatic metabolome remains largely unexplored.

Methods

Clinical perfusion data were analyzed from 27 donation after circulatory death liver grafts preserved between November 2020 and December 2024. Metabolic profiles were compared between livers preconditioned with DHOPE (n=10) followed by NMP and those undergoing NMP alone (n=17). Additionally, spatial quantitative metabolomics was applied on healthy livers (n=5) and livers transplanted after preservation by static cold storage (SCS, n=5), DHOPE (n=5), NMP (n=15) and sequential DHOPE-NMP (n=5).

Results

Livers preconditioned with DHOPE displayed lower gluconeogenesis during the first two hours of NMP, accelerated lactate clearance, and elevated bicarbonate levels, consistent with superior hepatic metabolic function. Reduced potassium efflux and elevated sodium concentrations suggested enhanced Na^+/K^+-ATPase activity, resulting in lower potassium levels after reperfusion in the recipient. Transaminase release was attenuated in the DHOPE-NMP group, indicating reduced hepatocellular injury, while higher bile bicarbonate secretion suggested improved cholangiocyte recovery during early perfusion. Spatial quantitative metabolomics identified DHOPE as a critical preconditioning step that replenishes cellular energy reserves and mitigates redox stress, thereby modulating livers for sequential perfusion and transplantation.

Conclusions

DHOPE modulates hepatic and biliary metabolism during NMP, potentially improving graft quality through mitochondrial recovery, reduced redox stress and stabilized membrane potential. Ongoing work will apply spatial quantitative metabolomics to elucidate cell-type-specific metabolic signatures across perfusion modalities.