FULL ORAL

OS01 - KIDNEY ALLOCATION AND THE GAP BETWEEN OFFERING AND ACCEPTANCE

OS001 ACCELERATED ORGAN ALLOCATION PROCEDURE (AOAP) FOR KIDNEY DONATION (REAL, RESCUE, CENTER OFFER) IN THE EUROTRANSPLANT KIDNEY ALLOCATION SYSTEM (ETKAS) IS IT WORTH? - 5-YEAR, SINGLE CENTER EXPERIENCES

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Background: Germany, the most populous member of Eurotransplant (ET) Alliance, has seen a >30% decline in post mortem kidney donation since 2010, as there are currently only 9 to nearly 10 donors per million inhabitants. Thus, waiting times for a kidney transplantion (ktx) for German recipients (recp) on dialysis are increased to over 8 years and more. In this situation of lack of organ donation, every effort is now made to allocate each donated kidney organ so that it has a transplant opportunity. In practice, this means that, in the event of repeated kidney offer refusal by at least 5 transplant centers, Eurotranspant will accelerate the allocation process (AOAP) by offering the kidney donation competitively to several transplant centers.
Material/Methods: Comparing ktx of AOAP offers to ktx of ETKAS primary offer 12/2013 – 12/2018, $n = 264$ ET donor ktx, AOAP = 56 (21%), ETKAS = 208.
Results: -AOAP donors are older and significantly more likely diabetics, but do not differ in renal function on explantation -AOAP recp have waiting time on list, median 3.3 years, compared to ETKAS recp median 6.6 years. -AOAP recp do not experience a significantly prolonged hospital stay. -AOAP transplants (2 year completed, $n = 37$ (66%) show no significant difference on renal function on month 6, 12, 24. -AOAP transplants show more frequently delayed graft function (> 1 dialysis post transplantation) -AOAP transplants show more lost of function within 3 years (12,5%) compared to ETKAS (5,8%)
Conclusion: Our 5-year retrospective analysis shows that it is worthwhile for recipients to take part in the AOAP because compared to the ETKAS recipients they only have to accept half of the waiting time until transplantation after being put on the waiting list. AOAP recipients show a non-significant difference in renal function compared to the ETKAS recipients after only 6 months, even though the donors are older, more frequently diabetics and the transplants have more primary DGF in comparison to ETKAS.

OS002 DECLINED KIDNEY OFFERS: REASONS AND OUTCOMES. A SINGLE CENTRE EXPERIENCE

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Background: In the UK, kidneys are normally offered for transplantation to a 'named patient'. In deciding whether to accept or decline an offer various donor and recipient factors are taken into account. Declined offers are now audited centrally. However, reasons for decline are poorly recorded and the implications for individual patients unknown.
Methods: Details of all kidney offers to the Queen Elizabeth University Hospital, Glasgow over a two-year period were recorded prospectively. Nature of offer, acceptance and reason for decline were recorded. All named patients with offers were followed-up for at least six months to assess future offers/transplantation.
Results: 637 offers and 119 screening calls were received resulting in 219 transplants. 75% ($n = 313$) of offers were made on a 'named patient' basis. 95 offers were declined based on recipient factors (unfit, positive crossmatch, recipient decline, donor/recipient mismatch). 208 offers were declined immediately for a variety of donor factors (high infectious risk (BBV) ($n = 32$), other infectious risk ($n = 34$), history of malignancy ($n = 33$), renal function ($n = 47$), extreme extended criteria ($n = 54$)). 107 offers were initially accepted and then subsequently declined (non-proceeding donor ($n = 55$), retrieval findings ($n = 56$) including 10 indeterminate lesions in which it was not possible to obtain pathology). 165 of 'named patient' offers proceeded to transplant (53%). Of the other 148 patients, 58 received a kidney transplant in the follow-up period. Only 24 (16%) received no further offer. 5 (3%) > 3 more offers. Median time to first offer was 134 days.
Conclusions: A vast range of 'quality' exists in kidneys offered for transplantation. Decline should not be undertaken without due consideration. However, most 'named patients' do receive further offers and the decision whether or not to accept a 'marginal kidney' should be taken in conjunction with the patient and without pressure from external sources

OS003 RENAL MASSES IN DECEASED DONOR KIDNEYS; POTENTIAL TO EXPAND THE DONOR POOL THROUGH IMPROVED ORGAN UTILISATION

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Introduction: Increasing deceased donor age may lead to greater incidental renal masses detected at retrieval. Small renal masses ≤ 4 cm have low metastatic potential and 20% are benign. We aim to report the incidence of renal masses in potential deceased donors and utilisation of kidneys for transplantation.
Methods: Retrospective 10 year national data(2008–2018), provided by NHS Blood & Transplant, was searched using key-words 'mass', 'tumour', or 'cancer' in deceased donor solid organ offers. For additional donor information, electronic offering system (EOS) was consulted. Those inappropriately coded

Comparative features of masses within donor kidneys

Cystic Lesion 49% (86/147 transplanted) (82/193 not transplanted)

Single 43/86			Multiple 34/86			Unrecorded 9/86	
	T	NT		T	NT		T
Small	35	13	Small	21	15	Small	6
Medium	3	3	Medium	0	4	Medium	0
Large	3	6	Large	3	7	Large	1
Unknown	2	2	Unknown	10	12	Unknown	2
	43	24		34	38		9

Solid Lesion (Including benign, malignant and nodule) 20% (25/147 transplanted) (42/193 not transplanted)

	T	NT
Small	16	20
Medium	2	6
Large	0	4
Unknown	7	12
	25	42

Mixed Lesion (Including solid/cystic) 4% (2/147 transplanted) (10/193 not transplanted)

	T	NT
Small	1	6
Medium	0	1
Large	1	3
Unknown	0	0
	2	10

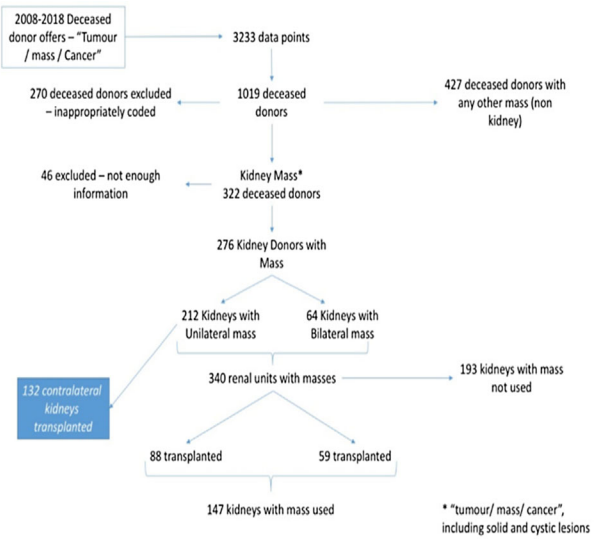
Scarred Lesion 4% (7/147 transplanted) (6/193 not transplanted)

	T	NT
Small	3	1
Medium	1	0
Large	0	1
Unknown	3	4
	7	6

Unknown nature of lesion 24% (27/147 transplanted) (53/193 not transplanted)

	T	NT
Small	11	6
Medium	2	3
Large	1	3
Unknown	13	42
	27	53

T= transplanted
NT= not transplanted



or with insufficient data were excluded. We categorised renal mass size into small(<4 cm), medium(5–7 cm), or large(>8 cm).
Results: 12121 deceased donor offers took place during the study period. The key-word search extracted 3233 matches in 1019 solid organ deceased donor offers. 427 offers related to 'mass', 'tumour', or 'cancer' in other solid organs and 318 offers were excluded due to inappropriate coding or lack of information. 276 potential donor offers had a kidney mass identified(64 bilateral kidney masses; 212 unilateral). This equates to 340 kidneys with a mass and 212 unaffected paired kidneys offered for transplantation.

Of 340 kidneys with a mass offered for transplantation, 147(43%) were transplanted. Of the 147 transplanted, there were 6 unknown malignancies and good functional outcome at 1 year. Of the 212 contralateral unaffected kidneys from donors with a unilateral mass, 132(62.3%) were transplanted with good functional outcome at 1 year and 2 unknown malignancies at 5 years.
Discussion: Overall 259 kidneys were transplanted and 293 discarded. Good functional and oncological outcomes in our cohort leaves the potential to improve utilisation. This in an appropriate recipient, from an adequate donor in the presence of appropriate infrastructure(histopathology and surgical skill for SRM excision). Longer term prospective data is needed.

OS004 THE UK KIDNEY FAST TRACK OFFERING SCHEME: 12-MONTH RECIPIENT OUTCOMES AT A SINGLE UK CENTRE

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Aims: The Uk Kidney Fast Track Scheme (KFTS) was devised in 2012. The primary aim was to maximise utilisation of organs from deceased donors at risk of discard, whilst simultaneously minimising ischaemic times. Such organs were often declined by several UK-centres via the Standard National Kidney Allocation Scheme (NKAS), based on less favourable donor criteria. KFTS was implemented at our centre in 2015. This retrosepctivestudy highlights 12-month primary outcomes of recipients transplanted via a KFTS offer.
Methods: 33 recipients were identified as receiving a renal transplant via the KFTS during the period of October 2015 - November 2018. Donor forms were used to obtain donor criteria. Electronic records were used to asess recipient data and subsequent outcomes.
Results: Donor criteria and recipient outcomes are summarised below. Means (+/- SD) are used unless otherwise specified.
Discussion: Mean recipient age was 60.5 years (21–76). Average BMI was 26.6. 7 recipients received dual kidney transplants (DKT). Mean recipient creatinine at 1,3 and 9 months post-transplant was 189, 159, and 172 respectively. 12-month creatinine was 155 umol/l (eGFR 52). DGF was observed in 42.4%. There were no episodes of rejection. 2 recipients required dialysis by 12 months due to graft failure. 1 patient required ITU post op secondary to sepsis. 1 recipient underwent an emergency laparotomy for upper GI bleeding. 1 mortality due to overwhelming urosepsis (terminal creatinine 210). 12-month graft survival was 94%. Average cold ischaemic time was 13hrs06mins (+/-5hrs10mins). Average total ischameic time was 14hrs40mins (+/-4hrs49mins). The average anastomosis time was 39mins (+/-7.5mins), depending on whether the transplant was DKT.
Conclusions: Early outcomes suggest that the KFTS is a valuable organ source, with certain outcomes comparable to NKAS results. Further longitudinal studies are required to make direct comparisons to NKAS recipient outcomes at 2, 5 and 10 years.

DONOR DETAILS		RECIPIENT OUTCOMES	
Age (years)	52 (+/- 17)	Age (years)	60.5 (+/-13)
Sex (M:F)	23:10	Sex (M:F)	2:1
Commonest cause of Death	Hypoxic brain injury (45%)	BMI	26.6 (+/-26.6)
History of diabetes	6%	Diabetes	39.4%
History of hypertension	27%	Hypertension	84.8%
Terminal creatinine (umol/l)	112 (+/- 98.2)	Primary non-function (PNF)	0%
Terminal eGFR	67 (+/- 23.8)	Delayed graft function (DGF)	42.4%
		Episodes of rejection	0%
		Creatinine 7 days (umol/l)	516 (+/-292)
		Creatinine 1 month (umol/l)	189 (+/-130)
		Creatinine 3 months (umol/l)	159 (+/- 79)
		Creatinine 9 months (umol/l)	172 (+/-115)
		Creatinine 12 months (umol/l) / eGFR	155 (+/-85) / 52 (+/-21)
		Mortality	3%
		12-month graft survival	94%

OS005 KIDNEY TRANSPLANTATION AFTER RESCUE ALLOCATION – METICULOUS SELECTION YIELDS THE CHANCE FOR EXCELLENT OUTCOME

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Background: Due to permanent organ shortage with persistently high numbers of patients on the waiting-list, it gets more necessary to enlarge the amount of transplantable kidneys. Yet, facing the progressing demographic change, both donors and recipients are older and have more comorbidities, which could have an impact on the graft function. To facilitate the use of organs of potentially poor quality, Eurotransplant (ET) generated the rescue allocation (RA) modus. Data on outcome of these transplants are scarce.

In our centre we accept RA kidneys according to a distinct algorithm including age-difference, donor comorbidities and cold-ischemia time (CIT). This retrospective study was performed to analyse the outcome of kidney transplantation after RA as compared to standard allocation (SA).
Methods: 258 recipients transplanted at our transplant centre between December 2010 and June 2018 were included: RA ($n = 64$) vs. SA ($n = 194$) and donor and recipient specific data were compared with regards to patient and graft outcome.
Results: RA donors were older, had higher mean body mass index, showed higher last serum creatinine levels and had a higher rate of pre-existing diabetes or hypertension than SA donors. Compared to SA, RA recipients were also older, showed less HLA-matches, had higher rates of CMV high risk constellations and a longer waiting-time. Mean CIT differed between 15.2 h in RA and 10.8 h in SA ($p \leq 0.001$). Although basic criteria varied in both groups, censored outcome after kidney transplantation resembled: 5-year graft survival after RA was 83.2% and 81% after SA ($p = 0.59$), and patient survival was 80% and 87.6% ($p = 0.14$), respectively.
Conclusion: Since opinions regarding the use of rescue allocated organs with lower quality on paper differ distinctively, our data show that, when selected meticulously, RA kidneys could generate a similar transplant outcome. The increasing use of those organs could help to provide patients with grafts.

OS006 DISCARD OF KIDNEYS FROM EXPANDED CRITERIA DONORS AFTER FROZEN SECTION PREIMPLANTATION BIOPSY ANALYSIS COULD LEAD TO AN UNJUSTIFIED INCREASE OF ORGAN WASTING

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The additional utility of zero-time renal transplant biopsies in the decision-making process of acceptance of kidney from expanded criteria donors (ECD) is not yet clearly validated. However, zero-time biopsy data are one of the main causes for kidney discard in the USA.

We conducted a single-center study of zero-time renal transplant biopsies performed for kidney acceptance decision for ECD between November 2005 and December 2014. All the ECD kidney grafts in our center ($n = 622$) had a zero-time biopsy, but only in some cases a frozen tissue section analysis was performed for kidney acceptance decision.

During this period, 92 (14.8%) zero-time frozen tissue section analysis were performed in ECD donors. After analysis, 48% of kidneys were accepted and 52% were discarded. ECD whose kidney was accepted or discarded were not significantly different regarding clinical (donor age, past history of hypertension or diabetes mellitus and the cerebrovascular cause of death) and biological data (serum creatinine) data. However, histology of discarded kidneys showed more sclerotic glomeruli (22% vs. 8%; $p < 0.001$), increased interstitial fibrosis (1 [0–2] vs. 0 [0–1]; $p = 0.072$) and more severe arteriolar lesions (2.5 [2–3] vs. 1.5 [1–2]; $p = 0.001$). Finally, we used a propensity score to select a group of 43 kidney allograft recipients matched for donor zero-time histology and age with donors whom kidney was discarded. Interestingly this group had a similar 2 and 8 years graft survival compared to the whole cohort of ECD recipients.

In conclusion, when performed, zero-time frozen tissue section analysis was a decisive element for kidney discard decision in our center. However, low quality preimplantation histology was not associated with worst graft survival among ECD in a matched control cohort.

OS007 DISPARITIES IN THE ACCEPTANCE OF DECEASED DONOR KIDNEYS AND CONSEQUENCES FOR TRANSPLANT ACCESS: NATIONWIDE ANALYSES OF PRACTICE IN THE US AND FRANCE

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Background: Approximately 3,500 donated kidneys are discarded in the US each year. The aim was to estimate the effects of a more aggressive allograft acceptance practices on the donor pool and allograft survival.
Method: This is a nationwide study using validated registries from the US and France of deceased donors with organs offered to kidney transplant centers between 2004 and 2014. The primary outcome was kidney allograft discard. The secondary outcome was allograft failure after transplantation. We used logistic regression to model organ acceptance and discard practices in both countries. We then quantified the number of kidneys discarded in the US that a more aggressive system would have used for transplantation. Finally, based on actual survival data, we quantified the years of allograft life that a redesigned US system would have saved.
Results: In the US, 156,089 kidneys were recovered from deceased donors, of which 128,102 were transplanted, and 27,987 (17.9%) were discarded. In France, among the 29,984 kidneys recovered, 27,252 were transplanted, and 2,732 (9.1%, $p < 0.0001$ vs US) were discarded. Kidney quality showed little change in the US over time (mean kidney donor risk index [KDRI] 1.30 $\pm$ 0.48 in 2004 versus 1.32 $\pm$ 0.46 in 2014), while a steadily-rising KDRI in France reflected a temporal trend of more aggressive organ use (mean KDRI 1.37 $\pm$ 0.47 in 2004 versus 1.74 $\pm$ 0.72 in 2014, $p < 0.0001$). We applied the French-based allocation model to the population of US deceased donor kidneys and found that 17,435 (62%) of kidneys discarded in the US would have instead been transplanted under the French system. We further determined that a redesigned system with more aggressive organ acceptance practices translated to an additional 132,445 allograft life years in the US over the 10-year observation period.
Conclusions: Greater acceptance of kidneys from older deceased donors in the US could provide major survival benefits to the population of waitlisted patients.

OS008 A NEW KIDNEY OFFERING SCHEME IN THE UK

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Background: In 2015, three working groups were established to consider if changes were required to the 2006 UK Kidney Allocation Scheme to reflect the increased use of donors after circulatory death (DCD) and generally older, more challenging donor kidneys. The three groups were tasked with reviewing the current scheme, looking at philosophy of allocation and looking at histocompatibility and immunogenetics, respectively. The groups agreed that a new Kidney Offering Scheme should be introduced to better match patient and graft life expectancy, to give more priority to difficult to match patients and, where HLA matching is deemed appropriate, all loci should be considered (HLA-A,B,Cw,DR,DQ).
Methods: In line with agreed objectives, a series of computer simulations were used to explore a number of different offering scheme algorithms. The simulations were developed using 4100 UK deceased kidney donors that resulted in a transplant between 2013 and 2016, and 5300 patients listed in the UK for a kidney only transplant at 1 January 2012 and 8200 patients newly listed for a kidney only transplant, between 2012 and 2016. Each simulation represented four years of constant activity.

Simulation results of different possible schemes were compared according to characteristics of the simulated transplant and waiting list pools in order to find the best compromise between competing objectives. The simulations included use of donor and recipient risk indices developed with the working groups.
Conclusions: The new Kidney Offering Scheme has been developed promptly with the use of high-quality registry data. The ability to simulate multiple versions of a new scheme using registry data has led to a scheme that has the potential to deliver real benefits to patients. The quantifiable benefits of the scheme are; increased access to transplant for difficult to match and ethnic minority patients, better kidney longevity matching and improved equity of access across different patient groups.

OS02 - ALLOCATION IN LIVER TRANSPLANTATION

OS009 DONOR AGE DOES NOT NECESSARILY IMPACT LONG-TERM SURVIVAL AFTER PEDIATRIC SPLIT LIVER TRANSPLANTATION

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Background: Split liver transplantation (SLT) was introduced to expand the number of grafts available for pediatric recipients. Large studies have found that donor age affects patient and graft survival. However, universal agreement defining the optimal donor criteria is lacking. For example, maximum donor age varies between 40–50 years among different countries. We sought to investigate the impact of donor age on pediatric SLT recipient outcomes.
Methods: A retrospective cohort study was performed including all pediatric (recipient age < 18 years) SLTs performed in the Netherlands between 1987–2015. Donor data were derived from Eurotransplant. Young donors were defined as age 10–50 years, old donors > 50 years. Kaplan-Meier survival analyses were performed with log-rank testing, with subsequently Cox proportional-hazards regression analyses to evaluate recipient outcome.
Results: A total of 154 SLT were performed, of which 124 were derived from a young and 30 from an old donor. After a median follow-up of 6.2 years, 52 (34%) patients deceased and 59 (38%) experienced graft loss. We found no significant differences in graft (HR = 0.72; 95%CI 0.23–2.23; $p = 0.56$; Figure 1a,c) or patient survival (HR = 0.89; 95%CI 0.24–3.30; $p = 0.87$; Figure 1b,d) among SLT recipients from young or old donors, when corrected for donor, recipient and surgical variables. Cold ischemia time was significantly lower in SLT from old donors (548 vs 577 min; $p = 0.035$). This can be explained by a significantly higher use of old donors at a regional (national) level when compared to young donors (83% vs 54%; $p = 0.003$).
Conclusion: Although previous large European studies found increased patient and graft mortality after pediatric SLT with donors aged > 50 yr, accepting older donors may be safe at a national level when limiting CIT by using regionally allocated grafts.

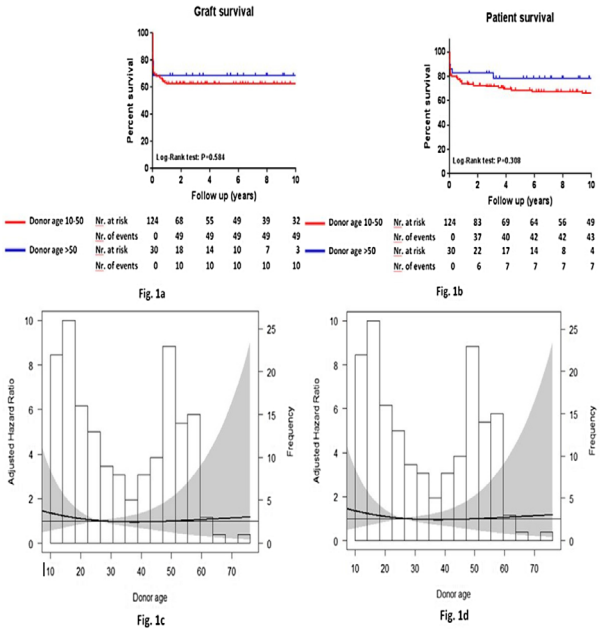

Figure 1. Adjusted hazards ratio for donor age on all-cause graft and patient survival

OS010 WAITLIST DYNAMICS IN ADOLESCENTS AND ADULT PATIENTS WITH BELOW AVERAGE BODYWEIGHT LISTED FOR LIVER TRANSPLANTATION, RESULTS FROM THE EUROTRANSPLANT DATABASE

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Background: Adult patients with below-average bodyweight waitlisted for liver transplantation (LT) may face a shortage of size-matched liver grafts. Primary objective of this study is to compare time to transplantation in adult patients with a bodyweight < 60 kg (BW < 60 kg) to patients with a bodyweight ≥ 60 kg (BW ≥ 60 kg).
Methods: The prospective Eurotransplant (ET) database was used, 11,686 patients listed for LT between 2010 and 2015 were included. Paediatric recipients, recipients of living donor LT, repeat LT or approved organ combinations, and patients with an initial high urgency status were excluded. Time to transplantation for patients with a BW < 60 kg was compared to patients with a BW ≥ 60 kg. Time to transplantation was compared with use of a multivariate cox proportional-hazards model controlling for recipient sex, recipient age, country of listing, year of listing, listing MELD-score and listing on the kidney waitlist.
Results: In total, 1,296 patients with a BW < 60 kg were compared to 10,390 patients with a BW ≥ 60 kg. In multivariate analysis a BW < 60 kg was associated with a lower chance for LT (hazard ratio 0.82, 95%CI: 0.75–0.90, $p < 0.0001$). At 12, 24 and 36 months after listing transplant rates were respectively 34%, 45% and 48% for patients with a BW < 60 kg *versus* 48%, 56% and 58% for patients with a BW ≥ 60 kg. Median waiting time was 548 days for patients with a BW < 60 kg and 307 days for patients with a BW ≥ 60 kg. At the end of follow-up waitlist mortality was 23.5% for patients with a BW < 60 kg *versus* 18.8% for patients with a BW ≥ 60 kg. Patients with a BW < 60 kg received a cadaveric split LT near three times more often (BW < 60 kg: 3.4% *versus* BW ≥ 60 kg 1.2%).
Conclusion: Small adults with a BW < 60 kg are disadvantaged for receiving a size matched liver graft in the ET region. These patients may benefit from increased use of intention-to-split policy, living donor LT or assignment of exceptional MELD points.

OS011 DCD LIVER TRANSPLANTATION AND AUTOIMMUNE LIVER DISEASES - AN INCOMPATIBLE COMBINATION?

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Background: Previous studies showed that patients with primary sclerosing cholangitis (PSC) may benefit from DCD liver grafts, however, graft survival appears to be inferior. In experimental models, prolonged ischemia augmented grafts alloimmune injury through several innate immunogenic pathways. The aim of the study was to explore the clinical outcomes of DCD liver transplantation for autoimmune liver diseases [PSC, primary biliary cirrhosis (PBC) and autoimmune hepatitis (AIH)], and undertake a histological analysis of the explant pathology for patients re-transplanted due to graft failure.
Methods: Data on DCD liver transplant recipients (2005–2017) was retrospectively collected in two UK liver transplant centres. Graft survival for patients transplanted for PSC, PBC and AIH was the primary end-point. Univariate and multivariate (Cox-regression) analyses were performed. A descriptive analysis of the explant pathology of the failed grafts requiring re-transplant was undertaken.
Results: 216 DCD liver transplants were undertaken (55 for autoimmune indications). Survival curves (Fig. 1) showed that patients transplanted for autoimmune disease had significantly lower graft survival ($p = 0.036$). Ischemic cholangiopathy (IC) was noted in 9 patients (50%) out of a total 18 who lost their grafts. A Cox-regression model showed that DCD liver transplant for autoimmune diseases is a predictor of graft failure (HR = 1.85, 95% CI = 1.03–3.33, $p = 0.039$). Descriptive analysis of the explant pathology of patients re-transplanted confirmed IC as main reason for graft failure.
Conclusion: DCD liver transplantation leads to significantly worse graft survival in autoimmune liver diseases. Further analysis of alloimmune mechanisms is warranted.

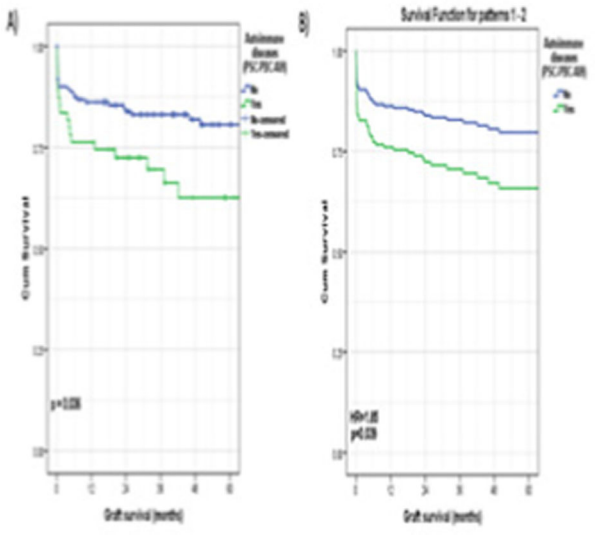

Figure 1. A) Kaplan Meier analysis for graft survival in patients transplanted for autoimmune diseases. B) Survival probability for graft survival after adjustment in a Cox-regression model.

OS012 NONAGENARIAN GRAFTS FOR LIVER TRANSPLANTATION. A COMPARISON WITH IDEAL YOUNG DONORS

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Background: Use of very old donors in liver transplantation (LT) has shown favorable results and is growing worldwide. However, this practice is not yet universally implemented.
Materials and methods: This was a retrospective analysis of whole-size, primary, ABO-compatible, adult LT from donors after brain death (DBD) between January 2014 and September 2018. Recipients of DBD graft ≥ 90 years were compared to patients transplanted with donors aged 18–39 years.
Results: A total of 16 DBD transplants from nonagenarian donors was compared to 37 recipients of younger grafts. Overall, the two groups were comparable in terms of indication for LT, HCV serology and pre-LT MELD score. The median (IQR) follow-up was 16 (6–33) months for older grafts versus 25 (15–36) for younger grafts ($p = 0.23$). No graft loss or patient death was observed in the elderly graft group versus 3 cases among younger grafts. There were no cases of early allograft dysfunction (EAD) in the older group vs 4 cases in the younger group ($p = 0.42$). Three cases of post-reperfusion syndrome were observed in the older group vs 8 in the younger one ($p = 0.89$). The post-LT ALT peak was lower in the older graft group (367 vs 593; $p = 0.03$), but the latter had better post-LT INR peak (1.3 vs 1.4; $p = 0.01$).The median interval to return to normal range was 7.5 versus 6 days for AST ($p = 0.08$); 14.5 versus 13.5 days for ALT ($p = 0.72$); 6.5 vs 5 days for total bilirubin ($p = 0.07$), and 4 vs 3 for INR ($p = 0.25$) in older and younger grafts, respectively. The median (IQR) hospital stay was 15 (11–16) days for older grafts versus 11 (9–15) for younger grafts ($p = 0.71$).
Conclusion: Our preliminary experience shows that age should not preclude consideration of any donor for LT.

OS013 PREDICTIVE FACTORS OF EARLY ALLOGRAFT DYSFUNCTION AND ITS IMPACT ON PATIENT POSTOPERATIVE DEATH AND LONG-TERM GRAFT SURVIVAL

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Early allograft dysfunction (EAD) is a multifactorial syndrome associated with higher morbidity in the early post-LT period and may compromise graft survival. We aimed to determine predictors of EAD (Olthoff criteria) and assess its impact on death within 90 postoperative days (POD) and on long-term graft survival.

All the 1329 LTs performed in our center between 2007 and 2016 were reviewed retrospectively. LDLT and domino were excluded. Recipient (7 variables), donor (5 variables), intraoperative data (6 variables) and postoperative data (5 variables) were used to assess the predictors of each endpoint. Potential risk factors were included in a multivariate logistic regression model or a Cox model when adequate.

The incidence of EAD was 36% overall and 27% during the last two years, with 10% of re-LT (3.6% in non- EAD, $p < 0.0001$). Analysis of the study cohort of 1212 LTs revealed 7 independent predictors of EAD: partial graft (RR = 2.22, $p = 0.003$), SCOT preservation solution (RR = 1.67, $p = 0.04$),

D/R graft weight ratio (RR = 1.37, $p = 0.006$), MELD score at LT (RR = 1.03, $p = 0.0007$), cold ischemia time (RR = 1.00, $p < 0.0001$), recipient age ≥ 60 yrs (RR = 0.73, $p = 0.04$) and combined kidney transplant (RR = 0.50, $p = 0.02$). We afterwards assessed if EAD has an impact on POD. EAD (RR = 1.94, $p = 0.04$) with two other factors: use of another solution than IGL-1 (RR = 2.15, $p = 0.03$) and number of transfused blood units (RR = 1.05, $p = 0.002$) were independent predictors of POD. Finally, EAD was a strong independent predictor (RR = 1.43, $p = 0.003$) of graft survival (79%vs. 91% at 1 year, $p < 0.0001$), with five other factors: number of transfused blood units (RR = 1.02, $p = 0.002$), recipient age (RR = 1.02, $p = 0.0002$), donor age (RR = 1.01, $p = 0.007$), length of ICU stay (RR = 1.01, $p < 0.0001$) and recipient BMI (RR = 0.96, $p = 0.001$).
Conclusion: the incidence of EAD was 36% in our series. Seven independent factors were predictive of EAD. EAD impacted significantly the POD and graft survival even in the absence of re-LT.

OS014 MODEL FOR EARLY ALLOGRAFT FUNCTION IS PREDICTIVE OF SURVIVAL IN DCD LIVER TRANSPLANTATION, BUT SHOULD NOT BE THE SOLE DRIVER FOR RETRANSPLANTATION

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Background & AIMS: Donation after circulatory death (DCD) liver transplantation is associated with higher rates of early allograft dysfunction, primary non-function and poorer survival.The Model for Early Allograft Function (MEAF) has been shown to predict outcome in donation after brainstem death (DBD) liver transplantation is unclear. In this paper, we explore whether MEAF can be applied to the setting of DCD liver transplantation.
Methods: We performed a retrospective analysis of prospectively collected data from all adult DCD (Maastricht 3) livers transplanted in Cambridge and Edinburgh between 1st January 2011 and 30th June 2017.
Results: 187 DCD liver transplants (without any form of machine perfusion) were undertaken during the study period.

DCD liver transplants with a lower MEAF score had a significantly better survival as compared to high MEAF score (Mantel-Cox $p < 0.0001$); this observed difference was largely due to early graft loss. However, in those whose grafts survived the first 28 days, there were no significant long-term graft or patient survival differences according to the grade of MEAF (Mantel Cox $p = 0.64$ and $p = 0.43$ respectively).

The MEAF score correlated with the length of stay in ICU ($p = 0.0011$) and hospital ($p = 0.0007$), but not with the requirement for retransplantation for ischaemic cholangiopathy ($p = 0.37$) or readmission ($p = 0.74$).
Conclusions: A high MEAF *predicts* early graft loss, but a high MEAF score in itself should not be the *soledriver* for retransplantation following DCD liver transplantation.

OS015 VON WILLEBRAND FACTOR FACILITATES MELD-INDEPENDENT RISK STRATIFICATION ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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Background & Aims: Model of End-Stage Liver Disease (MELD) is used for clinical decision making and organ allocation for orthotopic liver transplantation (OLT). However, MELD may underestimate complications arising from portal hypertension or infection. Von Willebrand factor antigen (vWF-Ag) correlates with portal pressure and seems capable of predicting complications in cirrhotic patients. Accordingly, this study aimed to evaluate vWF-Ag as an adjunct surrogate marker for risk stratification on the waiting list for OLT.
Methods: vWF-Ag at time of listing was assessed in patients listed for OLT. Clinical characteristics, MELD and mortality on the waiting list were recorded. Prediction of three months waiting list survival was assessed by receiver operating characteristics and net reclassification improvement.
Results: Patients dying within three months on the waiting list displayed elevated levels of vWF-Ag ($p < 0.001$). Indeed, MELD and vWF-Ag were comparable and independent in their predictive potential for three-month mortality on the waiting list (AUC: vWF-Ag = 0.739; MELD = 0.766). Importantly, a vWF-Ag cut-off at 413% identified patients at risk for death within three months of listing with a higher odds ratio (OR) than the previously published cut-off at MELD of 15 points (vWF-Ag: OR = 10.873, 95%-confidence interval: 3.160 – 36.084, $p < 0.001$; MELD: OR = 6.527, 95%-confidence interval: 2.216–19.227, $p = 0.001$). Ultimately, inclusion of vWF-Ag into the MELD-system significantly improved prediction of three-month waiting list mortality (AUC: MELDvWF = 0.822).
Conclusions: A single measurement of vWF-Ag at listing for OLT predicts early mortality. Combining vWF-Ag levels with MELD improves risk stratification and may help to prioritize organ allocation in order to decrease waiting list mortality.

OS016 CASE-MIX MODELS TO PREDICT 6-MONTH PATIENT SURVIVAL AND IDENTIFY FUTILITY AFTER LIVER TRANSPLANTATION: A MULTICENTER ITALIAN STUDY

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Background: Short-term patient survival (PS) after liver transplantation (LT) is predicted by MELD. The study aimed to identify, besides MELD, factors predicting 6- and 12-month PS after LT, in order to develop case-mix models. Primary endpoint was 6-mo PS; 2ndary end-points were 6-mo graft survival and 12 mo PS. LT was considered futile if associated with 5 yrs PS < 50% and/or 6 mo PS < 60%.
Method: 14 Italian LT Centres collected recipient and donor characteristics of 1680 consecutive adult LT recipients (2016–2017) with a median follow-up of 24 mo. Intraoperative parameters were included.
Results: At univariate analysis, factors associated with PS were: MELD ($p < 0.001$); PV Thrombosis (PVT) Yerdel 3–4 ($p = 0.002$); dialysis (DIA) ($p < 0.001$) and mechanical Ventilation (MV) 72 h before LT ($p < 0.001$); recipient age ($p = 0.067$); packed red blood cells units (PRBC), Class 6–10: $p < 0.001$; Class 16–20: $p < 0.001$; Class > 20: $p < 0.001$) and packing (PA) at the end of surgery ($p < 0.001$). At the multivariate analysis, 2 predictive models for 6 and 12 mo PS after LT (model A, for pre-LT and model B for both & and post-LT) were identified.

In the model A, predictors were MELD score ($p < 0.001$); PVT ($p = 0.013$); DIA ($p < 0.001$); MV ($p = 0.016$) and recipient age ($p = 0.034$). In the Model B, MELD score ($p = 0.009$); DIA ($p < 0.001$); MV ($p = 0.019$); PRBC (Class 6–10: $p = 0.013$; Class 16–20: $p = 0.007$; Class 20 and over: $p = 0.005$); PACKING ($p = 0.006$) and recipient age ($p = 0.043$) were identified as predictive factors for 6 mo PS after LT. Accordingly, in the final model B based on the case-mix analysis, for each patient (or Centre) a risk-score was calculated. The extreme case-mix level was set at the 95th percentile. Cases in the 1–95th percentile area were highlighted (green box). For each Centre, the 95th percentile level was identified. Centres were arbitrarily named.
Discussion: The results may be useful to prevent futile LT. The models may be also used by stakeholders to plain regulatory policies.

OS03 - CMV AND BK INFECTIONS AFTER RENAL TRANSPLANTATION

OS017 INCREASED EXPRESSION OF THE COINHIBITORS PD-1 AND BTLA ON CMV-SPECIFIC T-CELLS IS ASSOCIATED WITH SYMPTOMATIC CMV INFECTION IN RENAL TRANSPLANT PATIENTS

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Introduction: Cytomegalovirus (CMV) infections occur frequently in renal transplant patients due to immunosuppressive therapy inhibiting CMV-specific T-cell immunity. It was the aim of this study to investigate if the expression of inhibitory molecules on CMV specific T-cells is associated with the clinical course of renal transplant patients.

Methods: Peripheral blood was sampled from 30 renal transplant patients and stimulated with CMV lysate, SEB or control serum in presence of anti-CD28/CD49d. After stimulation, the coinhibitors PD-1 and BTLA were determined on CD154 + CD3 + T-cells. Symptomatic CMV infection was defined as CMV syndrome or tissue invasive disease. Asymptomatic CMV infection was defined as detectable CMV replication in absence of clinical manifestations.
Results: Two renal transplant patients were at low risk for CMV infection according to donor /recipient CMV IgG sero-status at the time of transplantation (D neg / R neg). Seven patients were at high risk (D pos /R neg) and the remaining 21 patients were at intermediate risk (D pos /R pos, D neg / R pos). Patients with low risk were excluded from further analysis. PD-1 expression was significantly enhanced on CMV-specific CD3 + T-cells in patients with a history of symptomatic CMV infection ($n = 6$) as compared to patients with asymptomatic CMV ($n = 14$) infection (CD3 + CD154 + : % of PD-1 + 63.8 $\pm$ 16.0% vs. 37.2 $\pm$ 19.4%, $p = 0.006$). Likewise, expression of BTLA on CMV-specific T-cells was significantly increased in patients with symptomatic versus asymptomatic CMV infection (CD3 + CD154 + : % of BTLA+ 89.3 $\pm$ 9.5% vs. 66.0 $\pm$ 22.0%, $p = 0.003$).
Conclusion: Patients with symptomatic CMV infection had enhanced expression of PD-1/BTLA on virus-specific T-cells. The coinhibitors PD-1/BTLA usually promote T-cell suppression. Therefore, increased expression of PD-1/BTLA on CMV-specific T-cells may compromise viral control and could serve as biomarker to stratify patients at risk.

OS018 EFFECT OF ANTI-THYMOCYTE GLOBULIN ON CMV INFECTION IN KIDNEY TRANSPLANT RECIPIENTS: THE RISK IS NOT INCREASED IN D+R- AND DEPENDS ON PREFORMED CELL-MEDIATED IMMUNITY IN R+

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Background: Rabbit anti-thymocyte globulin (rATG) induction is associated with profound immunosuppression, leading to a higher risk of cytomegalovirus (CMV) infection as compared to anti-interleukin 2-receptor antibody (anti-IL2RA). However, this risk depending on the baseline CMV serological recipient/donor status is still controversial.
Methods: The CMV infection-free survival between rATG and anti-IL2RA-treated patients was analysed in D+R- and R+ patients in one discovery cohort of 559 kidney transplant recipients (KTR) and two independent cohorts (351 and 135 kidney KTR). Furthermore, the CMV-specific cell mediated immunity (CMI) at baseline and at different time-points after transplantation was assessed using an IFN-gELISPOT assay.
Results: rATG increased the risk of CMV infection/disease in R+ but not in D+R- KTR. R+CMI+ rATG-treated patients had a higher CMV infection rate than anti-IL2RA-treated patients, no difference was observed among R+CMI- patients. Longitudinal follow-up demonstrated a deeper depletion of preformed CMV CMI in R+ rATG-treated patients.
Conclusions: D+R- KTR have the highest risk of CMV infection but rATG adds no further risk. Baseline CMV CMI has allowed us to stratify the risk of CMV infection among R+KTR : the least prone being R+CMI+ without rATG, then R+CMI+ with rATG and finally R+ CMI-. Using this stratification, further studies could define an individualized CMV preventive strategy.

OS019 THE USE OF IVIG IN TREATMENT OF BK VIRUS NEPHROPAHTY – SINGLE CENTRE EXPERIENCE

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Background: BK virus nephropathy (BKVN) in kidney transplant recipients is caused by the reactivation of BK virus in the recipient due to the use of potent immunosuppressive therapy protocols. Incidence of BKVN among renal transplant recipients is up to 10%, and it can cause up to7.5% of graft loss. BKVN is treated by modification of immunosuppressive therapy, introduction of antiviral drugs and the use of high dose IVIG. Here we present our results in treatment of BKVN with high dose IVIG and simultaneous modification of immunosuppressive therapy.
Methods/Materials: In this retrospective study we analyzed medical records of 2030 patients in our transplant centr. We selected patients that had biopsy proven BKVN and were treated with IVIG (2 g/kg) combined with immunosuppressive therapy modification. In follow up graft function and BK blood viral load were assessed.
Rerults: In 14 patients (86% male), BKVN was diagnosed by biopsy. Average blood viral load at time of diagnosis was 3,9 $\pm$ 1,5x10E4 copies. At the time of diagnoses 86% of patients received tacrolimus (tac), 14% received cyclosporine (CysA) with corticosteroids and mycophenolic acid (MMF) in their immunosuppressive protocol. Patients were treated with IVIG 2 g/kg. Immunosuppression was modified in 4 different approaches: in 7 patients MMF was converted to everolimus (evero), in 2 patients tac was converted to evero and MMF was reduced, in 4 patients tac was converted to CysA and MMF was reduced and in 1 patient tac was converted to CysA and MMF to everolimus. At 6 months after treatment 72% of our patients had BK blood viral load lower than 1000 copies. During follow up all our patients had preserved graft function, and 2 patients died with a functioning graft.
Conclusion: In this study we have shown that high dose IVIG combined with immunosuppressive therapy reduction and modification results in a significant reduction of BK virus copies in blood. During follow up all our patients had a stabile graft function.

OS021 INTRAVENOUS IMMUNOGLOBULINS PREVENT BK VIRUS REPLICATION IN KIDNEY TRANSPLANT RECIPIENTS, A PILOT STUDY

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Background: In kidney transplantation (KT), BKV replication could lead to BKV-associated nephropathy and graft loss. BKV replication post-KT is mostly of donor's origin. There are no BKV-specific therapies. In a previous work, we demonstrated that BKV genotype-specific neutralizing antibodies (NAb) were protective against BKV replication above the 4 $\log_{10}$ threshold and that intravenous immunoglobulins (IVIg) exhibited high anti-BKV neutralizing activity in vitro and ex vivo. We investigated whether administration of IVIg prevents BKV replication after KT.
Methods: Patients who underwent KT in Strasbourg in 2017 were included. Donors and recipients NAb titers were measured the day of KT. Patients at high risk of BKV replication were defined as those having NAb titer below 4 $\log_{10}$ against the donor's BKV strain (or against the most common strain (genotype I) if the sample of the donor was unavailable). KT Patients with secondary immunodeficiency ($n = 44$) or antibody mediated rejection ($n = 3$) received 1 to 3 doses of IVIg spaced by 3 weeks at a dose of 0.4 g/kg or 2 g/kg depending on the indication. BKV Nab titer and viremia were monitored until 1 year after KT. BKV viremia incidence in high risk patients receiving IgIV were compared with low risk patients who did not receive IVIg treatment in the current cohort (2017, $n = 41$) and with patients at high risk who did not receive IVIg treatment in a previous cohort (2012–2014, $n = 35$)
Results: among 111 patients who underwent KT in 2017, 47 were at high risk of BKV replication and received IVIg. At M12, the incidence of BKV viremia in the high-risk group treated with IVIg was reduced to that of the low-risk group (6% vs 12%, $p > 0.05$). Also, this incidence was significantly lower than that of non-treated high-risk patients in the previous cohort (6% vs 43%, $p < 0.0001$).
Conclusion: IVIg may represent an important strategy to prevent BKV replication after KT. A larger randomized prospective cohort study will start soon to confirm these results.

OS022 IL-10 AS A KEY PLAYER IN CHRONIC BK-VIRUS INFECTION OF RENAL TRANSPLANT RECIPIENTS

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Background: It has previously been shown in a mouse model of chronic LCMV infection that sustained IL-10 production induces increasing N-glycan branching of surface molecules on CD8 + T cells, resulting in decreased sensitivity of virus-specific T cells and viral persistence (Smith LK et al, Immunity 2018).
Materials and Method: We analyzed intracellular cytokine responses, CD4 + T helper function and in-vitro B cell responses pretransplant and up to 24 months posttransplant in a prospective study of 105 renal transplant recipients, who were randomized to a CsA/MMF (n = 35), Tacr/MMF (n = 37) and Tacr/ERL (n = 33) regimen, respectively. 18 drop-outs were excluded from analysis.
Results: Pretransplant, increased IL-10R expression was detected in patients developing BK viremia (CD4 + T cells, p = 0.005; CD8 + T cells, p = 0.004; CD14 + monocytes, p = 0.004). Posttransplant, we found an increased CD4 helper activity (p = 0.008, 4 months) and increased IL-10 responses of CD4 + and CD8 + T cells (CD4: p = 0.003, 1 year; p = 0.038, 2 years; CD8: p = 0.013, 1 year) in these patients.

Risk of BK viremia was lowest in Tacr/ERL and highest in Tacr/MMF patients (CsA/MMF: 4/30 (13%); Tacr/MMF: 14/36 (39%); Tacr/ERL: 1/21 (5%); p = 0.005). Tacr/ERL patients showed the lowest CD4, CD19 and CD14 cell IL-10 responses (CD4: p = 0.009, 1 year; CD19: p = 0.002, 4 months; CD14: p = 0.048, 2 years), but increased T-dependent B cell responses (p = 0.004, 4 months; p = 0.019, 1 year) compared to CsA/MMF and Tacr/MMF patients. Luminex-based screening, however, showed no significant differences in HLA class I and II or MICA antibody formation between the immunosuppressive regimens ($p \geq 0.510$).
Conclusion: Our data suggest that IL-10 plays a major role in chronic BKV infection after renal transplantation. Immunosuppressive treatment with Tacr/ERL significantly downregulates IL-10 responses and thereby appears to affect the key player in chronic BKV infection, resulting in a significantly diminished BK viremia incidence.

OS023 SIMILAR LONG-TERM OUTCOMES WITH PREEMPTIVE AND PROPHYLACTIC ANTI-CYTOMEGALOVIRUS STRATEGY IN KIDNEY TRANSPLANT RECIPIENTS

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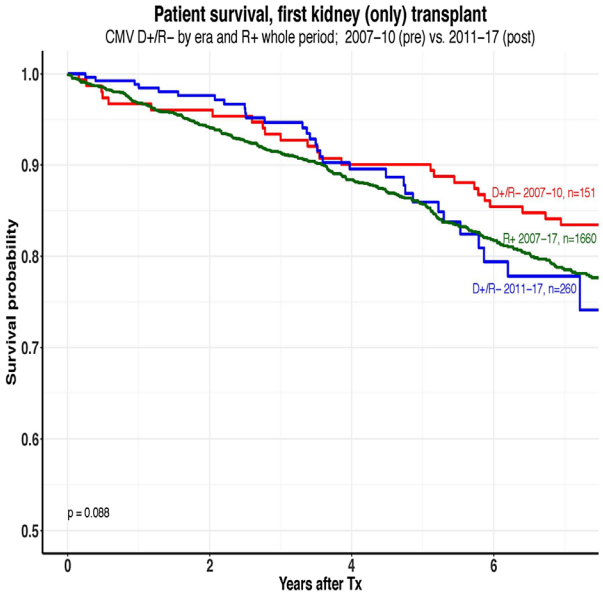
Background: Cytomegalovirus (CMV) naïve kidney transplant recipients (R-) transplanted with an organ from a CMV positive donor (D+) are at high risk for CMV disease. For the D+R- recipients international guidelines indicate equal efficacy by both the prophylactic or preemptive preventive approach, provided an adequate surveillance of CMV PCR when the preemptive approach is used. Our center switched from a preemptive approach, with active surveillance, to routinely 6 month valganciclovir (vGCV) prophylaxis in 2011. Whether the long-term outcomes are different with these alternate strategies is not known.
Methods: Altogether, complete national data from 410 D+R- kidney transplant recipients were available (2007–2010; 151 recipients with active surveillance receiving preemptive vGCV therapy vs. 2011–2017; 260 recipients whom received vGCV prophylaxis from time of engraftment, 900 mg once daily adjusted for renal function). All 1660 R+ kidney transplant recipients in the period 2007–2017 served as controls. Long-term graft and patient outcomes were retrieved from the Norwegian Renal Registry. All patients have given written informed consent for use of their data.
Results: The actuarial 5 years patient survival in D+R- patients was not different between the two approaches; preemptive 89% [95% CI: 85%-95%] vs. prophylactic 86% [81%-92%] (Figure 1, p = 0.23). Also, the crude and death censored graft survival were similar; 85% [80%-90%] vs. 77% [71%-84%] (p = 0.13) and 92% [88%-97%] vs. 87% [82%-93%] (p = 0.29), respectively. In control patients (all R+) the corresponding 5 years patient- and death censored graft survival rates were unchanged in the two time eras.
Conclusion: The long-term outcomes of preemptive therapy or prophylaxis for CMV prevention in high-risk kidney transplant recipient were similar. These nation-wide data support the international consensus guidelines which recommend the use of either strategy as preferred by the different transplant centers.



OS024 EFFICACY AND SAFETY ACCORDING TO DOSE OF VALGANCICLOVIR FOR CYTOMEGALOVIRUS (CMV) PROPHYLAXIS IN TRANSPLANTATION: NETWORK META-ANALYSIS USING RECENT DATA

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Introduction: Valgancivlovir is importantly used to prevent post-transplant CMV infection among kidney transplantation patients. However, the dose of such drug being used still remains controversial since the continuous use of drug decrease kidney functions and induces leukopenia in some of the cases. Accordingly, the purpose is to measure the appropriate dose of the drug required for preventing CMV using network Meta analysis.
Methods: We searched the Cochrane Register, OVID MEDLINE, EMBASE, and Pubmed until Sep 15, 2018.. Definition of low dose valganciclovir group is 450 mg and standard dose one is 900 mg. Studies evaluating among valganciclovir 900 mg, 450 mg and controls were evaluated. We performed direct and indirect network meta-analysis using Bayesian models and generated rankings of the different dose of valgaciclovir agents by generation mixed treatment comparison.
Result: Twenty-three studies involving 3,478 participants were eligible. As a result of analyzing among three groups, following completion of the research, the analysis revealed that the glomerular filtration rate, graft loss, tacrolimus level, antibody mediated rejection, fungal, and *Candida* infection rates were not different among groups. Compared with control, there was no difference between low dose 0.79 [95% CrI, 0.50–1.40] and standard dose 1.0 [95% CrI, 0.61–1.60] groups when CMV incidence was compared. In the Rank probabilities table, the best order for lowering the CMV event was as high as dose of 450 mg (71.1%). Incidence of leukopenia showed a significant difference, 4.3 times higher in the high dose group [CrI, 2.69–7.10], which was 2.9 times higher in the high dose group compare with low dose group [CrI, 1.88 -4.67].
Conclusion: The use of valganciclovir did not show any difference in other side effects, but the use of low doses of leukopenia significantly reduced side effects. The incidence of CMV was not different among the three groups, but the tendency was also decreased at low dose.

OS04 - KIDNEY REJECTION AND HISTOLOGY: CLINICAL FACTORS ASSOCIATED WITH OUTCOME AFTER KIDNEY TRANSPLANTATION

OS025 CLINICAL PATTERNS AND OUTCOMES OF THROMBOTIC MICROANGIOPATHY RELATED TO KIDNEY TRANSPLANTATION: A NATION-WIDE MULTICENTRE STUDY

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Background: Thrombotic microangiopathy (TMA) is a life-threating unfrequent condition associated to kidney transplantation (KTX) driven by complement Therapy is based on Plasmapheresis (PLASMA) and Eculizumab® (ECU).
Study Design: Multicentre retrospective cases study. Joint initiative from KTX Research Public Net and Genetic-Complement reference lab.
Case definition:: 1: Proved TMA superimposed on KTx (Novo-TMA Group). 2: Profilaxis for TAM recurrence in patients with previous TAM diagnosis who receive a KTx (PRO group).
Results: *TMA Group* 22 cases (47,7 year 45,5% W, no previous) received graft from 15 Brain death-BDD, 5 Cardiac Death CDD, 2 Living donor (LD) 20 cases 1st KTx.

15 cases early presentation (2 to14 d postKTx) 66% with immediate graft function, nadir Hb 8.5 g/dL, 55.000 plat/mm3 LDH 824 mg/dL No any trigger added to KTx. 11 received PLASMA and got 1 complete & 7 hematologic remission. Then received ECU in 12 cases and got: 7 global remission, 4 partial and 1 Nephrectomy. 11 cases spent 2 month on ECU and 1 still on ECU. No serious adverse event (SAE), no risk-factors from Genetic study, nor IS regimen or type of donor.

7 *late cases* (> 1 year postKTx) with triggers (Infections and tacro) all received PLASMA with partial remission, then all received ECU and 5 got total remission.

PRO Group 11 cases (30.0 y & 54.5% W) all with biopsy proved TMA on dialysis 8 complement mutation. They received a graft (8 BDD, 1 CDD 2 unrelated LD) with thymoglobuline® induction. 8 patients receive pre-emptive ECU without recurrences. 3 cases without ECU got 2 recurrences. One case (no mutations) withdraw ECU after 1 month others still on it (3,2 years), all cases who receive ECU alive and without dialysis. No SAEs.
Conclusions: We have defined different clinical profiles & therapy approach in a real life TMA clinical series. ECU present good efficacy and safety profile. Preemptive use of ECU allow successful KTX with graft coming from different donors. REDInREN ISCiii 16/009

OS026 OUTCOME AND RISK FACTORS OF RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION

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Background: Recurrent focal segmental glomerulosclerosis(FSGS) is common after kidney transplantation. We conducted a retrospective cohort study with the aim to investigating the long-term outcome and risk factors of recurrent FSGS after kidney transplantation.
Method: We retrospectively collected 92 kidney transplant recipients with FSGS as the primary disease from January 2000 to December 2011. The patients were followed up for at least 5 years. Baseline characteristics including age,gender, proteinuria level, progress of primary FSGS were recorded. Proteinuria levels after transplant were monitored, and recurrent FSGS was diagnosed by allograft biopsy when proteinuria reappeared.
Results: 34(37.0%) patients suffered recurrent FSGS after kidney transplantation, which was diagnosed by allograft biopsy. The median recurrent time was 26 months. Proteinuria was found in all patients with recurrent FSGS, and the mean proteinuria level was 4.21 g/ 24 hours. Kaplan-Meier analysis showed that the 1-, 5-, and 10-year death censored graft survivals were much lower in recurrent FSGS recipients compared to non-recurrent FSGS recipients (97.1%, 47.1% and 28% vs. 100%, 87.9%, and 58.9%). The median survival time was much shorter in recurrent FSGS recipients than non-recurrent FSGS recipients (57 months vs. 142 months, $p = 0.0002$). Logistic multivariate regression showed that young age (<18 years old), proteinuria more than 7 g/24 h before transplant, and rapid progress of primary FSGS(<3 year from onset to uremia) were independent risk factors for recurrent FSGS ($p < 0.05$).
Conclusion: Recurrent FSGS is common after kidney transplantation and prognosis is poor. Young age, heavy proteinuria before transplant, and rapid progress of primary FSGS are independent risk factors for recurrent FSGS.

OS027 TROMBOTIC MICROANGIOPATHY AFTER KIDNEY TRANSPLANTATION IS ASSOCIATED WITH PRETRANSPLANT COMPLEMENT ABNORMALITIES OF RECIPIENT SUPERIMPOSED ON ENDOTHELIAL INJURY OF DONOR KIDNEY

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Introduction: Thrombotic microangiopathy (TMA) is a rare cause of kidney graft dysfunction. Although it is most often associated with use of certain drugs or antibody mediated rejection (ABMR), recently genetic mutations in complement regulatory genes have been reported in up to a third of these patients. Irrespective of the etiology of TMA, endothelial cells are the main targets of immunologic attack driven by antibodies, complement or both.
Methods: Kidney transplant recipients (KTRs) with TMA without criteria of ABMR were assessed ($n = 6$) and compared to age and gender matched controls with unremarkable kidney biopsy ($n = 6$). Preimplantation biopsies of patients and controls were examined in order to exclude preexisting changes, including TMA, and evaluate electron microscopic (EM) vascular changes. The EM differences in vascular injury were validated by semiquantitative score. Complement assays were performed using pretransplant frozen plasma samples. The activity of the classical complement pathway (CH50), alternative pathway (AH50), concentration of C3, C4, factors B, H, I, MAC and C3Nef inhibitor were evaluated.
Results: All patients that experienced TMA have extremly decreased AH50 (49,07, range 0,9–89,9 vs 2,16, range 0–8,6; $p = 0,008$).), among which all patients except one have decreased factor I, while 3 patients had antibodies against factor H. Preimplantation light microscopy findings of TMA patients and controls were unremarkable, however in TMA patients EM signs of more pronounced endothelial injury in different compartments were present (Table).
Conclusion: KTRs who experienced TMA received grafts with severe preimplantation endothelial injury and have abnormalities of AH50, with decreased factor I and/or antibodies against factor H. It is possible that extensive preimplantation injury to the endothelium inicited exposition of endothelial antigens and activation af defective alternative pathway, which converged pathogenesis on final pathway of TMA.

OS028 ASSOCIATION BETWEEN AGE OF RED BLOOD CELL FOR TRANSFUSION AND OUTCOMES AFTER KIDNEY TRANSPLANTATION: A LONGITUDINAL NATIONWIDE ANALYSIS

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Background: Red blood cell (RBC) transfusions are frequently required in the early kidney post-transplant period. However, the consequences of RBC transfusions on long-term outcomes are largely unrecognized. Moreover, whether RBC storage duration affects transplant outcomes is unknown as well.
Methods: We conducted a nationwide cohort study based on the crossing of data from two prospective French national registries. All patients having received a first kidney transplantation between 2002 and 2008 in France were identified from the CRISTAL registry of the *Agence de la Biomédecine*. Transplant parameters and outcomes were extracted. Those transfused at time

		GLOMERULAR CAPILLARY LOOPS		PERITUBULAR CAPILLARIES		ARTERIOLES	
	Subendothelial distensions	Swelling	Arcadic structures	Swelling	Arcadic structures	Swelling	Arcadic structures
TMA patients	0,2 ± 0,0	1,2 ± 0,74	1,3 ± 0,4	1,03 ± 0,47	0,33 ± 0,0	1,16 ± 1,02	0,5 ± 0,5
controls	0,33 ± 0,43	0,08 ± 0,0	1,25 ± 0,25	0,08 ± 0,0	0,08 ± 0,0	0 ± 0,0	0,13 ± 0,0
P	0,35	0,01	0,89	0,02	0,05	0,11	0,05

of transplantation and up to 14 days post-transplant were identified from the national database of the *Etablissement Français du Sang* and transfusions characteristics were collected. The primary endpoint was transplant failure.
Findings: Of 12559 patients having received a first kidney transplantation during the study period, 3483 (28%) received an early post-transplant transfusion. Median follow-up was 7.6 years. Multivariate analysis determined that post-transplant transfusion was associated with an increased risk in transplant failure (HR 1.650, 95%CI [1.538;1.771] $p < 0.0001$). Propensity score analyses recapitulated this
Result: Longer minimum storage duration of transfused RBC reduced the effect of transfusion on transplant failure (HR 0.989, 95%CI [0.982;0.997] for each additional day, $p = 0.048$). Patients transfused with at least one RBC stored > 20 days had a 5% crude increase in transplant survival at 3 years and 7% at 5 years compared to those transfused with only RBC stored less than 20 days.
Interpretation: Post-transplant transfusions are significantly associated with a decrease in transplant survival. Short RBC storage duration is associated with reduced survival among transfused recipients.

OS029 OUTCOMES FOLLOWING SECOND KIDNEY TRANSPLANT: RESULTS FROM THE IRISH KIDNEY TRANSPLANT PROGRAMME

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***Introduction*:** For patients who have undergone primary kidney transplant (PKT) and returned to dialysis, second kidney transplantation(SKT) offers improved quality of life and survival advantages. However, SKT is associated with greater immunologic and non-immunologic risk. Despite these challenges, outcomes following SKT are acceptable with reported 5-year graft survival of up to 86%. We report outcomes and experiences following SKT from the Irish Kidney Transplant Programme.
***Methods*:** We identified all patients receiving SKT at a single transplant unit between January 1993 and August 2017 using a prospectively maintained database. Outcomes assessed included graft survival rates following SKT, incidence of acute rejection(AR) and delayed graft function(DGF). We assessed both donor and recipient risk factors for AR, DGF and long-term graft failure. Statistical analysis was completed using SPSS v22.
***Results*:** A total of 394 SKT were carried out over the study period. Follow up data was complete for 98.7% of patients. Median follow-up was 155(13–309) months. At the end of the study period, 239/394 recipients had at least 10 years of follow up completed. Median survival of PKT was 6(0–34) years

The 1-,5- and 10-year death censored graft survival rates following SKT were 93.7%, 86.7%, 74.7% respectively. An independent finding showed length of survival of primary graft < 6 years was predictive of poor outcome with SKT (HR0.6, $p < 0.05$), subgroup analysis of this cohort is underway. As expected, episodes of AR (HR1.6, $p < .05$), DGF (HR 2.0, $p < .05$) and HLA-DR MM (HR 1.7, $p < .05$) at SKT were associated with reduced SKT graft survival. The incidence of AR at SKT was 18.3%. AR at time of PKT significantly predicted AR at SKT ($p < 0.001$)
***Conclusion*:** We report the largest single centre experience of SKT outcomes. We have demonstrated that SKT can yield desirable outcomes for patients with a failed PKT. However, early PKT loss predicts a poorer outcome with sequential transplant.

OS030 TAILORED INDUCTION IMMUNOSUPPRESSION BASED ON PRETRANSPLANT DONOR SPECIFIC ANTIBODIES TO PREVENT ANTIBODY MEDIATED REJECTION

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Background: Sensitization to HLA antigens remain a large barrier to successful kidney transplantation and peritransplant desensitization is advocated in patients with preformed donor specific antibodies (DSA). Here we aimed to adapt induction immunosuppression based on DSA MFI category.
Methods: 111 patients who had undergone kidney transplantation in 2013–2018 with pretransplant DSA (anti HLA-A, -B, -DR antibodies with MFI > 1000) were included in this observational study. Peritransplant desensitization was adapted based the pretransplant risks (actual PRA, DSA levels, retransplantation and patient history), based on pretransplant immunological background and induction treatment used 3 groups were formed: dual induction with rATG/IVIg, triple induction with rATG/IVIG+plasmapheresis (PP) and quadruple induction with rATG/IVIG/PP+rituximab, all patients received triple maintenance immunosuppression. Negative CDC crossmatch was a condition to proceed to transplantation (Tx). Protocol biopsies were performed at 3 months and predictors of 3-year outcomes were evaluated.
Results: 3-year death-censored graft and patient survival was similar in all groups. The acute antibody mediated rejection (ABMR) incidence was significantly higher in quadruple induction group ($p < 0.01$). The 3-month protocol biopsy findings revealed more normal findings in dual induction group than in other two cohorts where capillaritis and tubulitis were more frequent. Multivariate binary regression revealed FXCM-B positivity to be a predictor of ABMR (OR = 8.9, 95% CI: 2.6–30.2, $p < 0.001$). Flow cytometry crossmatching (FCXM) tests predicted the incidence of ABMR with 72% sensitivity and 84% specificity, contrary to DSA category (MFI < 5000 vs. MFI > 5000) which had poor predictive value.
Conclusion: Tailored immunosuppression based on pretransplant DSA in sensitized patients failed to prevent from ABMR. FCXM is the only reliable tool to predict ABMR and should be used in all sensitized patients prior to Tx.

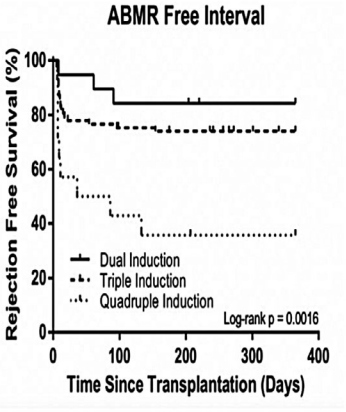

Figure 1: Acute antibody mediated rejection free interval expressing the 1-year incidence of ABMR within the cohorts.

OS031 IMPACT OF STEROID-FREE IMMUNOSUPPRESSION ON INTERSTITIAL FIBROSIS QUANTIFIED BY AUTOMATED DIGITAL ANALYSIS: RESULTS OF A PROSPECTIVE, RANDOMIZED, MULTICENTRE PHASE IV STUDY

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Aim: No randomized study evaluated quantification of interstitial fibrosis (IF) by computer-assisted image analysis following renal transplantation.
Patients: An institutional open prospective randomized multicentre study selected 193 primary and re-transplant patients, without pre-existing DSA; 188 were randomized and final evaluation was available in 178: 90 patients did not receive steroids (No Steroid Group; NSG) and 88 received standard steroids (Steroid Group; SG) for at least one year. All patients received ATG or anti-IL2-R MoAb, tacrolimus (Prograf® or Advagraf®) and mycophenolate mofetil or mycophenolique acid.
Results: Digital quantification of IF showed no inferiority in the NSG at 0, 3 and 12 months (no inferiority margin = 10%); mean difference at 12 months = 3.50% CI 95% [-0.51%; 7.50%]. For comparison, all biopsies were blindly reviewed by two pathologist experts for semi-quantitative IF grading: score 2–3 was not different on day 0 and 3 months but higher (31 vs 15%) in the NSG at 12 months; 16.12% CI 95% [0.00%; 31.81%]; *p = 0.04*. No inferiority of renal function (e-GFR) in the NSG was not demonstrated (no inferiority margin = -4 ml/min). However, no inferiority of protein/creatinine urinary ratio (threshold 10 mg/mmol) was indeed demonstrated in the NSG. Acute rejection incidence did not differ among groups: 13% in the NSG and 9% in the SG; de *novo* DSA: 2,2% in the NSG and 3,4% in the SG; 3 grafts (3,3%)

were lost in the NSG and 7 (8%) in the SG; NODAT: 11% in the NSG and 20% in the SG. The non-inferiority of the NSG was not confirmed among these secondary end-points.
Conclusion: The absence of steroids from the day of surgery did not favor more and/or progression of IF when quantified by computer-assisted image on protocol renal biopsies at 0, 3 and 12 months following transplantation. This methodology, in contrast to current histopathological grading, avoids wide interobserver variation and may allow reliable comparison across centres.

OS032 THE GRAFT AND PATIENT SURVIVAL OF KIDNEY TRANSPLANTATION ACCORDING TO ETHNICITY IN US KIDNEY TRANSPLANT RECIPIENTS

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Background: African American kidney transplant recipients experience disproportionately high rates of graft loss. The aim of this analysis was to use a UNOS data set that contains detailed baseline and longitudinal clinical data to establish and quantify the impact of the current overall graft loss definition on suppressing the true disparity magnitude in US AA kidney transplant outcomes.
Methods: Longitudinal cohort study of kidney transplant recipients using a data set created by United Network for Organ Sharing (UNOS), including 266,128 (African American 70,215, Non-African American 195,913) transplant patient between 1987 and December 2016. Multivariable analysis was conducted using 2-stage joint modeling of random and fixed effects of longitudinal data (linear mixed model) with time to event outcomes (Cox regression).
Results: 195,913 non-African American (AA) (73.6%) were compared with 70,215 AA (26.4%) recipients. 10-year-graft survival of AA in all era is lower than that of non-AA (31% in deceased kidney transplants (DKT) AA recipient and 42% in living kidney transplantation (LKT) non-AA recipient). 10-year-patient survival of AA with functioning graft in all era is similar that of non-AA. Multivariate Cox regression of factors associated with patient survival with functioning graft are acute rejection within 6 months, DM, hypertension and etc. Pre-transplant recipient BMI in AA show the trend as a protective factor in patient survival with functioning graft although not significantly in statistics
Conclusions: African American kidney transplant recipients experience a substantial disparity in graft loss, but not patient death with functioning graft.

OS05 - HCC IN LIVER TRANSPLANTATION

OS033 LIVER TRANSPLANTATION AFTER SUCCESSFUL DOWNSTAGING OF HEPATOCELLULAR CARCINOMA MACROVASCULAR INVASION

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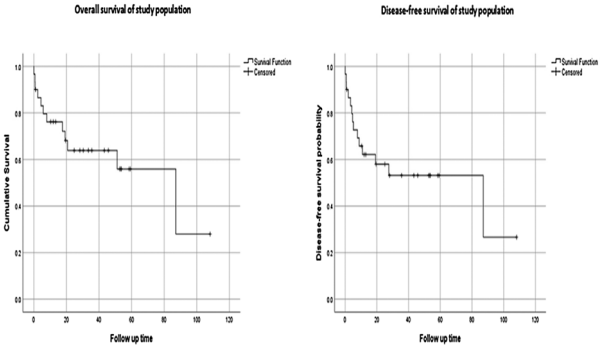
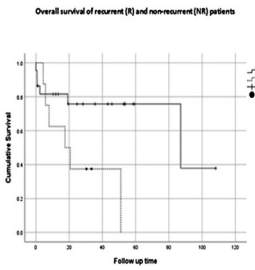
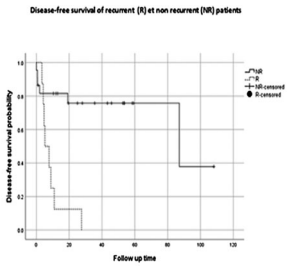
Introduction: Macrovascular invasion (MVI) is considered a contraindication to liver transplantation for hepatocellular carcinoma (HCC) because of a high risk of recurrence. However, it can now be treated by loco-regional means, re-opening the discussion. The aim of the present collaborative study was to explore the post-transplant outcome after successful downstaging of MVI.
Methods: Medical records of 45 patients with transplantation after successful downstaging of MVI were collected from ten university transplant centers and retrospectively reviewed. In order to improve the homogeneity of the radiological diagnosis of MVI, the images were assessed centrally by an expert liver radiologist. Images for second radiological assessment were available in 36 (80%) cases and diagnosis of MVI was confirmed in 30 (83.3%) cases. Predictors of recurrence were defined by comparing patients with and without recurrence.
Results: A total of 30 patients (25 males and 5 females, median age of 58 years, range: 44–68) was included.

	Total *n* = 30	Non-recurrent *n* = 22	Recurrent *n* = 8	P value
Epidemiological and clinical data				
Median age, yrs (range)	58 (44–68)	57 (44–68)	61 (44–67)	0.159
Male/female, *n*	25/5	18/4	7/1	0.931
Underlying liver disease, *n* (%)				0.672
HCV	15 (50)	12 (55)	3 (37)	
HBV	7 (23)	4 (18)	3 (37)	
HCV+HBV	3 (10)	2 (9)	1 (13)	
Other	5 (17)	4 (18)	1 (13)	
Median MELD score at LT, (range)	8 (2–41)	8 (3–40)	9 (2–41)	0.559
Data at MVI diagnosis				
Type of MVI, *n* (%)				0.215
Vp1	7 (23)	5 (23)	2 (25)	
Vp2	12 (40)	8 (36)	4 (50)	
Vp3	5 (17)	5 (23)	0	
Vv1	1 (3)	0	1 (12.5)	
Vv2	3 (10)	2 (9)	1 (12.5)	
Vv3	2 (7)	2 (9)	0	
Median number of HCC, *n* (range)	1 (1–6)	1 (1–10)	1.5 (1–6)	0.585
Median diameter of the largest HCC, cm (range)	5.9 (2–15)	6 (2–15)	3.5 (2–7.5)	0.063
Median AFP, ng/mL (range)	71.6 (1.2–231100)	70.5 (1.2–77890)	79 (6.1–231100)	0.472
Data at transplantation				
Median number of HCC, *n* (range) *	1 (0–4)	1 (0–2)	1 (0–4)	0.322
Median diameter of the largest HCC, cm (range) *,#	1 (0–4)	2.8 (1–8)	2.5 (1.4–5.5)	0.547
Beyond Milan criteria, *n* (%) *	7 (26)	4 (18)	3 (43)	0.327
Median AFP, ng/mL (range)	7.5 (1.0–12000.0)	5 (1.0–7053.0)	94 (4.4–12000.0)	0.019
Downstaging treatment				
LRT type to treat MVI, *n* (%)				
TACE	15 (50)	9 (41)	6 (75)	
SIRT	9 (30)	8 (37)	1 (12.5)	
LR	5 (17)	4 (18)	1 (12.5)	
Other	1 (3)	1 (4)	0	
Median number of LRT to treat MVI, *n* (%)	1 (1–6)	1 (1–6)	1 (1–5)	
Time from MVI diagnosis to successful downstaging, months (range) *	6.1 (0.7–24.5)	5.8 (0.7–21.1)	6.1 (2.3–24.5)	0.853
Time from successful downstaging to transplant, months (range)	11.4 (0.8–43.3)	11 (0.8–43.3)	9 (1.9–19.6)	0.576







The median post-transplant follow-up time was 26 months (range: 1–108). Recurrence was observed in 8 patients (26.7%) after a median time of 6.5 months (range 3.4–27.5).

The 5 years overall survival and disease-free survival was 63.9% and 53.1%, respectively, with a better survival in patient without recurrence.

AFP was the only pre-transplant variable predicting recurrence with an area under the curve of 0.78, and with 11.1% of recurrence when AFP was < 10 ng/ml. The number of viable tumor nodules ($p = 0.008$), the presence of residual HCC ($p = 0.036$) and satellite nodules ($p = 0.001$) on the explant were also significantly different between patients with and without recurrence.

Conclusion: HCC patients with MVI can be considered for liver transplantation, provided that they previously underwent successful downstaging resulting in a complete radiological MVI disappearance and in a pre-transplant AFP inferior to 10 ng/ml.

OS034

THE IMPACT OF DIRECT ACTING ANTIVIRALS ON HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION: A MULTICENTRIC RETROSPECTIVE STUDY

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Background: There are conflicting reports regarding the risk of hepatocellular carcinoma (HCC) following hepatitis C (HCV) treatment with direct-acting agents (DAA). Our aim was to assess the impact of antivirals on the risk of HCC recurrence post liver transplantation (LT) for HCC.

Methods: We retrospectively reviewed LT recipients, from five high-volume LT centres in North America and Europe, who were transplanted for HCC-HCV from 2005 to 2015. Patients were divided according to the antiviral treatment they received after HCC diagnosis (pre or post-LT): DAA, interferon (IFN) or no treatment. Recurrence incidence was compared by the Kaplan Meier method. Multivariable Cox regression was performed to identify risk factors for HCC recurrence.

Results: Of the 875 HCV-HCC transplant recipients, 121 (13.8%) received pre-LT DAA, 112 (12.8%) pre-LT IFN, 395 (45.1%) post-LT DAA, 105 (12.0%) received post-LT IFN and 142 (16.2%) patients were antiviral naïve. The median follow-up was 3.7 (2.1-6.6) years. Of the patients treated prior to LT, the 5-year recurrence-free survival was 93.4%, 84.8%, 73.9% for the pre-LT DAA, pre-LT IFN and antiviral naïve groups, respectively, $p < 0.001$ (Figure 1-A). After multivariable regression, the use of pre-LT DAA was not associated to risk of recurrence [HR = 0.44 (95%CI 0.19-1.00)]. Among patients who received antiviral after LT, the crude recurrence incidence was 2.6 (95%CI 1.5-4.5), 2.8 (95%CI 1.4-5.6), 3.3 (95%CI 2.6-4.3) per 100 person-year in post-LT DAA, post-LT IFN and treatment naïve patients, respectively, $p = 0.04$ (Figure 1-B). In a multivariable model, post-LT DAA was not related to increased risk of recurrence [HR = 0.62 (95% CI 0.33-1.16)].

Conclusion: In this multicenter study, DAA therapy (either pre- or post-LT) was not found to be a risk factor for HCC recurrence post-LT after adjusting for known risk factors for tumor relapse.

OS035

EARLY VERSUS LATE HCC RECURRENCE AFTER LIVER TRANSPLANTATION: LONG-TERM OUTCOME RESULTS

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Background: Hepatocellular carcinoma (HCC) is currently the most common indication of liver transplantation (LT). HCC recurrence is the main complication affecting short and medium term outcome after liver transplantation (LT). The aim of this study is to analyze the outcome of patients who developed HCC recurrence according to post-transplant time of recurrence.

Patients and Methods: Consecutive patients who underwent LT for HCC between 2000 and 2017 at our centre were recruited. Characteristics of patients, recurrence, modalities of treatment and outcome were collected retrospectively. Patients were divided according to time of recurrence: early (≤ 2 years post-transplant) and late (> 2 years post-transplant).

Results: 433 patients (mean age: 57.8 ± 8.5 years; 83.8% were males) underwent LT for HCC. Mean follow-up was 74.6 ± 58.6 months. Seventy-five patients (17%) developed HCC recurrence with a mean time to recurrence of 29.7 ± 31.8 months. Recurrence site at diagnosis was intrahepatic only (16.0%), extrahepatic only (61.3%) and intrahepatic and extrahepatic (22.7%). Early recurrence developed in 46 patients (61.3%) and late recurrence occurred in 29 patients (38.7%). The 5 and 10-year patient survival of the whole cohort were respectively 74.6% and 59.0%. The overall 5 and 10-year recurrence free survival rate were 80.9% and 75.6%. Only one patient survived at 5 and 10 years among patients who developed an early HCC recurrence. The 5 and 10-year survival of patients with early recurrence was therefore similar 6.7%, and significantly shorter than those patients with late recurrence respectively at 5 and 10 years, 64.0% and 27.1% (logrank $p < 0.0001$).

Conclusion: In this large cohort with long-term follow-up, late HCC recurrence has been associated with a good long-term survival. Early HCC recurrence is associated with very bad prognosis, probably related to more aggressive tumor and either tumor progression or bad selection criteria at time of transplant.

OS036

EXPANDED CRITERIA FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA BASED ON THE JAPANESE NATIONWIDE SURVEY: THE 5-5-500 RULE

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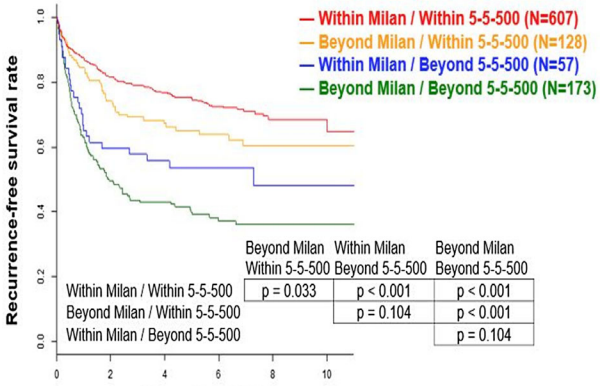
Expansion of the liver transplantation indication criteria for patients with hepatocellular carcinoma (HCC) has long been debated. Here we propose new, expanded living-donor liver transplantation (LDLT) criteria for HCC patients based on a retrospective data analysis of the Japanese nationwide survey. A total of 965 HCC patients undergoing LDLT were included, 301 (31%) of whom were beyond the Milan criteria. Here, we applied the Greenwood formula to investigate new criteria enabling the maximal enrollment of candidates while securing a 5-year recurrence rate (95% upper confidence limit) below 10% by examining various combinations of tumor numbers and serum alpha-fetoprotein (AFP)/des-gamma-carboxy prothrombin (DCP) values, and maintaining the maximal nodule diameter at 5 cm. Finally, new expanded criteria for LDLT candidates with HCC, the 5-5-500 rule (nodule size ≤ 5 cm in diameter, nodule number ≤ 5, and AFP ≤ 500 ng/ml), were established as a new regulation with a 95% confidence interval of a 5-year recurrence rate of 7.3% (5.2-9.3), achieving the maximal number of eligible patients by 19% increase. In addition, the 5-5-500 rule could identify patients at high risk of recurrence, among those within and beyond the Milan criteria. The recurrence free suvival by each criteria and 5-year patinet survival/recurrence rate were presented in the figure and the table, respectively. In conclusion, the new criteria – the 5-5-500 rule – might provide rational expansion for LDLT candidates with HCC.



	Beyond Milan Within 5-5-500	Within Milan Beyond 5-5-500	Beyond Milan Beyond 5-5-500
Within Milan / Within 5-5-500	p = 0.033	p < 0.001	p < 0.001
Beyond Milan / Within 5-5-500		p = 0.104	p < 0.001
Within Milan / Beyond 5-5-500			p = 0.104

At risk	0 year	1 year	3 years	5 years	10 years
Within Milan / Within 5-5-500	607	531	401	270	17
Beyond Milan / Within 5-5-500	128	108	77	53	8
Within Milan / Beyond 5-5-500	57	38	29	25	3
Beyond Milan / Beyond 5-5-500	173	109	69	48	6

OS037 LIVER TRANSPLANTATION FOR COLORECTAL METASTASES, 10 YEAR FOLLOWUP

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Introduction: Surgical removal of colorectal liver metastases (CLM) is the only treatment option with curative potential; however, many patients are not candidates for surgical resection due to extensive bilobar affection. These patients have poor prognosis, with only about 10% survival at five years on palliative chemotherapy. A pilot study on liver transplantation (Lt) for non-resectable CLM was performed at Oslo University Hospital between 2006 and 2012. In the initial report ($n = 21$), the 5 year Kaplan Meyer estimate of overall survival (OS) was 60% (95% CI 32-85%). (1) Four significant preoperative risk factors for reduced survival were identified (CEA > 80, tumor size > 5,5 cm, progressive disease at time of Lt, > 2 years from primary surgery to Lt), and potential for further improved patient selection was thus established. (1) Now, the material has matured; all living patients have reached at least 5 years of observation and the first patients have reached 10 years post liver transplantation. An additional two patients that were operated around the time of the previous publication were also included. Here we present current status on the SECA study of those 23 patients.
Objectives: To report 10 years follow up data after a prospective pilot study that investigates the potential for long-term OS after liver transplantation for CLM and to re-evaluate the prognostic factors established in the initial paper.
Methods: A prospective pilot study on Lt for non-resectable CLMs was performed at Oslo University Hospital from 2006 to 2012. Requirements for inclusion were liver only CLM, excised primary tumors, and at least 6 weeks of chemotherapy.
Results: Median observation time was 58 months (range; 6-144). At 5 years post Lt, OS was 43,5%, and at 10 years the Kaplan Meyer estimate of OS was 26.1%. Three of the factors found predictive in the initial report was still significantly associated with survival (CEA > 80, tumor size > 5,5 cm, progr

OS038 LIVING DONOR LIVER TRANSPLANTATION FOR ADVANCED HEPATOCELLULAR CARCINOMA WITH PORTAL VEIN TUMOR THROMBOSIS AFTER CONCURRENT CHEMORADIATION THERAPY

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Locally advanced hepatocellular carcinoma (HCC) with portal vein thrombosis carries a 1-year survival rate < 10%. Localized concurrent chemoradiotherapy (CCRT), followed by hepatic arterial infusion chemotherapy (HAIC), was recently introduced in this setting. Here, we report our early experience with living donor liver transplantation (LDLT) in such patients after successful down-staging of HCC through CCRT and HAIC. Between December 2011 and December 2017, nineteen patients with locally advanced HCC with portal vein tumor thrombosis (PVTT) at initial diagnosis were given CCRT, followed by HAIC, and underwent LDLT at the Severance Hospital, Seoul, Korea. CCRT [45 Gy over 5 weeks with 5-fluorouracil (5-FU) as HAIC] was followed by HAIC (5-FU/cisplatin combination every 4 weeks for 3–12 months), adjusted for tumor response.. The 1-year overall survival and disease-free survival rate were 90.9% and 87.5%, respectively. The 3-year overall survival and disease-free survival rate were 72.7% and 49.0%, respectively. There were eight instances of post-transplantation tumor recurrence during follow-up monitoring (median, 46 months; range, 1-72 months) Median survival time from initial diagnosis was 33 months (range 11-110 months). Using an intensive tumor down-staging protocol of CCRT followed by HAIC, LDLT may be a therapeutic option for selected patients with locally advanced HCC and portal vein tumor thrombosis.

OS039 EARLY OCCURRENCE OF SOLID DE NOVO NEOPLASMS IN PATIENTS TRANSPLANTED FOR HEPATOCELLULAR CARCINOMA

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Background and Aims: Patients with hepatocellular carcinoma (HCC) are at higher risk for second primary malignancies compared with general population. Such risk could be even higher after liver transplantation (LT). HCC has become the leading indication for LT, however, evidences on the additional risk that it could confer for de novo neoplasms (DNN), are lacking.
Method: A cohort study was conducted among 9 Italian centers between 1985-2014. Patients were excluded if: ≤18 years old, follow-up shorter than 90 days or cancer diagnosis within 90 days after LT. Person-years (PYs) at risk for DNN were computed from 90 days post-LT to date of death, cancer diagnosis or end of follow-up. Hazard ratios (HR) of DNN development and CI95% were estimated for patients transplanted for HCC (HCC patients) compared to those with no previuos neoplasm (non-HCC patients). All models were adjusted for sex, age and calendar year at LT, and liver disease etiology.
Results: A total of 2653 patients were followed up for 17,903PYs of observation during which 189 (7.1%) developed 202 DNNs. Out of 946 HCC-patients 62 (6.6%) developed 64 DNNs, while out of 1707 non-HCC patients 127 (7.4%) developed 138 DNNs. There was a significant difference in occurrence timings: median time from LT to first DNN diagnosis was 2.4 years for HCC-patients and 4.1 years for non-HCC ($p < 0.01$). This difference was relevant specifically for solid tumors (2.7 vs 4.5 years, $p < 0.01$). No significant association with the risk of all DNN emerged for HCC-patients as compared to non-HCC (HR = 1.2). In the analysis by specific tumor types, a significant increased risk emerged for bladder cancer (HR = 12.8) and skin melanoma (HR = 3.0).
Conclusion: In our cohort, HCC-transplanted patients were at higher risk for bladder cancer and skin melanoma. Furthermore, they presented early solid-DNN occurrence. Pre-trasplant liver neoplastic history should be taken into account during risk-stratification and surveillance-individualization.

OS06 - Immunosuppression and outcomes in pancreas and islet cell transplantation:

OS040 EXPERIENCE WITH ALEMTUZUMAB INDUCTION WITH TACROLIMUS/MYCOPHENOLATE ± STEROIDS IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT RECIPIENTS WITH PORTAL-ENTERIC DRAINAGE

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Wake Forest Baptist Health

Background: At present, <20% of simultaneous pancreas-kidney transplants (SPKT) in the US are performed with portal-enteric (P-E) drainage or alemtuzumab (Alem) induction. The study purpose was to analyze retrospectively our outcomes in primary SPKT patients (pts) undergoing P-E drainage and Alem induction ± early steroid withdrawal (ESW).
Methods: From 2005-2019, 134 primary SPKTs with P-E drainage were performed. All pts received single dose Alem with FK/mycophenolate (MP) ± steroids. ESW was performed unless pts were African-Americans (AA) < age 40 ($n = 21$), sensitized with a PRA > 20% ($n = 16$) or had kidney delayed graft function ($n = 4$).
Results: The study group included 94 Caucasian, 36 AA, and 4 other; 24 pts had pre-transplant C-peptide levels ≥ 2.0 ng/ml, suggesting a type 2 diabetes phenotype. Mean follow-up was 7 years; 53 pts had at least 8-year f/u. Overall pt, kidney and pancreas (insulin independence) graft survival rates (GSR) were 87%, 75%, and 68%, respectively, and did not differ by ethnicity, pre-transplant C-peptide status, or in pts ± ESW. ESW was attempted in 86 (64%) pts, 45 (52%) of whom remain steroid-free. There were no significant differences between 1-year and overall rates of acute rejection (AR) in ESW (26%, 34%) versus non-ESW ($n = 48$; 28%, 40%) pts. Death-censored kidney and pancreas GSRs were 83% and 77%, respectively. Death with functioning graft and AR/chronic rejection were the most common causes of kidney and pancreas graft loss whereas cardiovascular events and infection were the most common causes of death. Most AR episodes were heralded by dose reduction in either FK or MP because of infections or specific drug toxicities. Most pts could not tolerate full doses of FK and MP, with 16 pts (12%) unable to tolerate either drug.
Conclusion: Although ESW is durable in about half of selected SPKT pts, one must carefully weigh the benefits/risks of such a strategy, given that rates of AR are high and most diabetic pts cannot tolerate full doses of FK and MP.

OS041 CURRENT RESULTS AFTER PANCREAS TRANSPLANTATION IN NORWAY

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Background: After switching from jejunal drainage (DJ) to duodenal drainage (DD) in pancreas transplantation (PTX) in 2012, we found in 2016 a technical failure rate of 9%, a reoperation rate of 32% and 1 year graft survival (GS) of 90% for SPK and 74% for PTA. In June 2016 we added platelet inhibitor to Fragmin® from day 0; restricted the procurement to 4 experienced surgeons and introduced scheduled postoperative ultrasound and CT-scan. Here we present our results after the modifications.
Patients and Methods: We included 46 PTX (22 solitary PTX and 24 SPK) performed between June 2016 and Dec 2018. 36 PTX with DD and 10 with DJ. Scheduled ultrasound was performed within 6 hours and CT scan between day 3 and 5. Endoscopic pancreas biopsies were performed at week 6 and 52. The transplant was performed by the senior surgeon on call.
Results: Median follow up time was 549 days. Patient survival was 100% and GS was 94%. No grafts were lost in technical failures. Total rejection rate was 20%. Seven patients were treated for rejection in the pancreas and 2 patients were treated for rejection in the kidney. Three solitary PTX were lost in rejection after 7, 19 and 23 months respectively and 2 of these developed *de novo* DSA. Ten patients required an early reoperation and 5 of these due to bleeding or hematomas. Three patients had endoscopic intervention for duodenal bleeding. Four patients developed venous thrombosis and had a successful percutaneous thrombectomy followed by high dose anticoagulation for at least 3 months.
Conclusions: After an initial learning curve and after minor adjustments in 2016, our current results after PTX are excellent. However, solitary-PTX is still prone to rejection and graft loss. We still experience a 9% venous thrombosis rate, but due to active radiological surveillance these were detected in time and the grafts were rescued by percutaneous thrombectomy.

Table 1	Median / #	Range / %
Donor Age - years (range)	26,3	4,7 - 54,9
Donor BMI - kg/m² (range)	22,6	13,9 - 33,2
Donor Female gender - n (%)	21	46 %
Recipient Age - years (range)	41,3	25,2 - 62,0
Recipient BMI - kg/m² (range)	24,1	19,4 - 31,9
Recipient Female gender - n (%)	25	54 %
Time on waiting list - days (range)	185	9 - 2173
Solitary PTX - n (%)	22	48 %
PTX with Duodeno-duodenostomy - n (%)	36	78 %
Cold Ischemia Time - min (range)	467	227 - 1086
ATG dosage/kg - mg (range)	6,5	3,2 - 10,0
SAG within 30 days - units (range)	0	0 - 16
Stay in Hospital - days (range)	16	7 - 68
Venous extension - n (%)	33	72 %
Reoperations within 30 days - n (%)	10	22 %
Venous percutaneous thrombectomies - n (%)	4	9 %
Rejection in the Pancreas - n (%)	7	15 %
Rejection in the Kidney - n (%)	2	8 %
Rejection episodes treated - #	12	na
Graft losses - n (%)	3	7 %

OS042 ROUX-EN-Y PANCREATIC DUCT DRAINAGE IN PANCREATIC TRANSPLANTATION – WHAT IS THE EVIDENCE?

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Background: Pancreas transplantation is a successful treatment for selected patients with diabetes. However, it represents major surgery in a group of patients with multiple comorbidities. Exocrine drainage of the donor pancreas may be managed via the bladder, direct duodeno-jejunostomy (DJ) or roux-en-y (ReY) enteric drainage. It has been hypothesised that ReY confers an advantage over DJ as it distances the small bowel contents from the transplant duodenal anastomosis, potentially minimising the impact of enteric leaks, reported to occur in 3-6% of transplants. There are no direct, prospective studies available to guide the decision for ReY drainage over DJ.
Methods: Data was obtained from NHSBT on pancreatic-kidney transplants performed in the UK at 9 centres between 2002-2017. Transplants performed with ReY were compared to those with DJ for patient and graft survival, graft function at three months post-transplant, pancreatitis, number of laparotomies in the first three months and length of stay.
Results: 2172 transplants were included in the analysis. Groups were comparable for recipient and donor variables. In a multivariate analysis, no protective effect of ReY drainage was seen on graft survival (HR 0.89, CI 0.70 - 1.14; $p = 0.37$). There was no difference in rates of pancreatitis or patient survival. Although we did observe a higher rate of return to theatre (26% vs 34%, $p = 0.01$), this did not translate to a longer LOS. We did observe an association between transplant centre and duct management technique, and thus a centre-effect could not be excluded.
Conclusions: We found no evidence to support the use of ReY drainage over DJ to reduce rates of pancreatitis or improve graft survival. The extra surgical time and complexity associated with ReY pancreatic drainage cannot be justified by this study.

OS043 IMPACT OF ISCHEMIA TIME ON ISLET ISOLATION SUCCESS AND POST-TRANSPLANTATION CLINICAL OUTCOMES: A RETROSPECTIVE STUDY ON 452 PANCREAS ISOLATIONS

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Introduction: Many variables can affect the islet isolation process including ischemia time (IT) of the pancreas before the initiation of isolation procedure. In our laboratory, a total ischemia time (TIT) of < 8 hours is considered optimal and TIT between 8 and 12 hours is acceptable but considered suboptimal. We investigated the impact of IT on isolation success and post-transplantation clinical outcomes.
Materials and methods: A retrospective analysis of all islet isolations performed in our center between 2008 and 2018 was done. Cold ischemia time (CIT), organ removal time (ORT) and TIT (CIT + ORT) were analyzed. Variables related to donors and organ procurement in successful and failed islet isolations and clinical outcome after transplantation were evaluated.
Results: 452 pancreata met the inclusion criteria. 218 pancreata were successfully isolated and transplanted. No difference was founded in term of number of grafted islet preparations, number of islet equivalent (IEQ), viability and islets function when comparing total ischemia time from less than four hours until twelve hours and more. Pre and post-transplantation HbA1c, C-peptide values

and insulin requirement were compared between the two groups and no statistic difference was founded. The same observation was made for CIT and ORT.
Conclusion: This study showed no difference in term of islet isolation success and post-transplantation clinical outcomes between groups with < 8 hours of TIT and > 8 hours. IT should always be as short as possible but cut off for TIT can be pushed until 12 hours. This must be taken into consideration when IT during organ procurement may become a limiting factor for pancreatic removal.

OS044 TEN YEAR RESULTS OF A SINGLE CENTER STUDY OF RABBIT ANTI-THYMOCYTE GLOBULIN COMPARED TO ALEMTUZUMAB INDUCTION IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Robert Stratta, Giuseppe Orlando, Alan Farney, Jeffrey Rogers, Colleen Jay, David Harriman, Venkat Gurram, William Doares, Scott Kaczmorski, Amber Reeves-Daniel, Alejandra Mena-Gutierrez, Michael Gautreaux
Wake Forest Baptist Health

Introduction: Alemtuzumab (Alem) and rabbit anti-thymocyte globulin (rATG) are the most commonly used depleting antibody induction agents in simultaneous pancreas-kidney transplant (SPKT). The study purpose was to analyze 10-year outcomes at a single center.
Methods: From 2/02 thru 12/10, 114 primary SPKT patients (pts) received either multi-dose rATG ($n = 57$; minimum of 3 daily doses at 1.5 mg/kg) or single dose Alem induction ($n = 57$; 30 mg intra-operatively); 45 (39.5%) were in a randomized trial comparing the two induction regimens. All pts received FK/MPA ± steroids.
Results: Mean donor (30 rATG vs 26 years Alem) and recipient ages (43 rATG vs 45 yrs Alem) were comparable as were other characteristics (21% were African American). All pts in the rATG had at least 10 yrs follow-up (mean 144 months) whereas all pts in the Alem group had at least 8 yrs f/u (mean 116 months). 10-year pt survival rates were 77% rATG vs 75% Alem. Mean time to death was 108 months rATG vs 68 months Alem; 9 pts in the rATG group died after 10 years vs none in the Alem group (38 had at least 10 yr f/u). Major causes of death were C/V (5 in each group), malignancy (4 rATG vs 1 Alem), and infection (9 rATG vs 2 Alem, $p = 0.053$). 10-year kidney (60% rATG vs 61% Alem) and pancreas graft survival rates (GSR, 47% rATG vs 51% Alem) were comparable. The proportion of pts who died with both grafts functioning (14% rATG vs 16% Alem) and who experienced death-censored dual graft loss (GL, 7% rATG vs 5% Alem) were comparable between groups. Death-censored kidney (56% rATG vs 72% Alem, $p = 0.17$) and pancreas GSRs (43.5% rATG vs 64% Alem, $p = 0.059$) were slightly higher in the Alem group. The frequency of late kidney (17.5% rATG vs 12% Alem) and pancreas GLs (26% rATG vs 12% Alem, $p = 0.095$) were slightly higher in the rATG group.
Conclusion: Similar long-term results can be achieved with either rATG or Alem induction although Alem may be associated with fewer late deaths from infection and fewer late pancreas GLs from rejection.

OS045 PANCREAS TRANSPLANTATION ALONE VERSUS ISLET TRANSPLANTATION ALONE: A COMPARISON OF PERIOPERATIVE COMPLICATIONS AND GRAFT FUNCTION

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Introduction: It has been recently recognized that, even in the absence of insulin independence, Islet Transplantation Alone (ITA) providing marginal beta cell function may reduce the risk of hypoglycemia and/or glycemic variability/lability, outweighing the risks of immunosuppressive therapy. We sought to compare metabolic outcomes and perioperative complications associated with ITA and pancreas transplantation alone (PTA).
Methods: Data from 65 patients who underwent ITA and 36 patients who underwent PTA between February 2001 and February 2018 were retrospectively analyzed. The recent Igls criteria, based on glycated haemoglobin, frequency of severe hypoglycaemia, insulin requirements and c-peptide levels, were used to define optimal/good graft function. Perioperative complications were also recorded.
Results: Patients were followed up for up to 11.9 years. Overall graft survival was higher in the PTA group. At 5 years, 46.8% of PTA and 21.9% of ITA patients had optimal/good graft function. Median survival time was 826 days in the PTA group and 214 days in the ITA group ($p = 0.02$). However, further analysis showed that, in the first 3 years after the last islet infusion, graft survival between the PTA group and ITA patients who received 2 or 3 islet infusions, was similar.

Procedure-related complications were overall more common in the PTA vs. the ITA group (13 episodes of thrombosis, 7 graft removals, 11 episodes of acute rejection vs. none in the ITA group), except for bleeding (12 vs. 14 episodes, $p = 0.07$). Rates of infections and worsening renal function were similar in the two groups.
Conclusions: Graft survival over three years is comparable between PTA and ITA recipients of ≥ 2 islet infusions. However, over the long-term PTA provides better graft survival than ITA. Being PTA characterized by a higher rate of complications, ITA should be considered as a suitable alternative to PTA in selected patients, unsuitable for major surgery.

OS046 TACROLIMUS VERSUS SIROLIMUS AS CORNERSTONE IMMUNOSUPPRESSION AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION: 5-YEAR RESULTS OF AN OPEN LABEL, NON-INFERIORITY, RANDOMIZED CONTROLLED TRIAL

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Background: Standard maintenance immunosuppression (IS) after simultaneous pancreas and kidney (SPK) transplantation combines a calcineurin inhibitor, an antimetabolite and steroids. Tacrolimus (TAC) has well-known nephrotoxic and diabetogenic effects. Sirolimus (SRL) has been used in SPK in combination with TAC but never as cornerstone therapy. We hypothesized that a SRL based-regimen could spare TAC and avoid its nephrotoxic and prodiabetogenic effects.
Methods: We performed an open label, non-inferiority, randomized controlled trial comparing TAC versus SRL after SPK for 5 years. IS initially consisted of TAC, mycophenolate mofetil (MMF) and steroids. Patients were randomized to change IS at month 3 for TAC/MMF or SRL/MMF without steroids. Primary endpoint was kidney and pancreas survival or death at month 12.
Results: One hundred SPK recipients were enrolled (50 patients randomized in each group). Kidney graft loss or death during the first year occurred in 1 patient (2%) in the SRL group and 1 patient (2%) in the TAC group. Pancreas graft loss or death during the first year occurred in 7 patients (14%) in the SRL group and 10 patients (20%) in the TAC group. Non-inferiority of SRL was demonstrated at month 12. At 5 years, kidney graft loss or death occurred in 8 patients (16%) in the SRL group and 9 patients (18%) in the TAC group whereas pancreas graft loss or death occurred in 13 patients (26%) in the SRL group and 15 patients (30%) in the TAC group. Kidney graft rejection occurred in 11 patients (22%) of the SRL group and 9 patients (18%) of the TAC group, pancreas rejection in 11 patients (22%) in the SRL group and 6 patients (12%) in the TAC group. Thirty-four patients (68%) in the SRL group had definitive SRL withdrawal compared to 3 patients (6%) in the TAC group.
Conclusion: We showed the non-inferiority of a SRL-based immunosuppressive regimen compared to a TAC-based regimen one year after SPK. Clinical tolerance of SRL was poor.

OS047 IMPACT OF A CNI-FREE IMMUNOSUPPRESSIVE REGIMEN ON DONOR SPECIFIC ANTIBODIES AND HISTOLOGY FOLLOWING SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION

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Background: We conducted a prospective and randomized controlled trial comparing tacrolimus (TAC) versus sirolimus (SRL) as cornerstone immunosuppression after simultaneous pancreas and kidney transplantation (SPK). We prospectively looked for anti-human leukocyte antigen (HLA) antibodies and donor specific antibodies (DSA) for the 5-year study follow-up, as well as kidney histology performed one year posttransplant.
Methods: From June 2004 to April 2012, 100 recipients of primary SPK were randomized at the time of transplantation to be maintained after month 3 on TAC/mycophenolate mofetil (MMF) ($n = 50$) or SRL/MMF($n = 50$). Screening for anti-HLA antibodies was performed before transplantation, at 3 months and every year during 5 years. DSA were considered positive for an MFI above 1000 by single antigen assay. We performed protocol kidney transplant biopsy 1 year posttransplant. Histology was scored according to the Banff classification.
Results: 50 patients were randomized in each group. 2 patients (4%) in the TAC group and 1 in the SRL group (2%) had pre-formed DSA. 1 year after SPK, we detected *de novo* DSA in 9 patients (18%) in the SRL group and 1 patient (2%) in the TAC group ($p = 0.0154$); all DSA were against HLA class II antigens. At 5 years, we detected DSA in five patients (14%) in each group.

Protocol 12-month biopsy was available in 33 patients (66%) in the TAC group and 42 (84%) in the SRL group. Histology was considered normal in 14 patients (42%) in the TAC group and 16 patients (38%) in the SRL group. Subclinical cellular rejection was detected in 1 biopsy (2%) in the SRL group. Features of chronic humoral rejection were present on 4 biopsies in the SRL group (10%) and none in the TAC group.
Conclusion: Significantly more *de novo* DSA and histological features of humoral rejection were observed at 1 year in SPK patients under SRL. These results highlight a lower immunosuppression level of SRL compared to TAC in recipients of SPK transplants.

OS07 - DETERMINANTS OF OUTCOMES IN DECEASED DONOR KIDNEY TRANSPLANTATION

OS048 A UK AND US REGISTRY COLLABORATION: WHAT CAN WE LEARN FROM EACH OTHER?

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Introduction: The importance of international comparisons in healthcare is well established. In transplantation, meaningful global comparisons in organ utilisation are lacking due to fundamental differences in organ offering systems, variations in donor types and demographics. International discussions between transplant professionals in the US and UK led to the realisation that the two countries' approaches for quantifying kidney discard rates may not be directly comparable. This collaborative between UK and US national transplant organisations aimed to develop a comparable metric to facilitate valid inter-country comparisons, which can form the basis for global discussions.
Methods: Data from the UK Transplant Registry and the OPTN database were analysed; deceased donor kidneys (recovered and transplanted) from 2006 to 2017 were considered. To identify a comparable kidney 'Utilisation Rate' (UR), several denominators were assessed. Rates were stratified according to numerous parameters including donor type and Kidney Donor Risk Index (KDRI).
Results: Regardless of definitions, kidney URs have been steady in both countries for the last 5 years (Figure 1). The donor age and KDRI of transplanted kidneys in the UK are higher than the US, though small paediatric kidney transplantation is more common in the US (Figure 2). Only 0.8% of kidneys transplanted in the UK were en bloc compared with 2.6% in the US. In 2017, 41% of utilised kidneys in the UK were from DCD donors (UR amongst recovered kidneys, 84%) compared with 19% in the US (UR 79%). URs across KDRI deciles in the UK varied much less than the US (range 79%-97% versus 36%-99%).
Discussion: Collaborations can facilitate global learning; the US may benefit from the UK experience of organs from older and DCD donors, the US may offer insights into the expanded use of kidneys from very young donors in the UK. Further work is underway to enable valid international comparisons of kidney URs.

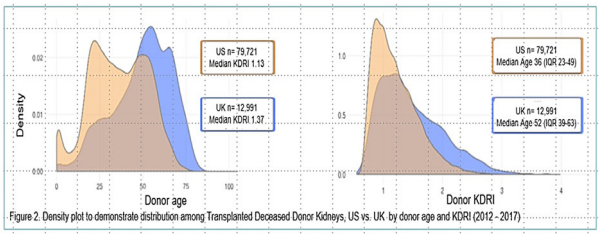

Figure 2. Density plot to demonstrate distribution among Transplanted Deceased Donor Kidneys, US vs. UK by donor age and KDRI (2012 - 2017)

OS049 OPTIMAL FLUID MANAGEMENT USING NON-INVASIVE HEMODYNAMIC MONITORING IN DECEASED DONOR

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Recently, non-invasive monitoring, such as pulse pressure variation (PPV) and stroke volume variation (SVV), has been applied to critical. However, it is unclear whether these parameters can be useful for deceased donor (DDs). We compared the several parameters with traditional hemodynamic parameters.

Twenty-three DDs were evaluated using uncalibrated arterial pressure wave form analysis (FloTrac/Vigileo™) in the setting of tidal volume (6-8 mL/kg) and minimal positive end-expiratory pressure (5-8cmH2O). Among them, 17 donors with a net amount of over 500 ml were enrolled for 8 hours. The donors were divided into two groups which were responder (M/F 5:2, mean age 40.7 ± 8.8 yrs) and non-responder (M:F 10:0, mean age 51.2 ± 14.8 yrs) based on the 15% changes in cardiac output (CO) after fluid therapy.

There was no difference in basic characteristics between two groups. Baseline PPV was significantly higher in the responder (22.9 ± 8.4 vs. 12.7 ± 9.5, $p = 0.038$). After volume replacement, CO tended to increase from 2.59 ± 1.07 to 6.54 ± 1.9 ($p = 0.054$) in the responder group. After fluid therapy, PPV was significantly changed in the responder (-10.7 ± 9.3 vs. -1.1 ± 5.9, $p = 0.015$) and SVV was also decreased more in the responder (-7.71 ± 6.5 vs. 2.3 ± 3.6, $p < 0.001$). However, CVP and heart rate were not different between two groups in both before and after volume replacement. The serum albumin level was significantly higher in the responder than the non-responder (3.22 ± 0.61 vs. 2.62 ± 0.52, $p = 0.04$).

To examine the reason why fluid therapy was not effective in non-responder with high PPV, the non-responder group was divided into two groups based on median PPV. The CRP level tended to be higher in the group with higher PPV than with lower PPV (20.1 ± 6.9 vs. 11.3 ± 5.4, $p = 0.058$). This result showed that volume replacement could not be effective in patients with systemic inflammation. In conclusion, PPV and SVV were better parameters than CVP and HR in evaluating volume status, and volume management in DDs.

OS051 THE KIDNEY DONOR PROFILE INDEX (KDPI) PREDICTS THE RISK OF GRAFT LOSS IN PATIENTS WITH A KIDNEY TRANSPLANT FROM MAASTRICHT TYPE III ASYSTOLIC DONORS

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[1]H.R.U CARLOS HAYA; [2]HUR M

Introduction: Recent years have seen an increase in the number of kidney transplants (KT) from Maastricht type III asystolic donors, resulting in the acceptance criteria for these organs being widened.
Objective: To assess the KDPI score as a risk factor for graft loss in patients with a KT from a deceased donor in type III asystole.

Material and Methods: This analysis involved 157 KT patients with grafts from type III asystolic donors at our centre from 2010 to 2017. ROC curves were made to show the predictive and discriminatory power of the KDPI in these donors. The Youden index was calculated to determine the point at which the KDPI was the most predictive and discriminatory for death-censored graft loss.
Results: The mean age of the recipients was 55 ± 13 years and of the donors it was 55 ± 9 years. The cold ischaemia time was 11 ± 4 hours. In all cases the immunosuppression used was induction with thymoglobulin (95%) or basiliximab (5%), steroids, mycofenolate mofetil and tacrolimus. Sixteen patients (10%) lost their graft during the follow-up (22 months; IQR 13-36). The area under the ROC curve of the KDPI to predict graft loss was 67.8% (95% CI, 0.529-0.828; $p = 0.02$). The Youden index showed that a KDPI > 90 was the best predictor of censored graft loss.

Graft survival at one and three years was significantly lower in patients with a KDPI > 90 (86%, 75% vs. 98%, 94%; $p = 0.007$). Bivariate Cox analysis, adjusted for acute rejection, delayed graft function, cold ischaemia time, total warm ischaemia, type of preservation, retransplant, recipient gender and time on dialysis showed that a KDPI > 90 was significantly associated with graft loss (Table).
Conclusion: These results show that the KDPI score has enough sensitivity and specificity to predict the risk of graft loss in patients receiving a kidney from a Maastricht type III donor in asystole. Accordingly, its use should be considered in this type of donor.

Adjusted for:	HR (95% CI)	*p*
KDPI > 90/ Acute rejection	4.5 (1.3-15.3) / 4.0 (0.5-31.5)	0.017 / 0.187
KDPI > 90/ Delayed graft function	4.1 (1.2-14.1) / 1.3 (0.4-4.3)	0.028 / 0.631

1. *Continued*

Adjusted for:	HR (95% CI)	*p*
KDPI > 90/ Cold ischaemia time	5.5 (1.5-20.9) / 0.8 (0.7-1.0)	0.012 /0.059
KDPI > 90/ Preservation type	3.3 (1.1-9.9)/ 1.9 (0.6-6.3)	0.034 /0.321
KDPI > 90/ Retransplant	4.4 (1.5-12.9)/ 1.4 (0.3-6.2)	0.007 /0.658
KDPI > 90/ Recipient gender	4.2 (1.4-12.4) /1.4 (0.5-3.9)	0.009/ 0.506
KDPI > 90 Time on dialysis	4.0 (1.4-11.6)/ 1.0 (0.9-1.0	0.012 /0.548

OS052 KIDNEY DONOR RISK INDEX (KDRI): IS VALID TO PREDICT KIDNEY TRANSPLANT OUTCOME IN ALL POPULATIONS?

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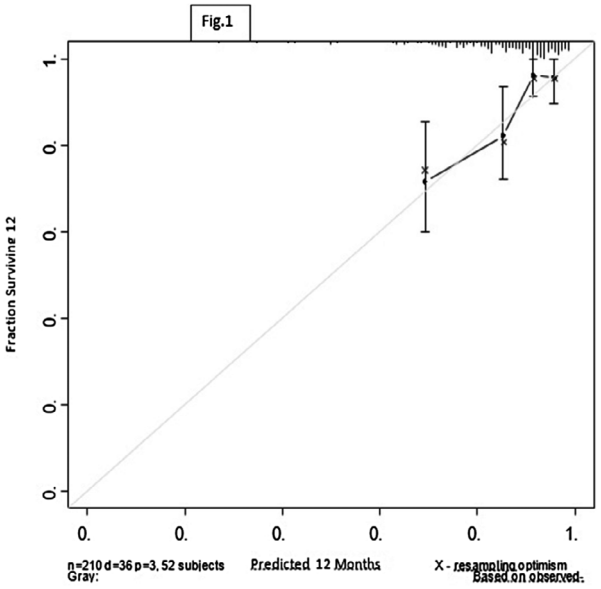
Background: Grafts from expanded criteria donors(ECD) and donation after circulatory death(DCD) are frequently discarded. Reasons are often based on variables of low prognostic value. KDRI was internal validated in the US(Rao et al) to predict graft outcome and external validated in the UK and the Netherlands(but c-statistics were low: 0.63 and 0.62, respectively).The *aim* of the study was to external validate KDRI in a Spanish population of ECD and DCD
Material/methods: *Population*: Data prospectively collected from 214 recipients of a 1st kidney transplant. Minimum follow-up:6 months. Ethical approval was obtained. *Outcome*:1 and 3-year graft survival (yGS). *Predictors*: KDRI factors are: age, height, weight, ethnicity, hypertension, DM, cause of death, creatinine, HCV and DCD status. KDRI is calculated from each donor using coeficients available at https://optn.transplant.hrsa.gov/resources/guidance/kidney-donor-profile-index-kdpi-guide-for-clinicians/*Calibration*:Our graft population was divided in quintiles and compared to KDRI quintiles from Rao et al. *Discrimination*: was tested with Harrell's c stat
Results: Table 1 shows distribution of KDRI quintiles in our population and 1 and 3-yGS

			1yGS		3yGS	
KDRI quintiles	N	%	KDRI (Rao)	Study cohort	KDRI (Rao)	Study cohort
0.45-<0.79	0	0	95.5		89.0	
0.79-<0.96	1	0.6	95.0		87.5	
0.96-<1.15	10	5.6	94.0	90.0	83.5	60.0
1.15-<1.45	27	15.0	91.0	92.6	81.5	92.6
1.45+	142	78.9	87.5	87.3	75.5	81.0
Total	180	100.0				

Results obtained in0.96- < 1.15, 1.15-<1.45, 1.45 + quintiles are similar in both groups. Only 3-yGS in0.96- < 1.15 quintile was lower in our group (60.0 vs 83.5). But this date is not accurate (only 10 recipients in this quintile). Calibration was good.Harrell's c index was 0.51(not discrimate power).

As an alternative to KDRI, we internal validate our own model. Included variables were: DCD status, donor age and type of dialysis. Hazard ratios were 11.8 (95%CI:3.5-39.7, p:0.00), 1.07(95%CI:1.0-1.2, p: 0.04) and 1.5 (95% CI:1.0-2.3,p:0.05), respectively. Calibration (Fig. 1) and discrimination were good: Harrell's c index: 0.74.
Conclusion: KDRI does not predict 1 and 3yGS in our population. We propose a simpler model that includes DCD status, donor age and type of dyalisis.<



OS053 KIDNEY TRANSPLANTS FROM EXPANDED CRITERIA DONORS AFTER CONTROLLED CIRCULATORY DEATH ARE ASSOCIATED WITH INCREASED GRAFT LOSS AND DEATH OF THE PATIENT

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Introduction: Controlled donation after circulatory death (cDCD) has allowed to significantly increase the deceased donors pool. However, while excellent previous reports have been shown using cDCD with deceased donors younger than 65-years old.The aim of this study was to evaluate in a large cohort of kidney transplant patients from 4 different transplant centre in Barcelona (Spain).
Patients and methods: In this retrospective analysis we included all consecutive kidney transplant patients from a deceased donor since the initiation of the cDCD program in each Hospital, until March 2017 (n = 992). Donor types were classified in 4 categories: DBD of standard or expanded criteria (DBD-SCD; DBD-ECD) and cDCD of standard extended criteria (DCD-SCD; DCD-ECD). Mean follow-up 39 + /-21 months. Kidney graft and patient survival were considered as main outcomes and yearly kidney graft function was also evaluated.
Results: Out of the 992 kidney transplants performed during the study period, 248(25%) were cDCD transplants. In, donors and recipients' characteristics are described. Mean 1 and 3-years graft survival were: 93% and 91% for DBD-SCD; 88% and 82% for DBD-ECD; 90% and 86% for DCD-SCD and 74% and 67% for DCD-ECD (Log Rank $p < 0.001$). Primary non-function (PNF) or graft thrombosis were main causes of graft loss in 2.6%, 3.7%, 3.1% and 7.8%, respectively ($p < 0.001$), as well as patient's death in 1.5%, 7.5%, 4.2% and 15% ($p < 0.001$). Estimated GFR (MDRD-4) at 1 year was 59 $\pm$ 21 ml/m/1.73 m2 in DBD-SCD; 43 $\pm$ 16 ml/m/1.73 m2 in DBD-ECD, 55 $\pm$ 22 ml/m/1.73 m2 in DCD-SCD and 40 $\pm$ 13 ml/m/1.73 m2 in DCD-ECD ($p < 0.001$). Graft and patient survival after the first year was comparable across groups (data not shown).
Conclusions: Kidney transplant patients DCD-ECD patients showed worse patient and graft outcome as compared to all other groups. This data has to be taken with caution and should be balanced with patient death probability while remaining on dialysis therapy

	DBD-SCD	DBD-ECD	DCD-SCD	DCD-ECD	P-value
N	266	478	95	153	
Donor age (years)	45 ± 10	71 ± 8 a	50 ± 9 a,b	70 ± 7 a,c	<0.001
Donor gender (m/f)	144/122	231/247	67/28	102/51	<0.001
Donor with arterial hypertension (*n*/y)	213/40	145/323	63/29	58/93	<0.001
Donor with Diabetes mellitus (*n*/y)	246/20	348/120	88/4	124/27	<0.001
Donor KDRI	1.11 ± 0.44 (*n* = 213)	1.99 ± 0.56[a] (*n* = 355)	1.18 ± 0.24b (*n* = 63)	2.21 ± 0.65 a,b,c (*n* = 107)	<0.001
Remuzzi Score	2.3 ± 1.4 (*n* = 68)	2.8 ± 1.5a (*n* = 282)	2.1 ± 1.5b (*n* = 47)	3.1 ± 1.3a,c (*n* = 84)	<0.001
Recipient age (years)	48 ± 10	66 ± 9a	53 ± 9 a,b	66 ± 10 a,c	<0.001
Recipient gender (m/f)	184/82	311/167	54/41	111/42	0.0506
1° Tx/ >1 Tx	206/60	397/81	80/15	134/18	0.0370
cPRA (%)	15 ± 33	11 ± 28	16 ± 34	12 ± 29	ns
HLA A+B+DR mismatches	3.9 ± 1.2	4.2 ± 1.1a	4.2 ± 1.1	4.4 ± 1.0 a	0.019
Cold ischemia time (hours)	17 ± 6	18 ± 6a	13 ± 6a,b	14 ± 6a,b,c	<0.001
Delayed graft function (%)	27%	32%	41%	54%	<0.001
Acute rejection (%)	16%	14%	17%	19%	ns

OS054 PRESENCE OF SCLEROSIS IN EXPANDED AND STANDARD CRITERIA DECEASED DONOR KIDNEYS

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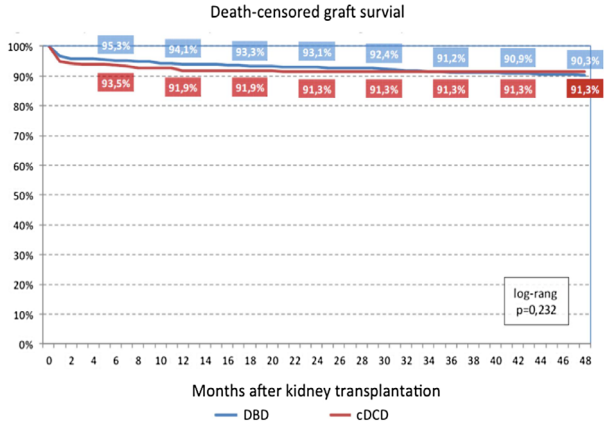
Background: Analysis of the deceased donation of the last years shows increasing frequency of expanded criteria donations and also higher frequency of co-morbidities in deceased donors (DD), limiting the chance to ensure kidney transplantation (KT) for younger recipients.
The Aim: of this study was to analyse association of sclerotic changes revealed in DD pre-transplant biopsies with KT worse outcomes and to check the frequency of such changes in different categories of DD.
Materials/methods: In this study we analysed all consecutive DD KT performed during the period since 01.01.2004 till 31.12.2010, where pre-transplant donor kidney biopsies were performed and recipients were available for 8-year follow-up (189 KT from 109 DD, of them expanded criteria (EC) were met in 23% of cases). Biopsies were performed by tru-cut biopsy needle just before the start of organ perfusion. The presence and percent of interstitial sclerosis (IS), glomerular sclerosis (GS) and arteriosclerosis (AS) and their impact on posttransplant outcomes (delayed graft function (DGF), acute rejections, surgical complications, graft function postoperatively and graft and patient 8-year survival) were analysed.
Results: IS of any grade was revealed in 57.8% of DD (IS > 10% in 28.4% and IS > 20% in 9.2% of cases), GS of any grade was revealed in 25.7% of DD (GS > 10% in 18.3% and GS > 20% of cases), and AS in 30.3% of cases. Analysis of KT results showed that IS of higher grade was associated with higher rate of DGF and vascular complications in early posttransplant period ($p < .05$), whereas GS was related with higher rate of DGF, vascular and urological complications and lymphocele formation postoperatively ($p < .05$), acute rejections ($p = .056$) and higher serum creatinine level at discharge from hospital (0.12 + 0.03 vs. 0.15 + 0.03 mmol/l, $p < .05$). In the late posttransplant period only presence of higher grade IS showed relation with higher mortality, associated with al



graft function (DGF) was higher in cDCD KT group (40.1% vs 22.9%, $p < 0.001$) without differences in primary non-function rates (2% vs 0.8%, $p = 0.12$). No differences in death-censored graft survival were observed (See Figure). Renal function was slightly better in DBD group (eGFR 51.6 ml/min vs 46.9 ml/min, $p = 0.012$). In multivariate analysis, recipient age > 75 yr and previous cardiovascular disease were independent risk factors for patient death (RR 10.06 and 2.24, respectively). DGF (RR 1.67) and cPRA > 50% (1.66) increased graft loss. The type of donation (cDCD vs DBD) was not an independent risk factor neither for patient survival nor graft loss.
Conclusions: In contemporary recent cohort, graft survival from cDCD and DBD donors is comparable. Type of donation does not impact patient and graft survival. Recipient age > 75 years, DGF and cPRA > 50% are risk factors for graft loss

OS055 COMPARISON OF KIDNEY TRANSPLANTATION OUTCOMES BETWEEN DONORS AFTER CONTROLLED CIRCULATORY DEATH AND BRAIN DEATH DONORS IN CATALONIA, SPAIN

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Background: The number of kidney transplants (KT) from controlled cardiac death donors (cDCD) has exponentially increased in Spain during the last years. Results from cDCD KT have been reported to be comparable to brain-death donors (DBD) KT in countries with long tradition of retrieving organs from cDCD. No studies have compared KT outcomes between these two types of donors in Spain, a country without this activity until recent years.
Patients and methods: Observational retrospective analysis including 1374 KT from DBD and 458 KT from cDCD, performed from January 2013 to December 2017 in Catalonia, Spain. Data were obtained from the Catalonian Registry of Renal Patients (RMRC) including donors, recipients and process of donation-transplantation. Median follow-up after KT was 20 months. A multivariate analysis was performed to identify risk factors for graft loss.
Results: Both donors and recipients mean ages were significantly higher in the cDCD group compared to DBD group. (61 ± 13 vs. 58 ± 17 for donors, $p < 0,001$; 60 ± 12 vs. 56 ± 15 for recipients, $p < 0,001$). Incidence of delayed

OS056 DONATION AFTER CIRCULATORY (DCD) DONORS IN THE EMILIA-ROMAGNA REGION (ERR): PROCUREMENT AND TRANSPLANTATION

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Emilia-Romagna Transplant Reference Centre

Introduction: In the face of gap between patients on waiting list and organ supply for transplantation, the ERR, a northern Italy region of 4,448,841, started DCD organ procurement in 2016, according to the DCD National Programme (implemented in Italy in 2015).

All DCD donors were part of category III according to the Maastricht Classification revisited (expected cardiac arrest in ICU; controlled).

Aim of the study was to evaluate organ procurement and transplantation activity from DCD donors from 2016 to 2019.
Methods: We analyzed all DCD donors in the ERR and related transplants with graft and recipient survival from the 14th of January 2016 to the 28th of January 2019. All data sources were the Italian Informative Transplant System (S.I.T.) and the ERR Informative Transplant System (R.R.T.). Graft and recipient survival at 1 year were assessed by Kaplan-Meier-analysis.
Results: During the study period 22 DCD controlled donors (Maastricht category III) were procurred, 17 males and 5 females, age average 55.23 years old (range 22 – 71 years old), median age 58.5 years old; causes of death were Anoxic Brain Damage (10 cases), Head Injury (4 cases), Ischaemic Stroke (4 cases), Haemorrhagic Stroke (3 cases) and Brain Abscess (1 case). All donors were submitted to veno-arterial extra corporeal life support (ECLS) upon the end of "no touch period" (20 minutes in Italy) and to hypothermic machine

perfusion after their removal. 18 out of 22 donors were utilized, allowing 15 liver transplantations, 21 single kidney transplantations and 4 double-kidney transplantations. Graft and recipient survival at 1 year were: 93% for liver graft, 84% for kidney graft, 100% for liver recipient and 88% for kidney recipient.
Conclusion: Because of organ shortage and age average increment of potential deceased donors (65 years old in ERR), the implementation of DCD organ procurement represents a way to increase the donor pool. Graft and recipient survival rates, even

OS057 A TEN YEAR EXPERIENCE OF DUAL KIDNEY TRANSPLANTATION

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Introduction: Bridging the disparity between the kidney waiting list and donor pool continues to pose challenges globally. For highly sensitised patients and older recipients the wait is contributing to an unacceptably high waiting list mortality. In the UK concerted efforts has seen a significant rise in DCD transplants and furthermore specialist centres have made increasing efforts to widen their donor acceptance criteria. Fast track and aggressive screening policies have paved the way for techniques such as dual kidney transplantation. First described by Remuzzi in 1996 there has been significant debate around solitary vs dual graft implants from marginal donors. Our centre has over 10 years of experience in Dual Kidney Transplantation DKT, and this work summarises our overall experience to date.
Methods: We analysed all DKTs performed at our institution to date (2007 – present). We specifically looking at recipient and donor characteristics, initial graft outcome and 30 day creatinine. Both grafts were placed in an Ipsilateral manner. Immunosuppression remained as standard. There was a Day 0 biopsy at time of implant and an USS on day 1
Results: Between 2007 – present 65 DKTs were performed. There were 43 male recipients and 22 female. Median recipient age was 65 years (48-78). There were 47 DCD and 15 DBD grafts. Overall median donor age was 73 (43-83). Primary function was present in 65% of patients. There was only 1 case of primary non function (PNF). The remaining 34% of patients experienced DGF between 2 and 22 days (median 6 days). 30 day creatinine levels ranged between 73 μmols/L to 547 μmols/L with a median of 160 μmols/L.
Conclusion: Dual kidney transplants provide a feasible option for previously discarded grafts giving outcomes comparable to solitary grafts in carefully matched donor recipient pairs.

OS058 OUTCOMES OF KIDNEY TRANSPLANTATION IN LOW WEIGHT PAEDIATRIC PATIENTS: A SINGLE CENTRE EXPERIENCE

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Background: Kidney transplantation is the best form of treatment for patients with end stage renal disease. However, it is very difficult to find size matched donors for low weight paediatric patients. Kidney from adult donors can cause significant problems with the anastomosis (due to vascular diameter mismatch), wound closure as well as hemodynamic instability, which can lead to graft loss. We aimed to determine the outcomes of low weight pediatric patients (<15 kg) who received kidney from adult donors.
Methods: Patients aged < 18 years who received kidneys between January 2011 to June 2017. Patients were divided in to higher weight group (HWG: >15 kg) and low weight group (LWG: <15 kg). The results are reported as mean for continuous variables and as number and proportion for categorical variables. Fisher's exact test and independent t-test were used, where appropriate.
Results: A total of 213 patients were included, 172 (81%) from the living donors and 41 (19%) from the deceased donors. Mean age of recipients and donors was 9.9 and 32 years respectively. Mean weight and body surface area of the recipients and donors were 26 and 70 kg and 0.92 and 1.75 m2 respectively. Sixty patients were in LWG and 153 in HWG. Rates of delayed graft function and acute rejection were higher in the HWG ($p < 0.01$ and $p = 0.01$ respectively), majority of episodes were in patients receiving kidneys from deceased donors. However, surgical complications, which occurred in 5.2% of the recipients, did not differ between the groups ($p = 1.00$). In the LWG, two patients required re-exploration, one for the vascular kink and the other for compartment syndrome. One patient in the LWG and 4 in the HWG lost the graft in the first year. One-year patient survival was 98.3% and 98.7% in the in the LWG and HWG respectively.
Conclusion: Our study has shown that low weight pediatric patients can receive kidneys from adult donors despite significant age and weight discordance.

OS08 - IS WARM WINNING THE COLD WAR IN MACHINE PERFUSION?

OS060 A CASE-CONTROL MATCHED COMPARISON OF KIDNEY TRANSPLANTATION FOLLOWING CONTINUOUS HYPOTHERMIC MACHINE PERFUSION VS. COLD STORAGE

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Background: Improved kidney preservation remains an unresolved issue in kidney transplantation. The aim of this study was to assess the effect of hypothermic machine perfusion (HMP) vs. cold storage (CS) in kidney transplantation.
Methods: All kidney transplantations performed at the Medical University of Innsbruck between August 2015 and December 2018 ($n = 422$) were evaluated. HMP was applied in 105 kidneys, the remaining 317 kidneys were transplanted following CS. The comparison was performed employing propensity score matching. The assessment eventually included 210 patients (105 HMP, 105 CS) fitting the criteria. DGF was defined as > 1 hemodialysis.
Results: Mean CIT in HMP and CS kidneys was 17:01 and 13:35 hours, respectively. Patient survival after a median follow-up of 20 months (range 1 – 41 months) was 97.2% (CS: 95.7% vs. HMP: 97.2%; $p = 0.796$). Graft survival was 89.1% in CS kidneys and 96.5% in the HMP organs (p=n.s.). Delayed graft function (DGF) occurred in 38.8% and was less frequent in SCD donors compared to ECD organs (15.3% vs. 23.4%; $p = 0.010$). DGF occurred less frequently after HMP compared to CS (15.8% vs. 23.0%; $p = 0.029$). There was a tendency towards less frequent DGF in ECD organs transplanted following HMP compared to CS (10.5% vs. 12.9%). This was even more pronounced in SCD (5.3% following HMP compared to 10.0% after CS, $p = 0.034$).
Conclusion: Our results indicate, that HMP is beneficial not only for ECD kidneys but also for SCD kidneys. HMP should be used as desirable method of preservation.

OS061 EX VIVO NORMOTHERMIC MACHINE PERFUSION OF PORCINE KIDNEYS WITH AN ERYTHROCYTE SUPLEMENTED PRESERVATION SOLUTION AS A SUBSTITUTE FOR BLOOD

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Background: Renal transplantation is limited due to kidney donor shortage. To increase the number of transplantable kidneys, donation after circulatory death (DCD) kidneys, albeit of inferior quality, are increasingly used. Normothermic machine perfusion (NMP) is designed for graft assessment and repair. Using blood-based solutions during NMP is now standard, but limited availability of donor blood warrants an alternative perfusion solution. We tested [AQIX® RS-I], a non-phosphate buffered, serum-like preservation solution, in combination with different colloids as protectant against edema and with the addition of washed red blood cells (RBCs) as oxygen carriers during *ex vivo* NMP of DCD kidneys.
Methods/Materials: Porcine kidneys retrieved from the abattoir, underwent 30 min of warm ischemia, followed by 3 h of oxygenated hypothermic machine perfusion. Then, kidneys ($n = 6$) were reperfused for 4 h with either 1) diluted blood (control), 2) Aqix with 2.2% bovine serum albumin (BSA), 3) Aqix with 3.5% Dextran 40 (DEX), 4) Aqix with 2.2% BSA & RBCs (BSA+RBC), or 5) Aqix + 3.5% Dextran 40 + RBCs (DEX+RBC).
Results: Throughout reperfusion, oxygen consumption was significantly higher in the RBC containing groups (308% $P < 0.0001$), in-line with the significantly higher ATP levels after 30 min of NMP (89% $P < 0.05$). The energy demanding process of fractional sodium reabsorption was also significantly improved in the RBC groups (45% $P < 0.001$). In terms of filtration the control and BSA+RBC groups had a significantly higher creatinine clearance than the other groups ($P < 0.05$). Total creatinine clearance was 18% higher in the BSA+RBC group compared to the control.
Conclusion: This study shows that RBCs significantly contribute to supplying sufficient oxygen to kidneys under normothermic conditions. Erythrocyte and BSA-supplemented Aqix appeared equivalent to blood-based solutions in terms of renal and tubular function during NMP and thus could be a relevant alternative perfusion solution.

OS062 PROLONGED NORMOTHERMIC MACHINE PERFUSION OF HUMAN DISCARDED DONOR KIDNEYS: FIRST RESULTS OF THE PROPER STUDY

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Introduction: In order to maximize the regenerative potential of normothermic machine perfusion (NMP) on kidneys, a longer period of continuous perfusion would be beneficial. The aim of this study is to test the effects of prolonged NMP using a previously published one-hour perfusion protocol against new developed protocol (PROPER protocol).
Methods: Eight discarded donor kidneys were perfused for 6 h. Kidneys were perfused with a pulsatile pressure of 75 mmHg at 37°C using an open drainage system and oxygenated with 95%O_2/5%CO_2. Group 1 (n = 4) kidneys were perfused by the one hour protocol, as previously published by (Hosgood et al. 2017 BMJ). Group 2 (n = 4) kidneys were perfused with a dedicated NMP perfusate, including washed red blood cells (RBCs), albumin, specified electrolyte concentrations and nutrients. Glucose and pH were corrected only if necessary. When urine was produced, this was recirculated. Blood gas analyses were performed hourly during NMP. Pump parameters, urine production and kidney injury and function as well as histology was assessed. Data are given in mean ± SD.
Results: No statistically significant demographic differences were found between the groups. In group 1, the flow continuously decreased from start until 6 hours of perfusion (75 ± 37 vs 65 ± 29 ml/min/100gr, resp. p = 0.03). On the contrary, flow in kidneys perfused within group 2 increased significantly (t = 0: 35 ± 20 vs t = 6 h: 80 ± 29 ml/min/100gr, p = 0.02). Kidneys in group 2 tended to produce less urine in 6 h time (265 ± 253 and 53 ± 93 ml, p = 0.17). Compared to group 1 kidneys in group 2 maintained more stable and physiological pH and electrolyte levels during perfusion (p = 0.04), potentially caused by urine-recirculation and washing the packed cells.
Conclusion: This study confirms that prolonged perfusion of discarded kidneys using NMP is feasible. It also demonstrates that for a prolonged NMP a modified perfusate is required to allow maintenance of viability.

OS063 NORMOTHERMIC MACHINE PERFUSION IS A FEASIBLE PRESERVATION TECHNIQUE AND A PROMISING STRATEGY FOR DONOR KIDNEYS IN THE EUROTRANSPLANT SENIOR PROGRAM (ESP)

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Introduction: Due to suboptimal quality of elderly donor kidneys in the ESP program, graft outcomes have shown to be inferior. Recently, normothermic machine perfusion (NMP) was identified as a tool to optimize marginal donor kidneys. We aimed to investigate the safety of implementing NMP in the ESP population to improve graft outcomes.
Methods: In 2018, ESP patients awaiting deceased donor kidney transplantation were prospectively asked to participate in a pilot study. Before transplantation, the donor kidney was placed on 2 hours NMP at 37°C with an oxygenated, plasma-free red cell-based solution at a mean pressure of 75 mmHg with additional nutrients to maintain homeostasis. Biopsies, perfusates and urine samples were collected during NMP to assess organ quality. Outcomes assessed were the incidence of delayed graft function (DGF) or primary non function (PNF), 3 and 6 months eGFR, and biopsy proven acute rejection (BPAR) within 3 months. The results were compared to ESP controls transplanted without NMP (Jan 2016-Dec 2018).
Results: 11 patients were included and the outcomes were compared to 54 ESP controls. Median follow-up at time of analysis was 5.4 months in NMP patients (3.8-9.0) and 14 months (10.9-12.3) in the ESP controls. Cold ischemic time (CIT) was significantly longer in the NMP group (NMP: 12.5 hours (10.0-16.4), controls: 10.0 hours (8.0-12.0), p = 0.027). Other donor and recipient characteristics were similar. The incidence of DGF/PNF was significantly lower in the NMP group (NMP group: 27%, controls: 63%, p = 0.045). BPAR within 3 months was similar. No significant difference was shown in 3 months eGFR (NMP: 31 (26-42), controls: 30 (22-39), p = 0.690) and 6 months eGFR (NMP: 36 (26-49), controls: 34 (27-39), p = 0.683).
Conclusion: Despite longer CIT, our preliminary results show lower incidence of DGF/PNF with equal 3 and 6 months eGFR in NMP patients. NMP is safe and feasible, and can be implemented in the ESP program.

OS064 THE FIRST CASE OF ISCHEMIA-FREE KIDNEY TRANSPLANTATION IN HUMANS

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Background: Ischemia-reperfusion injury (IRI) has been considered an inevitable event in organ transplantation since the first successful kidney transplant was performed in 1954. To avoid IRI, we have established a novel procedure called ischemia-free organ transplantation. Here, we describe the first case of ischemia-free kidney transplantation (IFKT).
Methods: The kidney graft was donated by a 19-year-old brain dead donor. The recipient was a 47-year-old man with end-stage diabetic nephropathy. The graft was procured, preserved and implanted without cessation of blood supply using normothermic machine perfusion.
Results: The graft appearance, perfusion flow and urine production suggested the kidney was functioning well during the whole procedure. The creatinine dropped rapidly to normal range within three days post-transplantation. The levels of serum renal injury markers were low post-transplantation. No rejection, vascular or infectious complications occurred. The patient had an uneventful recovery.
Conclusions: This paper marks the first case of IFKT in humans. This innovation might offer a unique solution to optimize transplant outcomes and overcome organ shortage in kidney transplantation.

OS065 PROTEOMICS REVEALS MOLECULAR WINDOW AND METABOLISM OF NORMOTHERMICALLY PERFUSED HUMAN KIDNEYS

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Background: Proteomic profiling by mass spectrometry (MS) can rapidly identify significant changes to proteins. The purpose of applying proteomics to tissue samples was to determine differences between normothermically perfused discarded human kidneys with and without urine recirculation (URC).
Methods: Biopsies from 19 NMP kidneys were prepared for proteomics. Protein was extracted from 16 kidneys with URC and from 3 kidneys without. For each kidney analysed with URC (n = 8 DBD and n = 8 DCD kidneys, at least 12 h of NMP), the zero biopsy and tissue taken after 6, 12 or 24 h underwent protein extraction. The proteins were identified and quantified by MS. Quantitative MS data were uploaded to Perseus for data visualization and statistical analysis.
Results: Damage-associated molecular patterns (DAMPs) known to be contributing to ischaemia reperfusion injury (IRI) were significantly downregulated in kidney tissue after 6 h of NMP with URC compared to kidneys without. Mitochondrial succinate dehydrogenase proteins were significantly downregulated with URC. The protein for the gene angiotensinogen (AGT) was upregulated in kidneys without URC and downregulated in kidneys with URC. The protein for carbonic anhydrase (CA1), maintaining acid-base balance, was upregulated in kidneys with URC and downregulated without. Key enzymes involved in glucose metabolism, including mitochondrial MDH and GOT, were downregulated in DCD zero biopsies compared to DBD. After 12 and 24 h of NMP, enzymes involved in glucose metabolism were more upregulated in DCD tissue compared to DBD. The cytosolic and the mitochondrial phosphoenolpyruvate carboxykinase (PCK) were more upregulated after 24 h of NMP in DCD compared to DBD tissue.
Conclusion: NMP with URC is an optimal and feasible preservation method to minimize IRI in discarded human kidneys. Kidneys become metabolically active during NMP. DCD organs seem to benefit more from NMP with/without URC, showing more active glucose metabolism.

OS066 COMPARISON OF NORMOTHERMIC MACHINE PERFUSION AND REMUZZI SCORE IN THE ASSESSMENT OF EARLY GRAFT FUNCTION IN DONATION AFTER CIRCULATORY DEATH (DCD) KIDNEYS

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Background: Despite the increase in organ utilisation from both DCD and extended criteria donors (ECD) a significant number of kidneys are discarded due to concerns regarding their quality. Several quality assessment methods have been established to determine suitability of organs for transplantation. The aim of this study was to compare the use of normothermic machine perfusion (NMP) and Remuzzi biopsy score in the assessment of early graft function in DCD kidney transplants.
Methods: 40 DCD kidneys underwent 1 hour of NMP prior to implantation. Kidneys underwent assessment scoring based on parameters including total urine output (mL), mean renal blood flow (mL/min/100 g), and macroscopic appearance, to give an overall score from 1 (highest quality) to 5 (lowest quality). Pre-implantation biopsies were processed for histopathological Remuzzi analysis with each kidney scored for severity of chronic injury based on the presence or absence of global glomerular sclerosis, tubular atrophy, interstitial fibrosis, arterial narrowing, to give an overall score out of 12 (0-3 mild injury, 4-6 moderate injury, 7-12 severe injury).
Results: Incidence of delayed graft function (DGF) was 27%, 1 case of primary non-function of graft (PNF), and 5 cases of biopsy proven acute rejection. During NMP assessment 36% of kidneys scored 1, 36% scored 2, 14% scored 3, and 14% scored 4. Remuzzi analysis resulted in 90% kidneys scoring 0-3, 5% scoring 4-6, 5% scoring 7-12. There was no significant correlation between Remuzzi score and early graft function (P = 0.7615, R^2 0.0039). NMP score correlated significantly with creatinine day 7 post-transplant (P = 0.0015, R^2 0.2790) and eGFR at 1 month (P = 0.0085, R^2 0.2228).
Conclusions: Parameters measured during NMP can be used to predict early graft function in DCD kidneys. Remuzzi score showed no correlation with early graft function. Future work should examine the relationship between NMP and Remuzzi score on long-term graft function and survival

OS067 EVALUATION OF A MARINE OXYGEN CARRIER (HEMO2LIFE®) FOR ORGAN PRESERVATION: FIRST USE IN KIDNEY TRANSPLANTATION IN HUMANS

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Background: The medical device HEMO2life® is an extracellular hemoglobin extracted from Arenicola Marina and featuring high oxygen carrying capabilities. Preclinical studies demonstrated its perfect safety as an additive to organ preservation solutions and its beneficial effect on ischemia/reperfusion injuries.
Methods: OxyOp is a multicenter open-labeled study evaluating for the first time in human the safety of the use of HEMO2life®, added (1 g/l) to the preservation solution of 58 kidneys retrieved and transplanted locally within the 6 participating centers. Their contralateral kidneys (same donor) transplanted elsewhere in France did not receive HEMO2life®. Totality of the adverse events (AE) were analyzed by an independent DSMB.
Results: Grafts were preserved in static mode (64%) or machine perfusion (36%). Mean ages of donors and recipients were 50 and 51 years. Among the donors, 23 (38%) were ECD. The mean cold ischemia time was 740 min. The patient survival was 100%, the rate of DGF (at least one dialysis session) 24.1%. At 3 months, 490 AE (41 serious) were reported including 2 graft losses and 2 acute rejections (3.4%). No immunological, allergic or pro-thrombotic effects were reported. According to the IDSMB, all these AE were in line with what was expected according to the donor and recipient populations. Pre-implantation and 3 month biopsies did not show signs of thrombosis or alteration of the microcirculation. Secondary efficacy end points with comparison with the contralateral kidneys showed less DGF and a better renal function in the HEMO2life® group. Data of Kaplan–Meier survival analysis of time to reach a creatinine value < 250 μmol and Cox regression analysis showed that in the subgroup of grafts preserved on static mode, HEMO2life® had a beneficial effect on DGF independently of cold ischemia time (p = 0.048).
Conclusion: This first study in humans confirmed that HEMO2life® added to preservation solution is safe and shows promising efficacy data.

OS068 DISPARATE REGIONAL REPERFUSION SIGNATURES IN HUMAN KIDNEYS DURING NORMOTHERMIC MACHINE PERFUSION

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Background: The healthy renal medulla (RM) functions on the edge of hypoxia to facilitate urine concentration. Yet damage to the RM during transplantation is understudied. We hypothesised that during transplant reperfusion, the RM would be disproportionately affected by tissue hypoperfusion, hypoxia and acute inflammation.
Methods: In a model comparing cortical and medullary responses to transplant reperfusion, human kidneys declined for transplantation (n = 20) underwent 90 min normothermic machine perfusion (NMP). Fibreoptic probes in cortex and medulla simultaneously measured laser-doppler flux (microvascular blood flow, MBF) and fluorescence lifetime oximetry (tissue oxygenation, tPO2). Paired end-reperfusion tissue samples of cortex and medulla (n = 6) underwent nanostring nCounter multiplex analysis to compare relative inflammatory gene expression.
Results: In the first 5 min reperfusion, medullary MBF was significantly higher than cortex, before falling significantly lower for the remainder of the reperfusion. In contrast, tPO2 was higher in the cortex throughout. Medullary MBF correlated with urine output whereas no cortical parameter did. Significant over-expression of several immunomodulatory genes including CCL2, CXCL2 and IL6 was seen in medulla vs. cortex.
Conclusion: This is a novel description of early medullary dyscirculation and inflammation in a human transplant reperfusion model. Medullary reperfusion injury differs significantly from that in the cortex, suggesting distinct strategies may be needed to ameliorate injury across the whole kidney.

OS069 MIR-493-5P IN HYPOTHERMIC MACHINE PRESERVATION SOLUTION AS AN INDEPENDENT PREDICTOR OF DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: Acute tubular necrosis (ATN) is the leading cause of graft dysfunction in the immediate post-transplant (KT) period. ATN determines short and long-term kidney function.

At present, biochemical biomarkers available in the preservation solution during Hypothermic Machine Preservation (HMP) do not have enough diagnostic accuracy. Our group has proved the viability of the Detection de miRNAs in the preservation solution.
Objective: To identify miRNAs as biomarkers of the graft function in the preservation solution during HMP.
Materials: A screening study of the expression of 762 different miRNAs was carried out following the selection of 4 experimental pairs in a cohort of expanded criteria brain death donors (ECD) under HMP in response to the development of ATN and its subsequent validation by RT-QPCR in $n = 35$ kidney recipients.

Simultaneously, LDH and lactate were determined as biomarkers of cellular injury. A network of interaction of the miRNAs was generated that show correlation with some of the parameters studied, based on the prediction of their targets. In addition, an analysis of enrichment of the biological processes orchestrated by these targets has been performed.
Results: A total of 11 miRNAs complied with the pre-established parameters (DCT < 40) and were included in the analysis. miR-493-5p in the final sample during HMP showed significant differences in response to the development of post-transplant ATN. miR-493-5p additionally showed a significant direct correlation with LDH and lactate levels in the final sample ($p = 0.001$ and $p = 0.017$, respectively). C-statistic was 0.71 for isolated miR-493-5p and increased to 0.91 in combination with LDH and lactate.
Conclusions: In grafts from ECD, elevated levels of miR-493-5p in the preservation solution during HMP were associated with an increased risk of ATN. miR-493-5p showed a direct correlation with LDH and lactate levels, biochemical parameters traditionally used as biomarkers associated with

OS070 OXYGENATED HYPOTHERMIC MACHINE PERFUSION OF KIDNEYS DONATED AFTER CIRCULATORY DEATH: AN INTERNATIONAL RANDOMISED CONTROLLED TRIAL

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Background: A double-blinded, randomised, paired phase 3 trial determined the effect of oxygenated (HMPO) vs non-oxygenated hypothermic machine perfusion (HMP) on 1y graft function in controlled DCD kidneys from donors $\geq$ 50y.
Methods: One kidney from each donor was randomly assigned to HMPO, the other to HMP. The primary endpoint was estimated glomerular filtration rate (eGFR) at 1y (CKD-EPI) with 90% power at α=0.05 to detect 8 ml/min/1.73 m^2 difference. A pre-specified sensitivity analysis accounted for cases where no 1y eGFR was available due to graft loss (eGFR imputed by 10 mL/min/1.73 m^2) or patient death with functioning graft (last known eGFR carried forward). Secondary endpoints were delayed graft function, primary nonfunction, acute rejection, graft and patient survival. Primary analysis was performed according to intention to treat.
Results: Belgium, the Netherlands, and part of UK randomised 197 kidney pairs (median donor age 56y (50-78)), of which 106 were successfully transplanted (recipient age 61y (21-79)). Median total warm ischemia time was 28.5 min (8-114), cold time was 11 h (4.6-27.6) in HMPO and 10.3 h (3.5-27.1) in HMP. Kidneys were pumped for 6.9 h (1.7-24.3) vs 7.4 h (1.3-23.8).

For the primary analysis, 83 pairs were eligible (23 pairs excluded due to all-cause graft loss of at least 1 kidney). No difference in eGFR at 1y was observed in HMPO vs HMP (mean(SE): 50.5(2.1) vs 46.7(1.8)mL/min/1.73 m^2, p = 0.12). However, when accounting for all-cause graft loss, eGFR was higher in HMPO (47.6(1.9) vs 42.6(2.0)mL/min/1.73 m^2, p = 0.035). Graft loss and acute rejection were lower after HMPO; other secondary outcomes were similar (Table).
Conclusion: This first randomised controlled trial comparing HMPO with HMP suggests that oxygenation improves 1 year graft function when accounting for the beneficial effect on graft survival.

	HMPO (N = 106)	HMP (N = 106)	p-value
Delayed graft function	38	38	0.99
Primary nonfunction	3	5	0.48
Acute rejection	15	30	0.014
Graft loss	3	11	0.021
Patient death	7	8	0.80

OS071 HYPOTHERMIC MACHINE PERFUSION AS A NATIONAL STANDARD PRESERVATION METHOD FOR DECEASED DONOR KIDNEYS

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Introduction: Transplantation professionals in collaboration with the Dutch Transplant Foundation have completed a two year project to implement hypothermic machine perfusion (HMP) as standard preservation method for deceased donor kidneys. The scope of this study was to assess the effect of the implementation of machine perfusion on early outcomes after kidney transplantation.
Materials & methods: All kidneys donated within the Netherlands from January 11th 2016 to December 31st 2017, and allocated to Dutch recipients were intended to be preserved by HMP. A historical cohort (2010-2014) with static cold storage (SCS) as standard preservation method was chosen as control group. Follow up data from these transplants were collected via the National Organ Transplant Registry. Results of the evaluation included delayed graft function (DGF), graft function defined by eGFR, graft survival one year after transplantation and safety of HMP preservation.
Results: Of all 924 kidneys procured during this project, 681 were transplanted in Dutch recipients. No kidneys were discarded due to the use of HMP. Within the historical cohort, 1812 kidneys were transplanted within the Netherlands, all preserved by SCS. DGF occurred in 38 percent of the project cohort versus 46 percent of the historical cohort (p = 0,001). A multivariate regression analysis showed an odds ratio of 0,7 (0,5 – 0,9) for the risk of DGF when implementing HMP (p = 0,001). At one year after transplantation the median eGFR for the project and the historic cohort was 44 (3 – 168) and 46 (5 – 141) ml/min/1.73 m2 (P=NS). One year graft survival did not show a significant difference with 94,4 percent in the project cohort compared to 93 percent historically.
Conclusion: The use of hypothermic machine perfusion as standard preservation method for all deceased donor kidneys in the Netherlands was associated with a significant reduction of DGF. To assess long term follow-up, a longer follow-up period and data is required.

OS09 - SURGICAL TECHNIQUE LIVER

OS073 CLINICAL COURSE OF HEPATIC ARTERY THROMBOSIS AFTER LIVING DONOR LIVER TRANSPLANTATION USING RIGHT LOBE

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Background: Hepatic artery thrombosis (HAT) can result in biliary tree necrosis and graft loss, necessitating retransplantation. The most effective treatment approach is still controversial. This study was performed to review the outcomes of HAT after living donor liver transplantation (LDLT) and to clarify the feasibility of different strategies.
Materials and Methods: From May 1996 to August 2017, LDLT using the right lobe was performed in 827 adult patients in our center. Our technique of hepatic artery (HA) reconstruction is end to-end anastomosis under a microscope (10 ×). Diagnosis of HAT was performed using Doppler sonography and computed tomography (CT) angiography. HAT was initially treated with surgical or endovascular procedure, and retransplantation was considered according to the graft condition.
Results: Among the 827 cases of LDLT using the right lobe, HAT occurred in 16 (1.9%) cases within 1 month after transplantation. Within the first week, 7 of these HAT cases (43.8%) occurred (early HAT), while the remaining 9 cases (56.2%) occurred between the first week and 1 month (late HAT). The incidence of graft failure was high in early HAT (42.9%), and the frequency of biliary complications was high in late HAT (77.8%). The success rate of HA recanalization was 62.5% (10/16): 100% (5/5) after reoperation and 45.5% (5/11) after the endovascular procedure. Of the patients in whom treatment failed in late HAT ($n = 5$), 4 underwent neovascularization during observation. A total of 5 patients underwent graft failure, and 3 of these patients underwent repeat liver transplantation (LT). Mortality occurred in 3 patients including 1 in the surgical group and 2 in the endovascular group.
Conclusion: Early diagnosis and aggressive treatment of HAT are necessary and the choice of treatment depends on various factors. Although further studies are required, early HAT requires preparation for graft failure, while late HAT requires treatment for bilary complications.

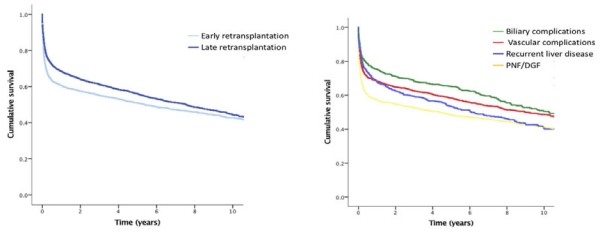

Figure 1. Left: Overall patient survival stratified by early (<1 month) versus late (≥1 month) retransplantation. **Right:** Overall patient survival stratified by indication for retransplantation.

OS074 RISK FACTORS FOR HEPATIC ARTERY COMPLICATIONS IN PEDIATRIC LIVER TRANSPLANTATION

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Introduction: Although liver transplantation has become the standard for treatment of end-stage liver disease in children, there are still some complications that adversely affect the post-transplant outcome. The aim of this study is to identify the risk factors for hepatic artery complications in pediatric liver transplantation
Methods: Data from 237 pediatric patients who underwent primary LT at Seoul National University Hospital from March 1988 to September 2015, were retrospectively analyzed. Treatment era was divided into 3 groups; 1988–2006, 2007–2011, and 2012–2015.
Results: Univariate analyses showed that age (< 1 vs. ≥ 1 year), body weight (< 6 vs. ≥ 6 kg), PELD score (<20 vs. ≥20), Child-Pugh score (< 7 vs. ≥ 7), transplant type (living vs. deceased), graft type (living vs. whole vs. split), and variant graft type (whole graft vs. standard partial graft vs. variant partial graft) were not significant factors related to hepatic artery complication ($P > 0.05$). However, the era of transplantation (early vs. mid vs. recent) ($P = 0.006$) and disease category (chronic liver disease vs. not) ($P = 0.001$) were related to hepatic artery complications. Fulminant hepatic failure, metabolic liver disease except Wilson disease, hepatoblastoma, and other not chronic liver diseases were categorized as "not". Multivariate analysis showed that disease category was the only significant factor related to hepatic artery complication (odds ratio: 8.768, confidence interval 2.549-30.156, $P = 0.001$)
Conclusion: The rate of hepatic artery complication could increase in patients without portal hypertension, especially in infants and small children.

OS075 ANALYSIS OF 124 CONSECUTIVE LAPAROSCOPIC AND ROBOTIC LIVING DONOR LEFT LATERAL SECTIONECTOMIES FOR PEDIATRIC LIVER TRANSPLANTATION AT THE KING FAISAL SPECIALIST HOSPITAL (RIYADH- SAUDI ARABIA): TOWARDS A GOLD STANDARD?

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Objectives: The adoption of fully laparoscopic living donor hepatectomy approach (LAP) in our institution in May 2013 is the standard approach for pediatric liver transplantation. Recently, the robotic-assisted approach (ROB) has been also implemented. Herein we describe our results and future perspectives.
Methods: From May 2013 until November 2018,a total of 124 left lateral sectionectomies (LLS) have been done. Five out of 124 donor hepatectomies were carried out with the robotic-assisted approach. The parenchyma transection was done using the surgical ultrasonic aspirator (LAP) and the harmonic scalpel (ROB). The trans-umbilical approach was routinely applied. After cutting the hilar plate and the bile ducts, the transection plan followed the line until the confluence of the left hepatic vein into the IVC. The S2-3 artery stump was secured with two Hem-O-lock clips, the left portal vein and the LHV secured and transected by the 45 mm vascular stapler after preparing a short Pfannestiel incision for graft extraction.
Results: The M/F ratio was of 60/64. The mean BMI was of 24.5 ± 3.8. Graft weight was of 224 ± 47 g. The operative time was of 264 ± 28 min. and 375 ± 31with an estimated blood loss of 111 ± 93 ml vs 37 ± 14 ($p = 0.0001$ and 0.07 respectively for LAP and ROB). The hilar dissection time was of 65 ± 12 min. in the Lap vs 50 ± 5 min in the ROB cases (p=ns). Overall donor complications were 4 (3.2%)(LAP). The conversion rate was 2.4% ($n = 3$ cases, LAP). The overall 3-y actuarial recipient survival was of 92.7%.
Conclusions: Laparoscopic LLS for donor hepatectomy is a safe and efficient procedure with a very low conversion rate. The ROB approach could be the ultimate evolution potentially shortening the hilar dissection time and providing its intrinsic and valuable advantages for the surgeon as better ergonomy, stable view, detailed anatomy and less manipulation of the graft. Further data are needed to validate this.

OS076 COMBINED LIVER KIDNEY TRANSPLANTATION IN PRIMARY HYPEROXALURIA TYPE 1: THE CHALLENGE OF CHOOSING THE RIGHT COMBINATION. A MONOCENTRIC RETROSPECTIVE ANALYSIS

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Background: Combined liver–kidney transplantation(CLKT) is a therapeutic option for different diseases as primary hyperoxaluria(PH1). Kidney graft loss is often reported as major complications after CLKT.
Methods: Between 2001 and 2018, 2402 LT were performed in our institution both in paediatric and adult recipients; 62 (2.6%) were CLKT and 13/62 (21%) performed for PH1, 6 in paediatric, 7 in adult recipients. We divided the whole population in two groups, group 1_kidney graft loss ($n = 3$) vs group 2_kidney graft survival ($n = 10$) to evaluate potential risk factors for kidney graft loss.
Results: Median[IQR] recipient age was 28.3[12.0-33.2] years; donor age 28.3[12.0-33.2] years while donor body weight was 68[40-76]. During a median [IQR] follow-up of 5.7[1.4-8.7] months, only one (8%) patient died 46 day after CLKT due to multiple organ failure; 3 (23%) kidney grafts were lost all in pediatric recipients: one case for primary non function due to long cold ischemia, one due to relapse of massive oxalate renal accumulation despite haemodialysis in the first month after transplantation, in another case, due to relapse of stone obstructive nephropathy evolved to end stage renal failure at 12 years of age. Donor's age, weight and recipient's age at CLKT were significantly lower in group_1 ($p = 0.01$). At multivariable logistic regression no risk factors for kidney loss were identified. 5-years liver and kidney graft survival was respectively 92% and 77%. One patient received a new uncomplicated kidney transplant after 2 years, whereas the other 2 are still in haemodialysis.
Conclusions: In our experience, despite the small population's size, kidney graft loss is the major CLKT complication especially in children.Pre-emptive liver transplantation with sequential kidney transplantation may be a better strategy to reduce kidney loss due to high serum oxalate level in children although the immunological protection of the combined transplant frome the same donor would be lost.

OS077 ANALYSIS OF FACTORS ASSOCIATED WITH BILIARY ANASTOMOTIC STRICTURES IN PEDIATRIC PATIENTS AFTER LIVING DONOR LIVER TRANSPLANTATION

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Background: Introduction of pediatric living donor liver transplantation (LDLT) have significantly reduced waiting list mortality. However, a higher morbidity is observed, including an increased rate of biliary anastomotic strictures (BAS). The aim of this study is to determine the rate of BAS and its associated risk factors.
Methods/materials: Retrospective cohort study of 330 children (<18 years of age) who underwent a primary LDLT between October 1999 and January 2018. Patients who did and did not develop BAS were compared to identify risk factors.
Results: A total of 31 patients (9.4%) develop BAS after LDLT. The median follow-up period for non-BAS and the BAS group was 79.6 and 82.4 months, respectively ($p = 0.59$). Duct-to-duct anastomosis and early hepatic artery thrombosis were risk factors associated with developing BAS ($p = 0.045$ and $p = 0.019$, respectively). There was no difference in patient or graft survival between non-BAS and BAS group.
Conclusions: In pediatric LDLT, Roux-en-Y bilioenteric anastomosis is an optimal method of biliary reconstruction. An inadequate arterial supply to bile tract due to early hepatic artery thrombosis is associated with the occurrence of BAS.

OS078 LIVING DONOR LIVER TRANSPLANTATION FOR HIGH-MELD PATIENTS: IS IT JUSTIFIED?

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Background/Aims: Living donor liver transplantation (LDLT) for patients with high MELD score is a controversial issue in terms of indication, graft selection and limitations. The purpose of the study is to retrospectively analyzed our data and clarify whether LDLT is justified for high MELD patients.
Patients/Methods: A total of 653 adult patients who underwent LDLT were included in the study. Preoperative disease severity was surrogated by MELD scores. Patients were divided into 3 groups according to MELD score: Group N (MELD < 25, $n = 552$), Group M (MELD 25≦, <30, $n = 55$) and Group H (MELD≧30, $n = 39$). Patients with retransplantation ($n = 7$) were excluded. Furthermore, patients were divided into 2 eras according to the date of LDLT: early (1997-2007, $n = 235$) and late (2008-2018, $n = 411$).
Results: Proportion of grafts (Left/Right /Posterior/Dual) were comparable among three groups. The GV/SLV(%)were 41.8%, 43.5% and 42.1%, respectively (p=NS). Operative time (768, 742, and 739 min) and blood loss (7550, 6243, 6778 ml) were also comparable. The incidence of small-for-size graft syndrome (14.6 15.7, and 19.4%) and sepsis (8.6, 13.7, and 18.9%) were comparable. The 1-,5-, and 10-year overall survival (OS) rates in each group were Group N (90.0, 82.7, 76.9%), Group M (89.6, 81.0, 81.0%) and Group H (74.4, 71.6, 66.5%), respectively (p=NS). The 1-year OS according to the graft type were comparable in Group N and M, however, that of patients with left lobe grafts was significantly worse in Group H ($p < 0.05$). Furthermore, the 1-year OS in all groups were significantly improved in the late era, especially in Group M (79.0% to 93.1%, $p < 0.05$) and Group H (50% to 84%, $p < 0.05$).
Conclusions: LDLT for high MELD patients can be justified, however, right lobe grafts with sufficient volume should be the choice for such patients.

OS079 POSTOPERATIVE AND INTRAOPERATIVE HEPATIC ARTERY COMPLICATIONS IN HEPATOCELLULAR CARCINOMA PATIENTS TREATED WITH TRANS-ARTERIAL CHEMOEMBOLIZATION (TACE) BEFORE LIVER TRANSPLANTATION, A MULTICENTER COHORT STUDY

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Background: Hepatic artery (HA) complications after liver transplantation (LT) may have devastating consequences, resulting in biliary complications, graft loss or mortality. Recent studies suggested an increased risk for HA complications in patients pre-treated with TACE. The present study aims to assess the risk for intra-operative HA interventions and postoperative HA complications in hepatocellular carcinoma (HCC) patients pre-treated with TACE in a multi-center cohort.
Methods: Patient records of 876 HCC patients transplanted between 2007 and 2016 in six centers were reviewed. Primary endpoints were occurrence of intra-operative HA interventions and post-operative HA complications. Intra-operative arterial interventions included re-do arterial anastomosis, thrombectomy, alternative arterial reconstructions, arterial conduit, and other interventions. Postoperative HA complications included thrombosis, stenosis, and (pseudo)aneurysms. Incidences of intraoperative HA interventions and post-operative HA complications were statistically compared between patients with and without TACE pre-treatment.
Results: In total, 425/876 patients were pre-treated with TACE. Baseline characteristics and outcomes are summarized in the Table and Figure. Pre-transplant TACE was not associated with an increased incidence of intra-operative HA interventions (TACE: 26; 6.7% *versus* no-TACE: 29; 7.8%; $p = 0.85$; $N = 759$) or postoperative HA complications (TACE: 27; 6.4% *versus* no-TACE: 31; 6.9%; $p = 0.79$; $N = 876$). Mean arterialisation time, defined as time between portal and arterial reperfusion, was similar between TACE and no-TACE patients (TACE: 34.2 ± 20 minutes *versus* no-TACE: 36.4 ± 24 minutes; $p = 0.5$; $N = 367$).
Conclusion: Pre-LT TACE was not associated with an increased incidence of either intra-operative HA interventions or post-operative HA complications. TACE treatment in HCC patients listed for LT is a safe bridging strategy.

	TACE (N = 425	No TACE (N = 451)	P
Recipient			
≥ 2 TACE cycles	215 (51%)	-	-
Radio frequent ablation	91 (21%)	178 (39%)	-
Age (years)	60 ± 7.3	59 ± 8.4	0.152
Sex (male)	353 (83%)	362 (80%)	0.296
BMI (kg/m2)	27.3 ± 4.6	27.8 ± 4.6	0.117
MELD at LT	12.8 ± 5.8	14.5 ± 6.4	<0.001
Insulin dependent	91 (21%)	89 (20%)	0.504
Anti-hypertensive drug use	166 (39%)	153 (34%)	0.091
Alternative HA anatomy	42 (10%)	53 (12%)	0.58
Number of tumours (pre-bridging)	1.8 ± 1.3	1.5 ± 0.8	0.005
Size largest tumour (cm, pre-bridging)	3.1 ± 1.7	2.6 ± 1.7	<0.001
Cumulative tumour size (cm, pre-bridging)	4.0 ± 2.5	3.3 ± 2.6	<0.001
Donor			
Age (years)	53 ± 16.4	52 ± 16.9	0.202
Sex (male)	234 (55%)	274 (64%)	0.1
BMI (kg/m2)	25.8 ± 4.1	27.8 ± 4.1	0.385
DCD	67 (16%)	122 (29%)	0.001
Split-graft	5 (1%)	12 (3%)	0.143
Back-table HA reconstruction	70 (16%)	78 (18%)	0.928
Alternative HA anatomy	91 (21%)	105 (25%)	0.516
Warm ischemia time (min)	43.6 ± 13.3	41.4 ± 12.7	0.006
Cold ischemia time (min)	462.3 ± 153.7	434.4 ± 146.2	0.025
Donor risk index	2.1 ± 0.6	2.1 ± 0.6	0.443
Outcomes			
Intra-operative HA interventions	26 (6.7%)	29 (7.8%)	0.85

1. *Continued*

	TACE (N = 425	No TACE (N = 451)	P
Re-do anastomosis	15 (3.9%)	16 (4.3%)	
Arterial Thrombectomy	4 (1%)	5 (1.4%)	
Arterial conduit	9 (2.3%)	9 (2.4%)	
Alternative arterial reconstruction	12 (3.1%)	10 (2.7%)	
Other	1 (0.3%)	0	
Postoperative HA complications	27 (6.4%)	31 (6.9%)	0.787
Thrombosis	15 (3.5%)	17 (3.7%)	
Stenosis	9 (2.1%)	13 (2.9%)	
(Pseudo)aneurysm	3 (0.7%)	2 (0.4%)	
Other	1 (0.2%)	1 (0.2%)	
Arterialisation time (min)	34.2 ± 20	36.4 ± 24	0.498

OS080 INDICATIONS AND OUTCOMES OF PEDIATRIC LIVER RETRANSPLANTATION IN EUROPE. ANALYSIS OF A EUROPEAN LIVER REGISTRY-BASED COHORT

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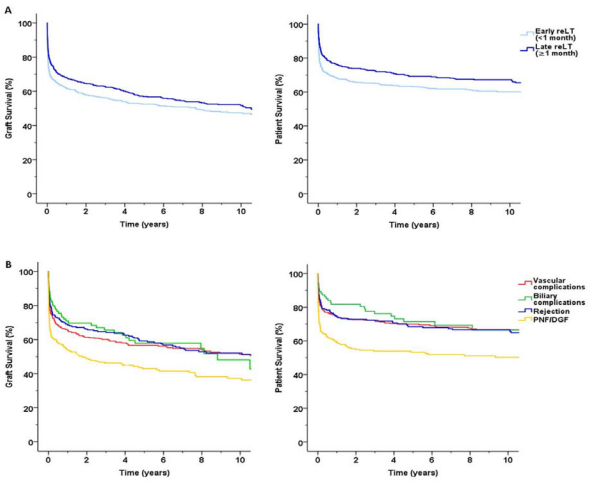
Background: Although survival after pediatric liver transplantation has improved over the years, a substantial proportion of recipients require retransplantation (reLT) due to a variety of causes. The purpose of this study was to investigate the impact of different indications for pediatric reLT on long-term outcomes.
Methods: Donor, graft and recipient data of reLT in recipients aged < 18 years were collected from the European Liver Transplantation Registry database (1995–2016). The Kaplan-Meier method was used to estimate survival by indication for reLT, stratified by early (<1 month) and late (≥1 month) reLT.
Results: Out of 12,075 pediatric liver transplantations, a total of 1,361 (11.3%) reLTs were performed. Of these, 668 (49%) recipients underwent early reLT after a median waiting list time of 2 (IQR 1-4) days, whereas 693 (51%) recipients underwent late reLT after 72 (20-191) days. 95% of early reLT recipients had a high urgency status, when compared to 21% after late reLT ($P < 0.001$). Early reLT was mainly performed for vascular complications (51%), or primary non-function (PNF; 38%), whereas main indications for late reLT were rejection (41%), vascular (18%), or biliary complications (18%). Overall, ten-year graft (52% vs. 47%; $P = 0.041$) and patient survival (67% vs. 60%; $P = 0.006$) were better after late reLT, when compared to early reLT (Figure 1a). Ten-year graft and patient survival were the highest for reLT for rejection (52% and 67%) or vascular complications (51% and 67%), whereas the lowest survival rates were observed after reLT for PNF (37% and 50%; Figure 1b).
Conclusions: In Europe, over the last two decades early pediatric reLT was mostly performed for vascular complications or PNF, and was associated with inferior long-term survival.
Figure 1. Graft and patient survival stratified by early and late ReLT (A) and stratified by indication for ReLT (B).



OS081 MULTICENTRE MATCHED-PAIR ANALYSIS OF EXTENDED RIGHT LOBE VERSUS WHOLE ORGAN LIVER TRANSPLANTATION

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Introduction: Split liver transplantation allows expansion of the limited organ pool. Available data suggest a comparable outcome between extended right lobes liver transplantation (ERLT) and whole organs. However, excellent liver graft quality in ERLT in contrast to largely marginal donors used for whole organ LT in the recent transplant era, makes conclusions not reliable.
Methods: Retrospective multicentre study of 7 large transplant centres in Germany between 2007 and 2015. We performed a 1:1 matched-pairs analysis of 121 patients with ERLT and whole organ LT each, using the matching criteria recipient and donor age and recipient MELD score.
Results: Patients with ERLT and whole organ LT were comparable concerning recipient age (40.3 ± 19.9 vs. 41.8 ± 20.7y), BMI (23.6 ± 6.9 vs. 23.3 ± 5.2), MELD score (both 19 ± 11points) and donor age (29.1 ± 14.5 vs. 31.2 ± 15.5y). We found a significant ($p = 0.000$) longer cold ischemic time in the ERLT group (779 ± 149 min versus 640 ± 143 min). Graft survival was significant reduced in patients after ERLT in contrast to whole organ LT (1-/5-/10-y graft survival rates 74%/66.2%/53% vs. 89%/75%/70.7%; $p = 0.046$), whereas patient survival was comparable. In the ERLT group 27.3% biliary complications occurred, including 16 biliary leakages, 10 biliary stenoses and 7 ITBL. 25.6% of the patients following whole organ LT suffered from biliary complications (biliary leakages $n = 7$, biliary stenoses $n = 17$, ITBL $n = 8$) without significant difference ($p = 0.884$). Likewise overall vascular complications were comparable between the ERLT group ($n = 8$) and the whole organ group ($n = 6$; $p = 0.784$).
Conclusion: In patients undergoing LT from comparable high-quality donors we found an elevated risk for graft failure after ERLT compared to whole organ LT. In an otherwise matched cohort, this appears to be most likely due to the significantly longer cold ischemic time. Consequently, efforts should be made to reduce cold ischemic time by improved allocation and reduced transportation time.

OS082 ASSOCIATED BALANCE OF RISK SCORE – COMPREHENSIVE COMPLICATION INDEX FOR THE PREDICTION OF LONG-TERM SURVIVAL AFTER LIVER TRANSPLANTATION: STARTING FROM THE ABC

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Background: In past years, several scoring systems were developed to predict early post-LT graft function. However, many of them showed poor accuracy in predicting long-term survival. Moreover, the majority of available scores are composed of many evasive variables, making user-friendly predictive models hard to generate. Recently, the pre-transplant Balance of Risk (BAR) and the post-LT Comprehensive Complication Index (CCI) have

been created. However, external validation and integration of the two scores in liver transplantation is absent.

This study aims to produce a user-friendly scoring system based on the combination of a low number of pre- and immediately post-liver transplant (LT) independent variables, in order to accurately predict long-term graft survival after LT.

Methods/Materials: A Training Set was created, composed of 1,262 retrospectively analysed first-LT performed in four European Centres (Brussels, Rome Sapienza, Ancona and Padua). A Validation Set from the Karolinska Institute (N = 520) was also obtained, for external validation of the results coming from the Training Set.

Results: The Associated Balance of risk-Comprehensive complication index (ABC) was generated in the Training Set, based on the combination of HCV status, BAR and CCI. At internal validation, the ABC showed the best discriminative power for the risk of five-year graft loss, with an area under the curve (AUC) = 0.80. The external validation confirmed the good accuracy of the score (AUC = 0.70).

Conclusions: The ABC score shows excellent predictive power for five-year graft survival, and its accuracy is greater than several pre-transplant (i.e. MELD, D-MELD, BAR) and post-transplant scores (i.e. CCI and Early Allograft Dysfunction score) (ClinicalTrials.gov NCT03723317).

OS083 COMPARISON BETWEEN CADAVERIC WHOLE LIVER AND PARTIAL LIVER TRANSPLANTATION IN HIGH RISK PATIENTS WITH MELD SCORE MORE THAN 40

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Asan Medical Center

Two types of grafts are possible for liver transplantation. Cadaveric whole liver graft(CLT) gives sufficient volume but usually considered suboptimal functionally. live donor partial liver graft(LDLT) has optimal functionally but has volume limitation. Although, the results from both type of graft are similar, but whole liver grafts are preferred then partial liver grafts if the recipient's condition is very poor. So we analyzed the results of whole and partial liver graft transplantation which recipient's MELD score was more than 40.

From Dec. 1994 to Dec. 2016, 5241 liver transplantation were done in Asan Medical Center. 269 recipient's MELD score were more than 40. Among them, 44 cases were excluded due to salvage transplantation, multiple organ transplantation, split or two donor transplantation or retransplantation and 225 cases were analyzed. CLT were 84 cases (male 61, female 23 and mean age was 49 years). LDLT were 141 cases (male 105, female 36 and mean age was 45 years) and 125 right lobe graft, 16 left lobe grafts were used. The GRWR(graft vs recipient weight ratio) were 2.20(1.16 -3.40) in CLT group and 0.98(0.67 – 1.58) in LDLT group. There's no difference in MELD score in both groups (CLT 43.4 vs LDLT 44). In hospital mortality in CLD were 18 cases (21.4%), infection in 11, primary non function(PNF) in 2, intracranial hemorrhage(ICH) in 3 and stress induced cardiomyopathy in 1 and sever pulmonary failure in 1 case. mortality in LDLT group were 21 cases(14.9%), infection in 11, PNF in 5, ICH in 4, and acute hepatic arterial thrombosis in 1 case. There were no difference between both group in ICU stay and post-operative hospital days and outpatient course.

In conclusion, with precise selection and careful operation, LDLT can get comparable or better results to whole liver graft transplantation.

OS10 - INFECTIONS - RISK FACTORS AND TREATMENT

OS084 THE USE OF 16S RIBOSOMAL RNA PCR TO INVESTIGATE DONOR DERIVED TRANSPORT FLUID INFECTIONS IN PATIENTS UNDERGOING RENAL TRANSPLANTATION: A RETROSPECTIVE AUDIT OF 55 DECEASED DONORS

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Introduction: 16S ribosomal RNA (rRNA) gene polymerase chain reaction (PCR) is emerging as a novel, high-yield molecular method for the detection and identification of bacterial pathogens in clinical specimens with a high suspicion for infection. 16S rRNA PCR has been investigated as an alternative approach to conventional microbiological cultures in various clinical settings. 16S rRNA has the potential of providing results faster than conventional culture.

Methods: Transport fluid was obtained from 55 deceased donors and was assessed by two different methods. 16S rRNA PCR was compared with conventional microbiological culture for the detection of potential pathogenic bacteria.

Results: Of 55 deceased donor transplants 39 had 16S rRNA PCR performed. 18 (of 39) transplants had a positive culture (46%). 5 (of 39) transplants has a positive 16S rRNA result (13%). Compared with conventional culturing 16S rRNA demonstrated 100% specificity and 28% sensitivity for the detection of pathogens. The positive predictive value (PPV) for 16S rRNA compared to culture for detection of pathogens was 100% The negative predictive value for 16S rRNA was 62%.

Discussion: Transplant associated infections are associated with high levels of morbidity and mortality. 16S rRNA PCR offers the possibility of rapid high yield analysis of transport fluid for pathogens before the results of conventional culture. Despite the low sensitivity demonstrated, 16S rRNA PCR still demonstrates potential clinical utility as 28% of transport fluid with a positive culture could be detected at an earlier stage, additionally low sensitivity of 16S rRNA PCR may be an advantage due to reduced risk of detecting contaminants.

Conclusion: There is limited understanding of regarding the use of 16S rRNA PCR for detection of infection in deceased donors. 16S rRNA analysis of transport fluid is a novel technique which shows potential clinical utility in the detection of pathogens. Further investigation is required.

OS085 IMPACT OF SARCOPENIA ON OUTCOME AFTER LIVER TRANSPLANTATION

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Background: The loss of skeletal muscle mass, quality and strength, is associated with an increased morbidity and mortality after surgery. Since sarcopenia is common in liver transplant candidates this study was designed to analyze both its prevalence and impact on outcome after liver transplantation (LT).

Methods: 132 patients who underwent LT between 2008-2017 at the Dept. of Surgery, University Hospital of Graz were retrospectively analyzed. CT scans were used to determine muscle mass in the area of the third lumbal vertebra to index sarcopenia. Gender specific cut-off-values were defined ($\leq$ 38.5 cm2/m2 in female and $\leq$ 52.4 cm2/m2 in male patients). The 30-days-mortality, 1-year-survival, 5-years-survival, early and late complications according to the Clavien-Dindo score, the length of ICU-stay and total postoperative hospital stay were compared.

***Results*:** In male individuals, sarcopenia is much more common as compared to female patients (p = 0.003). Sarcopenia dramatically decreased survival only at one year after LT from 89.5% to 13.3% (p = 0.019). Furthermore, sarcopenia is associated with an increasing length of ICU stay (p = 0,037); however, there was no impact on the total length of postoperative hospital stay nor on the incidence of complications.

***Conclusion*:** Patients with sarcopenia must be carefully selected for LT in times of organ shortage for utility reasons.

OS086 CAN PYURIA HELP RISK STRATIFY RENAL TRANSPLANT PATIENTS WITH BACTERIURIA?

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Background: Asymptomatic bacteriuria (ASB) is common post transplantation and recent evidence suggests there is no treatment benefit. ASB is defined as the presence of > 105 bacterial colony-forming units per ml of urine in the absence of local or systemic symptoms. The presence or absence of pyuria has not been incorporated into ASB definitions. Pyuria is often seen in transplant patients with UTIs and maybe a way of determining the difference between host response to bacteria versus colonisation.

The aim of this study is to determine the clinical relevance of pyuria in renal transplant patients with bacteriuria.

Method: We studied 786 renal transplant recipients and categorised them into 3 groups according to urine microscopy post-transplant: no bacteriuria (B-), B+W- (bacteriuria with no pyuria) and B+W+ (bacteriuria and pyuria). Pyuria is defined as the presence of > 50 white cells per cubic millimetre, our centre's cutoff for reporting. Bacteriuria is defined as above. Median follow up is 3.79 (3.6-3.9) years.

Results: There were 427(54.3%) B-, 166(21.1%) B+W- and 192(24.4%) B+W+ patients. Significant differences in the demographics are shown below.

There was no difference is bacteraemia episodes between the B- and B+W- groups, at 11(2.6%) and 8(4.8%), p = 0.16; which were significantly less than the B+W+ group, 52(27.1%), p < 0.001. Allograft outcomes are shown below.

	B- (N%)	B+W- (N%)	B+W+ (N%)	P value
Females	97(22.7)	66(39.8)	100(52.1)	<0.0001
Age	50.4±13.2	53.8±12.8	54.5±13.3	<0.0001
Deceased donor	267(62.5)	117(70.5)	138(71.9)	0.035
Diabetes	96(22.6)	43(26.1)	61(33.9)	0.013

Conclusion: The presence of pyuria may help stratify those patients at risk of detrimental allograft outcomes associated with bacteriuria, and maybe an objective finding to guide which patients with ASB will benefit from treatment.

OS087 OUTCOME AFTER KIDNEY TRANSPLANTATION IN HEPATITIS SURFACE ANTIGEN-POSITIVE PATIENTS

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Background: Hepatitis Surface Antigen (HBsAg) positive status in renal transplant recipients (RTRs) is known to be associated with higher rate of mortality, graft failure and HBV reactivation. Current guideline recommends that RTRs who are HBsAg positive must undergo suppression of HBV DNA by antiviral agent before transplantation. Because of the low prevalence of HBsAg positive RTRs, only a few reports have evaluated the actual outcome of these patients. This study aimed to provide real-world outcome of HBsAg-positive RTRs in Korea.
Method: This was a retrospective single-center cohort study. Inclusion criteria were (1) recipients of kidney alone transplantation, (2) HBsAg positive status at the time of transplantation. Outcomes including mortality, graft survival and HBV reactivation were investigated.
Results: Between January 2010 and December 2017, a total of 1255 patients were transplanted at Seoul National University Hospital. Of these, 52 (4.1%) patients who were HBsAg positive at the time of transplantation were enrolled. Mean ± SD age was 49.6 ± 9.5 years and 37 (71.2%) were male. Six (11.5%) patients received ABOi or DSA (+) transplants, 3 (5.8%) had previous kidney transplants, and 20 (38.5%) were donated by a deceased donor. 48 (92.3%) patients received a triple immunosuppressive protocol as maintenance immunosuppression and 3 (5.8%) received rabbit anti-thymocyte globulin as induction therapy. Rituximab was administered in 5 (9.6%) patients before transplantation. The majority of patients (90.4%) received antiviral treatment at the time of transplantation. Overall patient and allograft survival was 94.2% and 90.4% at a mean follow-up of 4.9 years. Two (3.9%) patient developed HBV reactivation and both did not start antiviral treatment at the time of transplantation.
Conclusion: Renal transplant with antiviral treatment in HBsAg positive RTRs is associated acceptable outcome.

OS088 ARE DIRECTLY ACTING ANTIVIRAL DRUGS IN RENAL TRANSPLANT RECIPIENTS AS SAFE AS WE BELIEVE?

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Background: Although considered as highly effective and well tolerated with minimal side-effects, limited data exist on safety of directly acting antiviral (DAA) drugs for treatment of hepatitis C virus (HCV) infection in renal transplant recipients in the real-life setting.
Methods: A retrospective cohort analysis of all HCV positive patients who received renal allograft at our center and who have been treated with DAAs. Virologic response, graft function, proteinuria, donor specific antibodies (DAA), and acute rejection were analized.
Results: 12 patients received DAA after kidney transplantation (KT). Median age at time of treatment with DAA was 53 yrs. 41,6% were female. 8 had genotype 1b, 2 genotype 1a and 2 genotype 3a. The median time from the beginning of renal replecement therapy to initiation of DAA was 26,5 (range 15-38) years. Median number of HCV RNA copies was 7,5 x105 (range 0.25-13.9 x105). Ombitasvir / paritaprevir / ritonavir/dasabuvir was used in 5 patients, 4 received ledispavir+sofosbuvir+ribavirin, 1 sofosbuvir/veltapasvir and 1 glecaprevir/pibrentasvir. 10 were negative at one month, all had negative HCV RNA at the end-of treatment and achieved SVR. Frequent CNI monitoring enebled stable trough levels. 4 patients developed de-novo DSA (three had proteinuria and one had elevated serum creatinine) and had biopsy-proven acute rejection. The treatment of rejection was administered concomitantly with the DAA therapy in one patient, while others developed acute rejection 6,3 (range 1-14) months after the end of DAA treatment. One patient had severe hypertension with fluid retention during the treatment, one had severe liver toxicity during the treatment which was interrupted after 20 days.
Conclusion: Our results demonstrate that DAAs may be associated with increased risk for acute rejection in renal transplant recipients. Patients should be carefully followed for worsening of allograft function or development of proteinuria.

OS089 PRE-TRANSPLANT PSOAS MUSCLE DENSITY AS A READY-TO-USE AND LOW COST PREDICTOR OF PATIENT SURVIVAL AFTER LIVER TRANSPLANT

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Objective: Sarcopenia, defined as low muscle mass together with low muscle function, is frequently encountered in cirrhotic patients, and is a major predictor of adverse clinical events, including post-transplant (LT) outcome. In the present study, we assessed the impact of sarcopenia, using computed tomography (CT)-based measurements, on post-LT mortality and complications.
Methods: We analyzed the post-transplant outcome of 287 cirrhotic patients who underwent LT between 1 January 2008 and 15 June 2016, and for whom a CT-scan 3 months prior to LT was available. Psoas muscle density (PMD) was detected for every patient using the standard instruments present in the radiological workstation, and was related to post-operative course.
***Results*:** Post-operative mortality was 6.3% (18 patients). At least one grade III-IV post-operative complication was experienced by 121 patients (42.2%); respiratory and infective complications occurred in 30 and 32 patients (10.5% and 11.1%), respectively. PMD was an independent predictor of post-operative mortality ($P = 0.021$), respiratory complications ($P = 0.015$) and post-operative infections ($P = 0.010$). ROC analysis identified a PMD $\leq$ 43.72 HU as the best cut-off value for predicting 90-day mortality after LT.
Conclusions: PMD accurately predicted post-LT mortality and complications; its easy and low-cost determination allowed a widespread use of this parameter, in order to improve clinical care and help with the decision to give these patients some priority on the transplant waiting list.

OS090 TREATMENT WITH EVEROLIMUS LEADS TO CMV-PROTECTION DUE TO INCREASED POTENCY OF CMV-SPECIFIC CD4 + T CELLS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS COMPARED TO A STANDARD REGIMEN: 12 MONTHS DATA OF THE ATHENA STUDY

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Purpose: CMV reactivations pose a clinical challenge after de novo kidney transplantation [KTx]. Clinical evidence indicates that mTOR-inhibitors lieke everolimus [EVR] can decrease reactivation rates, but underlying mechanisms are not yet fully understood. In the ATHENA trial and a dedicated CMV-substudy the effect of EVR-therapy on CMV-replication and CMV-specific T-cells was further investigated.
Methods: In this 12 month [M] prospective, open-label study, 612 patients [pts] were randomized 1:1:1 at time of KTx to EVR+tacrolimus [TAC], EVR+Cyclosporin A [CyA] or TAC+mycophenolic acid [MPA]. CMV-donor [D]/recipient [R] status at baseline was balanced across groups, D+/R- and D+/R+ pts received valganciclovir prophylaxis for 3M. Blood samples for CMV-specific stimulation assays were prospectively collected from 121 pts. Expression of functional anergy markers (CTLA-4;PD-1) and cytokine profiles of CMV-specific T-cells were characterized in pts on-treatment at M12.
Results: ATHENA showed significantly fewer CMV infections under EVR-treatment (21%TAC+MPA vs 6%EVR+TAC vs 3%EVR+CyA;$p < 0.01$) in *de novo* KTx recipients. Flow-cytometric analysis of stimulated CMV-specific CD4 + T cells revealed that: median CTLA-4 and PD-1 expression was lower in samples obtained from EVR+TAC or EVR+CyA treated pts compared to TAC+MPA pts samples (median CTLA-4 MFI: 744($n = 16$), 463($n = 8$), 1282($n = 28$);$p = 0.05$ and $p = 0.02$) (median PD-1 MFI: 227($n = 15$), 320($n = 8$), 351($n = 28$); $p = 0.02$ and $p = 0.59$). In addition, the percentage of multifunctional IL-2, IFNγ and TNFα triple-positive CMV-specific CD4 + T cells was higher in samples from EVR+TAC and EVR+CyA treated pts compared to TAC+MPA treated pts (median:28%($n = 16$),27%($n = 8$) vs 14%($n = 28$); $p = 0.02$,$p = 0.13$).
Conclusions: ATHENA confirmed the previously described beneficial effects of EVR on CMV replication. We found for the first time that CMV-specific T-cells of EVR-treated pts show a more potent functionality that might lead to an increased protective potential.

OS091 ARE INTRAVENOUS IMMUNOGLOBULINS EFFECTIVE IN PREVENTING PRIMARY EBV INFECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS?

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Introduction: About half of children ≤ 5 years are seronegative for Epstein-Barr virus (EBV) and are at risk of contracting primary EBV infection after transplantation, especially if the donor is EBV-seropositive. Posttransplantation lymphoproliferative disorder (PTLD) is the most harmful complication of EBV infection in transplant recipients. In the literature, there are no univocal recommendations on prevention of EBV primary infection in pediatric renal transplant recipients
Aims: EBV-seronegative (negative EBNA) kidney transplant-recipients (R-) of EBV-seropositive (positive EBNA) donors (D+) were serially administered intravenous immunoglobulins (IVIG) during the first six months after transplantation (PT), in order to evaluate if IVIG can prevent primary EBV infection and enhance protective immunity in a 12-24 months-follow up.
Materials and Methods. Between 2012 and 2015, IVIG (200 mg/kg/dose) were administered to 12 children (M/F:7/5, average age 6 years) according the following schedule: day 0 (time of transplantation), day 1-7-14 and 21 PT. Then, every 3 weeks for 3 months, and then monthly until the sixth month PT. All children received basiliximab/thymoglobuline+steroids, and then calcineurine inihibitor+mycophenolate mofetil/mTOR inhibitor+steroid. EBV-DNA and EBV antibodies (VCA, EA, EBNA) were regularly monitored and evaluated on month 6, 12 and 24 PT.
Results: EBV-DNA positivisation was observed in 50% of patients during the first 6 months PT. No one had developed protective immunity against EBV (negative EBV-EBNA) by month 12 PT. The same results were osbserved in a group of 12 R- patients with the same clinical features, who were transplanted between 2014 and 2017 but did not receive IGIV. Nobody developed PTLD in a 24-months follow up.
Conclusions: Despite the small number of patients and the short follow up, our data do not seem to support the use of IGIV as a tool to prevent EBV primary infection in pediatric R- who receive the graft from D + .

OS092 OPPORTUNISTIC INFECTIONS AFTER CONVERSION TO BELATACEPT IN KIDNEY TRANSPLANTATION

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Background: Belatacept rescue therapy seems to be a valuable option for calcineurin inhibitor (CNI) chronic toxicity in kidney transplantation. Nevertheless the risk of infection associated with belatacept is not well reported.
Methods: We report the rate of opportunistic infections (OPI) after a switch to belatacept in a multicentric cohort of 280 kidney transplant patients.
Results: Forty-two OPI occurred in 34 patients (12.1%), on average 10.8 ± 11.3 months after the switch. With a cumulative exposure of 4928 months of belatacept treatment, we found an incidence of 0.008 OPI per month of exposure, and 10.2 OPI per 100 person-years. The most common OPI were CMV disease in 18/42 OPI (42.9%) and pneumocystis pneumonia in 12/42 OPI (28.6%). Two patients presented a progressive multifocal leucoencephalopathy and 2 patients developed a cerebral EBV-induced post-transplant lymphoproliferative disease. OPI led to death in 9/34 patients (26.5%) and graft failure in 4/34 patients (11.8%). In multivariate analysis eGFR < 25/mL/1.73 m² on the day of the switch and and the use of immunosuppressive agents before transplantation were associated with the occurrence of OPI.
Conclusion: The results of this study show that the risk of OPI is high in this setting and justifies a specific monitoring of infection and presumably a prophylactic regimen, particularly regarding pneumocystis pneumonia and CMV disease. These data have to be confirmed in a larger case control study.

OS093 CLINICAL RELEVANCE OF SARCOPENIA IN LIVER TRANSPLANT CANDIDATES

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Background: Sarcopenia,characterized by loss of skeletal muscle mass,has recently emerged as an independent factor associated with elevated mortality in end-stage liver disease patients and in liver transplant (LT) candidates.Moreover, sarcopenia has been recently associated with peri-transplant morbidity e post-LT outcome.
Methods: 410 cirrhotic patients,who received a LT at Niguarda Hospital,from January 2012 to December 2016 were enrolled.Skeletal muscle index at the third lumbar vertebra was measured by CT scan,and sarcopenia was defined using previously published gender and BMI–specific cutoffs.
Results: 365 patients (69%) were male, with a median age at LT of 54 years.The most common etiologies of cirrhosis were HCV (52%), alcohol (16%) and autoimmune diseases (6%).Sarcopenia was diagnosed in 69 patients (16%), and was more frequent in those with refractory ascites (p = 0.000), and higher MELD score at LT (p = 0.000).While on waiting list, sarcopenic patients were more frequently admitted to the hospital for bacterial infections (p = 0.000) and to ICU to manage major cirrhosis complications (p = 0.000).Sarcopenic patients had longer ICU (p = 0.001) and hospital stays (p = 0.002), and a higher rate of bacterial and fungal infections (0.001) peritransplant.Moreover, MDR infections, especially caused by Klebsiella Pneumoniae Carbapenemase-producing (KPC) bacteria were more represented in sarcopenic patients (p = 0.014).The median survival after LT was 1282 days for sarcopenic and 1411 for non-sarcopenic patients (P = 0.016).At multivariate analysis, older age at LT and pre-LT sarcopenia as well as post-LT MDR infections,use of CRRT and prolonged ventilation in ICU were all independently associated with mortality.
Conclusion: Sarcopenia is one of the most common complication in patients with cirrhosis and it is predictive of longer hospital stays,higher risk of waiting-list and post-LT bacterial infections, including MDR infections, and is associated with increased mortality after-LT.

OS12 - HEART TRANSPLANTATION

OS096 CASE REPORT CONVERSION TO CERTICAN RECIPIENT AFTER HEART RETRANSPLANTATION, A PERSONALIZED APPROACH OF IMMUNOSUPPRESSIVE THERAPY

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The results of survival of recipients after heart transplantation last ten years decades have improved significantly. As a result of heart transplantation, a group of patients who need to use heart retransplantation with the development of graft dysfunction. Thus, according to the results of the ISHLT report for 2017, about 2.9% of patients who had undergone heart transplantation need heart retransplantation. This group of patients needs a personalized approach to immunosuppressive therapy. The purpose of our report is to demonstrate the successful case of conversion of the recipient after heart transplantation to certican after heart retranslantation and to evaluate the effectiveness of this drug during the observation year after heart retransplantation.

OS097 CHANGES IN WAVEFORMS DURING SIX MINUTES WALKING TEST IN PATIENTS WITH H-VAD: A NEW MARKER OF FUNCTIONAL CAPACITY

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Introduction: Left ventricular assist device (LVAD) allows improvement of survival and quality of life in potential heart transplant candidates. Quality of life in these patients is related to tolerance to exertion, and upon the tailored optimization of LVAD support. We analyzed the variability of HVAD

(HeartWare) parameters in a group of patients undergoing six-minutes walking test (6MWT) and right heart catheterization (RHC) to investigate how these changes may predict functional capacity during exercise.
Methods: We included all consecutive patients with HVAD who underwent RCH and 6MWT for routine follow-up between June 2018 and March 2019. We excluded patients who had not completed rehabilitation. Estimated average, afterload and preload flows were measured before and after 6MWT. Right ventricle stroke work index (RVSWI) was considered as indicator of right ventricle function.
Results: Nine 6MWT were performed in 9 patients. Average distance walked was 466 ± 85 m and Borg scale was 4.22 ± 2.10. Afterload (6.28 ± 0.56 to 6.96 ± 0.48 l/min, $p < 0.01$) and preload (1.81 ± 1.24 to 2.5 ± 0.98 l/min, $p < 0.01$) flows significantly rose after exercise. LVAD flow changes and flow pulsatility were associated with distance walked ($P = 0.02$). RVSWI was correlated with baseline flow pulsatility (0.64; $P = 0.05$) and preload flow change ($R = 0.65$; $P = 0.05$) during exercise. Aortic valve opening was associated with larger changes in preload flow ($P = 0.02$) and tended to be associated with longer distance walked ($P = 0.08$)
Conclusions: In this pilot study, changes in waveforms during exercise are associated with functional capacity. RV function is associated with LVAD pulsatility and with pre-load flow changes; aortic valve opening is a marker of improved functional capacity and increase in LVAD flow. Overall, these data support the concepts that RV optimized function influences the coupling of LVAD flow with exercise tolerance, and that LVAD waveforms may predict functional capacity and RV function.

OS098 SINGLE CENTER EXPERIENCE WITH MODERN TECHNIQUES OF APHERETIC MEDICINE IN PATIENTS UNDERGOING HEART TRANSPLANTATION

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The improvement of immunosuppressive strategies has reduced significantly the risk and the mortality of cellular rejection after Heart Transplantation (HTx). Recently, Humoral Rejection and antibodies have been recognized as a major problem in the management of recipients during the follow-up.

23 patients out of more than 700 recipients undergoing HTx and 6 undergoing retransplantation required techniques of apheretic medicine to manage Humoral Rejection episodes or to lead to transplant patients with Donor Specific Antibodies (DSA).

In our experience, 4 patients were treated with photopheresis with excellent tolerability, no adverse events, and no rejection episodes. Photopheresis was added on top of standard immunosuppressive therapy in patients requiring minimization of calcineurins due to other clinical conditions. 19 patients experiencing humoral rejection were treated alternatively with Plasma Exchange (8 patients) or with immunoadsorption. Plasma Exchange was preferred in acute patients requiring removal of inflammatory factors other than antibodies whileImmunoabsorptionn was better tolerated and adopted to reduce the metabolic impact and coagulative disorders when the patient was more stable.

Apheretic Medicine has opened a new door and represents an efficient weapon in the armamentarium of an HTx center. The complexity of the management of this new diseased in frail patients highlights the need for a multidisciplinary group establishing the right treatment for every patient.

OS099 OUTCOMES OF EVEROLIMUS AFTER HEART TRANSPLANTATION

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Purpose: To estimate the outcomes of patients managed with everolimus (EVL) after heart transplantation (HTx).
Materials and methods: From 2010 to 2018 it was performed 112 HTx (47 ± 14 yrs-old, $n = 82$ – male). Patients were managed with triple-drug therapy (tacrolimus (TAC), mycophenolate mofetil (MMF), steroids) plus induction (basiliximab – 82%; thymoglobulin – 18%). We retrospectively estimated outcomes of EVL treated patients.
Results: From 1 month to 6 years after HTx immunosuppressive regimen was changed to concentration-controlled EVL (initial dose 1.5 mg/day, C0 target 3-8 ng/ml) and reduced-exposure TAC in 29% ($n = 32$) of patients (49.9 ± 13.4 yrs-old; $n = 21$ - male). There was no *de novo* use of EVL following HTx. Indications for EVL treatment were as follows: chronic kidney disease (CKD; $n = 19$), cardiac allograft vasculopathy (CAV; $n = 8$), oncology ($n = 6$: 1 – lung cancer, 1 – basal cell carcinoma, 4 – colorectal polyps), severe leucopenia ($n = 3$) and clinically significant tremor ($n = 2$). EVL was discontinued in 7 patients from 3 to 6 months after conversion due to infectious complications ($n = 3$: 2 - pneumonia, 1 - acute cholecystitis with subhepatic abscess), interstitial pneumonitis (IP; $n = 3$: 2 – one month after initiated treatment), steroid-resistant and recurrent rejection ($n = 2$). IP was successfully managed with 1-3 months steroid treatment. There was no difference in a frequency of rejection between patients on TAC+MMF or TAC+EVL. Three EVL treated recipients died due to VFib ($n = 1$; also associated with AKI and infectious complications), chronic rejection, CAV ($n = 1$) and lung cancer ($n = 1$).
Conclusion: One-fourth of patients were managed with EVL. Frequent indications for EVL were CKD and CAV. Concentration-controlled EVL (C0 target 3.0-6.5 ng/ml) in combination with TAC achieved good efficacy and safety, higher C0 target was associated with frequent infectious complications. Patients need to be screened for EVL adverse effects, especially during first 6 months.

OS100 CHRONIC PAIN 1-5 YEARS AFTER HEART TRANSPLANTATION

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Background: The extent to which heart recipients experience chronic bodily pain in the years after heart transplantation is a neglected field. Neither the prevalence nor consequences of chronic pain after heart transplantation have been fully explored or understood. Therefore, the aim was to present a multidimensional assessment of self-reported pain 1-5 years after heart transplantation and its relationship with transplant specific wellbeing.
Methods: This nationwide, cross-sectional cohort study is part of the Self-management after thoracic transplantation study. A total of 79 heart recipients, who were due for their annual follow-up at one ($n = 28$), two ($n = 17$), three ($n = 11$), four ($n = 17$) and five years ($n = 5$) after heart transplantation were included. We used three instruments; the Pain-O-Meter (POM), which provides information about pain intensity, sensation, location and duration and the Organ Transplant Symptom and Wellbeing Instrument (OTSWI) and the Psychological General Wellbeing Instrument. The findings were compared with a cohort of lung recipients ($n = 117$) followed during the same period and using the same instruments.
Results: The overall prevalence of pain was 57% after 1 year, 76% after 2 years, 73% after 3 years, 35% after 4 years and 50% after 5 years. Women experienced more pain than men. The three most common pain locations were feet, back and legs. Heart recipients with pain reported lower transplant specific and psychological wellbeing as well as higher symptom distress from other symptoms than pain. There was no difference in pain intensity and sensory or affective burden between heart and lung recipients (Table 1).

Domain	Heart recipients ($n = 46$)	Lung recipients (=73)	p-value
Pain O Meter-VAS-median score	7.75	7	.893
Pain O Meter-Words-median score	15	14	.309
Pain Intensity Score-median score	25.25	21	.420

Conclusion: Chronic bodily pain up to 5 years after heart transplantation reduces perceived wellbeing. Heart recipients with pain report higher symptom distress than those without pain. Heart and lung recipients suffer from chronic pain to an equal extent.

OS101 SYMPTOM PREVALENCE AND SYMPTOM DISTRESS 1-5 YEARS AFTER HEART TRANSPLANTATION

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[1]Institute of Health Sciences; [2]Thoracic Unit, Skåne University Hospital; [3]Transplant Unit at Sahlgrenska University Hospital

Background: Heart transplant recipients are expected to play an active role in their recovery process. This includes symptom-management, which is part of the concept of self-management. Experienced symptoms post-transplantation is common and possibly affecting the recipients' level of self-management. Post-transplant symptoms may vary in perceived distress. Thus, it is vital to identify both the most common and the most distressing symptoms experienced by the transplant recipient.
Materials/Methods: This is a nationwide Swedish, cross-sectional cohort study. A total of 79 adult heart recipients, who were due for their annual follow-up, 1-5 years, after heart transplantation were included. Mean age was 53 years, and 32% ($n = 25$) were female. The Organ Transplant Symptom and Well-being Instrument (OTSWI) was used for assessment of experienced symptoms. OTSWI covers 8 transplant specific domains: sleeping problems, joint and muscle pain, foot pain, fatigue, cognitive function, basic ADL, mood and economy. It also includes 20 transplant specific symptoms.

Results: The most problematic domains were sleeping problems, fatigue and joint and muscle pain while the most common symptoms were tremor, decreased libido and dyspnea. Women reported significantly more nausea (p = .003), and embarrassment with their looks (p = .033) than men, who reported increased appetite (p = .047). Heart recipients younger than 50 years (n = 30) were considerably more concerned about their economy and reported a higher symptom distress in general than those older than 50 years (n = 49). Participants treated with VAD before transplantation (n = 24), reported significantly more fatigue (p = .019) and decreased appetite (p = .019) than those without VAD treatment.
Conclusion: Heart recipients suffer from symptom distress. Tremor and decreased libido are the most prominent problems. Special attention should be paid to heart recipients younger than 50 years since their symptom burden is more profound.

OS102 HEALTH-RELATED QUALITY OF LIFE ONE YEAR AFTER HEART TRANSPLANT

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Background: The quality of life in patients in need of heart transplantation is poor and is significantly improved after heart transplantation. The aim of this study was to investigate health-related quality of life (HRQoL) in adults one year after heart transplantation.
Method/Materials: Data was collected from the one year follow-up after heart transplantation at Sahlgrenska University Hospital in Gothenburg, Sweden during 2010-2013 (n = 84). HRQoL was measured using EQ-5D-3L, a validated, widly used, standardised instrument for measuring HRQoL covering 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Variables for heart and kidney function as well as exercise test were also collected. This was analysed using descriptive statistics as well as Spearman's Rho.
Results: The results show that the overall HRQoL in patients one year after heart transplantation was fairly good, and almost half of the patients (43.8%) experienced no problems within the dimensions measured by EQ-5D. The most common complaint was experiencing moderate or severe pain or discomfort (43.7%). Women were at a higher risk of suffering from anxiety and depression (p = 0.000) and patients who performed poorly in the exercise test had a worse HRQoL (p = 0.003).
Conclusion: It is of great importance to measure and continue to measure HRQoL regularly after heart transplantation. To comprehend which variables have an impact on HRQoL is a pre-requisite in directing treatment and supporting patients to improve their HRQoL.

OS103 SPIRONOLACTONE IMPROVES EVENT-FREE SURVIVAL IN HEART TRANSPLANT RECIPIENTS: SINGLE CENTRE PROSPECTIVE STUDY

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Shumakov National Research Center of Transplantology and Artificial Organs

Objectives: To evaluate the effects of aldosterone inhibitor spironolactone in heart transplant recipients.
Patients and methods: Patients who received a heart transplant between January 2013 and April 2016 in Shumakov National Research Centre of Transplantology (Moscow) and met inclusion criteria were randomly assigned to receive spironolactone (12.5-25 mg o.d.) in a 1:4 ratio. We included patients who survived 14 days after transplantation without severe renal dysfunction or hyperkalemia. Eligible participants continued to receive conventional immunosuppressive therapy and other treatments. The primary outcome was a composite of death from any cause or retransplantation.
Results: Out of 478 heart recipients, 398 patients (mean age 45.7 ± 2.4 years, 53 females and 345 males) enrolled in the study. Eighty patients were assigned receive spironolactone, 318 included to the control group. The mean follow-up was 728.9 ± 52.7 (95% CI = 573.3-1095.0). Nine (11.3%) patients in the spironolactone group and 19 (5.9%) in the placebo group — discontinued study participation due to the development of renal failure and were not included in the outcome's analysis (intergroup comparison p = 0.09). Treatment with spironolactone was associated with increased serum creatinine and potassium levels, but no significant differences in tacrolimus levels, rejection episodes or any other surrogate indices were observed. Patients receiving spironolactone had significantly better event-free survival than the control group (log-rank p = 0.04).
Conclusion: In heart transplant recipients survived 14 day after cardiac transplantation without severe renal failure and hyperkaliemia, treatment with aldosterone inhibitor spironolactone significantly improves composite outcome.

OS104 SELF-REPORTED ADHERENCE TO IMMUNOSUPPRESSIVE DRUGS AFTER HEART TRANSPLANTATION

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Sahlgrenska University Hospital

Background: Heart transplantation (Htx), is an established treatment for terminal heart failure. Post transplantation lifelong treatment with immunosuppressive drugs is a prerequisite for graft survival. If the patient doesn't adhere to the required treatment there is a risk of serious consequences, such as acute rejection, development of donor specific anti bodies or death. Non-adherence (NA) after Htx has not previously been studied in a Swedish Htx population. Thus, our aim was to investigate the frequencies of NA one year after Htx in relation to gender and age.
Method/Materials: The study was retrospective, cross-sectional and descriptive statistics were used (frequencies and $\chi 2$), SPSS 25.0. Adults < 18 years old who were Htx during the period 2012-2016 at Sahlgrenska University Hospital in Gothenburg were included. They should have attended the one year follow-up after Htx and also responded to the self-reported adherence instrument (the BAASIS©). The BAASIS measures 4 dimensions of adherence, i.e. taking, timing (every 12 h), dosing and skipping. In total 99 persons were included to participate.
Results: The majority of the respondents were male (73/99) and the mean age at Htx was 52 years (20-70 yrs). The frequency of self-reported NA was 27% (27/99). Not taking all doses, was reported by 16 persons (59%) and 18 (67%) individuals reported not being punctual with timing. No one reported changing doses or skipping medication 24 h or more, but 5 (18%) had more than one adherence problem, i.e. taking and timing. Of those who reporting NA, 43% had had one or more rejections.
Conclusion: The frequency of nonadherence among Htx recipients is high, however similar to other studies. Therefore, it is vital to screen for NA regularly in the clinical setting. Utmost importance should be given the transplant professionals to support the heart transplanted person to adhere to the immunosuppressive medication and create individual solutions.

OS105 THE IMPACT OF EXTRACORPOREAL PHOTOPHERESIS ON CARDIAC ALLOGRAFT REJECTION AND ON LYMPHOCYTE SUBSETS

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Background: Cardiac allograft rejection and consequences of immunosuppressive therapy (IS) continue to be major limiting factors of graft and recipient survival after heart transplant. The immunomodulatory extracorporeal photopheresis (ECP) may complement standard IS. Helper and cytotoxic T cells can differentiate into regulatory cells suppressing rejection or into effector cells promoting it. Regulatory T cells are essential for terminating rejection, B lymphocytes and natural killer (NK) cells contribute to it. We aimed to investigate the anti-rejection efficacy and the effect of ECP on peripheral blood lymphocyte subsets in adult heart transplant recipients.
Methods: 12 patients treated with ECP were included in our single-centre retrospective study (2013-2019). We evaluated the grade of rejection in endomyocardial biopsies (EMB) and we analysed the distribution of helper, cytotoxic and regulatory T cells, B lymphocytes and NK cells with fluorescence activated cell sorting both before and after the ECP treatment course. Data values were given as mean ± standard deviation or median[min-max].
Results: Patients underwent 26[2-39] ECP treatments beside standard IS. The average grade of cellular rejection improved significantly post ECP therapy (ISHLT grade 1.25 ± 0.45 vs. 0.50 ± 0.53; p = 0.022). The percentage of helper and cytotoxic T cells increased significantly (3.43% ± 2.24% vs. 5.98% ± 3.64%; p = 0.017 and 2.33% ± 1.46% vs. 4.16 ± 2.98%; p = 0.027). The rise in regulatory T cell percentage approached near significance (0.20% ± 0.22% vs. 0.37% ± 0.20%; p = 0.060). Neither B lymphocyte nor NK cell counts showed any significant changes.
Conclusion: ECP was effective in preventing cardiac allograft rejection. The significant reduction in rejection rates might indicate that ECP promotes the predominance of anti-inflammatory helper and cytotoxic T cell subpopulations and the propagation of regulatory T cells. Though, small sample size and effect of IS on lymphocytes may present limitations.

OS106 HEART TRANSPLANTATION

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[1]La Pitié Salpêtrière Hospital; [2]Paris Transplant Group; [3]Saint Louis Hospital; [4]Pitié Salpêtrière; [5]HEGP

Background: Heart allograft monitoring is based on iterative protocolar endomyocardial biopsies (EMB). The individualization of the monitoring is an unmet clinical need. Our aim was to analyze the incidence of rejection and to determine the risk factors for biopsy-proven rejections following heart transplantation (HTx) in a large cohort of highly phenotyped HTx recipients.
Methods: We performed a retrospective, observational study in 2 French referral centers enrolling patients transplanted from 2004 to 2016. We included all patients with at least 1 EMB. All EMB performed before 2012 were retrospectively reviewed and graded according to ISHLT guidelines. Rejections were defined as cellular rejection ≥ 1R1B and/or pAMR ≥ 1. Patients underwent an extensive evaluation comprising clinical, biological, histological and immunological parameters. Risk factors for rejection were identified using Cox proportional hazard model.
Results: A total of 1,053 patients were included. 13,677 EMB were performed during the first-year post-transplant. Almost one-third of patients were transplanted with pre-formed anti-HLA donor-specific antibodies (DSA, $n = 324$; 31.1%). Biopsy-proven rejections were diagnosed in 489 patients (46.4%) representing 1,009 EMB (7.3%, mostly low-grade rejections: 1R1B or 1R2: $n = 724$). Risk factors for rejection included recipient's age (HR = 0.988 per 1-year increment, $p = 0.002$), type of transplantation (combined compared to isolated HTx: HR = 0.27, $p < 0.001$), pre-formed DSA (HR = 1.42, $p < 0.001$), HLA A-B-DR mismatches (HR = 1.13 per 1-mismatch increment, $p = 0.02$) and the type of induction (basiliximab compared to ATG: HR = 1.72, $p = 0.01$). Sensitivity analyses were performed in patients alive ≥ 6 months post-transplant and found similar results.
Conclusion: Recipient age, type of transplantation, pre-formed DSA, number of HLA A-B-DR mismatches and the type of induction therapy were significantly associated with the risk of allograft rejection.

OS107

HEART TRANSPLANT RECIPIENTS WITH CARDIAC ALLOGRAFT VASCULOPATHY HAVE INCREASED PLATELET AGGREGATION BEFORE AND AFTER LOW-DOSE ASPIRIN THERAPY

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Background: Long-term survival after heart transplantation (HTx) is reduced mainly due to coronary allograft vasculopathy (CAV). Using optical coherence tomography, we have recently shown that layered fibrotic plaques resembling organized clots are the dominant plaque component in CAV. Thus, thrombosis is suggested as a possible mechanism to development and progression of CAV. There is no guideline recommended treatment. Aspirin is widely used but the antiplatelet effect of aspirin has not been thoroughly examined in HTx-patients.
Aim: To investigate baseline platelet aggregation and the antiplatelet effect of aspirin in HTx-patients with and without CAV.
Methods: We included 68 HTx-patients (median 8.6 years from HTx). In 66 patients taking 75 mg aspirin for a minimum of 7 days, platelet aggregation was measured using impedance aggregometry with adenosine diphosphate (ADP) and arachidonic acid (AA) as agonists. Baseline platelet aggregation was measured in 59 patients as it was not considered clinically safe to interrupt ongoing aspirin treatment for one week prior to blood sampling in 9 patients. CAV burden was determined by coronary angiography and echocardiography based on international classification. Patients were divided into two groups; no CAV ($n = 37$) and CAV ($n = 29$).
Results: We found significantly increased ADP-induced platelet aggregation at baseline in patients with CAV vs. no CAV. AA-induced aggregation was also higher in patients with CAV vs. no CAV, though non-significant. Even though aspirin reduced AA-induced platelet aggregation in both groups, patients with CAV had significantly increased AA-induced platelet aggregation compared with patients without CAV on aspirin treatment (Figure 1).
Conclusion: HTx-patients with CAV have increased platelet aggregation before and after aspirin treatment compared with HTx-patients without CAV. Aspirin monotherapy may not provide sufficient platelet inhibition in HTx-patients with CAV.

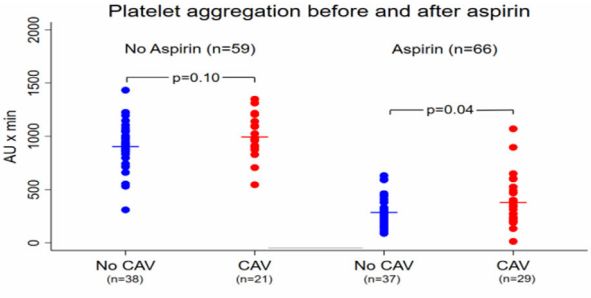

Fig. 1. Arachidonic acid-induced platelet aggregation before aspirin therapy and after a minimum of 7 days of aspirin therapy in heart transplant recipients with and without cardiac allograft vasculopathy (CAV).

OS13 - KIDNEY REJECTION AND HISTOLOGY: GRAFT HISTOLOGY AND OUTCOME AFTER KIDNEY TRANSPLANTATION

OS108

AN INTEGRATIVE APPROACH FOR THE ASSESSMENT OF PERITUBULAR CAPILLARITIS EXTENT AND SCORE IN LOW GRADE MICROVASCULAR INFLAMMATION-ASSOCIATIONS WITH TRANSPLANT GLOMERULOPATHY AND GRAFT LOSS

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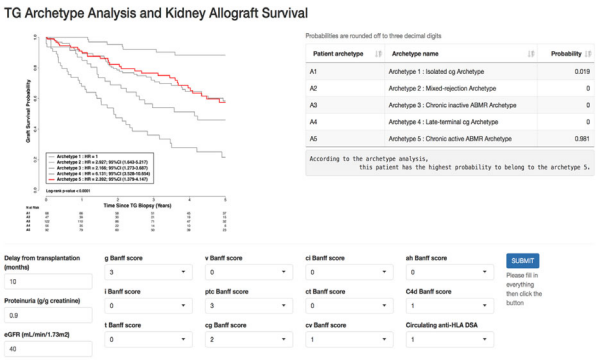
Background: Peritubular capillaritis (ptc), reported by the ptc score, is a major feature of kidney allograft rejection and microvascular inflammation (MVI). MVI sum scores (ptc+g ≥ 2) are accepted diagnostic surrogates of HLA antibody-antigen interaction. Low-grade microvascular inflammation is however frequent and ptc scores (number of leukocytes/capillary) may not mirror all aspects of ptc morphology. More recently we observed a highly significant relationship of diffuse extent of ptc (inflammation of > 50% the renal cortex) with graft loss and significantly higher DSA levels suggesting a potential of diffuse ptc as an additional surrogate of current HLA antibody interaction.
Methods: We sought to assess how a combination of ptc score and extent in low-grade inflammation (ptc 1) affects TG and graft loss risk. We included 616 patients (Tx 1999-2006) with adequate material for interpretation of MVI and C4d staining in their first indication biopsy. Cases with ptc score 1 but diffuse extent ($ptc1_{diffuse}$, g-score = 0, $n = 26$) were considered additional surrogates of HLA antibody-antigen interaction. Outcomes measured were prediction of any TG in all indication biopsies ($n = 1619$) and death-censored graft loss until 01.01.2017.
Results: Ptc was diagnosed in 26% of the biopsies (ptc scores 1, 2 and 3 were present in 12%, 12% and 2%, respectively) and MVI ≥ 2 in 19%. $Ptc1_{diffuse}$ and MVI score ≥ 2 subjects had worse graft survival (42% and 59%) compared to MVI score < 2 (70%), $p = 0.002$. The incorporation of $ptc1_{diffuse}$ to the MVI score ≥ 2 increased the ROC curve for TG [AUC: 0.602, $p = 0.008$] compared to the Banff MVI score ≥ 2 [AUC: 0.56, $p = 0.12$]; cases with baseline TG were excluded. In multivariate analysis $ptc1_{diffuse}$ remained independently related to TG (OR 3.89, $p = 0.008$) and graft loss (HR 2.64, $p = 0.001$) even after inclusion of all rejection episodes.
Conclusions: An integrated view of ptc morphology including diffuse ptc in MVI is superior for TG and graft loss risk assessment.

OS109

ARCHETYPE ANALYSIS IDENTIFIES DISTINCT PROFILES IN RENAL TRANSPLANT RECIPIENTS WITH TRANSPLANT GLOMERULOPATHY ASSOCIATED WITH ALLOGRAFT SURVIVAL

Olivier Aubert[1], Sarah Higgins[1], Yassine Bouatou[1], Daniel Yoo[1], Marc Raynaud[1], Denis Viglietti[1], Marion Rabant[1], Luis Hidalgo[2], Denis Glotz[3], Christophe Legendre[4], Michel Delahousse[5], Nikhil Shah[6], Banu Sis[2], Patricia Campbell[2], Michael Mengel[2], Jean-Paul Duong[1], Carmen Lefaucheur[1], Alexandre Loupy[1]
[1]Paris Translational Center for Organ Transplantation; [2]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton; [3]Saint Louis Hospital; [4]Necker Hospital; [5]Foch Hospital; [6]epartment of Medicine, Division of Nephrology and Transplant Immunology, University of Alberta, Edmonton

Background: Transplant glomerulopathy (TG) is a common glomerular lesion observed after kidney transplantation associated with bad prognosis. However, TG is not a specific entity but rather the end-stage of overlapping disease pathways. The heterogeneity of TG has not been precisely characterized to date.
Methods: Consecutive kidney transplant recipients from 3 Paris centers Necker, Saint-Louis and Foch hospitals and 1 center in Edmonton, Alberta presenting with a diagnosis of TG (Banff cg score ≥ 1 by light microscopy) in biopsies performed between January 2004 and January 2014 were included. Comprehensive pathology, clinical, immunological, and outcome data were used in unsupervised archetype analysis.
Results: Among the 8,207 post-transplant allograft biopsies performed during the inclusion period, 552 presented with TG (incidence of 6.7%). The median time to TG diagnosis post-transplant was 33.18 months (IQR: 12.12 – 78.72 months). Kidney allograft survival rates after TG diagnosis were 69.4%, 57.1%, 43.3% and 25.5% at 3, 5, 7 and 10 years, respectively. An unsupervised learning method integrating clinical, functional, immunological and histological parameters revealed 5 TG archetypes characterized by distinct functional, immunological, and histological features and associated etiologies. The 5 TG archetypes displayed distinct allograft survival profiles with incremental graft loss rates between archetypes, ranging from 88% to 22% allograft survival rates 5 years after TG diagnosis ($p < 0.0001$). Based on those results, we built an online application, which can be used in clinical practice (Figure).



Conclusions: A probabilistic data-driven archetypical approach applied in a large well-defined multicentric cohort refines the diagnostic and prognostic features associated with TG. Reducing heterogeneity among TG cases can improve disease characterization, enable patient-specific risk stratification, and open new avenues for archetype-based treatment strategies in TG.

OS110 PREDICTORS OF GRAFT SURVIVAL AT DIAGNOSIS OF ANTIBODY-MEDIATED RENAL ALLOGRAFT REJECTION

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Background: Antibody-mediated rejection (ABMR) is a major cause of premature graft loss in renal transplantation. We assessed the predictive value of clinical, pathological and immunological parameters at ABMR diagnosis for graft survival in a retrospective cohort study.
Methods: We investigated 54 consecutive patients with biopsy-proven ABMR. Patients were treated according to our current standard regimen followed by triple maintenance immunosuppression. Patient characteristics, renal function and HLA antibody status at diagnosis, baseline biopsy results and immunosuppressive treatment were recorded. The risk of graft loss at 24 months after diagnosis and the eGFR slope were assessed.
Results: Multivariate analysis showed that eGFR at diagnosis and chronic glomerulopathy independently predict graft loss (HR 0.94; 95%CI 0.89; 0.98; p = 0.018 and HR 1.57; 95%CI 1.01; 2.58; p = 0.045, respectively) and eGFR slope (beta 0.46; 95%CI 0.22; 0.69; p < 0.001 and beta -5.47; 95%CI -8.44; -2.51; p < 0.001, respectively). Cyclophosphamide treatment (6x15 mg/m2) plus high-dose intravenous immunoglobulins (IVIG) (1.5 g/kg) was superior compared to single-dose rituximab (1x500 mg) plus low-dose IVIG (30 g) (HR 0.10; 95%CI 0.02; 0.54; p = 0.008 and beta 10.70; 95%CI 1.95; 19.45; p = 0.017, respectively) and one cycle of bortezomib (4x1.3 mg/m2) plus low-dose IVIG (30 g) (HR 0.16; 95%CI 0.02; 0.99; p = 0.049 and beta 11.21; 95% CI 2.73; 19.69; p = 0.010, respectively) regarding graft loss and eGFR slope.
Conclusions: Renal function at diagnosis and histopathological signs of chronic ABMR predict graft survival independent of the applied treatment regimen. Stepwise modifications of treatment including the implementation of cyclophosphamide treatment seem to improve outcome. Prospective studies are needed to confirm our results and to define an effective standard of care.

OS111 C5B9 DEPOSITION IN GLOMERULAR CAPILLARIES IS ASSOCIATED WITH POOR KIDNEY ALLOGRAFT SURVIVAL IN ANTIBODY-MEDIATED REJECTION

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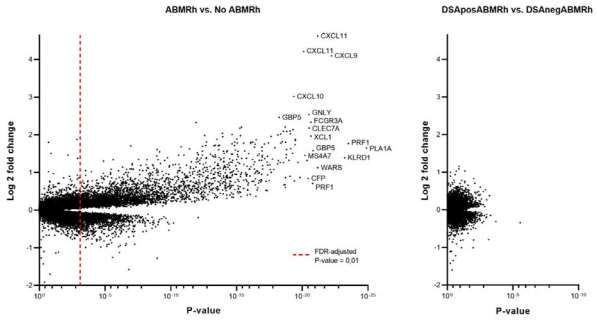
Background: C4d deposition in peritubular capillaries (PTC) reflects complement activation in antibody-mediated rejection (ABMR) of kidney allograft. However, its association with allograft survival is controversial. We hypothesized that capillary deposition of C5b9 — indicative of complement-mediated injury — is a severity marker of ABMR. This study aimed to determine the frequency, location and prognostic impact of these deposits in ABMR.
Methods/Materials: We retrospectively selected patients diagnosed with ABMR in two French transplantation centers from January 2005 to December 2014 and performed C4d and C5b9 staining by immunohistochemistry.
Results: Fifty-four patients were included. Median follow-up was 52.5 (34.25–73.5) months. Thirteen patients (24%) had C5b9 deposits along glomerular capillaries (GC). Among these, seven (54%) had a global and diffuse staining pattern. Twelve of the C5b9 + patients also had deposition of C4d in GC and PTC. C4d deposits along GC and PTC were not associated with death-censored allograft survival (p = 0.42 and 0.69, respectively). However, death-censored allograft survival was significantly lower in patients with global and diffuse deposition of C5b9 in GC than those with a segmental pattern or no deposition (median survival after ABMR diagnosis, 6 months, 40.5 months and 44 months, respectively; p = 0.015; Figure 1). Double contour of glomerular basement membrane was diagnosed earlier after transplantation in C5b9 + ABMR than in C5b9– ABMR (median time after transplantation, 28 vs. 85 months; p = 0.058).
Conclusion: We identified a new pattern of C5b9 + ABMR, associated with early onset of glomerular basement membrane duplication and poor allograft survival. Complement inhibitors might be a therapeutic option for this subgroup of patients.

OS112 RENAL ALLOGRAFT HISTOLOGY OF ABMR WITHOUT ANTI-HLA DSA: SIMILAR HISTOLOGY AND TRANSCRIPTOMICS, BUT DIFFERENT OUTCOMES

Jasper Callemeyn[1], Aleksandar Senev[1], Evelyne Lerut[2], Maarten Coemans[1], Dirk Kuypers[1], Wilfried Gwinner[3], Marie Essig[4], Dany Anglicheau[5], Pierre Marquet[6], Maarten Naesens[1]

[1]Department of Microbiology and Immunology, KU Leuven; [2]Department of Imaging and Pathology, KU Leuven; [3]Department of Nephrology, Hannover Medical School; [4]Department of Nephrology, Dialysis and Transplantation, University of Limoges; [5]Necker-Enfants Malades Institute, French National Institute of Health and Medical Research U1151; [6]U850 INSERM, University of Limoges

Background: Despite increased sensitivity of detection techniques, anti-HLA donor-specific antibodies (DSA) are often not detectable in serum of renal allograft recipients with biopsies demonstrating histology of antibody-mediated rejection (ABMRh). C4d deposition was added in the 2017 Banff revision as an alternative third diagnostic criterion for ABMR. However, it remains unclear whether DSA negative ABMRh represents a distinct clinical and molecular phenotype.
Methods: We performed microarray analysis of 224 biopsies collected in a multicenter study. ABMRh was termed for biopsies fulfilling the first two Banff criteria. Differentially expressed genes were analyzed with Ingenuity Pathway Analysis (IPA). CIBERSORT deconvolution with CD45 adjustment was used to estimate leukocyte infiltration.
Results: ABMRh was identified in 52/224 biopsies (23.2%), in 24/52 cases (46.2%) without detectable DSA. ABMRh biopsies had upregulation of 3860 probesets compared to other biopsies. After stratification for DSA and C4d positivity, no probesets were different between ABMRh subgroups (Figure). IPA showed similar activation of pathways in DSAposABMRh compared to DSAnegABMRh. In comparison to TCMR and borderline biopsies (N = 24), only natural killer (NK) cells were more abundant in DSAposABMRh and DSAnegABMRh (P = 0.029 and P = 0.029). DSA and high NK cell load were independently associated with graft failure (HR 2.28 [95% CI 1.11-4.66] and HR 3.26 [95% CI 1.39-7.68]).
Conclusion: ABMRh represents a robust transcriptomic profile that is not influenced by DSA or C4d deposition. NK cell infiltration discriminates DSA positive and DSA negative ABMRh from TCMR and borderline rejection. Despite transcriptional homogeneity, allograft survival in ABMRh is independently determined by DSA and NK cell load. Investigation into DSA-independent causes of NK cell activation after renal transplantation is necessary.



OS113 PROTOCOL BIOPSIES IN PATIENTS WITH SUBCLINICAL DE NOVO DSA AFTER KIDNEY TRANSPLANTATION

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Background: De novo DSA are associated with antibody-mediated rejection (ABMR) and allograft loss. This retrospective multicentric study (9 french kidney transplant units of the Spiesser Group) included patients with a de novo DSA (One Lambda, MFI > 1000) without graft dysfunction and biopsied for DSA apparition. Clinical, biological and histological characteristics of the patients were studied.
Methods: 123 patients (85M/38F; mean age: 49,5 ± 13,1 years old) were biopsied 3.7 months (median) after the occurrence of a de novo DSA and after 65.3 months (median) after kidney transplantation. Graft function was stable at least in the last 3 months before biopsy (eGFR: 55,3 ± 18,9 ml/min/1,73 m²).
Results: Fifty one subclinical ABMR (41.4%) were diagnosed in which 32 active sABMR (26%), 19 chronic sABMR (15.5%) and 72 biopsy with no ABMR (58,5%). Predictive factors associated with the diagnosis of active sABMR was MFI of iDSA > 4000, MFI of sDSA > 6300, age of the recipients < 45 y and the absence of steroids on the day of the biopsy. For the diagnosis of chronic sABMR, the presence of a proteinuria > 200 mg / g of creatininuria on the day of the biopsy was predictive. The decrease of eGFR at 5 years post biopsy and was significatively higher in patients with acute sABMR (- 25,2 ± 28,3 mL/min/1.73 m²) and graft survival significatively lower. Specific therapy for acute sABMR could help to preserve graft function in order to extend the lifetime of the kidney graft, especially in C4d positive active sABMR. For those without sABMR lesions, a close monitoring have to be realized, especially when, even stable, eGFR is lower (eGFR < 45 mL/min/1,73 m2: HR = 8,38; p = 0,0057) at time of dnDSA detection.
Conclusion: Performing a kidney graft biopsy for the occurrence of de novo DSA without renal dysfunction lead to the diagnosis of a subclinical ABMR process in up to 40%. This screening, guided by antibodies intensity, might allow the clinicians to initiate a specific treatment early before the organ dysfunction.

OS114 RISK PHENOTYPES OF EARLY BORDERLINE CHANGES IN KIDNEY ALLOGRAFTS

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Introduction: Borderline changes (BL) represent a frequent histological finding in kidney allograft with unclear prognosis.
Methods: In this single center, retrospective, observational study, the Early BL.
Results: Progression of BL into TCMR significantly increased the risk of graft failure during 5 year posttransplant (HR 6.8, 95% CI: 3.1-14.5; p < 0.001). Multivariate regression analysis identified delayed graft function (DGF, HR = 1.96, 95% CI: 1.1-3.4; p = 0.019), higher tubulitis (HR = 1.8, 95% CI: 1.3-2.6; p = 0.001) and vascular fibrosis intimal thickening (cv) scores (HR = 1.5, 95% CI: 1.1-2.1; p = 0.009) as significant variables for progression into TCMR. Those patients had higher intragraft expression of transcripts associated with immune and inflammation processes (GO terms: leukocyte migration in inflammatory response (p = 0.03), antigen processing and presentation via MHC class (p = 0.048), lymphocyte, monocyte and neutrophil chemotaxis (p = 0.003, p = 0.041 and p < 0.0001, respectively). RT-qPCR validation confirmed higher expression of chemokine *CXCL2* (p = 0.01) in biopsies in patients with later progression to TCMR.
Conclusion: Early borderline changes in kidney allografts represents heterogenous diagnosis with different patients' outcomes. Besides clinical (DGF) and morphological (Banff' t and cv scores) predictive factors, higher intragraft inflammatory molecular profile identified patients at risk for TCMR progression.

OS115 INTIMAL ARTERITIS IN ASSOCIATION WITH MICROVASCULAR INFLAMMATION LEADS TO INFERIOR GRAFT SURVIVAL REGARDLESS DSA

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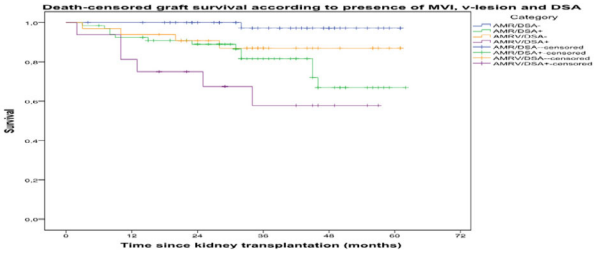
Background: Antibody-mediated rejection (AMR) is a major obstacle for long-term kidney graft survival. DSA-negative AMR phenotype represents diagnostic challenge with unclear outcome.
Materials and Methods: We retrospectively assessed 881 patients transplanted between Jan 2014 and Dec 2017 in order to evaluate outcome of distinct features of AMR. We found microvascular inflammation (MVI) and DSA positivity in 67 patients (category AMR/DSA+, N = 67), MVI and intimal arteritis (V) and DSA positivity was found in 16 (AMRV/DSA+, N = 16), MVI in absence of DSA occurred in 53 (AMR/DSA-, N = 53) and MVI and intimal arteritis in absence of DSA was observed in 33 patients (AMRV/DSA-, N = 33).
Results: Kaplan-Meier estimate of death-censored graft survival at 12 months was 100% in AMR/DSA-, 91% in AMR/DSA+, 87% in AMRV/DSA- and only 58% in AMRV/DSA + . Mean graft survival time was 60 months (95% CI, 59-62) in AMR/DSA-, 52 months (95% CI, 47-57) in AMR/DSA+, 55 months (95% CI, 50-61) in AMRV/DSA- and 40 months (95% CI, 30-51) in AMRV/DSA+, Log Rank = 0.001 (Fig. 1).

Mean transplant glomerulopathy-free survival (TG-free) was 50 months (95% CI, 45-56), 40 months (95% CI, 34-47), 42 months (95% CI, 33-50) and 21 months (95% CI, 11-32) in AMR/DSA-, AMR/DSA+, AMRV/DSA- and AMRV/DSA+ respectively, Log Rank = 0.0003.
Conclusion: Microvascular inflammation without DSA represents a benign AMR phenotype. Interestingly, intimal arteritis along with microvascular inflammation are associated with worse prognosis even in the absence of DSA.



OS14 - MACHINE PERFUSION IN LIVER TRANSPLANT

OS116 HYPOTHERMIC OXYGENATED MACHINE PERFUSION REDUCES HOSPITAL COMPREHENSIVE COMPLICATION INDEX AND IMPROVES GRAFT SURVIVAL IN LIVER TRANSPLANTATION WITH DONORS AFTER BRAIN DEATH

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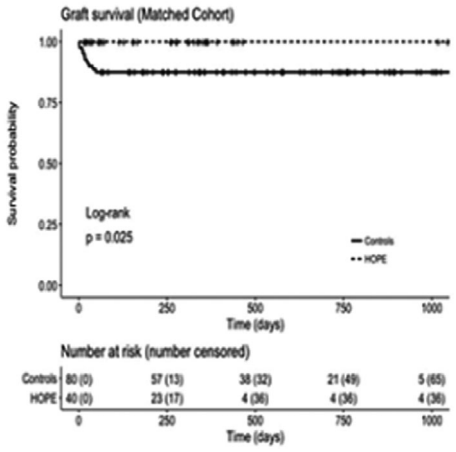
Background: Clinical benefit of hypothermic oxygenated machine perfusion (HOPE) has been shown in liver transplantation (LT) with donors after circulatory death, whereas its value is less clear when donors after brain death are used.
Methods: Retrospective analysis of prospectively collected data in the period March 2016-February 2019. Dual end-ischemic HOPE was employed on a case-per-case basis according to donor age and history, graft steatosis, and LT logistics. Early and long-term LT outcomes were evaluated. To overcome differences due to selection bias, 1:2 propensity score (PS) matching was used.
Results: 40 out of 358 adult recipients of primary single LT were treated with HOPE for a median (IQR) time of 180 (139-201) minutes during recipient hepatectomy. In HOPE group donors were older (74.8 vs 62.3 years; p < 0.001), rate of macrosteatosis > 15% was higher (25% vs 12.5%; p = 0.05), as well as D-MELD (1075 vs 842;p < 0.001) and donor risk index (2.15 vs 1.82;p < 0.001). These variables were used to calculate PS. HOPE reduced AST peak in recipients of grafts from donors older that 75 years (767 vs 1354;p = 00.9). In the matched cohort, HOPE reduced postoperative complications quantified using comprehensive complication index (32.2 vs 24.1;p = 0.03) and the rate of severe post-reperfusion syndrome (17.5% vs



0%;p = 0.01), and was associated with improved 1-year graft survival (100% vs 87.5%;p = 0.02; Figure).
Conclusion: While awaiting results of ongoing trials, this preliminary experience evidences that selective use of HOPE is associated with improved clinical outcome also in the setting of DBD LT.

OS117 INTRODUCTION OF NORMOTHERMIC MACHINE PERFUSION IN CLINICAL ROUTINE: A SINGLE CENTER EXPERIENCE

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Introduction: Normothermic machine perfusion (NMP) of donor livers has been successfully applied in clinical studies and has been shown to be safe. However, establishing a NMP-program in clinical routine has not been described so far. We herein present our experiences in order to help other centers in implementing NMP and to overcome encountered hurdles.
Methods: On 01.02.2018 an NMP program for livers was started at the Medical University of Innsbruck. Initially training as well as management was strictly reserved to perfusionists and the transplant surgeons. However in order to ensure a 24/7 coverage next steps were involment of transplant coordinators, anaesthesiological team, nursery, blood bank as well as laboratory staff. Specific technical as well as theoretical training sessions took place with the different involved disciplines after single key tasks were collectively set up. Additionally an SOP for set-up as well as handling of NMP was constituted with special attention to key problems observed in the initial cases. Furthermore, a specific perfusion protocol including donor specific key parameters as well as time-points for lab value-sampling was composed to optimally monitor and track the perfusion process as well as to evaluate organ quality. Alltogether we applied NMP in 23 cases without any organ loss. 18 livers were successfully transplanted and 5 discarded due to poor organ quality.
Conclusion: In order to successfully start a NMP-program in clinical routine, involvement of different disciplines is absolutely necessary in order to ensure a frictionless 24/7 coverage and enhance the benefit for patients in need for liver transplantation.

OS118 LIVER TRANSPLANTATION IN NORWAY WITH NORMOTHERMIC REGIONAL PERFUSION CDCD GRAFTS

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Background: In order to meet the increasing demand for donor organs, the concept of donation after circulatory death (DCD) was introduced in Norway. We here report the current Norwegian experience with liver transplantation utilizing DCD donors.
Methods: The donation process followed the Norwegian protocol for controlled DCD (cDCD). After acceptance from next of kin, life support was withdrawn and cardiac arrest observed. After a five minute "no-touch" period, extracorporeal membrane oxygenation for post mortem regional normothermic regional perfusion (NRP) by an ECMO circuit was established. Data from all liver transplant recipients receiving cDCD livers in Oslo were analyzed.
Results: From November 2015 to May 2017, 8 patients underwent liver transplantation with donor livers procured by cDCD in Norway. The indications for liver transplantation in the 7 patients were: 1) Steatohepatitis, 2) HCV, 3) PSC, 4) Post resection liver failure after resection for HCC, 5) Re-transplantation after graft failure of an ABO incompatible graft in an acute on chronic patient,6) Non-resectable colorectal metastases, and 7) NASH with HCC and 8) Cryptogen possible AIH. Median MELD was 26, (range 6-40).
Median observational time is 26 months (16-40 months) All patients are alive, there were no cases of delayed graft function or graft loss. No patients has ischemic type biliary lesions associated with cDCD. There was one instance of HAS at the anstomosis, which was managed with endovascular technique. All in all there were 1 patient with Clavien Dindo Grade IIIb, 1 patient with grade IVa (dialysis after liver transplantation). Two patients have recurrence of primary disease. All patients had normalized liver function at last follow-up.
Conclusion: The results after liver transplantation using NRP cDCD liver are excellent. The rate of complications seems to be within the same range as when using conventional DBD grafts without an apparent increase in ischemic cholangiopathy.

OS119 REAL-TIME HEPATIC METABOLISM ASSESSMENT DURING NORMOTHERMIC MACHINE PERFUSION OF EXTENDED CRITERIA DONOR LIVERS: MARKER FOR GRAFT QUALITY?

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Erasmus MC

Background: The persistent organ shortage has resulted in a higher utilization of extended criteria donor (ECD) livers to reduce mortality on the waiting list. Nonetheless these grafts are under-utilized for potential safety issues, especially in donation after circulatory death. To effectively increase the donor pool an objective assessment of ECD livers, focusing on residual graft function rather than graft injury, should be implemented. So far, no reliable liver function test is available to use during normothermic machine perfusion (NMP) of the liver. The maximum liver function capacity (LiMAx) test is a clinical cytochromal breath test based on 13C-methacetin metabolism. The aim of this study is to investigate whether the LiMAx-test can be used to measure liver metabolism during NMP of ECD grafts.
Method: Nine donor livers, declined from transplantation, were perfused for 4 hours using NMP. After one hour of stabilization, LiMAx-testing was performed. LiMAx-signal was obtained from the membrane oxygenator of the NMP device. In addition, lactate, ALT, AST and hepatocyte-derived microRNA (miR-122) were measured to relate these parameters to LiMAx-outcome.
Results: During NMP, CO2 concentrations could be measured form the air outlet of the membrane oxygenator. However, the 13C-methacetin dose needed to be adjusted to liver weight, i.e. 25% of the clinical dose.
All dose- and CO2-adjusted LiMAx-values were between 28 and 409 μg/kg/h. A significant inverse association was found between LiMAx-value and both ALT (R2 = 0.73; P = 0.003), AST (R2 = 0.52; P = 0.029) and the level of hepatocyte derived miR-122 in the perfusates (R2 = 0.76; P = 0.005). However, no association was found between LiMAx-value and lactate clearance.
Conclusion: The LiMAx-test is feasible to assess liver metabolism during NMP after adjusting the ^{13}C-methacetin dose to liver weight. LiMAx-testing could quickly identify fully functional ECD livers on NMP with good potential for transplantation.

OS120 SEQUENTIAL USE OF LOCOREGIONAL ABDOMINAL PERFUSION AND END-ISCHEMIC NORMOTHERMIC MACHINE PERFUSION IN DCD LIVER TRANSPLANTATION USING GRAFT WITH PROLONGED WIT

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Background: The Italian law requires 20 min of continuous flatline EKG to declare death for both controlled (cDCD) and uncontrolled (uDCD) deceased donors. This prolonged warm ischemia time (WIT) has prompted introduction of abdominal normothermic regional perfusion (NRP) immediately after death declaration followed by post-procurement, end-ischemic, ex-situ graft perfusion. At our institution we started a program of end-ischemic normothermic machine perfusion (NMP) for DCD liver transplantation (LT).
Methods: uDCDs suffer out-of hospital cardiac arrest, undergo cardiopulmonary resuscitation and are transferred to hospital under mechanical chest compression. NRP is started immediately after death declaration. Functional (f-WIT) is the time from cardiac arrest to start of NRP. After procurement, grafts are shipped to the transplant center and reperfused.

Results: Between January 2018 and January 2019, 15 DCDs were evaluated at our center. Based on NRP data, 7 (47%) were considered eligible for procurement (6 uDCD, 1 cDCD) and reperfused with NMP. Six LT were performed. One uDCD graft could not be transplanted due to recipient cardiac arrest at anesthesia induction. Median donor age was 48 years (range 41-62); median f-WIT 164 min (21-175); median duration of NRP 342 min (294-372), and median duration of NMP 188 min (120-360). The median lactate at end of NRP was 13 mg/dl (0.9-24) and median AST peak 290 IU/L (93-691). The median perfusate lactate at end of NMP was 1.0 (0.6-6.2) and median perfusate AST peak 1157 IU/L (604-3164). All grafts except one produced bile, and the lowest bile pH at 2 hours was 7.37. No PNF was observed. One patient was retransplanted due to portal vein graft thrombosis and died of carbapenemase-resistant E. coli infection. No biliary complications have been observed.
Conclusions: In DCD LT, a strategy of NRP coupled with NMP allows to overcome the 20 minutes no-touch rule. Strict selection criteria are necessary to achieve favorable results.

OS121 DUAL HYPOTHERMIC LIVER PERFUSION TO RECONDITION HIGH-RISK LIVER GRAFTS PRIOR TO TRANSPLANT

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Introduction: Livers for transplantation are increasingly being referred from "marginal" deceased donors including donors after circulatory death (DCD), overweight and elderly donors. These organs are invariably associated with increased reperfusion injury, post-transplant morbidity and graft loss. Early experience with hypothermic perfusion has been promising in both America and Europe.
Methods: We adapted the Hosgood/Nicholson perfusion circuit to dual perfuse livers with oxygenated UW solution prior to implantation after a period of static cold storage. Inclusion criteria for perfusion were either DCD livers or DBD livers declined by at least 1 other centre due to adverse donor factors.
Results: 16 livers were perfused and 10 livers transplanted after 2 to 3 hours of perfusion. Of the 10 transplanted livers, 7 were DCD. The median UK Donor Liver Index (DLI) was 1.71(+/-0.38). All D-HOPE liver recipients are alive with a median followup of 26 months (18-33). There has been 1 re-transplant in HOPE group, performed 11 months after transplant due to rejection. To date there have been no episodes of clinically-significant ischaemic cholangiopathy (IC) in any of the 10 HOPE patients. However, 2 patients have developed anastomotic strictures requiring ERCP and stenting. 33% of the DCD recipients in our comparator historical cohort ($n = 9$) developed clinically-significant IC requiring intervention (2 retransplants and 1 further death due to IC) compared to none of the HOPE transplanted livers to date (non-significant, $p = 0.15$). The cost of consumables for each perfusion was approximately £700 (excluding perfusate).
Discussion: We have safely implemented D-HOPE perfusion with excellent clinical outcomes in "high-risk" liver transplants. There have been no incidences of clinically significant IC after at least 1 year follow up. Our setup can cost-effectively perfuse livers for transplantation

OS122 RECIPIENTS OF DCD LIVERS FROM DONORS UNDERGOING IN SITU NORMOTHERMIC REGIONAL PERFUSION HAVE LESS ACUTE KIDNEY INJURY THAN RECIPIENTS OF STANDARD DCD LIVERS OR DCD LIVERS UNDERGOING EX SITU NORMOTHERMIC PERFUSION

James Richards[1], Rohit Guarav[2], Vasilis Kosmoliaptsis[3], Joanna Leithead[2], Andrew Butler[3], Chris Watson[4]
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Background: Acute kidney injury (AKI) is common in recipients of livers donated after circulatory death (DCD). We sought to determine whether *in situ* normothermic regional perfusion (NRP) or *ex situ* normothermic liver perfusion (NLP) modulated renal injury post liver transplant.
Methods: All DCD livers transplanted in our centre between 1/1/14 and 31/12/18 were studied. AKI was defined by the RIFLE criteria (AKI = increase of ≥ 2 fold in creatinine above baseline in first 7 days); GFR was determined using the CKD-Epi equation and reported as the percentage difference between the baseline pretransplant value and the values at 6 and 12 months.
Results: 162 DCD livers were transplanted in the study period. 41 (25%) underwent NRP and 38 (24%) underwent NLP either from the time of donation (5) or once the liver arrived at our centre (33); one underwent both NRP and NLP and was excluded from the analysis. The table summarises the demographics and results.
Conclusion: *In situ* normothermic regional perfusion, and not *ex situ* NLP, reduces acute kidney injury following DCD liver transplantation and is associated with a lower (but non-significant) fall in GFR from baseline to 6 and 12 months.

OS123 INCREASED AND SAFE UTILIZATION OF HIGH-RISK DONOR LIVERS FOR TRANSPLANTATION AFTER EX SITU RESUSCITATION AND ASSESSMENT USING SEQUENTIAL HYPO- AND NORMOTHERMIC MACHINE PERFUSION

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Background: Despite persisting organ shortages, a high number of donor livers is currently not used for transplantation. We aimed to increase the number of transplantable livers by resuscitating and assessing hepatobiliary viability of initially declined high-risk livers using a protocol of end-ischemic sequential *ex situ* hypothermic and normothermic machine perfusion.
Method: In a prospective clinical trial, all nationwide declined livers were eligible for inclusion (Netherlands Trial Registry NTR5972). The protocol consisted of one hour hypothermic oxygenated perfusion (10°C) for resuscitation, one hour of controlled oxygenated rewarming, and subsequent normothermic machine perfusion (NMP) for viability testing. A perfusion fluid containing a hemoglobin-based oxygen carrier was used for all temperature phases. During the first 150 min of NMP, hepatobiliary viability was assessed, using the following criteria: perfusate lactate < 1.7 mmol/L, pH 7.35-7.45, bile production > 10 mL and biliary pH > 7.45. Livers meeting these criteria were transplanted. Primary endpoint was safety and feasibility, as reflected by a 3-months graft survival rate of at least 80%.
Results: Between August 2017 and October 2018, 16 livers underwent machine perfusion after an average of 288 (241-480) min of static cold preservation. All livers were derived from donation after circulatory death donors, with a median age of 63 (range 42-82) years. During NMP, all livers cleared lactate and produced sufficient bile volume, but in 5 cases biliary pH remained < 7.45. The 11 (69%) livers that met all viability criteria were successfully transplanted, increasing the number of deceased donor liver transplants by 20%. Patient and with graft survival at 3 months was 100%.
Conclusion: Sequential hypo- and normothermic machine perfusion enabled resuscitation and selection of initially declined high-risk donor livers. This method offered a valuable tool to safely increase the number of transplantable livers by 20%.

Values are median and interquartile range unless indicated. Times in minutes

	Cold stored livers $n = 82$	NLP livers $n = 38$	NRP livers $n = 41$	p
Recipient UKELD	55 (53-58)	53 (50-55)	54 (51-60)	0.0386
UK Donor liver index	2.0 (1.7-2.1)	2.0 (1.7-2.3)	1.9 (1.6-2.2)	0.382
Withdrawal to perfusion time	13 (10-18)	14 (10-20)	13 (10-21)	0.850
Asystolic warm time	12 (10-14)	12 (11-13)	15 (13-17)	<0.0001
Perfusion duration		377 (283-481)	133 (110-142)	
Cold ischaemic time	439 (397-483)	390 (349-437)	376 (312-449)	<0.0001
Total preservation time	439 (397-483)	873 (759-983)	498 (441-569)	<0.0001
AKI (RIFLE criteria)	38/82 = 46%	17/38 = 45%	10/41 = 24%	0.053
Baseline GFR	100 (88-112)	96 (80-109)	91 (62-109)	0.140
% GFR fall at 6 months	33 (16-52) ($n = 74$)	33 (7-40) ($n = 26$)	20 (6-39) ($n = 36$)	0.132
% GFR fall at 12 months	31 (15-47) ($n = 73$)	31 (21-39) ($n = 23$)	23 (7-38) ($n = 29$)	0.219

OS15 - EPITOPE MATCHING AND DSA

OS124 HIGH HLA DQ EPITOPE-MISMATCH LOADS AND LOW TACROLIMUS LEVEL ARE ASSOCIATED WITH DEVELOPMENT OF DE NOVO DSA

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Maryknoll Medical Center

Introduction: HLA matching has been an essential role in the risk assessment for long-term graft outcome in kidney transplantation recipients. Recent HLA epitope matching at HLA-DR and HLA-DQ loci between donor and recipient are better predictors for the development of de novo DSAs and graft outcome. Purpose of our study is to evaluate the clinical significance of HLA class II epitope mismatch loads for the development of de novo DSA and graft outcome.
Method: We examined 178 kidney transplant recipients for the development of de novo DSAs from June 2001 to June 2018. We excluded patients whose data on HLA-DQ matching and HLA class II epitope matching were not available. A nadir FK trough level was collected over 6 months prior to de novo DSA.We compared HLA-DR/DQ epitope mismatch loads and a nadir FK level over 6 month prior to DSA occurrence for the development of de novo DSA and graft outcome.
Result: 25 of 178 stable KTRs (14.0%) had HLA class II DSAs on SAB, The median follow-up was a 90.0 $\pm$ 5.9 month. Mean HLA mismatch number was 3.5 $\pm$ 0.2. Six (3.4%) of 25 de novo HLA class II DSA had biopsy-proven CABMR. Three of 5DQ-DSA positive-patients and one of 1DR-DSA positive patient were lost graft function to CABMR. Not High DR epitope mismatch load (DR epitope mm $\geq$ 10) but High DQ epitope mismatch loads(DQ epitope mm $\geq$ 17) and the lowest FK trough level (<6 ng/ml) over 6 month prior to de novo DSA occurrence are significantly associated with the development of de novo DQ-DSA. Independent predictors of graft failure on multivariate analysis were CABMR, development of de novo DQ DSA.
Conclusion: We demonstrated high DQ-epitope mismatch loads and the lowest FK trough level over 6 month prior to DSA occurrence are significantly associated with the development of de novo DQ-DSA which subsequently lead to CABMR and graft failure. Our study needs to verify whether intensifying immunosuppression can prevent the development of de novo DSA among patients with high DQ-epitope mismatch loads

OS125 EARLY CXCR5 + PD1 + ICOS+ CIRCULATING T FOLLICULAR HELPER CELLS ARE ASSOCIATED WITH DE NOVO DONOR-SPECIFIC ANTI-HLA ANTIBODIES AFTER RENAL TRANSPLANTATION

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Background: Donor-specific anti-HLA antibodies (DSAs) are a major risk factor associated with renal allograft outcomes. As a trigger of B cell antibody production, T follicular helper cells (Tfhs) promote DSA appearance.
Methods: We measured circulating Tfh (cTfh) levels on the day of transplantation and one year after transplantation in blood from a prospective cohort of 237 renal transplantation patients without DSA during the first year post-transplantation. Total cTfh were characterized as CD4 + CD45RA-CXCR5 +, and the three following subsets of activated cTfh were analyzed: CXCR5 + PD1 +, CXCR5 + PD1 + ICOS+ and CXCR5 + PD1 + CXCR3-.
Results: Immunizing events (previous blood transfusion and/or pregnancy) and the presence of class II anti-HLA antibodies were associated with increased frequencies of activated CXCR5 + PD1 +, CXCR5 + PD1 + ICOS+ and CXCR5 + PD1 + CXCR3- cTfh subsets. By contrast, ATG-depleting induction and calcineurin inhibitor treatments decreased the total level of cTfhs, and activated cTfh subsets were increased at one year post-transplantation. In multivariate survival analysis, we reported a decrease in activated CXCR5 + PD1 + ICOS+ at one year after transplantation in the blood of DSA-free patients and a significant association with the risk of developing dnDSA after the first year ($p = 0.018$, HR = 0.39), independent of HLA mismatches ($p = 0.003$, HR = 3.79).
Conclusions: These results highlight the importance of monitoring activated Tfhs in patients early after transplantation and show that current treatments cannot provide early, efficient prevention of Tfh activation and migration. These findings indicate the need to develop innovative treatments to specifically target Tfhs to prevent DSA appearance in renal transplantation.

OS126 THE RISK OF ALLOGRAFT REJECTION ACCORDING TO HLA MISMATCH LEVEL USING THE CURRENT UK RENAL TRANSPLANT MATCHING SCHEME

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Background: The current UK renal transplant donor-recipient HLA matching scheme has been operating since 2006. Cadaver donor HLA-A, -B and –DR mismatches (mm) are ranked into 4 levels in the national matching run. Level 1 (000 mm) is the best match and Level 4 the worst match, with the algorithm weighted for better matching of broad HLA-DR and –B antigens.
Methods: We retrospectively collected data from 1,327 patients from the Royal Free Hospital who received renal transplants between 2006 - 2017, ~80% of these grafts were cadaveric donors.
Results: 14.1% of these renal grafts had one of more episodes of biopsy-proven cellular and/or vascular rejection within the first 6 months of transplantation, despite standard immunosuppression with Basiliximab induction, early steroid withdrawal, tacrolimus and mycophenolate mofetil maintenance. We have stratified the relative frequency of rejection episodes according to UK HLA match Levels 1-4 and tested for association with rejection by univariate analyses using the Chi-Square test for heterogeneity to generate Odds Ratios with 95% confidence intervals (CI). Initially a 4x2 comparison of match Levels 1-4 versus the presence or absence of rejection generated a combined Chi-Square of 8.8, $P = 0.031$ (3 degrees of freedom). Testing the relative frequency of rejection episodes in the better matched grafts (10.6% in HLA match Levels 1 and 2 combined) versus the less well matched grafts (15.9% in Levels 3 and 4 combined) generated an OR of 0.63 (95% CI = 0.44
Conclusion: Our analyses indicate a significant inverse trend between the relative frequency of rejection and better HLA matching as defined by the current UK renal transplant matching scheme, despite the use of modern immunosuppression.

OS127 THE RE-EXPOSURE TO MISMATCHED HLA IN THE ABSENCE OF PRE-FORMED DONOR-SPECIFIC ANTIBODIES IS NOT ASSOCIATED WITH WORSE ALLOGRAFT OUTCOMES IN KIDNEY RE-TRANSPLANTATION

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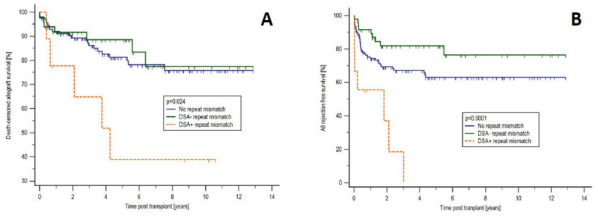
Background: Kidney re-transplantation has been linked to reduced graft survival, and re-exposure to the same HLA antigens that were mismatched with the previous graft (RMM) has been considered a risk factor for immunological memory and injury. However, reports thus far have lacked data on the impact of the presence of low level (luminex positive alone) pre-formed donor-specific antibodies (DSA) against a RMM antigen. The aim of this study was to determine whether the absence of low level DSA can help risk stratify patients receiving a RMM allograft.
Methods: We retrospectively analysed a cohort of patients who received a kidney transplant at our centre between 2005-2017. We excluded recipients of HLAi (defined by a positive cross match (XM+)), ABOi and SPK transplants, and patients where the full HLA type of the previous transplant were unknown. A, B, Cw, DR and DQ antigens were considered. All remaining patients were XM-. We divided the patients into 3 groups according to RMM and DSA status: RMM-DSA-; RMM+DSA- and RMM+DSA + .
Results: Of 1955 patients, 188 patients receiving a $\geq$ 2nd transplant were considered for the analysis, with 129(68.6%), 50(26.6%) and 9(4.8%) in the RMM-DSA-, RMM+DSA- and RMM+DSA+ groups respectively. Comparison of the baseline patient demographics showed less Black patients in the RMM-DSA- group ($p = 0.039$), who also had a better overall HLA mismatch ($p < 0.01$). All other demographics were comparable including immunotherapy regimen. As shown Figure 1, rejection free survival and death censored allograft survival was inferior in the RMM+DSA+ recipients compared with the RMM-DSA- and RMM+DSA- recipients. There was no difference in outcomes between the RMM-DSA- and RMM+DSA- recipients.
Conclusions: The exposure to a RMM is associated with inferior graft outcomes in the presence of targeted HLA antibodies detected by Luminex alone. A RMM otherwise does not confer further risk compared with re-transplants against no RMM.



OS128 THE IMPACT OF EPLET MISMATCHES ON DE NOVO DSA OCCURRENCE AND GRAFT FAILURE AFTER KIDNEY TRANSPLANTATION

Aleksandar Senev[1], Maarten Coemans[1], Vicky Van Sandt[2], Evelyne Lerut[1], Ben Sprangers[1], Dirk Kuypers[1], Marie-Paule Emonds[2], Maarten Naesens[1]
[1]KU Leuven; [2]HILA, Red Cross-Flanders

Background: Evaluating HLA eplet mismatches (MM) instead of antigen MM could theoretically enable better assessment of the donor-recipient HLA incompatibility and provide better risk assessment and outcome prediction. We aimed to evaluate the impact of the eplet MM on kidney transplant outcome and *de novo* DSA formation in a large cohort of donor-recipient pairs with full HLA genotyping at high-resolution (HR) level.
Methods: All consecutive adult kidney recipients transplanted at a single center between 2004 and 2013 were included in this study. In total, 926 transplant pairs were retrospectively genotyped at HR. HLAMatchmaker was used to determine the number of HLA eplet MM for each transplant pair.
Results: Pretransplant DSA were present in 10% of the recipients, while *de novo* DSA occurred in 5% of the patients. Univariate and multivariate analysis confirmed that the classical split HLA-A/B/DR/DQ antigen MM were significantly associated with graft failure ($p = 0.006$). The total number of eplet MM was not associated with an increased risk of graft failure. Only antibody-verified (abv) epitope MM were associated with graft failure ($p = 0.02$), which was entirely explained by DQ ($p = 0.008$). In concordance with this, abv epitope MM in Class II associated with *de novo* DSA occurrence, again fully explained by DQ. Class II abv epitope MM were significantly more predictive for *de novo* DSA occurrence than the number of Class II antigen MM, which lost its significance in multivariate analysis (*Table 1*).
Conclusion: For the first time in a European context, we demonstrate that abv epitope MM in DQ confer a significant risk for development of *de novo* DSA and graft failure after kidney transplantation, with a better prediction of *de novo* DSA formation than standard antigen MM analysis. The total number of eplet MM in the other HLA loci are not associated with DSA formation or graft outcome after transplantation.

Table 1. Multivariate hazard ratios for de novo Class II DSA occurrence in the cohort (n=926).

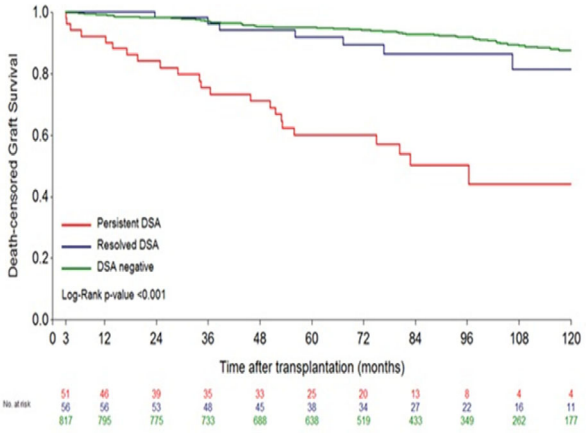
Variables	No. of patients	No. of events	HR	95% CI	*p*-value
Multivariate model-1					
Antibody-verified Class II epitope MM (0-34)	926	36	1.08	1.01 – 1.15	**0.02**
No. of HLA-DR/-DQ antigen MM (0-4)	926	36	1.38	0.83 – 2.29	0.22
Multivariate model-2					
Antibody-verified DQ epitope MM (0-17)	926	36	1.17	1.07 – 1.28	**0.0006**
No. of HLA-DQ antigen MM (0-2)	926	36	1.24	0.56 – 2.76	0.59

All multivariate models were corrected for donor and recipient gender, donor and recipient age, recipient race, recipient body mass index, donor type, cold ischemia time, repeat transplantation and presence of pretransplant HLA antibodies.

OS129 SPECIFICITY, STRENGTH AND EVOLUTION OF PRETRANSPLANT DONOR-SPECIFIC HLA ANTIBODIES DETERMINE OUTCOME AFTER KIDNEY TRANSPLANTATION

Aleksandar Senev[1], Evelyne Lerut[2], Vicky Van Sandt[3], Maarten Coemans[1], Jasper Callemeyn[1], Ben Sprangers[1], Dirk Kuypers[1], Marie-Paule Emonds[3], Maarten Naesens[1]
[1]KU Leuven; [2]UZ Leuven; [3]HILA, Red Cross-Flanders

Background: The association between the evolution of pretransplant donor-specific antibodies (preDSA) levels and outcome after kidney transplantation is currently not well known. In this cohort study (N = 924), we investigated the evolution and clinical significance of preDSA, positive with the single antigen beads assay but negative in CDC crossmatch.
Methods: The donor specificity of the preDSA (N = 107 patients) was determined by retrospective high-resolution genotyping of all donor-recipient pairs and evaluating all HLA-A/B/C/DRB1/DRB345/DQA1/DQB1/DPA1 and DPB1 loci.
Results: We found that in 52% of the patients with preDSA, the DSA spontaneously resolved within the first 3 months after transplantation, without receiving specific therapy for removal of the preDSA. PreDSA that persisted after transplantation had higher pretransplant MFI values and more specificity against HLA class II (78.5%), especially against DQ (49%). Although patients with resolved and persistent preDSA both had a high incidence (53.6% and 58.8%, respectively) of histological picture of antibody-mediated rejection ($ABMR_h$), the patients with preDSA that persisted after transplantation had worse 10-year graft survival compared to resolved preDSA and DSA-negative patients (44% vs. 81% vs. 87%, $p < .0001$) (). Compared to cases without preDSA, Cox modeling revealed an increased risk of graft failure in the patients with persistent preDSA, in the presence (HR = 8.3) but also in the absence (HR = 4.3) of $ABMR_h$. In contrast, no increased risk of graft failure was seen in patients with resolved preDSA, again independent of the presence or absence of $ABMR_h$.
Conclusion: We conclude that persistence of preDSA after transplantation has a negative impact on graft survival, beyond the diagnosis of $ABMR_h$. Even in the absence of antibody-targeting therapy, low-MFI DSA, and non-DQ DSA often disappear early after transplantation and are not deleterious for graft outcome.



OS130 COMPUTATIONAL SIMULATIONS DEMONSTRATE THE FEASIBILITY AND BENEFIT OF EPITOPE MATCHING FOR KIDNEY TRANSPLANTATION

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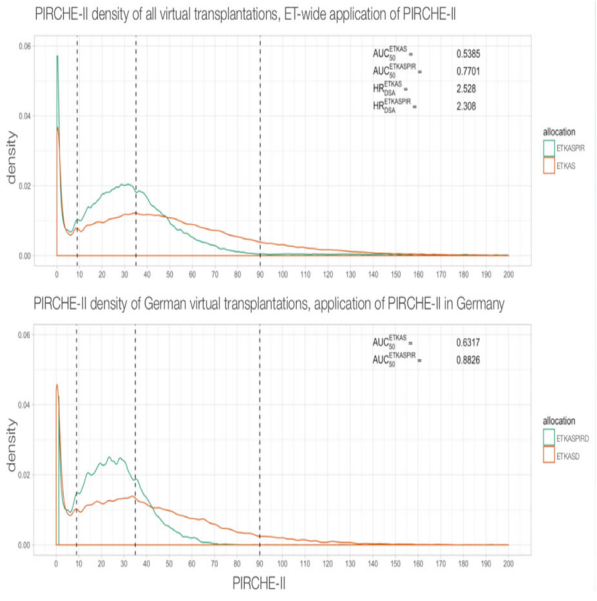
Background: The Eurotransplant (ET) Kidney Allocation System (ETKAS) aims at allocating organs to patients on the waiting list (WL) fairly whilst optimizing HLA matching. Evidently, epitope matching (EM) is biologically and clinically more reasonable. Here, we performed ETKAS-based computer simulations to evaluate the potential benefit of EM on allocation efficacy.
Method: A virtual population of European descent comprising 400,000 individuals and a WL of 10,400 patients were built and maintained during simulation matching the 2015 ET WL characteristics published in the annual report. Within 10 simulated years, 22,600 kidneys were allocated virtually. Epitope compatibility was calculated using the pirche.com algorithm. Besides comparing four EM scenarios, the impact of applying EM in all ET countries was compared to applying EM only in selected countries.
Result: The best-balanced scenario (ETKASPIR) prioritized A-B-DR fully matched donors, replaced the HLA match grade by PIRCHE-II score and exchanged the HLA mismatch probability (MMP) by an epitope MMP



polynomial. This setup showed negligible impact on kidney exchange rates and waiting time, whilst HLA match grades decreased slightly. However, considering previously reported data, the projected 10-year incidence rate of *de novo* donor-specific HLA antibodies (dnDSA) is expected to be relatively reduced by 13% in ET when EM is applied in all ET countries, and respectively by 10% / 7% in Germany / the Netherlands when EM is only applied in Germany / the Netherlands, with no further effect on other ET countries in terms of HLA matching, waiting time or transplant numbers.
Conclusion: The anticipated reduced graft loss rates may not only benefit transplanted patients but also patients on the WL while the reduced risk for dnDSA increases chances for a subsequent retransplant. We conclude that EM may lead to an improved outcome while keeping equal balances on the WL.

OS131 CLASS II HLA EPLET MISMATCH IS A RISK FACTOR FOR DE NOVO DONOR-SPECIFIC ANTIBODY DEVELOPMENT IN KIDNEY TRANSPLANTATION RECIPIENT

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Background: De novo donor-specific antigen (dnDSA) was associated with a long-term prognosis of kidney transplant recipient. Recently, HLA compatibility between a solid organ transplant recipient and donor is being defined at the epitope level thereby providing greater structural discernment than has historically been provided at the allelic level. We investigated: (1) the correlation between HLA eplet mismatches and immune status and (2) between HLA eplets mismatches and dnDSA in kidney transplant recipients.
Method: We conducted a retrospective study of 53 kidney recipients between 2012 and 2018. The HLA Matchmaker software package (version 2.1) was used to characterize epitope mismatches. To monitor alloimmune responses, multiparameter mixed lymphocyte reaction (MLR) assay, wherein the number and phenotype of alloreactive precursors are quantified by combining CFSE-labeling and FCM analyses was performed.
Result: The recipient's median age was 47 years (18-73 year), 34 recipients were males and 19 recipients were females. (1) HLA class I eplet mismatches were associated with CD4 + T cell precursor frequency (PF), CD8 + T cell mitotic index (MI) and PF ($p = 0.0467$, 0.0088 and 0.0268) determined by MLR assay. HLA II eplet mismatches were significantly associated with CD4 + T cell PF after 3 years transplantation($p = 0.0224$). Especially, DQB1 eplet mismatches and CD4 + T cell PF were significant difference ($p = 0.0049$). (2) The number of eplet mismatches were compared between those with ($n = 7$) and without ($n = 46$) de novo DSA. Class HLA I eplet mismatches showed no significant difference to dnDSA($p = 0.7820$). On the other hand, Class HLA II and DRB1 eplet mismatches were significantly associated with dnDSA development ($p = 0.0155$ and 0.0097).
Conclusion: On long-term observation, number of HLA II eplet mismatches might be affected immune status of transplant recipients. HLA II eplet mismatch is a risk factor for dnDSA in kidney transplantation recipients.

OS16 - BROKEN HEARTS AND ARTERIES: DIAGNOSIS AND PROGNOSIS

OS132 FERUMOXYTOL MR ANGIOGRAPHY: A NOVEL IMAGING TECHNIQUE FOR THE ASSESSMENT OF POTENTIAL KIDNEY TRANSPLANT RECIPIENTS

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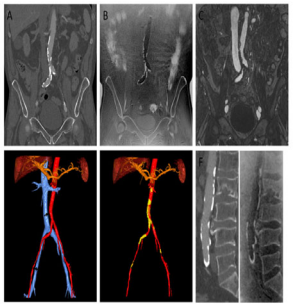
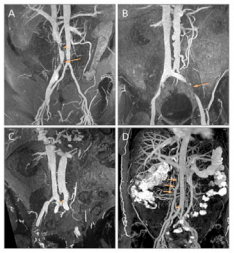
Background: Ferumoxytol, an iron oxide nanoparticle, provides an alternative to gadolinium for magnetic resonance angiography (MRA). Computed tomography angiography (CTA), the current standard technique for the evaluation of kidney transplant candidates, is limited due to concerns of nephrotoxicity. The aim of this study was to compare ferumoxytol-enhanced MRA (FeMRA) with CTA in assessment of the vasculature of kidney transplant candidates.
Methods: Thirty-six kidney transplant candidates underwent both CTA and FeMRA. Two independent readers analysed the FeMRA and a third reader the CTA. Comparisons of arterial and vein lumen diameter, calcification, and signal intensity at predefined vascular sections were performed. Interclass correlation coefficients (ICC), mean differences (with 95% CI) and Bland-Altman plots were used to examine intra- and inter-reader variability. In addition two transplant surgeons independently evaluated the scans with respect to significant findings that would impact on surgical planning.
Results: FeMRA showed excellent intra- and inter-reader repeatability (ICC 0.79-0.99). Between FeMRA and CTA there were no significant differences in arterial diameter and calcification (-0.36-0.89 mm and -0.05-0.06 mm^2, respectively) (Figure 1). Measurement of the vein diameter showed significant systematic difference (1.53-2.44 mm, $p < 0.001$) due to poor venous enhancement with CTA. Characterisation of the veins with FeMRA identified vein





abnormalities in 11% of patients (Figure 2), which influenced surgical decisions for venous anastomosis none of which were recognised with CTA. All these patients had prior intra-abdominal surgery.
Conclusions: FeMRA is comparable to CTA for the evaluation of arterial diameter and calcification with the significant advantages of a) improved venous depiction which can affect surgical decisions and b) no nephrotoxicity. These findings favor FeMRA and have the potential to improve clinical practice.

OS133 A CROSS-SECTIONAL PROSPECTIVE STUDY OF SERUM ADIPONECTIN LEVEL IS POSITIVELY ASSOCIATED WITH VASCULAR REACTIVITY INDEX IN KIDNEY TRANSPLANTATION PATIENTS

Wei-Chen Lin, Bang-Gee Hsu, Ming-Che Lee
Tzu Chi General Hospital

Introduction: Adiponectin plays an important role in CV disease through its anti-inflammatory, anti-diabetic, and anti-atherogenic properties. It is interesting to investigate a potential association between serum adiponectin levels and endothelial function among kidney transplant (KT) patients.
Methods: Fasting blood samples were obtained from 70 KT patients. The endothelial function and vascular reactivity index (VRI) were measured using digital thermal monitoring (DTM) test (VENDYS). Serum adiponectin levels were measured using a commercially available enzyme immunoassay kit. In this study, $VRI < 1.0$ was used as the poor vascular reactivity, $1.0 \leq VRI < 2.0$ was used as the intermediate vascular reactivity, and $VRI \geq 2.0$ was used as the good vascular reactivity.
Results: Ten KT patients (13.3%) were categorized as poor vascular reactivity, 25 KT patients (35.7%) were categorized as intermediate vascular reactivity, and 35 KT patients had good vascular reactivity. Increase serum alkaline phosphatase (ALP, $P = 0.026$) and lower serum adiponectin level ($P = 0.001$) was associated with poor vascular reactivity. Advanced age ($r = -0.300$, $P = 0.012$), serum ALP level ($r = -0.323$, $P = 0.006$), and serum logarithmically transformed triglyceride level (log-TG, $r = -0.317$, $P = 0.007$) were negatively, while serum adiponectin level ($r = 0.332$, $P = 0.005$) were positively correlated with VRI values. After multivariable forward stepwise linear regression analysis noted that age ($\beta = -0.267$, adjusted R2 change = 0.059; $P = 0.011$), serum ALP level ($\beta = -0.290$, adjusted R2 change = 0.106; $P = 0.006$), serum log-TG level ($\beta = -0.260$, adjusted R^2 change = 0.057; $P = 0.013$) and serum adiponectin level ($\beta = 0.308$, adjusted R^2 change = 0.097; $P = 0.004$) were significantly and independently associated with VRI values in KT patients.
Conclusion: Serum fasting adiponectin level was positively associated with VRI values and negatively associated with endothealial function among KT patients.

OS134 ULTRASOUND DOPPLER VASCULAR STUDIES AS PART OF RENAL TRANSPLANT WORK-UP: UNNECESSARY EXPENSE? OUTCOMES OF A NATIONAL SURVEY OF CONSULTANT SURGEONS

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Introduction: There is no agreed national protocol regarding iliofemoral and carotid doppler vascular studies prior to renal transplant (RTx) surgery. Work-up varies between institutions based on established local guidelines. Ultrasound doppler studies have been used to evaluate the extent of peripheral vascular disease in target anastomosis vessels at an average cost of approximately £120 (GB) per scan. This study reports outcomes of a national survey involving UK RTx consultant surgeons in the UK, and current trends.
Methods: An online survey was deployed, aiming to explore various factors influencing doppler study use, including indications, scan findings and overall efficacy in the assessment of recipient vascular disease. Opinion was sought on

doppler studies relating to duration of RRT and further alternative imaging modalities, in particular where doppler assessment was thought to be sub-optimal.
Results: Response rate was 40% ($n = 35$) representing 76% of all UK RTx centres.

15% of respondents perform carotid dopplers, estimating a cost of £20-£299. Iliofemoral dopplers are performed by 22%, estimating a cost of £20-£400. 31% of respondents felt that doppler studies were useful, with evidence of vessel stenosis being the most significant finding. A history of claudication/PVD was the modal indication (97%), followed by previous CVA/TIA (73%).16% of respondents stated they had declined recipients based on doppler study imaging, as opposed to 69% following CT within the last 12 months. 72% recommend CT angiography for patients requiring further imaging. 97% would consider surgical exploration of target vessels irrespective of doppler or CT findings as an alternative to imaging.
Conclusion: Our study suggests most recipients are declined based on CT findings rather than ultrasound doppler studies. CT should be considered as the primary imaging modailty, reducing workup costs by £240 (GB), and providing a more accurate vascular assessment to assist surgery.

OS135 NONENHANCED CT-BASED QUANTIFICATION OF ABDOMINAL AORTIC CALCIFICATION PRIOR TO KIDNEY TRANSPLANTATION

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University Medical center Groningen

Background: A high degree of vascular calcification is commonly encountered in patients undergoing kidney transplantation, but the prognostic value is unclear. Therefore, this study focused on the association of abdominal aortic calcification (AAC) prior to kidney transplantation and all-cause mortality.
Methods/Materials: From 2005 to 2018, renal transplant recipients referred for a nonenhanced CT procedure within 3 years prior to kidney transplantation, were included in a single-center study. Primary endpoint was all-cause mortality after kidney transplantation. AAC was retrospectively quantified using a semiautomated tool, as a modified Agatston score. Patients were stratified into quartiles based on the AAC quantification results. A Kaplan-Meier curve, with Log Rank analysis, and a Cox proportional hazards model were used for time-to-event analysis. Multivariate analysis included the AAC score in quartiles, recipient age, sex and Body Mass Index (BMI), duration of dialysis prior to transplantation and history of smoking.
Results: We evaluated 305 patients, 259 (84.9%) had detectable calcifications, median time between CT and transplantation was 1.0 (IQR 0.5 – 1.4) years, and 38 (12.5%) patients died during a median follow-up of 2.1 (IQR 1.2 – 3.6) years. The Kaplan-Meier curve indicated that a higher AAC score was associated with a higher all-cause mortality ($p < 0.001$) (Fig 1). Similarly, in univariate Cox proportional hazard analysis a higher AAC score was associated with a higher all-cause mortality 2.1 (95% CI 1.5 – 3.0, $p < 0.001$). This association remained significant upon multivariate analysis (HR 1.8 (95% CI 1.2 – 2.8), $p = 0.007$).
Conclusion: A significant association between the degree of AAC, assessed by nonenhanced CT-based quantification, and all-cause mortality was identified. A validated scoring system for AAC could guide clinicians in decision-making with regard to risk stratification and expected mortality after kidney transplantation.

OS136 THE ASSOCIATION BETWEEN BONE MINERAL DENSITY AND AORTIC CALCIFICATION: THE EXISTENCE OF A BONE-VASCULAR AXIS AFTER RENAL TRANSPLANTATION

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University Medical Center Groningen

Background: Chronic kidney disease mineral and bone disorders is often seen in end-stage renal disease and remain after renal transplantation. The bone-vascular axis hypothesis holds a plea for related pathophysiological mechanisms driving both bone-loss and vascular calcification, which contributes to excess cardiovascular risk in renal transplant recipients (RTR). We hypothesized that, in RTR, lower bone mineral density (BMD) is associated with higher abdominal aortic calcification (AAC).
Methods: From 2004 to 2014, RTR referred for a dual-energy X-ray absorptiometry procedure within 6 months after transplantation were included. Areal BMD was measured at the proximal femur, and AAC was quantified (8-point scoring system) from lateral single-energy images of the lumbar spine. Patients were divided into 3 AAC-categories (AAC-scores 0, 1-3 and 4-8; negative finding, low-AAC, high-ACC, accordingly). Multivariable-adjusted multinomial logistic regression models were performed to study the association between BMD and AAC.
Results: We included 678 RTR (51 ± 13 years-old, eGFR 51 ± 15 mL/min/1.73 m^2), of whom 366 (54%) had prevalent BMD disorders, and 266 (39%) had detectable calcification (AAC-score ≥ 1). AAC-categories distribution was different across subgroups by BMD ($P < 0.001$), *e.g.*, high-AAC was observed in 9%, 11% and 25% of RTR with normal, osteopenia, and osteoporosis BMD, respectively. Higher BMD (T-score, continuous) was associated with lower likelihood of prevalent high-AAC (OR 0.60, 95%CI 0.43-0.85; $P = 0.001$), independent of age, sex, renal function, and immunosuppressive therapy. In comparison to RTR with osteoporosis, those with normal BMD were less likely to have high-AAC (OR 0.23, 95%CI 0.08-0.65; $P = 0.01$).
Conclusion: Reduced BMD is highly prevalent in RTR. The inverse association between BMD and AAC may support the existence of a bone-vascular axis, and may provide insights into an overlooked and substantially prevalent modifiable cardiovascular risk factor in RTR.

OS137 INTRACRANIAL ANEURYSMS IN PATIENTS RECEIVING KIDNEY TRANSPLANTATION FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Asan Medical Center, University of Ulsan College of Medicine

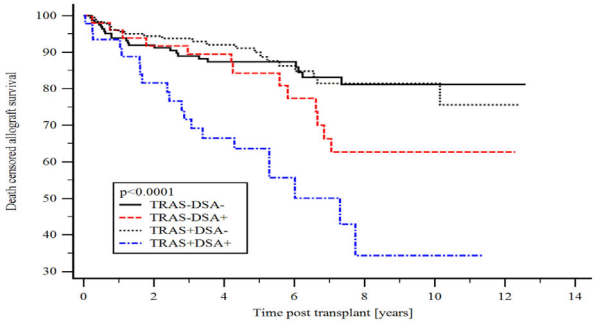
Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disease, commonly leading to the development of kidney failure requiring renal replacement therapy and eventually kidney transplantation. One of the most serious extrarenal complications of ADPKD is the high risk of intracranial aneurysms. The aim of this study was to evaluate the prevalence, rupture rate and results of treatments which are important for establishing the management and surveillance of these patients.
Method: 154 patients of 18-80 years of age with a documented diagnosis of ADPKD receiving kidney transplantation at Asan Medical Center in Seoul, South Korea from 1994 to December 2018 were reviewed. Currently, we routinely perform bilateral nephrectomy and kidney transplantation as a one-stage operation for ADPKD patients receiving transplants from both living and deceased donors
Result: Among 154 patients received kidney transplantation for ADPKD, 113 (73.4%) patients were screened for intracranial aneurysms preoperatively with CT angiography, MRA or four-vessel angiography. 23 patients (14.9%) showed intracranial aneurysms on preoperative imaging studies. 9 patients (5.8%) had rupture of aneurysms and the mean age of rupture was 34.9 years. 52.2% of the patients presented with multiple aneurysms. Nearly half of the aneurysms were located in the MCA territory and the most common location of aneurysms was MCA bifurcation (34.9%) followed by AcomA (20.9%). Clipping was the most common treatment in both ruptured and unruptured aneurysms (88.9% and 26.5%).
Conclusion: Intracranial aneurysms are more frequent in patients with ADPKD and the average age of rupture in patients with ADPKD is earlier than in the general population. These finding should be considered when counseling ADPKD patients regarding the appropriate management of intracranial aneurysms.

OS138 POOR OUTCOME FOLLOWING STENT PLACEMENT IN DSA POSITIVE TRANSPLANT RENAL ARTERY STENOSIS DEMONSTRATES THE HETEROGENEITY OF MACROVASCULAR DISEASE IN TRANSPLANTATION

Salim Hammad, Na Hyun Kim, Richard Corbett, David Taube, Wady Gedroyc, Mohamad Hamady, Michelle Willicombe
Imperial College Renal and Transplant Centre, Imperial College Healthcare NHS Trust

Background: Donor specific antibodies (DSA) have been shown to be associated with both mico- and macrovascular disease in transplantation. Whether management of DSA+ macrovascular disease requires the preferential targeting of traditional cardiovascular risk factors, alloimmune injury or both is not known. In this study of the largest reported series of transplant renal artery stenosis (TRAS), we aim to compare the outcomes following treatment by stent according to DSA status.
Methods: 234 TRAS+ cases, treated with PCI and stent were compared with 215 angiographically confirmed TRAS- cases. All patients were tested for the presence of DSA. Clinical outcomes were analysed, with a median follow up of 5.78 ± 3.16 years post angiogram.
Results: The median time to TRAS diagnosis was 2.76 months. TRAS was more common in recipients of deceased donors [117(75.5%), $p < 0.001$], older patients [54.4 ± 12.5, $p < 0.001$], non-caucasoids [160(68.4%), $p = 0.04$], patients with diabetes [141(60.3%), $p = 0.002$] and patients on dialysis pre-transplant [208 (89.7%), $p < 0.001$]; all variables which may be associated with traditional cardiovascular disease.

Unadjusted allograft survival was inferior in TRAS+ compared with TRAS- patients, $p = 0.028$. Although there was no difference in death censored allograft survival, $p = 0.44$, survival was dependent upon DSA status. Whilst TRAS+DSA- cases had a comparable survival to TRAS-DSA- cases as shown below, $p = 0.66$; TRAS+DSA+ patients had significantly inferior survival compared TRAS-DSA+ ($p = 0.012$), TRAS+DSA- ($p < 0.001$) and TRAS-DSA- ($p < 0.001$).



Conclusion: This study highlights the heterogeneity of TRAS and the importance of considering the likely aetiology when managing patients. It also emphasizes the need for further research to define and manage macrovascular disease in transplantation.

OS139 AORTO-ILIAC CALCIFICATION IS A RISK FACTOR FOR MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS; A SYSTEMATIC REVIEW AND META-ANALYSIS

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Erasmus Medical Center

Introduction: While atherosclerotic iliac arteries in potential kidney transplant recipients are becoming more common, little is known about the clinical outcome after transplantation. We performed a systematic review and meta-analysis to investigate patient and graft survival of kidney transplant recipients with aorto-iliac calcification (AIC) compared to recipients without aorto-iliac calcifications (nAIC).
Methods: We performed a literature search in 5 databases including Embase, Medline, Cochrane, Web of Science and Google Scholar. Articles from January 1st, 2000 until March 5th, 2018 were included. Article selection was in accordance with the PRISMA statement. Relevant outcomes for meta-analysis were patient survival, (death-censored) graft survival and delayed graft function (DGF). The quality of the evidence was assessed using the Newcastle-Ottawa scale.
Results: Twenty-one observational studies were identified from which 9 were eligible for meta-analysis. Short- and long term mortality risk was significantly increased in recipients with AIC (1-year mortality risk: RR 1.81, 95% CI 1.25-2.61, $p < 0.001$, 5-year mortality risk: RR 2.25, 95% CI 1.66-3.05, $p < 0.001$). The risk of uncensored and death-censored graft loss was similar in recipients with and without AIC. The risk of DGF was increased in recipients with AIC (RR 1.26, 95% CI 1.03-1.55). Mean 1-year patient survival, uncensored graft survival and death-censored graft survival from kidney transplantation on a prosthetic graft was 93.5%, 93.5% and 89.1% respectively.
Conclusion: Short- and long term mortality risk is significantly increased in kidney transplant recipients with AIC which is possibly due to cardiovascular comorbidity. Pretransplantation cardiovascular risk profiling is important to identify potential high risk recipients to prevent postoperative mortality. Allocation policies should focus on finding ways to maximize organ longevity in recipients with decreased life expectancy.

OS17 - ISCHEMIA-REPERFUSION; SCIENCE IN CHARGE!

OS140 CELLULAR SENESCENCE AND THE DEVELOPMENT OF BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION

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[1]SCRM Centre for Regenerative Medicine, University of Edinburgh; [2]IGMM, University of Edinburgh; [3]Edinburgh Transplant Centre, The University of Edinburgh

Introduction: Ischemic cholangiopathy (IC) is one of the most common complications after liver transplantation, occurring in 3 to 44% of the recipients, whereby the structure of the biliary tract is progressively destroyed, impairing liver function and jeopardizing the life of the patient. IC remain therapy-resistant resulting in graft loss, re-transplantation and significantly increased direct medical care costs. Furthermore, the aetiology of IC remains undefined, thus hampering the study of these conditions and the development of new therapeutics.

Here, we identify cellular senescence (CS) as a new potential mechanism implicated in the pathogenesis of IC, promoting cellular damage, biliary inflammation and fibrosis.
Methods: We have developed new murine models of cold storage that mimic the clinical handling of donor livers prior to transplantation. In these models we performed immunohistochemical, molecular biology and mass-spectrometry analysis to define a CS profile, applying state of the art technology such as CRISPR editing and high content screening to determine the role of CS in the regenerative/senescent response of the biliary tract.
Results: Our results indicate that biliary senescence might be a detrimental mechanism for the development of BC after liver transplantation.
Conclusion: In this study we identify differential mechanisms of regeneration/senescence that apply to different cell populations in the liver, potentially accounting for the repair and/or lack of repair seen after transplantation. By doing so, we propose the use of the CS profile as a prognostic tool to identify senescent biliary tracts prior liver transplantation and recommend novel therapeutic targets to limit senescence-dependent aggravation of IC. Furthermore, since CS is a common biological trait, the results of this study could potentially be applied to different organs and pathologies, improving and increasing the pool of available donors for transplantation.

OS141 EX-VIVO NORMOTHERMIC MACHINE PERFUSION OF A PORCINE KIDNEY WITH THREE DIFFERENT PERFUSION SOLUTIONS

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UMCG

Background: In the Netherlands, hypothermic machine perfusion (HMP) is clinically used to preserve deceased donor kidneys. Normothermic machine perfusion (NMP) could comprise an even better preservation strategy and provides the opportunity for pre-transplant organ diagnostics and interventions. At this time, a suitable perfusion solution has to be established for NMP. The purpose of this study was to evaluate three different perfusion solutions and determine which is most suitable for a longer period of NMP.
Methods: Porcine kidneys and autologous blood were obtained from a local slaughterhouse. Warm ischaemia time was standardised at 20 min and subsequent HMP with UW-MP at 2-3 hours. Next, kidneys underwent NMP at 37°C during 7 hours with autologous red blood cells (RBCs) and 3 different perfusion solutions ($n = 5$ per group). Group 1 consisted of RBCs and a perfusion solution based on Williams' Medium E. Group 2 consisted RBCs, human albumin and an outbalanced electrolyte composition. Group 3 contained RBCs and a medium based on a British clinical NMP solution. Vital parameters were monitored during NMP and perfusate and urine samples were taken regularly. Biopsies were taken to assess renal histology.
Results: During perfusion all kidneys were functional and most kidneys produced urine. Injury markers aspartate aminotransferase (ASAT) and lactate dehydrogenase (LDH) increased during perfusion with highest end-levels in group 3. N-Acetyl-β-D Glucosaminidase (NAG) levels were significantly lower in group 2 in comparison with group 1 ($p = 0.02$) and group 3 ($p = 0.01$). Histologically all groups showed glomerular dilatation, tubular dilatation and acute tubular necrosis, consistent with ischemic injury in this donation after circulatory death model.
Conclusion: In conclusion, perfusion of porcine kidneys with three different perfusion solutions proved feasible. However, group 2 showed the lowest levels of injury markers indicating that this perfusate is probably most suitable for prolonged NMP of a porcine kidney.

OS142 ACTIVATION OF INNATE IMMUNE CELLS BY FERROPTOSIS IN HEPATIC ISCHEMIA REPERFUSION INJURY

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Background: Organ damage as a consequence of ischemia and reperfusion is an important problem in clinical organ transplantation, especially in the context of extended criteria donors. In the pathomechanism of hepatic ischemia reperfusion injury (IRI) two important mechanisms are involved: Regulated cell death (RCD) events like ferroptosis and necroptosis and innate unconventional effector T cells, namely γδ T cells. However, the mechanisms underlying the T cell-RCD crosstalk are poorly understood. In this study, we investigate the effect of IRI induced ferroptosis on early γδ T cell activation.
Methods: In this study we investigated early immunological events in a well-established model of hepatic IRI in genetically targeted mice to study the role of γδ T cells and their IL-17 production. We used genetically modified mice (ferroptosis pathway up- or downregulated) which underwent a 90 min partial warm ischemia, followed 24 hours of reperfusion. Hepatocellular injury was

evaluated by HE-histology and serum-transaminase measurement. Hepatic leukocyte subsets, cytokine secretion and major effector molecules were characterized by immunohistochemistry, ELISA, RT-PCR and polychromatic FACS.
Results: We found that unconventional CD27-γδTCR+ and CD4-CD8- double-negative (DN) T cells, which are the major effector cells in hepatic IRI, are significantly elevated in the livers of those mice, where the RCD pathway is activated. Consequently, these mice show aggravated hepatic liver injury. In contrast, mice with insufficient ferroptosis activation show significantly reduced numbers of activated effector T cells in IRI livers, while hepatic liver injury was significantly diminished.
Conclusion: Severity of ferroptosis directly correlates not only with hepatic liver injury, but also with infiltration of innate unconventional CD27-γδTCR+ and CD4-CD8- double-negative (DN) T cells. This finding leads to the conclusion, that innate first line responding T

OS143 ALDEHYDE DEHYDROGENASE-2, AMPK AND MTOR IN STEATOTIC LIVER COLD ISCHEMIA INJURY

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Background: Aldehyde dehydrogenase-2 (ALDH2) has been reported to play a role in the cardioprotection against ischemic injury. However, no data are reported of the potential involvement of ALDH2 in fatty liver preservation. In this communication we demonstrate the relevance of ALDH2 activity in the underlying pathophysiological mechanisms responsible for the fatty liver graft protection against cold ischemia injury when two solutions, as HTK and IGL-1, are used.
Material and methods: Fatty liver from Male obese Zücker rats (11 weeks aged) were washed and stored in IGL-1 and HTK solutions at 4°C. After rinsing with Ringer solution, livers were stored at -80°C for subsequent analyses. We measured liver damage with alanine aminotransferase and aspartate aminotransferase (ALT/AST), mitochondrial damage with glutamate dehydrogenase (GLDH), aldehyde dehydrogenase 2 (ALDH2), adenosine monophosphate protein kinase (AMPK), mammalian target of rapamycin (m-TOR), several autophagy markers (beclin-1, beclin 2 and LCB3) and apoptosis (caspases 9 and 3). Nitric oxide generation (eNOS and nitrites/nitrates) and High mobility box 1 (HMGB1) were also measured.
Results: Data revealed that ALDH2 was more enhanced in liver preserved in IGL-1 than in HTK, correlating with increases in phosphorylated AMPK and a p-mTOR expression decrease. Data also showed increases in autophagy markers, which were accompanied by significant decreases in apoptosis. All these changes well correlated with decreases in AST/ALT and GLDH levels.
Conclusions: These data confirm that ALDH2 plays an essential role in liver graft protection against cold ischemia injury, being part of the underlying protection mechanism of AMPK/mTOR autophagy induction and apoptosis prevention. These data suggest that ALDH2 could be a promising marker of graft protection against cold ischemic injury during static preservation.

OS144 SEX-DIFFERENCES ON PLATELET AGGREGATION AND MICROVASCULAR PERFUSION AFTER BRAIN DEATH IN RATS

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Background: Several studies highlight the impact of brain death (BD) on organ viability. BD leads to a systemic inflammatory process associated to the activation of coagulation, that seems to be associated with decreased microcirculatory perfusion. There are clinical evidences that females exhibit significantly higher platelet aggregability. Thus, we investigated the sex differences on platelet behavior, coagulation process and microcirculatory compromise after BD.
Methods: Male and Female (proestrus) Wistar rats were submitted to rapid onset BD. Non-manipulated animals were used as controls (Naive). Experiments performed 180 min thereafter included: (a) intravital microscopy to evaluate mesenteric perfusion and leukocyte infiltration; (b) platelet aggregation assay and (c) rotational thromboelastometry.
Results: After 3 h of BD, female rats maintained the mesenteric microcirculatory perfusion, while male rats showed pronounced reduction on the percentage of perfused vessels (Female-Naive: 81.19 ± 0.63; Female-BD: 78.63 ± 3.46 and Male-Naive: 95 ± 1.67; Male-BD: 35.41 ± 2.75, $P < 0.0001$). Male-BD animals presented higher platelet aggregation in comparison to controls (Male-Naive: 45.94 ± 5.9; Male-BD: 81.6 ± 5.16, $P < 0.0001$). In contrast, Female-BD reduced platelet aggregation compared to Naive animals (Female-Naive: 72.73 ± 3.04; Female-BD: 34.03 ± 4.2, $P < 0.0001$). The thromboelatometry showed reduction of clot firmness in the Female group, in parallel with increased clothing time in comparison to the Male group after BD.
Conclusions: Data evidenced the different microcirculatory effect of BD between sexes and its connection with platelet role and clothing process. In addition, it was evidenced that the reduction of microcirculatory perfusion in Male is related to intravascular microthrombi formation, suggesting a possible influence of anticoagulation therapy on donor organ viability.

OS145 LOWERING TEMPERATURE INDUCES A PROGRESSIVE DISCREPANCY BETWEEN REDUCTIONS IN MITOCHONDRIAL OXYGEN CONSUMPTION AND RADICAL OXYGEN DAMAGE

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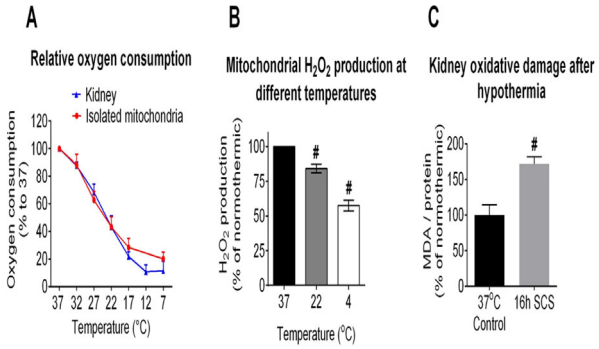
Background: Hypothermia, leading to mitochondrial inhibition, is widely used to reduce ischemic injury during transplantation. However, the exact effect of hypothermic versus normothermic temperatures on mitochondrial activity and mitochondrial failure remains unclear. We evaluated mitochondrial (mal)function in different models at temperatures ranging 7-37°C.
Methods: As a marker for mitochondrial function, respiration was measured in whole porcine kidneys, human kidney cells (HEK293) and isolated porcine mitochondria. Kidneys were connected to a closed perfusion circuit, perfused at different temperatures and oxygen consumption was calculated. The Oroboros oxygraph was used for cells and isolated mitochondria. As markers for mitochondrial malfunction, lipid peroxidation (MDA) levels and mitochondrial H_2O_2 production were measured. Eventually, scavenging capacity was assessed in cells by quantification of MnSOD, MDA and survival after treatment with the exogenous oxidant H_2O_2 and anti-oxidant trolox.
Results: Lowering temperature in perfused kidneys, cells and isolated mitochondria showed a rapidly decreased oxygen consumption (65% at 27°C versus 20% at 7°C compared to normothermic). Decreased oxygen consumption at lower temperatures was accompanied by a less pronounced reduction in mitochondrial H_2O_2 production, amounting only 50% of normothermic values at 7°C. Consequently, MDA levels increased in cold stored kidneys and cells. Moreover, we found a decreased ability to deal with oxidative stress paralleled by decreased MnSOD levels in hypothermia. Eventually, by using a powerful exogenous anti-oxidant, cells were protected to cold-induced oxidative stress.
Conclusion: In conclusion, temperature shifts in organ transplantation highly affect mitochondrial function, resulting in a progressive discrepancy between mitochondrial respiration and ROS production. This observation highlights the necessity to develop new strategies to decrease the formation of ROS during hypothermic organ preservation.



OS146 INVESTIGATING THE EFFECTS OF OXYGENATION ON DE NOVO METABOLISM AND CELL VIABILITY IN A PROXIMAL TUBULE CELL LINE MODEL OF HYPOTHERMIC MACHINE PERFUSION

Ohema Powell[1], Alpesh Thakker[2], Kamlesh Patel[2], Jay Nath[2], Christian Ludwig[2], Thomas Smith[2]
[1]Univerisity of Birmingham; [2]Institute of Metabolism and Systems Research

Background: Recent studies involving porcine kidneys have shown potential functional benefits when oxygenating perfusate during hypothermic machine perfusion. Using tracer-based metabolism and cell viability assays applied to a human proximal tubule cell line model, we aimed to replicate results of animal studies and refine the optimal concentration of oxygen delivery during HMP.
Methods: Telomerase-immortalised human proximal tubule cells were used for this cell line model experiment. Cells were seeded onto nine 100 cm2 for each of the three replicates. Cell media was exchanged for KPS-1 solution

including a carbon-13 labelled glucose tracer to enable detection of *de novo* metabolism. All hypothermic experiments were performed for 18 hours, after which metabolic profile of cell extracts was defined using a combination of Nuclear Magnetic Resonance Spectroscopy and Mass Spectrometry. The LDH assay was used to assess membrane damage, and the SRB assay used to assess differences in cellular viability.
Results: Metabolic analysis revealed profound changes in glucose metabolism as a consequence of the oxygen environment cells were stored in, with the hyperoxic environments resulting in greater intracellular levels of glutamate and aspartate. LDH was not found to differ between cells stored under hyperoxia or atmospheric oxygen. In contrast, the SRB data shows reduced SRB levels for hyperoxic compared to atmospheric conditions.
Conclusion: Active perfusate oxygenation during HMP is predicted to improve transplant outcomes, however the optimal oxygenation strategy is not yet defined. The close similarities between the in vitro findings here, and the latest research using whole organ models suggests our approach forms an effective screening tool for the elucidation of the optimal oxygenation strategy for a given cell lineage.

OS147 HYPOTHERMIC PROTECTION ATTENUATES RENAL FIBROSIS IN RENAL ISCHEMIA-REPERFUSION INJURY IN MICE

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Introduction: Hypothermia attenuates the renal injury induced by ischemia-reperfusion(IR). However, the detailed molecular pathway remains unknown. Although there has been reported that hypothermia protects acute renal damage, there is little known that hypothermia reduce renal fibrosis in IR kidney injury. We evaluated hypothermic protection against renal fibrosis in renal IR injury.
Methods: C57Bl/6 mice were divided into the following groups: sham-operated (cold, 32C) vs normal temperature (37C); IR mice (32C vs 37C). Kidneys were harvested 10 and 27 minutes after induction of renal ischemia and 24, 72, 168 hours after iIR injury. Functional and molecular markers of kidney injury were evaluated.
Results: The blood urea nitrogen and serum creatinine levels and the histologic renal injury scores were significantly lower in 32C IR than 37C IR kidneys (all P values $< .05$).In kidney harvested 10 and 27 min, the extent of renal AMPK,ERK, and HIF1 phosphorylation was significantly increased in the kidneys of 32C compared to 37C IR mice. In kidney harvested 27 min, 24 hr, 72 hr, and 168 hr, the expression levels of SOX9, TGF beta, alpha SMA, collagen IV, and fibrinogen decreased in 32C IR compared to 37C IR mice. In addition, in kidney harvested 72 hr, and 168 hr, the stained area of TGF beta, alpha SMA, and masson trichrome, were significantly decreased in 32C IR compared to 37C IR mice.
Conclusions: Hypothermia attenuates the renal fibrosis induced by Ischemia reperfusion.

OS18 - LUNG TRANSPLANTATION

OS148 LUNG TRANSPLANTATION FROM UNCONTROLLED DONATION AFTER CARDIAC DEATH PROGRAM: REPORT OF 5 YEARS EXPERIENCE

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Lung procurement from donation after circulatory death (DCD) donors is a developing method to increase the organs pool. The uncontrolled setting is the most stimulating because of its potentiality and minor ethical implications. On the other hand, it is undeniable that there are challenges to overcome regarding organization and preservation and evaluation of the graft. After a long preclinical and educational phase, in 2014 our lung-DCD projectstarted for isolated lung procurement from uncontrolled DCD donors (Maastricht class II). We report our 5 years' experience.

Our approach consists of an *in situ* open and ventilated normothermic lung preservation (i.e. recruitment manoeuvres and cPAP) and an *ex situ* assessment (i.e. ex-vivo lung perfusion, EVLP) (Table 1).

From 2014 to 2019, our donor recruitment system has been activated for 33 potential donors from 3 different hospitals. In 19 cases (57%) the system aborted for un-matching of inclusion criteria or lacking of consent; the lungs were judged not suitable in situ or at the back table in 3 cases (10%) and in 7 cases (21%) after EVLP evaluation. Finally, successful bilateral lung transplantation was performed in 4 cases (12%) (Table 2).

Clinica events	Definition	Notes
Cardio-circulatory arrest	Absence of respirazione and pulsa pressure	Exclusion criteria= un-witnessed collapse, no-flow of > 15 min, low flow > 60 min; age > 65 years, smoking, massive lung contusion,
Stop cardiopulmonary resuscitation		
Diagnosis of death	No touch = 5 min	
In situ preservation	Recruitment manoeuvres + continuous positive end-expiratory pressure	
Declaration of death	Flat ECG = 20 min	
Consent	Next of kin	
Heparin	10000 UI e.v.	3 min of cardiopulmonary resuscitation
Chest x-ray; bronchoscopy		
Surgery		
Incision		
Lung inspection + evaluation	Recruitment manoeuver	
Cold flushing	Fibrinolytic agent + preservation solution	15 mg rTPA; 60 ml/kg Perfadex
Retrograde flushing		250 ml/vein Perfadex
Cold storage		
Ex-vivo lung perfusion		Low-flow, open atrium and low hematocrit technique

	Case 1	Case 2	Case 3	Case 4
Donor				
Sex	Male	Male	Male	Male
Age (years)	46	20	56	50
Smoking history	No	No	No	Yes
Bronchoscopy	Negative	Aspiration	Fluid	secretions
Negative				
Chest x-ray	Negative	Infiltrates	Lobar opacity	Negative
Procurement				
Cardiac arrest-Flushing (min)	295	305	200	187
Ex-vivo lung perfusion duration (min)	370	255	1054	330
Cardiac arrest-Reperfusion first lung (min)	1335	1332	1930	1286
Cardiac arrest-Reperfusion second lung (min)	1551	1544	2009	1373
Recipient				
Sex	Female	Female	Male	Male
Age (years)	36	26	32	58
Lung allocation score	46	45	37	37
Disease	Cystic fibrosis	Cystic fibrosis	Cystic fibrosis	Emphysema
Primary graft dysfunction grade 3	No	Yes	No	No
Follow-up (days)	1580	240	38	7
Alive at follow-up	Yes	Yes	Yes	Yes
Anastomotic complications	No	No	No	No

Uncontrolled DCD is frequently perceived as a challenge due to increased logistical requirements and limited pre-procurement assessment; our approach demonstrated the possibility to overcome those limits. We are working to increase the number of hospitals involved.

OS149 REAL-TIME SHARING OF MEDICAL IMAGING: AN INNOVATION FACILITATING DECISION-MAKING FOR TRANSPLANTS

Beatrice Serrano Gonzalez, Patricia Poulat, Olivier Huot, Géraldine Malaquin
Agence de la Biomedecine

Transplant efficiency and the lack of grafts has led professionals to offer organs from donors using "expanded criteria", where evaluation using medical imaging has become essential.

In its role as regulation and allocation, the French Agence de la biomédecine provides transplant professionals with an online tool named "Cristal". This 24-hour accessible tool contains anonymized administrative, medical and biological data, updated in real time before explant. However, medical imaging was not available within this tool when it was first developed.

To provide experts and medical teams with the opportunity to examine medical imaging, thus allowing them to estimate the viability of the organs offered and to get a better pairing between donor and recipient; while respecting the answering delay (20 min).

At the end of year 2015, The ABM, helped by the GCS SESAN, has developed the software "Cristal Image" relying on the Regional Télémédecine Tool of Ile-de-France and the national network "Etiam Connect", technical support on these trades, allowing the connection of the 180 establishments involved in organ transplants

Two and a half years, all transplantation centers are equipped and all harvesting centers are able to transfer the images in real-time.

Since 2016, 4 854 donors have been evaluated with medical imaging and 11 471 833 images have been transferred with overall 10 251 views by the transplant medical teams.

We observed a slight reduction of the mortality of 0.5% thanks to Cristal Image. This software also clearly facilitated the medical team's decisions, as there was medical imaging in 100% of the donors files refused. It means that the medical teams had a better analysis of the risk/benefit balance for their recipients. In addition, using this tool saves time, money and human energy because it allows a diminution of unnecessary trips.

Real-time image sharing of donors is a real breakthrough in transplant efficiency, which could benefit other countries.

OS150 EXPANDING THE DONOR POOL BY EXTENDED DCD LUNG DONATION

Eva Koffeman, Joep Droogh, Alexander Veen, Michiel Erasmus, Tji Gan, Huib Kerstjens, Massimo Mariani, Erik Verschuuren
University Medical Center Groningen

Introduction:
Almost half of the lung transplantations in the Netherlands are performed with donation after circulatory death (DCD) donors. However, over 25% of the DCD donations are cancelled because the agonal phase exceeds the current maximum length for donation: 120 minutes. Pig models testing lungs ex-vivo (EVLP) have shown that a prolonged agonal phase doesn't compromise the quality of the lungs. Given the possibility to test lungs on EVLP before transplantation the length of the agonal phase might be less important in DCD lung donation. In 2017 four suitable DCD lung donations out of 20 DCD procedures in our center were cancelled due to a prolonged agonal phase. In 2018 four out of 19 DCDs were cancelled. We therefore present a protocol to accept DCD lung donation irrespective of length of the agonal phase.
Methods:
Informed consent will be obtained from patients on the lung transplant waiting list from our center to receive extended DCD (eDCD) lungs. When a donor exceeds the 2 hour agonal phase limit for regular organ donation, the donor becomes an eDCD donor and donation then is limited to the lungs. When a donor passes, after five minutes 'no touch', the donor will be transported to the OR for intubation. Lungs will be inflated by CPAP until the thoracic surgeons are available for procurement. After opening of the chest the lungs will be ventilated according to Dutch DCD guidelines. All eDCD lungs will be evaluated during EVLP after procurement. When the lungs are suitable for transplantation after evaluation on the EVLP they will be transplanted.
Discussion:
Currently, many potentially suitable lungs are not procured due to the prolonged agonal phase. It is going to be a logistic challenge to procure these lungs after a prolonged agonal phase. However, with the use of EVLP, lungs can be evaluated before transplantation and logistics can be managed. Therefore, we expect to increase the number of lung donations in our center with 3-5 per year by eDCD.

OS151 LUNGS TRANSPLANTED FROM DONORS AFTER CONTROLLED CARDIOCIRCULATORY DEATH (CDCD) HAVE SIMILAR PULMONARY GRAFT DISFUNCTION (PGD) THAT THOSE OBTAINED FROM DONORS AFTER BRAIN DEATH (DBD). DACMECITOS STUDY. PRELIMINARY CLINICAL DATA RESULTS

Alberto Sandiumenge[1], Irene Bello[1], Elisabeth Colf[2], Marina Pérez[3], Maria Angeles Ballesteros[4], Aroa Gómez[1], Silvana Crowley[3], Sara Naranjo[4], Javier Pérez[1], Judit Sacanell[1], Cristopher Mazo[1], Alberto Jauregui[1], Fernando Mosteiro[5], Jose Maria Dueñas[6], Maria Deu[1], Teresa Pont[1]
[1]University Hospital Vall d Hebron; [2]Organización Nacional de Trasplantes; [3]Hospital Universitario Puerta de Hierro Majadahonda; [4]Hospital Universitario Marqués de Valdecilla; [5]Complejo Hospitalario Universitario A Coruña; [6]Hospital Universitario Reina Sofia

Introduction: Despite suffering longer functional warm ischemia times, lungs trasplanted from cDCD have similar graft and recipient survival rates than those obtained from DBD (Krutsinger D.J Heart Lung Trasplant 2015; 34(5): 675-84). In 2018 a multicentre prospective study was started with the aim to investigate the inflamatory response pattern of lungs transplanted from DBD and cDCD and its influence on the development of PGD.
Methods: Lung donors and recipients from DBD and cDCD of 5 spanish lung transplant centres during 2018 were prospectively followed. Clinical data (demographic and admission characteristics) of donors and recipients, retrieval and implant procedure variables and post transplant outcome were registered. Blood samples were collected from the donor during the retrieval process, and from the recipient, during and 24/48/ and 72 hours after the lung transplant. Inflammatory response and clinical outcome variables will be compared between DBD and DCD groups. We present preliminary clinical data
Results: A total of 113 lung transplants were included (32DCD/81DBD). Demographic and admission characteristics from donor and recipient of both groups were similar except for a larger number of cDCD donors requiring ECMO during ICU stay (12.5vs2.5;$p < 0.05$). A total of 82 recipients (72%) developed PGD. The need of Cardiopulmonary bypass and hemoderivate transfusion was associated with higher PGD (96%vs70.9% and 83%vs 64%; $p < 0.02$) and PGD III (73%vs28% and 46%vs23%; $p < 0,02$) rates. Recipients from cDCD had a lower incidence of PGD (68.8%vs76.5%) and PGD III (32.3% vs38.3%) than those from DBD, although no statistical significance was reached.
Conclusions: Controlled DCD is a safe alternative to DBD lung transplantation with a trend to lower PGD rates. Differences in the inflamatory response triggered by the dying process may explain those findings.

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OS152 THE NEW METHOD FOR LONG-TERM HYPOTHERMIC LUNG PRESERVATION WITH CONTINUOUS VENTILATION

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Background: Lung transplantation (LTx) has done for end-stage respiratory failure. According to the guideline, total ischemic time should be within 8 hours, however total ischemic time is often over 8 hours in our program. We have performed 106 cadaveric LTx in Tohoku University lung transplant program and the average total ischemic time of all our LTx was over 9 hours (557.5 ± 139.9 min, average $\pm$ SD), because we need to use public transportations for delivery. So we invented ventilated lung preservation system in order to supply oxygen to donor lungs. The objective of this study is to investigate the effect of continuous ventilated lung preservation.
Materials & Methods: We divided Pig isolated lungs into 3 groups; deflation group (isolated lung keeps deflated in preservation), inflation group (isolated lungs keep inflated) and ventilation group (isolated lungs keep ventilated). All isolated lungs kept cold during preservation. We preserved these isolated lungs for 24 hours and then performed left LTx with these lungs in pig.
Results: The oxygen concentration in airway of isolated lungs was stable in ventilation group, however that was decreased in deflation group and inflation group. Moreover, the concentration of carbon dioxide in airway was significantly increased in deflation group and inflation group at the end of ischemic time. When we compared ATP in lung tissue between before and after lung preservation, the concentration of ATP in lung tissue was decreased in deflation group and inflation group, however that was stable in ventilation group. P/F ratio after left LTx was better in ventilation group compared to the other two groups. And also wet/dry ratio was the lowest in ventilation group in these groups.
Conclusion: Ventilation during preservation provides oxygen to isolated lung tissue and isolated lung could keep aerobic metabolism during preservation, therefore transplanted lung showed better condition than the conventional methods of lung preservation.

OS153 A SINGLE CENTER EXPERIENCE OF EX-VIVO LUNG PERFUSION PROGRAM: EARLY AND LONG TERM POST-TRANSPLANT OUTCOME

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Introduction: Ex vivo lung perfusion (EVLP) potentially allows to reduce the donor pool shortage, however its efficacy has been recently questioned.
Methods: We analyzed donors and recipients characteristics and early and long term outcomes of transplant procedures performed at the Milan Lung Transplant Center from January 2011 to December 2018comparing transplants from standard lung donors versus organs undergone EVLP.
Results: One hundred ninety-one lung transplants have been performed throughout the study period. Fifty EVLP procedures were performed resulting in 31 lungs accepted for transplantation. In the EVLP cohort 7 lungs were retrieved from donors after cardiac death and 24 lungs from donors after brain death with suboptimal function. Recipient characteristics were similar in the two cohorts with a trend toward higher severity score in the EVLP cohort. EVLP treated lungs underwent longer total preservation time. Early after transplantation, recipient of lungs undergone EVLP showed lower oxygenation and slight prolongation in the duration of mechanical ventilation without this affecting the duration of intensive care unit stay and early mortality rate. Long-term probability of overall survival and of survival free of chronic lung allograft disease did not differ between the groups (Log Rank Kaplan-Maier analysis, p value respectively 0.581 and 0.327).

	STANDARD Group (n = 160)	EVLP Group (n = 31)	p value
DONORS			
PaO2/FiO2, mmHg	456 [387; 518]	289 [230; 323]	< 0.001
Total Preservation Time 1st Lung, min	307 [240; 375]	867 [706; 939]	< 0.001
Total Preservation Time 2nd Lung, min	520 [456; 589]	1052 [968; 1175]	< 0.001
RECIPIENTS			
Disease, n (%)			0.577
Cystic Fibrosis	77 (48)	18 (58)	
Pulmonary Fibrosis	52 (32)	7 (22)	
COPD	14 (9)	3 (10)	
Other	17 (11)	3 (10)	
LAS	39.2 [34.6; 49.5]	44.9 [36.0; 60.5]	0.079
ECMO bridge to LuTx, n (%)	20 (12)	4 (13)	0.815
OUTCOME			
PaO2/FiO2 at 24 h, mmHg	304 [230; 378]	260 [199; 292]	0.005
PGD 2-3 at 72 h, n (%)	35 (22)	7 (23)	0.910
Ventilator Free Days (28 days), days	27 [22; 28]	25 [19; 27]	0.035
ECMO post-operatory, n (%)	29 (18)	11 (35)	0.053
ICU LOS, days	4 [2; 9]	6 [3; 12]	0.218
30 days survival, n (%)	159 (99)	30 (97)	0.735

Conclusions: The EVLP program allowed to increase the number of transplants by about 20% and to expand the lung donor pool to donors after cardiac death. Recipient of lungs undergone EVLP required more ventilatory support in the early phase after transplantation without affecting early and long term outcomes.

OS154 ELECTROLYTE BALANCE STABILIZATION BY CONTINUOUS DIALYSIS DURING EX VIVO LUNG PERFUSION IN PIG MODEL

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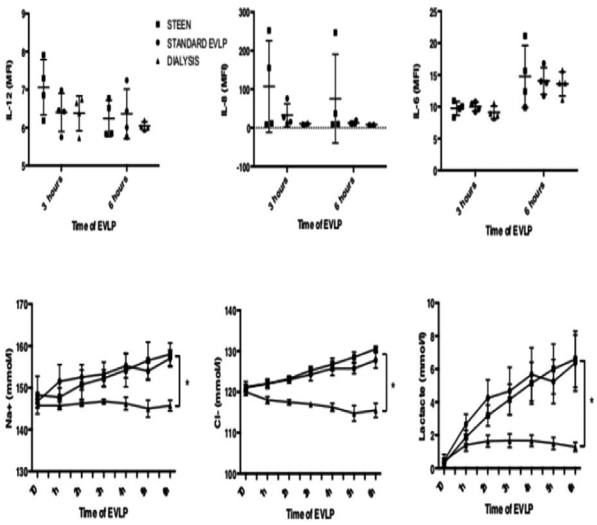
Introduction: Ex vivo lung perfusion (EVLP) has improved the lung donor management in different kind of situation. Unfortunately, stability of the process is limited around few hours. One of the reasons could be explain by an electrolytic and acid-base imbalance.

Our objective in this study was to test the safety and efficacy of continuous dialysis during EVLP in a pig model.
Methods: On a DCD swine model and after one hour of cold ischemia, a 6-hours EVLP procedure according to the Toronto protocol was performed. Three groups of four double lungs were compared. Group STEEN : no modification of perfusate. Group STANDARD EVLP : 500 mL of Steen solution is replaced every 2 hours. Group DIALYSIS : Perfusate was continuously run through a dialysis machine (Fresenius). EVLP physiologic and ventilatory parameters, perfusate biochemistry and inflammatory biomarkers were assessed every 30 minutes.
Results: Physiologic, ventilatory parameters and gaz exchange were comparable between the three groups. Electrolyte balance, determined by stabilization of sodium, potassium, calcium, magnesium ion concentrations in the perfusate, was significantly improved in the Dialysis group. Stability of the metabolic profile was obtained in the dialysis group while a significant variation with lactate accumulation and a decrease of glucose levels were significantly recorded in other groups. Proinflammatory Cytokine expression profile seems to be improve by dialysis.
Conclusion: Continuous perfusate dialysis is effective and safe during short EVLP for stabilizing electrolyte balance. Since this procedure improve the perfusate solution, further studies are needed to evaluate the beneficial effect on prolonged EVLP and post-transplant lung function.



OS155 TARGETING LATENT CYTOMEGALOVIRUS (CMV) WITH A NOVEL FUSION TOXIN PROTEIN USING EX VIVO LUNG PERFUSION (EVLP) AS A PLATFORM

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Background: Donor to recipient CMV mismatch leads to high incidence of CMV infection post lung transplantation causing devastating impacts in patient outcomes. EVLP is a potential platform to modify grafts prior to transplantation. We hypothesized that EVLP delivery of F49A-FTP, a fusion toxin protein that targets with ultra-high affinity cells expressing the latent CMV protein *US28*, may safely clear latent CMV from donor lungs, thus attenuating viral reactivation post transplant and leading to better clinical outcomes.
Methods: Human donor lungs rejected for transplantation were placed on EVLP alone (n = 2) or EVLP with 1 mg/L of F49A-FTP (n = 2) for 6 hours. Lung viral burden was quantified through RT-qPCR measurements of US28 and since F49A-FTP induces apoptosis of the cells expressing US28 (CD34 + stem cells and CD14 + monocytes), flow cytometry was used to quantify the proportion of these cells in lung tissue collected pre- and post-perfusion.

Results: F49A-FTP was delivered successfully through vasculature of the lung on EVLP and physiological data recorded during perfusion exhibit no acute adverse events. Regarding viral burden, a 5-fold decrease in US28 levels was observed in the F49A-FTP group compared to only a 0.4-fold in control group. The ratio of post to pre perfusion live and apoptotic CD34 and CD14 cells was used to assess the efficacy of F49A-FTP to target cells expressing US28. Lungs perfused with F49A-FTP demonstrated lower live CD34 + and higher apoptotic CD34 + cell frequency after perfusion vs control lungs (mean ratio live cells = 0.65 vs 1.08; apoptotic cells = 2.87 vs 1.00). Same trend was not noticed in CD14 + cells.
Conclusion: Initial results from our study shows that F49A-FTP seems to have the capacity to attenuate CMV latent burden in donor lungs using EVLP with no evident acute toxic effects. Although promissing, we need more data to confirm these trends.

OS19 - LIVING KIDNEY DONATION - EXPANDING THE LIMITS

OS156 COMPARISON OF CLINICAL OUTCOMES BETWEEN 100 CASES OF ABO INCOMPATIBLE AND 900 CASES OF ABO COMPATIBLE KIDNEY TRANSPLANTATION

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Introduction: ABO incompatible(ABOi) kidney transplantation(KTP) is a safe and proven method of increasing donor pool and reducing cadaveric KTP waiting time. It is also widely practiced in many countries, but there are still many countries and transplant centers that are not implemented globally. If the clinical outcome of ABOi compared to ABO compatible(ABOc) can confirm non inferiority and satety, it may be a conner-stone that can be used for ABOi transplantation in more transplant centers.
Method: We retrospectively evaluated 100 cases of ABOi KTP recipients and 951 cases of ABOc KTP recipients from June 1996 to December 2018 in Bong Seng Memorial Hospital. The first ABOi KTP operation was performed in June 2009. The primary outcome was patient survival and graft survival. The secondary outcome was CMV infection, Biopsy-proven rejection, bacterial or fungal infection.
Results: There was no statistical difference in the baseline characteristics between ABOi and ABOc KTP. Among the ABOi group, there were 5 deaths. Overall ABOi patient survival tended to decrease compared to the ABOc group (P-value 0.015), but there was no statistically significant difference between the two groups since 2012(P-value 0.128). Graft survival was not different between the two groups in both the all patients and the recent patients(P-value = 0.292, 0.872). There was no difference in complications such as PTDM, angina, and myocardial infarction after transplantation. There were no significant differences in infection and rejection.

Conclusion: ABOi transplantation was not inferior to ABOc and showed no difference in safety. In the future, ABOi is a safe and effective method of KTP that can be performed more easily at more centers.

OS157 ALTROISTIC DONATION IN A PAIR EXCHAGE PROGRAM SIGNIFICANTLY INCREASES TRANSPLANTABILITY OF HIGHLY SENSITIZED PATIENTS

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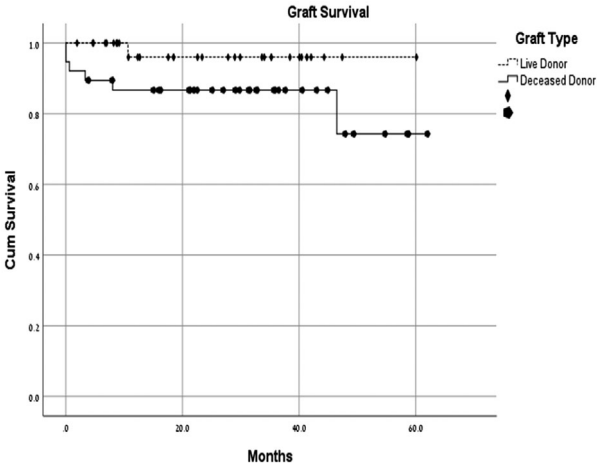
Altruistic donors are usually included in pair exchange program to open a chain of transplants. In Israel altruistic donors forms about 50% of all live-donor transplants and the majority are coming from the religious Jewish sector through a non-profitable organization "Matnat Haim" (gift of life). Donors who agree to be included in our pair exchange pool are matched preferably to highly sensitized recipients. In the deceased donor kidney transplant allocation highly sensitized patient are also prioritized by granting them extra-points. We sought to compare the chance of finding a match for highly sensitized patients between the two programs, the pair exchange live-donor (LD) versus the deceased donor(DD) transplants.
Material and Methods: We retrospectively review our 6-year experience with pair exchange LD kidney transplantation (n = 117 patients) and compare those to DD transplantation done at the same period (n = 428). We specifically looked at the proportion of highly sensitized recipients (PRA > 50%) and compared graft survival in these two groups.
Results: Between 1/2013-12/2018 34 of 117 highly sensitized patients (29%) were transplanted within our pair exchange program compared to 38 of 428 (8.8%) patients transplanted at the same time period from DD. In the pair exchange there were 42 pairs, 1 triplet, 1 four transplants and 1 chain of five. Another 21 single donors donated a kidney to highly sensitized patients. The mean waiting time on dialysis until transplant in the two groups was



73.75 months and 100 months respectively (ns). The 1, 3 and 5 year graft survival in the two groups were 96%, 96% and 96% in the first group and 86.7%, 86.7% and 74.3% in the second group (p = 0.11).
Conclusion: Including altruistic donors in our pair exchange program significantly benefit highly sensitized patients who otherwise would wait a longer time for a deceased donor match.

OS158 HEALTH LITERACY IN LIVING KIDNEY DONORS

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Background: Living donor kidney transplantation (LDKT) is the gold standard treatment for patients with advanced kidney disease. Limited health literacy (LHL) is known to be a major factor in preventing patients from engaging in the treatment process and contributing to healthcare decisions. Currently there are no studies investigating correlations between health literacy and living kidney donation in a European population. This cross-sectional study sought to investigate these correlations in a single centre with increasing referrals for living donation.
Method: We surveyed patients who donated a kidney, attended outpatient clinic for donor follow-up, or were undergoing work-up for donation between 1st of January 2018 to the 31st October 2018. Data on health literacy, demographic and socioeconomic status (SES) were collected using a questionnaire and patient notes. LHL was defined as a > 2 in the Single Item Literacy Screener (SILS). Health literacy was also assessed using the Brief Health Literacy Screener (BHLS). Univariate analyses were performed to assess which variables significantly correlated with donors' health literacy.
Results: Of 236 eligible donors, 136 (58%) participated in the study. Using the SILS, LHL prevalence was 1.5%. This did not significantly vary according to the stage of donation, donor relationship with the recipient, donor demographics, or SES. Subgroup analysis also showed the prevalence of LHL after LDKT has remained constant, regardless of the length of time since donation. Univariate analysis of BHLS scores suggested that only Asian ethnicity (n = 2) was associated with a slightly lower degree of health literacy compared with Caucasian donors (p = 0.030).
Conclusion: Living donors have very low rates of LHL, especially when compared to other estimates of LHL in kidney transplant recipients, and the wider Scottish population. This low prevalence of LHL was found to be true of all kidney donors, regardless of demographic or SES.

OS159 ADRENAL FUNCTION AFTER LIVING DONOR NEPHRECTOMY

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Introduction: Outcomes after living donor nephrectomy (LDN) are subject to a degree of heterogeneity that is largely unexplained. The hypothalamic-pituitary-adrenal axis (HPAA) is known to affect post-operative recovery and it may be altered after nephrectomy. We aimed to assess the HPAA response after LDN and the effect on post-operative outcomes.
Methods: Patients undergoing LDN were recruited into this study. Plasma and serum samples were collected at 6 time points. The levels of

adrenocorticotrophic hormone (ACTH) and cortisol were measured to establish their time dependent kinetics and define those with potential adrenal insufficiency. This was correlated with postoperative outcomes including hospital stay, complications, EQ5D scores, renal function at 30 days and 1 year and markers of the systemic inflammatory response.
Results: 51 living kidney donors were analysed.

Mean preoperative cortisol levels in the cohort were 347 nmol/L. This was elevated to a mean of peak Cortisol level of 462 nmol/L in the immediate postoperative period. The general trend was for falling cortisol levels thereafter until Day 30 which was also seen with ACTH levels.

20 patients representing 39% of the kidney donors on this cohort, had lower cortisol values in the immediate and day 3 postoperative periods than their initial preoperative recording suggesting adrenal insufficiency.

There was no association between a blunted cortisol response and preoperative factors or post-operative outcomes. Correlation of patient reported outcomes using the EQ5D questionnaire model demonstrated a reduced 30-day score in the blunted cortisol donors compared to normal response donors (0.72 V 0.8 $p = 0.04$). This association remained significant when the 30-day EQ5D index was adjusted for its preoperative index value in a linear regression model (coefficient -0.1 $p = 0.024$).
Conclusion: Adrenal dysfunction is present after LDN. This does not impact on immediate surgical complications but may impair

OS160 INCREASE IN 24-HOUR PROTEIN EXCRETION IMMEDIATELY AFTER DONATION IS ASSOCIATED WITH DECREASED FUNCTIONAL RECOVERY IN LIVING KIDNEY DONORS

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Background: In this study we evaluated the occurrence of proteinuria in living kidney donors during the immediate postdonation period, aiming to determine its clinical significance in renal function recovery.
Methods: We enrolled living kidney donors with predonation protein excretion rate (PER) < 150 mg/24 h. Participants were divided into two groups according to immediate postdonation PER (4 days after nephrectomy): non-microproteinuria (non-mPr; PER < 150 mg/24 h), $n = 244$; and immediate postdonation microproteinuria (ImPr; PER ≥ 150 mg/24 h), $n = 605$.
Results: Estimated glomerular filtration rate (eGFR) did not differ significantly between groups immediately after nephrectomy but was consistently lower in the ImPr group 1 week to 1 year postdonation (1-year postdonation eGFR: ImPr group, 63.6 ± 12.1 mL/min/1.73 m²; non-mPr group, 68.6 ± 12.3 mL/min/1.73 m²; $p = 0.001$). Immediate postdonation microproteinuria was an independent predictor of eGFR at 1 year postdonation (β (SE) = -2.68 (1.15), 95% CI -4.94 to -0.42, $p = 0.02$), along with predonation eGFR, age, and sex. Immediate postdonation microproteinuria was more common in donors who were older or male and occurred in 71.3% of kidney donors, suggesting renal injury in this period.
Conclusion: Although proteinuria generally resolves, its impact persists and can impair renal function recovery. Donors who are older and male are more likely to undergo immediate hyperfiltration after donation.

Table 2. Logistic regression analysis of factors predicting immediate post-donation hyperfiltration

	Univariate analysis			Multivariable analysis		
Independent Variable	β	OR (95% CI)	p-value	β	OR (95% CI)	p-value
Age	0.040	1.041 (1.027~1.055)	<0.001	0.060	1.062 (1.044~1.080)	<0.001
Gender (base=male)	-0.395	0.674 (0.497~0.914)	0.011	-0.871	0.418 (0.289~0.606)	0.004
Predonation eGFR(MDRD)	0.001	1.001 (0.993~1.009)	0.772			
Predonation PER	0.008	1.008 (1.001~1.014)	0.015			
Systolic BP	0.011	1.011 (1.000~1.022)	0.047			
Hemoglobin	0.101	1.106 (1.002~1.221)	0.046			
T. chol	0.008	1.008 (1.003~1.012)	0.001			
LDL chol	0.008	1.008 (1.003~1.014)	0.003			

OS161 PROPHYLAXIS OF WOUND INFECTIONS - ANTIBIOTICS IN RENAL DONATION (POWAR) STUDY: A MULTICENTRE UK DOUBLE BLINDED PLACEBO CONTROLLED RANDOMISED CONTROLLED TRIAL

Zubir Ahmed[1], Raphael Uwechue[1], Pankaj Chandak[1], Nicos Kessaris[1], Carolynn Hemsley[2], David vanDellen[3],Jamie Barwell[4], Laszlo Szabo[5], Sarah Heap[6], Jonathon Olsburgh[2], Nizam Mamode[2]
[1]Guy's and St Thomas NHS Foundation Trust; [2]Guy's and St Thomas' NHS Foundation Trust; [3]Dept of Renal and Pancreas Transplantation, Manchester University NHS Foundation Trust, Manchester, UK.; [4]Renal Transplant Unit, Derriford Hospital, Plymouth Hospitals NHS Trust; [5]5Department of Nephrology & Transplant Surgery, University Hospital of Wales, Cardiff & Vale University Health Board; [6]Renal Transplant Unit, St. George's Hospital, London, United Kingdom.

Background: Postoperative infection following hand assisted laparoscopic donor nephrectomy (HALDN) confers significant morbidity to a healthy patient group. This UK NIHR funded trial assessed if a single preoperative antibiotic dose could reduce post HALDN infections.
Methods: Eligible donors in 5 UK Transplant centres were randomly and blindly allocated to preoperative single dose intravenous co-amoxiclav or saline. The primary composite endpoint was clinical evidence of any postoperative infection at 30 days with pre defined criteria for surgical site infection (SSI), urinary tract infection (UTI) and lower respiratory tract infection (LRTI). The study aimed to detect a 10% or greater reduction in the primary endpoint with 90% power (α 0·05). All analyses were by intention to treat (ITT).
Findings: 293 participants underwent HALDN (148 antibiotic arm and 145 placebo arm). 99% (291/293) completed follow up. The total infection rate was 42·1% (61/145) in the placebo group and 26·4% (39/148) in the antibiotic group ($p = 0·005$). Superficial SSIs were 20·8% (30/45) in the placebo group vs 10.1% (15/148) in the antibiotic group ($p = 0·012$). LRTIs were 9% (13/145) in the placebo group and 3.4% (5/148) in the antibiotic group ($p = 0.046$). UTIs were 7.6% (11/145) in the placebo group and 7.4% (11/148) in the antibiotic group ($p = 0.96$). Adverse events occurred in 22 patients per group (14·7% (antibiotic) vs 15·2% (placebo), $p = 0·54$). Overall antibiotic prophlaxis conferred a 17.7% absolute risk reduction, with 6 patients requiring treatment to prevent one infection. Furtermore kaplan meier analysis demonstrated reduction in the rate of early and late postoperative infections (LR test $p < 0.001$).
Interpretation: The administration of a single preoperative antibiotic dose is safe and confers significant reduction in the risk of developing postoperative infection following HALDN. Surgeons performing HALDN should institute antibiotic prophylaxis as a routine component of their practice.

OS162 WHAT MEDIATES SOCIOECONOMIC INEQUITY IN ACCESS TO LIVING-DONOR KIDNEY TRANSPLANTATION? RESULTS FROM A MULTICENTRE CASE-CONTROL STUDY

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Background: A living-donor kidney transplant (LDKT) is the best treatment for most people with kidney failure, but there is evidence of socioeconomic inequity in access. We aimed to identify variables that mediate the described socioeconomic inequity and are amenable to intervention.
Methods: We undertook a case-control study at 14 UK renal units. Cases were LDKT recipients and controls deceased donor kidney transplant (DDKT) recipients. We posted questionnaires to adults transplanted at the centres between 1/4/13-31/3/17. We collected data on potential mediators identified in qualitative work: perceived social support (ISEL-12), patient activation (PAM13), and transplant knowledge (R3K-T), and patient demographics. We performed multivariable logistic regression to look at the association between the measured variables and receipt of a LDKT, and mediation analyses to investigate what proportion of the effect of socioeconomic position on case-control status was mediated by each variable.
Results: 1239 questionnaires were returned (39%). Receiving a LDKT over a DDKT was associated with higher levels of social support (OR per + 1 ISEL-12 score 1.06, 95%CI 1.04-1.09), higher levels of patient activation (OR per + 1 PAM level 1.36, 95%CI 1.28-1.45), and greater transplant knowledge (OR per + 1 point R3K-T score 1.57, 95%CI 1.48-1.67).

People with higher socioeconomic position were more likely to receive a LDKT: OR per £1000 increase in income OR 1.14, 95%CI 1.11-1.17. Mediation analyses revealed that the following mediated the socioeconomic inequity:

- social support (% of total effect mediated (TEM) 21.1, 95% CI 17.5-24.6);
- patient activation (%TEM 5.6, 95% CI 4.8-7.0)
- transplant knowledge (%TEM 43.3, 95% CI 35.8-56.0).

Conclusions: There is evidence that the variables of transplant knowledge, social support and patient activation are mediators of the well described UK socioeconomic inequity in access to LDKTs. The next step is to trial interventions that target these.

OS163 THE CHANGING DEMOGRAPHIC OF UNSPECIFIED KIDNEY DONATION IN THE UK

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[1]Xxxxxxx; [2]Guy's and St Thomas' NHS Foundation Trust; [3]University of Warwick; [4]NHS Blood and Transplant

Introduction: Unspecified kidney donation (UKD) is still a relatively new practice that remains illegal in many parts of the world. The BOUnD (Barriers and Outcomes in Unspecified Donation) study is a national UK study aiming to comprehensively assess the practice of UKD and compare it to specified kidney donation (SKD). This analysis compares current demographic trends with UK data published from the early years of UKD, when the practice was in its infancy.
Methods: Along with demographic questions, both specified (SKDs) and unspecified kidney donors (UKDs) were asked about other altruistic behaviours and their motivations to donate.
Results: 418 donors were recruited to the study between January 2016 and October 2018 (223 SKDs, 195 UKDs). Numbers of UKDs in the UK have dropped significantly since their peak in 2014. Most significantly, the current cohort of UKDs are significantly younger than those donating between 2007 and 2013 (48.5 yrs (SD 15.58) vs 54 yrs (SD 13.58), meaning there is no longer a significant difference between the groups. Additionally, a smaller proportion of UKDs held religious beliefs (36.6% UKDs identifying as religious vs 54.5%). The data also showed no significant difference in age, gender or ethnicity ($p > 0.05$) but persistent differences in relationship and parental status ($p < 0.001$). As demonstrated previously, UKDs were significantly more likely to engage with other altruistic behaviours, such as blood donation, and being on the organ donor register ($p < 0.001$). Both groups were primarily motivated by a desire to help someone in need (SKD 160 (98.2%) vs UKD 164 (91.6%). UKDs took longer to donate than SKDs (SKD 189d vs. UKD 310d; $p = 0.013$).
Discussion: The demographic profile of UKDs is changing in the UK. UKDs are becoming younger, and a lower proportion hold religious beliefs. Concerns regarding religion as a motivator should not be of specific concern to those undertaking UKD living donor assessments.

OS21 - IT'S ALL ABOUT ETHICS!

OS164 SURVEY ON THE AWARENESS OF THE VALUE OF DONATION

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Background: In Italy around 30% of the population opposes organ and tissue donation.In the last two years the number of citizens in favor has increased due to the fact that citizens wishing to be an organ donor can declare this preference to the municipalities on the occasion of the release of their identity card.This led us to undertake an educational and fact-finding project aimed to identify the most common sources of information regarding the donation of organs and tissues in a pool of people from the general population
Methods/Materials: Over the course of 1 year we distributed to individuals within our hospital an anonymous questionnaire valid to test the level of knowledge on the possibility of donating organs and tissues and on the importance of transplantation as a life-saving therapy.Other aspects investigated are also:sources of information,the expression of personal will and the ways to declare it
Results: We obtained a pool of 772 subjects, 515 females and 257 males, over the age of 18.

1.9% of women and 2.7% of men had never heard of organ donation.

5% of women and 8.2% of men had never heard of transplantation.

The most information comes from the media,only 3.1% had been informed by the GP.

79.6% declared themselves in favor of the donation,2.9% were against it, 9% said they did not know and 8.2% had never thought about it.

53% said they knew how to express their willingness to donate but only 35% reported having done so.

Conclusion: In spite of a high percentage of subjects who considered themselves to be in favor of the donation, only a small part knew how to express their will and an even smaller percentage had done so.No gender differences were observed.

The results gathered show that there is a lack of training in GPs and highlight the necessity to optimize the educational and didactive role of the mass media to increase the number of people declaring their desire to become organ donors.

OS165 CHANGES IN BODY AND MIND: THE PSYCHO-SOCIAL CONDITION OF PATIENTS 6 MONTHS AFTER TRANSPLANTATION – A PILOT STUDY

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Background: Liver transplantation (LTx) improves the quality of life (QoL) but as a major life event, it may increase depression, anxiety, and thus a worsening of the complaince. The aim of this study was to assess the psychosocial condition of recipients 6 months after LTx (T2) with the condition on waiting list (T1).
Methods: 6 months after LTx, psycho-social status of 11 female and 6 male recipients were evaluated by Short-form 36 Questionnaire, short form of Beck Depression Inventory (rBDI), State-Trait Anxiety Inventory (STAI-S/T), Illness Intrusiveness Rating Scale (IIRS), Athens Insomnia Scale and their changes compared to value on waiting list (Δ=(T2-T1)/max$*$100) in relation with personality dimension determined by Eysenck Personality Questionnaire and demographic data. Data was analysed with SPSS 20.0.
Results: After LTx, the depression and anxiety decreased (rBDI:16→9; STAI-T/S:47→40/45→40; $P < 0.01$) and the QoL improved (physical functions: 55→7, physical role: 42→59, mood: 59→74, vitality: 50→67, general health: 32→66, $P < 0.05$). The reduction of clinically significant depression and sleeping disturbances was found by 10% and 29%. The male had higher depression (rBDI: 13.2 vs. 6.2; $P = 0.049$) and worse mood (63.3 vs. 79.3, $P = 0.029$). In those above 55 years ($n = 9$), marital and family relations were less limited by LTx (ΔIRRS: -22.2%/+14.3%, $P = 0.029$). Improving of emotional stability reduced the depression and anxiety (ΔrBDI/STAI-T/S: OR:0.720/0.513/0.527, $P < 0.05$) and increased QoL (Δphysical role/emotional role/social interaction/physical pain/mood: OR: -0.486/-0.528/-0.572/-0.584/-0.576, $P < 0.05$), predominantly in subjects with a higher level of education (OR: -0.531, $P = 0.028$).
Conclusions: The psycho-social condition and quality of life of recipients was overall improved by LTx. In spite of all this, a deterioration of psychosocial status was arisen in younger, less qualified patients, therefore this cohort's follow-up is absolutely necessary.

OS166 RESULTS OF THE BEHAVIOR TOWARDS DEATH (DEATH PROFILE) OF THE FAMILIES OF POTENTIAL ORGAN DONORS AND RECIPIENTS

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Background: One of the most difficult situations that the Potential Organ Donors and Recipient families are facing is death. Families are saddened and need significant support. This is considered one of the most painful forms of mourning, because it is unexpected and often sudden.
Method/Material: An interventional study was conducted, monitoring at a specific time the beliefs, values and culture of the Potential Organ Donors and Recipient family as a catalyst for transplantation. The tool used to collect the data is Death Profile.
Results: From the participants' responses, 62% ($n = 31$) of the participants agreed or fully agreed that death was without doubt a morbid experience, 44% ($n = 22$) agreed or fully agreed that the prospect of their own death creates anxiety and similarly 40% ($n = 20$) agreed or totally agreed that they were disturbed by the certainty of death. In addition, 34% ($n = 34$) agreed or fully agreed that they had a strong fear of dying, 36% ($n = 18$) agreed or totally agreed that the issue of life after death is a matter of great concern the 32% (v = 26) agreed or totally agreed that the fact that death means the end of all things frightens them.
Conclusion: From the analysis of the data it was observed that the participants primarily adopt an attitude of fear and avoidance towards death while to a lesser extent adopt an attitude of escape, neutral acceptance or acceptance of death. Conclusions on the dimensions of death behaviour have shown that there is a significant difference based on the level of education of the participants in avoiding, accepting and escaping behaviours. The results showed that those who were graduated compulsory level education were less likely to adopt avoidance-avoidance behaviours than those who held a postgraduate or doctoral degree. Therefore, with the right information, knowledge and awareness, there will be a change of attitude and behaviour of the families and the donors or recipients.
Keywords: behavior, families, potential

OS167 OPO AGGRESSIVENESS INDEX: A NOVEL OPO PERFORMANCE METRIC THAT INCENTIVIZES PURSUIT OF MARGINAL DECEASED DONOR CANDIDATES IN THE UNITED STATES

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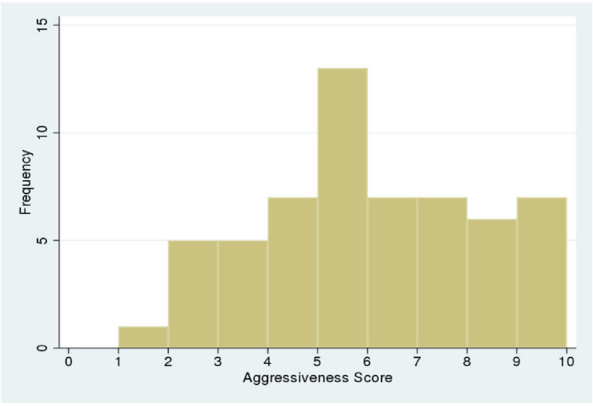
Of 2.5M deaths in the US every year, only 10,000 are classified by Organ Procurement Organizations (OPOs) as "consented eligible deaths"; recovery of organs from older donors is rare although similar donors are routinely used in Europe. Current policy and metrics used to evaluate OPO performance may disincentivize OPOs from pursuing marginal donor candidates. We present an OPO aggressiveness index to identify OPOs that aggressively pursue marginal kidney donors.
Methods: Using SRTR data 2013-2017, we evaluated the proportion of eligible deaths in each OPO that fell into one of 7 categories of "marginal donor candidate" (age > 60, BMI > 35, KDPI > 85%, serum creatinine > 2) and evaluated correlation between these proportions and deceased donors per 1000 total deaths in each OPO in 2015 ("overall donor rate"). We used decile scores of four of these categories (age > 60, BMI > 35, KDPI > 85%, SCr > 2) to construct an index of OPO aggressiveness ("aggressiveness score"), and compared this and current OPO performance metrics to overall donor rate.
Results: Of 7 categories of marginal donor candidate, four were correlated with total death rate ($r > 0.2$). The OPO aggressiveness score demonstrated substantial variation between OPOs (Figure). OPO aggressiveness score was more strongly correlated with overall donor rate ($r = 0.37$) than were the standard OPO performance metrics of standardized donation ratio ($r = 0.24$), organs transplanted per donor ($r = 0.29$), or observed: expected ratio ($r = 0.35$).
Conclusions: OPOs differ in their willingness to classify marginal donor candidates as "eligible deaths". Our results suggest that OPOs that are more aggressive in pursuing marginal kidney donors have more deceased donors available for transplant as a percentage of total deaths. Altering OPO performance metrics to incentivize aggressive classification of eligible deaths may expand the deceased donor pool in the United States.



OS168 LIVING DONORS IN JORDAN; ALTRUISM REWARDED WITH FORGETFULNESS

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Introduction: Living donors endure several challenges throughout the organ donation process. The physical-related effects are further compounded by social and emotional challenges. There have been no previous studies that addressed the motives and the impact of organ donation on living donors in Jordan.
Methodology: We conducted a qualitative exploratory study to understand the experience of a random sample of living genetically and legally related donors in Jordan. Participants were identified through the Directorate of the Jordanian Center for Organ Transplantation database. Our sample included Jordanians and non-Jordanians who donated a Kidney or liver. Data were collected by phone interview with living donors. Donors were asked about their experiences during the periods before and after the process of donation including their feelings, emotions and motives. Interviews were analyzed using thematic analysis approach.
Results: 125 donors (kidney $n = 118$, liver $n = 7$)(Jordanians $n = 107$,non-Jordanians $n = 18$) completed the interview. The time of the donation ranged from 14 days and 7 years before the interview. Pre-donation period was characterized by fear and confusion. After donation, the majority of donors described positive emotional state that was marked by self-satisfaction, pride and increased support of organ donation. However, many of them stated the feel of forgetfulness. The majority of donors were motivated by social solidarity and others invoked the role of their religious beliefs as the main motive. Other motives included improving the recipient life and fear that patients will be abandoned.
Conclusion: The emotional suffering of living donors during the pre-donation period emphasizes the need for social and psychological support in addition to medical evaluation. Donors who had post-donation positive experience can play a role in advocating donation. Finally, in Jordan the social solidarity and religious beliefs are the most important factors that motivate the donation.

OS169 MANDATORY REPORTING OF TRANSPLANT TOURISM

David Matas
David Matas

Background: The advent of legislation penalizing extra-territorial complicity in organ trafficking raises the question whether this legislation is enforceable without mandatory reporting by health professionals to state authorities of the transplant tourism of their patients. The Council of Europe Convention against Trafficking in Human Organs, which obligates states parties to enact extra-territorial legislation prohibiting complicity in organ trafficking, does not impose a requirement that the legislation include mandatory reporting.
Methods/Materials: The paper would consider mandatory reporting which already exists in other areas - for instance for gunshot wounds or child abuse.

The Canadian Senate enacted an extra-territorial prohibition against complicity in transplant tourism with a provision on mandatory reporting which the House of Commons then removed. The insertion and then removal of the reporting requirement led to substantial debate about mandatory reporting which the paper would canvass.

Israel, which has enacted extra-territorial legislation prohibiting complicity in transplant tourism, does not have mandatory reporting, but has instead allows health officials to examine medical records of organ recipients. This system allows the officials to gather information about transplant tourism. The paper would assess this mechanism as an alternative to mandatory reporting.
Results: Mandatory reporting need not breach medical patient confidentiality. Even reporting with identities disguised would give at least statistical information.

Mandatory reporting which includes identify information need not lead to the prosecution of patients. The prohibitions could target only intermediaries. Prosecutorial discretion could prevent prosecution of patients.
Conclusion: The fact that there is nothing much in the way of voluntary reporting systems indicates the need for mandatory reporting systems. Without mandatory reporting, we get caught

OS170 THE ETHICS OF ORGAN PROCUREMENT POLICIES: MODELS OF CONSENT, PERSONAL AUTONOMY AND THE ROLE OF THE FAMILY

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Background: The goal of this study is to offer an overview of the different models of consent for deceased organ donation, to clarify the role that family can take in the decision-making process, and the different understandings of autonomy behind each system.
Methods: A systematic description of all systems of consent is provided according to three variables: (1) the deceased's preferences regarding organ donation after death, (2) the roles families are allowed to play in the decision-making process of organ procurement, and (3) the default option when no preferences have been expressed by the deceased. An analytical discussion is carried out on the underlying models of autonomy for each model. Finally, we identify ethical issues related to personal autonomy, policy defaults or *nudges*, and family's involvement.
Results: We identify 4 levels of family involvement (no role, witness, surrogate and full decisional capacity) and 10 models of consent (deceased's wishes only, deceased's wishes prevail, deceased's wishes or agreement, agreement only, family's wishes or agreement, family's wishes prevai, family's wishes only, refusal prevails, consent prevails, and default only). Some models give more importance to the preferences of the deceased than to those of the family, while others do the opposite.
Conclusion: Policy decisions about models of consent deal with competing interests between respecting prospective donors and benefiting patients on the waiting list. These compromises are informed by concerns on public trust and the family preferences are a key element of ensuring that organ procurement is not perceived as an abuse of authority. Each jurisdiction deals differently with these tensions depending on historical and cultural

OS171 IT'S TIME TO STOP FREE-RIDING AND PROMOTE SOLIDARITY — WHY THE PRIORITIZATION OF RECIPROCITY IN TRANSPLANT ALLOCATION IS NOT ONLY PERMISSIBLE, BUT MORALLY IMPERATIVE

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Background: Germany's system of organ donation attracted attention recently when the Federal Minister of Health Jens Spahn re-introduced a pivotal question of deceased organ donation (DOD) to the political agenda: Should the donation process continue to require explicit consent with «NO» set as the default answer, or should we change that default to a «YES» and treat all non-objectors as consenting? Aiming for an increase in donation numbers, Jens Spahn suggested a switch to the latter, and rightly so. If it is morally acceptable to assume a default attitude of non-free-riding regarding lifeboat services like transplant medicine, shifting the administrative burden onto those who reject this attitude seems acceptable. Those who prefer to object to DOD could still do so at the mere price of having this attitude registered somewhere. So all would be fine, wouldn't it?
Methods: By mobilizing a liberal ethical framework and by insisting on our personal authority regarding our bodily remains, I'll provide evidence why such a solution is still falling short.
Results: It remains unsatisfactory as it continues to (i) exempt free-riders from the negative consequences of their choices by (ii) granting equal access to transplants despite unequal participation in donation, and thereby (iii) exploiting consenters by non-posteriorizing those who do not share the potential burden of providing the bottleneck resources for transplant medicine.
Conclusion: To heal this defect, I will argue in favor of two things, resulting in some kind of «club model solution»: a general posteriorization of objectors as default allocation and an individual option to exempt objectors from such posteriorization regarding one's own potential donation. According to this account, organs should not be viewed as a public resource and the state should respect the individual's authority to decide what should happen with his or her body after death – not only for the given reasons, but also for the greater good.

OS22 - HEART TRANSPLANTATION

OS172 OUTCOMES OF ECMO IMPLANTATION AFTER HEART TRANSPLANTATION

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Purpose: to estimate a number of patients who were supported with extracorporeal membrane oxygenation (ECMO) early-term after heart transplantation (HTx) and their outcomes.
Methods: From January 2010 to February 2019 it was performed 114 HTx (47 ± 14 years-old, $n = 84$ – male), 12% ($n = 14$) of them underwent mechanical circulatory support (MCS) implantation prior to HTx: ECMO ($n = 7$), Berlin Heart EXCOR ($n = 8$). We retrospectively analyzed post-transplant data.
Results: Early-term after HTx ECMO was implanted in 8% ($n = 9$) recipients (29 [20;66] year-old, $n = 5$ - male) due to right heart failure (RHF), duration on support was 15,5 [1;42] days. Causes of heart failure were IHD ($n = 4$), DCM ($n = 3$), HCM ($n = 1$) and cardiac sarcoidosis ($n = 1$). Three of them were supported with MCS prior to HTx: EXCOR ($n = 1$, female) and ECMO ($n = 2$: 1 – male). Seven of them died less than 3 months after HTx due to RHF, infectious complications ($n = 5$), bleeding ($n = 1$), mesenteric venous thrombosis ($n = 1$). Three from nine ECMO supported recipients underwent tricuspid valve repair due to severe tricuspid valve regurgitation. All of them were treated with inhaled NO, 67% – with Levosimendan and 44% – with Sildenafil. Before HTx PADP (27 [24;29] vs. 19 [13;25] mm Hg, $p = 0,02$) in these patients were worse in compare with others but results of PASP, PVR were comparable with others. There were correlations between ECMO implantation and post-HTx duration on respiratory support ($r = 0,506$; $p < 0,001$), 30-day ($r = 0,612$; $p < 0,001$) and long-term mortality ($r = 0,374$; $p < 0,001$), donors' gender ($r = -0,334$; $p < 0,001$) and donor/recipient mismatch ($r = 0,339$; $p < 0,001$). We did not find any difference of recipients' and donors' ages and recipients' gender ($p > 0,05$).
Conclusion: Possible factors of RHF development with following ECMO implantation are donors' gender and donor/recipient mismatch. There was a high mortality in post-transplant recipients supported with ECMO due to RHF. In 5 from 7 patients causes of death were infectious complications.

OS173 THE OBSESSION ABOUT ANTICOAGULATION IN LVAD PATIENTS: IS TTR USEFUL TO REDUCE THE RISK OF PUMP THROMBOSIS?

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Background: Anticoagulation is crucial to prevent pump thrombosis and stroke in patients with left ventricular assist devices (LVAD). Data from large registries showed that INR < 2 and low doses of aspirin are associated with a significant risk of thrombosis; however, the time in therapeutic range (TTR) of anticoagulation is poorly reported. The aim of our study is to investigate the role of a tight control of anticoagulation on pump thrombosis through TTR assessment.
Methods: All LVAD patients (pts) coming at our outpatient Clinic between 2016-18 whose anticoagulation was managed by our Hospital were included. We collected prospectively data about INR, aspirin and TTR (Rosendaal's method) during all follow up. The primary endpoint was the 2-yrs combined incidence of pump thrombosis and ischemic stroke, collection of TTR values was censored at endpoint occurrence. A low dose of aspirin was considered as ≤100 mg/day
Results: Among 16 pts (15 HVAD, 1 Heartmate-III; 6 bridge to transplant, 9 destination therapy, 1 bridge to recovery), INR was controlled every 7.2 ± 3.0 days; mean TTR was 73.1 ± 10.7%. 3 events occurred (2 pump thrombosis, one ischemic stroke); INR was > 2 in all cases. A TTR < 80% (highest quartile) led to an higher incidence of the endpoint (33.3 ± 16.1% vs 0%, $p < 0.001$). No major bleedings occurred in pts with TTR > 80%. Low aspirin dose didn't predict the endpoint. Looking at the data retrospectively, TTR was numerically lower in pts having a previous thrombotic event (60.6 ± 15.7% vs 75.9 ± 12.1%, $p = 0.08$). Controlling INR less frequently than every 7 days seemed to influence slightly the achievement of a TTR > 80% (12.5 vs 37.5%, $p = 0.2$).
Conclusions: This small single center study, while confirming that pump thrombosis and stroke occur frequently in LVAD patients despite tight anticoagulation control, seems to suggest that a TTR > 80% may be helpful in reducing this devastating complication and bleeding risk. Larger studies are needed.

OS174 WHAT WILL HAPPEN TO A BRAINLESS HEART?

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Introduction: Brain injuries are usually followed by serious cardiac complications that increase the mortality rate of inflicted patients. Neurogenic cardiac injury is caused by catecholamine surge and neuro-inflammatory responses instigated by brain damages. Neurogenic Stunned Myocardium (NSM), induced by local release of norepinephrine from sympathetic nerve terminals in myocardium after subarachnoid hemorrhage (SAH), is specified with increase or decrease in blood pressure, abnormal electrocardiogram (ECG), cardiac arrhythmias, increased rates of heart injury biomarkers and left ventricle dysfunction.
Materials and methods: For this purpose, we studied all brain dead cases transferred to Masih Daneshvari hospital organ procurement unit (OPU), Tehran, Iran, with respect to their cardiac evaluations from November 2018 to February 2019. These evaluations did include a base ECG, heart injury biomarkers, B-type natriuretic peptide (BNP), heart echocardiogram and in some cases (not all) a myocardium biopsy scrutinized by a pathologist. We considered and excluded cofounding events (e.g. history of previous cardiac dysfunctions, cardiopulmonary resuscitation, other traumatic heart injuries and possibility of propofol infusion syndrome) to exclusively analyze the recently induced complications attributable to brain death.
Results: 52 cases (31 male, 59.6%) were studied for cardiac complications. The most common casualty was ECG abnormalities (53.8%). Pathologic BNP alterations (40.3%), Elevation of cardiac troponin I (cTnI) in (34.6%) and Impaired LV contractility, hyperkinesia, and low ejection fractions were observed in total 15 cases (28.8%). In addition myocardial biopsy showed different patterns of cardiomyopathy in 8 cases (15.3%). Female gender showed significantly more sequelae fallowed by brain death (66.6% vs. 41.9% and P-value = 0.02)
Conclusion: Neurogenic Stunned Myocardium remains a major hold on for increasing donor pool for cardiac transplantation

OS175 OUTCOMES OF MECHANICAL CIRCULATORY SUPPORT IMPLANTATION IN HEART TRANSPLANTATION WAITING LIST

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Almazov National Medical Research Centre

Purpose: to estimate outcomes of patients bridged to heart transplantation (HTx) with mechanical circulatory support (MCS).
Methods: From January 2010 to February 2019 we included 212 patients in HTx waiting list (HTx WL; 74% - male): 54% (n = 114) of them underwent HTx, 22% (n = 46) - died, 4% (n = 9) – refused, 10% (n = 21) – improved and were excluded from HTx WL and 2% (n = 5) – were excluded due to contraindications. We analyzed HTx WL and post-transplant data.
Results: Prior to HTx 13% (n = 27) of patients underwent MCS implantation. Before HTx 20 patients (37 ± 17 years-old, 70% - male) were supported with extracoproreal membrane oxygenation (ECMO): 7 of them died on support, 3 – were switched to biventricular assist devices (BiVAD) Berlin Heart "EXCOR" (n = 1 – HTx), 2 – were switched to new left ventricle assist devices (LVADs: "AVK-N", "STRIM CARDIO"), 7 (n = 1 - was supported with EXCOR prior to HTx) – underwent HTx and 2 – improved and were excluded from HTx WL. Only 3 from 7 patients survived more than 1 month after HTx, others died from right or biventricular heart failure, stroke or infectious complications. So ECMO implantation was an effective "bridge" to transplant or to recovery in 55% (11 from 20) of patients. BiVAD "EXCOR" prior to HTx was implanted in 5% of patients (n = 10; 26 (16-41) years-old; 6 – male; duration on support – 186 (11-301) days): 8 of them were heart transplanted, 2 - died. Two recipients bridged with EXCOR died in early-term after HTx due to pulmonary embolism and infectious complications and 3 - in long-term due to chronic rejection, cardiac allograft vasculopathy. Two patients (16 and 35 year-old male) underwent LVAD implantation (duration on support – 274 and 39 days) and wait for HTx.
Conclusion: Using MCS is an effective treatment of end-stage heart failure as a "bridge" to HTx or recovery in 55% of patients due to ECMO implantation and in 60% - due to EXCOR. And 45% of patients bridged with ECMO died in HTx WL and 20% - bridged with EXCOR.

OS176 SHORT-TERM MECHANICAL CIRCULATORY SUPPORT AS BRIDGE TO HEART TRANSPLANTATION

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Background: Patients (P) with refractory cardiogenic shock have high short-term mortality, requiring hemodynamic support to access a heart transplant. Short-term mechanical circulatory support devices (STMCS) allow bridge to transplantation (BTT). This study aims to describe clinical characteristics and outcomes between P assisted with levitated centrifugal pump (CP) or extracorporeal membrane oxygenation (ECMO) as BTT.
Methods: STMCS used as BTT between 2006 and 2018 were evaluated retrospectively. Categorical parameters were provided as numbers and percentages, continuous data as mean ± standard deviation. Survival was depicted using Kaplan–Meier method and groups were compared using the log-rank test. A p value < 0.05 was considered statistically significant.
Results: STMCS were used as BTT in 38 P, 30 P (79%) underwent transplantation and 7 P (18,4%) were declare futile on support. Among the 15 P on ECMO, 14 (93,3%) received a heart transplant, whereas 16 P (69.5%) of the 23 P in CP were transplanted. Overall mean time on support until transplantation was 11,38 ± 16,36 days. P on CP were more frequently reoperated for bleeding (11 P 47,8% vs. 0 P; p = 0.01), required more blood products (48,35 ± 32,08 vs 22,33 ± 32,47; p = 0,04) and presented more acute kidney injury during support (15 P 65,2% vs 3 P 20%; p = 0,04). Post-transplant overall mortality was 23,3% (7 P) and there were no differences between ECMO and CP regarding this or other outcomes. In the multivariate analysis, independent predictors of mortality were acute kidney injury on MCS, post-transplant vasoplegic syndrome and time in intensive care unit.
Conclusions: Short-term MCS as BTT are an effective approach in a developing country, allowing successful transplantation in the majority of cases. P on ECMO had fewer reoperations for bleeding, transfusion requirements and acute kidney injury without differences in post-transplant mortality or other complications. We need further research in this area.

OS177 OUTCOMES OF PATIENTS WITH INFECTION RELATED TO VENTRICULAR ASSIST DEVICE AFTER HEART TRANSPLANTATION

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Background: Despite significant advances in durable mechanical support survival, infectious complications remain the most common adverse event after the perioperative VAD period and the leading cause of early death after transplantation. In this study, we aim to describe our local infectious epidemiology in a contemporary VAD population bridged to transplantation (BTT), present short term survival and infectious incidence rates in the post transplantation period and assess risk factors for infectious episodes after transplantation.
Methods: Retrospective single-center study of all consecutive adult heart transplant patients from 2008-2017. Survival data was estimated and summarized using the Kaplan-Meier method: We quantified and evaluated the difference in the incidence rate between patients with and without infection using a Fine-Gray model. The outcome of interest is the time to first infection diagnosis with post-transplant death as the competing event.
Results: Among 278 patients undergoing heart transplantation, 74 (26.5%) underwent LVAD implantation. Twenty-one patients (28.3%) developed an infection while supported by an LVAD. When compared to patients supported by an LVAD without a preceding infection, BMI was significantly greater (31.2 vs. 27.8 kg/m2, p = 0.03). Median follow-up post transplantation was 3.01 years. Significant risk factors for the competing risk regression for infection after heart transplantation include LVAD infection (HR 1.94, [95% CI] 1.11-3.39, p = 0.020) and recipient COPD (HR 2.14, [95% CI] 1.39-3.32, p = 0.001) when adjusted for recipient age, gender, comorbidities and body mass index.
Conclusions: Patients with LVAD-related infection had a significantly increased risk of infectious complications after heart transplantation. Further research on the avoidance of induction agents and reduced maintenance immunosuppression in this patient population is warranted.

OS178 TEMPORARY MECHANICAL CIRCULATORY SUPPORT AS A BRIDGE TO HEART TRANSPLANTATION. CLINICAL OUTCOMES BETWEEN UNI OR BIVENTRICULAR SUPPORT

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Favaloro Foundation

Background: Extracorporeal membrane oxygenation has long served as the standard of care for short-term mechanical circulatory support. It is unknown whether newer-generation temporary mechanical circulatory support (TMCS) devices afford a meaningful survival advantage over other devices. The aim of this study was to review the trends of use, support duration and clinical outcome of TMCS as a bridge to transplant strategy.
Methods: TMCS used as BTT between 2006 and 2018 were evaluated retrospectively. Twenty eight P assisted as bridge to transplant were only included. Categorical parameters were provided as numbers and percentages, continuous data as mean ± standard deviation, survival was depicted using Kaplan–Meier method and groups were compared using the log-rank test. A p value < 0.05 was considered statistically significant.
Results: TMCS were used as BTT in 9 P as univentricular (Uni) and 19 as biventricular (Biv) support. The mean age was 46.5 ± 17.62, 16P (57.1%) were men, and dilated cardiomyopathy was the main aetiology (12P, 42.8%). Mean time in TMCS was 12.5 ± 17.8 days, P on Biv required more blood products transfusion (57.1 ± 32.6 vs. 27.5 ± 15.2 units; p = 0.05) without differences in acute kidney injury, mechanical ventilation length or vasoplegic syndrome compared with Uni. Seventeen p were transplanted, six were declared futile and five died during support. After heart transplantation, overall mortality was 23.5% (4 P) and there were no statistical significant differences between uni or biventricular support regarding this or other outcomes.
Conclusions: The use of temporary mechanical circulatory support devices have raised rapidly in recent years, led by the growth of magnetically levitated centrifugal flow pumps. This kind of support can be used to bridge patients with cardiogenic shock towards transplant. Continued surveillance of outcomes is critical to improving patient selection and decreasing adverse events in patients with advanced heart failure.

OS179 SUPERIOR LEFT VENTRICULAR FUNCTION AFTER SIX HOURS OF PRESERVATION WITH OXYGENATED MACHINE PERFUSION AT 20°C COMPARED TO STATIC COLD STORAGE IN PORCINE DONOR HEARTS

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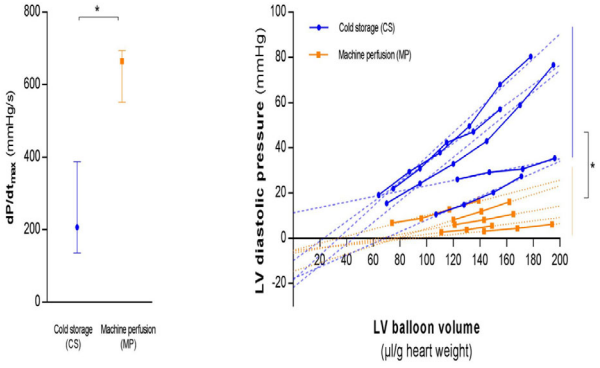
Background: Machine perfusion (MP) of donor hearts is becoming clinical reality. We evaluated the metabolic and functional effect of 6 hours of MP at 20°C on porcine hearts in comparison to 6 hours of cold storage (CS), the current clinical standard.
Methods: Pig hearts were harvested following cardioplegia and stored for 6 hours using either cold storage [CS, $n = 5$] or oxygenated MP at 20°C [MP, $n = 5$]. After preservation, hearts were reperfused using a Langendorff system. Biochemical parameters including myocardial oxygen consumption (MVO_2) and lactate production were analyzed. Flow parameters and heart weight were registered. Functional evaluation was performed using a balloon in the left ventricle (LV).
Results: There were no significant differences for MVO_2 ($p = 0.69$), veno-arterial lactate difference ($p = 0.10$), or coronary flow ($p = 0.55$) between both groups. 75 minutes after onset of reperfusion, developed LV pressure (P_{dev}) was significantly higher in MP (125.6 mmHg [106-128] vs 60.7 mmHg [43-80] for CS, $p < 0.01$). Maximum rate of pressure change, dP/dt_{max}, was significantly superior in MP (769.3 mmHg/s [708-816] vs 381.5 mmHg/s [292-537] for CS, $p < 0.01$). The diastolic elastance was significantly lower in MP at 75 min after onset of reperfusion (0.10 mmHg/µl [0.07-0.17] vs 0.43 mmHg/µl [0.19-0.51] for CS, $p < 0.05$).
Conclusion: MP at 20°C for 6 hours resulted in a greater functional recovery of the left ventricle of the porcine heart graft compared to 6 hours of cold storage, as shown by a higher developed pressure P_{dev}. There was significant superiority in both diastolic function, with a lower diastolic elastance, as well as systolic function, reflected by the higher dP/dt_{max}. MP at 20°C could offer safe and possibly superior storage of hearts for transplantation.



OS23 - DIABETES, CALCIUM AND NUTRITIONAL STATUS IN KIDNEY TRANSPLANTATION

OS181 RISK FACTORS OF HYPERCALCEMIA AFTER KIDNEY TRANSPLANTATION

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Background: Kidney transplantation (KT) is the best choice for patients with end-stage kidney disease (ESKD) because KT improves complications of ESKD and patient's outcomes. However, complications of ESKD after kidney transplantation are not all solved, and one of them is hypercalcemia. The purpose of this study was to identify the risk factors of hypercalcemia after KT.
Methods: One thousand eighty kidney transplant recipients was enrolled in multicenter observational cohort study (KNOW-KT) between July 2012 and August 2016. Nineteen patients with parathyroidectomy before KT excluded. Nine hundred forty-eight patients with calcium and albumin level at pretransplant and 1 year after KT were reviewed. Hypercalcemia was defined as albumin-corrected calcium $\geq$ 10.2 mg/dL.
Results: Serum corrected calcium level (mg/dL) at pre-transplant and 1 year after KT were 8.83 $\pm$ 0.88 and 9.22 $\pm$ 0.61, respectively ($p < 0.001$). Parathyroid hormone (PTH) level (pg/mL) at pre-transplant and 1 year after KT were 275.2 $\pm$ 268.7 and 86.3 $\pm$ 66.5, respectively ($p < 0.001$). Percentages of hypercalcemia at pre-transplant and 1 year after KT were 5.5 and 7.0, respectively($p < 0.001$). However, PTH level (pg/mL) at 1 year after KT between patients with and without hypercalcemia at 1 year after KT showed the significant difference (79.7 $\pm$ 73.4 vs. 195.1 $\pm$ 125.5 pg/mL; $p < 0.001$).

When divided into four groups using corrected calcium levels at pretransplant and 1 year, PTH levels (pg/mL) at pretransplant were 353.9 $\pm$ 269.7 in the persistent hypercalcemia group, 244.7 $\pm$ 504.9 in the improved hypercalcemia group, and 518.5 $\pm$ 350.6 in the developed hypercalcemia group. PTH levels (pg/mL) at 1 year were 242.2 $\pm$ 157.4 in the persistent hypercalcemia group, 75.2 $\pm$ 52.6 in the improved hypercalcemia group, and 176.3 $\pm$ 106.6 in the developed hypercalcemia group.
Conclusion: Hypercalcemia and high parathyroid hormone level at pretransplant were risk factors of hypercalcemia at 1 year after KT.

OS182 A RANDOMIZED STUDY COMPARING PARATHYROIDECTOMY WITH CINACALCET FOR TREATING HYPERCALCEMIA IN KIDNEY ALLOGRAFT RECIPIENTS WITH HYPERPARATHYROIDISM: 5 YEARS OF FOLLOW-UP

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Background: Tertiary hyperparathyroidism is a common cause of hypercalcemia after kidney transplant (KT). Persistent hyperparathyroidism has been associated with renal allograft calcifications and dysfunction, loss of bone mineral density and increased risk of fracture, vascular calcification, and increased risk of cardiovascular events.
Methods/Materials: A 12-month prospective, multicenter, open-label, randomized study demonstrated than subtotal parathyroidectomy is more effective than cinacalcet for controlling hypercalcemia caused by persistent hyperparathyroidism after KT. Now, we evaluate in the same cohort of patients if this effect is maintained after 5 years of follow-up. Laboratory assessment included serum calcium, serum phosphate, intact parathyroid hormone (iPTH), calcidiol levels, alkaline phosphatase, eGFR and proteinuria.
Results: At 5 years of follow-up, six of 13 patients in the cinacalcet group and ten of 11 patients in the parathyroidectomy group ($P = 0.03$) achieved normocalcemia. Subtotal parathyroidectomy maintained a greater reduction of iPTH compared with cinacalcet group. Normalization of iPTH was accomplished in 7 of 11 patients in the parathyroidectomy group versus zero of 13 patients in the cinacalcet group ($P = 0.001$). However, no statistically significant differences were observed in kidney function between both groups. In relation of treatment, 8 of 13 patients in cinacalcet group maintained treatment with cinacalcet after 5 years follow-up compared with zero of 11 patients in parathyroidectomy group ($P = 0.002$). Therefore, subtotal parathyroidectomy can be considered superior in terms of cost-effectiveness.
Conclusion: Subtotal parathyroidectomy continues to be superior to cinacalcet in controlling hypercalcemia and hyperparathyroidism in patients with kidney transplant after 5 years of follow-up.

OS183 INVESTIGATION OF FACTORS AFFECTING PERIOPERATIVE NUTRITIONAL STATUS IN KIDNEY TRANSPLANTATION

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Background: Kidney transplantation patients are doing dialysis and conservative treatment due to end stage kidney failure. It is thought that these patients have malnutrition disorders, and the perioperative nutritional status affects the postoperative prognosis.
Methods: We used Geriatric nutritional risk index(GNRI), in 106 patients who had kidney transplantation between 2008 and 2017 preoperative GNRI and postoperative 1 year GNRI were calculated and divided into two groups of malnutrition risk group(GNRI < 92) and non-malnutrition group(GNRI ≥ 92), and we examined frequency of complications and nutritional status after transplantation.
Results: There were 31 patients in the preoperative GNRI < 92 group. In these, the preoperative the serum-calcium value was significantly higher, and the serum-hemoglobin value was significantly lower for up to 1 week after transplantation. In addition, urinary tract infection, Cardiovascular disease (CVD), de novo malignant tumor occurred significantly than GNRI ≥ 92 group. Next, in the preoperative GNRI < 92 group, a similar examination was carried out by dividing it into a group in which the nutritional status was not improved even one year after the transplantation group (postoperative GNRI < 92) and improved group (postoperative GNRI ≥ 92). As a result, There were 6 cases in postoperative GNRI < 92 group. The low serum-hemoglobin value was prolonged after operation. In complications, there were significantly more

patients taking osteoporosis drugs, and glaft loss and death cases were significantly more than improved group.
Conclusion: In the preoperative malnutrition risk group, the risk of urinary tract infection and CVD becomes high, and in the group with not improvement of postoperative nutritional status, the risk of osteoporosis and graft loss cases increase. Therefore, improvement of nutritional status from preoperative was considered important in postoperative long term.

OS184 CENTRAL SARCOPENIA MEASURED BY PSOAS CROSS-SECTIONAL AREA PREDICTS POST-TRANSPLANT REHOSPITALIZATIONS IN CANDIDATES FOR A FIRST KIDNEY TRANSPLANTATION

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Background: CT scan-derived measurement of TPI (Total Psoas Index) is an objective tool for the assessment of central sarcopenia. It is a strong predictor of frailty in surgery and oncology. The aim of this study was to determine the impact of TPI on kidney transplant outcomes.
Methods: We retrospectively included 264 kidney recipients who had abdomino-pelvic CT-scan in the 3-year prior to their first transplantation between January, 1st 2007 and December, 31st 2013 at University Hospital of Montpellier (France). Total psoas index (mm^2/m^2) was measured as the cross-sectional areas of the left and right psoas muscle (TPA (mm^2)), normalized for height, at the level of L3 vertebra. Patients were classed and analyzed in TPI terciles stratified for sex.
Results: Mean TPI was 61.7 ± 12.1 mm^2/m^2 for men and 42.4 ± 14.2 mm^2/m^2 for women. Length of stay at transplantation was higher in low-TPI group compared to high-TPI group (19,71 ± 13,32 vs 15,39 ± 7,13 respectively, p = 0.01). After adjustment for age, Charlson index and delayed-graft function, this difference did not reach statistical significance. The number of rehospitalizations at one-year post-transplant and total rehospitalizations were higher in low-TPI group compared to high-TPI group (p = 0.03 and p = 0,003 respectively). In multivariate logistic regression models, small TPI was a strong risk factor for repeated rehospitalizations compared to large TPI (OR = 2,45 (1,26-4,76), p = 0,01); post-operative complications were also an independent risk for iterative rehospitalizations (OR = 1.88 (1 – 3.53), p = 0.05). Graft loss and death rate were not different between the terciles of TPI.
Conclusion: the measure of TPI seemed to be an objective and reproducible tool to assess central sarcopenia and frailty. It was associated with an increase of post-transplant morbidity.

OS185 OCCURRENCE OF DIABETIC NEPHROPATHY AFTER RENAL TRANSPLANTATION DESPITE INTENSIVE GLYCEMIC CONTROL: AN OBSERVATIONAL COHORT STUDY

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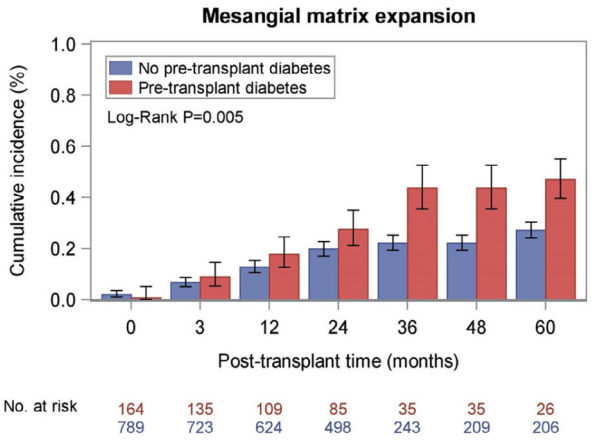
[1]KU Leuven; [2]Red Cross Flanders

Background: The kinetics and risk factors of diabetic nephropathy after kidney transplantation remain unclear. This study investigated the post-transplant occurrence of diabetic nephropathy and the contribution of post-transplant glycemic control.
Methods/Materials: In this single-center prospective cohort study, 953 individual renal allograft recipients were included, with histological data of 3458 protocol-specified renal allograft biopsies, obtained at time of transplantation and during the first 5 years after transplantation. We studied the effect of pre-transplant diabetes and post-transplant glycemic control on the histological evolution after transplantation.
Results: Prior to transplantation, diabetes was present in 164 of 953 (17.2%) renal allograft recipients, primarily type 2 (N = 146; 89.0%). Despite intensive glycemic control (glycated hemoglobin 7.00 ± 1.34% [53 ± 14.6 mmol/mol], 6.90 ± 1.22% [52 ± 13.3 mmol/mol] and 7.10 ± 1.13% [54 ± 12.4 mmol/mol], respectively at one, two and 5 years after transplantation), mesangial matrix expansion (mm) reached a cumulative incidence of 47.7% by 5 years after transplantation in patients with pre-transplant diabetes, vs. 27.2% in the absence of diabetes (Figure 1), corresponding to a hazard ratio of 1.55 (95% CI, 1.07 to 2.26; P = 0.005). The divergence of cumulative incidences was noted already by two years after transplantation. Pre-transplant diabetes was not associated with other structural changes of the glomerular, vascular or tubulo-interstitial renal compartments. The occurrence of mm was independent of post-transplant glycated hemoglobin levels.
Conclusion: Mesangial matrix expansion, an early indicator of diabetic nephropathy, can rapidly occur in patients with diabetes prior to transplantation, despite intensive glycemic control.

Figure 1. Cumulative incidence of mesangial matrix expansion over time after transplantation, according to pre-transplant diabetes state.



OS186 IMPACT OF STEROID-FREE PROTOCOL ON INCIDENCE OF POSTTRANSPLANTATION DIABETES MELLITUS: A PROSPECTIVE, RANDOMIZED, MULTICENTER, OPEN-LABEL, CONTROLLED TRIAL IN RENAL TRANSPLANT RECIPIENTS (SAILOR STUDY)

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Background: Steroid-containing, immunosuppressive therapy after renal transplantation is associated with an increased incidence of posttransplantation diabetes mellitus (PTDM). We compared steroid-free protocol with antithymocyte globulin (ATG) induction to steroid containing protocol with basiliximab induction, regarding the incidence of PTDM.
Methods/Materials: SAILOR study is an open-label, multicenter, randomized controlled trial where eligible patients received either ATG, low-dose tacrolimus and mycophenolate mofetil (MMF) (arm-A), or basiliximab, low-dose tacrolimus, MMF, and prednisolone (arm-B). Adult patients at low immunological risk, without pre-transplant diabetes mellitus, receiving single kidney transplant were included. The primary objective was the incidence of PTDM at one year. The secondary objectives included the incidence of biopsy-proven rejections (BPR), in both for cause and 1-year protocol biopsies, graft and patient survival, and renal function (m-GFR) at 2 years.
Results: A total of 222 patients were included and randomized to arm-A (N = 113) and arm-B (N = 109). The incidence of PTDM was overall low, 12.3% in arm-A vs. 18.3% in arm-B (p = 0.26) at 1 year. The incidence of all BPR was similar, 20.4% in arm-A vs. 17.4% in arm-B (p = 0.61), however acute T cell-mediated rejections (TCMR) were more frequent in arm-A 14.2%, compared to arm-B 4.6% (p = 0.02). Chronic active TCMRs occurred mainly beyond 6th months. Patient survival (99% in arm-A, 98% in arm-B) and graft survival (98% in arm-A, 98% in arm B) were excellent in both groups; m-GFR was comparable, 52.5 ± 18 ml/min in arm-A and 54.9 ± 18 ml/min in arm-B (p = 0.37). Higher proportion of patients in arm-B needed ≥ 3 antihypertensive drugs (arm-B 33% vs. arm-A 20%, p = 0.03).
Conclusion: Steroid-free immunosuppression with ATG induction and low-dose tacrolimus did not reduce the incidence of PTDM after renal transplantation, but offered good safety profile, as well as easily manageable hypertension.

OS24 - PRECLINICAL IMMUNOLOGICAL INTERVENTION STRATEGIES

OS188 HUMANIZED ANTI-IL-6 ANTIBODY ACTS ON ENDOTHELIAL CELLS TO REDUCE ANTIBODY MEDIATED COMPLEMENT ACTIVATION AND TO ALTER THEIR IMMUNOGENICITY

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Background: Interleukin-6 has been associated with allograft dysfunction both *in vitro* and in *in vivo* patient studies of antibody-mediated rejection. In the steady-state, microvascular endothelial cells produce IL-6 and this is increased under inflammatory conditions. Anti-HLA II antibody or DSA binding to endothelial cells, prior to co-culture with allogeneic PBMC, elevated IL-6 production and increased differentiation of pro-inflammatory Th17 $CD4^+$-T mediated by activation of Stat-3 (Taflin PNAS 2011, Lion Am J Trans. 2016). The ability of the humanized Interleukin-6-specific antibody (Clazakizumab) to directly act upon endothelial cells was studied.
Methods: Activation of the complement cascade (C5b-C9 detection) and of soluble factor production (ELISA assay) were tested after binding of HLA-II specific antibodies to endothelial cells and in the presence of IL-6-specific antibody. Additionally, cells were pre-incubated with IL-6-specific antibody prior to and during co-culture with allogeneic PBMC and differentiation of pro-and-anti-inflammatory $CD4^+$-T was assessed (intracellular cytokine staining and multicolour flow cytometry).
Results: We report that incubation of endothelial cells with anti-IL-6 antibody decreased IL-6 and CCL2 production in co-cultures with allogeneic PBMC. Moreover endothelial cell differentiation of pro-inflammatory Th17 and Th1 populations was reduced. Formation of the terminal complement complexe, C5b-C9, detected after HLA-II antibody binding to endothelial cells was significantly lessened when anti-IL-6-antibody was present.
Conclusions: These data reveal that anti-IL-6 antibody acts directly on endothelial cells. The combined outcomes of limiting formation of the C5b-C9 complex, reducing IL-6 and CCL2 production, decreasing pro-inflammatory Th17 and Th1 differentiation may contribute to an overall protection of the allograft endothelium in the context of chronic antibody mediated rejection associated with HLA-II specific alloantibodies.

OS189 INHIBITION OF FACTOR B REDUCES RENAL INFLAMMATION IN A RAT BRAIN DEATH MODEL

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Introduction: The majority of organs used for transplantation are retrieved from deceased braindead organ donors. In brain death, the irreversible loss of all brain function results in hemodynamic instability, hormonal changes, and immunological activation. Recently, brain death has been shown to activate the complement system, which is adversely associated with renal allograft outcome. Modulation of the complement system in the brain-dead donor might be a promising strategy to improve organ quality prior to transplantation. This study investigated the effect of an inhibiting antibody against factor B on brain death induced renal inflammation and injury.
Method: Brain death was induced in male Fisher rats by inflating a subdural balloon catheter. Anti-factor B(anti-FB) or saline was administered intravenously 30 min prior to the induction of brain death(n = 8/group). Sham-operated rats served as controls(n = 4). Blood, urine and organs were collected after 4 hours of brain death.
Results: Pretreatment with anti-FB resulted in significantly less renal complement activation in brain-dead rats. Moreover, anti-FB treatment improved renal function, reflected by significantly reduced serum creatinine levels. Furthermore, anti-FB significantly attenuated histological injury reflected by the reduced tubular injury score and renal deposition of kidney injury marker-1. In addition, anti-FB treatment significantly reduced neutrophil influx but did not affect macrophage influx. In accordance, renal gene expression of IL-6, MCP-1 and VCAM-1 were also significantly reduced after anti-FB treatment.
Conclusion: This study shows that donor treatment with anti-FB significantly improved renal function, reduced renal damage and inflammation prior to transplantation. Therefore, inhibition of the alternative pathway might be a promising strategy to reduce brain death induced renal injury in organ donors.

OS190 IGURATIMOD (T-614) INHIBITS THE DONOR-SPECIFIC ANTIBODIES (DSAS) PRODUCTION AND ATTENUATES THE ANTIBODY-MEDIATED REJECTION IN RAT KIDNEY TRANSPLANTATION

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Antibody-mediated rejection (ABMR) is now considered as the major cause of renal allograft loss. B cells are a group of diverse phenotype and function subsets, which was considered as the critical modulator in the pathogenesis of ABMR. Our study was designed to investigate the efficacy and related mechanisms of Iguratimod (T-614) in the inhibition of DSAs following kidney transplantation. A rat renal transplant ABMR model was established. Levels of de novo DSAs following skin transplant and renal transplant were detected by flow cytometry assay. Levels of Bregs (CD19 + Tim-1 +), Tregs (CD4 + CD25 + Foxp3 +), as well as the Th17 cells (CD4 + IL-17A+), in peripheral blood monocytes (PBMCs) collected from recipients were also examined. Various inflammatory cytokines, such as IL-2, IL-4, IL-10, and IL-17, were tested by ELISA assay. To further explore the mechanism involved, primary Bregs were extracted from the spleen of recipients and co-cultured with PBMCs of recipients in vitro. De novo DSAs were detected. Moreover, the Bregs and balance of Th17/Tregs were examined. We found that the administration of Iguratimod could induce the significant reduction of de novo DSAs in skin transplant and secondary DSAs following renal transplant. Moreover, the allograft function was remarkably improved in the treatment of Iguratimod. To further explore the related mechanisms, flow cytometry assay showed the significantly increased expression of Tregs, as well as the decreased expression of Th17 cells. Furthermore, our primary results from randomized controlled trials in our renal transplant center also supported the favorable efficacy of Iguratimod on decreasing the production of DSAs in sensitized renal transplant recipients, as well as the imbalance of Th17/Tregs. As a result, our study concluded that Iguratimod could significantly inhibit the production of DSAs and the progression of ABMR following renal transplant by modulating the imbalance of Th17/Treg.

OS191 BORTEZOMIB ATTENUATES THE PROGRESSION OF EPITHELIAL-TO-MESENCHYMAL TRANSITION THROUGH SMURF1/AKT/MTOR/P70S6K PATHWAY IN RAT ALLOGRAFT RENAL INTERSTITIAL FIBROSIS MODEL

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Allograft renal interstitial fibrosis was characterized by massive extracellular matrix (ECM) deposition caused by activated fibroblasts and myofibroblasts. Epithelial-mesenchymal transition (EMT) is recognized as an important source of myofibroblasts contributing to the pathogenesis of allograft renal interstitial fibrosis. Smad ubiquitination regulatory factor 1 (Smurf1) has been recently reported to be involved in the progression of EMT. Our study was to detect the effects of Bortezomib and Smurf1 in the EMT and allograft renal interstitial fibrosis. Biomarkers of EMT, as well as Smurf1, were examined in human proximal tubular epithelial cells (HK-2) treated with tumor necrosis factor-alpha (TNF-α) in various doses or at various time points by Western Blotting or qRT-PCR. We also knocked-down or overexpressed Smurf1 in HK-2 cells then detected the changes of biomarkers of EMT induced by TNF-α. Furthermore, rat allograft renal transplantation model was established and intervened by Bortezomib. Allograft renal tissues from rats were also collected and prepared for HE, Masson's trichrome, immunohistochemical staining and western blotting assays. As a result, we found that TNF-α significantly promoted the development of EMT in a time-dependent and dose-dependent manner through Smurf1/Akt/mTOR/P70S6K signaling pathway *in vivo* and *in vitro*. More importantly, Bortezomib could alleviate the progression of EMT and allograft renal interstitial fibrosis *in vivo* and *in vitro* by inhibiting the effects of TNF-α and expression of Smurf1. In conclusion, Smurf1 maybe play a critical role in the development of EMT induced by TNF-α

Conclusions: In HK-2 CELLS and allograft transplanted kidneys. Bortezomib can attenuate the Sumrf1-mediated progression of EMT and allograft renal interstitial fibrosis, which could be suggested as a novel choice for the prevention and treatment of allograft renal interstitial fibrosis.

OS192 MECHANICAL IRRITATION IN VASCULARIZED TISSUE ALLOTRANSPLANTATION TRIGGERS LOCALIZED SKIN REJECTION

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Medical University of Innsbruck

Background: "Atypical" forms of skin rejection have been described in some hand transplanted patients mainly manifesting on the palm after experiencing mechanical or thermal stress. The aim of the study is to investigate skin irritation and its effect on skin rejection after limb transplantation in rodents.

Methods: Orthotopic hind limb transplantations have been performed using male Lewis and Brown-Norway rats. Immunosuppression consisted of anti-lymphocyte serum (ALS 0.5 ml) and tacrolimus, which was individually tapered (final dose 0.1-0.2 mg/kg). Mechanical skin irritation was applied to the planta pedis of the transplanted limb using a mechanical irritation device. Irritation was performed for 10 days, four times/day for 10 minutes applying 5 Newton force. Skin biopsies were taken immediately after the last stimulation and after a five days' observational period. Samples were assessed histopathologically and protein expression was measured using luminex technology.

Results: Allogeneic transplanted + irritated animals displayed significant aggravated macroscopic skin alterations compared to naïve irritated ($p < 0.0001$) and syngeneic transplanted + irritated controls ($p = 0.0023$). Overall, histopathology showed a trend towards higher rejection/inflammation grades in allogeneic irritated animals than in syngeneic (2.3 ± 0.95 vs. 1.7 ± 0.81). After 10 days of irritation, minor skin alterations in syngeneic transplanted animals recovered quickly, however, in allogeneic transplanted animals' macroscopic features were more pronounced ($p < 0.0001$) and improved only little over the following five days without irritation. In allogeneic transplanted + irritated animals IL-1b and INF-y levels were up-regulated compared to irritated controls.

Conclusion: Standardized mechanical skin irritation in vascularized composite allotransplantation can trigger locallocalized skin alterations consistent with rejection.

OS193 DEFICIENCY OF EARLY COMPLEMENT COMPONENTS PROTECTS AGAINST BRAIN DEATH-INDUCED RENAL INJURY IN MICE

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Introduction: Brain-dead donors are still the major source of supply for renal transplantation. However, brain death is associated with hemodynamic instability, endocrine changes and a generalized inflammatory response which adversely affects the renal allograft. As part of the inflammatory response, the complement system is activated. Complement has been shown to play an important role in brain death-induced renal injury. Previous studies showed high systemic complement levels in the brain-dead donor. Therefore, the complement system might be a potential target to preserve the quality of renal allografts before organ retrieval. So far, the optimal complement therapeutic is controversial. In this study, we investigated which complement pathway is responsible for brain death-evoked renal injury.

Method: Brain death was induced in mice by inflation of a subdural placed balloon catheter. We subjected wildtype, C4-, properdin-, C3-, C5aR1- and C5aR2-deficient mice to 3 hours of brain death ($n = 8$/group). Sham-operated mice served as controls ($n = 3$/group).

Results: Renal injury and renal inflammation were significantly increased in brain death mice compared to sham-operated mice. All complement deficient mice had less renal injury, reflected by less histological injury and lower influx of infiltrating leukocytes. Furthermore, a significant upregulation of pro-inflammatory cytokines and chemokines was seen after brain death. In addition, brain death resulted in a deteriorated renal function in brain-dead mice compared to sham-operated mice. Absence of C4 significantly preserved renal function, as reflected by lower levels of blood urea nitrogen.

Conclusion: Given these results, we conclude that early complement components, especially C4, are essential in renal inflammation and injury in brain-dead mice. Therefore, complement inhibition in the brain-dead donor might be a potential therapeutic approach to diminish renal injury and inflammation.

OS194 THE EFFECTS OF AN IL-21 RECEPTOR ANTAGONIST ON THE ALLOIMMUNE RESPONSE IN A HUMANIZED SKIN TRANSPLANT MOUSE MODEL

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Background: Interleukin 21 (IL-21) is involved in regulating the expansion and effector function of a broad range of leukocytes, including T cells and B cells. In transplantation, the exact role of IL-21 in the process of allograft rejection is unknown. The aim of the present study was to test the effect of an IL-21 receptor (IL-21R) blocking antibody on allograft rejection in a humanized skin transplantation model in mice reconstituted with human T and B cells.

Methods: Immunodeficient Balb/c IL2rγ-/-Rag2-/- mice were transplanted with human skin followed by adoptive transfer of human allogeneic splenocytes. Control animals were treated with a PBS vehicle ($n = 7$) while the treatment group received humanized anti-IL-21R antibody (αIL-21R; $n = 8$). Mice were sacrificed 30 days after cellular infusion to assess skin rejection and inflammation.

Results: In control animals, human skin allografts were infiltrated with lymphocytes and developed a thickened epidermis with increased expression of the inflammatory markers Keratin 17 (Ker17) and Ki67. In mice treated with αIL-21R, signs of allograft reactivity were significantly reduced. Concordantly, STAT3 phosphorylation was inhibited in this group. Of note, treatment with αIL-21R attenuated the process of T and B cell reconstitution after adoptive cellular transfer.

Conclusions: These findings demonstrate that blockade of IL-21R signaling can prevent allograft rejection in a humanized skin transplant model and is of interest for improving clinical transplantation outcome.

OS195 RESVERATROL EXERTS CYTOPROTECTIVE EFFECTS THAT REDUCE DONOR SPECIFIC ANTIBODIES CYTOTOXICITY ON ENDOTHELIAL CELLS

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Background: Donor specific antibodies (DSA) trigger acute antibody-mediated rejection and play a major role in late allograft failure. DSA damage the transplant endothelium through complement-dependent cytotoxicity, antibody-dependent cell cytotoxicity and/or a complement independent direct effect. Resveratrol, a polyphenol with antioxidant properties, is known to exert protective effects on endothelial cells in vitro and in vivo. We hypothesized that Resveratrol could participate to endothelial cell protection against DSA aggression. Methods/materials

In a porcine model of alloimmunisation, donor porcine aortic endothelial cells (PAEC) and IgG from immunized recipients containing DSA were isolated. Complement dependent cytotoxicity of DSA on donor PAEC was evaluated in vitro with a functional test of calcein release. Quantitative PCR on reverse transcribed mRNA was performed by Taqman on PAEC.

Results: In vitro, 24 h incubation of PAEC with Resveratrol 200 μM induced a significant decrease of DSA complement dependent cytotoxicity as compared to no incubation. In these conditions, qPCR analysis showed a significant decrease of VCAM-1 mRNA expression compared to no incubation ($p = 0.0002$), an increase of HMOX1 ($p = 0.0006$), FTH1 ($p = 0.0002$), CD59 ($p = 0.019$), CD55 ($p = 0.011$) and CD46 ($p = 0.0002$) mRNA expression. The effect was dose-dependent and changes were already visible after incubation with Resveratrol at 50 μM. However, 6 or 12 hours incubation with Resveratrol were insufficient to induce changes in these molecules mRNA expression.

Conclusion: Incubation of PAEC with Resveratrol up-regulated transcription of genes coding for complement regulatory proteins (CD55, CD59, CD46) and cytoprotective molecules (HO-1, ferritin) and decreased transcription of VCAM-1 coding gene, an adhesion molecule. This protected phenotype renders EC less sensible to DSA toxicity in vitro. Resveratrol could be used in transplantation in combined strategies to reduce DSA early deleterious effects.

OS25 - KIDNEY IMMUNOSUPPRESSION-NEW ADVANCES

OS196 HOW RELIABLE ARE HLA ANTIBODY DETECTION ASSAYS UNDER IMMUNOSUPPRESSIVE REGIMENS?

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Background: Donor specific antibodies (DSA) trigger acute antibody-mediated rejection and play a major role Antibody mediated rejection (AMR) is one of the major complications after solid organ transplantation. Various studies have shown that donor specific HLA antibodies (DSA) can cause AMR and decrease graft survival. Intravenous immunoglobulins (IVIG) and/or rituximab (RIX) are commonly used to treat AMR. However, we observed an interference of IVIG with antibody detection assays when serum samples from a patient were analysed before and after IVIG treatment. Thus, we examined the effect of IVIG and RIX on Luminex mixed screen, single antigens (SA) and CDC and flow crossmatches.

After IVIG and rituximab were added (dilution 1:10) to negative patients' sera or negative and positive control sera, these sera were tested with Luminex mixed and SA, flow and CDC crossmatch assays.

In vitro treatment of negative sera with IVIG resulted in a broad pattern of reactivity in the Luminex SA and mixed screen, that were remarkably similar to our findings in the IVIG-treated patient serum. This pronounced pattern of reactivity was found with 4 different IVIG batches. However, spiking IVIG in a positive control serum did not affect Luminex assays. Also, IVIG did not affect CDC crossmatches, using 3 different donor cells, yielding a similar result as untreated serum. In contrast, RIX treatment of negative serum had no effect on Luminex assays, but gave false positive reactions in unseparated CDC and B cell flow crossmatches, using 3 different samples.

Results: Our results show that IVIG treatment interferes with Luminex assays of negative sera, but does not induce false positive crossmatches, probably because these antibodies are not complement-fixing or their titer is not high enough for CDC reactions. Similarly, our data reveal that RIX interferes with crossmatch assays, but not with Luminex assays.

Conclusions: In conclusion, these results highlight that the results of antibody detection assays must be interpreted with caution when patients recieve these immunosuppression drugs.

OS197 EVEROLIMUS BASED IMMUNOSUPPRESSION POSSIBLY SUPPRESS MFI VALUES OF DE NOVO DSA AFTER PRIMARY KIDNEY TRANSPLANTATION

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Purpose: *De novo*DSA production of EVR based immunosuppression for primary kidney transplant recipient who were involved in A1202 study from our institute was evaluated.

Methods: During March 2008 and August 2009, twenty-four recipients prospectively randomized into 2 groups. EVR group received reduced CSA (C0 25-50 ng/ml after 6 months), and EVR-C0 were adjusted 3-12 ng/ml. MMF group received standard CSA (C0 100-250 ng/ml after 6 months). Both groups received basiliximab and steroid. Flow PRA or LABScreen Mixed kits were employed for the screening. *De novo*DSA was identified in HLA antibody-positive recipients using LABScreen single antigen beads. MFI values > 1000 were considered positive. $P < 0.05$ was considered significant.

Results: Patient survival is 100% in both group and graft survival is 100% in EVR group and 90.9% in MMF group (mean observation 10.1 years). All patients are staying on primary protocol in EVR group but 3 patients (27.3%) were converted to tacrolimus due to DSA production and non-adherence. Estimated GFR was similar in both groups. None of EVR and 9.1% of MMF group was treated for clinical T cell mediated rejection. Banff borderline change on 6 or 12 months protocol biopsies were observed in 7.7% of EVR group and 18.2% of MMF group. None of EVR group revealed peritubular capillaritis while 9.1% in MMF group developed CAAMR. Luminex solid phase assay revealed accumulative class II DSA production rate of 15.4% in EVR group and 18.3% in MMF at 10 years respectively. There was no significant difference in DSA free survival between 2 groups. Mean MFI of HLA was significantly less in EVR group (average 1837 vs. 12399). When MFI cut-off level was set to 3000, DSA free survival was significantly better in EVR group.

Conclusions: EVR based immunosuppression provide quivalent clinical outcomes and possibly suppress MFI values of *de novo* DSA after primary kidney transplant at 10 years follow-up. Further follow-up is inevitable.

OS198 UGT2B17 AND GSTM1 BOTH NULL GENOTYPE SHOWED LOWER TACROLIMUS CLEARANCE IN KIDNEY TRANSPLANTATION PATIENTS

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Background: Tacrolimus is a major immunosuppressive drug with large intra-individual variability. Several pharmacogenetic studies revealed genetic determinants for intra-individual pharmacokinetic (PK) variabilities. For tacrolimus, however, only CYP3A5 genotypes are currently established as a genetic predictor. UGT2B17 and GSTM1 are known to related with various drugs of phase II drug metabolism. Yet, no study has been conducted to investigate the relationship with tacrolimus and UGT2B17 and GSTM1 copy-number variants (CNV). This study aims to investigate whether the CNV polymorphism in these genes affect tacrolimus drug PK using targeted next-generation sequencing panel.

Method: A total of 107 patients who received kidney transplantation at a single institution were enrolled. Considering the measured concentration, dosage and body-weight, the tacrolimus clearance (CL) was calculated at postoperative 1-week. Targeted pharmacogene panel (ADME-PGx panel with 114 pharmacogenes) sequencing was conducted using Illumina HiSeq 2500. CNV analysis based on coverage depth method was conducted for pharmacogenes. Patients were classified into two categories (Non-expressor: UGT2B17 and GSTM1 both null genotype, Expressor: present at least one copy of UGT2B17 or GSTM1).

Results: All patients ($n = 107$) were classified into three sub-group for Extensive metabolizer (EM), Intermediate metabolizer (IM), and Poor metabolizer (PM) by CYP3A5*3. Each group showed CL (L/h; mean ± SD) of 6.93 ± 2.04, 5.81 ± 1.56, and 4.77 ± 1.15, respectively. Statistical analysis using t-test between non-expressor and expressor in each group showed *P* values 0.332, 0.0068, and 0.0666 in the EM ($n = 8$), IM ($n = 31$), and PM ($n = 68$) group, respectively. Although the *P* values showed statistical significance only in the IM group, the mean CL in non-expressor was lower than expressor in all three groups.

Conclusion: Our study firstly showed that CNV polymorphism in UGT2B17 and GSTM1 may be associated with tacrolimus CL.

OS199 INFLUENCE OF CYP3A5*3 AND ABCB1 POLYMORPHISMS ON CHRONIC DAMAGE IN KIDNEY PROTOCOL BIOPSIES

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Tacrolimus (TAC) is the cornerstone of immunosuppresion in solid organ transplantation. Due to its narrow therapeutic window and pharmacokinetic variability, therapeutic drug monitoring is routinely applied. Implementation of pharmacogenetics may refine TAC assessment. The impact of CYP3A5, CYP3A4 and ABCB1 genetic polymorphisms on lesions in different compartments of kidney protocol biopsies has not been studied in recipients and donors.

This analysis included 258 protocol biopsies from kidney recipients (at month 6-12) treated with TAC. Biopsies were scored according Banff 2017 criteria. Chronicity score in different departments (glomerular (Cg), interstitial (Ci), tubular (Ct) and vascular (Cv) was analyzed. Inflammation in interstitial fibrosis and tubular atrophy (i-IFTA) and C4d was also recorded. Dose-adjusted TAC concentration at during the first year post-transplantation was collected. Recipients (258) and donors (205) polymorphisms of drug transport and metabolism genes were analyzed.

Renal transplant recipients with CYP3A5 non-expresser genotype (*3/*3, poor metabolizer) had double TAC dose-adjusted C0 during all follow-up compared with CYP3A5 expresser genotype (*1 carrier, high metabolizer). *3/*3 patients showed higher frequency and score of tubule-interstitial chronic lesions (ci, ct, i-IFTA) (Table 1). Any correlation was found with CYP3A4 (*1/*22 or *22/*22) and chronic damage. Protocol biopsies in the homozygous TT recipients for for the C3435T variant in ABCB1 revealed higher (ci and ct) score. Combined recipient homozygosity TT for ABCB1 and *3*3 for CYP3A5 resulted in an increase of chronic tubular and interstitial damage. Either donor CYP3A5, CYP3A4 and ABCB1 genotype or combinations donor/recipient polymorphisms did not contribute to tubule-interstitial lesions in the protocol biopsy.

More TAC exposure in the CYP3A5 non-expressers genotype recipients lead to higher tubule-interstitial damage and i-IFTA in kidney protocol biopsies.

Banff	CYP3A5 PM (*3/*3)	CYP3A5 (*1 carrier)	CYP3A4 PM (*22 carrier)	CYP3A4 (*1/*1)	ABCB1 (C3435T) TT	ABCB1 (C3435T) C carrier	CYP3A5 (*3/*3) + ABCB1 (C3435T) TT	CYP3A5 (*1 carrier) + ABCB1 (C3435T) C carrier
0	215 (97.7%)	37 (100%)	15 (100%)	237 (97.9%)	203 (98.1%)	48 (98.0%)	41 (97.6%)	210 (98.1%)
1	4 (1.8%)	0 (0%)	0 (0%)	4 (1.7%)	4 (1.9%)	0 (0%)	0 (0%)	4 (1.9%)
≥ 2	1 (0.5%)	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	1 (2%)	1 (2.4%)	0 (0%)
		p = 0.651		p =0.854		p =0.075		p =0.053
0	104 (47.3%)	23 (62.2%)	6 (40%)	121 (50%)	102 (49.0%)	24 (50%)	17 (41.5%)	109 (50.7%)
1	93 (42.3%)	14 (37.8%)	6 (40%)	101 (41.7%)	91 (43.8%)	16 (33.3%)	16 (39%)	91 (42.3%)
≥ 2	23 (10.5%)	0 (0%)	3 (20%)	20 (8.3%)	15 (7.2%)	8 (16.7%)	8 (19.5%)	15 (7%)
		p = 0.066		p =0.291		p =0.086		p =0.035*
0	96 (43.6%)	24 (64.9%)	6 (40%)	114 (47.1%)	99 (47.6%)	20 (41.7%)	14 (34.1%)	105 (48.8%)
1	107 (48.6%)	13 (35.1%)	7 (46.7%)	113 (46.7%)	99 (47.6%)	21 (43.8%)	20 (48.8%)	100 (46.5%)
≥ 2	17 (7.7%)	0 (0%)	2 (13.3%)	15 (6.2%)	10 (4.8%)	7 (14.6%)	7 (17.1%)	10 (4.7%)
		p = 0.028*		p =0.538		p =0.049*		p =0.008*
0	184 (84.4%)	32 (88.9%)	11 (73.3%)	205 (85.8%)	177 (86.3%)	38 (79.2%)	31 (75.6%)	184 (86.8%)
1	26 (11.9%)	3 (8.3%)	3 (20%)	26 (10.9%)	20 (9.8%)	9 (18.8%)	9 (22%)	20 (9.4%)
≥ 2	8 (3.7%)	1 (2.8%)	1 (6.7%)	8 (3.3%)	8 (3.9%)	1 (2.1%)	1 (2.4%)	8 (3.8%)
		p = 0.782		p =0.422		p =0.188		p =0.068
0	90 (47.4%)	22 (73.3%)	4 (33.3%)	108 (51.9%)	90 (50%)	21 (53.8%)	16 (47.1%)	95 (51.4%)
1	80 (42.1%)	8 (26.7%)	5 (41.7%)	83 (39.9%)	75 (41.7%)	13 (33.3%)	13 (38.2%)	75 (40.5%)
≥ 2	20 (10.5%)	0 (0%)	3 (25%)	17 (8.2%)	15 (8.3%)	5 (12.8%)	5 (14.7%)	15 (8.1%)
		p = 0.017*		p =0.116		p =0.508		p =0.470

OS200 NATURAL KILLER CELLS PROMOTE KIDNEY GRAFT REJECTION BY EVADING CYCLOSPORINE A THERAPY

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Background: Immunosuppressive drugs e.g. calcineurin inhibitors, are primarily targeting T cells, whereas their efficacy in suppressing other immune subsets such as NK cells might be limited. As NK cells have recently been recognized as key players in chronic graft failure comprehensive studies are required to address whether NK cells can escape immunosuppressive regimens.

Methods: Influence of Cyclosporin A (CyA) on NK cell function was studied in a mouse model of allogenic kidney transplantation (KTX, BALB/c to C57BL/6). Recipients were daily treated with CyA (10 mg/kg) for 7 (acute rejection) and 14 days (survival groups). Immunophenotyping was performed by flow cytometry and allograft function was assessed by measuring serum creatinine and urea levels.

Results: Application of CyA to C57BL/6 recipients resulted in a significant improvement of allograft function and morphology until day 7 post transplantation. Frequencies of CD4 + and CD8 + T cells were significantly reduced in renal transplants derived from CyA treated recipients and illustrated a reduced capacity of IFNy production. In contrast, NK cell frequencies remained completely unaffected and IFNg production as well as cytotoxicity of NK cells was not reduced compared with controls. Importantly, the additional depletion of NK cells resulted in a further improvement of kidney function in the acute rejection setting and prolonged the overall graft survival until day 56 as compared to the untreated controls ($p = 0.006$). Surviving animals demonstrated higher intragraft frequencies of activated CD4 + FoxP3 + Ki67 + regulatory T (TREG) cells as well as higher frequencies of CD8 + CD122 + TREG.

Conclusion: We show for the first time that NK cell depletion combined with CyA synergistically improves graft function and prolongs graft survival, suggesting that selective NK cell targeting constitutes a novel approach to ameliorate KTX outcomes.

	Banff	CYP3A5 (*3/*3)	CYP3A5 (*1 carrier)	CYP3A4 (*22 carrier)	CYP3A4 (*1/*1)	ABCB1 (C3435T) TT	ABCB1 (C3435T) C carrier	CYP3A5 (*3/*3) + ABCB1 (C3435T) TT
Cg	0	215 (97.7%)	37 (100%)	15 (100%)	237 (97.9%)	203 (98.1%)	48 (98%)	41 (97.6%)
	1	4 (1.8%)	0 (0%)	0 (0%)	4 (1.7%)	4 (1.9%)	0 (0%)	0 (0%)
	≥ 2	1 (0.5%	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	1 (2%)	1 (2.4%)
			p = 0.651		p = 0.854		p = 0.075	
Ci	0	104 (47.3%)	23 (62.2%)	6 (40%)	121 (50%)	102 (49.0%)	24 (50%)	17 (41.5%)
	1	93 (42.3%)	14 (37.8%)	6 (40%)	101 (41.7%)	91 (43.8%)	16 (33.3%)	16 (39%)
	≥ 2	23 (10.5%)	0 (0%)	3 (20%)	20 (8.3%)	15 (7.2%)	8 (16.7%)	8 (19.5%)
			p = 0.066		p = 0.291		p = 0.086	
Ct	0	96 (43.6%)	24 (64.9%)	6 (40%)	114 (47.1%)	99 (47.6%)	20 (41.7%)	14 (34.1%)
	1	107 (48.6%)	13 (35.1%)	7 (46.7%)	113 (46.7%)	99 (47.6%)	21 (43.8%)	20 (48.8%)
	≥ 2	17 (7.7%)	0 (0%)	2 (13.3%)	15 (6.2%)	10 (4.8%)	7 (14.6%)	7 (17.1%)
			p = 0.028 *		p = 0.538		p = 0.049 *	
Cv	0	184 (84.4%)	32 (88.9%)	11 (73.3%)	205 (85.8%)	177 (86.3%)	38 (79.2%)	31 (75.6%)
	1	26 (11.9%)	3 (8.3%)	3 (20%)	26 (10.9%)	20 (9.8%)	9 (18.8%)	9 (22%)
	≥ 2	8 (3.7%)	1 (2.8%)	1 (6.7%)	8 (3.3%)	8 (3.9%)	1 (2.1%)	1 (2.4%)
			p = 0.782		p = 0.422		p = 0.188	
i-IFTA	0	90 (47.4%)	22 (73.3%)	4 (33.3%)	108 (51.9%)	90 (50%)	21 (53.8%)	16 (47.1%)
	1	80 (42.1%)	8 (26.7%)	5 (41.7%)	83 (39.9%)	75 (41.7%)	13 (33.3%)	13 (38.2%)
	≥ 2	20 (10.5%)	0 (0%)	3 (25%)	17 (8.2%)	15 (8.3%)	5 (12.8%)	5 (14.7%)
			p = 0.017 *		p = 0.116		p = 0.508	

OS201 EFFECTS OF CYP3A5 POLYMORPHISM AND INTRA-PATIENT TACROLIMUS VARIABILITY ON KIDNEY ALLOGRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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Background: High intra-patient tacrolimus variability (IPV) has been proposed as a risk of poor allograft survival after kidney transplantation. Genetic factor, CYP3A5 polymorphism, is one of the possible causes affecting the IPV and may alter the outcome. However, the association of the CYP3A5 polymorphism, IPV and kidney allograft survival has not been established.
Methods: In this single-center retrospective cohort, data including CYP3A5 polymorphism were collected between 2009 and 2019. IPV was calculated using various methods and compared their prognostic value to predict the composite allograft survival endpoint; death-censored graft loss, biopsy-proven interstitial fibrosis and tubular atrophy, rejection and 50% reduction in glomerular filtration rate. The composite endpoint was analyzed in low and high IPV group using median IPV of the most accurate method as cut-off value.
Results: A total of 223 kidney transplant recipients were included, 51.1% were CYP3A5 expresser. IPV calculated by coefficient of variation of tacrolimus trough level was the most accurate predictor for allograft survival, with the cut-off value of 27% (sensitivity 70.5%, specificity 54.7%). High IPV was an independent risk factor for poor composite allograft survival (hazard ratio 2.343; 95% confidence interval [CI], 1.201-4.571; $p = 0.01$) and also found to be related with CYP3A5 expresser (odd ratio 1.902; 95% CI, 1.109-3.262, $p = 0.02$). No significant difference in the composite allograft survival between CYP3A5 expresser and nonexpresser group, however effect of CYP3A5 expresser was significant in the low IPV group, while it was not in the high IPV group (log-rank test, $p = 0.018$).
Conclusion: High IPV is associated with CYP3A5 expresser and poor composite allograft survival. IPV and CYP3A5 polymorphism are considered to beuseful data to identify at-risk patients and improve clinical outcomes.
Keywords: intra-patient variability, CYP3A5, tacrolimus, kidney transplantation

OS202 CNI-FREE THERAPY WITH ISCALIMAB (ANTI-CD40 MAB) PRESERVES ALLOGRAFT HISTOLOGY COMPARED TO STANDARD OF CARE AFTER KIDNEY TRANSPLANTATION

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Iscalimab (CFZ533) is a fully human, non-depleting, IgG1 mAb preventing CD40 pathway signaling and activation of CD40 expressing cell types. In a recent multicenter RCT (NCT02217410), iscalimab therapy showed improved renal function, reduced risk for new onset diabetes and similar rejection and infection rates compared to tacrolimus. Allograft biopsies were performed on a subset of study patients. At 1 site, a protocol amendment allowed for extended therapy and biopsies at month 24 in 6 patients. At a 2nd site, 3-4 surveillance biopsies were performed per routine within 12 months. A pathologist, blinded to therapy, reviewed and scored all biopsy slides using the established Banff criteria and calculated the chronic allograft damage index (CADI). A CADI of 1 or less was considered as 'normal renal histology'. Two patients were excluded from the analysis, since they started on iscalimab and were switched as per protocol to tacrolimus at 2 months. Three of five patients (60%) on iscalimab had 'normal renal histology' versus none of seven on tacrolimus, as assessed by CADI scoring, $p < 0.01$. The average CADI at final biopsy was 1.6 ± 0.6 for iscalimab and 5.1 ± 0.8 for tacrolimus, $p < 0.01$. Four patients had longitudinal biopsies, with stable CADI scores after iscalimab (+1, -1), and increased CADI in tacrolimus treated controls (+4, +4). One patient on iscalimab, with a CADI score 3, had significant BK viremia, 20K copies/ml. Compared to current standard-of-care, iscalimab was associated with lower CADI scores, with close to normal histology maintained in a high proportion of allografts. These findings, albeit in a limited number of patients, confirm previous observations in non-human primates. Further confirmation of our findings are needed and will be tested in the ongoing Phase 2b trial (Cirrus I, NCT03663335). If confirmed, iscalimab is likely to improve long-term outcomes compared to current standard-of-care, potentially providing *'One Transplant for Life'*.

OS203 IMLIFIDASE FOR DESENSITIZATION IN SENSITIZED KIDNEY TRANSPLANT PATIENTS: POOLED ANALYSIS OF PHASE 2 TRIALS

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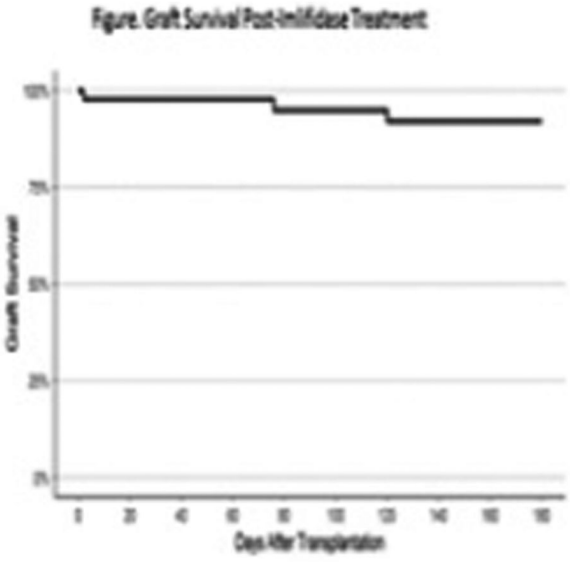
Background: Many patients on the transplant wait list have high levels of human leukocyte antigen (HLA) antibodies and about 15% have a calculated panel reactive antibody [cPRA] $\geq$ 80% (i.e., 'highly sensitized'). High PRA predicts a low probability of finding a suitable allograft for transplantation. Current desensitization strategies have suboptimal effectiveness and require multiple treatments well ahead of transplantation, limiting efficacy for the deceased donor setting. Imlifidase, an enzyme that inhibits the IgG-mediated immune response by specifically and rapidly cleaving IgG antibodies, is given once prior to transplantation. This permits a cross-match conversion at the time of organ offer, thus negating the difficulties of long desensitization planning time.
Methods: Four single arm, 6-month open label, phase 2, trials assessed the efficacy and safety of imlifidase in sensitized patients prior to transplantation with deceased ($n = 39$) or living ($n = 7$) donor kidneys.
Results: 46 patients were included (median age 43 years; 54% male; 70% re-transplants; 93% DSA positive; 85% crossmatch positive pre- treatment; median cPRA: 97%). Following imlifidase, the DSA levels rapidly decreased and positive crossmatches were converted to negative, thus enabling transplantation of all 46 patients. The majority of patients who were DSA positive before imlifidase had DSA rebound to levels at or below the pre-dose level. Antibody mediated rejection (AMR) occurred in 27% of patients; all were successfully treated. At 6 months, all patients were alive; graft survival was 94% (43/46); three patients experienced graft loss unrelated to imlifidase.
Conclusions: Imlifidase treatment inactivated DSA antibodies and converted positive crossmatches. AMR incidence was consistent with expectations and successfully managed. Imlifidase is a promising desensitization treatment for patients who would otherwise remain on dialysis without access to a potentially life-saving transplant.



OS26 - SURGICAL TECHNIQUE LIVER

OS204 EVEN EXTENSIVE PORTAL VEIN THROMBOSIS SHOULD NOT LIMIT ACCESS TO LIVE DONOR LIVER TRANSPLANTATION

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Background: Portal vein thrombosis (PVT) is a common (incidence up to 26%) manifestation of chronic liver disease particularly when decompensation necessitates liver transplantation (LT). The impact of PVT on LT survival is debatable, but large, registry-based studies have noted inferior 30-day and 1-year outcomes. Based on this, extensive PVT remains a relative contraindication at some institutions especially in the setting of live donor LT (LDLT) on account of its additional anatomic challenges. The objective of our analysis, is to further clarify the influence of extensive PVT on LT outcomes.
Methods: 564 adult LTs were performed at our center between January 1, 2011 and June 30, 2018. Pre-LT contrasted imaging (CT/MRI) was combined with operative findings to generate PVT classifications via the Yerdel grading system. Operative management, including the utilization of venous grafts were reviewed, and outcome analyses focused on portal inflow patency and patient survival.
Results: PVT was noted in 10.1% ($n = 57$) of the LT recipients, 68% ($n = 39$) of whomunderwent LDLT. PVT severity grades were as follows: I 33.3% ($n = 19$), II 43.9% ($n = 25$), III 17.5% ($n = 10$), and IV 5.3% ($n = 3$). Thrombectomy established adequate PV inflow in 93% ($n = 53$) of the cases; five patients, all LDLT cases, required venous interposition grafts to complete end-to-end portal anastomoses. Meso-portal ($n = 2$) and varico-portal ($n = 2$; both Yerdel IV) venous jump grafts were utilized sparingly. Three patients (5.3%) developed recurrent PVT and the 1-year actual patient survival was 86%. None of the thirteen patients with extensive clot burden (Yerdel III & IV) re-thrombosed and they had a comparable 85% 1-year survival rate. Receiving a live donor graft did not compromise these outcomes.
Conclusion: Our experience suggests that PVT is a manageable challenge and should not contraindicate LDLT. This holds true for even extensive PVT provided that the requisite surgical expertise and

OS205 LEARNING CURVE OF LAPAROSCOPIC LIVING DONOR RIGHT HEPATECTOMY: REVIEW OF A SINGLE SURGEON'S 103 LAPAROSCOPIC CASES COMPARED TO 96 OPEN CASES

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Purpose: To evaluate the feasibility of laparoscopic living donor right hepatectomy.
Methods: Data of living donors who underwent right hepatectomy by a single surgeon at Samsung Medical Center were reviewed. Comparisons regarding the anatomy, operation, and recovery were performed between open and laparoscopy group. Surgical videos were reviewed for each procedure. Linear regression was used for analyzing operational procedures showed linear decrease in time.
Results: During the period, 96 and 103 donors underwent open and laparoscopic living donor right hepatectomy, respectively. Median estimated blood loss was smaller (300 vs. 200 mL, $P < 0.001$) and mean operation time (301.3 ± 63.3 vs. 252.2 ± 42.8 minutes, $P < 0.001$) and median hospital stay was shorter in the laparoscopy group. (10 vs. 8 days, $P < 0.001$). There was no difference in complication rate. (24.0% open vs. 14.6% laparoscopy, $P = 0.092$) Although overall bile duct openings were more than expected in the laparoscopy group, ($P = 0.022$) it showed improvement with the increase in case numbers. ($P = 0.022$) Total operation time of laparoscopy showed linear decrease along with increase in laparoscopic cases. (R^2=0.407, β=-0.914, $P = 0.001$) and it significantly decreased after nearly 50 cases (2nd to 3rd and 3rd to 4th, $P = 0.001$ and $P = 0.023$, respectively). Inflow control and ischemic line marking (R^2=0.238, β=-4.4), parenchymal transection time (R^2=0.290, β=-22.4) and graft placement in laparoscopic plastic bag (R^2=0.204, β=-1.7) showed the most significant decrease in time. ($P < 0.001$ for each)
Conclusion: Although bile duct division is challenging in laparoscopic living donor right hepatectomy, it showed comparable feasibility to open surgery along with the learning curve.

OS206 THE IMPACT OF A TEMPORARY PORTOCAVAL SHUNT AND INITIAL ARTERIAL REPERFUSION ON PERIOPERATIVE BLOOD LOSS IN LIVER TRANSPLANTATION

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Background: The use of a temporary portocaval shunt (TPCS), as well as the order of reperfusion (initial arterial reperfusion (IAR) versus initial portal reperfusion (IPR)) in orthotopic liver transplantation (LT) is controversial, and its beneficial effect on perioperative blood loss has yet to be determined. The aim of this study was to evaluate possible determinants on perioperative blood loss by using multivariate analysis.
Methods/Materials: Between January 2005 and May 2017 all orthotopic, first liver transplantations performed in our center were included in a retrospective cohort study, including liver transplantations from both donation after brain death and donation after circulatory death. Logistic regression was used to analyse independent determinants.
Results: Of all 365 recipients included, logistic regression showed IAR to be an independent determinant on less perioperative transfusion of red blood cells (RBCs). When analyzing recipients with, and without, portal hypertension (PH) separately, a TPCS was significantly beneficial on less perioperative transfusion of RBCs in recipients without PH. However, in recipients with PH, IAR was significantly beneficial on less transfusion of RBCs ($p = 0.001$). No statistical difference was found in operative time between all four possible combinations.
Conclusion: In conclusion, the use of a TPCS and IAR are statistically beneficial in less need for transfusion in LT depending on the presence of PH. The combination of a TPCS and IAR does not lead to a longer operative time and should therefore be considered as a surgical option in liver transplantation.

OS207 OUTCOME OF RENO-PORTAL BYPASS IN LIVER TRANSPLANTATION WITH NON TUMOROUS PORTAL VEIN THROMBOSIS

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Background: Although not representing an absolute contraindication, portal vein thrombosis (PVT) may increase the risk and technical complexity of liver transplantation (LT). Several technical options are currently available to manage PVT during LT. Reno-portal (R-P) bypass may be particularly interesting in the presence of a spontaneous spleno-renal shunt (SRS).
Methods: Since October 1997 we performed 1568 liver transplants (902 adult and 667 pediatric). In this study we retrospectively analyzed clinical data of the 10 patients underwent R-P bypass, intraoperative and postoperative outcomes. We also evaluated the patency of the R-P bypass by MRI portal flowmetry technique.
Results: Nine patients were adults. Median MELD score was 16. The only one pediatric patient was a 16 yr female with PFIC in a setting of complete situs inversus who underwent the 4th LT. All grafts were from dead brain donors. Median total ischemic time was 406 minutes and operative time was 413 minutes. Before transplant all patients had a SRS documented by CT scan with a median diameter of 28.9 mm. PV findings at transplant according to Yerdel's classification were: one grade II, 8 grade III and one grade III-IV. R-P bypass was the first choice in 7 patients (70%). Three patients required a vein graft interposition (30%). At median follow up of 26.4 months, 7 out of 10 patients are alive with documented normal liver function. Causes of death were not related to surgery. 0nly one patient developed acute kidney injury treated with dialysis. All patients experienced self-limiting ascites. Two patients were submitted to percutaneous trans-hepatic venoplasty because of R-P anastomosis stenosis. In all survivors the patency of the R-P bypass was documented by a phase contrast MRI after a median of 21.4 months post LT.
Conclusion: R-P bypass in the presence of SRS is safe, feasible, easily reproducible and effective with low morbility and no mortality related to surgery.

OS208 USING GLISSON SHEATH AS AN ALTERNATIVE WAY TO PREVENT BILIARY STRICTURE IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Owing to organ shortage and culture difference, living donor liver transplantation (LDLT) becomes a standard treatment for end stage liver disease in East Asia. Many surgical techniques have been developed to prevent biliary complications. In our institution, we came up with a new suture method, which was inspired by Kasai procedure, to reconstruct bile duct in 2014. Instead of duct-to-duct anastomosis, we connected recipient bile duct to

graft Glisson sheath for restoring biliary drainage. The aim of this study is to investigate the surgical outcome of new suture technique.
Methods and Materials: Between January 2007 to December 2017, patients receiving adult to adult right lobe LDLT in Changhua Christian Hospital, Taiwan were included in this study. During the first era of our transplantation surgery, we performed duct-to-duct anastomosis in biliary reconstruction. Since 2014 January, we used Glisson sheath for biliary reconstruction. We used posterior wall continuously suture technique to connect recipient common bile duct and graft right intra-hepatic duct, then, we interruptedly suture the recipient CBD anterior wall to graft Glisson sheath. There are 320 patients included in this study, 120 patients in Duct-to-Duct group and 200 patients in Duct-to-Glisson group. In this study, we retrospectively investigated the biliary stricture rate in each group.
Results: Biliary stricture rate for Duct-to-Glisson group was 13.3% (27 of 200) which was relatively low compared with 28.3% in Duct-to-Duct group ($p = 0.001$). 18 patients in Duct-to-Glisson group experienced bile leak, 12 patients resolved spontaneously, 2 patients treated with percutaneous transhepatic biliary drainage (PTBD) and 4 patients received operation for T-tube insertion. Only 4 bile leak patients developed biliary stricture in Duct-to-Glisson group.
Conclusion: Using Duct-to-Glisson method for biliary reconstruction lowers the stricture rate in LDLT.

OS209

OPERATION ROOM (OR) LIVER TRANSPLANT (LT) RECIPIENT OROTRACHEAL EXTUBATION IS ASSOCIATED WITH LESS HOSPITAL AND ICU LENGTH OF STAY (LOS), AND LOWER BACTERIAL INFECTION, ACUTE RENAL FAILURE (ARF) AND TRANSFUSION RATE

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Background: Fast track anesthesia is an increasingly common practice in selected LT patients. We retrospectively analyzed its relationship with patient outcome, including LT performed in our hospital between years 2005 and 2017.
Methods/Materials: Patients with emergency status, retransplantation, combined liver transplants and living donor LT were excluded. We divided patients in two groups: group A (OR extubation, $n = 36$) and B (delayed extubation, $n = 77$). For all patients, anesthesia was based on propofol, remifentanil and isofluorane, and normovolemic hemodilution was performed when hemoglobin was > 10 grs/dL. Candidates to OR orotracheal extubation included those with no previous encephalopathy, hemodynamic stability (<0.3 μg/kg/min noradrenalin), core temperature ³35.5°C at the end of surgical procedure, and no respiratory acidosis (Sat O2 > 96% with FiO2 < 50% with spontaneous breathing).
Results: Patients demographics were similar between groups, including age, sex, BMI and cause of cirrhosis. Mean MELD score was significantly lower for group A compared to group B (18.5 vs. 24.1, $p = 0.01$). Immediate OR extubation was performed more frequently between years 2013 and 2017 ($n = 67$, 57% of patients). Group A vs. group B had respectively a lower red blood cells (RBC) transfusion rate (1.8 vs. 5.2, $p < 0.001$), less bacterial infections (20.8% vs. 45.5%, $p = 0.035$), less ARF (40% vs. 68.8%, $p = 0.04$), and shorter ICU LOS (3.6 vs. 12 days, $p = 0.009$) and hospital LOS (11.3 vs. 22 days, $p = 0.04$). These differences persisted when including in the analysis only patients with a MELD score ≤ 20 with the exception of ARF rate, which was similar between groups.
Conclusion: We concluded that OR extubation is associated with less hospital and ICU LOS, and lower bacterial infection, ARF and transfusion rate and a prospective trial should be carried out to validate these conclussions.

OS210

IMAGE-GUIDED SURGERY BASED ON 2D ILLUSTRATIONS AND 3D PRINTED MODEL OF DONOR ANATOMY DURING LIVING DONOR HEPATECTOMY

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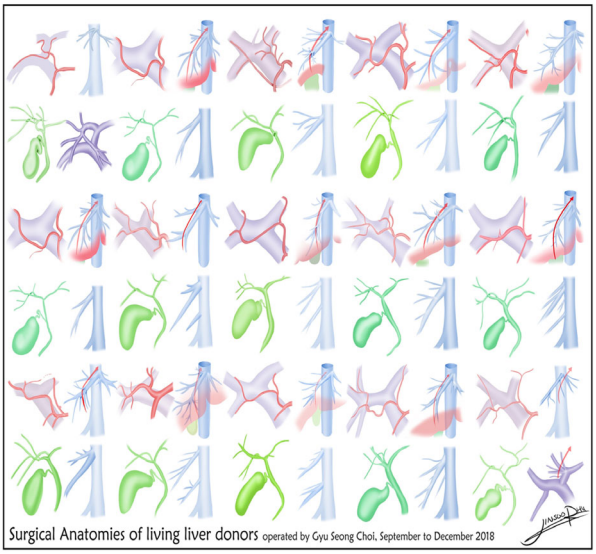
Samsung Medical Center, Sungkyunkwan University School of Medicine

Background: This study was designed to introduce our surgical know-how for using anatomical illustrations to facilitate the understanding of the donor's surgical anatomy for the surgical staffs attending the donor hepatectomy as an image-guided surgery.
Methods: Before living donor liver transplantation, every computed tomographies and magnetic resonance cholangiopancreatographies of the donors' liver were reviewed and illustrated by Jinsoo Rhu using Photoshop CC 2019 (Adobe systems, CA, USA). Donor's portal vein, hepatic artery, bile ducts and hepatic veins were illustrated and were displayed on the operating room.
Result: During the period of September 2018 to January 2019, 37 cases of living donor liver transplantations, 35 laparoscopic cases and 2 open cases, were performed with the assistance of anatomical illustrations of the donor. Among these 37 cases, 34 recipients were adults in which 32 right hemihepatectomies and 2 extended left hemihepatectomies were performed. The other



3 cases were performed as laparoscopic left lateral sectionectomies for pediatric recipients. A 3D-model of the donor's hilar structures and hepatic veins were printed for a case performed in February, 2019. Three-dimensional modeling was done by Jinsoo Rhu using Mimics Medical 21.0 (Materialise, Leuven, Belgium) and was printed with the assistance of Fusion technology corporation (Anyang, Gyeongi-do, Republic of Korea) and Jung-Yon Ko.
Conclusion: Anatomical illustration can be used for living donor liver transplantation, especially for laparoscopic living donor hepatectomy. However, both 2D illustrations and 3D printed model requires a biomedical visualization artist expertized in surgical anatomy of the liver with proper equipments.

OS211

PREOPERATIVE PROXIMAL SPLENIC ARTERY EMBOLIZATION: ALTERNATIVE PORTAL MODULATION FOR PROPHYLAXIS OF SMALL-FOR-SIZE SYNDROME

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Introduction: In living donor liver transplantation (LDLT), small-for-size syndrome (SFSS) has been a serious concern. Splenectomy has been established as portal modulation for prophylaxis of SFSS. While it would lead to surgical complexity and morbidities such as septic complication and portal thrombosis. We previously reported the efficacious use of preoperative proximal splenic artery embolization (PSE) as portal decompression (Trasplant Int 2007, Transplantation 2008).
Method: In this study, we analyzed the efficacy of PSE, compared with splenectomy from the view point of surgical outcome, SFSS occurrence, and morbidity. We retrospectively investigated 274 adult LDLT without previous history of splenectomy. The patients were divided into three groups which consisted of Group A (without-concomitant Splenectomy/-PSE, N = 147), Group B (PSE, N = 103), and Group C (Splenectomy, N = 24).
Result: In regards to background factors including MELD, donor age, and Graft size, there were no significance between 3 groups. The rates of SFSS (total / GW/RBW < 0.8%) were 19/30% in Group A, 10/10% in Group B, and 5/0% in Group C, respectively ($p = 0.08/0.045$). Splenectomy showed significantly increased operation time (Group A: 634, B: 595, C: 614 min.) and intraoperative blood loss (Group A: 116, B: 89, C: 141 ml/kg). On the other hand, PSE could contribute to shortened operation time and reduction of blood loss. Morbidity about splenectomy included post-transplant bacteremia (N = 13, 54%) and portal thrombosis (N = 8, 33%). And splenectomy marked the highest hospital mortality (Group A: 8.8%, B: 6.8%, C: 25%, $p = 0.021$). In Group C, fatal patients' MELD were higher than survivors (Ave. 24.6 vs 15.6, $p = 0.004$).
Conclusion: PSE could be an efficacious portal modulation as well as splenectomy. Considering surgical risks, it would be an alternative option to splenectomy in some specific cases.

OS27 - ORGAN DONATION AND ALLOCATION: BIG CHALLENGES-INSPIRATIONAL SOLUTIONS

OS212 EUDONORGAN - TRAINING AND SOCIAL AWARENESS FOR INCREASING ORGAN DONATION IN THE EUROPEAN UNION AND NEIGHBOURING COUNTRIES

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Introduction: EUDONORGAN, a service contract awarded by the European Commission, aims to provide training and increase social awareness in the European Union (EU) and neighbouring countries (NCs) to enhance positive attitude towards organ donation.
Methods: Spain as leader, Croatia, Italy and Slovenia joined the project, divided in two core work packages (WPs), WP1: *Training* and WP2: *Social Awareness* and two horizontal WPs.

In WP1, the training program employed a blended methodology. The beneficiaries included healthcare professionals (HPs) and other key players (OKPs) from the EU and NCs. The e-learning offered one route for HPs and another for OKPs. The face to face was practical and promoted best practice exchange. A survey on attitude towards donation was carried out among participants before and after.

In WP2, organ donation data was collected from EU and NCs for the organisation of six tailored awareness events in 2018-2019.
Results: In WP1, 101 participants from 28 countries completed the training: 79 HPs and 22 OKPs. The e-learning was evaluated with 4,45 (from 1-poor to 5-excellent), registering 25,22% of knowledge improvement among healthcare professionals and 29,47% among other key players. The face to face session was evaluated with 4,44 (from 1 to 5). 96 participants attended all sessions and were certified.

In WP2, 6 Member States agreed to organize awareness raising events. By March 2019, three awareness events (Warsaw, Budapest, Brussels) have been organized and the remaining three (Stockholm, Lisbon, Athens) are confirmed for March-April 2019. The events involve a variety of countries and stakeholders: 95 participants in Warsaw from 4 countries, 49 participants in Budapest from 7 countries, 127 participants in Brussels from 33 countries. A minimum of 500 participants will be reached by the end of the project.
Conclusions: EUDONORGAN is an innovative cross-sectorial project that aims at improving donation across the EU and neighbouring countries.

OS213 THE BENEFIT OF INFORMATION AND COMMUNICATIONS TECHNOLOGY (ICT) AND BROADCASTING ON YOUTUBE FOR IMPROVING ATTITUDE TO ORGAN DONATION IN AN INSTITUTIONAL EDUCATIONAL PROPOSAL

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Background: It is important for teenagers to have a favorable attitude toward organ donation and transplantation (ODT) in order to increase the number of future donors. Objective: to analyze the impact of an educational proposal based on the creation of short films about ODT recorded by teenagers and broadcast on YouTube.
Method: Experimental group: students from final year of Compulsory Secondary Education were randomly selected ($n = 543$). A questionnaire was applied about ODT. An educational intervention was carried out in which the teenagers were provided with a website in class with information for being able to make a short film. The audiovisual content of the website was hosted on a Youtube channel. The website consisted of three parts, 11 interviews given to important personalities who explained topics related to ODT; an archive with audiovisual contents about ODT; and an explanation was given about how to make a short film. At the time of handing in the short film the students completed a second questionnaire. Control group: 320 students were randomly chosen. The teenagers filled in similar questionnaires. Statistics: SPSS base statistics. The McNemar test was applied to compare the questionnaires (experimental and control group). The YouTube platform were used for the analysis of the viewings about the website and the short films.
Results: Experimental group: all the variables of the questionnaire improved, most notably: attitude toward donation organs ($p < 0.001$), knowledge of the brain death concept ($p = 0.003$), and social discussion about ODT ($p < 0.001$). Control group: no differences were found ($p > 0.05$). The YouTube channel received 1.142 viewings of the didactic contents and 104.912 viewings of the films. The most visited short film reached 8.688 viewings in this period.
Conclusions: An innovative educational intervention about ODT using ICT and social media has a positive influence on teenage attitude, knowledge, and social interaction about ODT.

OS214 MODELING MULTIPLE REGISTRATIONS AND THE IMPACT AT THE NATIONAL AND REGIONAL SCALE BASED ON KIDNEY TRANSPLANTATION IN THE UNITED STATES

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Current policies in the United States allow patients to register at multiple donor service areas (DSAs), provided they have physician approval and can cover additional costs. The ability to register in multiple DSAs may impact the waiting list size, time on the waiting list, and patient mortality. An agent-based queuing model was developed to analyze these potential effects.

In this model, simulated patients are added to the waiting list where they wait for a transplant an then either eventually receive a transplant or die while waiting. The model used 2017 kidney transplant and waiting list data of each DSA in the US to parameterize a simulation where a proportion of the patients on the waiting list are able to register in multiple DSAs. Each DSA has a simplified queue of patients waiting for a transplant and a proportion of the simulated patients in the model can register for up to four additional DSAs as secondary waiting lists. The model runs over a 20-year time span with different proportions of advantaged patients.

Results of this modeling practice found that: (1) Allowing multiple registrations decreases the overall patient mortality, but increases the average time patients spend waiting for a transplant; (2) patients that have multiple registrations receive proportionally more transplants; (3) advantaged patient mortality is lower; and (4) with approximately 40% advantaged patients in the simulation, deaths and waiting time reaches a steady state.

In the simulated transplant system, allowing multiple registrations decreases mortality and increases the time patients spend waiting for a transplant; patients with multiple registrations benefit the most, especially when the make up a low portion of the waiting list population (<40%). At a local level, disparities in waiting list time and patient mortality across regions decrease as there are more advantaged patients in the population, having a negative impact on DSAs with high transplant rates and low death rates.

OS215 SETTING TRANSPLANT RESEARCH PRIORITIES – A COMPARISON AMONG PATIENTS AND PROFESSIONALS IN THE SWISS TRANSPLANT COHORT STUDY

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Background: Involving patients in research is a recommended strategy to increase research efficiency and reduce research waste. Setting research priorities is one phase in the research cycle where patient's perspective is needed. We compared research priorities for transplant (Tx) research between Tx patients and Tx professionals in the Swiss Transplant Cohort Study (STCS).
Methods: The cross-sectional study was nested in the STCS. A convenience sample of 292 adult solid organ Tx patients and 175 Tx professionals (i.e., STCS members, Tx clinicians, researchers) were included. They scored 34 patient suggested research priorities (resulting from the qualitative analysis of three focus group interviews) and 56 variables to be assessed in the STCS data collection on a scale from 0 to 9 (not at all important to very important). Rank order was based on a cut-off of ≥ 7 and the groups were compared using a Chi-square test.
Results: Highest ranked research priorities by both, Tx patients and Tx professionals, were: "continuity of care" (91% and 93%, $p = 0.071$), "care begins even before Tx takes place" (92% and 86%, $p = 0.895$), and "dealing with illness by balancing emotions" (81% and 91%, $p = 0.085$). Highest discrepancies between patients and professionals were: "a good doctor sees you as a complete person and not just as a transplanted organ" (88% vs 53%, $p = 0.282$), "pregnancy after Tx" (47% vs 76%, $p = 0.001$). Highest importance in both groups in view of variables to be assessed in the STCS data collection were: graft functioning, quality of life, rejection and patient survival (all > 92%). Comparing the two groups in view of highest discrepancies are summarized in Figure 1.
Conclusions: While patients and professionals agree on important variables and research topics, discrepancies should be acknowledged in a mutual discussion on future research priorities. The STCS recently established a patient board to integrate the patients' perspective in its research agenda.

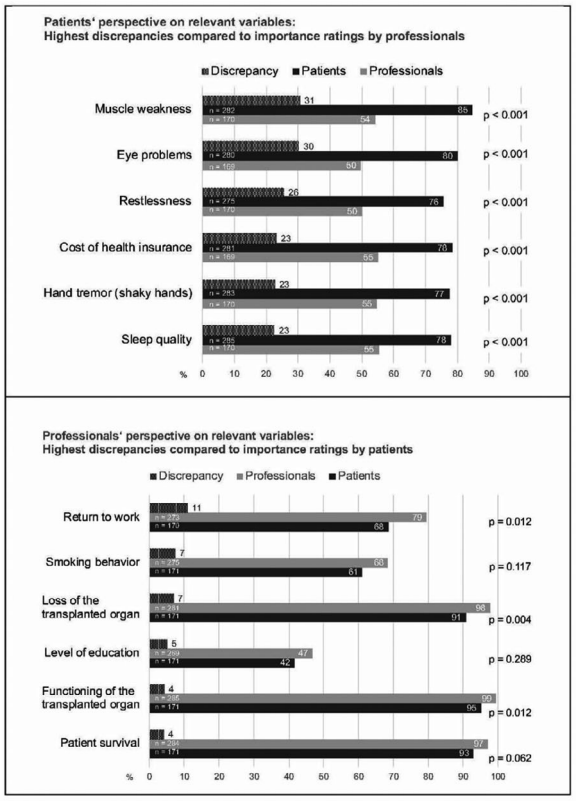

Figure 1. Discrepancies among patients' and professionals' importance ratings of relevant variables and research priorities

OS216

LEVEL OF CHRONIC ILLNESS MANAGEMENT IN TRANSPLANTATION: COMPARISON OF THREE DUTCH SOLID ORGAN TRANSPLANT PROGRAMS WITH INTERNATIONAL TRANSPLANT REFERENCE DATA

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Background: The level of Chronic Illness Management (CIM) refers to how well a system of care has been implemented integrating continuity of care, self-management support, preventive measures, decision-making support, clinical information systems, and prepared multidisciplinary teams. Higher levels of CIM are associated with better outcomes in chronically ill populations. We assessed the level of CIM in three solid organ transplant programs of the University Medical Center Groningen Transplant Center (UMCG-TC) from both transplant patients and clinicians perspective and benchmarked our data with international reference data.

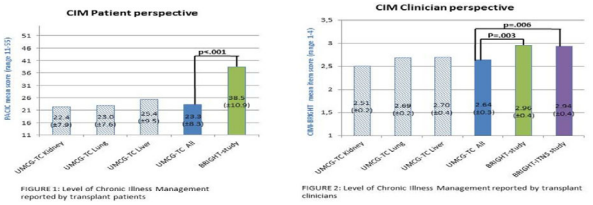

FIGURE 1: Level of Chronic Illness Management reported by transplant patients

FIGURE 2: Level of Chronic Illness Management reported by transplant clinicians

Methods/Materials: Using a cross-sectional comparative design we assessed CIM in the kidney, lung, and liver transplant program at the UMCG-TC. We used the Patient Assessment of Chronic Illness Care (PACIC-S) to assess transplant patients perspective (168/220, response rate 76%) and the Chronic Illness Management Implementation BRIGHT (CIMI-BRIGHT) questionnaire to assess the transplant clinicians perspective (14/19, response rate 74%) on CIM. Reference data were retrieved from two international transplant studies, i.e. the BRIGHT-study (36 heart transplant centers) and the BRIGHT-ITNS study (172 transplant clinicians). Aggregated center level data were summarized using descriptive statistics and compared with reference datasets using a T-test or ANOVA.
Results: Figure 1 & 2 provide the summary statistics of the level of CIM as perceived by patients and clinicians for the UMCG transplant programs, UMCG-TC total score, and reference data of the BRIGHT and ITNS studies. UMCG's PACIC and CIMI-BRIGHT-scores were significantly lower compared to reference scores of the BRIGHT and BRIGHT-ITNS study.
Conclusion: These findings indicate major opportunities to reengineer practice patterns in our transplant programs. Implementation science methods are needed to develop contextually appropriate solutions based on principles of CIM for trans

OS217

DIFFERENT DISTRIBUTION OF ORGAN DONORS ACCORDING TO SOCIOCULTURAL LEVEL OF THEIR RESIDENCY REGIONS IN TEHRAN

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Iranian Society of Organ Donation

Background: Organ donation as a social activity is influenced by cultural and mental variables. So, in order to examine the factors affecting organ donation, social and cultural environment of individuals and their access to these service providers should be considered. The geographical distribution of socio-cultural indicators in all regions of Tehran are not similar. In this study we investigated organ donors' distribution in different socio-cultural regions of Tehran.
Methods: This cross-sectional study was performed on 500 actual organ donors from 2011 to 2018 in Tehran, Iran. The information was collected through phone interviews with organ donor families by two trained questioners. The statistical analysis was carried out by SPSS v.16
Results: According to previous studies, 22 districts of Tehran municipality have been divided into five levels including A(1 developed region), B(4 upward developed region), C(1 middle developed region), D(11 downward developed region) and E(5 deprived region) based on social indicators. Many of organ donors were married men in all five regions but mostly did not have a donor card. The donor per million population (pmp) for seven years was 6.94 in A, 6.16 in B, 9.15 in C, 8.50 in D and 9.93 in E region. Most of donors lived in D region and many of them were family breadwinner men. In E area many donors had large families and were under-graduated. Although the mean age of donors in E region is lower than the others, the difference among them were not significant(p-value > 0.05).

Most donors were from the D and E regions, may be associated with high brain death rate in these area.
Conclusion: Socio-cultural level of donor's residency and social services' availability can have important role in organ donation. Most of the organ donors were from low Socio-cultural level regions that many of them in these regions were family breadwinner with large family size. Therefore, brain dead family support after organ donation is important issue

socio-cultural level	Age (Mean ± SD)	Donor distribution%	family breadwinner %	Marital status % (single)	Marital status % (married)	female %	male %	Family size % (1 person)	Family size % (2 person)	Family size % (3 person)	Family size % (4 person)	Family size % (5 person and upper)	Education % (Under diploma)	Education % (diploma)	Education % (bachelor)	Education % (Upper)	Donation card % (No)	Donation card % (made to will)	Donation card % (Yes)
A	41.18 ± 15.96	2.4	1.4	44.4	55.6	41.7	58.3	20	20	70	10	0	40	10	40	10	70	10	20
B	36.95 ± 16.24	10.3	10.7	32.4	67.6	35.3	64.7	8.1	16.2	78.9	29.7	13.5	45.9	35.1	18.9	0	78.9	10.6	10.5
C	40.45 ± 18.10	5.1	3.6	53.8	46.2	16	84	14.3	14.3	50	35.7	14.3	30.8	23.1	30.8	15.4	50	12.5	37.5
D	37.26 ± 14.28	52.7	58.6	35.5	64.5	34.5	65.5	9.1	24	54.4	25.5	12.5	33.8	43.5	19.8	2.9	54.4	22.8	22.8
E	35.33 ± 15.51	29.5	25.7	43.1	56.9	29.7	70.3	7.3	19.1	71.7	28.2	19	57.8	30.3	11.9	0	71.7	15.9	12.4

OS218 RECORD-BREAKING TRENDS IN DECEASED ORGAN DONATION AND TRANSPLANTATION IN THE UK

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NHS Blood and Transplant

Introduction: Over recent years, due at least in part to significant investment in a new organ donation infrastructure, the number of deceased organ donors (DD) in the UK has risen markedly, leading to increases in transplant numbers and a fall in kidney and liver transplant waiting times.
Results: Over the last ten years, the number of DD in the UK has increased by 75% to 24 per million of population (pmp), while DD transplants have increased by 57% and the number of patients on the active transplant list has fallen by 24%.

The number of DCD donors has more than doubled (to 619 in 2017/18), and the number of DBD donors has increased by 56% (to 955). Increases in referral of potential donors and family consent rates for organ donation have contributed to this change: DBD referral has increased by 11% to 99% and consent has increased by 9% to 72% last year; DCD referral has increased from 45% to 89% and consent has increased by 2% to 60%.

While other organ waiting times have not changed, the increase in DD transplantation has led to shorter kidney and liver waiting times: median waiting time to kidney transplant has fallen from over three years for patients registered in 2005-2009 to 2 years for patients registered more recently. In the same time, liver waiting times have fallen from 5 months to 3½. Despite increased use of older donor organs, post-transplant outcomes have not been adversely affected.
Conclusions: The increase in deceased organ donors in the UK over recent years has had beneficial impacts overall for patients waiting for transplant. The UK is now waiting to see the impacts of machine perfusion of organs and 'opt-out' legislation for organ donation over the next ten years.

OS219 THE LENGTH OF THE DECEASED ORGAN DONATION AND TRANSPLANTATION PROCESS IN THE UK

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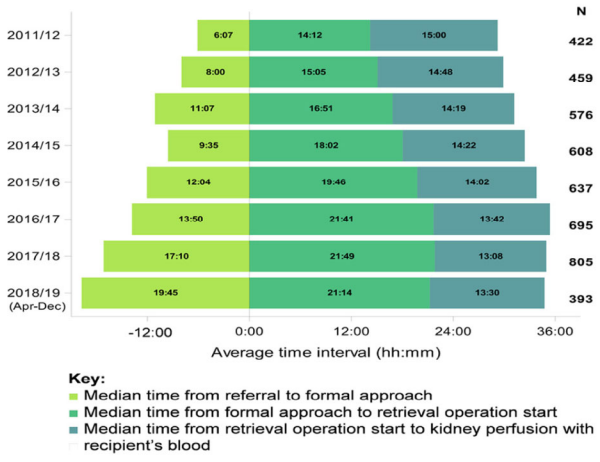
NHS Blood and Transplant

Background: Of all families declining organ donation in the UK, 12% of cases in 2015/16 were reportedly due to the length of the donation process being too long (146 of 1267 declines), with this figure rising to 13% in 2017/18 (150 of 1151 declines). Alongside this, analysis conducted in 2016 highlighted that the length of the organ donation and transplantation process in the UK was increasing. As such the process is now under regular review.
Methods: The organ donation process for donors after brain death (DBD) and donors after circulatory death (DCD) varies, therefore timings are reviewed separately. The time from the formal organ donation discussion with family to the time of transplantation of the donated organ is analysed, this is broken down into differing events depending on donor type. The median time between each event of interest is routinely calculated for full or partial fiscal years.

Time from referral to formal approach is monitored and has positively increased. This is due to early referral of potential donors, which is encouraged to allow time for planning and mobilisation of Specialist Nurses for Organ Donation.
Results: Data for 4595 patients from the DBD process and 2762 from the DCD process, facilitated between 1 April 2011 and 31 December 2018, were analysed. Results are presented in Figure 1 for DBD, and DCD results are similar.
Conclusion: Various events have been held involving relevant stakeholders to identify parts of the process that contributed to delays and to discuss initiatives to influence change in these areas. The most recent initiative is a feasibility pilot, taking place to encourage the donation process to occur within a certain timeframe.

Tackling the length of the process is a pressing priority as it is negatively impacting on donor hospitals and transplant centres. Most importantly, it is also impacting on donor families, especially in the setting of DCD donation. NHS Blood and Transplant will continue to monitor.

Figure 1 – Length of process for DBD donors



OS28 - METABOLIC PROFILE AND BODY COMPOSITION IN LIVER TRANSPLANTATION

OS220 ALCOHOL USE RELAPSE FOLLOWING LIVER TRANSPLANTATION FOR ALCOHOLIC LIVER DISEASE

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Background: Alcohol use disorders (AUD) affect 10% of European population; one of the consequences of AUD is an alcoholic liver disease (ALD) which is the most common indication for liver transplantation (LTx) in Slovakia.

AIMS. 1) to determine a proportion of the patients (pts) transplanted with ALD who relapsed to alcohol drinking after LTx,; 2) to determine a risk factors for the alcohol use relapse; 3) to compare clinical outcome according to the presence or absence of alcohol use relapse.
Material and Methods: Retrospective study of consecutive pts with ALD, who underwent LTx in a single transplant center between May 2008 and December 2017. We included only adult pts with LTx due to the chronic form of ALD. Exclusion criteria were death shortly after LTx (< 1 month) and age < 18 years (y). We recorded demographic and clinical characteristics; graft injury and overall mortality. And we compared them between relapsers and abstainers.
Results: During a study period of 115 months, we reviewed files of 196 LTx in 191 pts. We excluded 87 pts for non-ALD etiology and 15 pts by predefined criteria, the final analysis was carried out in 89 pts, aged 55 y, 24.7% women. Alcohol use relapse was diagnosed in 23 pts - 26% of LTx for ALD; we did not find any alcohol use in 153 pts transplanted for other etiologies than ALD [$p = 0.0001$]). We found harmful drinking in 52%, and occasional drinking in 48% in relapsers. From the independent risk factors scrutinized for association with alcohol use relapse we identified: smoking (OR = 5.92,$p = 0.006$), loss of social status (OR = 7.61,$p = 0.002$) and time after LTx(OR = 1.0008, $p = 0.02$). Graft injury was significantly more frequent in relapsers (OR = 12.7 and 36.6, $p < 0.001$), but overall survival was uneffected.
Conclusions: We documented alcohol use relapse after LTx for ALD in 26% of pts. Risk factors associated with relapse were time, smoking and loss of social status. Graft injury was more frequent in pts who relapsed, but mortality was similar.

OS221 LACK OF METABOLIC PROFILE AND RENAL FUNCTION IMPROVEMENT AFTER HCV ERADICATION – ANALYSIS AT 24 MONTHS AFTER INTERFERON-FREE TREATMENT IN LT RECIPIENTS

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Fundeni Clinical Institute

Background: Long term morbidity and mortality after liver transplantation (LT) is determined by the presence of complications such as cardiovascular disease, diabetes, metabolic syndrome, renal failure. Hepatitis C virus is involved in the occurrence of these extrahepatic manifestations in addition to immunosuppression effects. Aim: To investigate if presence of sustained virological response (SVR) after direct acting antiviral therapy in patients with post-transplant recurrent hepatitis C can influence metabolic factors and renal function.
Methods: Metabolic profile, cardiovascular risk scores, non-invasive evaluation of fibrosis, renal function was assessed in 89 HCV LT recipients at SVR and 24 months after achieving SVR with DAA. Results: There was a trend of fibrosis stage decrease evaluated by transient elastography (9 ± 6.6 vs 8.1 ± 5.9 kPa, $p = 0.06$), but a significant decrease of BARD (2.44 ± 1 vs 2.14 ± 1.23 kPa, $p = 0.03$) and FIB4 scores (2.2 ± 1.4 vs 2.0 ± 1.2 kPa, $p = 0.06$). NAFLD, APRI, MetS and Framingham scores remained stable. Steatosis grade 3 evaluated by CAP did not differ in LT recipients between the two time moments ($p = 0.22$). There was a significant weight gain between SVR and 24 months after SVR ($p = 0.004$), a significant increase of platelet

count ($p < 0.0001$), ALT ($p = 0.01$), serum glucose ($p = 0.006$), LDL-cholesterol ($p = 0.01$), creatinine ($p = 0.003$), and a significant decrease of estimated glomerular filtration rate calculated by MDRD6 ($p = 0.007$). LT recipients with steatosis grade 3 had the following features: significantly higher weight ($p < 0.0001$) and BMI ($p = 0.0001$), higher serum glucose ($p = 0.01$), triglycerides ($p = 0.03$), as well BARD ($p = 0.04$), MetS ($p = 0.001$), Framingham scores ($p = 0.02$).
Conclusions: Eradication of recurrent HCV infection by DAA therapy has a clear benefit for long term liver related complications, but has no beneficial impact on HCV extrahepatic manifestations.

OS222 EXERCISE TRAINING TO IMPROVE PHYSICAL FITNESS AND MUSCLE STRENGTH IN LIVER TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Maud Lormans[1], Katriona O'Donoghue[2], Stefan De Smet[1], Liset Pengel[2], Diethard Monbaliu[3]
[1]KU Leuven; [2]Royal College of Surgeons of England; [3]UZ Leuven

Background: Liver transplantation (LTx) recipients often suffer from muscle wasting and impaired physical fitness before LTx. Due to physical inactivity and immunosuppressive therapy, posttransplant, recipients are at higher risk of developing chronic fatigue, obesity, and metabolic syndrome. Although exercise training is likely to restore physical capacity, its effectiveness has not been reviewed systematically.
Methods: PubMed, Ovid EMBASE, Web of Science, Cochrane Library, Transplant Library, ClinicalTrials.gov, and World Health Organization International Clinical Trials Registry Platform were searched from inception until December 2018 for randomised controlled trials (RCTs) reporting the effect of exercise training on maximal oxygen consumption (VO_2max) and quadriceps muscle strength (QMS) in LTx recipients. Two reviewers independently determined study eligibility and extracted relevant data. Risk of bias was assessed using the Cochrane Risk of Bias tool. A random-effects meta-analysis was conducted to analyse VO_2max and QMS across studies.
Results: Two RCTs reported VO_2max and QMS. Overall risk of bias was scored as moderate, with low risk of bias scores in three to four of the seven domains (sequence generation, attrition bias, reporting bias and other bias). Except high risk of performance bias (blinding of participants), the remaining domains were scored as unclear risk. Pooled data did not show improved VO_2max after exercise training (standardised mean difference (SMD), 0.16; 95% Confidence interval (CI), -0.15 to 0.47; Chi^2 0.21; I^2 0%; Fig 1) or improvements in QMS after exercise training (SMD, 0.18; 95% CI, -0.33 to 0.68; Chi^2 2.33; I^2 57%; Fig 1).

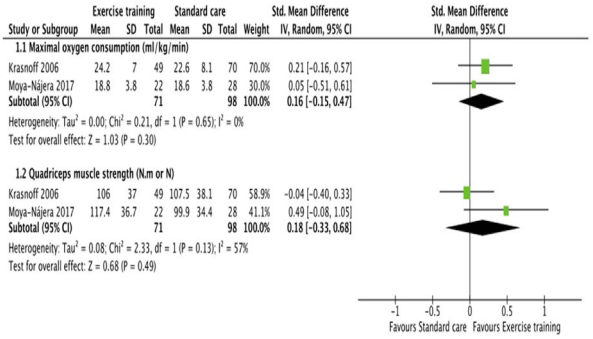

Figure 1. Maximal oxygen consumption and quadriceps muscle strength.
Conclusion: Evidence on the effects of exercise training on VO_2max and QMS in LTx recipients is limited. Further research is needed to confirm the effectiveness of exercise training on physical fitness and muscle strength post-LTx.

OS223 DONOR GENOTYPING COULD ASSIST IN PREVENTION OF NAFLD PROGRESSION AFTER LIVER TRANSPLANTATION

Irena Míková, Magdaléna Neřoldová, Jaroslav A. Hubáček, Dana Dlouhá, Milan Jirsa, Eva Honsová, Eva Sticová, Věra Lánská, Julius Špičák, Pavel Trunečka
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Background: The rs58542926 polymorphism in *TM6SF2* (transmembrane 6 superfamily member 2) is a genetic factor predisposing to nonalcoholic fatty liver disease. We aimed to explore the effect of recipient and donor *TM6SF2* rs58542926 genotypes on liver graft fat content after liver transplantation.
Methods: Steatosis was evaluated in liver biopsies from 268 adult recipients. The influence of recipient and donor *TM6SF2* genotypes, *PNPLA3* rs738409 genotypes and nongenetic factors on the steatosis grade assessed 6 - 30 months after transplantation was analyzed by ordinal logistic regression.
Results: The presence of the *TM6SF2* c.499A allele in the donor ($p = 0.007$), the *PNPLA3* c.444G allele in the donor ($p < 0.001$), posttransplant BMI ($p < 0.001$) and serum triglycerides ($p = 0.047$) independently predicted increased liver fat content on multivariable analysis. The effects of the donor *TM6SF2* A and *PNPLA3* G alleles were additive, with an odds ratio (OR) of 4.90 (95%CI 2.01-13.00; $p < 0.001$) when both minor alleles were present compared to an OR of 2.22 (95%CI 1.42-3.61; $p = 0.002$) when only one of these alleles was present.
Conclusions: The donor *TM6SF2* c.499A allele is an independent risk factor of liver graft steatosis after liver transplantation that is additive to the effects of donor *PNPLA3* c.444G allele. We assume, that donor *PNPLA3* and *TM6SF2* genotyping in liver transplant recipients with graft steatosis may identify patients at highest risk of progression to chronic liver graft disease who should strictly avoid development of obesity and dyslipidemia.
Funding: This study was financially supported by the Ministry of Health of the Czech Republic, grant No. 15-26906A, and the project for development of research organization 00023001 (IKEM, Prague, Czech Republic) – Institutional support.

OS224 PATTERN, RISK FACTORS AND CLINICAL IMPACT OF POSTOPERATIVE DELIRIUM AFTER LIVER TRANSPLANTATION

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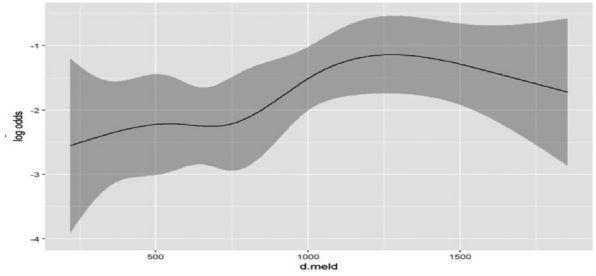
Background: Post-operative delirium (POD) is a surgical complication, occurring in 15-20% of patients. POD is associated with a higher complications rate and mortality after discharge. Moreover, patients developing POD have impaired functional and mental recovery. Literature on POD after liver transplantation (LT) is scanty; the available studies report an incidence of 10-47%.The aim of this study was analyzing pattern, risk factors and clinical impact of POD after LT at a single center.
Material and Methods: Data on consecutive adult (>18 years) LT recipients from March 2016 to May 2018 were prospectively collected and retrospectively analyzed. We collected data on donor and recipient characteristics, including mental and nutritional status at LT, and donor-recipient matching. Data on post-LT course and timing of onset of POD were also collected. Risk factors for POD were analyzed using logistic regression and Bayesian model averaging (BMA). Kaplan-Meier method was used for survival analysis.
Results: 309 patients underwent LT during study period; 3 were excluded due to perioperative death. Incidence of POD was 13.4% ($n = 41$). The median day of onset was the 5th (IQR[4-7]) with a median duration of 4 days (IQR[3-7]). POD was associated with pre-LT status (previous episodes of encephalopathy [$p = 0.004$], creatinine [$p = 0.03$]; INR [$p = 0.02$]; dialysis [$p = 0.04$]), postoperative course (grade ≥ 3 complications [$p = 0.01$], days in intensive care unit [$p = 0.06$]), graft quality (macrovesicular steatosis [$p = 0.004$]) and matching (D-MELD[$p = 0.05$]). At BMA, D-MELD, with a cut-off of 1016(image) was the variable exhibiting the strongest association with POD (70.5% inclusion probability). No differences in patient and graft survival were observed.
Conclusion: Incidence of POD after LT appears to be multifactorial. In our experience, D-MELD > 1016 was the strongest predictor of POD. These results help identify patients to be considered for interventions aimed at preventing the onset of POD.



OS225 INFLUENCE OF METABOLIC PARAMETERS ON THE HISTOPATHOLOGY OF THE GRAFT AFTER LIVER TRANSPLANTATION

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Background: Non-alcoholic steatohepatitis (NASH) is about to become one of the leading causes for liver transplantation. NASH relapse and the development of steatosis after liver transplantation remain poorly understood. The aim of this analysis was the evaluation and analysis of metabolic parameters and histopathological changes of the graft after liver transplantation during long-term follow up.
Methods: 1494 longitudinal liver biopsies of 414 recipients were evaluated during a follow up period of 5 to 10 years. Clinical and laboratory parameters as well as histopathological categories of steatosis, inflammation, fibrosis, and hemosiderosis were explored.
Results: Men showed higher BMI compared to women. After liver transplantation, significant weight gain occurred ($p < 0.01$). 27.5% patients had diabetes mellitus after one year, 33.1% patients after 5 years ($p < 0.01$). The BMI, diabetes mellitus, triglycerides and fasting glucose were significantly associated with the degree of steatosis of the graft. Inflammation was a precursor of fibrosis and fibrosis increased over the first 5 years ($p < 0.01$). There were significant correlations between the degree of steatosis and fibrosis. Severe graft dysfunction was not observed.
Conclusion: High BMI, postoperative weight gain and diabetes mellitus correlate with steatosis, relapse of and de-novo non-alcoholic fatty liver disease (NAFLD) after transplantation. Similar processes as in the original organ might lead to steatosis and NAFLD in the graft. Metabolic syndrome must be considered as a serious complication after liver transplantation forwarding severe histopathological alteration of the graft.

OS226 BODY COMPOSITION AND MORBIDITY FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION – THE VALUE OF QUALITY OVER QUANTITY

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Background: The significance of preoperative body composition is in the spotlight of interest in various diseases. Here we assessed the role of sarcopenia and myosteatosis as prognostic factors following orthotopic liver transplantation (OLT).
Methods: The data of 225 consecutive OLT recipients from a prospective database were analyzed retrospectively (05/2010-01/2018). Computed tomography-based lumbar skeletal muscle index-L3SMI, visceral adipose tissue area-L3VAT and mean muscle attenuation-MA were calculated using a segmentation tool (3DSlicer). Patients with sarcopenia (low L3SMI), visceral obesity (high L3VAT) and myosteatosis (low MA) were identified using predefined sex-specific cutoff values.
Results: The cutoff values of myosteatosis resulted in a good stratification of patients into low- and high-risk groups in terms of major morbidity (Clavien-Dindo-CD>=3b). Myosteatotic patients had significantly higher complication (90-days CCI 68 $\pm$ 32 vs. 44 $\pm$ 30, $p < 0.0001$) and early allograft dysfunction rates. These patients spent significantly longer time in hospital. The estimated costs were 44% higher compared to patient with superior muscle quality. A correlation was found between MA and various outcome parameters (ICU, hospital stay, CCI, costs). Cutoff values for the other used body composition parameters failed to identify high risk patients and did not correlate with outcome. Multivariable analysis identified myosteatosis as an independent prognostic factor for major morbidity (2.432 OR, 1.319-4.486, $p = 0.004$). Adding myosteatosis to the well-established Balance of Risk-BAR score resulted in an increase of the prognostic value for morbidity compared to the original BAR-score (Area-under-the-curve 0.710 vs 0.677).
Conclusion: Our results suggest the superior predictive value of muscle quality (myosteatosis) over quantity (sarcopenia) in terms of morbidity following OLT. Myosteatosis might be a valuable novel parameter in already established outcome prediction tools

OS227 A SYSTEMATIC REVIEW AND META-ANALYSIS ON OUTCOMES AND CORRELATES ASSOCIATED WITH BODY WEIGHT PARAMETERS IN LIVER TRANSPLANTATION

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[1]University of Basel; [2]University Medical Center Groningen; [3]Rush University College of Nursing; [4]Spitalregion Fürstenland Toggenburg

Background: High level evidence from systematic reviews on outcomes and risk factors remains scarce. We summarized and synthesized the evidence on (1) relationships between pre- and post-liver transplantation (LTx) body mass index (BMI), weight gain and obesity with post-LTx outcomes, and (2) pre- and post-LTx risk factors related to post-LTx BMI, weight gain, and obesity.
Methods: Outcomes examined were survival, metabolic and cardiovascular comorbidities, and health care utilization. Risk factor categories were genetic, sociodemographic, behavioral, biomedical, psychological, and environmental. Quality was assessed via a 19-item instrument. Odds ratios and 95% confidence intervals were calculated if outcomes and risk factors were investigated in ≥ 5 studies related to the same body weight parameter.
Results: The search retrieved 16495 articles, whereof 37 and 6 studies were included in the meta-analyses on outcomes and risk factors, respectively. Regarding outcomes, patients with pre-LTx BMI ≥ 30 kg/m^2 and BMI ≥ 35 kg/m^2 had lower survival than those with pre-LTx normal weight (72.6% and 69.8% vs. 84.2% $p = 0.02$ and $p = 0.03$, respectively). Those with pre-LTx BMI ≥ 30 kg/m^2 had worse graft survival than normal weight patients (75.8% and 85.4%, $p = 0.003$). Pre-LTx BMI and pre-LTx overweight were associated with new-onset diabetes ($p < 0.001$ and $p = 0.015$, respectively), but post-LTx BMI showed no relationship. There were no associations with health care utilization. Heterogeneity was high in all analyses. Regarding risk factors, the majority of studies examined biomedical variables. Neither tacrolimus ($p = 0.24$) nor cyclosporine ($p = 0.14$) were associated with post-LTx obesity.
Conclusions: Despite important findings on patient and graft survival, evidence is still scarce on cardiovascular outcomes and on risk factors, related to post-LTx body weight parameters. High heterogeneity and diverse definitions of measurements, outcomes and risk factors limited data extraction and meta-analysis.

OS29 - CARDIOVASCULAR OPTIMIZATION AND OUTCOMES IN RENAL TRANSPLANTATION

OS228 INTRAOPERATIVE FLUID MANAGEMENT FOR PATIENTS UNDERGOING UNDERGOING RENAL TRANSPLANTATION STROKE VOLUME VARIATION VERSUS CENTRAL VENOUS PRESSURE

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Introduction: Optimizing intravascular volume is crucial for early graft function after renal transplantation (RT). Central venous pressure (CVP) represents a standard decision-making tool in fluid management in RT, despite the various potential complications and limitations.Stroke volume variation (SVV) is a simple and less invasive hemodynamic variable for evaluating fluid responsiveness and preload status and its use was associated with improved outcomes in patients undergoing high risk surgery.The aim of this study was to evaluate the effectiveness of SVV versus CVP in guiding fluid administation during RT.Methods:We retrospectively analyzed two groups of recipients who underwent RT under general anesthesia and volume control ventilation: standard CVV-guided (Group A, $n = 16$) vs. SVV-guided (Group B, $n = 16$) fluid administration.The SVV was derived from the FloTrac/Vigileo system and the protocol consisted of a baseline sodium saline administration rate of 2 ml/kg/hr and any additional bolus if SVV > 12%.Vasopressors, mannitol and furosemide were used in both groups according to the institution protocol.We examined differences in intraoperative fluid volumes, graft dysfunction on 7th postoperative day as assessed by the need for RRT, length of hospital stay and 30-day survival between the two groups.
Results: The average volume of total fluids administered (calculated as total crystalloid over patient's weight and surgical time) was 14.6 $\pm$ 8.3 ml/kg/hr for the CVP group and 12.4 $\pm$ 6.6 ml/kg/hr for SVV group ($p = 0.04$). The total intraoperative fluid balance for the non-PGDT group was 3630 $\pm$ 1460 ml and for the PGDT group was 3010 $\pm$ 850 ml ($p < 0.001$).The median LOS was 6 5, 9.5] days for the CVP group and 5[4,7] days for the SVV group($p = 0.025$).30-day survival rates and graft dysfunction rates did not differ between the two groups.Conclusion:These results suggest that SVV may be a useful tool for optimizing intravascular volume during RT and could also lead to shorter LOS.

OS229 ENDOTHELIAL DYSFUNCTION IN KIDNEY TRANSPLANT RECIPIENTS (KTRS) IS ASSOCIATED WITH INCREASED MORTALITY AND GRAFT LOSS

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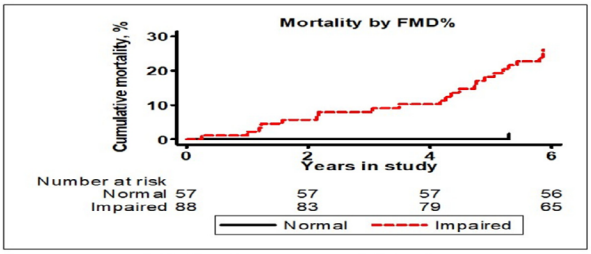
Background: Endothelial dysfunction is an early and potentially reversible stadium in the atherosclerotic process. We assessed endothelial dysfunction non-invasively in KTRs and evaluated the association with mortality and graft loss.
Methods/Materials: Flow-mediated dilation (FMD) was measured in the brachial artery by a 12 MHz linear array ultrasound probe (Zonare z.one, ZONARE Medical Systems, CA, USA), with baseline diameters obtained at rest and maximal diameters obtained during the reactive hyperemia occurring after 5 minutes of forearm occlusion with a sphygmomanometer cuff. FMD% was calculated as 100*(maximum diameter-baseline diameter)/baseline diameter. Clinical endpoints were collected from The Norwegian Renal Registry. The distribution of risk according to FMD levels was assessed in Cox regression using a restricted cubic spline function. To simplify the model, FMD was dichotomized using ROC analysis to identify optimal cut-points at maximal sensitivity and specificity.
Results: 152 out of 269 (56.5%) eligible KTRs were examined approximately 6 weeks after transplantation, 145 had successful FMD measurements. Patients were mean ± SD 54.9 ± 12.9 years old, 34% were women, 28% had diabetes, 26% had pre-transplant cardio- or cerebrovascular disease, and FMD% 4.4 ± 3.4. During a median follow-up of 6.5 years, 26 patients died, 11 patients lost their graft, and 34 experienced either graft-loss or death. Mortality increased with lower FMD levels until about 5%, below this level, a ceiling effect was seen (P for non-linearity < 0.003). An optimal cut-point of FMD<= 5.36% defined impaired endothelial function. FMD% below this level, compared to higher FMD% (n = 88 vs. 57), was associated with death, HR 9.80 (1.29-74.62), P = 0.03 (Table and Figure), uncensored graft loss, 7.80 (1.83-33.30), P = 0.01, but not death-censored graft loss, HR 4.58 (0.55-37.92), P = 0.16.
Conclusion: Impaired FMD was associated with increased mortality and uncensored graft loss in KTRs.



	Unadjusted		Adjusted	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	1.09 (1.04-1.13)	<0.001	1.07 (1.01-1.13)	0.02
Female	0.82 (0.48-1.40)	0.47		
DM or NODAT	1.87 (1.06-3.30)	0.03	2.08 (0.93-4.69)	0.08
Cor/Cer vasc.	1.71 (0.78-3.74)	0.18		
Pulse pressure	1.03 (1.01-1.04)	0.001	1.00 (0.98-1.02)	0.96
Dialysis pretx	1.81 (0.73-4.49)	0.20		
Time in RRT	1.02 (0.97-1.08)	0.36		
FMD% impaired	18.42 (2.50-136)	0.004	9.80 (1.29-74.62)	0.03

OS230 PRE-OPERATIVE LEFT VENTRICULAR DYSFUNCTION AND POST KIDNEY TRANSPLANT COMPLICATIONS: A SINGLE-CENTRE ANALYSIS

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Introduction: Guidelines for routine pre-operative echocardiograms for kidney transplant candidates differ. At our centre, echocardiograms are repeated every three years before transplantation in all candidates. Left ventricular (LV) dysfunction is common with advanced kidney disease but the link with increased mortality post-transplantation is poor. The aim of this study was to establish if pre-operative LV dysfunction is associated with post-transplant complications.
Methods: Data from hospital informatics for all transplant recipients between 2007-2018 was linked with recipients' latest pre-operative echocardiogram. Mortality, graft loss and 1-year creatinine values were cross-checked with the UK Transplant Registry. LV dysfunction was defined as any male or female with LV ejection fraction under 52% or 54%, respectively (as per latest recommendations).
Results: We analysed 691 transplant recipients, with 7.7% having pre-operative LV dysfunction. No association between LV dysfunction and age, gender, BMI, ethnicity, diabetes status or dialysis status was found. Graft function at 1-year in surviving kidneys showed worse estimated GFR (ml/min) in those with versus without LV dysfunction (46.0 versus 52.8 respectively, p = 0.045). Recipients with LV dysfunction had significantly increased risk for death post-transplant (17.0% versus 8.6% respectively, p = 0.046) and borderline increased risk for death-censored graft loss (28.3% versus 18.7% respectively, p = 0.068). However, in a Cox regression model, after adjustment for baseline variables, LV dysfunction was no longer significant for mortality.
Discussion: Pre-operative LV dysfunction is not an independent risk factor for post-transplant all-cause mortality. Our cohort only includes candidates who proceeded to transplantation leading to selection bias. We suggest LV dysfunction alone should not exclude potential transplant candidates but should alert professionals to increased risk for targeted counselling.

OS232 WHY PROGNOSTIC FACTORS FOR CARDIOVASCULAR COMLICATIONS IN PATIENS IN WAITING LIST FOR KIDNEY TRANSPLANTATION HAVE A LOW CLINICAL BENEFIT: STATISTICAL AND CLINICAL TRICKS

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Patients stratification by the risk of complications and death is widely used among patients with CKD. However, the high statistical significance does not always provide clinical efficacy.

This analysis is based on the study of results of treatment of 1862 patients. Figure 1 shows a typical result of a study of risk factors for death among patients with CKD. Consider this model in more detail.

Many risk factors (age, albumin, CRP, mean BP) - related to mortality become statistically insignificant when included in the model of stronger predictors. Paradoxically, but KT/V has shown no correlation with mortality, probably due to the reason that this parameter of almost all patients is within an optimal range.

The severity of diastolic dysfunction is strongly associated with mortality. The value of this predictor somehow reduces the lack of clear diagnostic criteria, the complexity of the measurement of highly informative parameters that are not included in the routine protocol of echocardiography. The exact values can be obtained by invasive measurement that is not applicable for widespread use.

Ejection fraction is also strongly associated with mortality. Herewith this parameter is stable: it does not change during the HD session, less depends on hyperhydration than PASP. Despite the fact that the AUCROC curve reaches 0.8-0.85, clinically valuable forecast may only be done in the field of limit values, i.e. approximately within 10-15% of patients. In other cases, positive predictive value and negative predictive value are close to 50-60%. Thus, PV as a prognostic factor actually becomes binary, which makes it less informative for risk stratification.

In addition, most risk factors are not modifiable, so it is impossible to properly manage risk.

Ways to improve: determinating of a smaller number of more informative, stable and most importantly - modifiable predictors, determinating the optimal endpoints.

	HR	95% CI	P-value
Age	1.03	0.99-1.06	0.39
BMI	1.02	0.97-1.05	0.68
Sex (M/F)	1.2	0.97-1.31	0.09
Hb	0.99	0.96-1.03	0.57
CRP	1.04	0.98-1.07	0.18
PTG	1.03	1.01-1.06	0.02
Albumin	0.96	0.81-1.05	0.61
Time on GD	1.09	0.98-1.08	0.13
MAP	1.01	0.99-1.03	0.77
kT/V	0.97	0.88-1.12	0.64
Cumulative illness rating score	1.11	1.07-1.17	0.001
Diastolic dysfunction (reference quantile) 0			
1	1.03	0.96-1.16	0.18
2	1.1	1.02-1.21	0.016
3	1.74	1.68-1.83	<0.0001
Ejection fraction (reference quantile) 50-59%			
40-49%	1.22	1.02-1.76	0.014
30-39%	3.21	2.04-6.1	<0.0001
<30%	4.72	3.23-7.44	<0.0001
PASP (reference quantile) <25mmHg			
25-45mmHg	1.03	0.93-1.13	0.56
45-65mmHg	1.46	1.1-1.95	0.01
>65mmHg	2.2	1.48-3.25	<0.0001
Qa (per each 100ml)	1.11	1.05-1.22	0.001
Qa/CO	1.12	1.07-1.18	0.001
CHF (reference quantile) NYHA 0			
1	1.14	0.92-1.4	0.21
2	1.72	1.12-2.4	0.01
3	3.1	2.31-4.16	<0.0001
Diabetes Yes/No	2.1	1.84-2.34	<0.0001
Pre-HD CHF Yes/No	1.59	1.28-1.89	<0.0001

OS233 APPLICATION OF NEW HYPERTENSION GUIDELINES TO RENAL TRANSPLANT RECIPIENTS: IMPACT ON CARDIOVASCULAR OUTCOME AND GRAFT SURVIVAL

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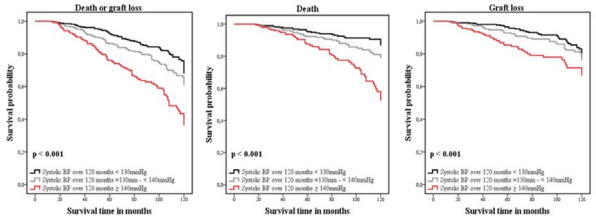
Background: Based on data of the SPRINT trial, American national guidelines recently reduced the blood pressure goal from 140/90 mm Hg to 130/80 mm Hg for subjects with increased cardiovascular risk, e. g. those with chronic kidney disease. To date it remains elusive whether renal transplant recipients benefit from these goals as well.
Methods: We performed a retrospective analysis of 877 patients who underwent kidney transplantation between 1997 and 2011 in transplant centers in Germany (Berlin and Bochum) with a follow-up of 12 - 120 months. Blood pressure was obtained at regular follow-up examinations in the transplant outpatient clinic.
Results: Patient and graft survival was defined as composite endpoint. Subjects were stratified according to mean systolic blood pressure (SBP) values < 130 mmHg, 130-139 mmHg, or ≥ 140 mmHg.
Results: Cumulative survival regarding the composite endpoint as well as its individual components was significantly different among the three groups being highest for those patients with a systolic blood pressure (SBP) < 130 mmHg, followed by 130-140 mmHg and ≥ 140 mmHg ($p < 0.001$ each). Both the composite endpoint and patient survival remained significantly different among the three groups in cox regression analyses adjusted for age, gender and mean eGFR of the first 12 months ($p = 0.007$ and 0.03, respectively). Graft survival tended to be better with lower SBP in cox regression ($p = 0.09$). Stratification by SBP values of the first 12 months resulted in significant intergroup differences in both the composite endpoint, mortality, and graft loss in Kaplan Meier analysis as well (p 0.001, 0.001, and 0.03, respectively). Conclusion

Renal transplant recipients who achieve a mean SBP < 130 mmHg have a lower mortality and a better allograft survival than those with a conservative blood pressure goal < 140 mmHg. The new blood pressure targets < 130 mmHg should be considered suitable for renal transplant recipients as well.



OS234 LIPID ABNORMALITIES AND CARDIOVASCULAR EVENTS IN RENAL TRANSPLANT RECIPIENTS RECEIVING EVEROLIMUS WITH REDUCED-EXPOSURE CALCINEURIN INHIBITOR REGIMEN: 24-MONTH ANALYSIS FROM TRANSFORM STUDY

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Background: Post-transplant lipid abnormalities are considered to increase the risk of cardiovascular (CV) events in renal transplant recipients (RTxRs). Here, we evaluate lipid profiles and cumulative incidences of dyslipidaemia and major adverse cardiac events (MACE) at month (M) 24 in *de novo* RTxRs receiving everolimus (EVR) + reduced-exposure calcineurin inhibitor (EVR+rCNI) or mycophenolic acid+standard CNI (MPA+sCNI) regimen from the TRANSFORM (NCT01950819) study.
Methods: Dyslipidaemia (hyperlipidaemia, hypercholesterolaemia, hypertriglyceridaemia, increased/abnormal lipids, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), non-high-DL (HDL-C), and decreased HDL-C) and MACE were reported by investigators as adverse events (AEs) or serious AEs. Lipid profiles and MACE were examined in the overall population and in the dyslipidaemia cohort, by treatment arms.
Results: In all, 384/1014 and 217/1012 RTxRs had dyslipidaemia in the EVR+rCNI and MPA+sCNI arms, respectively. In the overall population, M24 lipid levels and mean changes from baseline were higher in the EVR+rCNI vs MPA+sCNI arm. A similar trend was noted in patients with dyslipidaemia (Table). Although the proportion of patients with normal/optimal TC, LDL-C, and TG levels was significantly lower in the EVR+rCNI vs MPA+sCNI arm ($P < 0.05$), >80% of RTxRs had normal TC/HDL-C ratio across arms. All patients with dyslipidaemia received concomitant lipid-lowering drugs, most commonly atorvastatin (EVR+rCNI, 47.9% and MPA+sCNI, 45.6%). Overall incidence of MACE was low in the study and, in particular, was significantly lower in the EVR+rCNI arm among patients with dyslipidaemia (Table).
Conclusion: Despite a higher incidence of dyslipidaemia, the incidence of MACE was not higher in the EVR+rCNI vs MPA+sCNI arm. Dyslipidaemia associated with EVR+rCNI appears to be manageable and does not confer increased short-term CV risk up to M24.

Table. Lipid abnormalities and cardiovascular events in the overall population and patients with dyslipidaemia

	Overall population			Patients with dyslipidaemia		
Lipid parameters at M24, mean (SD)	EVR+rCNI	MPA+sCNI	*P* values	EVR+rCNI	MPA+sCNI	*P* values
	N = 640	N = 704		N = 294	N = 177	
TC, mg/dL	208.9 (47.98)	183.6 (41.94)	<0.001	210.5 (47.52)	182.1 (44.24)	<0.001
HDL-C, mg/dL	60.0 (18.32)	55.0 (17.48)	<0.001	58.2 (16.02)	56.2 (19.96)	0.256
LDL-C, mg/dL	121.6 (39.46)	108.7 (33.70)	<0.001	122.6 (38.28)	111.3 (37.84)	0.002
TC/HDL ratio	3.8 (1.73)	3.6 (1.22)	0.012	3.9 (1.39)	3.7 (1.40)	0.367
TG, mg/dL	195.8 (130.89)	157.0 (95.29)*	<0.001	207.5 (118.83)	180.1 (85.37)	0.004
	N = 596	N = 660		N = 277	N = 169	
Mean change from BL in TC (mg/dL)	43.0 (57.53)	19.4 (50.29)	<0.001	39.0 (58.50)	17.4 (51.19)	<0.001
Mean change from BL in HDL-C (mg/dL)	11.6 (15.57)	7.3 (16.14)	<0.001	10.9 (13.97)	8.4 (16.66)	0.107
Mean change from BL in LDL-C (mg/dL)	22.9 (48.81)	10.6 (41.42)	<0.001	19.0 (49.19)	6.5 (43.88)	0.007
Mean change from BL in TC/HDL ratio	0.1 (1.87)	-0.2 (1.58)	0.006	-0.1 (1.60)	-0.4 (1.68)	0.155
Mean change from BL in TG (mg/dL)	60.3 (126.76)	15.8 (116.09)*	<0.001	54.3 (118.60)	25.5 (105.87)	0.010
Proportion of patients at M24, n (%)	N = 640	N = 704		N = 294	N = 177	
Normal (<200 mg/dL) TC level	292 (45.6)	486 (69.0)	<0.001	132 (44.9)	106 (59.9)	0.001
Optimal (≥60 mg/dL) HDL-C level	298 (46.6)	236 (33.5)	-	121 (41.2)	59 (33.3)	-
Men	157/437 (35.9)	137/495 (27.7)	0.003	65/202 (32.2)	28/109 (23.9)	0.094
Women	141/203 (69.5)	99/209 (47.4)	<0.001	56/92 (60.9)	33/68 (48.5)	0.297
Optimal (<100 mg/dL) LDL-C level	199 (31.1)	309 (43.9)	<0.001	87 (29.6)	74 (41.8)	0.014
Normal (<5) TC/HDL-C ratio	542 (84.7)	623 (88.5)	0.061	241 (82.0)	149 (84.2)	0.814
Normal (<150 mg/dL) TG level	268 (41.9)	404 (57.5)*	<0.001	101 (34.4)	81 (45.8)	0.046
MACE ≥0.5% in any group, n (%)	N = 1014	N = 1012	RR (95% CI)	N = 384	N = 217	RR (95% CI)
Any MACE	62 (6.1)	81 (8.0)	0.76 (0.56, 1.05)	17 (4.4)	19 (8.8)	0.51 (0.27, 0.95)
Cardiac failure	13 (1.3)	11 (1.1)	1.18 (0.53, 2.62)	2 (0.5)	1 (0.5)	1.13 (0.10, 12.39)
Chronic cardiac failure	4 (0.4)	1 (0.1)	3.99 (0.45, 35.66)	0 (0.0)	1 (0.5)	0.00
Congestive cardiac failure	7 (0.7)	4 (0.4)	1.75 (0.51, 5.95)	4 (1.0)	1 (0.5)	2.26 (0.25, 20.10)
Cerebral haemorrhage	1 (0.1)	1 (0.1)	1.00 (0.06, 15.93)	0 (0.0)	1 (0.5)	0.00
Cerebrovascular accident	0 (0.0)	2 (0.2)	0.00	0 (0.0)	1 (0.5)	0.00
Acute myocardial infarction	7 (0.7)	6 (0.6)	1.16 (0.39, 3.45)	1 (0.3)	1 (0.5)	0.57 (0.04, 8.99)
Myocardial infarction	5 (0.5)	6 (0.6)	0.83 (0.25, 2.72)	1 (0.3)	0 (0.0)	-
Acute coronary syndrome	5 (0.5)	3 (0.3)	1.66 (0.40, 6.94)	2 (0.5)	2 (0.9)	0.57 (0.08, 3.98)
Angina pectoris	22 (2.2)	31 (3.1)	0.71 (0.41, 1.21)	9 (2.3)	8 (3.7)	0.64 (0.25, 1.62)
Arteriosclerosis coronary artery	0 (0.0)	3 (0.3)	0.00	0 (0.0)	1 (0.5)	0.00
Coronary artery disease	3 (0.3)	8 (0.8)	0.37 (0.10, 1.41)	1 (0.3)	4 (1.8)	0.14 (0.02, 1.26)

*N = 702; †N = 889

Cholesterol levels:- Normal: <200 mg/dL, borderline high: 200 - <240 mg/dL, high: ≥240 mg/dL; HDL-C levels:- low: <40 mg/dL for men and <50 mg/dL for women, normal: 40 - <60 mg/dL for men and 50 - <60 mg/dL for women; optimal levels: ≥60 mg/dL for men and women; LDL-C levels:- optimal: <100 mg/dL, near or above optimal: 100 - <130 mg/dL, borderline high: 130 - <160 mg/dL, high: 160 - <190 mg/dL, very high: ≥190 mg/dL; TC/HDL ratio:- normal: <5, high: ≥5 but ≤7, very high: >7; TG levels:- normal: <150 mg/dL, borderline high: 150 - <200 mg/dL, high: 200 - <500 mg/dL, very high: ≥500 mg/dL

Other MACE were acute cardiac failure, cardiogenic shock, left ventricular failure, cardiomyopathy, ischaemic cardiomyopathy, cerebral infarction, cerebral ischaemia, ischaemic stroke, subarachnoid haemorrhage, transient ischaemic attack, unstable angina, coronary artery stenosis, myocardial ischaemia, cardiac arrest, cardiogenic shock

A patient with multiple occurrences of a MACE is counted only once for the preferred term. A patient with multiple MACE within an SMQ is counted only once for the SMQ. A patient with multiple occurrences of a level under one treatment is counted only once for the same risk for that treatment

BL, baseline; CI, confidence interval; EVR, everolimus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, month; MACE, major adverse cardiac event; MedDRA, medical dictionary for regulatory activities; MPA, mycophenolic acid; N, total number of patients; rCNI, reduced-exposure calcineurin inhibitor; RR, risk ratio; sCNI, standard-exposure calcineurin inhibitor; SMQ, standardised MedDRA queries; SD, standard deviation; TC, total cholesterol; TG, triglycerids

OS30 - COMPOSITE TISSUE

OS236 TISSUE DONATION ACTIVITY IN A UNIVERSITY CENTRE. EXAMPLE OF A WIN-WIN MODEL FOR MEDICAL STUDENTS, HOSPITAL AND SOCIETY

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Introduction: Vall d'Hebron University Hospital (VHUH) is a 1106 bed tertiary centre with 7510 health care professionals, attending a referral population of 430,000 inhabitants and certifying around 1800 deaths per year. It is associated with a medical school, yearly training around 500 third-through-sixth year medical students. In 2001 the current hospital tissue procurement program was first implemented.
Methods: Tissue procurement program is carried out by a specifically trained and certified group of 5 medical students working as tissue coordinators (Tc) in a 24 hours on-duty schedule under senior Transplant Coordinator (sTC) supervision. Tc duty is to attend death, perform initial donor evaluation, conduct family approach and interviews, and set up logistical organization for tissue retrieval in collaboration with Banc de Sang i Teixits (BST) and, in some cases perform corneal tissue retrieval. We describe HUVH tissue procurement activity performed in the last 4 years.
Results: A total of 7,039 deaths were prospectively evaluated, 62% of whom (n = 4,388) presented medical contraindications for tissue donation. Of the remaining 2,651 (38%) potential tissue donors (PTD), 1,292 (49%) were not converted into real donors, mostly due to family refusal (36,3%; n = 964) followed by detection system failure and other logistical issues (12,9%; n = 342). A total of 1,390 corneal units, 185 skin grafts, 232 muscleskeletal grafts, 76 blood vessels, and 151 heart valves were obtained from the remaining 1,359 (51,3% of PTD) actual donors.
Conclusions: The tissue donation program performed by specifically trained students is successful in achieving a high and sustainable tissue donation rate in our university hospital.

OS237 CLINICAL RESPONSE TO HISTOPATHOLOGICAL FINDING IN UTERUS TRANSPLANTATION

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Purpose: Uterus transplantation has recently proven to be the first successful treatment for absolute uterine factor infertility, with demonstration of live births.
Methods: Uterus transplantation was done in five women from both deceased and living donors. Ectocervical biopsies (ECB) collected at predetermined time points were used to diagnose acute rejection (ACR). ECB were scored as: negative, borderline, grade 1, grade 2, or grade 3 for ACR. Clinical responses were recorded as: no action, increase in existing immunotherapy or steroid recycling. Protocol immunotherapy included Thymoglobulin induction and CNI with either mycophenolate (prior to pregnancy) or Azathioprine as maintenance.
Results: In total, 86 ECB (the majority as per protocol biopsies) were taken to detect histopathological signs of rejection. Two episodes of ACR were diagnosed in two recipients: one as grade 1 and one as grade 2. Twenty-nine ECB were categorized as borderline rejection. Steroid recycling was used to treat the two episodes of ACR and two borderline cases with complete resolution. All other borderline ECB episodes (n = 27) reversed without treatment. One of the treated women with borderline ACR delivered a healthy baby.
Conclusions: Rejection in uterus transplantation if detected early appears to be easily treated. Borderline rejection appears to spontaneously resolve in most cases. More experience and a modification of the existing scoring system are needed for a proper clinical response to histological changes.

OS238 TWO DECADES OF HAND TRANSPLANTATION: LONG-TERM OUTCOME WITH EMPHASIS ON REJECTION, FUNCTION AND PATIENT SATISFACTION

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Background: Between 2000 and 2014 five patients received a bilateral hand (n = 3), bilateral forearm (n = 1) and a unilateral hand (n = 1) transplant at the Innsbruck Medical University Hospital. We report novel insights on the correlation of rejection, function and patient satisfaction in the long-term follow-up.
Methods: Rejection was confirmed by histopathologic examination of a skin biopsy. The cellular infiltrate was characterized by immunohistochemistry and analyzed early (0-3 years), late (4-10 years) and very late (>10 years) posttransplantation. Hand function and psychological parameters/scores were correlated to rejection.
Results: 38 rejection episodes were recorded during a 5-19 years follow-up. Immunohistochemistry revealed that the proportion of CD3 + T-cells during acute rejection significantly increased after year 3 (67.57 ± 5.34 vs 82.47 ± 1.78 vs 81.08 ± 5.02, $p < 0.001$). The highest proportion of CD20 + B-cells was observed at 4-10 years (8.40 ± 1.27, $p = 0.012$), and for CD68 + macrophages early posttransplantation (15.48 ± 2.59, $p = 0.022$). No significant change in Foxp3 + T-regulatory cells was found over time. Endothelial C4d expression continuously improved with time posttransplant ($p < 0.05$). Hand function remained stable also during rejection episodes. A negative impact of rejection on patients' well-being and quality of life (QOL) was found. QOL scores were significantly lower during rejection, compared to scores in the absence of rejection ($p = 0.045$). Patient satisfaction significantly correlated with an overall acceptable upper limb function expressed by a high ARAT, HTSS and a low DASH, and good sensitivity, indicated by low s2PD.
Conclusion: We report stable functional results independently of rejection over two decades after human hand transplantation. Regain of allograft sensitivity may be most significant for patient satisfaction and happiness. The phenotype of the cellular infiltrate during rejection changes with time after transplantation.

OS239 HAND TRANSPLANT IN A TERTIARY CARE HOSPITAL IN INDIA

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Introduction: Upper extremity allotransplantation has become a reconstructive option for the treatment of major amputation of upper limb. Though hand transplant does not prolong life, the improvement in quality of life for an amputated patient by hand transplant is unmatched
Aim: To assess the outcomes of 5 hand transplant patients who underwent transplant at Amrita institute of medical sciences, Kochi, India
Materials and methods: This is a retrospective, cross sectional observational analysis of 5 hand transplant patients who underwent hand transplant at Amrita institute of medical sciences, Kochi, India
Results: 5 patients underwent hand transplant from 2015 to 2018. All patients received bilateral hand transplant. Average age at transplant was 29.6 years (19 yrs to 46 yrs). The mean follow-up of these patients were 2 yrs. The cause of graft loss was due to electrical burns (n = 2); crush injury (n = 2) and blast (n = 1). All patients were induced with ATG and maintenance immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone. The average cold ischaemia time was 320 minutes for each limb and the average warm ischaemia time was 15 minutes. 4 out of the 5 patients had atleast one episode of rejection (all were acute cellular rejection). The average number of rejection was 2.2 episodes. Rejcetion occured within the first two months. Most rejections were successfully treated with steroids. One patient alone received IVIG and rituximab for rejection but never occurred again. The infectious complications noted were CMV colitis (n = 1), herpes labialis (n = 1), Giardiasis (n = 1). One patient developed monomorphic B cell lymphoma of the gastrointestinal tract which was successfully treated with Rituximab and cure was attained. None of them had graft loss and all of them were functional.
Conclusions: Hand transplant's long term functional status remains good. With advances in immunosuppression and treatment for the complications this can be offered to a wider population.

OS240 TRANSPLANTING IMMUNOGICAL HIGH RISK PATIENTS WITH HLA MATCHED CORNEA – EXPERIENCE FROM THE DANISH PROGRAM

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Corneal transplantation without HLA matching is common and 600 corneal transplantations are performed annually in Denmark. HLA matching is beneficial in high-risk keratoplasty procedures such as in re-grafts and transplantation to a vascularized recipient bed.The disadvantage waiting for an HLA matched donor, is longer waiting time compared to waiting for a random donor cornea. One reason is the polymorphism of the HLA system and the

limited number of HLA typed cornea donors. Therefore, the chance of finding a HLA compatible donor should be assessed before enrolling in a program for HLA matched cornea transplantation.The Danish Program for HLA matched cornea transplantation was initiated in March 2016 in the western part of Denmark, and by June 2017 it has been a national program.

Patients eligible are high-risk patients (re-transplants, HLA immunized and/or previous rejections). The patients are assessed for immunization history. Genomic HLA type (HLA-A,B,DRB1) and HLA antibody screening and identification (LAbscreen mixed and -single antigen) are performed.The cornea donors allocated into this program, are deceased organ donors with consent given for donation of corneas. They are HLA typed using RT-PCR for the loci HLA-A,B,C,DRB1,DQB1,DQA1,DPB1,DPA1) as part of the normal kidney allocation rules.The patients are matched with at least 4/6 HLA split type match (HLA-A,B,DRB1) and no donor-specific antibodies.

Twenty-eight patients have been transplanted. Mean HLA match-grade was 4.2. Mean waiting time was 107 days (9-301). 7 rejections were observed in 7 patients. 2 of the 28 grafts have failed due to a immunological rejection episode. 13 were HLA compatible with one or more donors without receiving a transplant, mainly because there were no available donor corneas from the donors.

It is possible to allocate corneas from HLA typed deceased donors to high risk pts. with good short term results. HLA typing of non-organ, cornea donors will increase the donor pool.

OS241 UTERUS TRANSPLANTATION: A SINGLE CENTER'S EXPERIENCE OF PERI- AND POSTOPERATIVE COMPLICATIONS

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Background: Uterus transplantation allows women who do not have a uterus or a have a nonfunctioning uterus to become pregnant and deliver a baby. We analyze the first 15 cases of uterus transplantation with focus on recipient complications, follow-up and outcome.
Methods: Over a 2-year period we have performed 15 uterus transplantations in our institution using grafts from both deceased ($n = 2$) and living donors ($n = 13$). The recipients were followed regularly with gynecological examination, cervical biopsies and sonograms. The main outcome measurements were hospital stay, postoperative complications, and success rate.
Results: Five recipients had their uterine grafts removed within the first two weeks after surgery. Vascular complications, related to both inflow and outflow problems, were identified as the primary reason for three of the graft losses and organ related factors for two. Out of the six recipients with ongoing grafts, four have experienced vaginal strictures at the vagina-vagina anastomosis necessitating surgical interventions. Four recipients have been treated for ACR (grade 1, 2 and borderline) with steroid recycling with complete resolution. One of the treated women with borderline ACR delivered a healthy baby. All other borderline episodes resolved without treatment. One recipient developed CIN I but no action has been required. Six of the recipients had a total of 13 embryo transfers resulting in seven pregnancies. One recipient had a decreased kidney function during pregnancy which led to a decrease in her immunosuppression levels up until delivery and hysterectomy.
Conclusions: Uterine transplantation is a promising treatment of uterine factor infertility that affects 1-5% of women. The lessons learned from our initial 15 recipients have been instrumental to our success, and we aim to share our conclusions and build on knowledge in the field of uterus transplantation.

OS242 THE INNSBRUCK HANDTRANSPLANT PROGRAM: EIGHTEEN YEARS OF EXPERIENCE

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Background: Reconstructive transplantation represents a therapeutic option for severe tissue defects which are not amendable to conventional reconstructive attempts. We herein report long-term follow-up data over a period of 18 years (mean 11.2 years).
Methods: Between March 2000 and March 2014 five patients received a bilateral hand ($n = 3$), bilateral forearm ($n = 1$) and a unilateral hand ($n = 1$) transplant performed at the Medical University of Innsbruck.
Results: Hand function and sensitivity continuously improved during the first five years and remained stable with insignificant fluctuations thereafter. To reduce the burden of calcineurin inhibitors, m-TOR inhibitors ($n = 2/5$) and belatacept ($n = 3/5$) were added to the therapeutic regimen. At total of 38 rejection episodes was observed. The majority were cellular rejections (65,79%), while 11 (28.85%) were identified as antibody-mediated rejections (AMR) with presence of donor-specific alloantibodies (DSA). AMR manifested both early and late after transplantation. While it was successfully treated in two patients with anti-CD20, IVIG and immunoadsorption, the hand allograft of the unilateral transplant recipient had to be amputated at seven years after multiple, unmanageable AMRs with significant levels of DSAs, eventually resulting in severe allograft vasculopathy, and hence chronic rejection. The same patient was diagnosed with stage IV gastric adenocarcinoma 12 months after graft removal and passed away six months after diagnosis. The remaining four patients are currently rejection-free with moderate levels of immunosuppression and without any evidence of chronic rejection.
Conclusion: In immunologically stable patients, the introduction of belatacept was able to help reduce overall burden of immunosuppressive therapy. AMR is challenging, and early de-novo DSA was associated with a complex immunological course.

OS243 LIVING DONOR UTERUS TRANSPLANTATION: DONOR DEMOGRAPHICS AND OUTCOMES

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Introduction: Uterus Transplantation (UTx) is a solution to Absolute Uterine Infertility (AUI). We describe the demographics and clinical outcomes of the women who underwent hysterectomy for donation.
Materials and methods:: UTx was performed according to the IRB-approved protocol (ClinicalTrials.gov NCT02656550). Candidates of donation were recruited after voluntary referral and strict clinical, imaging and psychological evaluation. All hysterectomies were performed through a midline infraumbilical incision. Follow-up was structured after United Network for Organ Sharing (UNOS) living donor regulations.
Results: Since inception in 2016, 14 UTx have been performed, 12 with grafts from living donors (LD) and 2 from deceased donors (DD). Mean LD follow-up is 16 months (3-29). All LD but 1 were non-directed. 1 LD was postmenopausal (age 48). Average LD operative time was 5 hours (4-7) and average hospital stay was 5 days (4-6). Half of the LD did not show any complications (6/12). 2 LD suffered Clavien-Dindo grade 3 complications: 1 vaginal cuff dehiscence (14 weeks post-donation) and 1 fecal impaction; 3 LD, grade 2 complications: 3 urinary tract infections and 1 blood transfusion and 1 LD a grade 1: buttock claudication. All LD have fully recovered and have normal sexual function.
Conclusions: LD hysterectomy can be performed safely with complete return to normal functions. The complications are not different than the ones reported for hysterectomies performed for uterine pathologies. The length of hospital stay is due to return of bowel and bladder functions. The introduction of laparoscopy and robotic hysterectomy for LD may decrease hospital stay and overall discomfort for the donors.

Age	BMI	Pregnancies/Children	Delivery (V, vaginal; C, cesarean section)
42	27.9	2/2	V
56	25	3/3	V
45	20.4	5/3	V
35	22.8	2/2	V
36	19.1	4/4	V
39	27.5	3/4 (1 twin delivery)	V & C
35	25.9	7/7	V
48	21.4	2/2	V
32	26.2	4/4	V & C
33	23.1	2/2	C
39	20.3	3/3	V
32	24.9	1/1	V

OS31- OVERCOMING BARRIERS IN LIVING KIDNEY DONATION

OS244 IMPROVEMENT OF RENAL FUNCTION EVALUATION IN LIVING KIDNEY DONORS: ROLE OF RADIOISOTOPIC GLOMERULAR FILTRATION RATE AND OF RENAL FUNCTIONAL RESERVE

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Background: After donation, living kidney donors (KD) develop a partial loss of kidney function (KF), defined as AKI (Acute Kidney Injury). Its recovery is due to renal functional reserve (RFR), defined as the capacity to increase glomerular filtration rate (GFR). The aim was to analyze KD KF before donation, in the immediate postoperative period and 1 yr after and investigate the predictive performance of pre-donation RFR on AKI and 1 yr KF.
M-M: 48 KD KF was analyzed with serum creatinine (sCr), radioisotope GFR (rGFR) with 51Cr-EDTA and a sequential scintigraphy 99mTc-MAG to determine split KF, in the immediate postoperative period (sCr) and 1 yr after

(rGFR). 16 KD underwent a kidney stress test with protein load to assess their RFR before donation and 1 yr after.
Result: Mean sCr 0.7 mg/dL, rGFR 98 mL/min. At scintigraphy mean % of KF of right kidney was 47. After donation (all left nephrectomies) KD worsened KF: mean sCr was 1.2 mg/dL (1.1-1.4). 7 days after, renal recovery was observed in all. 1 yr after, rGFR was measured and compared with the split rGFR of right kidney before donation: 64 mL/min (44-87) vs 46 (38-65) respectively with mean compensatory increase of 18 mL/min (1-46) and in % 35 (1-110). Pre-donation RFR was 21.5 mL/min.There was no correlation between pre-donation RFR and AKI after donation while a strong linear correlation between RFR and the compensatory GFR increase 1 yr after was found ($r = 0.66$). 1 yr after, KD maintain their RFR (16.5 mL/min).
Conclusion: Radioisotopic evaluation is a feasible and precise determination of KF and compensatory GFR increase of the single kidney after donation. This is the first study demonstrating the validity and potential utility of a test that provides a dynamic evaluation of pre-donation KD KF with prognostic information on KF 1 yr after donation. RFR assessment may represent a useful screening tool for KD, providing more information about the quality of the kidneys and possibly increasing the number of KD.

OS245 CHANGING DEMOGRAPHICS IN UK LIVING KIDNEY DONORS 2006–2017

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Background: Living kidney donation (LKD) accounts for a third of UK renal transplant activity. Population cohort studies have shown lifetime donor risk is modified by age, sex, obesity, co-morbidity and relationship to the recipient. Most UK transplant units will extrapolate US donor cohorts to predict UK donor risks; however the difference between donors in the UK and US, and the change in UK donors over time has not been established.
Methods: Data on LKD as reported to NHS Blood and Transplant from January 2006 to December 2017 were assessed by age, sex, ethnicity, BMI, co-morbidity and relationship to recipient.
Results: Between January 2006 and December 2017 11,651 LKDs were reported to NHS Blood and Transplant.

Age: The proportion of donors aged > 65 years increased from 3.9 to 10.4% ($p < 0.001$). The mean age of donors increased from 45.8 to 48.7 years ($p < 0.001$).

Sex: A greater proportion of donors were women (53.4%), but this proportion did not change significantly over time.

BMI: At donation 17.4% of donors were obese (BMI > 30 kg/m^2). This proportion did not change over time.

BP: The proportion of donors with a diagnosis of hypertension did not significantly change over the study period (mean 2.8%).

Relationship: The proportion of non-related non-partner donations increased (p-value for linear trend = 0.01).

Ethnicity: No difference in the proportion of donors from non-white ethnic groups was observed over the 12 year period (mean 12.9%)
Conclusions: The mean age of living kidney donors has increased in the UK, and a greater proportion were aged > 65 years of age when compared to US donors. This change in donor profile has implications for both recipient and donor outcomes. Age differences between US and UK donor population may limit the generalisability of US donor risk data to a UK population. Despite rising need for organs from the black, asian and minority ethnic groups there has been no increase in the ethnic diversity of UK living kidney donors.

OS246 DEVELOPMENT OF KIDNEY EXCHANGE PROGRAMME IN LATVIA

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Background: Up to 1/3 of patients with a willing living kidney donor are excluded due to incompatible blood group and/or positive cross-match. To overcome those barriers desensitization methods are available but they are losing popularity due to inferior outcomes. Instead of them kidney exchange programmes (KEP) are gaining popularity because allow patients with related but ABO- or HLA- incompatible living donor to receive a compatible living donor transplant in return for the donation of a kidney from their incompatible donor to another individual.
Methods/Materials: All potential living donor/recipient pairs who approached Latvian Transplantation center in P. Stradins Clinical University hospital in last 5 years were included in study.
Results: 10 of 46 kidney transplantations from living donors were done within KEP during 2013-2018. Of the donors (mean age 45y) 40% were men and of the recipients (mean age 38y) 50% were men. 6/10 donors were spouses. The mean cold ishemia time was 4 hours and no recipient had delayed graft function. No rejection was diagnosed in this group of patients, but one recipient developed polyoma BK nephropathy. All recipients have good graft function with mean serum creatinine 121 μmol/l and as well all donors have good remaining kidney function with mean serum creatinine 102 μmol/l at the beginning of 2019. In 3 pairs exchange was done due to ABO incompatibility and in 2 pairs – due to possitive cross-match. In all cases organ sharing was carried out as paired donation and surgeries were done in the same day except a case in 2017 when a surgery for one of recipients in a pair was delayed for 2 weeks due to peritoneal dialysis related peritonitis but another recipient needed preemptive transplantation or start of dialysis.
Conclusions: In the last 5 years 1/5 of kidney transplantations from living donors were done within kidney exchange programme in Latvia. Kidney paired donation has become the fastest growing source of living donor kidneys.

OS247 CROSSING BORDERS TO ENHANCE LIVE DONOR KIDNEY TRANSPLANTATION: THE CZECH-AUSTRIAN KIDNEY PAIRED DONATION PROGRAM

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Kidney paired donation (KPD) is an efficient strategy to circumvent blood group and/or HLA antibody barriers. Small volume national European KPD programs, however, are limited by low match probabilities.

We merged two established national programs, which both have been designed to include ABO and HLA antibody-incompatible pairs. 48 Czech and 20 Austrian incompatible pairs have been referred since 2016. Computer-based matching runs prioritizing highest possible transplants, blood group compatibility, HLA match and avoiding DSA (>2000 MFI) were performed every 3 months.

Our merged algorithm identified 23 compatible combinations, and, until now, 23 kidney transplantations (6 two-way, 2 three-way and 1 four-way exchanges, 1 initiated by altruistic donor) have been performed, including 4 cross-border kidney shipments (CIT of 5-6 hours). In 2018, we initiated an altruistic donor-triggered open KPD chain with 6 transplantations (two cross-border exchanges) performed in three chain segments. Our merged KPD program included transplantations in 7 blood group O, 8 blood group B and 8 blood group A recipients. Fifteen recipients had anti-HLA antibodies and 4 patients had 10-26% cytotoxic panel reactivity. All recipients had negative flow- and CDC-crossmatches. Two transplantions were performed across major ABO barriers (in one case additional low-level anti-HLA class II DSA), applying immunoadsorption-based desensitization. ABO-incompatible pairs with O blood group recipients who did not find a match in 1-2 matching runs were offered ABOi transplantations in cases of higher HLA match (haplotype and higher). Thus, there were another 15 AB0i kidney transplantations in the Czech pool and 3 in the Austrian pool.

In conclusion, this first systematic international KPD program allowed 34% incompatible pairs to be transplanted via merged KPD, while another 26% of registered pairs received ABOi grafts. International joint initiatives are critical to maximize living donor kidney exchange.

OS248 MENTAL HEALTH AMONG UNSPECIFIED ANONYMOUS LIVING KIDNEY DONORS AFTER DONATION

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Background: Anonymous living donors donates to an unknown stranger. These donors undergo psychosocial assessment to evaluate likelihood of psychological harm of donation. The aim of this retrospective interview study was to investigate the psychological symptoms, psychiatric diagnoses, and whether these are attributable to the donation among anonymous living donors.
Methods: All 147 unspecified anonymous kidney donors (2000-2016) in our center were eligible to participate in a semi-structured audio recorded interview and to complete questionnaires. Questionnaires used were the Symptoms Checklist (SCL-90), Dutch Mental Health Continuum, the MINI-Screen, and on indication the MINI-Plus. We asked in open questions about expectations, anonymity, experiences, and the support received.
Results: The majority of these 147 donors was willing to participate in the study: Eleven donors had died (not related to donation) 109/136 gave consent, 18/136 declined and 7/136 are pending. 80/136 interviews have been conducted. In 36/80 (45%) donors a MINI-Plus was required based on the MINI screen. Results on the number of donors reporting psychological complaints, the type of diagnoses, type of required/received treatment, and the attribution to donation will be presented as well as qualitative findings from the interviews.

Discussion: Willingness of anonymous donors to participate in this study was very high, reflecting the cooperative and altruistic attitude of this population. Forty-five percent MINI-plus indication is understandable in view of the 43,5% lifetime prevalence of psychiatric diagnoses in the general population. Preliminary results indicate that the mental health of unspecified anonymous kidney donors is comparable to that in de general population.

OS249 THE EFFECT OF BEING OVERWEIGHT ON LONG-TERM RENAL FUNCTION AFTER LIVING KIDNEY DONATION

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Background: Obesity is considered a risk factor for developing renal failure. Little is known about renal failure in overweight living kidney donors. The aim of this study is to assess the risk of renal failure after living donor nephrectomy using different measures of body composition.
Methods: We included 1150 living kidney donors who donated between 1980 and 2018 at the University Medical Centre Groningen. Pre-nephrectomy measures of body composition were body mass index (BMI), body surface area (BSA), waist circumference, weight and waist-hip ratio. Post-donation renal function was assessed using measured glomerular filtration rate (mGFR) at 5 and 10 years follow-up.
Results: Mean donor age was 52 ± 11 years, 553 (47.7%) were male and median mGFR pre-donation was 113.5 ± 21.8 mL/min*1.73 m2. Baseline mGFR was higher in obese (BMI > 30) donors compared to non-obese donors (respectively 121.6 ± 23.7 vs. 108.0 ± 19.5, $p < 0.001$). At 5 years, BMI ($\beta = 0.21$, $p < 0.001$), BSA ($\beta = 0.55$, $p < 0.001$), female waist circumference ($\beta = 0.31$, $p < 0.001$), weight ($\beta = 0.48$, $p < 0.001$) and female waist-hip ratio ($\beta = 0.16$, $p = 0.03$) were associated with increased mGFR. At 10 years, BMI ($\beta = 0.22$, $p = 0.01$), BSA ($\beta = 0.45$, $p < 0.001$), female waist circumference ($\beta = 0.36$, $p = 0.02$) and weight ($\beta = 0.41$, $p < 0.001$) were associated with mGFR. In multivariable analysis, female waist-hip ratio was associated with increased delta mGFR between 2 months and 5 years after nephrectomy ($\beta = 0.17$, $p = 0.03$). There was no difference in type of body composition measurement on renal function.
Conclusion: This study shows that overweight living kidney donors have increased mGFR at 5 and 10 years post-nephrectomy, which may be an overestimation due to a supraphysiologic elevation in GFR in obese patients. Higher female waist-hip ratio is associated with less decrease in mGFR between 2 months and 5 years post-nephrectomy. These data can be used during donor screening and in donor education.

OS250 THE NEW UK GUIDELINES FOR LIVING DONOR KIDNEY TRANSPLANTATION: MEASURING THE IMPACT

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Introduction: The UK living donor guidelines were updated in March 2018. The acceptable GFR for donation become more conservative for some patients.

The purpose of this study was to evaluate the impact of these changes on our centre and potentially at a national level.
Method: Patients who donated their kidneys between May 2011 and Feb 2018 at our centres were identified using a prospective database. Comparison was made between their pre-donation corrected GFR (by Cr EDTA or iohexol) and the new guidelines. Follow up data was collected.
Results: There were 284 donations (M:F 129:155) in this period. Nineteen donors were identified with a GFR below the advisory range (M:F 11:8, mean age 48.9 years). Of these, 6 donors had a GFR of more than 4 points below advisory range. 3 were aged less than 30 years. In this group, Creatinine increased by 40.4 (20 – 66) from work up to most recent follow-up. In the first 6 months, the average Creatinine rise was 43.3 μmol/L and then this appeared to plateau and did not, on average, rise beyond the 6-month value.
Conclusion: 6.7% ($n = 19$) of donors would have been below the advisory level for donation under new guidelines.

In the UK there were 7307 living donor transplants in the same time frame. Extrapolating this data from our centre experience, 490 donors would have a GFR less than the new guideline. It is recognised that some patients would have chosen to continue with donation but would require further counselling to individual their risk.

OS251 OBESITY AND OUTCOME FOLLOWING RENAL TRANSPLANTATION; COMPARISON BETWEEN LIVING AND DECEASED DONOR TRANSPLANTS

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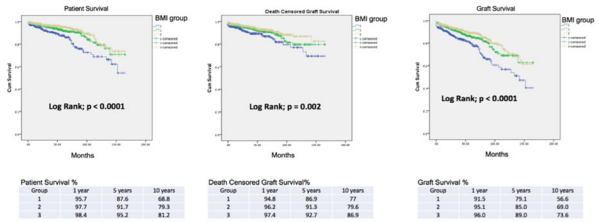
Background: Obesity is associated with metabolic comorbidities among kidney transplant recipients leading to increased mortality after transplant. The study aimed to compare the long-term graft and patient survival in obese and non-obese patients and compare those between recipients of live- and deceased donor transplantation.
Methods: In a retrospective analysis of kidneys transplantation preformed between 01/2005-05/2018 we compared the outcome among three groups: group 1,Obese patients (BMI > 30 kg/m2), group 2 (BMI = 25-30 kg/m2) and group 3 (BMI 18.5-25 kg/m2). Excluded were patients with BMI < 18 and recipients of another organ. Of the 1444 patients with anthropometric data included in the study, 314 (22%) were in group 1, 177 (56.4%) of whom received a living donor transplant (LD), 456 (32%) in group 2, 64.3% LD, and 630 (44%) in group 3, 64.9% LD. Kaplan-Meir Method with log rank test was used for survival analysis and Cox regression analysis to find risk factors for graft loss and death.
Results: One, 5- and 10-years *graft survival*s were respectively; 91.5%, 79.1% and 56.6% in group 1, 95.1%, 85.0% and 69.0% in group 2 and 96.0%, 89.0% and 73.6% in group 3 ($p < 0.0001$, group 1 vs. 2 + 3). The difference in survival was significant only for DD transplants, $p < 0.0001$, but not for the LD transplants. One, 5- and 10-years *patient survival*s were respectively; 95.7%, 87.6% and 68.8% in group 1, 97.7%, 91.7% and 79.3% in group 2 and 98.4%, 95.2% and 81.2% in group 3 ($p < 0.001$,group 1 vs. 2 + 3). Patient survival was significantly different between group 1 and 3 in both the DD and LD groups ($p < 0.001$). On Cox regression analysis IHD, weight, donor age, re-transplant, and DD type were independent risk factors for graft loss whereas the risk factors for death were recipient age,T2DM, IHD, and DD.
Conclusions: Recipient obesity at transplant is a risk factor for graft loss and death for the long-term mainly in the deceased donor group who have higher comorbidities.



Patient Survival %			
Group	1 year	5 years	10 years
1	95.7	87.6	68.8
2	97.7	91.7	79.3
3	98.4	95.2	81.2

Death Censored Graft Survival%			
Group	1 year	5 years	10 years
1	94.8	86.9	77
2	96.2	91.3	79.6
3	97.4	92.7	86.9

Graft Survival %			
Group	1 year	5 years	10 years
1	91.5	79.1	56.6
2	95.1	85.0	69.0
3	96.0	89.0	73.6

OS252 LIVING KIDNEY DONORS WHO LOSE WEIGHT IN ORDER TO BE ABLE TO DONATE, GAIN MORE WEIGHT AFTER DONATION

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Background: Living donor kidney transplantation is the treatment of choice for end-stage renal disease(ESRD). However, in recent years data have emerged which suggests potential long-term risks for kidney donors. Kidney donors are now widely counselled of the increased risk of ESRD. In line with changes in the general population, an increased proportion of live donor candidates are now overweight or obese. Obesity has been shown to be an independent risk factor for the development of ESRD. Our living donor programme concentrates much effort on lifestyle modification in live donor candidates. No data are currently available as to whether these recommendations are followed by live donors after donation.
Methods: We conducted a retrospective analysis of all live donors who proceeded to donation in the years 2014-15, and were followed up for at least 2 years in our centre. Comparisons in donors' Body Mass Index(BMI) over this period were made with matched pair analysis from initial assessment to preoperative assessment, 1 year and 2 years after donation.
Results: Our data demonstrate that at the time of surgery, 61/129 donors (47.3%) had a BMI between 25-30 kg/m^2, and 18/129 (14%) had a BMI of > 30 mg/m^2. Donors with a BMI > 30 kg/m^2 at presentation were seen to lose weight by the time of surgery (mean change in BMI -1.5, $p = 0.002$). However, data at 1 year follow-up shows that the donors with BMI > 30 at presentation gained weight after donation (mean change in BMI + 2.0 $p = 0.0045$), returning to their initial weight. These patients maintain their weight at 2 years (mean BMI difference 0.29; $p = 0.47$). No significant changes were seen in donors with BMI < 30.
Conclusion: These data underline the difficulties in maintaining lifestyle modifications, even in highly motivated and selected individuals. The impact of

weight gain on long-term donor risk needs further evaluation, and live donor programmes should consider continuing provide support with lifestyle modification after donation.

OS253 LIVING KIDNEY DONOR KNOWLEDGE OF PROVIDED INFORMATION AND INFORMED CONSENT – A PROSPECTIVE NATIONWIDE INVENTORY STUDY

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Background: Informed consent is important for living kidney donors, as they are healthy individuals undergoing surgery for the benefit of others. No standardized nationwide informed consent procedure is available for living kidney donors; informed consent procedures vary per center, even between healthcare professionals. By understanding what information potential donors need to prepare them for the operation, the basis for a standardized, uniform informed consent procedure for live donor nephrectomy can be created.
Methods: In this prospective, multicenter national study, donor knowledge of the procedure and postoperative course was evaluated by means of pop quizzes. All potential donors who were seen at the live donor clinic (Cohort A) completed a pop-quiz about the details of the donation procedure prior to receiving any information. A second group of donors completed the same pop-quiz on the day of admission for donor nephrectomy (Cohort B). Primary endpoint was donor knowledge. Secondary endpoints were donor satisfaction and current informed consent practices in all transplant centers.
Results: A total of 656 pop-quizzes were completed; 417 in Cohort A and 239 in Cohort B. Average donor knowledge score was 7.0/25 (± 3.9, range 0-18) in Cohort A and 10.5/25 (± 2.8, range 0-17.5) in Cohort B. Donors scored best on duration of admission and convalescence, and worst on long-term complications. Cohort B scored significantly higher on overall knowledge, feeling of preparation and individual item scores ($p < 0.0001$), except for long-term complications ($p = 0.91$).
Conclusion: Donor knowledge of the procedure and postoperative course significantly improves during the work up process for live kidney donation, but is still low. Twenty percent of all donors did not know about long-term complications after live kidney donation after receiving information. Long-term complications deserve more attention during the preoperative educational process of living kidney donors.

OS254 THE UK LIVING DONOR KIDNEY EXCHANGE PROGRAMME – THE LARGEST IN EUROPE

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Introduction: A national living donor kidney exchange programme (KEP) started in the UK in 2007. Matching is 3-monthly, identifying all possible exchanges involving two or three donor-recipient pairs and, since 2012, altruistic donor chains (ADC) which facilitate one or two transplants for patients in the KEP pool and one transplant for a patient on the deceased donor waiting list. Compatible pairs have been included since 2011.
Methods: Data on enrolled and transplanted pairs are summarised.
Results: By the end of 2018, 2127 patients (2348 pairs) and 252 non-directed altruistic donors had enrolled in the UK KEP. Of the 2348 pairs, 148 were compatible pairs - seeking to gain a better HLA match or age match.

Recent matching runs have included up to 290 possible recipients and identified 60-85 possible transplants. About half of all patients enrolled have HLA antibodies to ≥ 85% of the deceased donor pool. Despite this, approximately 1600 possible transplants have been identified, with 993 proceeding: 26% were 2-way exchanges, 37% 3-way exchanges, 21% short ADC and 16% were long ADC. 71 transplants were for compatible pairs (48% of those registered). Since 2012, 66% of identified transplants have proceeded and 40% of all registered pairs have been transplanted through the KEP, ranging from 13% for AB recipients with B or AB donors to over 60% for A or B recipients with O donors. Non-simultaneous surgery occurs in about 20% of exchanges.
Conclusions: The UK KEP is very successful, allowing two- and three-way exchanges and ADC. Last year, 16% of all UK living donor kidney transplants were through the KEP, with particular impact on immunologically complex recipients who wait a long time for deceased donor transplant. A concomitant reduction in antibody incompatible transplantation in the UK has been seen in recent years. The UK KEP continues to grow and now represents more than half of all European KEP transplants.

OS255 KIDNEY DISORDERS LEADS THE MEDICAL REASONS TO EXCLUDE POTENTIAL KIDNEY DONORS FROM DONATION

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Living kidney transplantation provides the best therapeutic option for patients with kidney failure; however significant numbers of donors are rolled out for medical reasons. We aim to study the medical reasons behind excluding them from donation by transplant selection committee.

We assessed all potential kidney donors presented to our center between January 2015 to December 2016. Data presented as means + Standard deviation for continuous variables and proportion for categorical variables. 852 potential donors were assessed, 352 (41%) of them proceeded for donation. We present here the data for 500 potential donors who were rolled out. The mean age was 34.1 + 9.1 years, 76% were male. Mean Body Mass Index (BMI) was 27.9 + 5.5 for all excluded donors and 35.3 + 6.6 for donors rolled out because of obesity. Family history of Chronic Kidney Disease (CKD), Diabetes, Hypertension and kidney stone was positive as follow; 87.5%, 60%, 60% and 10%.

Impaired glucose metabolism was seen in 30% of them with 7.5% had undiagnosed diabetes mellitus. The prevalence of hypertension, hematuria, Kidney stone and proteinuria was as follow; 12%, 17.5%, 5% and 2.5%. Table 1 summarizes the common reasons for donor exclusion. These collectively made kidney disorder as the main reason to exclude potential kidney donor. This finding may explain the reported higher rate of chronic kidney disease post donation in comparison to healthy individuals from general population.

Conclusion; Kidney abnormalities, obesity and impaired glucose metabolism constitute the most important reasons to exclude potential donors. The prevalence of these abnormalities is high and raises alarm on population health. Potential reasons for high prevalence might be attributed to high family history of these diseases on top of prevalent population risk.

Reason to exclude	Proportion
Impaired glucose	22%
BMI	17%
Kidney abnormality	33%
Psychosocial	10%
Hypertension	7%
Hypertension	4%
Others	10%

OS32 - INTESTINAL TRANSPLANTATION

OS256 FIRST INTESTINAL TRANSPLANTATION IN THE GULF COUNTRY COUNCIL

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King Faisal Specialist Hospital & Research Center

Introduction: Intestinal transplantation (ITX) is the least common form of solid organ transplantation and often considered to be the most difficult. Recently, the Intestinal Transplant Registry (ITR) database included patient information from 82 contributing centers providing data on 2887 transplants in 2699 recipients. For various reasons including improvements in medical care of patients with intestinal failure and difficulty in accessing transplant care, the actual number of intestine transplants has declined significantly over the past 6 years.

we report the first successful case of intestinal transplantation in Saudi Arabia and Gulf counteries Council with a follow up of more than 1 year. The

reported case illustrates the well-known difficulty of postoperative risk for rejection which is being observed within 50% of all recipients following intestinal transplantation. Close monitoring and timely reaction as presented here is the key in detecting rejection episodes early. Timely and targeted treatment is the key in successful treatment of these and might diminish the still high rates of graft loss especially in the setting of isolated ITX where the liver is not included in the transplant

OS257 SENTINEL SKIN FLAPS FOR IMMUNOLOGICAL SURVEILLANCE

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Introduction: Abdominal wall transplantation (AWTx) offered a potential solution to the often-challenging closure of the abdominal wall at the time of intestinal transplantation (ITx). However, besides facilitating closure, the AWTx has been proven a promising asset for early, patient led rejection monitoring. We have therefore also used sentinel skin grafts for solely graft monitoring purposes when there was no clinical need for AWTx.
Methods: We performed a retrospective analysis of all patients undergoing intestinal and vascularized composite allograft (VCA) transplantation. Clinical presentation of rejection was correlated with histology, stoma output, citrulline levels and endoscopy findings.
Results: From October 2008 to October 2018, 45 patients underwent ITx. Ten underwent a modified multivisceral transplant and 35 an isolated small bowel transplant. Mean age was 42.6 years (range 23- 73). M/F: 27:18. Median follow up was 1031 days (range 14- 3651). All patients had Campath induction (30 mg iv) followed initially by Tacrolimus based maintenance (trough level of 8-12 ng/ml). Thirty one patients received a VCA in addition to ITx. Twenty two of these were AWTx.

There were 5 intestinal biopsy proven rejections in the IT alone group (36%) and a further 5 patients in the same group were falsely treated for rejection, as this was later labelled as infection.

There were 10 patients with rejection in the VCA part of the IT+ VCA group (11/31, 35%). These patients presented with a rash limited to the VCA. Of those 11 patients, there were 5 with concurrent intestinal rejection (5/31, 15%) with a lead-time of 5- 7 days between VCA and ITx.
Conclusion: We report on a series of combined VCA and ITx. The skin component has been utilized as a dynamic canvas for remote immune monitoring of visceral grafts. It has so far been useful for patient led monitoring of the ITx graft since it is visible and presents the earliest and only sign of rejection.

OS258 USE OF ARTERIAL EMBOLISATION TO FACILITATE EXENTERATION DURING MULTI-VISCERAL AND INTESTINAL TRANSPLANTATION

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Introduction: Exenteration during multi-visceral (MVT) and intestinal transplantation (IT) is associated with significant blood loss that increases patient instability intra-operatively and may affect the subsequent post-operative course. This is particularly the case for MVT for porto-mesenteric thrombosis (PMVT).
Methods: Embolisation was undertaken in theatre following anaesthesia and placement of lines. Amplatzer arterial plugs, type I (up to 16 mm in length) & type II (18-22 mm) were utilised. In the case of full MVT, the plugs occluded both coeliac axis (CA) and superior mesenteric arteries (SMA). In circumstances where the stomach was retained the SMA, hepatic and splenic arteries were occluded and the left gastric artery preserved.
Results: Pre-operative embolisation was performed in 13 patients who have had either MVT, liver/small bowel transplant (LSB), or small bowel/ pancreas/ colon transplant (SBP).

Nine of the 13 cases were embolised for severe portal hypertension (PHT). We have compared blood loss and use of blood products in this group to a historical cohort of intestine containing transplants in patients with severe PHT (table 1).

By performing embolisation in the operating theatre there was minimal delay in the explant procedure and no increase in the cold ischaemic time.

There was a reduction in intra-operative blood loss, blood products and metabolic instability. One patient undergoing a full MVT for PMVT required no blood products intra-operatively.

There were no complications associated with the embolisation procedure.
Conclusion: We believe that arterial embolisation is a very useful technique to minimize the blood loss associated with severe PHT during IT & MVT. It reduces blood loss, blood products and metabolic instability. The use of arterial plugs substantially reduces the time required for embolisation and the selective occlusion of visceral branches allows for the preservation of the stomach.

	Embolised = 9 (median, range)	Non-embolised = 22 (median, range)	*p* value
Blood loss (ml)	8,000 (1,395 – 2,740)	15,400 (4,700 – 66,000)	$p = 0.04$
RBCs (units)	6 (0 - 32)	18 (4 - 82)	$p = 0.02$
FFP (units)	4 (0 - 26)	11 (4 - 26)	$p = 0.03$
Platelets (units)	0 (0 - 6)	4 (0 - 11)	$p = 0.04$
Cryopercipitate (units)	0 (0 - 10)	4 (0 - 20)	$p = 0.16$
Reperfusion lactate (mmol/L)	4.3 (1.9 - 11.0)	7.1 (2.6 - 10.7)	$p = 0.11$

OS259 HEROIC INTERVENTION FOR INTESTINAL TRANSPLANTATION - A NOVEL OPTION FOR END-STAGE VASCULAR ACCESS IN INTESTINAL FAILURE (IF) PATIENTS: THE HEMODIALYSIS RELIABLE OUTFLOW (HERO) GRAFT

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[1]University of Oxford; [2]Oxford Transplant Centre

Background: Intestinal failure (IF) patients are dependent on central venous access to receive parenteral nutrition and to facilitate intestinal transplantation. Longstanding central venous catheters lead to loss of access due to central venous stenosis/occlusion and are associated with lifethreatening catheter related blood stream infections (CRBSIs). The Haemodialysis Reliable Outflow (HeRO) graft is a device that is designed for end-stage access in haemodialysis patients and can maintain access in the presence of central venous stenosis/ occlusion. We describe a case series of HeRO graft use in patients with IF to facilitate or support intestinal trasplantion.
Methods: Four HeRO grafts were inserted into IF patients with end-stage vascular access to facilitate or support intestinal transplantation. Perioperative complications, infections, patency rates and interventions to retain patency were assessed.
Results: There were no blood stream infections, one surgical site infection and no procedure related peri-operative complications. The HeRO graft was used for phlebotomy, fluid therapy and parental nutrition in all patients and two of the patients were trained to self-cannulate. Primary patency was 1235, 177, 52 and 23 days. Secondary patency was 1748 and 359, two of the four patients died with a functioning graft (DWFG). One patient had repeated episodes of thrombosis (15 procedures) and the graft was removed on patient request.

Case	Transplant/IF Diagnosis: *SBS = Short Bowel Syndrome	Patency (days) Primary (P) Secondary (S) *Death with functioning graft (DWFG)	Infections	Interventions to retain patency
1	SBS	P: 1235 S: 1748	0	8
2	SBS	P & S: 52 days DWFG*	0	0
3	SBS	P & S: 177 days DWFG*	1	(Surgical Site infection)
0				
4	Crohn?s Disease	P: 23 days S: 359 days HeRO removed after 359 days	0	15

Discussion: We have shown that in a highly complex group of IF patients with central venous stenosis/occlusion limiting conventional access, a HeRO graft can be a feasible alternative. In all patients the HeRO graft allowed immediate vascular access and in 3 out of 4 patients it was used successfully for nutritional support despite limited life-expectancy.

OS260 17β-ESTRADIOL AS A NEW THERAPY TO PRESERVE MICROCIRCULATORY PERFUSION IN SMALL BOWEL DONOR

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Background: Intestine graft viability compromises harvesting in most brain dead (BD) donors. Small bowel transplantation is a complex procedure with

worse outcomes compared to other abdominal organs. The hormone 17β-estradiol has showed vascular protective effects in lung tissue of BD male rats. Thus, estradiol might be a treating option to improve the quality of small bowel grafts.
Methods: Male Wistar rats were divided in 3 groups (n = 11/group): trepanned only (SH); submitted to rapid onset brain death (BD); and BD rats treated with 17β-estradiol (E2, 280 μg/kg, iv; BD-E2). Experiments performed 180 min thereafter included: (a) laser Doppler flowmetry and intravital microscopy to evaluate mesenteric perfusion; (b) RT-PCR of endothelial nitric oxide synthase (eNOS) and endothelin-1; (c) immunohistochemistry of eNOS, endothelin-1, P-selectin, intercellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1 expression; (d) ELISA for cytokines and chemokines measurement.
Results: Treatment with 17β-estradiol restored microcirculatory perfusion after brain death. Values for the proportion of perfused small vessels were (mean ± SEM): BD rats (40 ± 6%); SH rats (75 ± 8%); BD-E2 rats (67 ± 5%) (p = 0.011). There were no changes in mesenteric blood flow between groups (p = 0.369). Treatment with 17β-estradiol was associated with 2-fold increase in eNOS protein (p < 0.0001) and gene (p = 0.0009) expression, with no differences in endothelin-1 expression among groups. BD-E2 rats exhibited a reduction in VCAM-1 expression (p = 0.0008), and reduced CINC-1 serum levels (p = 0.002).
Conclusion: Data showed that 17β-estradiol treatment was effective in restoring mesenteric perfusion in BD rats by increasing endothelial eNOS expression. Estradiol actions in the microcirculation may improve intestine donor viability.
Financial Support: FAPESP grant 2016/13632-3.

OS261 USE OF AVASCULAR RECTUS ABDOMINUS FASCIA FOR ABDOMINAL CLOSURE IN TRANSPLANTATION

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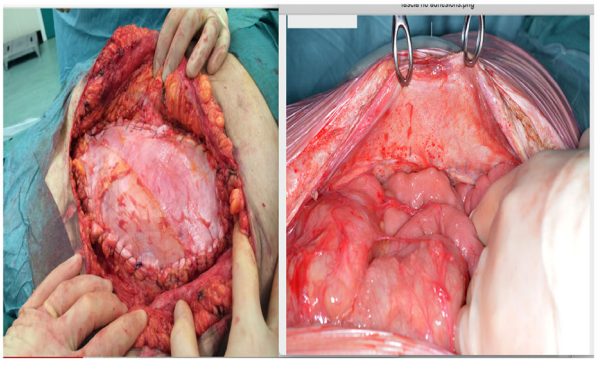
Introduction: Abdominal closure after intestinal transplantation (IT) is challenging. A variety of techniques have been described: tissue expansion, use of reduced grafts, autologous flaps and vascularized abdominal wall transplants.
Methods: The rectus abdominus and fascia are excised from the donor leaving subcutaneous tissues and skin.

The fascia is stored in UW solution on ice. Prior to use the fascia is isolated, anterior and posterior layers are preserved and any defects closed with prolene.

The fascia is implanted using tension free closure. Skin closure is achieved by mobilisation of the subcutaneous tissues, although use of a vac dressing onto the fascia and skin grafting is possible.
Results: We describe 21 transplant recipients (17 small bowel, 3 liver and 1 kidney) where abdominal closure was achieved using rectus abdominus fascia. In 3 patients fascia from a third-party donor was used.

In the 3 liver transplants, a fascial graft was used for a small patient with acute liver failure. This permitted organs from a donor with a weight ratio of 1.41 to that of the recipient to be used. Another recipient required abdominal wall reconstruction following loss of abdominal domain (3rd liver transplant with chronic biliary fistula). A third developed an enterocutaneous fistula following incisional hernia repair. The prosthetic material (Permacol) was removed and replaced with third party fascia with no subsequent sepsis or fistulation.

There have been no significant complications associated with this technique. Ten subsequent laparotomies through the fascia have been performed with minimal adhesions between the viscera and fascia. No herniae have developed. Where third party fascia has been used HLA antibodies to the fascia have been demonstrated. In addition, it is possible to transmit CMV with fascial grafts.
Conclusion: The use of avascular fascia is associated with good functional outcomes and is a technique applicable to a range of transplants.



OS33 - KIDNEY IMMUNOSUPPRESSION-CHALLENGES AND OPTIONS

OS262 THE USE OF THYMOGLOBULIN INDUCTION AND MTOR INHIBITORS TO PREVENT ACUTE CELLULAR REJECTION IN KIDNEY TRANSPLANTATION ON BELATACEPT REGIMEN

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Background: Belatacept is a costimulatory blocker that is used as maintenance immunosuppression in kidney transplantation to avoid toxic effects of calcineurin inhibitors. However, patients maintained on belatacept, mycophenolate, and corticosteroids, have been noted to have more frequent and severe acute rejection than in CNI. We developed a belatacept regimen incorporating thymoglobulin for induction and everolimus as part of the maintenance regimen.
Methods: We prospectively enrolled 67 kidney transplant recipients (43 deceased; 24 living donors) at our center to receive denovo belatacept from Aug 2012 to Oct2018. PBMCs were collected prior to transplant and at the time of biopsies. All patients received thymoglobulin for induction with belatacept 10 mg/kg administered on POD 1, 4, 14, 28, 56, and 84. Monthly maintenance dose of 5 mg/kg was given starting week 16. Patients were started initially on MPA but were converted to everolimus after 1 month, and all patients were maintained on prednisone. Protocol biopsies were performed at 6 months.
Results: In the first 12 months post-transplant, 16.4% developed acute rejection: 2 with ACR 1a, 1 with ACR 2a, 6 with ACR 2b, 1 with AMR, and 1 with simultaneous ACR 1a and AMR. All 11 rejections occurred in those who were on MPA and not on mTORi. 12 patients were found to have borderline rejection (5 on mTORi, 7 on MPA). 33 patients did not have any inflammation on biopsies. 57 patients remained on belatacept, and 10 patients were converted to tacrolimus. Our regimen with thymoglobulin maintained T regs, in contrast to phase III trial.
Conclusion: This trial of combining belatacept with mTORi shows that it is possible to significantly reduce the rate of acute rejection in belatacept-based regimens. The synergy between mTORi and belatacept may be related to mTORi's inhibitory effect on memory CD8 + CD28-CD38 + cells refractory to costimulatory blockade. In addition, induction with thymoglobulin prevents the depletion of T regs.

OS263 KIDNEY TRANSPLANTATION IN PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME: THE OSPEDALE MAGGIORE POLICLINICO EXPERIENCE OVER 35 YEARS

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Background: Due to very high recurrence rates after transplantation, poor kidney allograft survival has been reported for recipients with atypical hemolytic uremic syndrome (aHUS). More recently, prophylaxis with eculizumab has shown encouraging results but available data remain scarce.
Methods: In this single-centre retrospective study with a median follow up of 42 months, we reviewed data from 38 consecutive kidney transplants performed between 1983 and 2018 in patients with aHUS. Outcomes of transplants receiving prophylaxis with eculizumab (Eculizumab group, 14 allografts in 14 patients) were compared to those of transplants receiving no prophylaxis or prophylaxis with plasma-exchange (No-Eculizumab group, 24 allografts in 22 patients). If no otherwise specified, data refer to last visit.
Results: Baseline characteristics were comparable. Recipients in No-eculizumab had significantly longer follow up (p = 0.013). aHUS recurrence rate was 0% in Eculizimab and 46% in No-Eculizumab (p = 0.006) with 91% of the relapses recorded within 1 year of transplant. Recurrence led to transplant loss in 64% of the recipients experiencing such a complication. However, rescue therapy with eculizumab was effective in 100% of the graft treated. One-year graft survival was significantly better for patients in Eculizumab than No-Eculizumab (100% vs 71%; p = 0.0334) whereas overall patient survival (100%), primary non-function (0%), delayed graft function (8% vs 17%), and rejection (25% vs 29%) rates were similar (p = ns). Albeit not statistically significant (p = ns), Eculizumab and No-Eculizumab showed different intraoperative bleeding (17% vs 37%), overall infection (83% vs 48%), and severe infection (25% vs 15%) rates.
Conclusions: For patients with aHUS, recurrence represents the main cause of transplant loss. Eculizumab significantly reduces the risk of relapse and improves early graft survival. Aggressive perioperative infection control strategies are advised.

OS264 ANTI-CD40 (ISCALIMAB) TREATMENT RESULTS IN PRESERVED ALLOGRAFT HISTOLOGY IN NON-HUMAN PRIMATE KIDNEY TRANSPLANTATION COMPARED TO CALCINEURIN INHIBITORS

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The CD40-CD154 costimulatory pathway has been implicated in the pathology of transplant rejection, and blockade of this interaction using anti-CD40 antibodies significantly prolongs renal allograft survival in non-human primates (NHPs). Further, recent clinical data indicated that the anti-CD40 mAb Iscalimab (CFZ533) demonstrated comparable efficacy and superior renal function versus tacrolimus in de novo calcineruin inhibitor (CNI)-free kidney transplantation. One possible explanation for superior renal function was that Iscalimab treatment may have resulted in improved graft quality compared to CNIs. To examine this notion, allograft histology from baseline and up to one hundred days post-transplanted NHP kidney allografts from transplanted animals treated with Iscalimab, anti-CD154 mAb, Cycosporin, PKC inhibitors or FTY720 were reviewed and scored in a blinded fashion by a pathologist. Banff criteria and the chronic allograft damage index (CADI) were obtained. A CADI of 1 or less was considered as 'normal renal histology'. Additionally we performed molecular analyses of these samples. Our analyses indicated that the quality of allografts from Iscalimab treated animals was superior to that observed in animals dosed with other immunomodulatory agents. This was also reflected in the molecular analyses. Collectively our data indicated that prevention of allograft rejection by Iscalimab appears to be associated with lower CADI scores, with close to normal histology maintained in a high proportion of allografts.

OS265 LOW DOSE THYMOGLOBULINE INDUCTION IN LOW RISK KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Practically all kidney allograft recipients require immunosuppressive therapy to prevent rejection and loss of the allograft. The optimal regimen, including induction therapy, is not clear. The aim of this study was to determine the occurrence of biopsy proven acute rejection (BPAR) in low immunological risk kidney transplant recipients according to the type of induction (basiliximab versus low dose of Thymoglobuline – 3.5 mg/kg).
Material and Methods: 125 patients after primary kidney transplantation (KT) with low immunological risk were included in the retrospective analysis with 6-month follow-up. The immunosuppression regimen of all patients included tacrolimus, mycophenolic acid and corticoids.
Results: We did not find any significant difference in the occurrence of acute rejection or difference in the occurrence of infection complications. Patients in the Thymoglobuline group had a significantly longer period of cold ischemia, more frequently KT from expanded criteria donors (ECD) and significantly more mismatches in DR. We did not confirm any significant difference in the graft or patient survival between monitored groups. Delayed graft function was identified as an independent risk factor for BPAR.
Conclusion: Patients with low immunological risk and at the same time with a high risk of DGF benefit from the Thymoglobuline induction in dose of 3.5 mg/kg without the increased risk of infection complications with the assumption of good graft function in long-term post-transplant period.

	D0	D1	D2	D3-7	D8-14	D15-28	D29-3mes
methylprednisolon	500 mg i.v.	500 mg i.v.					
prednison			20 mg	20 mg	20 mg	15 mg	10 mg
mycophenolate sodium	2 g/1440 mg	2 g/1440 mg	2 g/1440 mg	2 g/1440 mg	2 g/1440 mg	2 g/1440 mg	1.5g/1080 mg
tacrolimus	0.2 mg/kg 1x per day	levels 10-15 ng/ml					levels 8-12 ng/ml
anti IL2-RA – protocol I	20 g before reperfusion and at D4						
rATG – protocol II	1.5 mg/kg	1.0 mg/kg	1.0 mg/kg				

ATG – rabbit antitymocyte globuline, **anti IL2-RA -** monoclonal antibody to IL-2R alpha

Table 1 Immunosuppressive protocols I, II

OS266 EFFECT OF DONOR AGE ON EFFICACY AND SAFETY OF DE NOVO RENAL TRANSPLANT RECIPIENTS RECEIVING EVEROLIMUS WITH REDUCED-EXPOSURE CALCINEURIN INHIBITOR REGIMEN: 24-MONTH RESULTS FROM THE TRANSFORM STUDY

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Background: Recipients (R) of allografts from older donors (D) are expected to have poor outcomes after renal transplantation (RTx). Here, we evaluate the 24-month (M) efficacy and safety outcomes in 2 cohorts of RTxRs based on D/R age (Cohort 1: D age at least 20 years more than R age and Cohort 2: D/R ages $\geq$ 65 years) from the TRANSFORM (NCT01950819) study.
Methods: In this 24M, multicentre, open-label study, *de novo* adult RTxRs were randomised to receive everolimus with reduced-exposure calcineurin inhibitor (EVR+rCNI, N = 1022) or mycophenolic acid with standard-exposure CNI (MPA+sCNI, N = 1015) with induction+steroids. Efficacy (composite of treated biopsy-proven acute rejection [tBPAR] or estimated glomerular filtration rate [eGFR] <50 mL/min/1.73 m^2 and composite of tBPAR/graft loss/death), renal function (mean eGFR [MDRD4] and urinary protein to creatinine ratio), and overall safety were assessed by treatment arms and cohorts.
Results: In all, there were 295 and 158 RTxRs in Cohorts 1 and 2, respectively (Table). The donor category was predominantly living-related for Cohort 1 (80.0%) and deceased for Cohort 2 (82.9%). Between-arm differences in incidence of efficacy endpoints, tBPAR, and eGFR < 50 mL/min/1.73 m^2 were comparable for both cohorts ($p > 0.05$). Mean eGFR was comparable between treatment arms, but at least 10 mL/min/1.73 m^2 lower in Cohort 2 versus Cohort 1. From Week 4 to M24, both treatment arms showed net eGFR decline in Cohort 1 and a net eGFR gain in Cohort 2. Safety outcomes were comparable between arms; however, incidence of cytomegalovirus infections was significantly lower with EVR+rCNI in both the cohorts (Table).
Conclusion: In RTxRs with age mismatched or matched older donors, EVR+rCNI regimen shows comparable efficacy, renal function and safety outcomes, with lower viral infection rates, as MPA+sCNI regimen up to 24-months post-RTx; however, younger RTxRs tend to have better outcomes than older RTxRs with age-matched donors.

OS267 GRAFT AND PATIENT SURVIVAL BY INDUCTION THERAPY IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS

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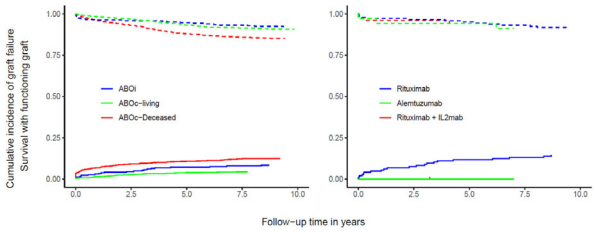
Background: Over a decade ago the first ABO-incompatible (ABOi) kidney transplantations were performed in The Netherlands. Initially, rituximab was used for induction. Later basiliximab was added or alemtuzumab was administered instead. We compared graft and patient survival between a) ABOi and ABO-compatible (ABOc) transplant recipients, and b) induction regimens in the ABOi group.
Methods: Data on all kidney transplantations performed since 2006 were obtained from the Dutch Organ Transplant Registry. Using propensity scores, ABOi recipients were matched to ABOc-living donor and ABOc-deceased donor from the same center in a 1:4:4 ratio.
Results: 10474 Kidney transplantations were performed between March 2006 and January 2018, including 263 ABOi procedures. All ABOi recipients were matched to ABOc-living donor and ABOc-deceased donor recipients. Baseline characteristics were similar after matching. The left figure below shows respectively the survival probability with a functioning graft and the cumulative incidence of graft failure for the three groups.

The ABOi group had similar risk of death with a functioning graft (HR = 0.81; 95%CI 0.51 – 1.29), but a higher risk of death-censored graft



failure compared to the ABOc-living donor group (HR = 1.91; 95%CI 1.17 - 3.13). However, the ABOi group had a lower risk of graft failure (HR = 0.64: 95%CI 0.42 – 0.99) and lower risk of death (HR = 0.46; 95%CI 0.30 – 0.72) compared to the ABOc-deceased donor group. The right figure above shows outcome by induction regimen.
Conclusion: ABOi kidney allograft recipients had similar survival compared to ABOc-living donor recipients. Alemtuzumab and rituximab+basiliximab treated ABOi recipients had superior graft survival compared to rituximab only induction.

OS268

EFFICACY OF CALCINEURIN INHIBITORS TRANSFERRING TO RAPAMYCIN IN LIVE KIDNEY TRANSPLANTATION FROM OLD DONORS TO YOUNG RECIPIENTS

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Background: Calcineurin inhibitor(CNI) nephrotoxicity is one of the major reasons for chronic allograft injury in live kidney transplantation from old donors to young recipients. Therefore we carry out a retrospective cohort study with the aim to evaluating whether calcineurin inhibitors transferring to rapamycin on 3 months after live kidney transplantation from old donors to young recipients could improve the long-term kidney allograft function.
Methods: We retrospectively collected 308 cases of live kidney transplantation with young recipients(age < 30 years old) and old donors(age > 50 years old) from January 2005 to November 2015. Among these recipients, 92 recipients transferred from CNI to rapamycin(Rapa group) on 3 months after kidney transplant, who was matched with 92 recipients who persisted on CNI (CNI group) according to the age and gender of donors and recipients. The 1 year graft function, long-term graft and patient survival, and complications after 3 months were compared between the two groups.
Results: The acute rejection rate was comparable between Rapa group and CNI group(17.4% vs. 15.2%, $p = 0.690$). However, incidence of chronic allograft injury was significantly lower in Rapa group compared to CNI group (13.0% vs. 25.0%, $p = 0.039$). the 1-year serum creatinine level was significantly lower in Rapa group (114.7 ± 48.2 vs.131.5 ± 55.4umol/L, $p = 0.029$). The new onset diabetes rate was higher in CNI group(10.9% vs. 3.3%, $p = 0.044$). The incidence of hyperlipemia was significantly higher in Rapa group(23.9% vs.9.8%, $p = 0.01$). The incidences of proteinuria, liver function impairment, infection, cerebral vascular diseases were all comparable between the two groups($p > 0.05$). The 1-,3-,5- year graft and patient survival were also comparable between the two groups($p > 0.05$).
Conclusion: Calcineurin inhibitors transferring to rapamycin can reduce chronic allograft injury and improve graft function in live donor kidney transplantation from old donors to young recipients.

OS269

EFFICACY AND SAFETY OF EVEROLIMUS-BASED REGIMEN IN RENAL TRANSPLANT RECIPIENTS WITH DELAYED GRAFT FUNCTION: 24-MONTH RESULTS FROM THE TRANSFORM STUDY

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Background: Delayed graft function (DGF) affects allograft and patient outcomes in renal transplant recipients (RTxRs). Here, we evaluate the effect of everolimus+reduced-exposure calcineurin inhibitor (EVR+rCNI) vs mycophenolic acid+standard-exposure CNI (MPA+sCNI) regimen in RTxRs with DGF from the TRANSFORM (NCT01950819) study.
Methods: In this 24-month (M), multicentre, open-label study, low-to-moderate risk *de novo* RTxRs were randomised to EVR+rCNI (N = 1022) or MPA+sCNI (N = 1015) with induction and steroids. Drug exposure, overall efficacy (estimated glomerular filtration rate [eGFR] <50 mL/min/1.73 m^2, tBPAR, graft loss or death), renal function, and safety were assessed at M24.
Results: Overall, 210 RTxRs developed DGF (EVR+rCNI [$n = 110$, 10.8%]; MPA+sCNI [$n = 100$, 9.9%]). In the DGF cohort, proportion of RTxRs with expanded criteria deceased donors was similar in both treatment arms (EVR+rCNI, 25 [26.3%]; MPA+sCNI, 26 [33.3%]), but cold ischaemia time > 20 h was more common with EVR+rCNI (34.5% vs 22.0%). Mean tacrolimus trough levels at Day 7 were within target range in EVR+rCNI (6.8 ng/mL; target 4-7 ng/mL) and MPA+sCNI (8.5 ng/mL; target 8-12 ng/mL) arms. Consistent with the overall population, incidences of efficacy parameters were comparable between arms in the DGF cohort at M24 (Table). Mean eGFR was comparable in EVR+rCNI vs MPA+sCNI. Proteinuria as an adverse event was more frequent in the EVR+rCNI arm (24.3% vs 12.0%); however, most patients in both arms had mild proteinuria (urine protein/creatinine ratio30- < 500 mg/g: EVR+rCNI, 30/39 [76.9%] vs MPA+sCNI, 46/50 [92.0%]). Overall incidence of infections and infestations, including cytomegalovirus (CMV) infection, was significantly ($p < 0.001$) lower in EVR+rCNI vs MPA+sCNI arm.
Conclusion: In *de novo* RTxRs with DGF, an EVR-based regimen provides comparable efficacy, safety, and renal function outcomes, with a lower rate of CMV infections relative to MPA+sCNI regimen up to 2 years post-transplant.

Table. Efficacy, renal function, and safety outcomes at M24 in RTxRs with DGF*

	DGF Cohort				Overall population			
Parameters	**EVR+rCNI (N=110)**	**MPA+sCNI (N=100)**	**Risk difference (95% CI)**	***P* value‡**	**EVR+rCNI (N=1022)**	**MPA+sCNI (N=1015)**	**Risk difference (95% CI)**	***P* value†**
Induction therapy, n (%)								
Basiliximab	87 (79.1)	74 (74.0)	-	-	849 (83.1)	844 (83.2)	-	-
rATG	23 (20.9)	26 (26.0)	-	-	171 (16.7)	171 (16.8)	-	-
Efficacy outcomes, n (%)								
eGFR <50 mL/min/1.73 m^2 or tBPAR	55 (50.0)[§]	51 (51.0)[§]	−0.01 (−0.15, 0.13)	0.885	489 (47.9)[§]	443 (43.7)[§]	4.2 (−0.3, 8.7)	0.067
eGFR <50 mL/min/1.73 m^2	47 (42.7)[§]	40 (40.0)[§]	0.03 (−0.11, 0.16)	0.689	474 (46.4)[§]	423 (41.6)[§]	4.7 (0.2, 9.2)	0.040
tBPAR, graft loss or death	37 (33.6)[§]	29 (29.0)[§]	0.05 (−0.08, 0.17)	0.470	169 (16.0)[§]	147 (17.3)[§]	0.8 (−4.6, 6.1)	0.782
tBPAR	22 (20.0)[§]	19 (19.0)[§]	0.01 (−0.10, 0.12)	0.855	118 (12.8)[§]	98 (12.1)[§]	0.7 (−4.4, 5.8)	0.794
Graft loss	9 (8.2)[§]	10 (10.0)[§]	−0.02 (−0.10, 0.06)	0.646	37 (3.7)[§]	32 (3.2)[§]	0.5 (−1.1, 2.1)	0.572
Death	10 (9.1)[§]	7 (7.0)[§]	0.02 (−0.05, 0.09)	0.579	32 (3.7)[§]	36 (4.2)[§]	−0.5 (−2.7, 1.6)	0.634
Renal function			**Mean difference (95% CI)**	***P* value§**			**Mean difference (95% CI)**	***P* value§**
eGFR (mL/min/1.73 m^2), mean (SE)	41.2 (2.00)	44.4 (2.46)	−3.13 (−9.33, 3.07)	0.321	52.6 (0.74)	54.9 (0.72)	−2.28 (−4.32, −0.24)	0.028
UPCR (mg/g), mean (SE)	362.2 (82.27)	209.6 (45.92)	152.6 (−35.7, 340.8)	0.110	290.2 (588.2)	233.1 (524.4)	-	-
Safety outcomes, n (%)	**EVR+rCNI (N=107)**	**MPA+sCNI (N=100)**	**Risk ratio (95% CI)**	***P* value¶**	**EVR+rCNI (N=1014)**	**MPA+sCNI (N=1012)**	**Risk ratio (95% CI)**	***P* value¶**
At least one AE/infection	106 (99.1)	99 (99.0)	1.00 (0.97, 1.03)	-	1000 (98.6)	992 (98.0)	1.01 (0.99, 1.02)	-
At least one SAE/infection	83 (77.6)	83 (83.0)	0.93 (0.82, 1.07)	-	632 (62.3)	633 (62.5)	1.00 (0.93, 1.07)	-
At least one AE/infections leading to study drug discontinuation	50 (46.7)	31 (31.0)	1.51 (1.06, 2.15)	-	276 (27.2)	152 (15.0)	1.81 (1.52, 2.16)	-
At least one AE/infection leading to study drug dose adjustment or interruption	35 (32.7)	63 (63.0)	0.52 (0.38, 0.71)	-	496 (48.9)	612 (60.5)	0.81 (0.75, 0.88)	-
Infections and infestations, n (%)								
Total	71 (66.4)	84 (84.0)	0.79 (0.67, 0.93)	0.003	584 (57.6)	664 (65.6)	0.88 (0.82, 0.94)	<0.001
CMV infection	3 (2.8)	17 (17.0)	0.16 (0.05, 0.55)	0.001	44 (4.3)	158 (15.6)	0.28 (0.20, 0.38)	<0.001
BKV infection	5 (4.7)	6 (6.0)	0.78 (0.25, 2.47)	0.671	46 (4.5)	87 (8.6)	0.53 (0.37, 0.75)	<0.001

*DGF was defined as need for dialysis within 21 days post-Tx following investigator-reported graft dysfunction or delayed graft function on the AE e-CRF form or investigator-reported delayed or slow recovery of graft function post-revascularization as primary suspected reason for rejection or delayed graft function as primary clinical diagnosis on the kidney allograft rejection eCRF form.
†Chi-square test; ‡P-value to test for no difference (EVR+CNI) - (MPA+CNI) = 0); §Incidence rates; ¶Kaplan-Meier incidence and *P*-value is from Z-test; ††T-test
AE, adverse event; BKV, BK virus; CI, confidence interval; CMV, cytomegalovirus; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; eCRF, electronic case report form; EVR, everolimus; M, month; MPA, mycophenolic acid; rATG, rabbit antithymocyte globulin; rCNI, reduced-exposure calcineurin inhibitor; RTxRs, renal transplant recipients; SAE, serious AE; sCNI, standard-exposure calcineurin inhibitor; SE, standard error; tBPAR, treated biopsy-proven acute rejection; Tx, transplantation; UPCR, urine protein creatinine ratio.

OS270

PROPHYLACTIC USE OF ECULIZUMAB IN PATIENTS AT HIGH RISK OF POST-TRANSPLANT AHUS RECURRENCE IMPROVES GRAFT OUTCOMES

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Purpose: Eculizumab has revolutionized the management of atypical Hemolytic Uremic Syndrome (aHUS). In 2012, recommendations were issued to advocate the prophylactic use of eculizumab in kidney transplant recipients with high and moderate risk of post-transplant aHUS recurrence. The impact of this strategy has never been assessed.
Methods: A nationwide retrospective multicenter study was conducted, involving 32 centers. Inclusion criteria were the following: 1- aHUS diagnosed before the transplantation; 2- An extensive complement work-up undertaken at the national reference laboratory; 3- At least one adult-onset kidney transplantation performed after January 1st 2007. Individualized risk assessment was based on complement investigations and history of post-transplant recurrence.
Results: Overall, 126 kidney transplantations, performed in 116 patients were included into the study. Overall, 58.7 and 33.3% of the transplantations were considered at high risk and moderate risk of aHUS recurrence. Full-blown clinical and subclinical aHUS recurrence occurred in 30 (23.8%) and 12 (9.5%) of the transplantations. Multivariate analysis identified high-risk group (HR = 2.94; $p = 0.003$) and prophylactic eculizumab (HR = 0.06; $p < 0.0001$) as factors associated independently with an increased and reduced risk of recurrence, respectively. Moreover, aHUS recurrence (HR = 3.74; $p = 0.006$) and eculizumab therapy (HR = 0.23; $p = 0.003$) were independently associated with increased and decreased risks of graft loss, respectively. Eculizumab prophylaxis significantly reduced the rates of recurrence in both high- ($p < 0.001$) and moderate-risk ($p = 0.02$) transplantations but only improved graft survival in the high-risk transplantation group ($p < 0.02$).
Conclusions: The present study demonstrates that the outcome of kidney transplantation in aHUS patients has dramatically improved since eculizumab approval and supports individualized risk stratification based on complement investigations and medical history.

OS271 PHENOTYPIC AND TRANSCRIPTOMIC LYMPHOCYTES CHANGES AFTER HIGH DOSES OF INTRAVENOUS IMMUNOGLOBULINS IN KIDNEY ALLOGRAFT RECIPIENTS

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[1]APHP Hôpital Henri Mondor; [2]Inserm U955 équipe 21

Effects of intravenous immunoglobulins (IVIG) are pleiotropic. Despite IVIG large use in the field of kidney transplantation, no phenotypic and transcriptional analyze of peripheral lymphocytes evolution after IVIG are available.

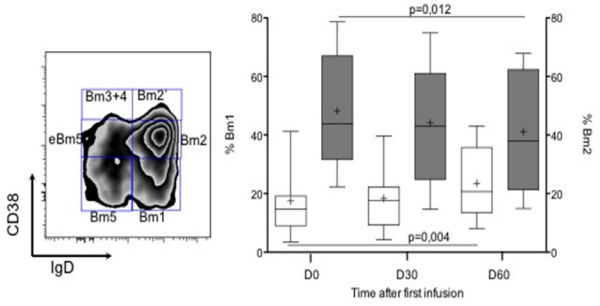
We designed a prospective cohort study of kidney allograft recipients treated with IVIG high doses each month during three months and never treated before with Rituximab. PBMC were collected before each IVIG infusion (Day 0, D30, D60, D90). Both transcriptional profile (13 genes selected to be mechanistically informative) and phenotypic characterization of peripheral lymphocytes were performed by real time PCR and flow cytometry, respectively.

Twelve renal transplant recipients have been included. All received three courses of high doses of IVIG. Phenotypic analysis of B cell subsets showed after 60 days a significant increase of Bm1 cells (%IgD+CD38-, naïves cells) and a significant decrease of Bm2 (%IgD+CD38low, activated naïves cells).

Phenotypic analyze of peripheral T lymphocytes did not show any difference at the end of IVIG treatment.

Transcriptomic analyses did not show any modification in blood gene expression after IVIG treatment.

Conclusion: In conclusion, high doses of IVIG in kidney transplant recipients increased significantly naïves B cells and decreased significantly activated naïves B cells. However, gene expression did not differ before and after treatment.



OS273 CONVERSION FROM CALCINEURIN INHIBITORS TO BELATACEPT IN KIDNEY RECIPIENTS DECREASES THE PATHOGENICITY OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES

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Conversion from calcineurin inhibitor (CNI)- to Belatacept-based regimen has been associated with improved graft function in low-immunologic risk kidney recipients. We investigated the efficacy and safety of conversion to Belatacept in kidney recipients with post-transplant anti-HLA DSAs.

We prospectively included 109 adult kidney recipients with post-transplant anti-HLA DSAs and biopsy-proven CNI nephrotoxicity (isometric vacuolization of proximal tubular cells, arteriolar hyalinosis with medial/peripheral nodules and/or striped pattern of IF/TA) who were converted to Belatacept between 2012-2017. We excluded patients with clinical AMR. Patients were systematically assessed for clinical, histological characteristics and DSA characteristics (specificity, MFI and IgG subclass composition using SAB) at the time of conversion and at one year post-conversion. Patients were followed-up to 2018 to evaluate graft survival.

Patients were converted at a median time of 13.0 (IQR, 3.0-66.1) months post-transplant and showed improved GFR at one year (39.8 $\pm$ 14.4 vs. 29.5 $\pm$ 13.9 mL/min, $p < 0.001$). GFR kinetics exhibited a linear component with rapid improvement within 3 months post-switch ($p < 0.001$) and a negative quadratic component with slow improvement beyond 3 months post-switch ($p < 0.001$). Patients exhibited decreased DSA MFImax levels at one year post-switch (4624 $\pm$ 5398 vs. 5320 $\pm$ 5553, $p < 0.001$). The prevalence of complement-fixing IgG1 and IgG3 subclasses diminished from 38.5% to 26.6% under Belatacept treatment ($p = 0.002$). Histologically, patients showed decreased prevalence of microcirculation inflammation (g > 0 and/or ptc > 0, 15.6% vs. 22.9%, $p = 0.027$) and of C4d deposition (6.5% vs. 29.4%, $p = 0.004$) at one year post-conversion.

Conversion from CNI- to Belatacept-based regimen in kidney recipients with post-transplant anti-HLA DSAs and nephrotoxicity is associated with improved graft function and decreased pathogenicity of anti-HLA DSAs.

OS34 - GROWING ORGANS AND CELL THERAPIES

OS274 DESIGN BY NATURE: IMPROVING CULTURE, EXPANSION AND DIFFERENTIATION OF HUMAN LIVER ORGANOIDS WITH CLINICAL GRADE LIVER EXTRACELLULAR MATRIX

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Introduction: LGR5 + liver organoids derived from human liver biopsies have great potential for personalized regenerative medicine purposes. Culture of such organoids is performed in non-clinical grade hydrogels derived from mouse tumor extracts, such as Matrigel®. These extracts lack tissue specific components, which inhibits differentiation towards functional hepatocytes. The aim of this study is create clinical grade hepatic micro-environments from human liver extracellular matrix (ECM) for the culture and differentiation of human liver organoids.

Methods: Human livers, deemed unsuitable for transplantation, were decellularized via perfusion with Triton-x-100 solution. ECM components were extracted by pepsin digestion in 0.1M acetic acid for 72 hours. After normalizing the pH, a viscous pre-gel solution was formed, which formed a hydrogel at 37°C. Composition and physical properties of the hydrogel were determined. Human liver organoids were cultured in the human liver hydrogel and analyzed for proliferation and differentiation capacities (N = 15).

Results: Human liver hydrogels solidified within 15 minutes, consisted of dense collagen networks and exhibited a higher stiffness (0.35 kPa) compared to Matrigel® (0.1 kPa). Liver organoids proliferated in the liver hydrogel and were passaged multiple times according to normal procedures. Metabolic assays showed similar cell proliferation compared to Matrigel. However, the human liver hydrogels improved differentiation towards hepatocytes, as gene expression for albumin was 15-fold higher compared to matrigel conditions.

Conclusion: This study shows the feasibility of creating clinical grade hydrogels from human liver ECM that can support the proliferation and differentiation of human liver organoids. The liver hydrogel could provide an important step forward in the clinical applications of liver organoids for personalized regenerative medicine purposes.

OS275 ENDOTHELIAL CELL REPLACEMENT - A NOVEL PLATFORM FOR BIOENGINEERING OF PERSONALIZED, TISSUE-ENGINEERED ORGANS FOR TRANSPLANTATION

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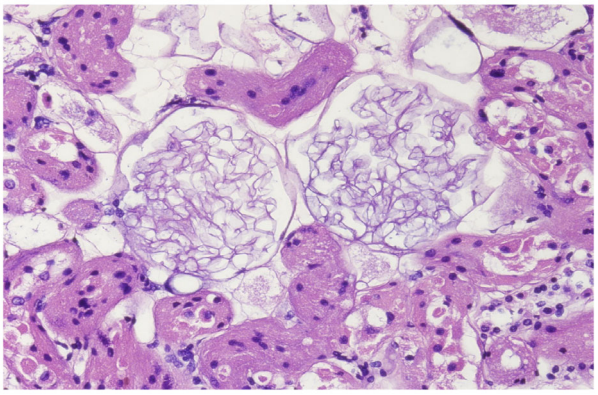
Background: Whole organ perfusion decellularization has been proposed as a promising method for the generation of non-immunogenic organs from allogeneic or xenogeneic donors. However, the ability to recellularize organ scaffolds with multiple patient-specific cells in a spatially-controlled manner remains challenging. Here, we describe a modified decellularization technique in an attempt to address these limitations.
Methods: Rat and porcine organs (including kidneys, liver, heart, lungs, limbs) were treated in order to selectively eliminate donor endothelial cells while keeping the remaining tissue intact and viable. Preservation of vascular patency was assessed by fluoroscopic angiography.
We used in-situ, isolated cold perfusion decellularization, followed by normothermic perfusion recellularization. This model allows an easily obtainable, single-site central cannulation, useful for accessing the desired target organ. Stem cells isolated from human placentae were used to assess the ability to replace endothelial cells in rat kidneys. Patient-specific endothelial progenitor cells isolated from peripheral blood are being tested as well.
Results: Perfusion decellularization of vascularized organs under controlled flow conditions resulted in successful selective removal of endothelial cells. Subendothelial tissues remained intact and viable. Placental stem cells were shown to readily engraft within de-endothelized glomeruli. Human identity of seeded cells within rat kidneys was confirmed by human-specific molecular staining techniques. In-situ organ perfusion while keeping it in its native anatomical location yielded minimal ischemic time, less peri-organ dissections and better control of perfusate leakage.
Conclusions: Our findings suggest that limited decellularization of donor endothelial cells followed by re-endothelization with non-immunogenic cells is feasible and may be used to generate possibly fully functional, tolerable organs for transplantation.



OS276 SPHEROID ENGINEERING FOR 3D CELL CULTURE: WHICH METHOD TO CHOOSE?

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Introduction: 3D cell culture by engineering spheroids offers a more realistic approach than 2D culture. It allows to control spheroid sizes and cells configuration. Furthermore, cell cell to cell interactions in 3D improve cell function, especially in insulin secreting cells. For this reason, a lot of progresses have been made to create spheroids with different techniques used over the last decades. Here we have compared four different methods of cell aggregation to evaluate the most effective one.
Material and methods: Rat pancreatic islets were dissociated into single cells before reaggregation. Spheroids were created either by self-aggregation in non-adherent petri dishes, 3D hanging drop culture method, 5D sphericalplate (Kugelmeier®) or in agarose molds containing 3D wells. We created spheroids of 250 cells, except for self-aggregation method, where the number of cells per spheroid could not be controlled. Cell function and morphology were assessed by glucose stimulation insulin secretion test (GSIS) and histology, respectively. The quantity of material and the time needed to create the spheroids were also analyzed between the different techniques. Results were compared with native rat islets.
Results: Native islets and self-aggregating spheroids showed an important heterogeneity in term of size and shape and were larger than spheroids generated with the other methods. 3D hanging drops, 5D sphericalplate and agarose molds showed homogeneous round shaped spheroids with a mean size of 90 μm. GSIS results showed a similar improvement of the spheroids created with the 3D hanging drops, the 5D sphericalplate and the agarose mold methods in comparison to native islets and self-aggregating spheroids. However, the 5D sphericalplate and the agarose mold techniques were faster and more economic in term of material.
Conclusions: Agarose molds and 5D sphericalplate showed the best results in term of morphology and function.

OS277 TOWARDS 3D-BIOPRINTING OF BIONIC PANCREAS: INFLUENCE OF THE BIOINK COMPOSITION DURING 3D BIOPRINTING OF PANCREATIC SCAFFOLDS ON THE FUNCTIONALITY AND VIABILITY OF PANCREATIC ISLETS

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Introduction: 3D bioprinting has great potential for preparing functional composite constructs. Perfect bioink should contain evenly distributed additives that "mimic", strengthen or replace the native microenvironment of the regenerated tissue and allows control of the properties of a construct, similarities to the natural extracellular matrix (ECM) and the ability to change its physical state after bioprinting (use of crosslinking agent). The most popular component used as a bioink is alginate, mainly due to its high ability to crosslink with calcium ions. Recently, it is also widely used as a potential encapsulating agent in islet studies.
Purpose: Investigating possibilities of using alginate as the main component of a bioink with pancreatic islets and identifying the perfect bioink for 3D-bioprinting with pancreatic islets.
Materials and methods:: Human's and porcine's pancreatic islets were used in experiments. For bioprinting with islets 2 types of bioprinters (EnvisonTEC, Cellink BioX) and 6 types of bioinks (gels) were used: 3% alginate (Gel1), 3% alginate with methacrylate gelatin (Gel2), 3% alginate with commercially available adds (Gel3), 3% alginate with biological adds (Gel4), bioink w/o alginate (Gel5), Cellink's Start (Gel6). Pancreatic islets were mixed with gels before bioprinting in the following ratios (gel:islets) 5:1; 2:1; 1:1; 1:2. Bioink rheological properties (e.g. viscosity) were analyzed for pure gels and mixtures (gels-islets) in the above ratios. Viability (FDA/PI) and functionality (GSIS) tests were performed: before and 1-7 days post-printing.
Results: All gels with islets were characterized by relatively low viscosity. Moreover, pancreatic islets survived the 3D bioprinting in prepared gels, but they had a 50% reduction of response to low and high glucose stimulation.
Conclusion: Bioinks with alginate decrease islets functional response. Mixing of gels with islets in 1:2 ratio or higher reduces mixture viscosity and makes it unprintable.

OS278 BIOLOGICAL ACTIVITY OF HUMAN LIVER STEM CELLS-DERIVED EXTRACELLULAR VESICLES IN A MURINE MODEL OF HEPATIC ISCHEMIA/ REPERFUSION INJURY

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Background: Ischemia-reperfusion injury (IRI) is an antigen-independent inflammatory event that affects several clinical procedures such as hepatic resection and liver transplantation. Human liver stem cells-derived extracellular vesicles (HLSC-EV) have been demonstrated to reduce liver damage in different experimental settings. This study aims to investigate the potential protective role of HLSC-EV on hepatic IRI and to define a dose-effect correlation.
Materials and methods:: An experimental mouse model of partial hepatic IRI (approximately 70% of the liver parenchyma) was obtained by selective clamping of intrahepatic pedicles for 90 minutes followed by 6 hours of reperfusion. HLSC-EV were administered systemically at the end of the ischemic period through the tail vein. Three different doses of HLSC-EV were compared to the control group; their effects on the liver were investigated by biochemical, histopathological, biomolecular and fluorescence analyses.
Results: The specific hepatic distribution of HLSC-EV was observed by In Vivo Imaging System, while their internalization into hepatocytes was

confirmed by epifluorescence analyses. The lower dose (3x10^9 particles) was able to significantly reduce ALT and LDH release, necrosis extension and cytokines expression (TNF-α, CCL-2 and CXCL-10) when compared to the control group. By contrast, livers treated with the medium dose (7.5x10^9 particles) were similar to controls in enzymes levels and histological phenotypes, although showing significantly lower cytokines expression. Finally, the higher dose (10x10^9 particles) was identified as the lethal dose, since it caused sudden death in all the animals.
Conclusions: This study confirms the ability of HLSC-EV to localize within the injured liver. The lower HLSC-EV dose is associated with protection from hepatic IRI, while the medium and higher ones are not.

OS279 THE FEASIBILITY OF TISSUE ENGINEERING THE VASCULATURE OF AN ALLOGRAFT INTO A FUNCTION AUTOGRAFT

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[1]BREONICS Inc.; [2]St. Antonius Hospital

Background: Organ tissue engineering organs has focused on decellularization with the goal of recellularization. Rather than destroying the 3-trillion cell kidney mass, we have focused on targeting its most immunogenic component. The vascular intima is the site of immune cell recruitment. Reducing endothelial cell (VEC) antigenicity represents a targeted approach to reducing alloresponses. We attempted to tissue engineer the most immunogenic component of allografts.
Methods: Human renal allografts ($n = 4$) were placed on warm perfusion. The VEC were first treated with a bioengineered interface of a basement membrane. Following placement of the membrane, $1.0x10^8$ fluorescently labeled VEC were introduced into the perfusion via the arterial line. Following 12 hours of perfusion, the majority of the VEC left the circulation ($<2.0X10^6$ remaining) and attached to the vascular intima. Mononuclear cells (MNC) were isolated from blood of the same source as VEC that were tested for a proliferative response to engineered blood vessels compared to untreated controls in a proliferation assay. Frozen sections were evaluated by fluorescent microscopy.
Results: Labeled VEC were found exclusively along the vascular lumens. The constructs consisted of native VEC surfaced with basement membrane and labeled VEC co-located to the vascular intima. The tissue engineered intima did not alter the perfusion pressures or vascular flow rate. The MNC from same donor as seeded VEC did not elicit proliferative responses. However, same MNC stimulated with the native allogenic VEC of untreated blood vessels elicited strong proliferative responses.
Conclusions: Results demonstrate tissue engineering the most immunogenic component of an allograft may be feasible. Rather than whole organ decellularization, it may be feasible to tissue engineer a targeted component. The tissue engineered construct provided a non-immunogenic lumen that prevented an allogeneic response.

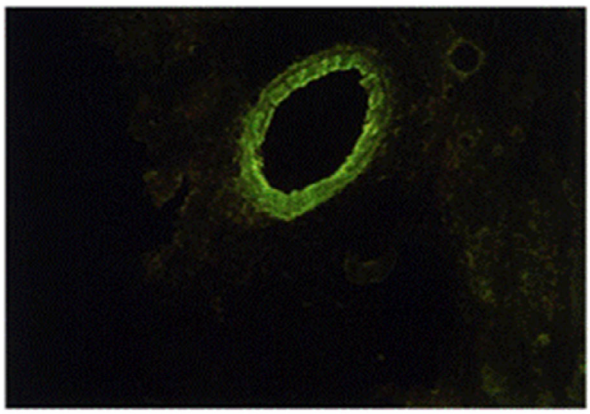

Figure 1: Tissue Engineered Renal Vessel

OS280 DEVELOPMENT AND CHARACTERIZATION OF BLOOD VESSEL IN PRE-CLINICAL SET UP

Debashish Banerjee[1], Nikhil B. Nayakawde[2], Uzair-Ul Haq[3], Deepti Antony[2], Ketaki Methe[1], Michael Olausson[4]
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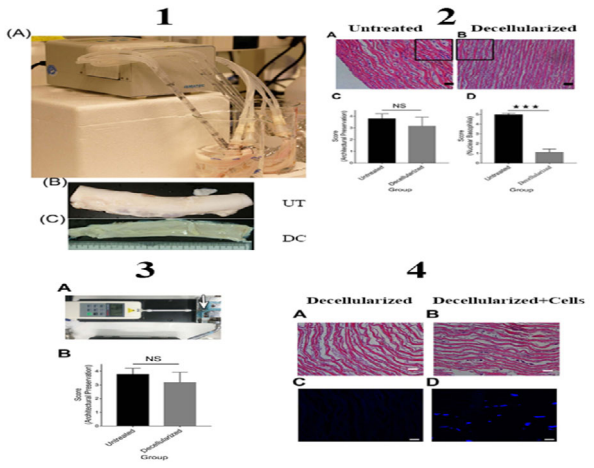
Background: Blood vessel disorders have been regarded as being one of the main cardiovascular human health problems. Tissue engineering, a modern technology through the use of natural and artificial scaffolds, suitable cells and signalling mechanisms, have been able to address the issue of organ shortage.
Methods and Materials: The purpose of the research work was to (i) develop an acellular blood vascular (decellularized) scaffold from a xenogeneic source of pig aorta and (ii) test the feasibility of the blood vascular scaffold to support cellular regeneration and growth under *ex vivo* condition involving (i) preparation of an acellular biological scaffold (decellularized, DC scaffold), (ii) characterization of the DC scaffold and finally (iii) testing of the suitability of the DC scaffold for cellular seeding and repopulation with human smooth muscle cells.
Results: The histological staining procedure showed that there is successful preparation of a decellularized scaffold with no marked change in the tissue architecture supported also from the mechanical strength assessment. Finally, the DC scaffold showed the feasibility for cellular repopulation. The results indicate that decellularized scaffold could preserve the essential extracellular matrix components while providing a more natural mechanical and biological environment capable for cellular repopulation.
Conclusion: Cardiovascular diseases including that of blood vessels have increased globally affecting human health and economic stability. In order to address the global shortage of donor organs, the advancement in tissue engineering is expected to solve the immediate need of alleviating human health. The current work shows the importance of the *ex vivo* preparation of a cellular vascular tissue, as an initial step to subsequent cellular repopulation strategy for preparation of functional organs.

The work is supported by a Travel grant from the Swedish Foundation for Transplant and Cancer Research, 2019.



1- Perfusion sytem (A) for comparison of untreated B, UT) *vs* decellularized (C, DC) pig aorta
2. H&E staining of untreated *vs* decellularized pig aorta
3. Mechanical testing of the untreated *vs* decellularized pig aorta
4. Cell survival and repopluation of decellularized pig aorta

OS281 HIGH-MOBILITY GROUP BOX 1 PROTEIN ANTAGONISMS THE IMMUNOSUPPRESSIVE CAPACITY AND THERAPEUTIC EFFECT OF MESENCHYMAL STEM CELLS IN ACUTE KIDNEY INJURY

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Zhongshan Hospital, Fudan University

Kidney ischemia reperfusion injury (IRI) is a common cause of acute kidney injury and an unavoidable consequence of kidney transplantation and still lacks specific therapeutics. In recent years, mesenchymal stem cell (MSC) emerges as a promising cell-based therapy. The reparative effects of MSC largely

dependent on its unique immunosuppressive property, which is primed and regulated by the microenvironments. In this study, we verified the expression of high-mobility group box 1 protein (HMGB1) is increased not only in the acute phase of IRI, but also during the relapse stage, and the HMGB1 upregulation is correlated with the injury severity. We found that HMGB1 could diminish the immunosuppressive capacity of MSC in the presence of pro-inflammatory cytokines *in vitro* and *in vivo*. Toll like receptor 4 (TLR4)-mediated inducible nitric oxide synthase (iNOS) inhibition might contribute to the effect of HMGB1 on MSCs. Importantly, we further demonstrated that HMGB1 blocking strategies would augment the therapeutic efficacy of MSCs on renal IRI. These findings demonstrate that HMGB1 plays a crucial role in shaping the immunoregulatory property of MSCs within the microenvironments, providing novel insights into the crosstalk between MSCs and microenvironment components, suggesting HMGB1 signals as a promising target to improve MSC-based therapy.

OS282 BILE DUCT RECONSTRUCTION USING SCAFFOLD-FREE TUBULAR CONSTRUCTS OF ALLOGENEIC PIG FIBROBLAST

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Background: Biliary stricture after bile duct injury or duct-to-duct reconstruction are serious complications those remarkably deteriorate the quality of life of patients due to the periodic stent replacement for treatment. The aim of this study was to fabricate a scaffold-free tubular constructs as an interposition graft for treating biliary stricture. We used fibroblast as a source of tubular constructs because it is easy to culture and proliferate in vitro, also exhibit promising mechanical strength in previous studies.
Methods: Allogeneic fibroblast derived from a pig femoral dermis were proliferated by the explant culture. The scaffold-free tubular construct of allogeneic pig fibroblast (hereinafter referred to as the fibroblast tube) was fabricated by a Bio-3D Printer. Five pigs underwent implantation. The fibroblast tube was implanted as an interposition graft for duct-to-duct biliary reconstruction. Serum levels of hepatobiliary enzyme was analyzed on postoperative days 0, 7, and 14. After the graft removal, the three-dimensional micro-computed tomography (mCT) and histological studies were performed.
Results: All pigs were in good health until their sacrifice on postoperative day 14. The serum levels of hepatobiliary enzyme remained stable during the experimental period. The mCT showed no biliary stricture, no biliary leakage and no dilation of the intrahepatic bile duct. The tubular structure was observed in all resected specimens, and the fibroblast tube existed in the lumen of the graft site. Although immunohistochemistry with CK7 and CK19 did not show the extension of biliary epithelium to the lumen of the fibroblast tube, angiogenesis in out layer of the fibroblast tube was detected by immunohistochemistry with CD31.
Conclusion: Present study demonstrated the successful reconstruction of the extrahepatic bile duct using the allogeneic fibroblast tube. The fibroblast tube has the possibility for a novel regenerative treatment for hepatobiliary diseases.

OS283 POTENTIATING CELLULAR REGENERATIVE THERAPIES USING A TISSUE ENGINEERING PLATFORM

Lauren Brasile[1], Bart Stubenitsky[2], Nicholas Henry[1]
[1]BREONICS Inc.; [2]St. Antonius Hospital

Background: Regeneration of ischemic tissue using stem cells is a focused area of research. Stem cells are thought to mediate effects via paracrine factors. It is not known whether stem cells require intimate contact to trigger their secretome. We evaluated ex vivo renal regeneration.
Methods/Materials: Paired ischemically damaged human kidneys were used to evaluate mesenchymal stem/stromal cell (MSC) ($1x10^8$) potentiated regeneration using a tissue engineering platform in one of the pairs. The kidneys were evaluated by histology, cytokine/chemokine/DNA synthesis, cytoskeletal repair and mitosis.
Results: DNA synthesis was first up-regulated at 6H of MSC treatment and continued to increase during 24H of perfusion. MSC treatment led to a significant increase in synthesis of ATP and growth factors in a time dependent manner with normalization of metabolism and the cytoskeleton by 24H of perfusion. The regeneration mediated by the MSC resulted in a reduced inflammatory state along with increased synthesis of growth factors associated with renal repair. Staining of MSC treated kidneys demonstrated a significant increase in the number of cells undergoing mitosis ($p < 0.05$) compared to controls.
Conclusion: It is necessary to delineate if the facilitated MSC effects are contact-independent mediated by ubiquitous effects or contact-dependent necessitating direct contact between the MSC and injured renal tissue. Our research is evaluating whether the MSC need to be "activated" by an injury signal from the kidney in order to optimize regenerative signals. This understanding will be important to determining whether synthesized paracrine factors can be produced that adequately mediate renal regeneration without the need for continuous contact between MSC and damaged renal cells. The ability to regenerate kidneys that today are too damaged to be transplanted would impact the kidney allograft shortage by providing significantly increased numbers of transplantable kidneys.

OS284 THERAPEUTIC POTENTIAL OF HEMATOPOIETIC STEM CELL-DERIVED NATURAL KILLER CELLS ON CANCER RECURRENCE AND VIRAL INFECTION AFTER LIVER TRANSPLANTATION

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Hiroshima University

Previously we have shown that Interleukin (IL)-2/OKT3 stimulated lymphocytes, containing much of NK (natural killer)/NKT cells, from donor liver graft have vigorous anticancer effect. We have successfully applied an adoptive immunotherapy to liver cirrhotic patients with hepatocellular carcinoma (HCC) in a phase I trial. However, single treatment with activated lymphocytes might lead to limited effects. We have now developed culture conditions for the efficient expansion of NK cells obtained from the circulated hematopoietic stem cells (HSCs) by using 5% AB-serum X-VIVO15 medium containing IL-7, IL-15, Flt3L (Fms-related tyrosine kinase 3 ligand) and stem cells factor (SCF). Populations of NK cells expanded under these conditions and after culturing for 17 days the viability of the activated NK cells was 88% $\pm$ 10.1 (range, 81-96%). Expanded NK cells strongly inhibited hepatic C virus (HCV) replication as compared to freshly isolated lymphocytes. When HSC-derived NK cells were co-cultured with HepG2, an HCC cell line, they showed vigorous anticancer activity. We therefore suppose that repeated adoptive immunotherapy using HSC-derived NK cells might contribute to the promotion for inducing innate immunity to decrease the incidence of cancer recurrence and viral infection after liver transplantation.

OS285 TOWARDS FUNCTIONAL TISSUE ENGINEERED EXTRAHEPATIC BILE DUCT CONSTRUCTS FOR REPLACEMENT OF DAMAGED DUCTAL TISSUE BY USING PATIENT SPECIFIC BILIARY ORGANOIDS AND DUCTAL EXTRACELLULAR MATRIX

Jorke Willemse, Monique Verstegen, Iris Voogt, Ksenia Burka, Floris Roos, Luc vanderLaan, Jeroen deJonge
Erasmus MC University Medical Center Rotterdam

Introduction: Bile duct-related complications are a common cause of graft failure after donation after circulatory death liver transplantation. Complicated surgical interventions, such as Hepaticojejunostomy or retransplantation, are required to manage severe complications. However, tissue engineered extrahepatic bile duct (EBD) constructs could be used to replace the damaged EBD tissue. Such constructs can be created by combining patient-specific ductal organoids with EBD extracellular matrix (ECM). The aim of this study is to establish a reproducible method to obtain ductal ECM by decellularizing EBD tissue and to explore recellularization with human LGR5 + bile duct-derived organoids.
Methods: EBD tissue is obtained from human donor livers, discarded for transplantation (N = 10). EBD tissue was decellularized using Triton-x-100. From the ductal ECM circular segments were cut. Ductal-derived organoids were initiated from healthy human EBD tissue and kept in culture according to normal procedures. An organoid-derived cell suspension was added to the luminal side of the ECM segments and kept in culture for up to 21 days.
Results: All cells, including DNA fragments, were removed from EBD tissue, while maintaining ductal architecture and ECM components. After addition of organoids, an epithelial monolayer covered the luminal surface of the ductal ECM. Microscopic analysis revealed a confluent and polarized monolayer. Cells exhibited a phenotype similar to that of large cholangiocytes. Moreover, cholangiocyte markers as cytokeratin-7 and 19 were detectable at mRNA and protein levels, indicating the presence of cholangiocyte-like cells.
Conclusion: This study shows feasibility of *in vitro* engineering ductal constructs for the replacement of damaged EBD. Recellularization of ductal ECM with biliary organoids showed the potential of the cells to completely repopulate the luminal surface of the ECM, thereby potentially restoring the vital barrier function of the EBD.

OS35 - KIDNEY TRANSPLANT SURGERY: CHALLENGES, INNOVATIONS AND OUTCOMES

OS286 CAN CONTRAST-ENHANCED ULTRASOUND (CEUS) BE REPLACED BY DIGITAL FLOW TECHNIQUES IN THE DETECTION OF BLOOD FLOW IN KIDNEY TRANSPLANTS?

Franz Josef Putz[1], Miriam Banas[2], Bernhard Banas[2], Ernst Michael Jung[2]
[1]Herr; [2]University Hospital Regensburg

Background: For the assessment of kidney transplants ultrasound is the first method of choice in daily routine and when problems are supposed. Modern ultrasound techniques e.g. contrast-enhanced ultrasound (CEUS) or digital flow methods (B-Flow) are developed recently. Aim of this study is to determine the applicability of different modern ultrasound methods including CEUS for the assessment of blood-flow in kidney transplants.
Methods: 50 examinations of 41 renal transplanted patients were examined by B-Mode, color-coded Doppler sonography (CCDS), B-Flow, CEUS and contrast-enhanced B-Flow (ceB-Flow). All examinations were performed by one independent examiner with a high-end ultrasound device. The reading was done by two experienced examiners in consensus using rating scales.
Results: Compared to other ultrasound modalities, CEUS had the highest informative value with the best image quality and questions could be answered in 100%. The highest penetration depth was reached in CEUS (8.6 ± 1.6 cm). B-Flow allows only the assessment of superficial organ regions (5.0 ± 1.1 cm) and is very susceptible to imaging artefacts. By contrast agent administration, the penetration depth of B-flow could be increased significantly (7.0 ± 1.7 cm). The ability to visualize slow blood flow was limited in CCDS compared to B-flow and CEUS.
Conclusion: For the assessment of renal transplants CCDS is still important for the evaluation of the hemodynamic. Digital flow methods are promising but need further improvements in penetration depth. CEUS was able to show the capillary microperfusion with the highest image quality and the highest diagnostic value. Therefore, the combination of all ultrasound modalities is necessary for a complete assessment of renal transplants.

OS287 RENAL AUTO-TRANSPLANTATION FOLLOWING EX VIVO TUMOUR RESECTION FOR COMPLEX RENAL MALIGNANCIES

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Oxford University Hospitals NHS Foundation Trust

Background: Partial nephrectomy is the gold standard treatment for patients with T1-2 renal tumours within a solitary kidney. Ex-vivo partial nephrectomy and renal auto- transplantation (EPN) can be used to treat complex renal tumours unsuitable for conventional treatment modalities.
Methods: Patients with highly complex T1-2 renal tumours in solitary kidneys were managed with EPN at our institution. All patients underwent a radical nephrectomy followed by cold perfusion and bench dissection of the tumours. After renal reconstruction the kidneys were auto- transplanted.
Results: A total of 33 patients with renal cell carcinoma were treated with EPN (median age 64, range 37- 82). The median tumour size was 6.3 cm; 31/33 patients had a RENAL nephrometry score greater than 10 (94%). EPN surgery was associated with a Clavien III-V complication rate of 55%. Over a median follow up of 54 months the cancer specific survival was 96%, the overall survival 88% and recurrence free survival 79%. 82% of patients still alive are currently dialysis free.
Conclusion: EPN offers patients with complex renal tumours and solitary kidneys an excellent chance of oncological control and avoidance of long-term dialysis. EPN should be considered before rendering a patient anephric and committing them to long-term dialysis.

OS288 INDICATIONS AND POSSIBILITIES FOR CONTRAST-ENHANCED ULTRASOUND (CEUS) IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

Franz Josef Putz[1], Eva Haneder[2], Miriam Banas[2], Ernst Michael Jung[3], Bernhard Banas[2]
[1]Herr; [2]University Hospital Regensburg; [3]University Ho

Background: For the assessment of kidney transplants (KTX) ultrasound is the first method of choice in daily routine and when problems are supposed. Contrast-enhanced ultrasound (CEUS) plays an increasing role in kidney imaging. Ultrasound contrast agent is not nephrotoxic and has no relevant side-effects. Aim of this study was to describe the indications and possibilities of CEUS in renal transplanted patients.
Methods: In total 265 CEUS examinations of the kidneys and KTX were performed at the University Hospital Regensburg between September 2014 and April 2018. 121 examinations of renal transplanted patients were included for the analysis.
CEUS was performed by experienced sonographers after bolus injection of 1.0 up to 2.4 ml sulphur hexafluoride microbubbles using a high-end ultrasound device with multifrequency probes and at a low mechanical index.
Results: The average age was 58 ± 14 years (20 to 76 years). 88.9% of the patients had GFR below 60 ml/min/1.73 m^2 and therefore a relative or absolute contraindication against contrast-enhanced CT or MRI. No adverse events were observed after the injection of contrast-agent.
70.5% of all examinations ($n = 87$) were related to pathologies of the KTX and in 29.5% ($n = 36$) to pathologies of the native kidneys. In KTX the assessment of the renal perfusion was the main issue (57.0% of all cases), followed by the evaluation of complex renal cysts (25.6%), infectious diseases (7.4%) and solid renal masses (4.7%). The objectives in the native kidneys were in 89.0% the evaluation of complex renal cysts and the assessment of solid renal masses (8.3%).
Conclusion: CEUS is a safe and excellent diagnostic tool for renal transplanted patients. It could be applied easily bedsides and allows an immediate assessment of a variety of indications.

OS290 ISIRIS™ FOR URETERIC STENT REMOVAL IN RENAL TRANSPLANTATION: AN INITIAL SINGLE CENTRE EXPERIENCE OF 150 CASES

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Manchester University NHS Foundation Trust

Background: Ureteric stents are inserted during renal transplantation to reduce post-operative urological complications, including anastomotic leak and ureteric obstruction. Transplant ureteric stent removal (TUSR) has historically been performed via flexible cystoscopy in a theatre environment. Isiris™, a single use cystoscope with integrated grasper designed for removal of JJ stents, allows TUSR to be moved away from the operating theatre, with the potential of improved patient experience and reduced resource burden. We aimed to report our unit's initial clinical and financial outcome.
Methods: A retrospective analysis of a contemporaneously maintained database was performed with review of case notes of TUSR in a single transplant unit (10/17-09/18). TUSR was performed in the outpatient setting by surgical middle grades with a single nurse assistant.
Results: 150 TUSR were performed in 145 transplant recipients (140 single and 5 dual transplants; mean age 50.2 years, SD $\pm$ 15.2; 61.3% male). 91.3% ($n = 137$) of cases were performed in the outpatient clinic. Median time from transplant to TUSR was 42 days (IQR 30-42) with 12 cases of urinary tract infection (UTI) with indwelling stent (8.1%). 147 procedures were successful with 3 failures (prior false urinary passage; technical difficulties; anxiety) with 1 post-TUSR UTI. Isiris™ use for TUSR has provided a £80,680 saving in this cohort.
Conclusion: Isiris™ safely and practically allows timely TUSR. It releases the procedure from the operating theatre to the outpatient clinic or community healthcare facility. This reduces the resource burden for healthcare providers and provides financial benefit, with the savings calculated conservative, as they do not include income gained from re-allocated use of operating theatre capacity. Further work is required to assess patient and surgeon satisfaction, environmental impact, and use in complicated TUSR. However, Isiris™ is safe and appropriate for use in the outpatient setting.

OS291 GOAL-DIRECTED NON-INVASIVE PROTOCOL FOR THE AMELIORATION OF FLUID MANAGEMENT DURING LAPAROSCOPIC LIVE DONOR NEPHRECTOMY

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Laiko General Hospital

Introduction: The aim of our study was to evaluate the impact of a goal-directed protocol(GDT) using a non-invasive system on the management of living kidney donors undergoing hand-assisted laparocopic nephrectomy.
Materials/Methods: A single center, non-randomized, prospective observational study was performed.All living kidney donors subjected to laparoscopic nephrectomy were eligible for inclusion.Hemodynamic parameters were measured non-invasively in Group A using a ClearSight sensor(EV1000 monitor/Edwards Lifesciences) and included arterial pressure, stroke volume (SV) and cardiac output(CO). Fluid administration was determined using a SV-targeted GDT protocol after estimating the optimal SV(Veelo et al). The trigger for intraoperatine fluid adminitration was an SV 10% below the optimum. The intravenous(IV) fluid therapy in the standard care group(group B) was guided by mean arterial pressure and diuresis.The collected data included, for the donor:the intraoperative volume of IV fluids,the postoperative urine output at day 1(POD1) and creatinine at discharge and for the recipient : the postoperative urine output-if any- at day 1(POD1) and 7(POD7), as well as creatinine at discharge.

Results: Fourteen donors were included in the study and divided equally in two groups.The mean operative time was 192 min.The use of intraoperative fluids was significantly lower in the intervention group(A)[mean 2324 vs 3320 ml, $p < 0.001$], without affecting donor renal function [POD1mean 4350 vs 5060 ml, $p = 0.149$ and creatinine 1.14 vs 1.16].The allograft function was documented by the recipient's POD1[4160 vs 5460 ml,$p = 0.75$],POD7[2100 vs 1890 ml, $p = 0.179$] and creatinine at discharge [1.3 vs 1.4, $p = 0.272$].There was a case of acute rejection(cellular and humoral) and 2 cases of delayed graft function.
Conclusion: Restriced intraoperative fluid guided by a dynamic preload variable(SV) appeared to prevent excessive third spacing without adversely affecting allograft outcomes.

OS292 COMPLICATION RELATED TO PROPHYLACTIC STENTING VESCICOURETERAL ANASTOMOSIS IN KIDNEY TRANSPLANTATION: OUR EXPERIENCE AND LITERATURE REVIEW

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Background: Vesicoureteral anastomosis is the most common technique to reconstruct urinary tract during kidney transplant, but it is linked to urinary complications (UCs). Vesicoureteral stenting has been employed successfully to treat UCs, but its role as prophylactic measure is still debated. Our aim is to evaluate benefits and complications associated with prophylactic routine use of stent.
Material and methods: We evaluated 745 transplanted patients in our center between 1977 and 2017 and performed a literature review in PubMed and EMBASE to examine articles about ureteral stenting of vesicoureteral anastomosis in renal transplantation. We included English-language articles published between 1995 and 2018.
Results: In our experience, based on routine prophylactic stenting, we have found stent-related complications in 65 patients: 2 endured capsular and parenchymal breakage because of stent malposition; 5 sustained subcapsular stent migration (all 7 treated endoscopically); in 3 cases the stent needed to be repositioned with a redo of the anastomosis; 2 patients suffered from severe urinary tract infection (UTI) that required an early stent removal. The other patients showed episodes of UTIs treated with antibiotic therapy. We have found 975 articles, of which 92 underwent a full-text analysis and 26 satisfied our inclusive criteria.
Discussion: The incidence of our complications related to prophylactic stenting is similar to the rates found in the studies about non-prophylactic stent's use. Though the results found in the literature are conflicting, the latest metaanalyses recommend routine prophylactic stenting, because it reduces UCs' incidence, without a significant increase of UTIs.
Conclusion: Our results agree with the findings in the literature. Prophylactic stenting allows a reduction of UCs, without causing an increase in stent-related complications. Early removal may reduce the UTI incidence, whereas it does not entail an improvement of the risk of UCs.

OS293 KIDNEY TRANSPLANT GRAFT CONTINUOUS PERFUSION MONITORING DURING THE EARLY POSTOPERATIVE COURSE

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Background: In the early post-transplantation period, vascular complications are ones of the most dangerous regarding the graft survival. They occur in up to 7,4% of cases and if not diagnosed within minutes, they can have fatal consequences for the kidney graft. This is in many cases nearly impossible using standard monitoring methods, such as urination and serum creatinine monitoring and doppler ultrasound. In cooperation with engineers, we designed a monitoring system for graft perfusion monitoring, based on the principle of near infrared spectroscopy (NIRS).
Material and Methods: We devised a NIRS based monitoring device. The system consists of in-vivo portion with NIRS emitter/sensor (placed on graft parenchyma) and ex-vivo battery and wireless transmitter. We established a laboratory model of kidney transplantation on 40 kg laboratory pig to mimic conditions after human kidney transplantation. We performed two series of tests to perfect and verify the system performance in 48 hour time graft perfusion monitoring after transplantation.
Result: We successfully devised a NIRS based system that can be used to monitor kidney graft perfusion in short post-transplantation period. The system can differentiate between arterial and venous complications. The system is wireless, acts also as drainage of the wound and can be safely applied on and removed from the graft without danger of further injury.
Conclusion: The continuous monitoring of graft perfusion can be very beneficial in short post-transplantation period. Especially in selected cases (e.g. complex graft anatomy) it can give us a chance for graft salvage in case of acute vascular complication without additional risks for the patient.

OS294 TREATMENT OF POST-RENAL TRANSPLANT LYMPHOCELES

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Introduction: Post-renal transplantation lymphoceles are not uncommon occurring in 5-15% of recipients. They can lead to infection, vascular and urological complications. Different therapeutic modalities are in practice including percutaneous drainage, laparoscopic or open marsupialization. Sclerosing iodine therapy is advocated as an alternative option. we report our experience in treating post-transplant lymphoceles.
Subjects and Methods: A retrospectively collected data between March 2005-December 2018 in 2 centres was analysed. Data included demographic data, recipient co-morbidities, type of donor and outcome measures including lymphocele presentation, complications and treatment modalities.
Results: A total of 1357 kidney transplants were performed including 77 re-transplants. Lymphoceles were reported in 82(6.04%) recipients. Intraoperative drains stayed in-situ for an average of 14 days(10-35). Out of these 50 (61%) recipients needed further intervention including laproscopic marsupialization in 6(7.3%), open drainage in 3(3.7%), guided reinsertion of drain in 24 (29.3%), 19 of them required Iodine sclerotherapy. Iodine was used in additional 17 recipients through the original intraoperatively inserted drain with a total of 36(44%) out of lymphocele population treated with iodine. Thirty two (39%) recipients recovered without further intervention with only longer original drain time (the majority were before introducing Iodine therapy). Infection was reported in 12(14.6%) patients. Vascular compromise noted in 5(6.1%) patients that warrant open drainage in 3 and laparoscopic drainage in 2. Compression on the renal pelvis and ureter noted in 4(4.9%) and treated laparoscopically. Seven out of the laparoscopic and open drainage group were done before iodine use.
Conclusion: Iodine sclerotherapy is a safe and efficient treatment for post-transplant lymphocele. Open/laparoscopic drainage of lymphoceles rarely used since iodine use.

OS295 ENDOVASCULAR TREATMENT OF TRANSPLANT RENAL ARTERY STENOSIS

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Purpose: Transplant renal artery stenosis(TRAS) is most common vascular complication following kidney transplantation (KT), which most clinicians regard percutaneous transluminal angioplasty(PTA) to be the treatment of choice for TRAS. The aim of this study was to review our experience with an endovascular approach to TRAS
Methods: We reviewed the KT recipients those who underwent PTA due to TRAS We analyzed the patient's baseline characteristics, postoperative renal function, blood pressure evolution, and the number of antihypertensive drugs pre- and postprocedure.
Result: A total 21 patients (15 men) were treated with endovascular technique. The mean age was 49.2 years (31-65 years), mean time to treatment was 44.8 days(4-230 days). The predominant presentation was graft function alteration (76.2%). Stenosis or hemodynamic kinking were located at the anastomosis 7, proximal 13, distal 1. Number of donor renal artery was single in 11, multiple in 10(double 8, triple 2). The PTA without stent placement was performed in 7, PTA with stent placement was performed in 14. Serum creatinine (SCr) levels demonstrate no difference between preprocedure and discharge day (1.61 mg/dl vs. 1.46 mg/dl, $p = 0.33$). The GFR also showed no difference between preprocedure and discharge day (53.6 ml/min to 57.0 ml/min ($p = 0.084$). Systolic and diastolic blood pressure varied from 137 mmHg and 84 mmHg to 129 mmHg and 79 mmHg, respectively ($p = 0.124$ and $p = 0.07$)). The preoperative number of antihypertensive medication was significantly decreased from 1.5 to 0.5 ($p = 0.023$). There was no technical failure and no procedure related complication or mortality. During follow up period free from reintervention rate was 100%, graft failure was occurred in 2(9.5%) due to rejection.
Conclusion: Endovascular procedure in TRAS shows high technical success rate. In our experience, its impact on Scr levels and GFR do not seem toimprove, however, antihypertensive drug could be reduce after procedure

OS296 EFFECT OF DONOR NEPHRECTOMY WITH VAGINAL EXTRACTION ON RECIPIENT AND GRAFT SURVIVAL

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Background: Laparoscopic approach has become the standard procedure for living donor nephrectomy in many transplant centers. In order to minimize the morbidity of the living donors, transvaginal extraction of the kidney has been introduced as a minimally invasive technique. Here, we aimed to investigate the effect of the surgical techniques regarding trasvaginal and standard donor nephrectomy on recipient and graft outcomes.
Material/Methods: This prospective data analysis included a total of 146 kidney transplant recipients whom all had female living donors. Group I included 37 recipients (4 female, 33 male) whose donors underwent laparoscopic nephrectomy with transvaginal extraction. Group II included 109 recipients (31 female, 78 male) whose donors underwent a standard laparoscopic nephrectomy. Parameters regarding recipient and donor ages, warm and cold ischemia times during the procedure, and 5-year recipient and graft survival rates, were compared between the two groups.
Results: Male gender and warm ischemia time were found to be significantly higher in Group I compared to Group II (89.2% and 71.6% male gender, 195 and 146 seconds in groups I an II respectively). On the other hand, no significant difference regarding recipient and donor ages, cold ischemia time during the procedure and follow-up duration were observed between the two groups. Most importantly statistical analysis revealed high recipient and graft survival rates in both groups (5-year recipient survival rates 96.8% and 98.8% in groups I and II respectively, 5-year graft survival rates 96.8% and 96.7% in groups I and II respectively).
Conclusions: Successful long-term outcomes of kidney transplant recipients whose donors had a laparoscopic donor nephrectomy with vaginal extraction, encourages the surgeons to perform this minimally invasive method in order to minimize the morbidity of the living donors.

OS297 RENAL TRANSPLANTATION INTO URINARY DIVERSIONS AND RECONSTRUCTED BLADDERS

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Introduction: Renal failure secondary to urological disorders can necessitate urinary diversion or reconstruction either pre or post-transplant (KT). Decision-making regarding timing of diversion/reconstruction may be affected by living (LD) or deceased (DD) donor options. We assessed KT outcomes into urinary diversions and reconstructed bladders.
Methods/Materials: Single-centre retrospective review of 4679 KTs between 1986-2018. Graft and patient survival (GPS) were calculated.
Results: 54 patients (mean age 38) who had 63 transplants (1.3%) required urinary diversion or reconstruction; 5 had initial diversion and subsequent undiversion/reconstruction. Mean follow-up was 141 months.

*Cutaneous ureterostomy (CU):*12 patients (7 LD; 6 DD); 10 at transplant. 1 patient required two sequential transplants; first was diverted to CU 3 years after transplant (for unrecognised neuropathic bladder), the second a planned CU. The other CU was 4 years post-transplant for a radiotherapy vesico-vaginal fistula from cervical cancer.

*Ileal Conduit (IC):*15 into pre-formed IC (7 LD; 8 DD). 7/15 died; 4/7 with functioning transplant.

*Post-transplant IC:*5 transplants into bladder but subsequent IC diversion (4 due to bladder cancer and 1 due to worsening bladder function from spina bifida).

*Reconstructed urinary tract:*20 transplants into augmented bladders using native ureter (2), gastric-segment (1), ileo-caecum (6) and ileum (16). 5 were augmented post-transplant; 2 were undiverted into neo-bladders post-transplant.

	Graft survival at 1 year	Patient survival at 1 year	Graft survival at 5 years	Patient survival at 5 years
Cutaneous ureterostomy	91%	91%	50%	67%
Pre-formed ileal conduit	93%	100%	77%	77%
Post-transplant ileal conduit	80%	80%	80%	80%
Reconstructed urinary tract	90%	100%	74%	96%
Overall kidney transplant survival in our centre (2009-2017)	95%	98%	92%	93%

Conclusion: Transplantation into urinary diversions and reconstructed bladders appears safe, with similar GPS to our general transplant population. DD kidney recipients with unsafe bladders may require initial CU before undiversion and reconstruction to prevent complications from a "dry" augment.

OS36 - HUMORAL AND CELLULAR FACTORS IN RENAL TRANSPLANTATION

OS298 RISK STRATIFICATION OF DONOR-SPECIFIC ANTIBODIES BASED ON MEAN FLUORESCENCE INDEX

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Background: Donor-specific antibodies (DSA) present prior to kidney transplantation can lead to post-transplant histological damage, often associated with antibody-mediated rejection (ABMR). However, it remains unclear which mean fluorescence intensity (MFI) threshold should be uphold for DSA to be hazardous. In this paper, we analyze the effect of different MFI thresholds of pre-transplant DSA on graft survival and on the occurrence of ABMRh (=histological picture of ABMR).
Methods/Materials: We performed a single center cohort study, including 985 kidney transplantations (2004-2013) and 3594 biopsies, obtained up to 5 years after transplantation. The effect of pre-transplant DSA on the occurrence of ABMRh and on graft survival was studied using mixed and survival models respectively. On top, in a joint longitudinal-survival model, we evaluated the mediation, via ABMRh, of the effect of pre-transplant DSA on graft survival.
Results: Pre-transplant DSA with an MFI above 1400 have a negative impact on kidney allograft survival, corresponding to a hazard ratio of 3.19 ($P < 0.001$). No effect of DSA is observed when the MFI lies between 500 and 1400 ($P = 0.162$). According to the MFI threshold of 1400, figure 1 shows the higher prevalence of ABMRh in the pre-transplant DSA group (odds ratio of 39.86, $P < 0.001$). Moreover, the significant effect of pre-transplant DSA on graft survival disappears after including ABMRh as predictor. This shows that the negative impact of pre-transplant DSA is mediated via the occurrence of ABMRh.
Conclusion: We conclude that patients with pre-transplant DSA, according to an MFI threshold of 1400, are more prone to develop ABMRh and are more susceptible to graft failure after kidney transplantation. In fact, the negative impact of pre-transplant DSA on graft survival is fully mediated by the occurrence of ABMRh.

Figure 1. Prevalence of ABMRh according to pre-transplant DSA (MFI > 1400) in (A) protocol and (B) indication biopsies.

OS299 IDENTIFICATION OF IMMUNOGENIC RECIPIENT HLA CLASS II AND DONOR-HLA-DERIVED PEPTIDE COMPLEXES: CLINICAL RELEVANCE TO DE NOVO DONOR-SPECIFIC HLA ANTIBODY FORMATION IN KIDNEY TRANSPLANTATION

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De novo donor-specific HLA antibody (dnDSA) production involves the indirect allorecognition pathway in which donor HLA is processed by the recipient's antigen-presenting cells and presented via recipient HLA class II to CD4 + T cells. Recently, particular peptide and HLA class II complex was proven to have a protective or promotive roll in producing the peptide-specific antibodies through the induction of peptide-specific regulatory or effector CD4 + T cells. Here we hypothesize that particular donor-HLA-derived peptide and recipient HLA class II complexes (pHLAs) may also have an impact on dnDSA formation in kidney transplantation.

All adult living recipient-donor pairs transplanted at Nagoya Daini Red Cross Hospital and Aichi Medical University Hospital between 2003 and 2018 were eligible for this retrospective study. In total, 536 transplants without preformed DSA have been analyzed. We checked HLA typing, and pre- and posttransplant follow-up for dnDSA surveillance. The donor-HLA-derived pHLAs were all calculated using the latest version of the PIRCHE-II algorithm (version 3.0). With the purpose of validating the immunogenic effect of these complexes, we performed co-culturing of donor-peptide-loaded recipient dendritic cells (DCs) and CytoTell(TM)-labelled-recipient CD4 + T cells. Recipient CD4 + T cell proliferation was analyzed by calculating stimulation index (SI). A SI value > 2.0 was considered enhanced.

PIRCHE-II score was higher in dnDSA+group ($n = 115$), compared with dnDSA-group ($n = 421$). (256.9 ± 142 vs 206.0 ± 140, $p < 0.05$). Some complexes were seen more frequently in dnDSA+group ($p < 0.05$). The top 3 complexes were shown in table.

Recipient HLA class II / donor HLA-derived peptide	Frequency in dnDSA positive group ($n = 115$)	Frequency in dnDSA negative group ($n = 421$)	Rerative Risk	p value
DRB1*12:01 / SFTVQRRVQPKVTVY (DRB1*15:01 or DRB1*15:02 or DRB4*01:03 derived)	7 (6.1%)	3 (0.7%)	8.7	0.002
DRB1*08:03 / GVVESFTVQRRVQPK (DRB1*15:01 or DRB1*15:02 or DRB4*01:03 derived)	9 (7.8%)	7 (1.7%)	4.6	0.007
DRB1*04:05 / RNTQIFKTNTQTYRE (B*51:01 derived)	6 (5.2%)	4 (0.95)	5.5	0.02

In pairs which contained these promotive complexes, proliferation of recipient CD4 + T cells were promoted compared with cases which didn't contain these complexes (SI > 2.0 vs 1.3 ± 0.3).

Some donor-HLA-derived pHLAs may play a promotive roll in dnDSA production in kidney transplantation.

OS300 INCIDENCE OF DONOR-SPECIFIC ANTIBODY FORMATION FOLLOWING INTRAOPERATIVE BUFFY COAT-DEPLETED RED BLOOD CELL TRANSFUSION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Immunological sensitization resulting from allogeneic blood transfusions can induce antibody-related rejection affecting long-term graft survival after kidney transplantation. Very few reports have assessed the impact of red blood cell transfusion on the prognosis of patients undergoing kidney transplantation.
Methods: Of 423 kidney transplant recipient between 2013 and 2016, 356 patients were enrolled in the present study after excluding patients with preformed donor-specific antibody (DSA) and pediatric patients. We assessed the incidence of anti donor-specific *de novo* antibody formation within 2 years after transplantation in cases with intraoperative transfusion.
Results: All the recipients had undergone induction with rituximab. Of the 356 kidney transplant recipients, 124 had received an intraoperative red blood cell transfusion. *De novo* DSA formation was detected during the period after kidney transplantation in 7 of these transfusion recipients (5.7%). The incidence of *de novo* DSA within 2 years after transplantation in the remaining 232 patients who did not receive an intraoperative transfusion was 6.0%; no significant difference was seen between two groups. In high risk cases such as those receiving a secondary transplantation or a kidney transplantation after the transplantation of another organ, however, the development of *de novo* DSA within 2 years after transplantation occurred more frequently among patients receiving an intraoperative transfusion compared with a non-transfusion group (22.2% vs. 8.7%)
Conclusion: Except in high risk cases, the incidence of *de novo* DSA formation during a 2-year period following kidney transplantation was relatively low overall and did not differ significantly between patients who did and those did not receive an intraoperative red blood cell transfusion. The administration of rituximab for induction might explain the low incidence of *de novo* DSA formation during the 2-year postoperative period.

OS301 HLA-A*02 SENSITISATION AND PAEDIATRIC RENAL ALLOGRAFT SURVIVAL - A RETROSPECTIVE COHORT ANALYSIS OF THE UK NATIONAL HEALTH SERVICE BLOOD AND TRANSPLANT (NHSBT) REGISTRY

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Background: Transplantation remains the gold standard of therapy in children with end stage kidney disease (ESKD). However, human leukocyte antigen (HLA) mismatch continues to be a significant hurdle to allograft survival. In the United Kingdom, approximately half of paediatric transplant recipients are sensitised to HLA-A*02, restricting the donor pool. This analysis tested the null hypothesis that prior HLA-A*02 sensitization does not affect renal allograft survival.
Methods: A retrospective cohort study from the prospectively collected NHSBT UK registry for all single kidney transplants performed from 0 – 18 years prior to November 2018. The HLA-A*02 sensitisation status was defined as the presence of antibodies. The primary outcome was renal allograft survival time in days, from transplantation to the diagnosis of ESKD, re-transplantation or the initiation of renal replacement therapy. Survival analyses were presented using Kaplan Meier method using Cox proportional hazard modelling.
Results: 5643 transplants were performed in 4953 individuals (59·4% M) with a mean recipient age of 11·8 (± 9·9). HLA-A*02 sensitisation occurred in 369 (6%) transplant procedures and increased the univariate hazard of failure (HR; 1·3 [1·12 – 1·5], 95% CI) however was non-significant at the multivariate level. In a subgroup analysis by transplant number, HLA-A*02 increased the univariate hazard of allograft failure of first transplant procedures (HR; 1·34, [1·1 – 1·62] 95% CI, $p < 0·001$), but not in subsequent procedures in childhood. In deceased donor transplantation HLA-A*02 sensitisation independently increased the hazard of renal allograft failure at the multivariate level once adjusted for significant covariables (HR; 1·31 [1·11 – 1·56], 95% CI, $p < 0·01$).
Conclusion: HLA-A*02 sensitisation negatively impacts renal allograft, therefore should be considered when predicting allograft survival, counselling patients as well as in matching algorithms when allocating renal allografts.

OS302 A COMPARISON OF IVIG VERSUS NO-IVIG DESENSITIZATION IN HIGHLY SENSITIZED RENAL ALLOGRAFT RECIPIENTS

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Objectives: The aim of this study was to compare the clinical outcomes of kidney transplantation (KT) in sensitized patients according to the desensitization protocol with or without IVIG using nationwide data from the Korea Organ Transplantation Registry (KOTRY).
Methods: This is a retrospective study using data extracted from the KOTRY database. Patients who underwent desensitization treatment prior to KT from January 2016 when the desensitization protocol started being recorded accurately to September 2017 were included. The desensitization treatment at each center consisted of rituximab and plasmapheresis (PP) with or without IVIG. After excluding 140 patients who underwent desensitization due to only ABO incompatibility, 125 patients were included in the analysis. These 125 patients consisted of 17 patients with positive complement-dependent cytotoxicity (CDC) XM, 40 patients with positive flow cytometric (FC) XM, and 68 patients with high-titer DSA. These patients were divided into no-IVIG (76 patients) and IVIG (49 patients) groups according to the use of IVIG in desensitization methods. Propensity score matching was performed to homogenize both groups.
Results: In total, 34 propensity score-matched recipients in both groups were identified. The one-year rejection rate showed no significant difference

between the no-IVIG and IVIG groups (two patients, 5.9% vs. four patients, 11.8%, $p = 0.21$). There were no cases of mortality or graft failure in either group. The univariate analysis to evaluate factors associated with acute rejection showed that the use of IVIG was not a significant factor (hazard ratio = 2.77; 95% confidence interval, 0.65–14.01; $p = 0.18$).
Conclusions: This study showed that the no-IVIG and IVIG groups showed similar clinical outcomes during one-year follow up.

OS303 ARE γδ T CELLS INVOLVED IN DONOR SPECIFIC ANTIBODY GENERATION?

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Introduction: The generation of donor-specific antibodies (DSA), the leading cause of graft failure in transplantation, requires that alloreactive B cells receive T-cell help. According to the molecular nature of their TCR, two main types of T cell (Tc) are distinguished: α/β or γ/δ.

While the importance of α/βTc in the generation of DSA is well established, the implication of γ/δTc is unknown. Data from the literature suggest that γ/δTc could i) directly help B cells or contribute indirectly by activating α/βTc (through the presentation of alloantigen).
Methods: A balb/c (H2d) heart graft was transplanted into 4 types of C57BL/6 (H2b) recipients: i) wild type (with α/βTc and γ/δTc), ii) CD3ε KO (deficient for both α/βTc and γ/δTc), iii) TCR αKO (deficient in α/β Tc only), or iv) TCR δKO (deficient in γδTc only). The DSA titer was quantified before transplantation and after each week post-transplant by flow crossmatch.

Our experimental results were confirmed in a cohort of 341 kidney transplant (KT) recipients for whom serum at 5 years post transplantation and γ/δTc measurement at baseline and 2 years post-transplantation was available.
Results: The 4 recipient strains had the expected T cell phenotype and a B cell compartment quantitatively and functionally normal. Unlike wild-type mice, CD3ε KO mice did not develop DSA after heart transplantation. While mice without α/βTc did not develop DSA, mice without γ/δTc showed a similar DSA response as wild-type mice. The clinical study confirmed the absence of correlation between the number of circulating γ/δTc (at baseline and 2 years post transplantation) and the risk of developing de novo DSA at 5 years post transplantation.
Conclusion: Our results confirm the importance of α/βTc in DSA generation and suggest that γ/δTc are not involved in this process.

OS304 TRANSPLANT GLOMERULOPATHY IN ABSENCE OF DONOR-SPECIFIC HLA ANTIBODIES: HISTOLOGICAL APPEARANCE AND INDICATION FOR OUTCOME

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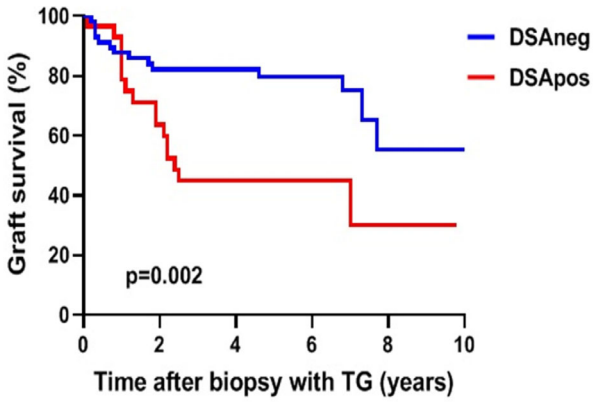
Background: Transplant glomerulopathy (TG) is a sign of chronic kidney allograft damage driven by donor-specific HLA antibodies (DSA). Recent studies showed that TG may, however, also results from other disease processes affecting the glomerular endothelium. So far, a direct comparison of DSA-dependent and DSA-independent TG has not been performed. In this study we investigated graft survival and histological appearance of cases with TG that developed in the absence of HLA-DSA, and compared this phenotype to cases of TG with HLA-DSA.
Methods: Patients who underwent kidney transplantation between March 2004 and February 2013, and who had at least one post-transplant biopsy, were included in this study ($n = 935$ patients with 4295 performed biopsies). Pre- and post-transplant anti-HLA antibodies were retested with Luminex.
Results: A total of 88 patients (9.4%) developed TG by light microscopy (Banff cg score > 0) during the follow-up period, on average at 2 years after transplantation. TG was diagnosed both in indication and in protocol biopsies. Of the patients with TG, 30 patients (34%) had pretransplant or *de novo*DSA ($DSA_{pos}TG$ group), while in 58 patients (66%) DSA were never detected ($DSA_{neg}TG$). Patients in the $DSA_{pos}TG$ group were younger and received more induction therapy compared to the $DSA_{neg}TG$ group ($p < 0.05$). The $DSA_{pos}TG$ group had more microcirculation (47% vs. 22%, $p = 0.02$) and interstitial inflammation (43% vs. 19%, $p = 0.02$) compared to the $DSA_{neg}TG$ group.- Patients in the $DSA_{neg}TG$ group were more likely to have received an older kidney (51.2 ± 14 vs. 42.7 ± 17 years; $p = 0.01$). When we performed 10-year death-censored graft survival analysis we found that the $DSA_{neg}TG$ group had a better graft survival than the $DSA_{pos}TG$ group (55.1% vs. 28.8%; $p = 0.002$ by log-rank analysis).
Conclusion: Transplant glomerulopathy occurs often in the absence of HLA-DSA and represents a different phenotype with better graft survival compared to TG developed in the presence of HLA-DSA.



OS305 ANGIOTENSIN II TYPE 1 RECEPTOR ANTIBODIES IMPROVE PRE-TRANSPLANT RISK STRATIFICATION FOR KIDNEY ALLOGRAFT LOSS

Carmen Lefaucheur[1], Denis Viglietti[1], Aurélie Philippe[2], Jean-Paul Duong Van Huyen[1], Jean-Luc Taupin[1], Olivier Aubert[1], Denis Glotz[1], Christophe Legendre[1], Alexandre Loupy[1], Duska Dragun[2]
[1]Paris Translational Research Center for Organ Transplantation; [2]Medical Faculty of the Charité Berlin

Current state-of-the-art pre-transplant risk stratification relies on the HLA system. Non-HLA agonistic angiotensin II type 1 receptor antibodies (AT1R-Ab) have been associated with allograft rejection. We investigated whether AT1R-Ab might improve current approach to pre-transplant immunological risk assessment.

We enrolled a prospective cohort of 1845 kidney recipients transplanted across a negative complement-dependent cytotoxicity crossmatch between 2008-2013. Patients were assessed at the time of transplantation for donor, recipient and transplant characteristics, anti-HLA donor-specific antibodies (HLA-DSAs) and AT1R-Ab using quantitative ELISA. Primary outcome was allograft loss until 2018.

We identified 438 (24%) patients with pre-transplant AT1R-Ab (>10 U/mL). Patients with AT1R-Ab showed decreased 8-year graft survival (73%, 95%CI: 68-77) compared to patients without AT1R-Ab (86%, 95%CI: 83-87, $p < 0.001$). Pre-transplant AT1R-Ab and HLA-DSAs had a synergistic deleterious effect: 8-year graft survival of 65% (95%CI: 55-73) in patients with both antibodies ($n = 132$), 76% (95%CI: 69-81) in those with HLA-DSAs alone ($n = 210$), 76% (95%CI: 71-81) in those with AT1R-Ab alone ($n = 306$) and 87% (95%CI: 85-89) in those without antibodies ($n = 1197$) ($p < 0.001$). Spline modeling showed dose-response effect between AT1R-Ab level and the risk of graft loss ($p < 0.001$). Pre-transplant AT1R-Ab were associated with antibody-mediated rejection (HR = 2.20, 95%CI = 1.69-2.87, $p < 0.001$) and graft loss (adjusted HR = 2.04, 95%CI = 1.59-2.62, $p < 0.001$) after adjusting on donor (age, gender, type, cause of death), recipient (age, gender, calculated panel reactive antibody, previous transplant, time since dialysis) and transplant (HLA-A, -B, -DR, and -DQ mismatches, pre-transplant anti-HLA DSAs, cold ischemia time, induction therapy) characteristics.

Evaluating AT1R-Ab antibodies could improve pre-transplant risk assessment in kidney recipients, independent from the presence of pre-transplant HLA-DSAs.

OS306 NOVEL NON-HLA ANTIBODIES AGAINST ARHGDIB ARE ASSOCIATED WITH KIDNEY ALLOGRAFT FAILURE

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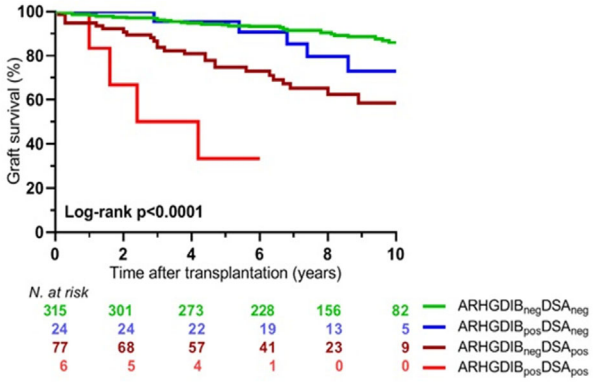
Background: The impact of donor-specific anti-HLA antibodies (DSA) on antibody-mediated rejection (ABMR) and graft survival has been well established. However, the clinical relevance of non-HLA antibodies remains unclear. We investigated the clinical relevance of antibodies (abs) against 13 non-HLA antigens in kidney transplant recipients and association with histology of ABMR.
Methods: In this study we included all single kidney transplant recipients (N = 203) with histological picture of ABMR ($ABMR_h$) and matched $ABMR_h$-free controls (N = 219) transplanted in a single centre between 2004 and 2013. Non-HLA antibodies in the recipient sera were detected by using a newly developed multiplex Luminex assay.

Results: Of all tested non-HLA abs (against agrin, APMAP, ARHGDIB, ARHGEF6, AT1R, ETAR, LMNB1, LPLUNC1, PECR, PLA2R, PRKCZ, TUBB4b, Vimentin), we did not find any non-HLA antibody to be more prevalent in $ABMR_h$ cases when compared to $ABMR_h$-free controls. With univariate analysis we found the antibody against ARHGDIB (adjusted MFI $\geq$ 1000 as a threshold for positivity) to be associated with graft outcome, which was confirmed by multivariate Cox modeling. Next, we grouped the patients according to HLA-DSA and anti-ARHGDIB abs. Compared to HLA-DSA-negative and anti-ARHGDIB negative patients, the adjusted Cox model showed a 20-fold increased risk for transplant failure in the patients positive with both HLA-DSA and anti-ARHGDIB antibodies, and almost a 5-fold increased risk in only HLA-DSA positive patients, but not in only anti-ARHGDIB positive patients ($p = 0.16$). This illustrates that anti-ARHGDIB antibodies potentiate the effect of HLA-DSA on graft outcome.
Conclusion: According to our results, presence of anti-ARHGDIB abs stratified the HLA-DSA positive kidney transplant recipients who are at the highest risk of graft failure. Other non-HLA abs did not contribute to risk stratification and could not explain the histology of ABMR in the absence of HLA-DSA.



OS307 INTRARENAL VIRAL DNA IN PROTOCOL BIOPSIES AND HUMORAL REJECTION: A RETROSPECTIVE STUDY IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Background: Viral infections can lead to transplant dysfunction and through the cytopathic effect and immune response they can lead to acute/chronic allograft rejection. It has been known that antibody mediated rejection (ABMR) represents one of major risk factors for reduced transplanted kidney survival. In order to evaluate if local virus mediated inflammation could be linked to development of anti-donor antibody and ABMR, we retrospectively reviewed histological, donor-specific antibodies (DSA), viremia and intrarenal virus data of transplanted patients and followed up at our pediatric center from 2011 to 2017.
Methods: Histological data were obtained from protocol biopsies performed at 6, 12 and 24 months after transplantation (Banff '15) in association with DSA +(with MFI > 3000). The detection of virus DNA was done by PCR for CMV, EBV, BKV, PVB19 in blood and bioptic tissue samples at the time of transplant (T0) and at the time of protocol biopsies.
Result: Analysis included 104 patients: 248 protocol biopsies, 52 diagnosed as acute/chronic rejection (69.2% cellular vs 30.8% humoral). The study did not highlight correlation between systemic viral infection and humoral or cellular rejection. Conversely, our data emphasized that the presence of at least one intrarenal virus, is more correlated to humoral rejection than to cellular rejection (68.8% vs 36.1%, $p = 0.038$). In particular, the presence of PVB19 is associated with humoral rejection compared to the cellular one (50% vs 19.4%, $p = 0.044$) and we could observe that only PVB19 has a prevalence in T0 biopsies (25.5%).
Conclusion: We speculate that Parvovirus B19 could increase the risk of humoral rejection, amplifying the exposition of MCH II antigens through INFg pathway. This retrospective study highlights a possible association between the presence of PVB19 intragraft and ABMR. The creation of a new multicentre study will allow increasing statistical power.

OS308 GENOME-WIDE NON-HLA MISMATCH IN KIDNEY TRANSPLANTATION

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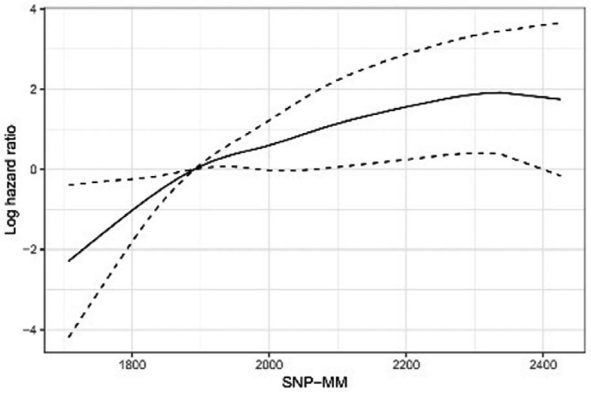
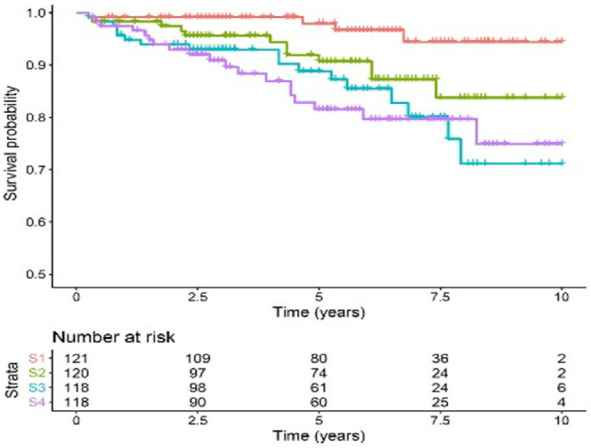
Background: The introduction of HLA matching of donors and recipients was a breakthrough in kidney transplantation. However, half of all transplanted kidneys still fail within fifteen years after transplantation. Epidemiological data suggest a fundamental role of non-HLA alloimmunity.
Methods: A total of 477 deceased donor and first kidney transplant recipient pairs from a prospective multi-center transplant cohort study were successfully genotyped. Genome-wide genetic mismatches in non-synonymous single nucleotide polymorphisms (nsSNPs) were calculated to identify incompatibilities in transmembrane and secreted proteins. Association of nsSNP mismatch and graft loss was estimated in a Cox proportional hazard model adjusting for HLA mismatch and clinical covariates. Customized peptide arrays were generated to screen for antibodies against genotype-derived mismatched epitopes in 25 patients with biopsy confirmed chronic antibody-mediated rejection (ABMR).
Results: The median nsSNP mismatch in immune-accessible transmembrane and secreted proteins between donors and recipients was 1,892 with an interquartile range (IQR) of 86. The degree of nsSNP mismatch was independently associated with graft loss in a multivariable model adjusted for HLA eplet mismatch *(HLA-A, B, C, DP, DQ, DR)*. Each increase by a unit of one IQR exhibited a HR of 1.68 (95% CI 1.17-2.41, $p = 0.005$).

A Kaplan-Meier analysis of graft loss stratified for the quartiles of nsSNP MM in transmembrane or secreted proteins is provided below.

Customised peptide arrays verified a donor-specific alloimmune response to genetically predicted mismatched epitopes.
Conclusion: Genetic mismatch of non-HLA haplotypes coding for transmembrane or secreted proteins is associated with an increased risk of functional graft loss independently of HLA incompatibility. As in HLA alloimmunity, donor specific alloantibodies can be identified against genotype derived non-HL





OS309 EXTENDED AND HIGH-RESOLUTION HLA GENOTYPING OF KIDNEY TRANSPLANT PAIRS IS NECESSARY TO CORRECTLY ASSIGN DONOR-SPECIFIC HLA ANTIBODIES PRIOR TO SOLID-ORGAN TRANSPLANTATION

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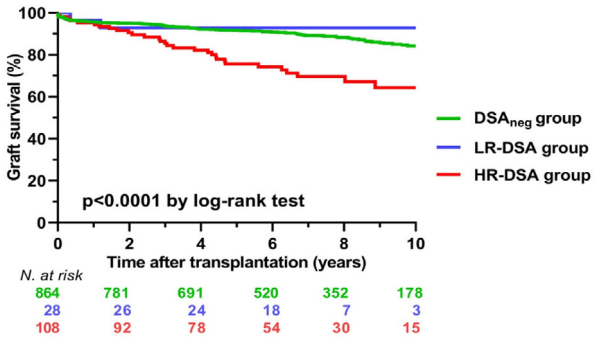
[1]Nephrology and Renal Transplantation Research Group, KU Leuven; [2]HILA, Red Cross-Flanders

Background: The need for high-resolution (HR) HLA typing to determine the compatibility between kidney transplant pairs in solid organ transplantation is currently widely debated due to high costs and questioned clinical importance. To date no studies have assessed the added value of HR extended HLA typing over low-resolution (LR) HLA typing in solid-organ transplantation. We analyzed the impact on graft survival of pretransplant DSA determined by HR HLA typing, compared to pretransplant DSA determined by LR typing.
Methods: We included 1000 single kidney transplant pairs transplanted in one centre between 2004 and 2013 and initially genotyped at LR HLA level. Anti-HLA antibodies were tested with Luminex and HR HLA genotyping was performed retrospectively.
Results: Based on LR HLA typings, serology or SSP for HLA-A/B/C/DRB1/DQB1, and Sanger sequencing for DPB1, pretransplant DSA were identified in 136/1000 patients and absent in 864/1000 patients (DSA_{neg} group). With HR extended typing of both donors and patients, we confirmed the presence of pretransplant DSA in 108/136 (79%) patients (HR-DSA group), and excluded DSA in 28/136 (21%) (LR-DSA group). Kaplan-Meier analysis showed that graft survival rates, censored for recipient death, were similar between DSA_{neg} and LR-DSA groups (86% vs. 93%; $p = 0.58$), which were both significantly better than the HR-DSA group (64%; $p < 0.001$).

In the LR-DSA group (N = 28), we found 34 misclassified DSAs in total, 21% of them were in HLA class I and 79% were in HLA class II. Analyzed per locus, 56% of DSAs were against DQ, while 15% were against DP. The main reasons for DSA misclassification were lack of 2nd-field HR typing (50%), incomplete HLA typing data of the donor (29%) and incomplete typing of patients (21%).
Conclusion: this cohort analysis illustrated that for a correct assessment of DSA prior to kidney transplantation, extended and HR HLA genotyping of the transplant pairs is needed, including DQA1 and DPA1 loci.

Figure 1



OS37 - PREDICTION AND OPTIMIZATION OF OUTCOMES IN KIDNEY TRANSPLANTATION

OS310 WHO SHOULD RECEIVE A PEDIATRIC KIDNEY? A NOMOGRAM FOR PREDICTING GRAFT SURVIVAL AFTER PEDIATRIC DONOR KIDNEY TRANSPLANT BY DONOR-RECIPIENT COMBINATION

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[1]The First Affiliated Hospital of Sun Yat-sen University; [2]Zhongshan School of Medicine, Sun Yat-sen University

Background: Kidney Donor Profile Index (KDPI) is used for deceased donor kidney allocation. However, KDPI could not accurately predict pediatric donor graft survival and impact of donor quality on post-transplant (PT) graft survival may vary by candidate condition. We aim to assess the PT pediatric graft survival by combination of donor quality and candidate condition.
Methods: Deceased pediatric donor under 18 years old between March 1994 and February 2016 were identified from Scientific Registry of Transplant Recipients. We estimated PT death-censored graft survival based on combination of donor and candidate factors known before transplantation using Cox Regression. A nomogram was then developed based on Cox Regression model for PT graft survival prediction.
Results: A total of 20813 pediatric donor kidneys recipients were included. Fourteen independent risk factors were found to predict death-censored graft survival (Table 1). The nomogram quantifying the relative contribution of each risk factor based on Cox Regression model was created with a C-index of 0.64, which performed better than the former KDPI or Child Donor Index and Adolescent Donor Index (Figure 1).
Conclusions: Our nomogram improves prediction accuracy in PT pediatric graft survival. With this nomogram, individualized allocation decision on pediatric donor kidneys can be made.

Table 1. Hazard models of post-transplant death-censored pediatric graft survival

Characteristics	HR	95%CI	P
Donor factors			
Donor age (months)	-0.002	0.997-0.998	<0.001
Donor race			
Black	0.411	1.145-1.988	0.003
Multiracial	0.211	0.697-2.192	0.468
Native	0.314	0.833-2.251	0.215
Pacific	0.494	0.876-3.068	0.122
White	0.224	0.956-1.639	0.103
Donor height			
Low	0.251	1.131-1.461	<0.001
Normal	0.103	1.003-1.225	0.043
Donor creatinine	0.036	1.017-1.057	<0.001
Recipient factors			
Recipient age			
12-17	0.296	1.145-1.577	<0.001
18-34	-0.211	0.700-0.937	0.005
35-49	-0.605	0.471-0.633	<0.001
50-64	-0.928	0.339-0.461	<0.001
65+	-0.941	0.321-0.474	<0.001
Recipient diagnosis			
Diabetes	0.034	0.937-1.141	0.505
Hypertension	0.038	0.951-1.135	0.400
Malignant disease	-0.257	0.401-1.493	0.444
Others	-0.098	0.839-0.979	0.013
Recipient race			
Black	0.648	1.647-2.216	<0.001
Multiracial	-0.694	0.124-2.013	0.329
Native	0.493	1.209-2.216	0.001
Pacific	0.229	0.810-1.953	0.307
White	0.113	0.968 -1.296	0.127
Recipient pretransplant dialysis	0.317	1.230-1.534	<0.001
Recipient history of transplant	0.175	1.088-1.305	<0.001
Recipient peak PRA	0.001	1.000-1.002	0.015
Recipient BMI	0.015	1.009-1.021	<0.001
Recipient pretransplant transfusion	0.136	1.075-1.222	<0.001
Known transplant factors			
HLA-DR mismatch			
1	0.133	1.060-1.231	<0.001
2	0.176	1.099-1.293	<0.001
Transplant type			
En bloc	-0.333	0.638-0.806	<0.001

PRA, Panel reactive antibody; BMI, Body mass index. P < 0.05 is considered as significant.

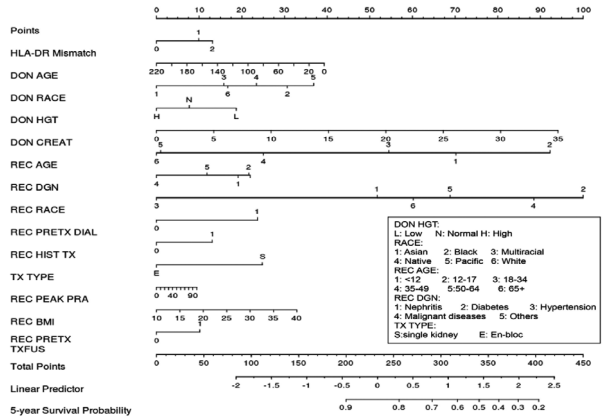

Figure 1. Nomogram for predicting the post-transplant death-censored pediatric graft survival (5-year). DON HGT, donor height; DON CREAT, donor creatinine; REC DGN, recipient diagnosis; REC PRETX DIAL, recipient pretransplant dialysis; REC HIST TX, recipient history of transplantation; REC PRETX TXFUS, recipient pretransplant transfusion; PRA, panel reactive antiboy; BMI, body mass index.

OS311 EXTENDED CRITERIA DONOR (ECD) KIDNEY TRANSPLANTATION: HISTOLOGICAL FEATURES AFFECTING LONG TERM GRAFT OUCOME

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Transplant Surgery Tor Vergata University, Roma

Background: Which donor Karpinski histological parameter at the pre-transplant biopsy affects long term graft outcome.
Methods: Between January 2005 and July 2017, 163 patients (pts) underwent kidney transplantation from ECD in our center. 143 pts (male = 91) received a single kidney transplant (SKT) and 20 pts (male = 15) a double kidney transplant (DKT). The recipient mean age was 62,1 (± 6,1) years in the SKT group and 65,9 (± 4,1) years in the DKT group. Donors mean age was 67 (± 7,3) years in the SKT group and 71 (± 8,6) years in the DKT group. Pre transplant wedge biopsy was evaluated according to Karpinski score. Thus in SKT group pts received graft with score 0 to 5; in DKT group pts received graft with score 3 to 6. The outcome was defined as both graft survival and function (MDRD at six months and then yearly). Mean follow up was 47.4 months (± 43) for SKT group and 57.8 months (± 27) for DKT group.
Result: No difference in 5 years graft survival was found between SKT and DKT groups. However MDRD was significantly higher in DKT group vs SKT group at 6 months (35.5 vs 54.3) (p = 0,0001), 3 years (40.2 vs 56) (p = 0,006) and 5 years (41.4 vs 57) (p = 0,049).

Among the SKT group, angiosclerosis (n = 93) was the only histological parameter adversely affecting graft survival at both 5 years (74.2 vs 93.6%) (p = 0,017) and 10 years (71 vs 89.4%) (p = 0,039). In the SKT group, donor age ≥ 70 years (n = 44) compared to donor age < 70 was found as a relevant factor adversely affecting graft survival both at 5 years (70.5 vs 85.9%) (p = 0,030) and 10 years (68.2 vs 81.8%) (p = 0,025).

The presence of both angiosclerosis and donor age ≥ 70 (n = 36), was dramatically affective on graft survival both at 5 years (61.1 vs 87.9%) (p = 0,0001) and 10 years (58.3 vs 84.1%) (p = 0,0001).
Conclusion: In our study ECD kidneys provide higher MDRD in DKT than in SKT. Kidneys ≥ 70 years and showing pre-transplant biopsy with angiosclerosis have higher survival when used in double transplant.

OS312 SIMILAR 1- YEAR RENAL FUNCTION IN KIDNEY GRAFTS FROM CONTROLLED DONATION AFTER CIRCULATORY DEATH USING NORMOTHERMIC REGIONAL PERFUSION AND DONATION AFTER BRAIN DEATH

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[1]Oslo University Hospital Rikshospitalet; [2]Department of Transplant Medicine, Oslo University Hospital Rikshospitalet; [3]Division of Emergencies and critical care, Oslo University Hospital Ullevål; [4]Department of Cardiothoracic Surgery, Oslo University Hospital Rikshospitalet

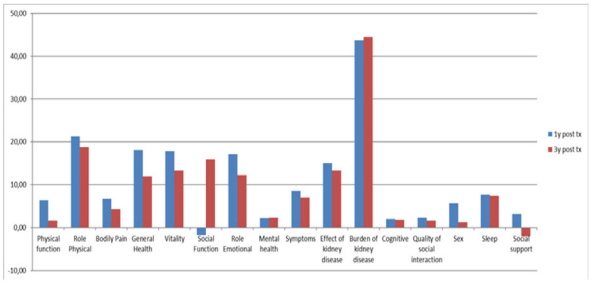
Background: With a marked increase in waitlisted recipients for kidney transplantation we implemented a Norwegian protocol for controlled DCD (cDCD) using normothermic regional perfusion. We hereby present the results from our first 32 cDCD kidney transplantations.
Methods: Kidney graft function was evaluated by comparing measured glomerular filtration rates (mGFR; plasma iohexol clearance) at eight weeks and one year after transplantation between cDCD grafts (n = 32) and DBD grafts (n = 163). Recipient and grafts were matched for recipient and donor age, immunosuppression and era. Mann-Whitney U test was used for comparison and two-tailed p-values < 0.05 were considered statistically significant.
Results: There was no significant difference in mGFR between the recipients of cDCD and DBD kidney grafts, neither at week 8 (55 vs 62 mL/min/L/1.73 m2, p = 0.43) nor at one year after transplantation; (61 vs 60 mL/min/L.73 m2, p = 0.57). The rate of delayed graft function was 22% in the cDCD group compared to 5% in the DBD group (p < 0.005) but this did not affect the one year graft survival was 96% in in both groups (p = 0.61).

At ESOT19, we also plan to present two- years data on kidney function and graft survival in addition to rejection rates.
Conclusion: The first 32 cDCD kidney transplants have clinical function in line with results from our DBD transplantations. The results have encouraged us to continue to address the shortage of organs for transplantation by utilizing cDCD kidneys.

OS313 "GETTING LIFE BACK" - KIDNEY TRANSPLANTATION IN THE ELDERLY PATIENT

Vasiliki Tsarpali[1], Lønning Kjerstl[2], Midtvedt Karsten[2], Tomm Bernklev[3], Nanna vonderLippe[4], Marit Helen Andersen[2], Kristian Heldal[2]
[1]Telemark Hospital Trust, Skien, Norway; [2]Department of Transplantation Medicine, Oslo University Hospital, Oslo; [3]Vestfold Hospital Trust, Tønsberg; [4]Oslo University Hospital, Oslo

Background: The number of elderly patients developing end stage renal disease (ESRD) who are eligible for kidney transplantation (KTx) is increasing, but their transplant rate is still low. Published data describing the long-term impact of KTx on health related quality of life (HRQoL) in this population are insufficient. We aimed to measure HRQoL and identify changes longitudinally from enlisting until three years post transplantation in a population of older kidney transplant candidates.
Methods: All patients ? 65 years old who were referred to our transplant center from Jan 2013 until Dec 2016 were asked to participate. The Kidney Disease Quality of Life Short Form version 1.3 questionnaire was used to measure HRQoL. Scores were obtained at enlisting and thereafter every 6 months until KTx, with latest answer representing baseline. A new set of questionnaires were answered 10 weeks, 6 months, 1 year and 3 years post-engraftment.
Results: Of 289 patients included, 214 (74%) had received a transplant and 90 had reached 3 years follow up by Mars 2019. 84 (93%) had completed the three years follow up questionnaire; 62 (74%) males, 61 (72%) on dialysis at enlisting, 20 (24%) KTx with a living donor. Mean age at the time of KTx was 71 years (65-82), mean time on the wait list was 15 months (2-50). Changes in HRQoL scores from baseline to 1 and 3 years post KTx are illustrated in the figure. Compared to baseline the scores improved after one year for most dimensions, except for social function (SF). At three years the SF score had improved significant, both clinically and statistically but physical function (PF) score declined to baseline level, probably due to ageing. The scores for the other dimensions remained relatively unchanged (Table)
Conclusions: HRQoL improves after KTx, also among older recipients. The most remarkable change is a marked improvement of social function, illustrating that the patients are finally "getting their lives back".



	Pre-KT (Mean ± SD)	1st Year (Mean ± SD)	3rd Year (Mean ± SD)	P - value (3rd Year vs pre-KT)
PF	66.7 ± 21.2	73.7 ± 23.0	68.5 ± 23.7	0.520
RP	25.3 ± 39.1	48.3 ± 45.5	44.7 ± 43.0	< 0.001
BP	65.6 ± 27.5	73.6 ± 26.7	70.0 ± 28.3	0.185
GH	50.8 ± 21.8	68.5 ± 23.0	63.0 ± 21.0	< 0.001
VT	42.3 ± 21.1	59.8 ± 21.7	55.4 ± 21.3	< 0.001
SF	65.5 ± 22.0	65.2 ± 19.0	81.5 ± 23.0	< 0.001
RE	55.5 ± 43.5	75.0 ± 40.8	67.9 ± 42.3	0.038
MH	79.1 ± 15.2	81.6 ± 18.5	81.5 ± 19.2	0.289
Symp	75.6 ± 16.1	84.5 ± 12.6	82.5 ± 12.8	< 0.001
EKD	70.8 ± 17.0	86.0 ± 14.1	83.8 ± 14.3	< 0.001
BKD	36.6 ± 25.8	81.0 ± 24.2	81.3± 22.3	< 0.001
Cogn	89.2 ± 13.5	92.0 ± 14.7	91.0 ± 14.1	0.346
QSI	84.6 ± 15.6	87.5 ± 14.4	86.2 ± 14.6	0.435
Sex	75.5 ± 25.1	78.8 ± 24.9	82.3 ± 21.0	0.810
Sleep	66.2 ± 17.8	73.3 ± 18.0	73.5 ± 16.6	0.001
Soc Supp	88.5 ± 1.2	91.05±20.2	86.3 ± 26.5	0.532

OS314 DUAL ADULT KIDNEY TRANSPLANTATION IN THE UK: AN UPDATED NATIONAL REGISTRY ANALYSIS

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[1]Guys and St Thomas and KIngs College London; [2]Addenbrookes Hospital, Cambridge; [3]NHS Blood and Transplant; [4]Leeds Teaching Hospital NHS Trust

Introduction: Dual adult kidney transplantation (DAKT) may have a role in increasing the utilisation of kidneys from older donors. Low patient numbers hampered previous national analyses and no current national guidelines exist. This study aims to 1) define DAKT practice in the UK and 2) compare outcomes of DAKTs to single kidney transplants (SKTs) from older donors.

Methods: Data were analysed from the UK transplant registry from 01/01/2005 to 31/12/2017. DAKTs were defined as 2 kidneys transplanted from deceased donors over the age of 5 years, and en bloc and multivisceral organs were excluded. Univariate and multivariable analyses were used, and graft and patient outcomes were considered.
Results: 450 DAKTs were performed over the study period, with 20,061 SKTs. DAKTs reached a peak of 71/annum in 2013 followed by a decline to 40/annum in 2017. DAKT median donor age was 71 (IQR 64-75) years, and median UK Kidney Donor Risk Index was 2.04 compared with 1.17 for SKTs. DAKTs had lower 5-year death-censored graft survival (DCGS) than SKTs (80.6% vs 85.9%; $p = 0.017$), however no statistical difference was observed when a Cox proportional hazards model adjusted for known risk factors was fitted (hazard ratio 1.05, 95% confidence limits 0.80-1.37, $p = 0.78$). When transplants from donors aged > 60 years were considered, 5-year DCGS were similar between DAKTs and SKTs (Figure 1). Median 12-month eGFR was 45 mL/min for DAKTs compared with 38 mL/min for SKTs aged 60 + ($p < 0.0001$), however primary non-function rates were comparable; 3.79% and 3.25% respectively ($p = 0.72$).
Discussion: Recipients of dual and single kidney transplants from donors aged over 60 years have similar kidney transplant survival and function. DAKT may allow the use of donor kidneys that would otherwise have been discarded. The appropriate selection of kidneys from older deceased donors remains uncertain and a major challenge for the transplant community.

OS315 THE IRISH EXPERIENCE OF KIDNEY TRANSPLANTATION AMONG RECIPIENTS WITH PRIOR NONRENAL SOLID ORGAN TRANSPLANT AND REPEAT KIDNEY TRANSPLANT

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Background: Renal failure is common complication among recipients of prior nonrenal solid organ transplants, predominantly due to calcineurin inhibitor toxicity. As a result of extended life expectancy and better quality of life, these patients are increasingly being referred for consideration for kidney transplantation. In this study we examined our experience of recipients of kidney transplant post nonrenal solid organ transplantation and compare them to age-matched repeat kidney transplant recipients.
Methods/Materials: This is a retrospective review of a prospectively maintained database from the National Kidney Transplant Service (NKTS) of Republic of Ireland. The study period was from January 1993 to August 2017 and included adult living and deceased donor kidney transplant recipients. Patients who received kidney transplant after other solid organ transplantation were reviewed and were compared to patients who received repeat kidney transplant in the same period.
Results: There were a total of 433 patients in the study cohort (38 recipients of kidney transplant post nonrenal solid organ transplant and 395 recipients of repeat kidney transplant). Baseline and transplant-specific characteristics of study population are outlined in Table 1. Death-censored 1-,5- and 10-year graft survival for the two groups were 94.7%/93.7%, 87.3%/86.4%, 78.6%/74%, respectively (P = 0. 509) (Figure 1).

	Kidney after other solid organ transplant (N = 38)	Repeat kidney transplant (N = 395)	P value
Recipient age at transplant, y, mean (sd)	44.5 (41.7)	41.7 (12.4)	0.193
Recipient sex, *n* (%)			0.21
Male	20 (52.6)	249 (63)	
Female	18 (47.4)	146 (37)	
Cold ischaemia time, h, mean (sd)	17.6 (5.6)	18.0 (6.6)	0.32
Recipient blood group, *n* (%)			0.73
O	22 (57.9)	219 (55.6)	
A	11 (28.9)	121 (30.7)	
B	5 (13.2)	43 (10.9)	
AB	0	11 (2.8)	
Type of dialysis at transplant, *n* (%)			0.34
HD	30 (78.9)	277 (71.1)	
CAPD	4 (10.5)	78 (20.2)	
PE	4 (10.5)	32 (8.3)	
Donor age, y, mean (sd)	38.8 (16.7)	38.4 (14.1)	0.86
Donor type, *n* (%)			0.08
DBD	37 (97.4)	330 (83.1)	
DCD	0	5 (1.3)	
LD	1 (2.6)	60 (15.2)	
DGF, *n* (%)	4 (10.5)	64 (16.2)	0.48

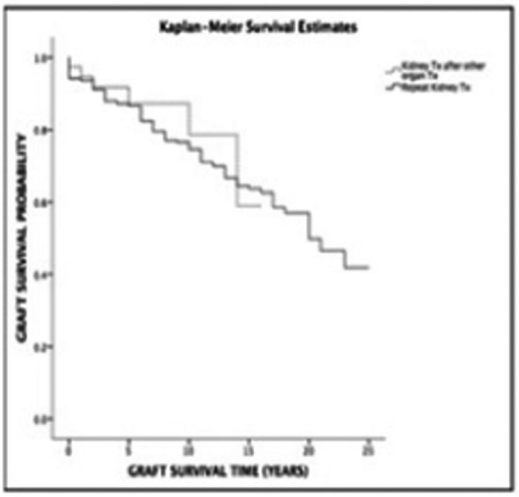

Figure 1. Kaplan-Meier allograft survival curve for kidney after other nonrenal solid organ transplant and repeat kidney transplant (P=0.509)

Conclusions: Our national experience demonstrates that patients receiving kidney transplant after nonrenal solid organ transplant can expect allograft survival similar to patients receiving repeat kidney transplant.

OS316 MULTIORGANIC AND MONORGANIC DONOR IN RENAL TRANSPLANT IN ARGENTINA 2007–2017

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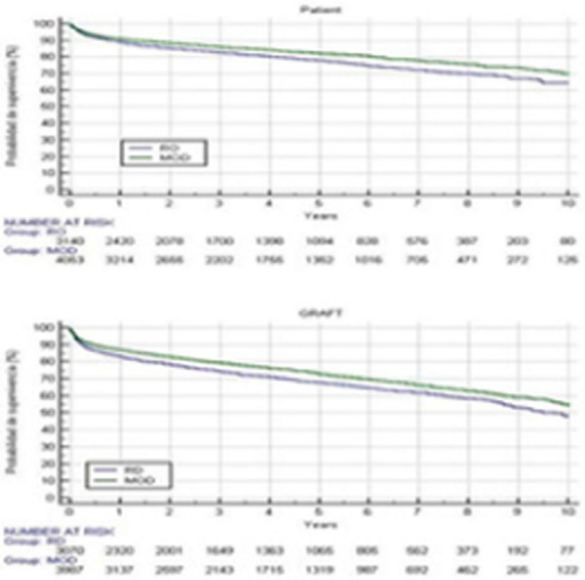
INCUCAI

Objective: To analyze patient and graft survival in Argentina in the last 11 years, in relation to the type of monorganic donor (Renal Donor = RD) and multi-organ donor (multiorgan donor MOD) and other associated variables.
Material and Methods: We analyzed 7708 patients over 18 years of age at the time of transplantation (TX) between January 1, 2007 and December 31, 2017. The information was extracted from SINTRA. The variables entered into the multivariate model were: type of donor, age and gender of donor and recipient, cause of death of the donor (CVA, Trauma, and Other), time of cold ischaemia CIT, years in WL (3), years on dialysis (7), etiology of admission to the waiting list WL, delay graft function (DGF) defined as dialysis need within 7 days post transplant, and missmatch.
Results: Of 7708 Tx analyzed, 43% were performed with RDMedian age of recipient and donor were, respectively, 51.3 years (95% CI 50.8-51.7) and 45.9 years (95% CI 45.4-46.4). 57% of the recipients were male, and 58% of donors. 54.10% of patients, DGF was observed in 3516 patients.

Median time in WL was 2.63 (95% CI 2.6-2.7) and median time on dialysis was 7.02 yrs (95% CI 6.9-7.1). Main causes of donor's death were CVA in 56% and Trauma 36%.

Multivariate Analisys is showing in Table 1

Donor's Variable	RD	MOD	*p*
Age (median-CI95%)	49.89 (49.2-50.6)	42.94 (42.3-43.7)	$P < 0.0001$
Sex (M/F)	1885/1453	2586/1784	$P = 0.0171$
BMI	27.34	26.06	$P < 0.0001$
Cause of death	CVA58% Trauma 32%	CVA 58% Trauma 38%	$P < 0.0001$
Creatinine (median-CI95%)	1.1 (1.1-1.15)	0.95 (0.93-0.97)	$P < 0.0001$
CIT Hrs (median-CI95%)	21 (20.8-21.3)	18.5 (18.2-18.8)	$P < 0.0001$
HLA Clase I mismatch (media-CI95%)	2.54 (2.5-2.6)	2.36 (2.3-2.4)	$P < 0.0001$
HLA Clase II mismatch (media-CI95%)	0.62 (0.6-0.64)	0.52 (0.5-0.54)	$P < 0.0001$
Recipient's Variable			
Age (median-CI95%)	52.74 (52.1-53.5)	50.13 (49.5-50.7)	$P < 0.0001$
Sex (M/F)	1935/1403	2438/1932	$P = 0.0171$
BMI (median-CI95%)	24.2 (23.9-24.3)	23.7 (23.5-23.8)	$P < 0.0001$
DGF	58%	51%	$P < 0.0001$
Dialysis duration (yrs) (median-CI95%)	5.8 (5.6-6.0)	7.0 (6.8-7.1)	$P < 0.0001$
Diabetes	9.11%	8.96%	N/S



In multivariate analysis recipient's and donor's age, DGF and the mismatch greater than 3, were associated in a statistically significant way with post-transplant mortality.

In graft's survival, variables that were associated in a statistically significant manner for graft loss were: recipient's age, time on dialysis, national distribution, DGF, and CVA as a cause of donor's death and having a greater mismatch of 3.

Conclusions: KM curve shows a slight improvement in patient's and graft's survival transplanted with MOD tan RD.

The type of donor does not show statistically significant differences in the multivariate analysis.

OS317 OPTIMISING OUTCOMES FOR OLDER PATIENTS: ARE ADULT CHILDREN AN UNDERUTILISED ALLY IN TRANSPLANTATION

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Introduction: Living donor (LD) transplantation is the optimal form of renal replacement therapy for suitable patients with end-stage renal disease (ESRD). The mean age of incident patients with ESRD continues to rise in the UK, but there is age-related inequity of access to LD transplantation.

The proposed change in the allocation of deceased donors (DD) in the UK is likely to result in older patients being offered poorer 'quality' kidneys, with potential for greater morbidity and mortality.

We reviewed the pattern of transplantation in older recipients in our region and considered the profile of their donors.

Methods: The records of all renal transplant recipients in this region from 01/01/2010 to 31/12/2018 were interrogated. Recipients older than 65 years at time of transplant were identified. Data were extracted from NI Renal Transplant Database and Electronic Care Record.

Results: There were 896 transplants in the study period. The recipient age range was 3-79 years, and 156 (17%) recipients ≥ 65 years old. Of these 45% received a LD kidney which is comparable to the 50-64 yr. cohort (143/289, 49%), lower than the 35-49 yr. group (175/276, 63%), with highest proportion of LDs being in the 18-34 yr. (109/140, 78%) and paediatric (26/ 35, 74%) cohorts. Adult children accounted for half of the living donors for the older recipients, details in Table 1.

Relationship	Number	Percentage (%)	Mean donor age (yr.)
Partner/spouse	15	21	58
Sibling/Sibling-in-law	14	20	63
Child/Child-in-law	36	51	44
Friend/Altruistic Donor	5	7	60

Discussion: In our region older (≥65 yr.) recipients have comparable access to LD transplantation to those aged 50-64 years. This may reflect the absence of prejudice against adult children or their spouses being living donors. The disparity in outcomes between LD and DD transplantation is likely to become more pronounced in older recipients with the change in DD allocation in the UK in 2019. As the physical risks to a LD are equivalent irrespective of the recipient demographics, this group represents an important opportunity to optimise the care of the older patients with ESRD.

OS318 ABSENCE OF ADDITIONAL PREDICTIVE ABILITY VALUE OF PREIMPLANTATION BIOPSIES FOR LONG-TERM ALLOGRAFT OUTCOME

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Background: A significant number of kidneys are discarded worldwide due to the suboptimal use of large kidney resources. The main cause of discard is the result of the preimplantation biopsy.

Method: We included patients who underwent kidney transplantations from a deceased donor in 2 French referral centers between 2004 and 2014 with preimplantation biopsy. Two external validation cohorts were included: 1,107 deceased donors from Belgium and 1,103 discarded kidneys based on biopsy results from the US.

Results: A total of 1,629 patients were included in the development cohort. After adjusting for donor, recipient, and transplant characteristics as well as for preimplantation biopsy findings (IFTA, cv and ah Banff score, and glomerulosclerosis percentage) and baseline immunological parameters, we identified the KDRI score (HR = 2.50; 95% CI, (1.38 to 3.40); $p < 0.001$), the presence of circulating DSA on the day of transplantation (HR = 1.76; 95% CI, (1.36 to 2.28); $p < 0.001$), prior kidney transplantation (HR = 1.34; 95% CI, (1.01 to 1.78); $p = 0.045$), and the IFTA score (HR = 1.51; 95% CI, (1.00 to 2.26); $p = 0.048$) as the main independent determinants of long-term allograft loss. However, the biopsy results had no additional value to predict long term allograft outcome when compared to the model without the biopsy results (Fig. 1). In the Belgium validation cohort, none of the biopsy results were associated with allograft loss. Kidneys discarded based on histology results in the US were matched to transplanted kidneys in France. French kidneys with similar histological results as discarded kidneys in the US did not have worse allograft survival compared to the unmatched transplanted kidneys ($p = 0.156$) (Fig. 2).

Conclusions: Given this result and the fact that preimplantation biopsies increase the cold ischemia time, the current practice of discarding kidneys based on preimplantation biopsy results may not be optimal for allocation decision-making.

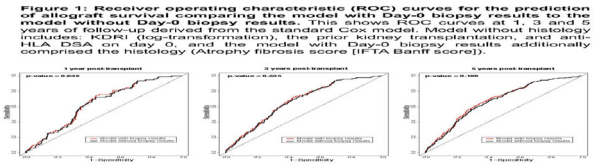

Figure 1: Receiver operating characteristic (ROC) curves for the prediction of allograft survival comparing the model with Day-0 biopsy results to the model without Day-0 biopsy results. This shows ROC curves at 1, 3 and 5 years of follow-up derived from the standard Cox model. Model without histology includes: KDRI (log-transformation), the prior kidney transplantation, and anti-HLA DSA on day 0, and the model with Day-0 biopsy results additionally comprised the histology (Atrophy fibrosis score [IFTA Banff score]).

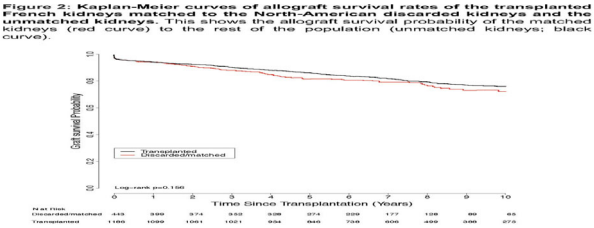

Figure 2: Kaplan-Meier curves of allograft survival rates of the transplanted French kidneys matched to the North-American discarded kidneys and the unmatched kidneys. This shows the allograft survival probability of the matched kidneys (red curve) to the rest of the population (unmatched kidneys; black curve).

OS319 EARLY GRAFT OUTCOMES IN KIDNEY TRANSPLANTATION: WHICH IS THE BEST SURROGATE FOR LONG TERM GRAFT AND RECIPIENT SURVIVAL?

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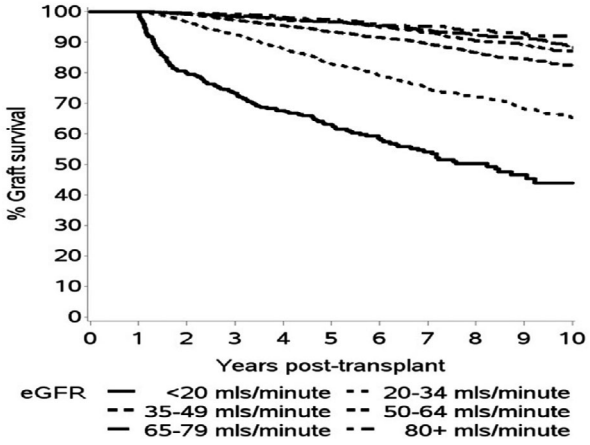
[1]University of Cambridge; [2]NHS Blood and Transplant

Introduction: Long term patient and graft survival are the most clinically-relevant endpoints in kidney transplantation but it is rarely viable to design and power clinical trials using these endpoints. The aim of this study was to compare the utility of the early surrogate endpoints delayed graft function (DGF), primary non function (PNF), acute rejection (AR) and eGFR in predicting long-term graft and patient survival.

Methods: First-time, adult recipients of kidney-only transplants in the UK during 2005-17 were included in the study. A stepwise variable selection method was used to develop separate Cox proportional hazard models for

death-censored graft and patient survival using donor, recipient and transplant characteristics. The surrogate endpoints were compared to graft and patient survival using Kaplan-Meier plots, and the risk-adjusted survival models. Model fit was tested using Akaike's Information Criteria.
Results: 17,102 patients were included in the study with 10,304 recipients of donation after brain death (DBD) and 6,798 recipients of donation after circulatory death (DCD) kidneys. DGF was associated with graft failure for both DCD and DBD donor kidneys (HR 1.6, 95% CI 1.4-1.8, $p < 0.0001$) with a positive interaction between donor type and effect of DGF ($p = 0.04$). AR was also associated with graft failure (HR 1.7, 95% CI 1.5-2.0, $p < 0.0001$). eGFR at 3 and 12 months post transplant were strongly associated with graft failure (fig 1). Similar associations were found between DGF, acute rejection and eGFR with patient survival. PNF was associated with early mortality (1 year patient survival for PNF vs graft function 77.7% vs 96.8% $p < 0.0001$). Model fit was best for eGFR 12 months post transplant.
Conclusion: Acute rejection, DGF and eGFR at 3 and 12 months post transplant are all strongly associated with graft survival. eGFR at 12 months is the best fit surrogate and so is recommended as a primary endpoint for future clinical trials in kidney transplantation.



OS320 DOES THE DURATION OF DELAYED GRAFT FUNCTION AFTER DCD DONOR KIDNEY TRANSPLANTATION INFLUENCE LONGER-TERM OUTCOMES? A UK REGISTRY ANALYSIS

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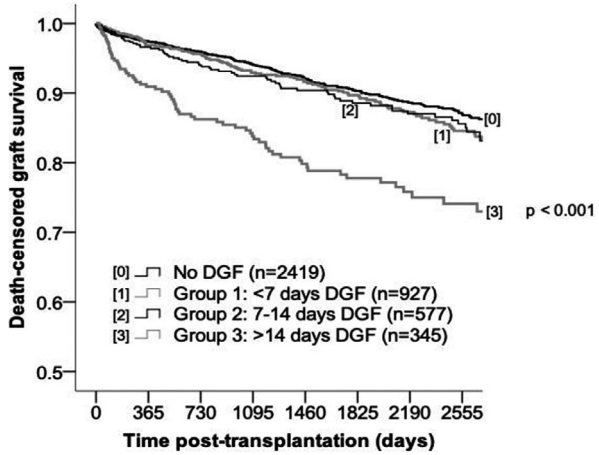
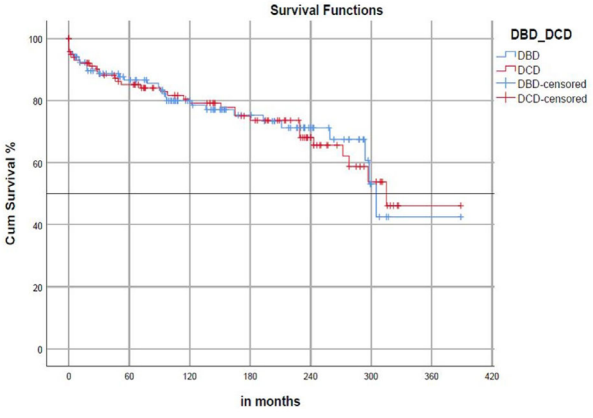
Introduction: Previous UK registry analyses have suggested that the presence of delayed graft function (DGF) does not influence longer-term graft outcomes after DCD donor kidney transplantation. However, the impact of prolonged DGF has not been examined. This study 1) determines if DGF duration affects longer-term outcomes; 2) identifies factors associated with prolonged DGF duration.
Methods: A UK registry analysis on first single kidney-only DCD transplants from donors aged ≥ 10 years old to adult recipients between 2006-2016 was performed. Recipients were grouped: no DGF; DGF < 7 days (group 1); DGF 7-14 days (group 2); DGF > 14 days (group 3). Pre-emptive recipients, those with missing data on dialysis status at transplantation, and those with PNF were excluded. Univariable and multivariable statistical analyses determined the effect of donor/recipient characteristics and DGF duration on post-transplant outcomes.
Results: Of 4268 recipients, 2419 (56.7%) had no DGF, with 927 (21.7%) in group 1, 577 (13.5%) in group 2, and 345 (8.1%) in group 3. There was no difference in death-censored graft survival (DCGS) between recipients with no DGF and those in groups 1 and 2; however group 3 had significantly worse DCGS relative to all other groups ($p < 0.001$), suggesting a threshold effect. DGF duration was an independent predictor of DCGS; those in group 3 had almost three times the risk of graft failure than those without DGF (HR 2.9 CI 1.8-4.5 $p < 0.001$). Surprisingly, duration of DGF was an independent risk factor for patient survival; those in group 3 had double the risk of death relative to recipients with no DGF (HR 2.0 CI 1.5-2.7 $p < 0.001$). Older, male, obese donors with longer CITs, and black, male recipients, were all independently associated with prolonged DGF > 14 days.
Conclusions: Unexpectedly, this updated registry analysis shows that duration of DGF > 14 days strongly impacts longer-term graft and patient survivals following DCD donor kidney transplantation.



OS321 LONG-TERM OUTCOME OF DCD KIDNEY TRANSPLANTATION

Amélie Müller[1], Kerstin Hübel[1], Christian Oberkofler[1], Kuno Lehmann[1], Pietro Cippà[2], Thomas Müller[1], Markus Weber[3], Pierre-Alain Clavien[1], Olivier deRougemont[1]
[1]University Hospital Zurich; [2]Ospedale Regionale di Lugano; [3]Stadtspital Triemli

Background: Donation after circulatory determination of death (DCD) represents up to 20% of used kidney grafts. Numerous studies have shown similar outcome compared to donation after brain death on the short- and mid-term. Until now, long-term outcome has though never been shown. The aim of this study was to complete long-term follow up and graft survival of a controlled-group study comparing DCD and DBD kidneys.
Methods: We retrospectively analyzed all patients transplanted at our institution between January 1985 and March 2000. All DCD recipients were matched one-to-one with patients transplanted with DBD grafts during this period. Graft survival was estimated with Kaplan-Meier method.
Results: Overall 1133 kidneys were transplanted during this period. Of these, 122 patients received a graft from a DCD donor and accordingly matched with 122 DBD recipients. Results showed similar graft-survival in both groups, with no significant difference ($p = 0.93$). Median graft survival after 33-years follow-up was 25 years (305 months) in DBD, and 26 years (315 months) in DCD. Delayed graft function occurred in 59 patients in the DCD group compared to 29 in the DBD group ($p = 0.001$).
Conclusion: This is the first study to show similar outcome in DCD kidneys compared to DBD after 30 years follow-up. Although the incidence of delayed graft function is higher after DCD, these graft are a valuable resource and should probably be handled in the same way as DBD grafts.



OS38 - ALLOCATION IN LIVER TRANSPLANT 2

OS322 SARCO-MODEL, A NOVEL SCORE TO BETTER PREDICT THE RISK OF DEATH IN CIRRHOTIC PATIENTS AWAITING LIVER TRANSPLANTATION

Quirino Lai[1], Paolo Magistri[2], Raffaella Lionetti[3], Alfonso W Avolio[4], Ilaria Lenci[5], Valerio Giannelli[3], Annarita Pecchi[2], Flaminia Ferri[1], Giuseppe Marrone[4], Martina Milana[5], Vincenzo Schinninà[3], Renata Menozzi[2], Michele Di Martino[1], Antonio Grieco[4], Tommaso M Manzia[5], Giuseppe Tisone[5], Salvatore Agnes[4], Massimo Rossi[1], Fabrizio Di Benedetto[2], Giuseppe M Ettorre[3]

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Background: Sarcopenia has been recently proposed as a useful tool for predicting death in cirrhotic patients waiting for liver transplantation (LT). However, the creation of a model integrating sarcopenia with the conventional scoring systems is needed, with the intent to identify patients not efficaciously captured by these allocation models. The study aimed at developing a score integrating sarcopenia and MELDNa able to predict the risk of death in cirrhotic patients enlisted for LT.
Methods: 1,082 patients enlisted in the Roman Liver Transplant Consortium (Training Set; $n = 855$), and in Modena University (Validation Set; $n = 232$) during the period Jan2013-Dec2018 were investigated. Exclusion criteria were: a) age < 18 years, b) non-cirrhotic liver disease. At-listing cross-sectional psoas muscle area at the level of L3 was used for evaluating the sarcopenic status.
Results: Sarco-Model was built using a competing-risk analysis of the cause-specific hazards, being based on the equation: 12*((0.069*MELDNa) + (0.027*age) + (0.056*BMI)-(0.039*psoas sum cm2)-(0.561*albumin mg/dL)). At external validation, Sarco-Model showed an AUC = 0.70 (P = 0.001) respect to MELD (AUC = 0.59; P = 0.1) and MELDNa (AUC = 0.68; P = 0.002). When investigated only in the patients with MELD score ?19, Sarco-Model showed a markedly superior diagnostic ability (AUC = 0.80; P < 0.0001). The Sarco-Model score ranged 6-40 like the MELDNa, consenting to calculate how many additive points should be added to the patient with the intent to

OS323 IMPACT OF CENTER VOLUME ON DONATION AFTER CARDIAC DEATH LIVER TRANSPLANT OUTCOMES. A RETROSPECTIVE SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS ANALYSIS

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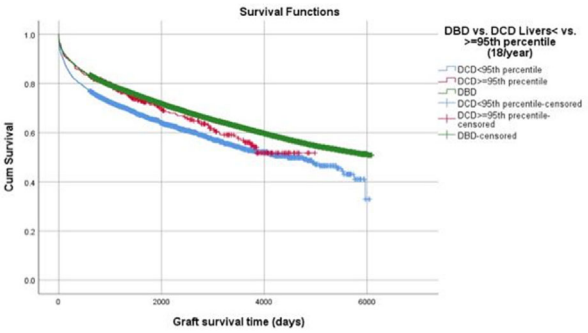
[1]UAMS Medical Center; [2]King's College Hospital; [3]Mayo Clinic Arizona

Background: Organ shortage necessitates the optimization of the utilization and outcomes of donation after cardiac death (DCD) liver allografts. Aim of the study was to assess the center volume effect on graft survival in DCD liver transplantation (LT).
Method: Retrospective SRTR analysis on deceased donor LTs performed during period 2001-2015. Exclusion criteria: age < 18 years, partial grafts, retransplants, multivisceral transplants, < 5 LTs per year. Cohort was sorted by time and location. Transplant centers were ranked in order of annual case volume. Center rank and group designation were annually recalculated. The observations were split into tertiles and then further subcategorized into annual DCD volume deciles. Log-rank analysis was performed comparing LT graft survival. Multivariate backward cox-regression analysis was performed.
Results: N = 69,387 LTs. DCD LTs were 3,536 (5.1%). 60% of DCD allografts were used by centers performing < 5 DCD/year; their survival was inferior to higher volume centers ($p = 0.024$). Low DCD volume center outcomes were consistently inferior to the outcomes of higher volume centers or DBD grafts, until the 95th percentile (≥18DCD/year); beyond this threshold, DCD graft survival became equivalent to DBD ($p = 0.224$).

Adjusted cox-regression analysis indicated that < 5 DCD/year, prolonged cold ischemia time, increased warm ischemia time, older donor age and ICU status at the time of transplant were predictors of inferior DCD graft outcome.
Conclusion: Presently, the majority of DCD allografts are transplanted at low DCD volume centers. DCD outcomes are persistently higher in busier DCD centers, becoming equivalent to DBD at centers performing 18 DCD/year. Expedited offering and allocation of potential DCD allografts to accredited regional DCD centers of excellence may therefore optimize DCD graft utilization and outcomes.



OS324 SHOULD WE REVISE MELD ALLOCATION FAVORING PATIENTS WITH HCC? ANALYSIS OF MORTALITY ON THE WAITING LIST

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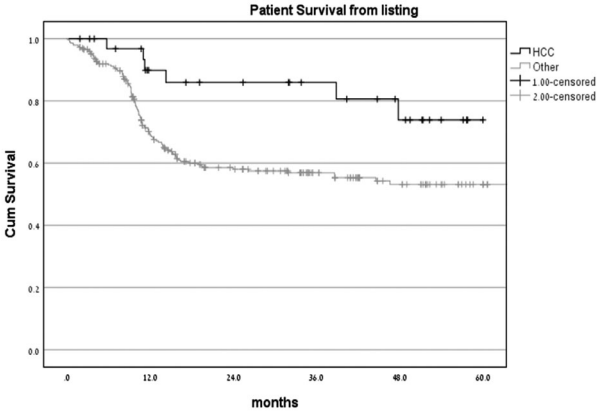
[1]Rabin Medical Center, The Liver Institute; [2]Rabin Medical Center, Dep. of Transplantation; [3]Rabin Medical Center

The MELD allocation gives liver transplant (LT) dates with HCC extra-points while surgery and various local treatments may control HCC progression with good outcome after transplant. We sought to determine whether the MELD allocation negatively affect other patients without a tumor.
Patients and Methods: We extracted data on listed patients for (LT) between 1/2013-9/2018. Waiting time and patient survival rate for the different disease categories (NASH, hepatocellular dis, cholestatic immune dis., HCC, and others) was calculated. Kaplan-Meier Method was used once for survival analysis from listing and then for survival after LT.
Results: During that period 408 patients were listed for LT, 60 were excluded from the analysis for the following reasons: delisting for deterioration in medical condition (47), fulminant liver failure (10) and tumor progression (3). Another 21 patients who underwent transplant elsewhere were also excluded leaving 327 patients for analysis. Of these patients, 159 patients underwent transplant (48.6%), 86 died on the waiting list (26.3%) and another 82 patients are on the list. Mean waiting time until transplant or death on the list for the whole group was 13.4 ± 15.6 mo. (2-68 mo.); 7.6 ± 7.3 mo. for HCC candidate vs. 14.1 ± 16.5 mo. for other patients ($p = 0.023$). Mortality on the waiting list occurred at a mean interval of 10.93 + 6.14 months after listing. Overall patient survival from listing was 71.4% and 60.9% for 1- and 2-years, respectively. The 1- and 2-years survival was 86.0% and 73.9% for HCC patients vs. 69.2% and 58.0% for all other patients ($p = 0.014$). Overall patient survival at 1- and 3- years after LT were 93.1% and 87.9% for HCC patients vs. 74.1% and 71.1% for all other patients ($p = 0.08$).
Conclusions: Current Meld allocation that advantages patients with HCC is associated with high mortality on the waiting list for other patients and thus should be revised



OS325 MELD-NA ALTERATIONS ON THE LIVER TRANSPLANT WAITING LIST AND ITS IMPACT ON LISTING OUTCOME

Gerd Silberhumer, Georg Gyoeri, Lukas Baumann, Sonja Zehetmayer, Thomas Soliman, Gabriela Berlakovich
Medical University Vienna

Background: Currently, MELD Score listing is state of the art for liver transplant recipients. Our department could show by our own data and confirmed by an ET- cohort that dynamic MELD deterioration (Delta MELD) during waiting time has a significant impact on postoperative survival. Aim of this study was to analyze the impact of MELD score (Delta MELD) alterations on waiting list behavior of liver transplant candidates.
Method: More than 51000 patients were listed in the UNOS data for a liver transplantation between 2011 to 2015.
MELD-Na was calculated according to this formula
MELD − Na − [0.025 × MELD × (140 − Na)] + 140(Na ranges from 125-140)
Patients were analyzed according to their delisting reasons, which were defined as transplanted, still listed, died on list, too good, too sick for transplantation or other.
Difference in outcome between MELD and MELD-Na were compared.
Results: Half of the listed patients (50.1) are already transplanted, 18.6% are still actively listed, 11.5% were removed due to poor conditions, 11% died on list, 2.6% were removed due to recovery and 6.3% of patients were removed due to other reasons.
MELD-Na did not show significant more impact on waiting list outcome than MELD alone.
MELD-Na On was significantly higher for patients who died on list compared to the other groups. Patients who finally died on the waiting list showed a mean Delta MELD-Na of 6.8 ± 8.5. Patients who are still awaiting a graft showed almost no Delta MELD-Na (-0.1 ± 5.1) and patients who where considered too healthy for transplantation improved by almost 3 points. The maximum MELD alteration was 10.1 ± 7.7 for patients who died on the waiting list, compared to 6.7 ± 6.5 in the group of finally transplanted patients.
Further details of the MELD and MELD-Na values are shown in table 1.
Conclusion: Dynamic alterations in the MELD/MELD-Na during waiting time have significant impact on waiting list behavior for liver transplant candidates.

MELD/ MELD Na	TX	Too good	Too sick	Died	Other	Waiting
ON	18.2/20.3	13.4/15.4	18.0/20.3	19.6/22.1	14.0/16.3	13.2/15.2
OFF	21.6/23.4	11.1/12.5	24.6/26.1	27.3/28.9	15.4/17.5	13.5/15.1
Delta	3.3/3.0	-2.3/-2.9	6.6/5.9	7.7/6.8	1.4/1.2	0.3/-0.1
Delta max	6.6/6.7	5.8/7.0	9.2/9.0	10.7/10.1	5.5/6.3	5.4/6.5
Delta last	-0.3/-0.3.	-0.4/-0.6	1.9/1.6.	2.4/2.0	0.5/0.4	-0.0/-0.1

OS326 NOVEL CLINICAL AND GENETIC RISK FACTORS FOR EARLY POST-OPERATIVE THROMBOSIS IN LIVER TRANSPLANTATION

Yanni Li[1], Lianne Nieuwenhuis[2], Michiel Voskuil[1], Ranko Gacesa[1], Shixian Hu[1], Bernadien Jansen[1], Maureen Werner[2], Hans Blokzijl[1], Bouke Hepkema[3], Ton Lisman[2], Rinse Weersma[1], Robert Porte[2], Eleonora Festen[4], Vincent deMeijer[2]
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Background: Post-operative thrombosis (PT) is one of the leading causes of graft loss and mortality after liver transplantation (LT), and is associated with a plethora of donor, recipient and transplant-related risk factors. While clinical risk factors can largely be accounted for, better knowledge of genetic risk factors for PT is essential for developing targeted strategies to improve graft survival.
Methods: A post-hoc analysis of a prospective cohort (www.trialregister.nl – Trial NL6334) of LT recipients between 1993-2017 was performed. Upon availability, donor and recipient DNA were genotyped with the Illumina Global Screening Array. Risk factors for early PT (<90 days) were analyzed in univariate and multivariate logistic regression models. To study genetic risk factors for PT, we performed genome-wide association (GWA) analysis.
Results: A total of 1099 recipients underwent 1337 LT procedures. Only primary adult LT (748 [55.9%]) were included in subsequent analyses. Multivariate regression analyses demonstrated that smoking status of the donor (OR = 2.505 [1.288-4.871]; P = 0.007), and nonalcoholic steatohepatitis (NASH) in the recipient (OR = 2.343 [1.057-5.193]; P = 0.036) were independent clinical risk factors for early PT. Using GWA analysis with donor genotypes, we identified 42 genetic loci associated with increased risk of PT at a suggestive genome-wide significance threshold ($P < 5x10^{-05}$). One of these variants (rs1336472 [$P = 1.2x10^{-05}$ OR = 1.84]), in a locus harboring the *AK4* gene, has been reported as a risk variant for venous thromboembolism, outside the context of LT.

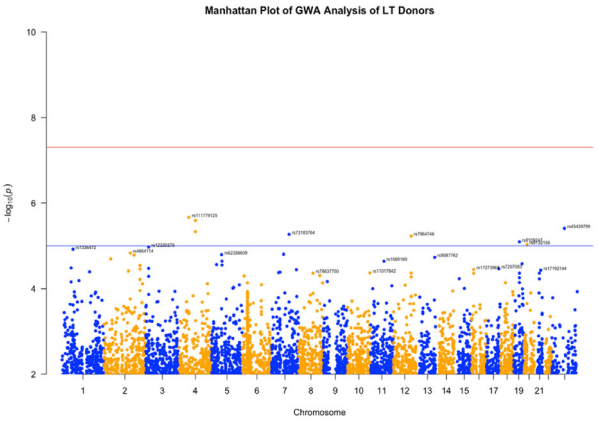

Figure 1. Manhattan plot of GWA analysis of LT donors.

Conclusion: We identified donor smoking status and NASH in the recipient as novel clinical risk factors for early PT. Moreover, we observed that genetic variation within the donor influences risk for early PT. These preliminary results warrant further investigation into the contribution of donor genetic risk factors for early PT.

OS328 THE CASE-MIX IN LIVER TRANSPLANTATION. DIFFERENT PERCEPTIONS (TRANSPLANT SURGEONS AND TRANSPLANT HEPATOLOGISTS) AND DIFFERENT CONCORDANCE LEVELS WITHIN CENTERS

R. Calia[1], A. Avolio[2], M. Luciani[3], Antonio Franco[1], Q. Lai[3], M. Vivarelli[4], A. Benedetti[4], L. Lupo[5], M. Rendina[6], Michele Colledan[7], S. Fagiuoli[7], M. Cescon[8], C. Morelli[8], F. Zamboni[9], L. Mameli[9], Luciano De Carlis[10], Luca Saverio Belli[10], G. Rossi[11], F. Donato[11], V. Mazzaferro[12], S. Bhoori[12], Fabrizio Di Benedetto[13], N. De Maria[13], W. Santaniello[14], G. Di Costanzo[14], Salvatore Gruttadauria[15], R. Volpes[15], Paolo De Simone[16], Paola Carrai[16], M. Spada[17], V. Nobile[17], S. Agnes[1], Antonio Grieco[1], G. Spoletini[1], G. Ettorre[18], Valerio Giannelli[18], G. Tisone[19], I. Lenci[19], M. Rossi[3], S. Ginanni Corradini[3], R. Romagnoli[20], S. Martini[20], A. Risaliti[21], P. Toniutto[21], U. Tedeschi[22], A. Carraro[22], Patrizia Burra[23], Umberto Cillo[23]
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A national study on case mix in liver transplantation (LT) is ongoing in Italy. As an add-on analysis the evaluation of perception of sustainable case mix among surgeons (SURGs) and hepatologists (HEPs) has been performed using a 30-item questionnaire.
Surgical directors and transplant hepatologists from 21 LT Centers were asked to quantify perception of the patient-death risk at 6 months for each supposed risk factor. Answers were assessed by visual-numerical analogue scale (0% = no impact; 100% = max impact, Spearman's Rho test). SURG-HEP concordance within the same Centre and between Centres was evaluated. The Italian case-mix database (1633 LTs, 2016-2017) was the reference. Acute patients were excluded (low number of cases).

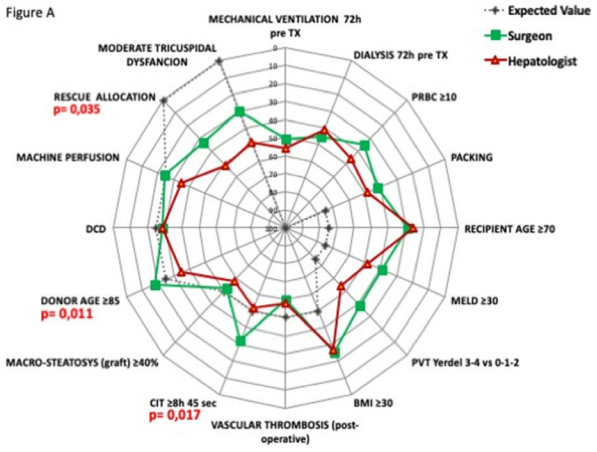
The number of correctly identified factors was low for SURGs and HEPs (median 1.5). However, when the answers were globally evaluated in the same Centre a 60% of correctly identified factors was observed. A better fit was observed when the question was to "identify the multifactorial fatal combination" (ρ= 0,64; p = 0.005). Differences between SURGs and HEPs are in figure A.

The detrimental effect of Mechanical Ventilation (72 hours pre-LT), Dialysis (72 hours pre-LT) PRBC transfusion ≥ 10, Intraoperative Packing, Age of Recipient, MELD ≥ 30, Portal Vein Thrombosis 3-4 vs 0-2 (Yerdel), BMI ≥ 30 were under-estimated by SURGs and HEPs, on the opposite the detrimental effect of Rescue Allocation and Moderate Tricuspidal Dysfunction were over-estimated by both SURGs and HEPs (Figure A).

SURG's perception of sustainable case-mix is different from HEP's one. Concordance between SURGs and HEPs varies between 32 and 78% (Figure B).

Conclusion: In conclusion integration of opinions within each Centre increases the accuracy of case mix perception. To improve adherence to reality, surgeons and hepatologists should group together when evaluating the impact of complex case-mix cases.

Figure A



OS329

DONOR SAFETY AND OUTCOMES REGARDING TO REMNANT LIVER VOLUME IN LIVING DONOR LIVER TRANSPLANTATION

Ali Ozer, Tonguc Utku Yilmaz, Hikmet Aktas
Mehmet Ali Aydinlar Acibadem University

Backround: Modifing donor selection criteria to expand the potential donor pool in living donor liver transplantation (LDLT) is a necessity in regions where shortage of deceased donor remains a problem. We have compared the results of living donors with different remnant liver rates in this retrospective study.

Methods/Materials: From July 2012 to August 2018, 356 right lobe LDLT were performed in our center. The donors were divided into 3 groups in regard to remnant/total volume ratio(RTVR): Group 1 RTVR < 30%, group 2 RTVR 31%-35%, and group 3 RTVR > 35%. There were 45, 178 and 133 patients in group 1,2 and 3 respectively. The features of donors that may affect postoperative liver function recovery was compared between three groups.

Results: The median age, and body mass index showed no significant difference in 3 groups. The median length of hospital stay was longer in group 1, but it was not statistically significant. We perform liver biopsy routinely in donors and the pathology results like the degree of steatosis were similar in all groups, The median remnant liver volume (RLV) were 389 ± 67,3, 423 ± 77,4 and 494 ± 94,7 in group 1, 2 and 3 respectively and group 1 had significant smallest RLV (p < 0,001). The median AST, ALT, total bilirubin and INR levels were significantly high on postoperative day 1 in group 1 (p < 0,001) but there was no significant difference on postoperative day 15 between the groups and liver function tests almost approached to normal values in all. The rate of recovery of liver function was the highest in group 1. The complications rates of Clavien grade 3 or above ranged from 2,8 to 4,4%. Postoperative complications rates were also similar in all groups. There was no donor mortality in this period.

Conclusion: In cases where the recipient has no other donor option and is at serious risk of life, right hepatectomy with an RTVR < 30% can be an alternative for carefully selected and well evaluated living donor

OS330

SHIFTING THE RISK FROM THE DONOR TO THE RECIPIENT – A SINGLE CENTER EXPERIENCE WITH FULL-LEFT LIVING DONOR LIVER TRANSPLANTATION AT UNIVERSITY HOSPITAL TUEBINGEN (UKT) 2008–2018

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University Hospital Tuebingen

Background: Left-LDLT (i.e. Seg2-4 grafts) decreases donor risk while raising recipient's risk for SFSS due to reduced graft volume resulting in need for Graft-inflow-modulation (GIM). Worldwide only small series and different results have been reported: good in Eastern countries, acceptable in US and poor in Europe as recently reported in a European multicenter study with 46 patients in 2018.

Aim: to report our single center experience with 15 Left-LDLT.

Methods: Retrospective single center study analysis of recipient and donor morbidity and mortality according to modified Dindo-Clavien-Classification as well as long term results after a mean FUP of 4.33 years(± 3.33).

Results:

GIM is used in 7 cases: Splenic artery ligation(n = 3), hepatic portocaval shunt(n = 1), Somatostatin(n = 3) and Epoprostenol(n = 5). Short and long-term outcome of donors was completely uneventful. 73.3% of recipients developed early complications*(s. chart)*.

Early complications (≤3 months)		
Bleeding	IIIb	n = 4, 26.7%
Leakage of biliary anastomosis	IIIb	n = 2, 13.3%
SFSS	IV	n = 3, 20.0%
Others		n = 2, 13.3%

Overall 1-,3- and 5-year graft survival was 80.0%, 62.3% and 62.3%, recipient-survival 93.3%, 86.2% and 86.2%,respectively. Early graft loss (≤90 days) due to HAT (n = 2) and SFSS (n = 1) was recorded for 3 patients, each leading to ReLT (n = 3). Late graft loss occurred in 3 patients (IVb) due to recurrence of disease(n = 2) and rejection(n = 1) ending in ReLT (n = 1) or death (n = 2).

Conclusion: As known this is the largest number per center for Left-LDLT in Europe presenting excellent results regarding donor's safety and good 1,3- and 5-year recipient and graft survival rates (cf. European results 90.9%,82.7%,82.7% and 59.4%,56.9%,56.9%, respectively). Regarding the high risk for ReLT and SFSS we recommend assessing presence of portal hyperflow, using GIM if necessary, low MELD, GBWR > 0.6 and precise selection of each recipient, donor and liver quality. In terms of grave organ shortage Left-LDLT seems a feasible method for recipients with low MELD and only small chance to receive time fashionable deceased LT while minimizing donor's risk.

Demographics:	
Recipient	
Gender	11 female, 4 male
Age	37.0 years (2 ≤16 years, 13 >16 years, range: 8-60)
BMI	20.6 (±3.7)
Indications	PSC (n=6) Cryptogenic cirrhosis (n=3) CF (n=1) CCA (n=1) CRLM (n=1) HCC in HCV-cirrhosis (n=1) Secondary biliary cirrhosis (n=1) C2-cirrhosis (n=1)
labMELD	10.2 (range: 5-19, n=14)
Donor	
Age	44.6 years (28-62)
Graft weight	378g (290-558)
GBWR	0.71 (0.45-1.40)

OS332 EAF SCORE, A NOVEL ALGORITHM BASED ON KINETICS OF ALT, BILIRUBIN, PLATELETS AND RECIPIENT DATA TO PREDICT EARLY ALLOGRAFT FAILURE AT 30 AND 90 DAYS AFTER LIVER TRASPLANTATION. A MULTICENTRE ITALIAN STUDY WITH UK VALIDATION

A. Avolio[1], Antonio Franco[1], Q. Lai[2], Salvatore Gruttadauria[3], L. Caccamo[4], Michele Colledan[5], S. Agnes[1], M. Vivarelli[6], V. Mazzaferro[7], Fabrizio Di Benedetto[8], M. Rossi[2], U. Tedeschi[9], Luciano De Carlis[10], M. Cescon[11], S. Meli[12], G. Spoletini[1], D. Ghinolfi[12], D. Patrono[13], D. Pagano[3], D. Dondossola[4], F. Tandoi[13], Stefania Camagni[5], R. Montalti[6], Marco Bongini[7], D. Bassi[14], P. Violi[9], P. Magistri[8], F. Ferla[10], M. Ravaioli[11], J. Hammond[15], W. Alrawashdeh[15], A. Schlegel[16], P. Muiesan[16], R. Romagnoli[13], Umberto Cillo[14], Paolo De Simone[12]

[1]Gemelli University Hospital, Rome; [2]Umberto I, Rome; [3]ISMETT, Palermo; [4]Maggiore Hospital, Milan; [5]Papa Giovanni XXIII, Bergamo; [6]University Hospital, Ancona; [7]National Tumor Institute, Milan; [8]University Hospital, Modena; [9]University Hospital, Verona; [10]Niguarda Hospital, Milan; [11]S. Orsola-Malpighi University Hospital, Bologna; [12]University Hospital, Pisa; [13]Molinette Hospital, Turin; [14]University Hospital, Padua; [15]the Newcastle Upon Tyne Hospitals NHS Fundation Trust, Newcastle; [16]Queen Elizabeth Hospital, Birmingham

Background: Use of DCD and reconditioned high-risk grafts mandates the development of algorithms to predict Early Allograft Failure (EAF) in order to list promptly liver transplants (LT) for re-LT. Prediction of EAF remains challenging.

Recently, a new algorithm (L-GRAFT) based on kinetics of transaminases, bilirubin, INR and platelets during pod 1-10 has been proposed. It was based on 40 determinations and predicts EAF (re-LT or death at 90 days) with a 0.85 C statistic.

The Italian LT population is characterized by high donor age, high MELD and high prevalence of HCC. Aim of the study was to validate the L-GRAFT.

Methods: Prospectively entered data (1760 LT, 2016-2017, 14 LT Centers, including 27 DCD and 81 reconditioned grafts) were used to develop an algorithm similar to L-GRAFT but based on fewer determinations.

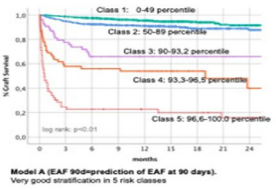
Results: We validated the original L-GRAFT formula (C-statistic = 0.81). Components of the L-GRAFT were tested to recalculate ß-coefficients. A model based on 16 variables including MELD and post-operative thrombosis was developed.

The model stratified graft survival as follows: 0-50th percentile = 99%; 50,1th-90.0th percentile = 95%; 90.1th-93.3th percentile = 78%; 93.4th-96.5th percentile = 57%; 96.6th-100.0th percentile = 34% (Figure 1).

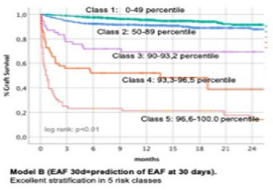
Finally, we developed a new predictive model at 30 days (EAF 30d). We further validated EAF 90d and EAF 30d in a UK database (Birmingham and Newcastle Centres). The C-statistics were 0.87 and 0.92 for the Italian multicenter database; 0.78 and 0.91 for the UK validation set (Figure 2).

Discussion: 1) an innovative algorithm based on fewer determinations, MELD, and diagnosis of post-operative thrombosis was built;

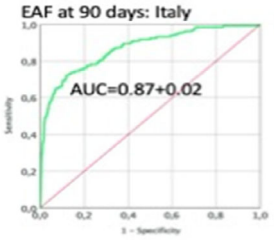
2) the algorithm shows a better performance in the prediction of EAF at 90 days and an excellent performance at 30 days; 3) patients in the two upper-risk classes should be considered for early re-transplantation; 4) the algorithms remain excellent in the external UK validation set.

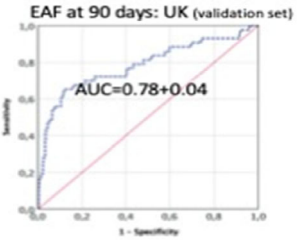


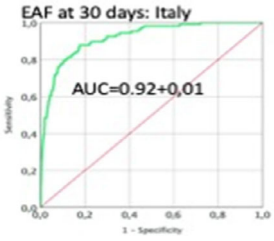
Model A (EAF 90d=prediction of EAF at 90 days). Very good stratification in 5 risk classes

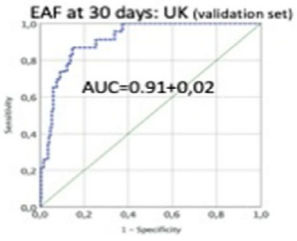


Model B (EAF 30d=prediction of EAF at 30 days). Excellent stratification in 5 risk classes









OS333 THE TORONTO POST LIVER TRANSPLANT HCC RECURRENCE CALCULATOR: A MACHINE-LEARNING APPROACH

Phillipe Abreu, Lawrence Lau, Walter Nelson, Andre Gorgen, Lauren Erdman, Anna Goldenberg, Gonzalo Sapisochin

University of Toronto

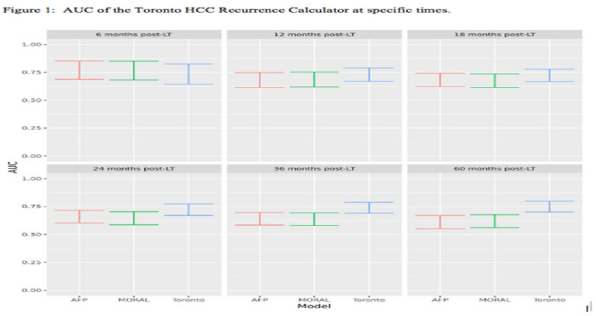
Background: The liver transplant listing criteria for hepatocellular carcinoma (HCC) is controversial. Policies aim to prevent recurrence but it is difficult to incorporate the numerous contributive factors. This study takes advantage of machine-learning to include all available features in a post-transplant recurrence prediction calculator.

Method: The calculator was developed using the Toronto General Hospital HCC database which includes all patients with HCC listed for liver transplantation between 2000-2016, and comprehensively includes serial imaging morphology, AFP, bridging therapy, treatment response, and post-transplant outcome. A Cox proportional hazards model was used to model recurrence following transplant. Over-fitting was limited by encouraging coefficient sparsity using a least absolute shrinkage and selection operator (LASSO). The coefficients were calibrated on 90% of the data. Performance was evaluated over 1000 iterations by assessing the AUC and concordance on the held-out data. Variables selected by LASSO in over 50% of iterations were selected to run the analysis of the 5-year recurrence risk in the model. Alternative recurrence risk algorithms (AFP score and MORAL) were compared.

Results: The dataset included 694 patients who underwent liver transplant for HCC. The overall concordance of score with disease-free survival was satisfactory (concordance 0.706, sd: 0.075). The AUC for prediction of recurrence show the predictive power of the model.

Including all variables meeting the selection criteria, the AUC at 5 years post transplantation was 0.742 (95% CI 0.736-0.748). By comparison, the AUC for AFP score at 5 years post transplantation was 0.605 (95% CI 0.598-0.611) and that of MORAL was 0.589 (95% CI 0.583-0.595).

Conclusion: A comprehensive HCC recurrence risk calculator using machine learning is possible with higher accuracy than other available scores.



OS39 - KIDNEY REJECTION AND HISTOLOGY: NON-INVASIVE IMMUNE MONITORING IN KIDNEY TRANSPLANTATION

OS334 PERIPHERAL BLOOD CHEMOKINE LEVELS IN KIDNEY ALLOGRAFT REJECTION

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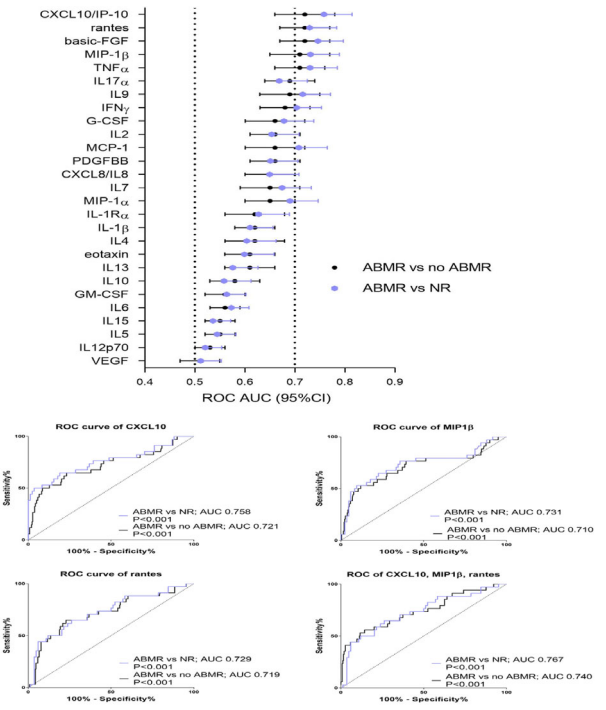
Background: Cytokines and chemokines play a critical role in acute rejection after kidney transplantation. They are important targets in the quest for better diagnostic markers and new therapeutic strategies for rejection. However, their specificity for the underlying mechanisms and histological lesions of rejection is not well known. We evaluated peripheral blood levels of 27 cytokines, chemokines and growth factors in acute rejection.
Methods: All for cause biopsies performed between 07/08/2012 and 13/07/2016 (N = 293 in 192 kidney transplant recipients) were included. In the concomitant peripheral blood samples, 27 cytokines, chemokines and growth factors were measured with multiplex analysis. Histology was scored according to Banff 2017 classification. Analysis of variance and associations were evaluated using ANOVA and logistic regression analysis in all biopsies, corrected with mixed models for multiple sampling and FDR correction for multiple testing.
Findings: Antibody-mediated rejection is associated with dysregulation of many cytokines in peripheral blood. These effects are not observed in T-cell mediated rejection. CXCL-10 and the MIP-1 family of chemokines (MIP-1?, MIP-1? and RANTES), ligands to the CXCR3 and CCR5 receptors, are most strongly associated with antibody-mediated rejection and its histology. The pro-inflammatory cytokine IL-6 that is being highlighted as possible therapeutic target in antibody-mediated rejection is not significantly associated with acute rejection subtypes in our study. Diagnostic performance of CXCL-10, MIP-1? and RANTES combined for diagnosis of antibody-mediated rejection vs no rejection is only fair (AUC of ROC 0.77, $p < 0.001$).
Interpretation: Ligands to the CXCR3 and CCR5 receptor play an important role in antibody-mediated rejection and could serve as therapeutic targets rather than targeting less specific cytokines like IL-6. Their diagnostic performance however seems insufficient to aid non-invasive monitoring.



OS335 DONOR-DERIVED CELL-FREE DNA IN DONOR SPECIFIC ANTIBODY POSITIVE KIDNEY TRANSPLANT RECIPIENTS

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Background: Donor-derived cell-free DNA (dd-cfDNA) is an emerging biomarker of kidney allograft injury. Studies examining the clinical validity of this biomarker have identified cut off values for kidney allograft rejection: <1% of dd-cfDNA level reflect the absence of active rejection and > 1% indicate a probability of active rejection(TCMR>IA or ABMR). This study concluded clinical experience using ddcfDNA to detect rejection in kidney transplant recipients.
Methods: Plasm dd-cfDNA was assayed in 32 patients with two reasons: high serum creatinine (13 patients) or DSA$^+$ (19 patients). Dd-cfDNA quantification through Target Region Capture Sequencing and calculated by Maximum Likehood Estimation (MLE). Samples with detection value greater than 1% or clinical suspicion of kidney injury were determined for graft biopsy.
Result: The mean level of quantification of dd-cfDNA in 32 patients is 1.22% ± 1.3%. 19 patients have DSA$^+$, but only 7 patients (37%) dd-cfDNA higher than 1%, allograft biopsy performance in 19 patients confirmed all of 7 patients (higher dd-cfDNA) show pathologically rejection: 4 patients (1.3%, 1.68%, 1.9% and 2.52%) have chronic active humoral rejection, 3 patients (2.08%, 4.04% and 5.71%) belong to ABMR. But none of allograft rejection evidence in remain 12 patients. The positive predictive value (PPV) for DSA$^+$ in ABMR was 37%.

25 patients (78%) detected dd-cfDNA lower than 1%. Among them, 17 patients clinically performed pathological biopsy: 1 patient (0.67%) pathologically show chronic active rejection, 5 patients (0.33%, 0.54%, 0.54%, 0.69% and 0.76%) show allograft IgAN but 2 patients show DSA$^+$, The remain 11 patients (0.59% ± 0.1%) show toxicity of CNI or board line change. The PPV for dd-cfDNA (level > 1%) in rejection was 100%, and negative predictive value (NPV) was 95% .
Conclusion: ddcfDNA is a specific biomarker to predict renal injury caused by AMR.

OS336 ANALYTICAL AND CLINICAL VALIDATION OF A DONOR-DERIVED CELL-FREE DNA (DD-CFDNA) ASSAY FOR RENAL ALLOGRAFT REJECTION

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Background: Published studies have demonstrated analytical and clinical validation of a SNP-based dd-cfDNA assay using mmPCR for detection of renal allograft rejection. We compare performance of this assay to estimated glomerular filtration rates (eGFR) and serum creatinine (SCr) levels.
Methods: Analytical validity was measured with 66 unique samples with 1064 replicates in cell line-derived reference samples, plasma-derived mixtures and transplant patient samples. Clinical validity was performed using 217 biopsy-matched plasma samples. Both validations applied a SNP-based mmPCR assay targeting over 13,000 SNPs, without the need for donor or recipient genotypes.
Results: Analytical validation of the cfDNA assay showed a limit of detection of 0.15% for unrelated and 0.29% for related donors. Precision measurements showed a coefficient of variation of < 2%. At a predefined cutoff of 1%, clinical validation demonstrated significantly higher median dd-cfDNA in samples with biopsy-proven active (2.3%) vs non-active (0.47%) rejection samples. Comparative statistics for dd-cfDNA, eGFR and SCr, respectively, were: sensitivity, 88.7% vs 67.7% vs 51.6%; specificity 72.6% vs 65.3% vs 67.5%. The area under the curve (AUC) was significantly greater for dd-cfDNA than SCr: 0.87 vs. 0.68 ($p = 0.04$). When restricted to adult patients (≥18 yr) the difference in AUC between the two markers increased: 0.88 vs. 0.64 ($p < 0.001$), and AUC was significantly greater for dd-cfDNA than eGFR: 0.88 and 0.67 ($p = 0.004$). Among adult samples, cfDNA showed better sensitivity and specificity in detection of AR in samples collected on protocol as opposed to for-cause (92.3% and 82.6% vs 86.4% and 67.9%), suggesting that cfDNA detects rejection prior to clinical presentation.

Conclusions: This dd-cfDNA assay has shown analytical and clinical performance superior to the current standard of care for renal allograft rejection monitoring; subanalysis demonstrated the improvement was even greater in adults.

OS337 DETECTING DONOR-DERIVED CELL-FREE DNA LEVELS TO IDENTIFY BKVN AND BKV INFECTION COMBINED TCMR

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AlloDx

Background: It is difficult to distinguish BK virus nephropathy (BKVN) from BKV infection combined TCMR in clinical practice. Donor-derived cell-free DNA (dd-cfDNA) is an emerging biomarker of kidney allograft injury. This study concluded clinical experience using ddcfDNA to identify BKVN and BKV infection combined TCMR.
Materials and methods:: Donor-derived cell-free DNA was assayed in 13 plasm samples (12 patients) and corresponding urine samples. We also measured the concentration of ddcfDNA in blood and the absolute amount of ddcfDNA in urine. DdcfDNA quantification through Target Region Capture Sequencing and calculated by Maximum Likehood Estimation (MLE).
Result: 3 patients (group A) tissue pathology show TCMR plus BKV infection, non-BKVN. The mean absolute ddcfDNA in urine is 4.17 $\pm$ 1.75 ng/ml, the mean ddcfDNA in blood is 1.44% $\pm$ 0.17. 5 patients (group B; 2A, 2B1 and 1B2)tissue pathology show BKVN and the mean absolute ddcfDNA in urine is 19.56 $\pm$ 3.5 ng/ml, and 0.72% $\pm$ 0.23 in blood.The mean absolute ddcfDNA in urine of 3 patients (group C) whose tissue pathology show TCMR only is 10.66 $\pm$ 0.91 ng/ml. While the mean level of quantification of ddcfDNA in blood is 1.46% $\pm$ 0.49. 1 patient show AMR plus BKV infection, non-BKVN, ddcfDNA in urine is 0.66 ng/ml and 2.2% in blood.The results indicate that urine ddcfDNA in group B is significantly higher than that in group A ($P < 0.001$), but an opposite change in blood ($P < 0.05$). No significant difference shows between the blood of group A and group C ($P > 0.05$), but a significant difference in urine ($P < 0.001$), suggesting that BKV infection affects the tubule injury caused by TCMR. The blood ddcfDNA in group C has no significantly difference from group B ($P > 0.05$), and ddcfDNA in urine of BKVN patients was greater than 14 ng/ml (Figure 1).
Conclusion: The results indicated that simultaneous detection ddcfDNA in blood and urine can distinguish BKVN from AR, especially BKV infection combined TCMR and BKVN.

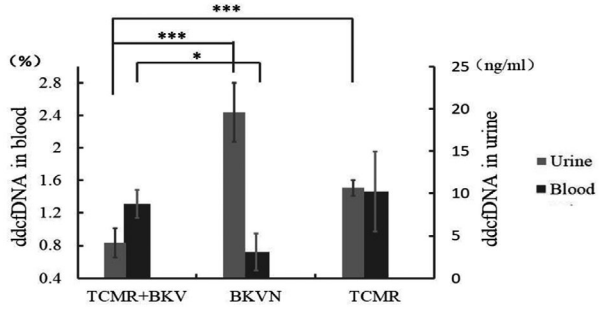

Figure 1. ddcfDNA levels in urine and blood

***: P<0.001 *: P<0.05

OS338 DETECTING AND QUANTIFYING DONOR DERIVED CELL FREE DNA IN THE BLOOD OF KIDNEY TRANSPLANT RECIPIENTS AS A BIOMARKER FOR GRAF

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Background: Development of diagnostic test(s) with non-invasive biomarker to monitor allograft status will gain quality of life of transplant recipients. Measurement of donor derived cell free DNA (dd-cfDNA) in the blood have been described as such a non-invasive biomarker for organ transplantations. To develop a diagnostic system to detect allograft rejection before diagnosis by biopsy, we have conducted a targeted deep sequencing.
Subjects/Methods: Ten Japanese donor and recipient pairs of kidney transplant including two recipients who have experienced acute rejection. Plasma collected after transplantation (1, 3, 5, 7, 14, 28 day after transplantation and when the recipients had an episode which was suspected graft injury) were examined. Cell-free DNA was extracted from plasma of recipients using NucleoSpin Plasma XS (MACHEREY-NAGEL). To select informative SNPs for separating cell-free DNA between donor and recipient, we used minor allele frequency data determine by exome sequencing of 1,208 Japanese individuals (the Human Genetic Variation Database). Fourteen primer sets were designed with length between 100 and 130 bases. Pre-amplified PCR fragments were sequenced by a MiSeq sequencer (Illumina) with 150 base single-end mode. The sequencing reads were mapped with BWA, Samtools, and Genome Analysis Toolkit.
Results: Each pair of donor and recipient had at least two informative SNPs (from two to seven SNPs). We have successfully detected dd-cfDNA in sera of kidney transplant recipients. the dd-cfDNA percentages were highly elevated on the first days after transplantation, but dd-cfDNA percentages were decreased gradually within 7-14 days in stable patients with on sign of rejection.
Conclusion: The quantification of dd-cfDNA is the promising method to detect graft injury at early stage. This non-invasive method enables us close follow up the grafy injury and prevent graft rejection

OS339 CLINICAL VALIDATION OF A STANDARDIZED ELISPOT-BASED ASSAY TO MONITOR CMV-SPECIFIC CELLULAR IMMUNITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Impaired cytomegalovirus (CMV)-specific cell-mediated immunity (CMV-CMI) is a major cause of CMV reactivation and associated complications in solid-organ transplantation. Reliably assessing CMV-CMI is desirable to individually adjust antiviral and immunosuppressive therapy. This study aimed to evaluate the suitability of a novel IFN-γ ELISpot assay (CE-IVD, T-Track® CMV), based on the stimulation of peripheral blood mononuclear cells with pp65 and IE-I CMV proteins, to monitor CMV-CMI following kidney transplantation.
Methods: A prospective, longitudinal, observational, multicenter study was conducted in 86 intermediate risk renal transplant recipients (D-/R+, D+/R+) under preemptive antiviral therapy. CMV-CMI, CMV viral load (CMV DNAemia by qPCR or pp65 antigenemia) and clinical complications (CMV disease, opportunistic infections and graft dysfunction) were monitored over six months post-transplantation.
Results: 95% and 88-92% of IFN-γ ELISpot test results were positive pre- and post-transplantation, respectively, demonstrating the sensitivity of the assay in immunocompromised patients. CMV-specific response was reduced following immunosuppressive treatment and increased in patients with graft rejection, indicating the ability of the ELISpot assay to monitor the patients' immunosuppressive state. Interestingly, median pp65-specific response was 9-fold higher in patients with self-clearing viral load compared to antivirally-treated patients prior to first viral load detection (MWU $p < 0.001$), suggesting that reactivity to pp65 represents a potential immunocompetence marker.
Conclusion: Altogether, this standardized IFN-γ ELISpot assay (T-Track® CMV) is a highly sensitive immune-monitoring tool, suitable for the follow-up of renal transplant recipients, and with a potential use for the risk assessment of CMV-related clinical complications.

OS340 CLINICAL SIGNIFICANCE OF DE NOVO DONOR SPECIFIC ANTIBODY IN KIDNEY TRANSPLANT RECIPIENTS WITH CHRONIC ANTIBODY-MEDIATED REJECTION

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Background: Chronic antibody-mediated rejection (CAMR) is still an important cause of late graft loss, but the prognosis of CAMR according to de novo donor specific anti-HLA antibody (dnDSA) is uncertain. We investigated clinical features of CAMR according to dnDSA.
Methods/Materials: We retrospectively analyzed 35 kidney transplant recipients (KTRs) diagnosed to CAMR between 2010 and 2018. We divided into two groups as follows: 14 KTRs with the dnDSA(-) and 21 KTRs with the dnDSA(+) groups. We investigated pathologic findings, allograft function at 1 year after diagnosis of CAMR, and allograft survival rate according to dnDSA at diagnosis of CAMR.
Results: In pathologic findings, the mean value of microvascular inflammation (g+ptc score) and proportion of chronic change (cg and cv scores) were significantly higher in the dnDSA(+) group compared to the dnDSA(-) group. There was no significant difference in the allograft function at 1 year after diagnosis of CAMR between the dnDSA(-) and dnDSA(+) groups, but allograft function got worse in the graft failure group. There was no significant difference in the amount of proteinuria at diagnosis of CAMR between the dnDSA(-) and dnDSA(+) groups. However, death-censored graft survival rate was lower in the high proteinuria group than low proteinuria group both dnDSA(-) and dnDSA(+) groups. The proportion of rituximab and intravenous immunoglobulin (RIT+I-VIG) treatment was higher in the dnDSA(+) group compared to the dnDSA(-) group. Death-censored graft survival rate was higher in the RIT+IVIG group than non-RIT+IVIG group, regardless of dnDSA.
Conclusion: There was no significant difference in the prognosis according to dnDSA, but the prognosis of KTRs with low allograft function, high proteinuria at diagnosis of CAMR, or without treatment with RIT+IVIG was poor. Therefore, aggressive treatments are needed in KTRs with risk factors, regardless of dnDSA.

OS341 UNIQUE AND SPECIFIC PROTEOBACTERIA DIVERSITY IN URINARY MICROBIOTA OF TOLERANT KIDNEY TRANSPLANTED RECIPIENTS

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Background: Host-microbiota interactions can modulate the immune system at both local and systemic levels, with potential consequences for organ transplantation outcomes. However, the precise nature of these interactions and their health consequences still remain to be defined. In this study, we hypothesized that differences in the urinary microbiota following kidney transplant would associate with post-transplantation status between stable (STA), minimally immunosuppressed (MIS) and tolerant patients (TOL).
Methods: A total of 113 urine samples were collected 6 months to 31 years after kidney transplantation from STA ($n = 51$), MIS ($n = 19$), TOL ($n = 16$) patients, and from sex and age-matched healthy volunteers (HV, $n = 27$). Characterization of the urinary microbiota was performed using 16S rRNA gene sequencing. Taxonomic classifications were compared with HV and within the 3 groups of recipients.
Results: Transplant recipients featured a significant increase in community diversity with higher bacterial biodiversity in both STA and TOL compared to controls. Transplant recipients were also characterized by a higher relative abundance of *Proteobacteria* at the level of phyla and families espacially in TOL compared to STA and MIS. Interestingly, 2 orders of Firmicutes were associated with TOL and negatively correlated with CNI and mTOR inhbitors. This specific and unique microbiota profile was stable over time
Conclusions: The higher relative abundance of specific bacterial phyla and families such as *Proteobacteria* or *Firmicutes* may favor stability or tolerance to the graft over time. Immunosuppressive drugs such as systemic corticosteroids, CNI or mTOR inhibitors were likey to impact microbial diversity and metabolic functions with distinct profiles according to transplant status. It remains to be established whether the tolerant state was responsible for the microbiota profile, or the microbiota induce the tolerant state.

OS342 RENAL TRANSPLANT PATIENTS HARBOR NEUTROPHILS SECRETING B CELL ACTIVATING FACTOR (BAFF) WHICH CAN BE SUPPRESSED BY MTOR-INHIBITORS

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Background/Aim: B cell activating factor (BAFF) is a cytokine which drives B cell survival and maturation. Several studies have shown that elevated BAFF levels in renal transplant patients are associated with increased risk for the development of donor specific antibodies and antibody mediated rejection. It was the aim of this study to investigate neutrophils as cellular source of BAFF in renal transplant patients.
Methods: Neutrophils (NT) were freshly isolated from whole blood of healthy controls (HC) and renal transplant patients (RTX). After isolation, purity of neutrophils was usually above 98%. Neutrophils were stimulated with LPS or TNFα in presence of Granulocyte-colony stimulating factor (GCSF) or Granulocyte macrophage colony-stimulating factor (GMCSF). In selected conditions, FK506 or rapamycin was added. Supernatants were harvested after 20 hours of culture and BAFF levels were determined by ELISA.
Results: GCSF/TNFα and GCSF/LPS were the most potent stimuli leading to BAFF secretion of NT in HC (403 ± 64 pg/ml and 421 ± 69 pg/ml). NT derived RTX showed similar capacity to secrete BAFF as compared to HC (GCSF/TNFα: 515 ± 31 pg/ml and GCSF/LPS: 539.4 ± 36 pg/ml). Treatment of cultures with rapamycin reduced BAFF levels (515 ± 100 pg/ml vs. 348 ± 27 pg/ml, $p < 0.001$). Treatment with FK506 was less efficacious (515 ± 31 pg/ml vs. 465 ± 31 pg/ml, $p = 0.01$).
Conclusion: NT may enhance of B cell maturation and survival via BAFF. BAFF-secretion by NT can be suppressed with mTOR inhibitors. In renal transplantation, NT might promote formation of allo-antibodies and drive antibody mediated rejection.

OS343 DECIPHERING ANTI-HCMV HLA-E-RESTRICTED UNCONVENTIONAL CD8 T-CELL RESPONSES IN SEROPOSITIVE HCMV+ KIDNEY TRANSPLANT RECIPIENTS: FREQUENCIES, INFLUENCING FACTORS AND PHENOTYPE

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Background: Human cytomegalovirus (HCMV) causes severe illness and poor outcome in immunocompromised hosts such as transplant recipients. Cytotoxic CD8 T cells against HCMV antigens (pp65, IE1) presented by classical HLA class-I molecules are major cellular components of the protective anti-HCMV immunity. HLA-E-restricted CD8 T cells targeting HCMV UL40 leader peptides (Lp) have been recently reported as unconventional T-cell responses also observed in some hosts but they still need clinical and functional characterization.
Methods/Materials: Our study aimed to provide a qualitative and quantitative *ex vivo* analysis of HLA-EUL40 CD8 T-cell responses, in a large cohort ($n = 161$) of kidney transplant recipients, and to elucidate determining factors.
Results: HLA-EUL40 CD8 T cells were detected in > 30% of seropositive HCMV+ hosts and may represent > 30% of total circulating CD8 αβT cells at a time point (mean value: 2.2%). We identified host-related genetic factors (HLA-A*02 and HLA-E genotype) and HCMV strain, determining the sequence of UL40Lp, as critical parameters for this response. HLA-EUL40 CD8 appear early post-infection as monoclonal or oligoclonal populations and persist for life. Although specifically induced in response to HCMV infection, a key feature of these cells is their potential ability to be also responsive against self and allogeneic HLA resulting from sequence homology between HLA-ILp and UL40Lp. Few weeks post-infection, HLA-EUL40 CD8 are terminally differentiated effector memory T (TEMRA) cells (CD45RA+,CCR7-,CD27-,CD28-, CD38 +) displaying low migratory properties but selective recognition of endothelial cells through CX3CR1. They express low (PD1, Tim3) or no (Lag3) level of inhibitory receptors suggesting that they are not exhausted but instead fully functional.
Conclusion: Unconventional HLA-EUL40 CD8 cells belong to the common immune arsenal against HCMV.Their role and potential side effect toward allogeneic transplant need investigations.

OS344 TARGETED PROTEOMIC ANALYSIS DETECTS ACUTE T CELL-MEDIATED KIDNEY ALLOGRAFT REJECTION IN BELATACEPT-TREATED PATIENTS

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Erasmus MC

Introduction: There is an unmet need for reliable minimally-invasive diagnostic biomarkers for immunological allograft monitoring and detection of acute kidney transplant rejection. Here, targeted proteomic analysis was applied to compare 92 proteins in sera of belatacept-treated patients who had a biopsy-proven, acute T cell-mediated rejection (aTCMR) with patients without an aTCMR.
Materials and methods:: Serum samples were collected from kidney transplant recipients who participated in a prospective, randomized-controlled trial between 2013 and 2015. Proximity extension immunoassay (PEA) was used to measure 92 inflammation-related protein concentrations in pre-rejection (day 30 after transplantation) and rejection sera of 11 patients with an aTCMR and 9 patients without an aTCMR. PEA uses two matched oligonucleotide-labelled antibody probes for each protein and PCR to measure normalized protein expression values.
Results and Discussion: Five proteins (CD5, CD8A, NCR1, TNFRSF4 and TNFRSF9) were expressed significantly higher in samples of patients with an aTCMR compared with samples of patients without an aTCMR (adjusted p-value < 1.14E-02) and had a good predictive capacity for an aTCMR (area under the curve of a receiver operator curve ranged from 0.83 to 0.91 [$p < 0.014$]). The pathways most enriched among these 5 proteins are related to T cell activation, T cell proliferation, and NK cell-mediated immune responses. Non-hierarchical clustering analysis showed distinct clustering of samples of patient with an aTCMR and of samples of patients without aTCMR. This clustering was not seen in pre-rejection samples. In pre-rejection samples, IFN-γ was expressed at a significantly lower level (NPX value median -0.15, IQR -0.27 - 0.04) than in samples of patients without rejection (median 0.13, IQR -0.07 - 0.15, adjusted p-value = 3.67E-03).
Conclusion: PEA appears to be a promising minimally-invasive technique to diagnose an aTCMR.

OS345 ASSESSMENT OF IN-VITRO ANTI-GRAFT IMMUNE RESPONSES AS PREDICTOR OF GRAFT OUTCOME: A QUEST FOR THE ULTIMATE TOOL IN TRANSPLANT IMMUNOLOGY

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Postgraduate Institute of Medical Education & Research, Chandigarh

Background: Unlike other immune mediated disorders, the 'onset' of anti-graft immunity is predictable and hence amenable. What is not predicable is the quantum of this response which decides the graft's acceptance or rejection. Eliciting and assessing this immune response to the prospective graft antigens *in-vitro* therefore seems to a logical test to pre-assess donor recipient compatibility.
Methods/Materials: We designed an assay wherein recipient's monocyte derived macrophages pulsed overnight with graft antigen were co-cultured with the recipient's lymphocytes. Fold change in cytokine gene expression of co-cultured lymphocytes and increment in cytokine levels in culture supernatants after co-culture were then analysed by an 86 gene set PCR array and cytometric bead array (CBA) respectively. A total of 50 haplo-identical donor recipient pairs were analysed of which 10 developed acute cellular rejection (ACR) with or without concurrent antibody mediated rejection (ABMR), 7 ABMR and 30 were stable allografts (SA). One case was excluded from analysis.
Results: On linear discriminant analysis and multivariate analysis of variance, a gene set comprising of C3, CCL3, IL1B, TOLLIP, CXCL5, ABCF1, CCR3, IL10RB, CXCL1, & IL1R1 differentiated the ACR from SA. In addition, a gene set comprising of IL10, C3, IL37, IL1B, CCL3, CARD18 & TOLLIP differentiated AMR from SA. Levels of IL-6, IP-10, MIP1α, & MCP-1 in culture supernatants were found to be high in ACR compared to non-ACR while IL-6, IL-1α, IL17A, and MIP1α were increased in rejection compared to SA.
Conclusions: Specific *in-vitro* cytokine profiles correlated with occurrence of rejection. It is proposed that such an *in-vitro* testing model would enable risk assessment in prospective recipients. This will help individualise immunosuppression in transplantation practice and should hence be explored by the transplant community.

OS40 - KIDNEY IMMUNOSUPPRESSION-MONITORING AND OUTCOMES

OS346 INDUCTION WITH ATG IN DCD KIDNEYS, DOSE EFFECT AND PREDICTORS OF OUTCOME

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Background: Thymoglobulin (ATG) is used in few UK centres as induction. We have shown good results with ATG for pancreas transplants.
Aim: The aim of this study is to see if the total ATG dose used for induction in DCD kidneys affected their outcome and if the initial impact to the blood cells and CD3 count was predictive of its efficacy.
Method: All 140 DCD patients who received ATG induction (standard of care in reporting centre) were included. Intended dose was 1.25 mg/kg for 5 days rounded to the nearest 25 and not exceeding 150 mg/dose. Some patients did not receive the total dose. Patients were separated to 4 quartiles according to the total dose/kg they received. Outcomes examined were total dose relation with rejection, and eGFR, and if the initial cell response to the ATG was predictive of those outcomes.
Results: Rejection (including borderline changes) was 12% in 3 years and was predictive of eGFR at 12 ($p = 0.05$) and 36 months ($p = 0.1$). The total dose or dose/kg was not predictive of rejection but they were both equally predictive of WCC at day5 ($p = 0.04$) and lymphocyte count at day5 ($p = 0.006$, Pearson correlation of dose/kg and day5 lymphocyte -0.36). Platelets dropped but had no correlation with dose/kg. In non-rejectors the lowest dose/kg quartile was associated with 10mls/min lesser eGFR at 12 months compared to the other quartiles ($p = 0.06$).
In a subset of patients (30) CD3 count was available at day3. Day3 CD3 was associated with rejection ($p = 0.001$) and inversely associated with eGFR at 12 and 36 months ($p = 0.03$).
Conclusion: There is variable response to ATG even within a tight dose range. WCC and lymphocyte count at day 5 better reflect the dose compared to platelets. Less than 4.5 mg/kg total ATG might be associated with worse outcome. Day 3 CD3 count is correlated strongly with rejection and eGFR.

OS347 EVEROLIMUS WITH LOW DOSE CYCLOSPORINE IS ASSOCIATED WITH BETTER GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS WITH BKV ASSOCIATED NEPHROPATHY

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Background: BKV associated nephropathy (BKVAN) portends adverse kidney graft outcome in most series, since substantial reduction of immunosuppressive therapy which is usually adopted, is associated with increased risk of acute rejection and loss of renal function. mTOR inhibitors-based immunosuppressive protocols proved to be effective in preventing BKV infection, but data are lacking on their effectiveness in KTRs with biopsy-proven BKVAN.
Methods: We prospectively evaluated 15 kidney transplant recipients (KTRs), mean age 59 yrs, who underwent graft biopsy for progressive worsening of graft function associated with BKV-DNA replication, occurring 9 ± 5 months after transplantation. All KTRs were administered tacrolimus, mycophenolate mofetil, and prednisone. Immunostaining with anti-SV40 antibodies was performed in all samples; biopsies were classified according to Banff 2017 criteria. Kidney graft function, BKV-PCR for BKV-DNA monitoring, and immunosuppressive agents trough levels were strictly monitored.
Results: Histological evaluation showed class 3 BKVAN in 7 patients, class 2 in 5 and class 1 in 3. Mean peak BKV copies/ml were 5.5×10^6. All patients showed concomitant reduction of eGFR (from 50.5 ± 13.7 to 24.8 ± 8 mL/min/1.73 m^2, p=<0.0001). Everolimus (EVR) was introduced in all immunosuppressive protocols (target trough levels 3-8 ng/mL), with low dose cyclosporine (target trough levels 50-100 ng/mL), and MMF withdrawal. After 29 ± 21 months no graft loss occurred, eGFR significantly increased (from 24.8 ± 8 to 33 ± 16.5 mL/min/1.73 m^2 $p = 0.032$) and reduction or even disappearance of BKV genomic copies was observed (from 5.5×10^6 to 1.9×10^5, P=<0.0001) was observed.
Conclusions: This is the first study to demonstrate that in KTRs with proven BKVAN an immunosuppressive regimen based on EVR and low dose cyclosporine is effective in the mid-term follow up in preventing kidney graft loss and inducing both an improvement in graft function and a reduction in BKV replication.

OS348

INFLUENCE OF TROUGH LEVEL IN TACROLIMUS ON THE APPEARANCE RATE OF DE NOVO DONOR SPECIFIC ANTIBODY (*DN*DSA) UNDER LOW DOSE-BASED TACROLIMUS PROTOCOL DURING 7 YEARS FOLLOW-UP AFTER RENAL TRANSPLANTATION

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Background: The suitable trough level in CNI has been controversial in terms of CNI toxicity and *de novo* anti-donor specific antibody (*dn* DSA). The purpose in this study is to investigate the relationship between maintenance trough level in tacrolimus and the appearance rate of *dn* DSA during follow-up after Tx.
Materials and methods:: Total 584 recipients (group 1 no-*dn* DSA, N = 420; group 2 *dn*DSA, N = 164) who were transplanted from living donors at our single center between 2000 and 2015, were included in this study. We investigated incidence rate of *dn* DSA according to recipient's sensitized immunological status and immunosuppressive regimen used as well as maintenance trough level in tacrolimus.
Results: Patients in both two groups were followed-up for 7.4 ± 2.6 years without any differences. *Dn* DSA in group 2 appeared at 812 ± 102 days on average. The number of mismatches in HLA-A/B/C/DR/DQ was significant more in group 2 than in group 1 (2.8 ± 1.5 in group 1 vs. 3.4 ± 1.3 in group 2; $P < 0.001$). Patients with preformed DSA showed higher incidence rate of *de* novo DSA production (27.1% in group 1, vs. 48.2% in group 2. $P < 0.001$). Graft function evaluated eGFR has been significantly much worse in group 2 than in group 1, since 1 to 3 years after Tx. Graft biopsies revealed much more incidence rate and severer findings of acute and/or chronic TCMR and ABMR in group 2 recipients. Death censored-graft failure was higher in group 2 than in group 1 (18/420, 4.3% in group1 vs. 28/164, 17. 1% in group 2, $P < 0.001$). Also, patients in group 2 complicated higher incidence rate of proteinuria.
Conclusion: In this study, higher incidence rate of *de* novo DSA production was observed in recipients with prior sensitization and in D/R combination with more HLA mismatches.However, there were no clear relationship between immunosuppressive regimen or trough level in tacrolimus and incidence rate of d*e* novo DSA production.

OS349

PHARMACOKINETIC EVALUATION OF LCP-TACROLIMUS AND MYCOPHENOLATE COMBINATION

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Background: Envarsus® is a novel extended-release formulation of tacrolimus with enhanced bioavailability. There is a lack of evidence for drug interaction in terms of pharmacokinetic parameters. In particular, the possible drug interaction between different prolonged release TAC and mycophenolate (Myc) has never been investigated. In the present study we investigated the pharmacokinetic interaction between LCP tacrolimus and mycophenolate and compare these results with the existing standard tacrolimus once daily formulation.
Methods: The possible pharmacokinetic interaction between the new immunosuppressive LCP tacrolimus (Envarsus®) and Myc was assessed by comparing routinely estimated mycophenolic acid (MPA) plasma trough levels of renal transplant patients at least 6 months posttransplant with stable allograft function receiving methylprednisolone and Myc in combination with LCP tacrolimus (31 patients) with standard tacrolimus once daily (TOD, Advagraf®) (27 patients), after switching patients from the tacrolimus twice-daily forumulation.
Results: Coadministration of LCPT and the full dose of Myc resulted with a decrease of the tacrolimus dose from 0,1 mg/kg to 0,015 mg/kg after 6 months what was significantly lower compared with the TOD (0,06 mg/kg to 0,04 mg/kg) ($p = 0,02$), with trough levels 5 (4,5 - 5,7) for TOD and 6,1 (4,8 - 7,6) ($p = 0,002$) for LCPT. Regardless of the tacrolimus prolonged-release formulation, GFR 12 months after the switch significantly correlated with the initial dose (Rho = 0,265 P = 0,04), as well as with the initial dose/kg body weight (Rho = 0,277 P = 0,04). Additionaly, the higher the initial tacrolimus C0, the higher was GFR at the end of follow-up (Rho = 0,296 P = 0,02).
Conclusion: This study revealed possible differences between the pharmacokinetic interactions of different prolonged release formulation and mycophenolate which need further investigations. Significanly lower doses of LCPT than TOD enable stable tacrolimus t

OS350

PHARMACODYNAMIC STUDY OF CALCINEURIN INHIBITION: FROM CLASSICAL FORMULATION TO NEW EXTENDED RELEASE TACROLIMUS

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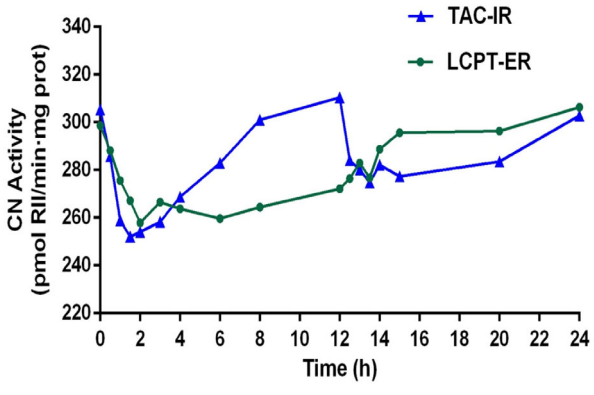
Introduction: Tacrolimus (TAC) is the cornerstone calcineurin inhibitors most commonly used in transplantation. New extended release formulation of tacrolimus (LCPT-ER) offers better bioavailability and less fluctuation compared to immediate-release formulation (TAC-IR). The correlation between TAC exposure of LCPT-ER with different pharmacokinetic (PK) profile and calcineurin activity (CNA) and the comparison of pharmacodynamics (PD) between both formulations have been not reported. The goal of this study is to compare CNA between LCPT-ER and TAC-IR in kidney stable transplant patients and the correlation with TAC exposure.
Methodology: An open-label, prospective, non-randomized study investigator-driven was conducted. Twenty-five stable patients receiving TAC-IR in steady state conditions (more than 6 months after transplant) were subsequently switched to LCPT-ER. Before and after conversion, an intensive PK and PD sampling AUC (16 points) were conducted among 24 hours. A validated method by UPLC-MS based on peptide dephosphorilation was used to measure CNA in peripheral blood mononuclear cells. TAC levels in whole blood were measured by UPLC-MS.
Results: LCPT-ER showed lower C_{max} and higher dose normalized AUC PK than TAC-IR statistically significant. TAC-IR presented higher maximum inhibition (I_{max}) in comparison with LCPT-ER, but LCPT-ER had prolonged CNA inhibition (lower PD AUC). No correlation was achieved between any PK and PD parameter in any formulations. Remarkably, only with LCPT-ER, we observed a good correlation between C_{max} and C_0, and between I_{max} and I_0.
Conclusions: The higher C_{max} achieved with TAC-IR was not translated to higher CNA inhibitions supporting the hypothesis of rate-limiting phenomena for calcineurin substrate. TAC exposure of LCPT-ER resulted in an optimized PD profile with a more sustained inhibition of CNA during dose intervals. In addition, with LCPT-ER CNA levels did not return to basal point (I_0) at any time.

N = 25	TAC-IR	LCPT-ER	p
C trough	6.9 [5.35-7.65]	5.9 [4.6-7.9]	0.805
C max	18.1 [14.5-22.83]	10.2 [9.2-16.9]	0.0003
T max	1.5 [1.0-2.0]	4.0 [4.0-6.0]	<0.0001
AUC PK	198.2 [171.4-226.7]	187.3 [144.9-291.7]	0.846
AUC PK/Dose	70.3 [41.5-92.2]	82.6 [63.02-121-1]	0.0003
I min	322.1 ± 60.2	315.3 ± 62.7	0.379
I max	212.2 [191.7-237.6]	238.1 [212.9-265.1]	0.048
T nedir	2.0 [1.5-3.0]	4.0 [1.5-7.0]	0.588
AUC PD	1702 [943.2-1971.0]	782.3 [508.6-985.6]	0.0002

Figure 1



Pharmacodynamic profiles of TAC-IR and LCPT-ER: Time course assay of CN activity on 25 patients receiving TAC-IR and their conversion to LCPT-ER.

OS351 INCREASING TIME-IN-THERAPEUTIC RANGE IS ASSOCIATED WITH SUPERIOR OUTCOMES IN LIVING KIDNEY TRANSPLANTS

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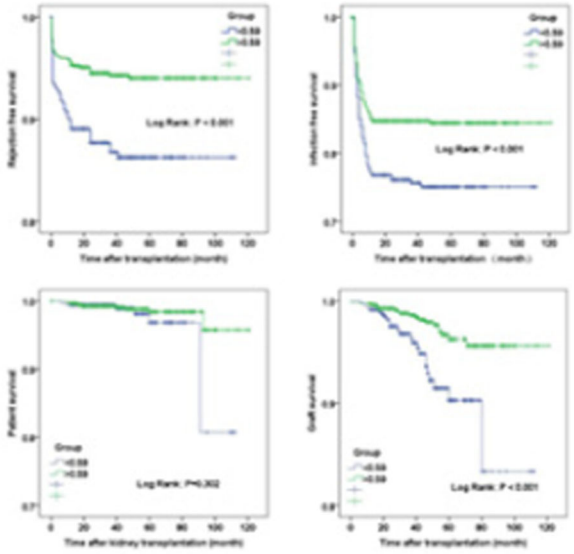
The narrow therapeutic index of tacrolimus (TAC) requires drug monitoring, and time in therapeutic range (TTR) is a novel method of TAC management assessment. The present study investigated whether TTR influenced acute rejection (AR) and long-term outcomes of kidney transplants. The TTR in the first post-transplant year was estimated retrospectively in 1421 living-donor kidney transplant patients. The target range was 5–12 ng/ml. The optimal TTR cutoff of 59% was estimated by receiver operating characteristic (ROC) curve analysis. Increasing TTR by 10% was associated with a significantly decreased risk of AR, with an odds ratio (OR) of 0.818 (95%CI:0.752–0.890) and graft loss (OR = 0.801, 95%CI:0.705–0.901). A TTR of > 59% reduced the risk of AR by 60.3% (OR = 0.397, 95%CI:0.223–0.707) and graft loss by 64.2% (OR = 0.358, 95%CI:0.189–0.678). Of note, infection was more frequent in those with a TTR of < 59% (23.8% vs. 15.2%, $p < 0.001$). Increasing TTR by 10% significantly lowered the risk of infection (OR = 0.888, 95%CI:0.834–0.946). Patient survival did not significantly differ in patients with TTRs above or below 59%, but patients with TTRs > 59% had better renal function. Increasing the TTR in the first year was associated with improved long-term outcomes; a TTR > 59% should be maintained.

Figure. Comparison between patient with TTR>59% and TTR<59%.



OS352 A NOVEL MITRA®-BASED ASSAY FOR THE QUANTITATIVE DETERMINATION OF TACROLIMUS CONCENTRATIONS IN CAPILLARY BLOOD SAMPLES FROM LIVER AND KIDNEY TRANSPLANT RECIPIENTS

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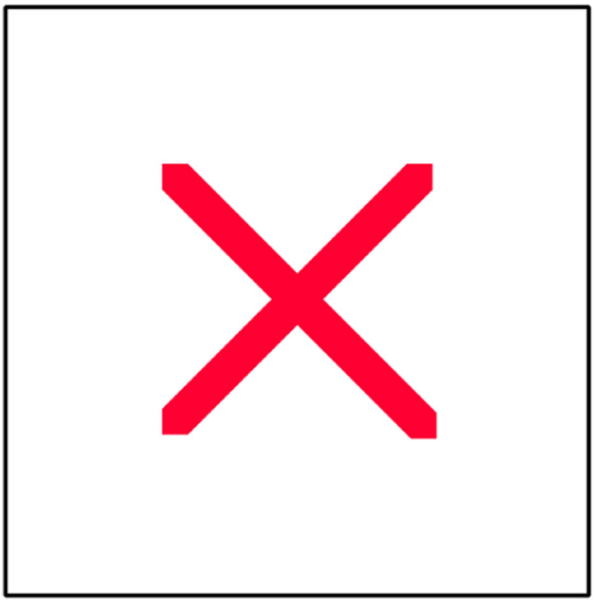
Background: Therapeutic drug monitoring (TDM) of tacrolimus (TAC) concentrations in transplant recipients currently necessitates regular visits to phlebotomy services for venous blood sampling. A new assay for determination of TAC concentrations in capillary blood samples that can be self-obtained by a fingerprick using the MITRA® Microsampler has been developed and validated. This study compares TAC concentrations in venepuncture samples with those in fingerprick samples obtained using the MITRA® Microsampler.
Methods: Paired venous and capillary (10 μL) blood samples were collected pre-dose, 1- and 3 hours post-dose during routine outpatient visits from stable adult liver or kidney transplant recipients receiving prolonged-release TAC (ADVAGRAF, Astellas Pharma Europe, BV)-based therapy (NCT03465969). Whole blood TAC concentrations were determined by validated high-performance liquid chromatography tandem–mass spectrometry (HPLC-MS/MS), and the concentrations obtained by the two sampling methods were compared by linear regression and Bland–Altman agreement analyses.
Results: Samples were available for 82 transplant recipients (kidney, $n = 41$; liver, $n = 41$). Mean ± SD age was 51 ± 14.8 yrs; mean ± SD TAC daily dose was 4.6 ± 2.44 mg. A high correlation was seen between TAC concentrations in capillary and venous blood samples (Pearson's correlation coefficient [r^2], 0.970; Lin's concordance coefficient, 0.870; slope of fitted line, >1.0). Bland–Altman agreement analysis showed TAC concentrations in capillary samples to be ~22.5% higher on average than the corresponding venous blood samples (95% limits of agreement, 0.5 to 44.6%). Similar results were seen in both subgroups.
Conclusion: The strong positive correlation seen between whole blood TAC concentrations in capillary and venous blood samples in this study suggests that the fingerprick MITRA® assay may be a convenient and reliable alternative to venepuncture for TDM in transplant recipients maintained on ADVAGRAF.



OS353 BIOAVAILABILITY OF THE DIFFERENT TACROLIMUS FORMULATIONS USED IN ROUTINE CLINICAL PRACTICE FOR THE MANAGEMENT OF DE NOVO KIDNEY TRANSPLANT RECIPIENTS: THE STUDY BETTER

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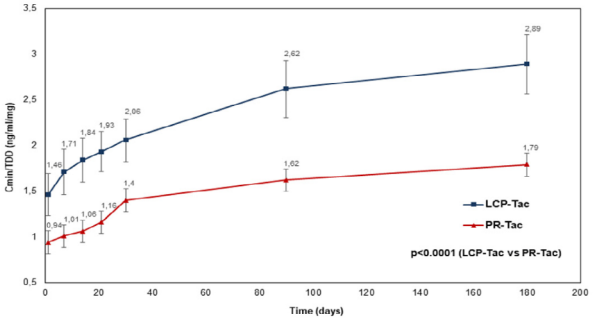
[1]Nephrology, University Hospital A Coruña, A Coruña,; [2]Nephrology, University Hospital del Mar, Barcelona,; [3]Nephrology, University Hospital Son Espases, Palma de Mallorca,; [4]Nephrology, Hospital Miguel Servet, Zaragoza,; [5]Nephrology, University Hospital Germans Trias y Pujol, Badalona,; [6]Nephrology, University Hospital Vall d'Hebron, Barcelona,; [7]Nephrology, University Hospital Doce de Octubre, Madrid,; [8]Nephrology, University Hospital Ramón y Cajal, Madrid,; [9]Nephrology, University Hospital Clínico de Valladolid, Valladolid,; [10]Nephrology, University Hospital Clínico San Carlos, Madrid,; [11]Nephrology, University Hospital Virgen del Rocio, Sevilla,; [12]Nephrology, University Hospital Virgen de las Nieves, Granada,; [13]Nephrology, University Hospital Bellvitge, Hospitalet de Llobregat,; [14]Nephrology, Fundación Jiménez Díaz, Madrid,; [15]Nephrology, University Hospital Regional, Málaga,

Background: Maintaining adequate tacrolimus (Tac) blood levels is essential to prevent organ rejection and toxicity after kidney transplant (KTX). This multicenter, prospective study compared the bioavailability of Tac formulations used to treat de novo KTX recipients.
Methods: Adult KTX recipients from deceased donors receiving treatment with Tac, MMF and corticosteroids were included ?14 days after KTX. Tac daily dose (TDD), trough levels (Cmin), bioavailability (Cmin/TDD), treatment failure,

viral infections, renal function and adverse events (AEs) were assessed over 6 months.
Results: Between October 2016 and August 2017, 251 KTX recipients from 15 centres were recruited. Data from 228 patients were evaluated: 129 on MeltDose® extended-release Tac (LCP-Tac), 89 on prolonged-release (PR-Tac) and 10 on immediate-release (IR-Tac). LCP-Tac showed the highest bioavailability, with a 55% and 60% increase vs IR-Tac and PR-Tac, respectively ($p < 0.0001$). We found no significant differences between groups in Cmin ($p = 0.5$) and a 30% reduction in TDD in LCP-Tac vs PR-Tac ($p < 0.0001$). Delayed graft function occurred in 20 (15.5%) and 16 (18%) patients treated with LCP-Tac and PR-Tac, respectively. Post-KTX diabetes developed in 8.5% (LCP-Tac) and 13.5% (PR-Tac) patients. Viral infections (CMV/BK) presented in 23.2% (LCP-Tac) and 21.3% (PR-Tac) patients. A higher but non-significant incidence of treatment failure (7.9% vs 3.9%) and premature withdrawal (5.6% vs 2.3%) was observed in the PR-Tac group compared to the LCP-Tac group. Mean eGFR and creatinine levels were similar regardless of the Tac formulation. AEs were registered in 82 (61.7%) LCP-Tac-treated patients and in 55 (57.3%) PR-Tac-treated patients.
Conclusion: LCP-Tac showed a greater bioavailability with a similar renal function and safety profile and a tendency to lower post-KTX diabetes, treatment failure and premature withdrawal compared to available Tac formulations.



OS355

VARIABILITY OF TACROLIMUS TROUGH LEVELS DURING THE INITIAL TWO YEARS AFTER RENAL TRANSPLANTATION AND GRAFT FUNCTION IN RENAL TRANSPLANTS

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Background: Intra-patient variability of tacrolimus trough levels (TAC-C0) during follow up has been associated with multiple factors including the impact of food, drug-drug interactions, suboptimal prescribing or patient non adherenceHigh TAC-C0 variability (>30%) has been related with a higher rejection rate, poorer renal function, progression of chronic lesions and graft loss. We aimed to characterize variability of TAC-C0 during the initial two years after transplantation and its impact on graft function in a consecutive cohort of patients treated with an extended release tacrolimus formulation.
Patients and methods: We evaluate consecutive kidney transplants performed at our center during 2015 and 2016 surviving more than 3 months and treated with tacrolimus (Advagraf®), MMF and steroids. All tacrolimus trough levels obtained during the initial 2 years after transplantation were retrieved from our electronical records. Mean TAC-C0, coefficient of variation (standard deviation/mean * 100, CV) of TAC-C0 and the time area under the curve of TAC-C0 (AUC-TAC-C0) were estimated at different time periods (0 to 3 months, 3 to 6 months, 6 to 12 months and 12 to 24 months). TAC-C0 was measured by CMIA and glomerular filtration rate was estimated by the CKD-EPI formula.
Results: During the study period 114 patients were evaluated. The mean, SD, CV and AUC-TAC-C0 at different time periods are shown in the attached table. About one third of patients displayed a CV-TAC-C0 > 30% from 3 to 24 months after transplantation. Patients with a 6 to 12 months CV-TAC > 30% displayed a poorer renal function at 12 (41 ± 13 vs. 50 ± 49 mL7 min/1.73 sqm; p-value < 0.05) and 24 months (37 ± 10 vs. 45 ± 19 mL/min/1.73 sqm; p-value < 0.05).
Conclusions: During the initial two years after transplantation one third of renal transplants displayed a high intra-patient variability of tacrolimus trough levels and this variability is associated with a poorer graft function.

Variable	0-3 months	3-6 months	6-12 months	12-24 months
Number of determinations	14 ± 6	6 ± 4	6 ± 5	6 ± 4
Mean TAC-C0 (ng/mL)	9.8 ± 1.7	8.7 ± 2.1	8.4 ± 1.7	7.7 ± 1.4
SD TAC-C0 (ng/mL)	4.4 ± 1.9	2.4 ± 1.8	2.3 ± 1.8	2.0 ± 1.4
CV-TAC-C0 (%)	44 ± 15	27 ± 17	27 ± 17	26 ± 15
CV > 30% (%)	82.7%	35.6	32.4	32.5
AUC-TAC-C0 (ng/mL/day)	8.5 ± 2.1	8.3 ± 2.9	7.9 ± 2.5	6.6 ± 1.8

OS356

CAPILLARY MICRO-SAMPLING MAKES PATIENT-CENTERED AUC-MONITORING OF TACROLIMUS POSSIBLE

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Background: AUC-guided tacrolimus (Tac) therapeutic drug monitoring (TDM) may help reducing side effects. TDM by trough-concentrations (C_0) is only used since multiple sampling is challenging in the clinic. Tac concentrations by capillary micro-samples may bypass this problem, as patients can take these samples themselves. In combination with limited sampling strategies (LSS) and population pharmacokinetic dosing tool, individual AUC measures is clinically applicable. The aim of the present study was to evaluate the use of 3 micro-sampled Tac concentrations to predict individual AUC:s.
Methods: 12-hour Tac concentration-time profiles (13 samples) were obtained from 27 renal transplant recipients on twice-daily Tac. Samples were obtained using finger prick micro-sampling (10 μL Mitra® Neoteryx, LLC) early after transplantation. A population model (Pmetrics) was used to calculate the individual reference AUC_{ref} using all 13 concentrations. Optimal LSS within 4- and 12-hours were determined: 0-, 0.5- and 4-hours and 0.75-, 4-, and 11.75-hours, respectively. $AUC_{4\ h\ LSS}$ and $AUC_{12\ h\ LSS}$ were predicted by the model using these times. In addition, AUC_{C0} was also estimated with the model using only C_0. The predictive performance of the two 3-point LSS and C_0 estimated AUC:s were evaluated by comparison with $AUC_{ref.}$ Relative bias with related standard deviation was calculated.
Results: Mean dose, C_0 and systemic exposure of Tac (AUC_{ref}) were 3.6 ± 1.7 mg, 6.3 ± 1.3 μg/L and 122 ± 30 μg*h/L. The LSS predictions, $AUC_{4\ h\ LSS}$ and $AUC_{12\ h\ LSS}$, had a relative bias of 3.2 ± 14.9% and -1.4 ± 9.2%, respectively. In comparison, when only using C_0 for prediction (AUC_{C0}), relative bias was larger and more variable; -4.8 ± 27.5%.
Conclusion: Taking advantage of micro-sampling, utilizing a 3-sample LSS method is possible and provide good predictions of individual systemic exposure of Tac. This approach will be suitable for AUC-targeted individualization of Tac doses. The bias for C_0 predicted AUC was high.

OS357

TACROLIMUS METABOLISER STATUS IS INDEPENDENTLY ASSOCIATED WITH INFERIOR LONG TERM RENAL ALLOGRAFT SURVIVAL

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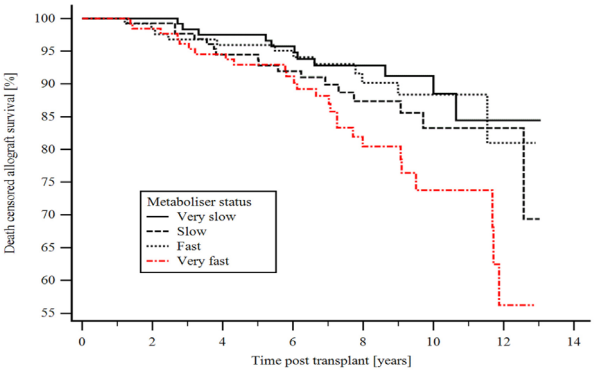
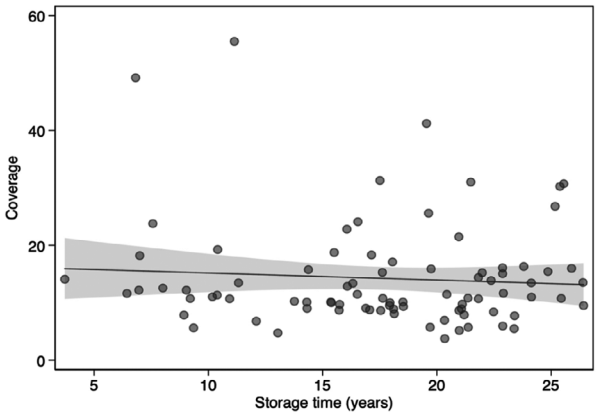
Imperial College Renal and Transplant Centre, Imperial College Healthcare NHS Trust

Background: A recent study has shown that in surveillance biopsies performed at 10 years post renal transplant, non-immunological injury predominates and arteriolar hyalinosis is the most common major histological lesion seen. Arteriolar hyalinosis may be associated with calcineurin inhibitor use, and risk of nephrotoxicity maybe related to individual pharmacokinetics. In this study we look at the impact of tacrolimus metaboliser status on long term allograft survival in patients who were stable at one-year post-transplant, with no rejection or DSA.
Methods: 515 renal transplant patients who had received alemtuzumab induction with tacrolimus monotherapy with a target 12 hour trough level of 5-8 ng/ml were analysed. Metaboliser status (very fast, fast, slow, very slow) was determined by the IQR of the average tacrolimus doses (mg/kg) prescribed between months 6-12 months.
Results: The median tacrolimus dose was 0.061(0.037-0.1)mg/kg. The baseline characteristics are shown in the table below, and demonstrates that fast metabolisers were more likely to be younger and of Black ethnicity.

Very fast metaboliser status was not associated with DSA, p = 0.44 or rejection, p = 0.78. However, on univariate analysis it was associated with death censored allograft failure, p = 0.022 as shown below. Very fast status was also associated with allograft failure on multivariate analysis, Exp(b) 1.89 (1.14-3.15), p = 0.015.



Conclusions: This study shows that patients who are stable at 1 year who receive higher tacrolimus doses (fast metaboliser status) have worse outcomes independent of rejection and DSA development. Interventions to minimise the tacrolimus exposure may help to prolong allograft survival in such patients.



The solid line represents the linear prediction. The shaded area represents the 95% confidence interval for linear prediction.

OS42 - NOVEL BASIC IMMUNOLOGICAL CONCEPTS

OS358 WHOLE-GENOME SEQUENCING BASED ON FORMALIN-FIXED PARAFFIN-EMBEDDED ENDOMYOCARDIAL BIOPSIES FOR GENETIC STUDIES ON OUTCOMES AFTER HEART TRANSPLANTATION

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[1]Clinical Sciences Lund, Cardiothoracic Surgery, Lund University and Skane University Hospital, Lund, Sweden; [2]Clinical Sciences Lund, Cardiology, Lund University and Skane University Hospital, Lund, Sweden; [3]Clinical Sciences Lund, Surgery, Lund University and Skane University Hospital, Lund, Sweden

Background: Whole-genome sequencing (WGS) of heart transplant recipient- and donor-derived cardiac biopsies may facilitate organ matching, graft failure prediction, and immunotolerance research. The objective of this study was to determine the feasibility of WGS based on formalin-fixed paraffin-embedded endomyocardial biopsies.
Methods: The study included donor- and serial recipient samples from patients who had undergone heart transplantation at Skane University Hospital, Lund, Sweden, between 1988 and 2009. DNA extraction and WGS were conducted. Additional WGS sequencing quality metrics and coverage were obtained with the *Genome Analysis Toolkit*.
Results: 455 endomyocardial samples from 37 heart transplant recipients were acquired from routine rejection monitoring and stored as formalin-fixed paraffin-embedded samples. They were analyzed after 3–26 years of storage. DNA was extracted from 114 samples and WGS was run on 85 samples. DNA extraction yielded 313 ng (IQR 96–601) for all samples. A coverage of 11.3x (IQR 9.0–15.9) was recorded for all WGS samples. Three samples stored for > 25 years yielded a coverage of ≥ 25x. Data were generated for 1.7 billion reads per sample (IQR 1.4–2.7). A Transition/Transversion (TiTv) ratio of 2.09 ± 0.05 was calculated for all WGS samples. No associations were found among storage time, DNA yield, or sequencing quality metrics.
Conclusion: The present study demonstrated the feasibility of whole-genome sequencing based on endomyocardial biopsies. This process could enable large-scale retrospective genomic studies using stored histopathological samples.

Data presented as medians and interquartile ranges, means and standard deviations, or percentages (%). Library sizes in gigabases.
Figure 1. Association between storage time and coverage (n = 85).

OS359 DEFINITION OF RENAL INFLAMM-AGEING – IMPLICATIONS FOR ALLOGRAFT QUALITY AND SURVIVAL

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Background: Donor age is a major risk factor for allograft outcome. However, renal senescence has been solely described at the molecular level, the underlying cellular mechanisms characterizing an aged kidney as well as the intragraft recipient's immune response towards it have not been addressed so far.
Methods: We performed a comprehensive immunophenotyping for intrarenal lymphocytes derived from aged (18-20 months) or young C57BL/6 (12-16 weeks) mice by flow cytometry. We further analyzed the intragraft cellular immune response in an allogeneic murine kidney transplantation model by transplanting aged/young C57BL/6 kidneys into young BALB/c recipients.
Results: Naïve aged kidneys harbor significantly more CD8 + T cells and produce more IFNy than their counterparts derived from young kidneys. Although aged kidneys are further characterized by more effector memory T cells (TEM), these cells are less proliferative. However, no differences could be detected for bulk NK cell frequencies in aged versus young organs, but senescent intrarenal NK cells upregulate the cytotoxicity receptor NKG2D as well as the chemokine receptor CXCR6; the latter has been described for NK cell-mediated memory. On day 7 post kidney transplantation, the kidney was completely repopulated by recipient derived cells and we detected increased frequencies of recipient-derived TEM infiltrating the aged kidney. More interestingly, these organs were characterized by an increased production of IFNy, granzyme B and perforin of CD8 + T cells indicating enhanced inflammation and cytotoxicity towards the aged kidney - which was not detected in spleen or lymph nodes.
Conclusion: Our data illustrate that intrarenal senescence also occurs at the immunological level (inflamm-ageing) and that senescent organs provoke an altered immune response in the graft. These results may deliver insights into the development of novel strategies towards pre-conditioning of the graft.

Table 1. Whole-genome sequencing quality metrics.

Variable	All n = 85	0-10 years n = 11	11-15 years n = 12	16-20 years n = 28	21-30 years n = 34	Min	Max
Coverage (x)	11.3 (9.0-15.9)	12.2 (10.7-18.2)	10.9 (9.6-14.6)	10.4 (9.2-17.7)	11.2 (8.4-15.4)	3.8	55.5
% Covered 20x	15.8 (12.4-29.4)	16.0 (11.2-29.7)	13.6 (11.3-22.0)	14.9 (13.9-31.2)	17.3 (11.1-29.4)	0.8	97.2
% Covered 10x	40.9 (25.3-58.4)	54.7 (43.4-61.5)	42.0 (28.4-0.9)	38.2 (26.3-63.2)	36.0 (20.3-53.2)	9.3	97.9
% Covered 0x	2.9 (1.9-4.0)	2.2 (1.9-3.0)	2.7 (2.0-3.7)	2.9 (1.9-3.5)	3.4 (2.2-4.7)	1.1	26.2
% Q20	77.0 (70.8-82.1)	80.8 (75.7-84.0)	79.4 (73.4-3.1)	76.8 (73.0-84.0)	74.2 (67.7-79.8)	40.5	93.9
Library size	1.7 (1.4-2.7)	2.8 (1.7-3.2)	1.7 (1.4-2.0)	1.7 (1.5-3.0)	1.6 (1.3-2.4)	0.87	8.61
Ti/Tv Ratio	2.09 (0.05)	2.09 (0.03)	2.09 (0.03)	2.08 (0.04)	2.09 (0.07)	1.94	2.28

OS360 MYELOID-DERIVED SUPPRESSOR CELLS IN LUNG TRANSPLANTATION

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Background: Myeloid-derived suppressor cells (MDSC) are a heterogeneous group of immune cells from the myeloid lineage. MDSCs expand in pathological situations, such as chronic infection, cancer, autoimmunity and allograft rejection. As chronic lung allograft dysfunction (CLAD) limits long-term survival after lung transplantation (LTx), MDSCs may play a role in its pathophysiology.
Methods: We assessed the phenotype and frequency of MDSCs in peripheral blood from lung transplant recipients and its relationship to post-transplant complications and immunosuppression. Granulocytic (G)-MDSC were identified and quantified by flow cytometry of blood from 4 control subjects and 20 lung transplant patients (stable $n = 6$, infection $n = 5$; CLAD $n = 9$). G-MDSC functionality was assessed in vitro by their capability to inhibit CD4 and CD8 T cell proliferation.
Results: More G-MDSC could be assessed using EDTA tubes compared to heparin tubes ($p = 0.004$). G-MDSC were increased in stable lung transplant recipients versus non-transplant controls (52.1% versus 9.4%; $p = 0.0095$). The infection or CLAD groups had lower G-MDSCs versus stable recipients (28.2%; $p = 0.041$ and 33.0%; $p = 0.088$, respectively), but were not different among CLAD phenotypes. G-MDSC tended to correlate with cyclosporine A and tacrolimus levels (r^2=0.18; r^2=0.17). CD4 and CD8 cells proliferation decreased by 50% and 80% if co-cultured with MDSCs (1:6 and 1:2 MDSC:T-cell ratio, respectively).
Conclusion: In conclusion, circulating MDSCs are measurable, functional and have a G-MDSC phenotype in lung transplant patients. Their frequency is increased in stable patients, decreased during post-transplant complications, and related to level of immunosuppression. This study may pave the way for further investigations of MDSC in the context of lung transplantation.

OS361 EFFECT OF REDUCED CALCINEURIN INHIBITOR EXPOSURE WITH BASILIXIMAB INDUCTION ON RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: Hepatocellular carcinoma (HCC) is an important indication for liver transplantation (LT), but post-LT tumor recurrence remains a major threat. Early post-LT immunosuppression (IS) has been proposed to affect HCC recurrence risk. In Gothenburg, the IS protocol was changed in 2010 from tacrolimus and steroids(± mycophenolate) to basiliximab induction with delayed-introduction of reduced-dose tacrolimus with mycophenolate.
Aim: To evaluate the impact on post-LT HCC recurrence of the new IS protocol with reduced early tacrolimus exposure.
Methods: We included consecutive HCC patients transplanted 2000-2017 in Gothenburg. The impact on HCC recurrence of basiliximab induction and mean tacrolimus concentration (TC) during the first 20 post-LT days was analyzed by Cox regression adjusted for relevant demographic and tumor characteristics.
Results: Study comprised 235 patients (mean age 57 yrs, men 80%, mean MELD score 13, HCV seropositive 58%, alcoholic cirrhosis 30%, within Milan criteria(MC) 57%). Mean TC during the first 20 days were 10.5 ng/mL before 2010($n = 92$) and 7.1 ng/mL after 2010 ($n = 143$). The cumulative 5-yr HCC recurrence rate among patients transplanted before/after 2010 were 28.6% and 19.7%, respectively. Basiliximab had no independent impact on HCC recurrence. High tacrolimus exposure (mean 20-day TC $\geq$ 8 ng/mL) increased HCC recurrence risk in univariate analysis (HR 2.22; $p = 0.008$), though non-significant in multivariate analysis ($p = 0.17$). Outside MC, high tacrolimus exposure predicted HCC recurrence (HR 3.68; $p = 0.012$) independently of number of nodules, size of largest nodule, differentiation, vascular invasion and AFP level; outside UCSF criteria, the corresponding HR was 9.61($p = 0.009$).
Conclusion: igh tacrolimus exposure early post-LT associated with an increased risk of HCC recurrence among patients outside MC. Prospective studies are needed to confirm if minimizing early CNI exposure by using basiliximab induction reduces HCC recurrence rates.

OS362 HUMAN KIDNEYS CONTAIN TISSUE-RESIDENT MUCOSAL ASSOCIATED INVARIANT T-CELLS

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Introduction: Mucosal associated invariant T (MAIT) cells are innate-like T-cells involved in the antibacterial response by recognizing bacterial riboflavin metabolites. They are present in human blood but are particularly abundant in the liver, lungs and intestines. Currently it is unclear whether MAIT cells are present in human kidneys.
Methods: We used a fluorescently-labelled MR1-tetramer in conjunction with 14-color flowcytometry to identify and characterize MAIT cells in normal renal tissue ($n = 5$), renal allografts explanted after allograft failure ($n = 13$) and in peripheral blood mononuclear cells (PBMCs) from healthy donors ($n = 21$). We performed an additional analysis of the allografts that clinically failed due to recurrent urinary tract infections (RUTI) ($n = 5$).
Results: MAIT cells were present in each of the measured renal samples. Both the absolute T-cell counts and the MAIT cell counts were significantly higher in the explanted allografts than in the normal kidneys ($p < 0.0001$ and $p = 0.004$, respectively). MAIT cells comprised an equal share of the total T-cell population, as defined by live CD3 + events, in the normal kidneys compared to the renal allografts and also the PBMCs, median 0.77% (range 0.2-1.7), 0.20% (0.01-9.7) and 0.38% (0.07-4.8), respectively. MAIT cell counts in the normal kidneys were too low to perform a phenotypic characterization. The renal allografts comprised a mainly CD4?CD8 + MAIT cell population that encompassed a substantial CD69 + and CD69 + /CD103 + 'tissue-resident' subset. Further analyses of MAIT cells in allografts that failed due to RUTI, revealed that these MAIT cells displayed a less cytotoxic phenotype.
Conclusion: MAIT cells are present in human kidneys and comprise a CD69 + CD103 + tissue-resident population. Remarkably, in allografts that failed due to RUTI, MAIT cells display a less cytotoxic profile than in allografts that failed for other reasons.

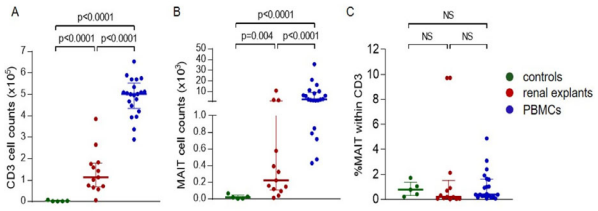

Figure 1. MAIT cells are present in renal tissue.
Renal tissue from normal kidneys (n=5), explanted renal allografts (n=13) and peripheral blood mononuclear cells (PBMCs) from healthy controls (n=21).
(A) T-cell and (B) MAIT cell counts per 2 million mononucleair cells, (C) percentage of MAIT cells within the T-cell population. Values are represented as median + IQR.

OS363 NEXT-GENERATION PORCINE LOW IMMUNOGENICITY ANTI-LYMPHOCYTE IMMUNOGLOBULINS SHOWS SELECTIVE DEPLETION OF T LYMPHOCYTES VERSUS TREG AND BREG

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Polyclonal anti-lymphocyte globulins (ALG) have been used for many years in organ transplantation. Their use as induction therapy is growing, owing to their higher efficacy as compared with other induction agents. ALG, however, decrease acute rejection at a cost of increased development of BK virus, CMV and bacterial infections. In addition, as any antibody from animal origin, ALG elicit antibodies anti-N-glycolylneuraminic acid carbohydrates that contribute to formation of immune complexes to a systemic inflammation called xenosialitis and have been associated with shorter kidney graft lifespan.

To address these issues, we developed LIS1, a new generation ALG from a1,3-GT and CMAH knockout swine, lacking carbohydrate xenoantigens. Since LIS1 is obtained after immunization with human T lymphocytes and given its modified glycosylation pattern, it possibly results indifferent outcomes in vivo as compared with existing ALG. We therefore analyzed lymphocyte depletion by LIS1 in Cynomolgus monkeys ($n = 13$).

In macaques receiving a daily dose for 5 days of LIS1, a rapidly and significantly depletion of circulating CD8 + T cells and CD4 + T cells was recorded. Subpopulations including recent thymic emigrants, naïve, stem cell memory, central memory and RA+ effector memory T cells were significantly depleted ($p < 0.002$), except for regulatory T cells that were not affected. Naive B cells, memory B cells and granzyme B+ B-reg cells were also unaffected, such as monocytes and polynuclear cells.

Taken together these results strongly suggest that LIS1 can be an attractive induction treatment with high efficacy and specificity, avoiding the deleterious side effects observed with current anti-lymphocyte/thymocyte globulins.

OS364 CIRCULATING T FOLLICULAR HELPER PROLIFERATION AND MEMORY B CELL ACTIVATION CORRELATE WITH DONOR-SPECIFIC ANTIBODY OCCURRENCE AND ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Crosstalk between T follicular helper cells (TFH) and B cells is necessary for class-switched antibody generation. The contribution of TFH and B cells to humoral response after transplantation is unclear.

Using 22-color spectral flow cytometry and *in vitro* functional assays, we concomitantly characterized circulating TFH (cTFH) and B cells phenotype in 88 kidney recipients. Patients with DSA with ($n = 20$) or without ($n = 28$) biopsy-proven antibody-mediated rejection (ABMR) were compared to patients without DSA ($n = 40$).

We identified a subset of proliferating (Ki67 +) cTFH (CD4 + CD45RO+CXCR5 +) expanded in patients with DSA, at the time of DSA first detection ($P < 0.001$). This proliferating cTFH subset expressed higher levels of CD38, co-stimulatory molecules ICOS, PD-1, CD28 and transcription factors associated with germinal center TFH Irf4 and c-Maf ($p < 0.001$ for all) as compared to patients without DSA. A subset of activated memory B (mB) cells (CD38loCD27 + CD21-CD20hi) was also expanded at the time of DSA occurrence ($p < 0.001$). These activated mB cells were associated with increased frequency of plasmablasts and decreased frequency of resting mB cells (CD38loCD27 + CD21 +) in patients with DSA as compared to patients without DSA ($p < 0.001$ for both). Moreover, both frequency of Ki67 + cTFH and activated mB were the highest in patients with ABMR ($p = 0.01$ and $p = 0.02$). To evaluate the functional potential of cTFH and mB cells, we co-cultured these subsets *in vitro* in presence of staphylococcal enterotoxin B. We found greater plasmablast formation, IgG, IL-6 and IL-21 production in co-cultures of patients with DSA than in patients without DSA ($p = 0.01$ for all).

Our data show that during an ongoing DSA response after kidney transplantation, cTFH are proliferating and functional to trigger B cell activation and differentiation into antibody-secreting cells. Therapeutic intervention limiting TFH-B interaction may represent an important strategy to prevent DSA formation and ABMR occurrence.

OS365 POTENTIATING REGULATORY T CELLS USING CHIMERIC ANTIGEN RECEPTORS FOR TARGETED TRANSPLANTATION TOLERANCE

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Background: Solid organ transplantation is limited by allograft rejection. Adoptive transfer of regulatory T-cells (Tregs) protects from graft rejection. Antigen-specific Tregs are superior to polyclonal Tregs, with chimeric antigen receptors (CAR) being one method to confer antigen-specificity. The aim of this study was to further improve the function of CAR-Tregs and to monitor the persistence of Tregs *in vivo*.

Methods/Materials: A cassette encoding an HLA-A2-specific CAR, a suppressive cytokine IL-10 and the radionuclide-fluorescence reporter gene NIS-RFP was generated. Human Tregs were CD4/CD25-enriched and lentivirally transduced and sorted for expansion. Resultant CAR-Tregs were analysed in vitro for phenotype, specificity, suppressive capacity and reporter gene function (99mTcO4- uptake for NIS).

Results: Tregs maintain NIS-RFP expression and are specific to A2 by dextramer-labelling. A2CAR releasing IL-10 resulted in an increased suppressive ability, 1000-fold more IL-10 secretion, and a decrease in proinflammatory IL-17 production by Teffectors compared to A2CAR alone. NIS- RFP engineered Tregs showed specific 99mTcO-4 uptake compared to untransduced Tregs

Conclusion: A first of-its-kind HLA-A2 CAR Treg releasing exogenous IL-10, equipped with a reporter gene for *in vivo* tracking was fully characterised *in vitro*. Results demonstrated superiority over polyclonal Tregs with no negative phenotypic impact.

OS366 DESENSITIZATION USING COSTIMULATORY BLOCKADE AND BORTEZOMIB DOES NOT PREVENT DSA FORMATION AND PREVENT REJECTION IN RECONSTRUCTIVE TRANSPLANTATION

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Background: Sensitization in form of donor-specific antibodies (DSA) and subsequent antibody-mediated rejection constitute some of the greatest risk factors for allograft rejection and long-term graft failure. Here we investigated the effect of dual targeted desensitization using costimulatory blockade and bortezomib on DSA levels and graft survival after hindlimb transplantation in the mouse.
Methods: C57BL/6 mice were sensitized with Balb/c skin transplants. All animals rejected the graft within 2 weeks and sensitization was confirmed by flow crossmatch. Group 1 received a desensitization protocol consisting of bortezomib (0.75 mg/kg) twice and CTLA4-Ig (500 μg) once per week for a total of 4 weeks before orthotopic hindlimb transplantation together with a tolerance induction protocol consisting of anti-Thy1.2 (2 mg/kg), total body irradiation (249.7 cGy), and cyclophosphamide (200 mg/kg). Animals in group 2 received the desensitization protocol after hindlimb transplantation and group 3 did not receive desensitization treatment whilst otherwise following the same protocol.
Results: Four weeks after skin transplantation, all animals developed a significantly increase in DSA levels (15.5 ± 7.7-fold increase; $p < 0.0001$). Despite the four week course of combined desensitization, animals in group 1 did not display a significant reduction in DSA levels. After hindlimb transplantation and application of the tolerance protocol, DSA levels significantly dropped to baseline levels in all groups. In group 3, median graft survival was limited to 37 days. Combined desensitization even shortened graft survival (median 15.5 and 19 days, respectively; $p = 0.26$).
Conclusion: Although effective in solid organ transplantation a combined desensitization protocol with CTLA4-Ig and bortezomib failed to show reduced DSA levels and improved allograft survival in a stringent VCA model.

OS367 THE SELF-PEPTIDE REPERTOIRE PLAYS A CRITICAL ROLE IN TRANSPLANT TOLERANCE INDUCTION

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Background: Expression of donor MHC I in recipient hepatocytes induces tolerance to donor skin grafts. Tolerance induction requires direct recognition of the intact foreign MHC I. Vector-encoded donor MHC I heavy chains (HC) pair with native β2-microglobulin and are loaded with various endogenous peptides before transport to the hepatocyte surface.
Methods: To determine the role of self-peptides in tolerance induction, we engineered AAV vectors expressing a single chain trimer (sct) of β2microglobulin, Kb heavy chain (HC) and a defined peptide sequence (KIITYRNL or SIINFEKL). Wild-type (WT) B10.BR (H-2k) or B10.BR-RAG mice reconstituted with 50,000 Des-RAG T cells (which recognise Kb bound to KIITYRNL) were inoculated with Kb (HC), sct Kb-KIITYRNL or sct Kb-SIINFEKL vectors. Transgene expression and peptide presentation were evaluated using flow cytometry and mass spectrometry (MS). Some mice received skin grafts bearing Kb.
Results: Comparable expression of Kb was achieved following transduction with either sct vector. Expression of sct-Kb-KIITYRNL excluded presentation of naturally-processed endogenous peptides. B10.BR-RAG mice reconstituted with Des-RAG cells accepted Kb-bearing skin grafts indefinitely when transduced with sct Kb-KIITYRNL but rejected grafts with a MST of 20 days after inoculation with sct Kb-SIINFEKL ($p < 0.0005$). Conversely, inoculation of WT B10.BR mice with either sct Kb-KIITYRNL or sct-Kb-SIINFEKL only prolonged graft survival by a few days. Kb-bound peptides were eluted from Kb (HC) transduced hepatocytes, spleen and skin. Recognition of shared peptide epitopes was determined using tetramer staining. From a pilot pool of peptides, we identified one immunodominant epitope which bound up to 27% of activated alloreactive CD8 T cells (fig). Further peptide screening is underway.
Conclusions: Self-peptides play a critical role in tolerance induction. Identification of individual pMHC epitopes is feasible using MS and multimer staining.

OS368 CHARACTERIZATION OF DE NOVO DSA WITH MASS SPECTROMETRY: HIGH PROPORTION OF IGG3 AND LOW SIALYLATED IGG3 PREDICTS ANTIBODY-MEDIATED REJECTION OCCURRENCE AND POORER OUTCOME IN RENAL TRANSPLANT RECIPIENTS

Vincent Pernin[1], Beyze Anais[2], Nicole Bec[3], Ilan Szwarc[2], Christophe Duperray[4], Valerie Garrigue[2], Georges Mourad[2], Christian Larroque[5], Moglie Le Quintrec[2]
[1]CHU Lapeyronie Montpellier; [2]CHU Lapeyronie; [3]INSERM U1183; [4]INSERM; [5]Institut du cancer de Montpellier

IgG subclass distribution and Fc glycosylation of DSA could have a major impact on their pathogenicity. Some studies have reported that the detection of IgG3 by Flow cytometry, adapting the Luminex Single Antigen test, was associated with poorer graft survival. However, this test does not allow a relative quantification of the different subclasses. We developed an innovative test using mass spectrometry for characterization of DSA after their isolation on Luminex HLA beads. Our objective was to investigate the role of the glycosylation and the relative IgG subclasses distribution of de novo DSA on ABMR occurrence and decline of graft function.

Between 2014 and 2017, 48 RT patients developed de novo DSA and were included in this study: 16 patients without (ABMR-) and 32 with ABMR (ABMR+). Interestingly, with MS, all IgG subclasses were present in all analyzed DSA with the following distribution: IgG1: 60.1%, IgG2: 23.7%, IgG3: 8.6% and IgG4: 7.3%. The proportion of IgG3 was significantly higher in ABMR+ group: 9% vs 5.8%, $p = 0.007$. In addition, patients with IgG3 > 7.25% had a higher C4d score (1.69 ± 1.3 vs 0.82 ± 1.2, $p = 0.017$), a tendency for more micro-vascular inflammation (g+cpt score: 3.3 ± 2.0 vs 2.2 ± 1.9, $p = 0.08$) and a significantly higher risk of GFR decline > 25% ($p = 0.01$, Figure 1).Furthermore, sialylation of IgG3 was significantly lower in ABMR+ vs ABMR- recipients (7.5% vs 8.8%, $p = 0.017$). A sialylation ratio of IgG3 < 7.5% was also associated with a higher risk of GFR decline ($p = 0.02$, Figure 2).
Conclusion: In conclusion, a higher proportion of IgG3 and a low sialylation of IgG3 are both associated with ABMR occurrence, ABMR severity and poorer graft outcome.

Figure 1

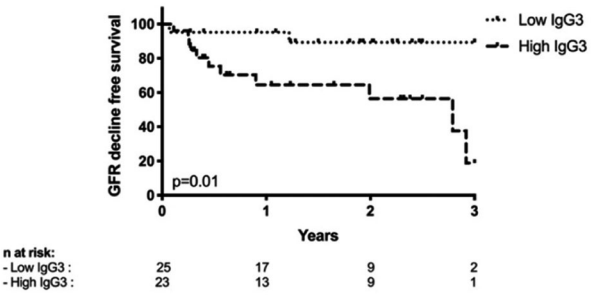
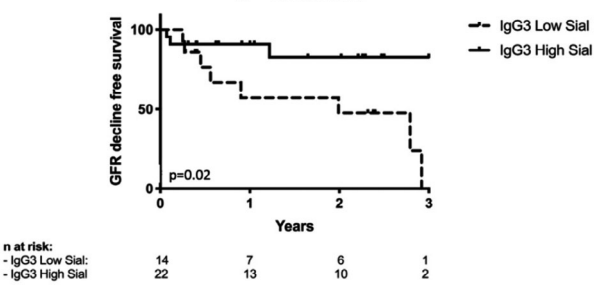


Figure 2



OS369 CHARACTERIZATION OF CIRCULATING T FOLLICULAR HELPER CELLS IN KIDNEY RECIPIENTS WITH ANTIBODY-MEDIATED REJECTION: INCREASED FUNCTION AND TH17 POLARIZATION

Kevin Louis[1], Camila Macedo[2], Elodie Bailly[1], Marilyn Marrari[2], Bala Ramaswami[2], Michelle Lucas[2], Beth Elinoff[2], Masaki Yamada[2], Xinyan Gu[2], Geetha Chalasani[2], Parmjeet Randhawa[2], Alexandre Loupy[1], Adriana Zeevi[2], Carmen Lefaucheur[1], Diana Metes[2]
[1]Paris Translational Research Center for Organ Transplantation; [2]University of Pittsburgh School of Medicine

T follicular helper cells (TFH) provide help to B cells that is critical for class-switched antibody generation. How TFH may participate to a deleterious donor-specific anti-HLA antibody (DSA) response that would trigger antibody-mediated rejection (ABMR) is unclear.

Using multiparametric flow cytometry and *in vitro* assays, we evaluated the heterogeneity of circulating TFH (cTFH) phenotypes, their relationship with B cell activation, DSA pathogenicity (strength, C1q-binding, IgG subclasses) and ABMR occurrence in 98 kidney recipients. Patients with biopsy-proven ABMR ($n = 23$) were compared to patients with DSA without ABMR ($n = 26$) and patients without DSA ($n = 49$).

Patients with DSA had higher frequency of proliferating (Ki67 +) cTFH (CD4 + CD45RO+CXCR5 +) that correlated with DSA strength ($r = 0.48$, $p = 0.0005$). Patients with ABMR had with higher frequency of Th17 cells within proliferating cTFH compared to ABMR-free patients ($p < 0.01$). There were no differences regarding Th1, Th2 and Th1/17 subsets. Proliferating cTFH-Th17 were increased in patients with C1q-binding DSA and patients with IgG3-positive DSA compared to those with non-C1q-binding and IgG3-negative ($p < 0.01$ for both). There were no differences in cTFH subsets according to IgG1, IgG2 or IgG4 DSA status. After stimulation with donor cells lysate, allo-reactive CD40L+ cTFH in patients with ABMR comprised higher IL-17 + and IL-21 + cells ($p = 0.01$ for both) compared to control groups. When co-cultured with memory B cells, cTFH-Th17 from patients with ABMR induced greater plasmablast differentiation, IgG3 production, IL-6, IL-17 and IL-21 secretion ($p < 0.05$ for all) as compared to Th1, Th1/17 and Th2 subsets.

We identified a subset of cTFH with Th17 polarization in patients with ABMR, associated with C1q-binding and IgG3 DSA *in vivo*, with the most potential to produce effector cytokines, trigger plasmablast and IgG3 response *in vitro*. Targeting TFH may represent an important strategy for therapeutic intervention in ABMR.

OS371 HAND-ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY (HARP) OPTIMIZES HEALTH RELATED QUALITY OF LIFE OF LIVING DONORS – ANALYSIS FROM THE RETROSPECTIVE PART OF THE QOLID-STUDY

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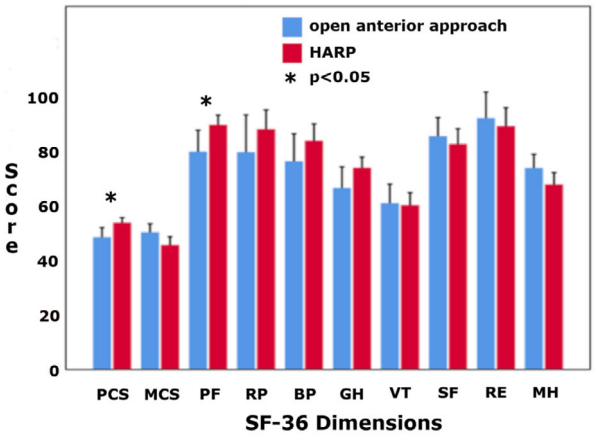
Introduction: Living kidney donation (LKD) has become essential for transplantation in Germany due to the low rates of deceased donors. In the long time follow up health-related quality of live (HRQL) and psycho-social aspects are important for the living donor. If the surgical technique of donor nephrectomy could influence HRQL is still no clear. Data regarding the HARP are scarce. Therefore, the QoLiD-study (Quality Of live in Living kidney Donors) was implemented. Aim of the first part of the study was 1) a status-quo analysis on HRQL and psycho-social aspects in living kidney donors and 2) the influence of the HARP-technique during the follow-up.
Methods: Single-center cross-sectional study
Results: 100 living donors were included (complete data $n = 96$). 28 donors were operated with open anterior approach (AA), 68 with HARP donor nephrectomy with a follow-up time of 33.3 ± 20.6 months (AA 58.7 ± 13.9 vs. HARP 22.6 ± 11.7, $p < 0.005$). Age was 54.9 ± 8.9 (HARP) vs. 59.2 ± 9.9 (AA, p=ns). Post-operative eGFR was 61.5 ± 13.5 ml/min (HARP) vs. 63.8 ± 12.2 ml/min (AA, p=ns). Length of the scar was 10.8 ± 2.2 cm (HARP) vs.19.4 ± 4.1 cm (AA, $p > 0.005$). There were no major surgical complications (≥3a° Clavien-Dindo). Normalized to the German population HRQL (SF-36-questionaire) was significantly higher for HARP in the physical health sum score (HARP vs. AA: 53.9 ± 7.6 vs. 48.6 ± 8.5, $p = 0.006$) without a difference in the mental health sum score (HARP vs. AA: 45.8 ± 12.3 vs. 50.4 ± 7.6, $p = 0.85$), neither in the multidimensional fatigue inventory (MFI-20) nor in the hospital anxiety and depression scale (HADS).
Discussion: Hand-assisted retroperitoneoscopic donor nephrectomy seems to optimize physical aspect of health related quality of life in living kidney donors during long-term follow-up in comparison to anterior approach donor nephrectomy.



OS372 KIDNEY TRANSPLANTATION IN PATIENTS AGED 60 YEARS AND OLDER IS NOT RELATED TO INCREASED RISK OF SURGICAL COMPLICATIONS - A SINGLE-CENTER, LONG-TERM, PAIRED-KIDNEY ANALYSIS

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Background: Increased rate of cardiovascular diseases (CVD) and diabetes in elderly patients can lead to complications in early and late period after kidney transplantation (KTx).The aim of the study was to analyse the incidence of surgical complications in kidney recipients aged 60 years and older compared to younger recipients of kidneys procured from the same donors in early and late postoperative period.
Material/Methods: Among patients treated with KTx in Katowice between 1998 and 2018, in case of 175 deceased donors one kidney was transplanted to a recipient aged 60 years and older (≥60), and the other - to a recipient younger than 60 years (<60). In order to reduce the influence of donor parameters on incidence of surgical complications early (up to 3 months) and long-term (3-60 months) results of KTx were compared between these two groups.
Results: Recipients ≥ 60 (median 64 years) compared to < 60 (median 47 years) presented higher BMI (26.1 ± 3.5 vs. 24.7 ± 3.4 kg/m2), and higher rates of CVD (34% vs 10%) and diabetes (21% vs 11%), but did not differ regarding to gender M/F (61.1/38.9% vs 60.6/39.4%) and dialysis vintage (35 months vs 32 months). There were less re-transplants in ≥ 60 group (6% vs 20%), however the rate of recipients with PRA > 25% was comparable (24% vs 27%). In early postoperative period the rates of artery or vein thrombosis (2.3% vs 2.9%), hematoma or hemorrhage (12% vs 16%), urinary leak or stenosis (6.3% vs 5.1%) and complications requiring surgery (12% vs 14.9%) were similar in both groups. In long term follow up the rates of graft artery stenosis (0.6% vs 2.3%), ureter stenosis (3.4% vs 1.1%), lymphocele (6.9% vs 3.4%), and complications requiring surgery (8% vs 4%) were comparable in recipients groups aged ≥ 60 years and < 60 years.
Conclusion: Despite higher incidence of cardiovascular diseases and diabetes in elderly patients the risk of surgical complications remains comparable to younger recipients in early and long-term period after KTx.

OS373 MINIMAL INVASIVE KIDNEY AUTO-TX FOR RENAL ARTERY ANEURYSM

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Background: Renal artery aneurysm (RAA) is in most cases an incidental finding. For aneurysms above 20 mm, our policy has been endovascular approach if possible or auto-transplantation of the kidney (auto-KTX) with ex vivo resection of aneurysm for complex hilar RAAs. Since 2009, along with development of laparoscopic donor nephrectomy (LDN), our standard approach has been hand-assisted laparoscopic nephrectomy and auto-transplantation of the kidney (HAL-auto-KTX) through a standard kidney TX (KTX) incision.
Material and Methods: Since 2009 until 2019, we have performed 42 auto-KTX due to RAA. Median age was 57 years, 74% were females and median BMI was 24. 67% had concomitant hypertension. The right kidney was affected in 62% and median aneurysm size was 24 mm [15-50]. 39 out of 42 were performed as HAL-auto-KTX and the remaining with conventional open technique. Radioisotope renography was performed preoperatively and after 1 and 12 weeks in the majority of patients.
Results: Median follow-up time was 38 months [5-118]. Patient survival (PS) was 100% and graft survival (GS) 95%. 1 graft was lost on day 1 due to thrombosis and 1 graft was lost on day 9 due to bleeding and urine leakage. Median number of arterial anastomoses was 3 [1-7], median total arterial flow was 300 ml [110-980] and median CIT was 137 min [112-404]. 19 patients (45%) received a temporary ureter stent. Median operative time was 372 min [281-571] and median stay in our department was 7 days [3-30]. 5 patients needed an early reoperation and 2 had an additional reoperation due to graftectomy. Median eGFR preoperatively was 91 [45-124] ml/min/1.73 m2 and median eGFR after 3 months was 86 [49-122] ml/min/1.73 m2 ($p = 0.18$).
Conclusion: HAL-auto-KTX through a standard KTX incision is a safe technique for complex hilar RAAs. Both GS and PS were excellent and median eGFR 3 months after auto-KTX did not differ significantly from baseline values. We recommend this surgical approach for complex hilar RAAs.

OS374 LEFT VERSUS RIGHT HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY. COMPARISON OF INDICATIONS AND OUTCOMES IN A LARGE CENTRE AND SURVEY OF NATIONAL PRACTICE

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Introduction: In this century almost all living donor nephrectomies are done laparoscopically. The left kidney is the preferred kidney due to the longer left renal vein and potentially easier approach technically however, there is some reticence in selecting the right kidney in a donor.

We analysed 739 donors done laparosopically in a large centre evaluating laterality and indications for a right donor nephrectomy,

Donor and recipient outcomes were compared and a survey of national practice was carried out.
Methods: All hand assisted laparoscopic donor nephrectomies (HALDN) and transplants done in a single centre from 01/2006 to 11/2018 were analysed retrospectively from all patient record sources. Recipient variables which were analysed included cold ischemia time (CIT) graft function, transplant renal artery stenosis, ureteric stenosis, graft loss and recipient death with or without a functioning graft. A analysis of national practice was extrapolated from anonymised CIT data provided by National Health Services Blood and Transplant (U.K.).
Results: The total number of HALDN analysed were 739 of which 604(84.3%) were left sided nephrectomies and 135 (15.7%) right sided. There was a slight female preponderance in both groups with 328 (54.3%) female donors who underwent left HALDN and 68 (50.3%) female donors who underwent right HALDN. There were 126 paediatric recipients and 613 adults. in total.

Of the right sided 60 (44.4%) were due to fewer arteries as compared to left when the split function was within British Transplantation Society guideline and 55 (40.7%) were due to much lower split function. In 20(14.8%) the reasons were varied including scarring, cysts, tumours, etc.

As tabulated below the outcomes in donors and recipients were comparable and there were no statistically significant differences ($p > 0.05$)
Discussion: Analysis of this large group shows that there is no impact on recipient outcome on the laterality. Right HALDN is a safe procedure

	LEFT (*n*)	LEFT (%)	RIGHT (*n*)	RIGHT (%)	TOTAL {*n*, (%) }
AVERAGE SURGICAL TIME (minutes)	181.4	-	166.8	-	172.1
AVERAGE WARM ISCHAEMIA TIME (minutes)	3.5	-	3.5	-	3.5
CONVERSIONS IN DONOR	2	0.3%	5	3.5%	7 (0.94%)
BLEEDING IN DONOR	10	1.3%	1	0.7%	12 (1.6%)
REEXPLORATION IN DONOR	18	2.5%	2	1.5%	20 (2.7%)
INCISIONAL HERNIAE IN DONOR	36	5.9%	7	5.2%	43 (5.8%)
SURGICAL SITE INFECTIONS	19	3.1%	6	4.4%	25 (3.38%)
AVERAGE HOSPITAL STAY	4.3	-	4.1	-	4.3
AVERAGE COLD ISCHAEMIA TIME (minutes)	204	-	221	-	197
GRAFT THROMBOSIS	7	1.2%	0	0	7 (0.94%)
BLEEDING IN RECIPIENT	5	0.8%	2	1.5%	7 (0.94%
TRAS	3	0.7%	0	0	3 (0.4%)
URETERIC STENOSIS	2	0.3%	1	0.7%	3 (0.4%)
PNF	1	0.2%	0	0	1 (0.71%)
REEXPLORATION IN RECIPIENT	11	2%	2	1.5%	13 (1.8%)
GRAFT FAILURE	32	5.3%	4	2.8%	36 (4.9%)
DEATH WITH FUNCTIONING GRAFT	20	3.3%	2	1.5%	22 (2.9%)

OS375 DONOR LAPAROSCOPIC NEPHRECTOMY: LEARNING CURVE AND EXPERIENCE IN A HIGH VOLUME CENTER

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Kidney and Pancreas Transplant Unit - Departement of Surgery, Oncology and Gastroenterology -University of Padua

Introduction: Laparoscopic nephrectomy is now considered the gold standard in living renal transplantation. It is a safe procedure with a low percentage of complications, reduced lengths of stay and post-operative recovery time.
Methods: We examined 343 laparoscopic nephrectomies performed by three different surgeons in our center between January 2010 and February 2018. The complications were evaluated via the Clavien Classification and the learning curve was elaborated via Cu-Sums Analaysis both for the individual operator and for the entire case study.
Results: The OR times significantly decreased secondary to the execution of the first 157 laparoscopic nephrectomies. They further decreased during the downwards slope of the learning curve. The average OR time of the downwards slope was of 187,32 $\pm$ 28,29 min vs. 272,71 $\pm$ 42,07 min of the upwards slope of the learning curve. No significant differences concerning the complication rates in the three phases of the learning curve were noted: these include a single case of conversion to laparotomy, 13 wound hematomas, 4 cases of anemia requiring hemotransfusions and 5 chyloperitoneums. Furthermore examining the learning curve of the operator that performed the greatest number of nephrectomies, the performance improves after the execution of the first 75 surgeries and 1 year after the execution of the first surgery.
Conclusions: Donor laparoscopic nephrectomy is a safe and standardised procedure with minimal post-operative complications. In a high volume center (>50 cases/year), laparoscopic training can be achieved in roughly 1 year.

OS376 FRAILTY TRAJECTORY AFTER KIDNEY TRANSPLANTATION

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UMCG

In today's aging population, an increasing number of patients are becoming frail. Frailty results from the body's failure to return to homeostasis after stressful events, leading to adverse outcomes. To study the dynamics of frailty in kidney transplant recipients we aimed to determine whether the degree of frailty and its specific domains are affected by kidney transplantation (KTx).

A total of 176 kidney transplant recipients, transplanted between 2015-2017, were prospectively included. The presence and severity of frailty was measured using the Groningen Frailty Indicator (GFI). Frailty was assessed preoperatively during admittance and during follow-up. Changes in frailty, the total score and the individual domains, were determined between the admittance and follow-up measurement. Specific changes in the different domains of the GFI and contributing patient characteristics were analyzed.

Mean age (SD) was 51.8 (14.1) years and 63% were male. Sixty percent of the patients were dialysis dependent prior to KTx and 83% received a kidney from a living donor. Thirty patients (17%) were considered frail (GFI > 4) at baseline. Compared to the baseline frailty state, 78 patients (44%) became more frail, 49 (28%) remained equally frail and 49 (28%) became less frail after a mean 23-month follow-up. Factors contributing to a more frail state were age ($p = 0.007$) and receiving a deceased donor kidney ($p = 0.001$). The individual frailty domains "limited cognition" (20%) and "limited psychosocial functioning" (28%) contributed most to a deterioration in degree of frailty.

More than 40% of patients become more frail after KTx. This deterioration is caused by kidney donor type and age at transplantation. These results can be used to inform patients on the impact of KTx and manage expectations regarding physical and cognitive decline after surgery. More emphasis needs to be put on specific, preventative interventions which combat the decline of the individual frailty domains.

OS377 HAND ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY AVOIDS INTRAABDOMINAL COMPLICATIONS: OUR EXPERIENCE WITH 816 CASES

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After 3 years of experience with Hand Assisted Laparoscopic Donor Nephrectomy consisting 71 living donors, we adopted Hand Assisted Retroperitoneoscopic Donor Nephrectomy(HARPDN). We performed 816 consecutive cases between February 2009 and December 2018. We reviewed the charts of donors and recipients retrospectively.

The paramedian($n = 688$)or Pfannensteil($n = 128$,15,7%)incision was performed with hand assistance. Two 12 mm trocars(subxiphoid for camera and subcostal for instruments) were introduced. 171 donors had right donor nephrectomy(21%). 63 recipients and 174 donors were lost in long term follow up. 5 donors and 46 recipients died during follow up period. The demographics were predominant with female sex(56%), mean age of 44.3,mean BMI of 27.2 $\pm$ 4.8 for donors. The mean follow up period was 50.9 months for recipients and 49.9 months for donors. No donor had intraabdominal organ injuries or bowel obstruction. The dissection time for right and left kidney was 94 min and 97 min respectively. 3 donors had intraoperative bleeding but none required blood transfusion. Wound infection(1%) and incisional hernia(1.7%) were the most frequent complications in donors. The rate of delayed and slow graft function was 1.7% and 3.5%. Two recipients had graft thrombosis. 10 recipients had urinary complications requiring surgery. The mean creatinine of recipients at 5th day and last follow up time was 1.28 $\pm$ 1 mg/dl and 1.6 $\pm$ 1.5 mg/dl. Graft survival for 1, 5 and 10 years was 97.2%,88.4% and 79.6% respectively. There was no statistical significance in donor and recipient demographics, operative parameters, donor complications, recipient outcome according to right and left kidney procurement even in situation of multiple arteries

HARPDN is a safe procedure that avoids intraabdominal complications. It has similar results at both left and right sided donor nephrectomy including multiple artery grafts. Therefore, HARPDN offers safety and successful utilization of right kidneys in living donation.

OS44 - ISCHEMIA-REPERFUSION INJURY AND OTHER ISSUE IN LIVER TRANSPLANTATION

OS378 PRE-TRANSPLANT ASSESSMENT OF MITOCHONDRIAL FUNCTION USING HIGH RESOLUTION RESPIROMETRY PREDICTS PRIMARY POOR FUNCTION IN CLINICAL LIVER TRANSPLANTATION

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Background: In order to further increase the usage of liver grafts from expanded criteria donor objective tools to assess graft quality prior to implantation are needed. Our aim was to assess donor liver quality using high resolution respirometry and to investigate its predictive value for clinical liver transplantation.
Methods: We performed a prospective clinical trial to assess the predictive value of high resolution respirometry as assessment tool for organ quality in deceased donor liver transplantation; results of high resolution mitochondrial respirometry in liver biopsies and was correlated with primary poor function (PPF). Biopsy results (confocal score), recipient, donor and transplant factors were analysed.
Results: A total of 35 liver transplant recipients (22 male, 62,8%) have been included the trial. Of these, 26 grafts originated from a ECD donor (74,3%). The median donor age was 53 years, the median recipient age was 59 years; Cold ischemia time was 7.4 $\pm$ 2.1 hours.

Overall, 13 (37.1%) recipients showed PPF. OXPHOS coupling efficiency was significantly lower in livers eventually developing PPF: 0,70 $\pm$ 0,08 in PPF vs. 0,76 $\pm$ 0,07 in the no PPF group, $p = 0,0403$. Most Importantly, OXPHOS coupling efficiency significantly correlated with the occurrence of PPF ($p = 0,0366$).
Conclusion: High resolution respirometry has a predictive value for primary poor function in clinical liver transplantation.

OS379 SHORT TERM RESULTS OF THE FIRST ITALIAN EXPERIENCE ON ORGANOX METRA MACHINE PERFUSION RECONDITIONED DISCARDED LIVER GRAFT

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Background: Because of donor shortage, about 20% of potential liver transplant (LT) recipients still die during waiting list. In order to increase donor pool, use of Extended Criteria Donors (ECDs) became a widespread practice.

Ex situ Normothermic Machine Perfusion (NMP), preserving organ in a functioning, physiological status, avoids damages caused by current standard static cold storage on marginal grafts.
Methods: At Tor Vergata University, Rome, from January to November 2018, five consecutive regional discarded liver grafts from brain death donors [age: 58 (range: 41-88) years, BMI: 27 (range: 21-32), Donor Risk Index (DRI): 1.5 (range: 1.2-2.0)] underwent NMP with OrganOx Metra. Primary aim of the study was to assess viability and safety of NMP used on regional discarded liver.
Results: four grafts fulfilled viability criteria and were transplanted. One fatty 3.5 kg liver graft was not considered eligible for LT after OrganOx Metra perfusion and split liver procedure was performed during NMP for research purpose only, in order to prove surgery feasibility. AST peak during first 7 days after LT was 1401 U/L (range: 69-1442). All recipients experienced Early Allograft Dysfunction. The median Intensive Care Unit stay was 3 days (range: 2-28), median hospital stay was 14 days (range: 9-70). One patient developed hepatic artery thrombosis on 2ndpost-operative day that required re-laparotomy and successful thrombectomy. The median follow-up was 4 months (range: 2-4). The 60-days patients and graft survival were 80%; one patient developed Primary Non Function (PNF) and died during re-transplant.
Conclusion: this is first Italian experience with OrganOx Metra NMP; we finally recruited 80% of regional discarded liver that finally showed acceptable feasibility and safety profile. Although it represents a preliminary experience, we could assert that NMP would be a valid option to recruit liver for well compensated recipients allowing minimization of waiting list time

OS380 VIABILITY ASSESSMENT DURING D-HOPE LIVER PERFUSION

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Introduction: Dual hypothermic oxygenated perfusion (DHOPE) can be used to recondition liver grafts prior to transplantation. Objective biochemical, haemodynamic and biliary parameters have proven successful in identifying livers for transplantation during clinical normothermic perfusion. We aimed to identify parameters associated with outcomes during DHOPE and develop an objective assessment tool.
Methods: We analysed perfusion characteristics, biochemical and molecular signatures from livers ($n = 16$) undergoing DHOPE perfusion. Mesoscale multiplex plates (MESO QuickPlex™ SQ120 multiplex analyser) were used to quantify tissue and vascular injury as well as inflammatory status at different time points. Receiver Operator Characteristics (ROC) curve analysis was performed to establish the optimum cut-off values for each molecule.
Results: 10 livers were transplanted (mild injury) and 6 livers (severe injury) were not transplanted on the basis of an integrated subjective assessment of donor and recipient factors. There were no significant differences between the two groups based on vascular flows, lactate clearance, bile duct flow, and oxygen consumption. Perfusate ALT level above 358U/L at 20mins was seen in all discarded livers, but 1 liver was successfully transplanted with a value of 2112U/L. ROC curve analysis revealed significant differences in various molecular patterns between the two groups. An algorithm integrating a specific combination of 6 molecules could discern between mild and severe injury with 100% sensitivity and specificity. Some
of these molecules are associated with specific damage pathways during ischaemic injury.
Discussion: Perfusate ALT alone can contribute to the assessment of livers ex-situ. However, a specific pattern of injury associated biomarkers have been identified that can successfully differentiate between severe and mild injury. This suggests objective scoring of livers using molecular analysis during hypothermic injury is achievable.

OS381 ORAL PRECONDITIONING OF DONORS AFTER BRAIN DEATH WITH CALCINEURIN INHIBITORS VS. INHIBITORS OF MAMMALIAN TARGET FOR RAPAMYCIN IN PIG KIDNEY TRANSPLANTATION

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Background: The systemic inflammatory cascade triggered in donors after brain death (DBD) enhances the ischemia-reperfusion injury (IRI) after organ transplantation. Data regarding donor preconditioning with calcineurin inhibitors (CNIs) and inhibitors of mammalian target for Rapamycin (mTORIs) is limited. The aim of this project is to investigate the effects of (oral) donor preconditioning with a CNI versus an mTORi compared to the conventional administration of steroid in the setting of DBD in porcine renal transplantation.
Methods: DBD pigs were randomly preconditioned with either Cyclosporine ($n = 9$) or Everolimus ($n = 9$) administered via nasogastric tube. Control donors received intravenous (i.v.) Methylprednisolone ($n = 8$). Kidneys were procured, cold-stored in HTK solution and transplanted in recipients after a mean cold ischemia time of 19.32 ± 2.92 (SD) hrs. No immunosuppression was performed to avoid confounding bias. Blood samples were obtained at 4 hrs postreperfusion and daily until postoperative day (POD) 5 for complete blood count, blood urea nitrogen (BUN), creatinine (Cr), and electrolytes. Graft protocol biopsies were performed 4 hrs after reperfusion.
Results: Serum BUN peaked on POD1 in all groups but trended to remain higher after donor preconditioning with Everolimus. Serum Cr also peaked on POD1 but was significantly higher after donor preconditioning with Cyclosporine on POD 1 ($p = 0.017$) and at the conclusion of the study on POD 5 ($p = 0.009$). There was no difference between serum Cr after donor preconditioning with Everolimus compared to steroids. Histological assessment of acute tubular necrosis revealed no significant differences between the groups.
Conclusion: donor preconditioning with Everolimus resulted in similar post-transplantat serum Cr compared to the conventional donor preconditioning with steroids after kidney transplantation. The histological tissue damages were the same in the three groups, showing no advantage in the conventional group

OS382 IDENTIFICATION OF NEW DRUG TARGETS TO PREVENT HYPOXIA-INDUCED BILE TOXICITY USING A HUMAN BILIARY ORGANOID MODEL

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Introduction: Ischemic cholangiopathy (IC) is the most severe complication after liver transplantation (LT). Hypoxia might accelerate bile toxicity in cholangiocytes, due to insufficient protection by CFTR-related bicarbonate (HCO_{3-}) secretion and contribute to IC development. Liver-derived organoids (LDOs) resemble cholangiocyte-like cells. Thus we investigated if LDOs have functional cholangiocyte transport channels and could serve as a model for hypoxia-related biliary injury as well as used for IC drug-discovery purposes.
Methods: LDOs, cultured from healthy individuals, were analyzed on mRNA and protein level for cholangiocyte-specific transporters. Channel-functionality was tested using an Ussing-chamber set-up in 2D-grown organoids ($n = 42$). Forskolin (cAMP-activator) addition, initiated CFTR activation which was inhibited by GlyH. Hypoxia was achieved by nitrogen gas ($95\%N_2/5\%CO_2$) exposure. To study bile-related toxicity, bile was added during oxygen and hypoxia. Finally, compounds were tested for the ability to abrogate the ischemia-induced inhibition of CFTR.
Results: CFTR was expressed in LDOs on gene and protein level. Moreover, CFTR could be activated. Activity significantly decreased when switching from oxygen to hypoxia (8.00 ± 1.19 vs. 5.89 ± 1.26, p = 0.02). Further experiments showed that CFTR indeed secrete HCO_{3-} in these conditions, confirming that hypoxia reduces apical HCO_{3-} secretion. When LDO were exposed to bile, it resulted in more cell death in hypoxic conditions (31.2% ± 4.32 vs.19.18 ± 4.81, p = 0.04). Most importantly, addition of compound C (AMPK-inhibitor) was able to rescue CFTR-activity during hypoxia.
Conclusion: LDOs provide an excellent model to study bile duct transporters. We demonstrate that hypoxia inhibits CFTR-related HCO_{3-} secretion and identified that a AMPK-inhibitor can restore this. This encourages further clinical studies to test whether AMPK-inhibitors can prevent hypoxia-related biliary injury during graft preservation and after LT.

OS383 FAS-SIRNA PRE-TRANSPLANT LIVER GRAFT THERAPY ALLEVIATES ISCHEMIA-REPERFUSION INJURY: PRELIMINARY RESULTS IN A RODENT LIVER TRANSPLANT MODEL

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Background: Severe ischemia reperfusion injury (IRI) limits the use of extended criteria donors (ECD) in liver transplantation (LT). Apoptosis has been shown to play an important role in IRI.
Aim: We sought to investigate if siRNA silencing of an apoptosis associated gene (FAS) could alleviate liver IRI.
Methods: In an arterialized rat liver transplant model, a single dose of 500 μg of FAS siRNA was administered in the donor 2 h before organ procurement. A prolonged static cold storage time of 22 h was used to intensify the IRI effects.

Additional transplants were performed with an *ex-vivo* siRNA treatment during the liver graft perfusion in a hypothermic machime perfusion system.
Results: Recipients of treated donors presented lower levels of AST (1067 ± 382 x 2087 ± 203 IU/L p = 0.03) and ALT (775 ± 161 x 1777 ± 542 IU/L p = 0.05) at 24 h post-LT when compared with the control group (Figure 1). Confocal microscopy confirmed siRNA uptake in liver grafts (Figure 2 right panel). Because donor treatment in clinical trial setting can raise potential ethical and logistical issues regarding the use of different organs by different transplant teams, we set up a model where FAS siRNA was administered to the liver during 4 hours in an ex-vivo hypothermic machine perfusion system. Here again, siRNA was uptaken by the liver and the recipients of treated grafts showed lower levels of ALT/AST at 24 h post-LT.
Conclusions: Our preliminary results suggest that silencing of apoptosis-associated genes could be used to alleviate IRI post-LT, which has the potential to increase the pool of transplantable liver grafts.

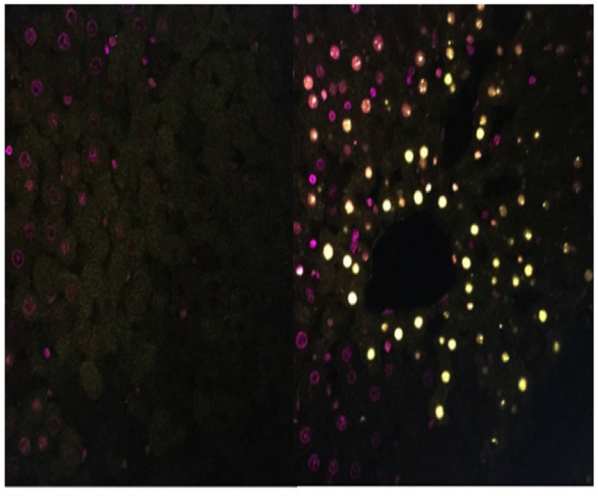

Figure 2: Confocal microscopy showing FAS-siRNA hepatocyte uptake at 24h post-LT.

OS384

NOVEL APPLICATION OF MOLECULAR HYDROGEN (H2) IN ORGAN TRANSPLANTATION: HYDROGEN FLUSH AFTER COLD STORAGE (HYFACS) AND HYDROGEN INHALATION AFTER REPERFUSION (HYIAR)

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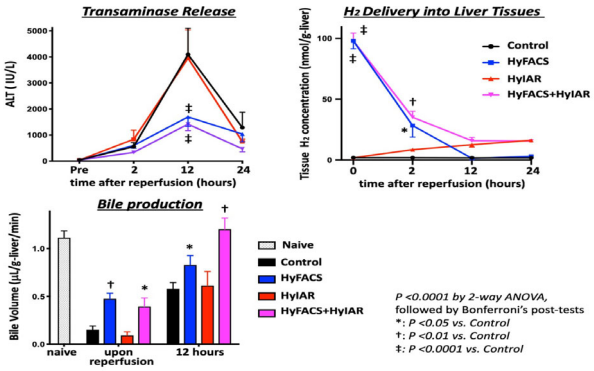
Background: Ischemia/reperfusion injury (IRI) remains a central issue in solid organ transplantation. We recently reported HyFACS (Hydrogen Flush After Cold Storage), just an end-ischemic H_2 flush directly into donor organs *ex vivo*, significantly ameliorates hepatic IRI. Here we investigated whether HyFACS combined with systemic H_2Inhalation After Reperfusion (HyIAR) confers additional protection in a rat model of orthotopic liver transplantation (OLT)
Methods: Male Lewis Rats (250-300 g) were used as donors and recipients. Whole livers were cold-stored in UW for 6 hours, then randomly assigned into the following 4 groups. Group-HyFACS: Livers were flushed *ex situ* with 1.0 ppm H_2-saline via portal vein and hepatic artery just before implantation; Group-HyIAR: Recipients were inhaled with 2% H_2 gas during/after surgery; Group-HyFACS+HyIAR: treated with the both; and Group-Control; treated with neither HyFACS nor HyIAR. Liver damages/function were evaluated at 2, 12, and 24 hours after OLT.
Results: HyFACS+HyIAR significantly improved hepatic microcirculation ($P < 0.001$), lactate ($P < 0.001$), tissue ATP restoration ($P < 0.01$), transaminase ($P < 0.0001$), and HMGB-1 release ($P < 0.001$) after reperfusion. Hyaluronic acid was significantly lower by HyFACS+HyIAR ($P < 0.01$), indicating better functional viability of sinusoidal endothelia. Bile production, LDH leakage therein, and total bile-acid secretion were all significantly ameliorated by HyFACS+HyIAR ($P < 0.01$). Of note, HyFACS enabled significantly-efficient H_2 delivery into liver tissues during early reperfusion, while H_2 concentration by HyIAR gradually increased and surpassed that in Group-HyFACS by 12 hours after reperfusion. HyFACS+HyIAR maintained the highest tissue H_2 conc. throughout reperfusion ($P < 0.001$), followed by significant attenuation of oxidative damage (8-OHdG release, $P < 0.001$).



OS385

THE EFFECT OF DONOR CARDIOPULMONARY RESUSCITATION DURATION ON LIVER TRANSPLANTATION OUTCOME: A PROPENSITY SCORE MATCHED ANALYSIS OF NATIONAL DATA

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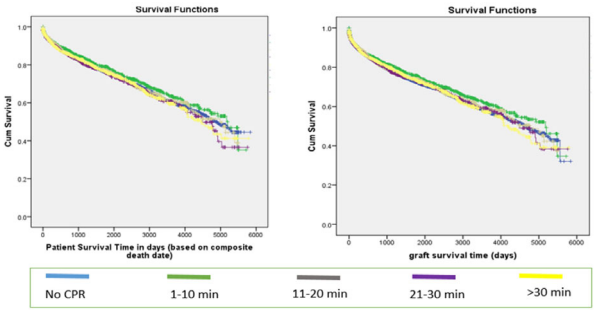
Introduction: The shortage of liver allografts is a major limiting factor for liver transplantation. The impact of cardiac arrest and cardiopulmonary resuscitation (CPR) in organ donors potentially results in ischemic organ injury and graft dysfunction.
Methods: We performed an 18-year (2001-2018) retrospective analysis of United Network for Organ Sharing (UNOS) database. We stratified the patients into two groups based on whether the donors did or did not receive CPR. The donors who received CPR were further stratified by the duration of the CPR: CPR of less than 10 minutes, CPR of 11 to 20, CPR of 21 to 30 minutes, and CPR exceeding 30 minutes. Propensity score matching was performed after adjusting for donor age, cold ischemia time, recipient age, gender, and MELD score. Our primary outcome measures were patient and graft survival rates. Secondary outcomes include primary allograft dysfunction, and hospital length of stay.
Results: 110,388 patients with liver transplantation were enrolled. After propensity score matching we included 10,244 patients (no donor CPR: 50%, 14% with donor CPR < 10 minutes, 12.6% with donor CPR 11 to 20 minutes, 8.7% with donor CPR 21 to 30 minutes and 14.7% patients with donor CPR > 30 minutes). Mean age of the population was 54.48 ± 10 years, 66% were male, and mean MELD score was 22 ± 10, mean CPR time was 21 ± 18.The post-transplant patient and graft survival rates, hospital length of stay and primary graft dysfunction were not significantly different among the groups. On multivariate regression analysis, showed CPR duration was not an independent risk factor for post-transplant graft failure.
Conclusion: Donor CPR duration does not adversely affect clinical outcomes and should not play a role in liver donor selection. Careful donor organ selection can lead to shorter wait list times and possibly extend the pool of organ donors



OS45 - SOCIOECONOMIC ASPECTS AND NEW DIRECTIONS IN KIDNEY TRANSPLANTATION

OS386 VULNERABLE ELDERS SURVEY (VES-13) SCORING IN GERIATRIC EVALUATION OF ELDERLY KIDNEY TRANSPLANT RECIPIENTS

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Background: Over the last decade, the percentage of kidney recipients older than 60 years has significantly increased. Long-term care over these patients should be defined with relevant standards and involve transplantologists, geriatricians and primary health care specialists. This extremely sensitive group of recipients require precise and standardized assessment due to the multitude of hazards and complications associated with the ageing process. Such evaluation can be achieved with VES–13 scale (Vulnerable Elders Survey). 3 or more points correlate with the increased risk of death or significant deterioration of health within two years and should entail the Comprehensive Geriatric Assessment as well as supplementary geriatric care.
Methods/materials: 300 kidney transplant recipients, 60 + years old, in various post-transplant period, were included into the study and evaluated with validated VES scale, supplemented with demographic data and questions regarding type of the post-transplant care.
Results: 94 (34,3%) patients received 3 ore more points in VES scale, 64 (71,3%) of them had high scoring (6 or 7 points) indicating urgent need for Comprehensive Geriatric Assessment and supplementary geriatric care. However, only 2 of them had received such care. VES-13 sore was associated strongly with patients physical activity: those declaring as physically active (41, 15,4%) received average of 1,34 points (SD $\pm$ 2,06), while those not performing any physical activity (75, 28,2%) were scored average of 3,65 (SD $\pm$ 2,64) points, $p < 0,05$.VES-13 evaluation correlated strongly with patient's self-assessment: recipients describing their well-being as "bad" scored average of 4,89 ((SD $\pm$ 2,27), while those presenting their physical condition as "good" or "excellent" received only 1,19 points (SD $\pm$ 1,61), $p < 0,05$
Conclusions: VES-13 can be applied as useful tool for geriatric evaluation of elderly kidney transplant recipients, identifying those in need for Comprehensive Geriatric Assessment

OS387 EXTENDING RENAL TRANSPLANTATION TO LMIC - CONVINCING POLITICIANS MAY BE THE BIGGEST CHALLENGE

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Since 2007, the UK registered charity Transplant Links (TLC) has supported the development of renal transplantation (RTx) in low and middle-income countries (LMIC), in Africa, the Caribbean and Asia. Support has included de novo program development, the extension of fledgeling programs and guidance to centres considering RTx. A bespoke approach has been taken to skill transfer based on each centres' need: on-site mentoring, the performance of living donor procedures, the facilitation of training fellowships in the UK and online learning all available by a group of TLC volunteer RTx clinicians and healthcare professionals.

TLC partner centres have now all made developmental progress, ranging from near sustainability (e.g. Trinidad), through continued extensive support (e.g. Ghana, Jamaica, Barbados) to initial mentoring (Uganda). While in each case significant progress has been made, attaining sustainability faces challenges beyond initial expertise and adequate infrastructure. Indeed, such matters can usually be addressed by mentoring and skill transfer, particularly as developing programs have clinicians eager to learn and make most of the available resources. However, more intractable is the lack of political engagement required to maintain developmental progress. In most countries, progress has been slowed by a lack of political understanding of the problems of renal failure resulting in an inadequate financial commitment that negatively affects service development and the job security of clinical staff. Such factors risk offsetting any development progress achieved through skill transfer.

Therefore, we assert that RTx program development in LMIC is enhanced by mentoring and skill transfer provided by outside experts. However, achieving sustainability in such programs is critically dependent upon political support. As such, the international transplant community not only has a responsibility to mentor clinicians

OS388 A PHASE IV, CHINESE, MULTI-CENTRE, RETROSPECTIVE STUDY ON THYMOGLOBULIN INDUCTION THERAPY IN RENAL TRANSPLANT PATIENTS RECEIVING ORGANS DONATED AFTER CARDIAC DEATH

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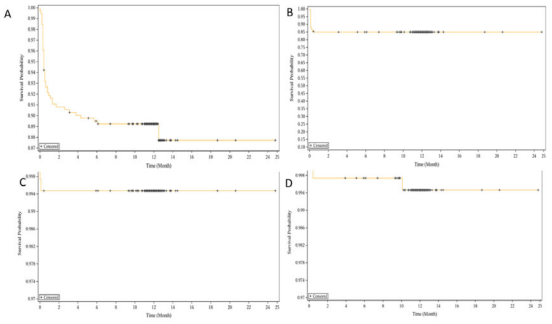
Background: Thymoglobulin induction therapy reduces acute rejection(AR) and delayed graft function(DGF). Donation following cardiac death(DCD) is associated with increased rates of DGF and AR. We report results of phase IV, multicentre study evaluating the efficacy of thymoglobulin induction therapy and risk factors for AR and DGF in DCD renal transplant recipients from China.
Methods: Between January 2012 and April 2015, patients who underwent DCD renal transplantation treated with thymoglobulin induction therapy in 6 centres in China were included. Objectives were to evaluate incidence of AR, DGF, graft and patient survival at 12 months, factors associated with AR and DGF, and safety profile.
Results: Mean accumulated dose of thymoglobulin in the 382 treated patients was 183.4 mg. Incidence of AR and biopsy proven AR(BPAR) were 11%(95% CI:8.0-14.6) and 2.6%(95%CI:1.3–4.8) respectively. The incidence of DGF, graft and patient survival were 14.9%(95%CI:11.5-18.9), 98.4%(95%CI:96.6-99.4) and 98.2%(95%CI:96.3-99.3) respectively. 12-month KM estimate (fig) for AR, BPAR and DGF were 10.8(95%CI:8.0-14.3), 2.6(95%CI:1.3-5.0) and 14.9(95%CI:11.7-19.9), while for graft and patient survival, KM estimate (Figure 1)

was 99.5(95%CI:97.9-99.9). Donor hypertension (OR:3.08;95%CI-1.19, 7.92;$P = 0.02$), warm ischemic time(OR:1.61;95%CI-1.15,2.27;$P = 0.006$), donor serum sodium level(OR:0.978;95%CI-0.96,0.99;$P = 0.02$), recipient age(OR:0.95;95%CI-0.92,0.99;$P = 0.01$) and height (OR:0.91;95%CI-0.85,0.98;$P = 0.01$) were the risk factors for AR($P < 0.05$) while donor serum creatinine level(OR:1.00;95%CI-1.00, 1.00;P = 0.04) and gender (OR:2.12;95%CI-1.08,4.43;$P = 0.03$) were risk factors for DGF($P < 0.05$). 174 patients experienced study drug-related adverse events like anaemia (14.7%), urinary tract infections(8.4%) and gastrointestinal disorders(13.9%).
Conclusion: Recombinant anti thymoglobulin induction therapy in DCD transplant recipients is effective with lower incidences of AR and DGF.

Figure 1- Kaplan Meier curve from the time of kidney transplantation to A) AR, B) onset of DGF, C) graft failure and D) patient death.



OS389 GENDER DISPARITIES, ALSO IN KIDNEY TRANSPLANTATION?

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Hospital Dr Peset

Introduction: In the last years there is an increasing interest in disparities related to gender in renal disease management. OBJECTIVES Our aim was to analyse gender disparities in our kidney transplantation environment. METHODS Retrospective study of our kidney transplanted series ($n = 1101$) until January 2019.RESULTS We compared 435 women (W) (39,5%) with 666 men (M) (60,4%). Median follow-up: 87 $\pm$ 72 months. There were no differences in recipient age, pretransplant cardiovascular risk, with the exception of smoking, more prevalent in M. Interstitial aetiology of ESRD was more frequent

in W, vascular disease in M. Sensitization percentage was higher in W, with no differences in retransplantation. Women were transplanted with a higher proportion of grafts from cerebrovascular death. Median serum creatinine was lower during the first 8 years of follow-up (p < 0,001) in W group. Graft or patient survival were similar.

When we analysed recipients < 60 years (*n* = 687): 59,5% M, 40,5% W, we observed a higher proportion of HLA sensitization percentage (p = 0,000) in W, but no differences in retransplantation, HLA compatibilities, months on dialysis or modality of dialysis. Women received a higher proportion of donors > 55 years (p = 0,01), female sex (p = 0,01) and worse creatinine (p = 0,01), without differences in cold ischemia time or immunosuppression. A higher graft failure was observed in W < 60 (p = 0,04), related to chronic dysfunction (p = 0,004), without differences in patient survival. Independent variables related to graft failure in W < 60 were prior sensitization (HR: 2,14, p = 0,000) and donors > 55 years (HR: 1,50, p = 0,009). CONCLUSIONS We didn't find any disparities related to recipient gender in graft quality, treatments or evolution postransplantation. we highlight the lower graft survival in women under 60 years old. The female gender, could condition a negative bias in the type of donors received that may be involved in a worse graft survival, above all in younger recipients.

OS390 EFFECT OF TIMING FROM BRAIN DEATH TO ORGAN PROCUREMENT ON DELAYED GRAFT FUNCTION AND GRAFT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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Background: Brain death may impair organ function through increased inflammatory activation, but it is still unclear how the duration of brain death affects transplant outcomes. Our aim was to assess the effect of time from brain death to organ procurement on kidney allografts in a nationwide cohort.
Methods: Consecutive deceased donor kidney transplantations in our country from June 2004 to December 2017 were followed until death, graft loss, or October 2018. The effect of time from brain death to organ perfusion on delayed graft function (DGF) and graft survival were analysed in multivariable models.
Results: Altogether 2388 kidneys from 1356 deceased donors were included. The median time from declaration of brain death to cold perfusion was 10 hours (range 3-38 hours). Of all kidneys transplanted 789 (33%) suffered from delayed graft function and 60 (2.5%) never gained function. Altogether 322 patients died and 269 grafts were lost during the follow-up (median 58 months). No association was seen between the time from brain death to organ procurement and the risk of DGF. In univariable models, shorter time from brain death to organ perfusion was associated with lower graft survival. In a multivariable model adjusted for donor factors (age, gender, cause of death, resuscitation, hypertension, kidney function, cold ischemia time), recipient factors (age, gender) and posttransplant events (delayed graft function, acute rejection), lowest quartile of time from brain death to organ perfusion (<7.8 hrs) was associated with an increased risk of graft loss (HR 1.35, 95% CI 1.13-1.62).
Conclusions: No benefit from shorter time from brain death to organ procurement was observed. On the contrary, shorter time was associated with an increased risk of graft loss. Reasons behind this observation require further exploring.

OS391 COST SAVINGS GENERATED BY PERFORMING PRE-EMPTIVE KIDNEY TRANSPLANTATION (KT) OVER TRADITIONAL DIALYSIS THERAPY: A COST ANALYSIS

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Mayo Clinic

Objective: To assess the cost savings generated by performing pre-emptive KT in comparison to dialysis therapy prior to KT using economic evaluation methods.
Design: We performed a cost analysis by building Markov Models in TreeAge Pro and using Monte Carlo micro simulation methods to obtain estimates of renal replacement therapy costs over a period of 5 years. We included two arms: those with pre-emptive KT and those who first initiated dialysis. Markov health states included improvement, wait list (with or without receiving dialysis), post-transplant period, graft failure, and death. Separate subtrees and health states were created for living and deceased donors to accommodate the probabilities of patient and graft survival. Models were run separately for commercial (C) and Medicare (M) populations using appropriate cost estimates. Patients fell out of the model if they experienced graft failure, death, or improvement. Model estimates, such as transition probabilities and costs, were obtained from existing literature on KT.
Population Studied: We simulated 10,000 hypothetical patients through the model to obtain 5-year cost estimates, with the purpose of the model representing the average M or C patient. Resulting cost estimates are relevant to the average adult patient listed for a first, kidney-only transplant.
Results: Mean (median) cost estimates over 5 years for dialysis were $550,548 ($630,270) with a range of $6,243 to $799,061 for C and $355,105 ($404,712) with a range of $3,951 to $511,424 for M. In comparison, estimates for pre-emptive KT were $147,643 ($144,835) with range $1,207 to $201,308 and $123,525 ($113,725) with range $948 to $168,823 for C and M patients respectively. This amounts to average (median) cost savings in the vicinity of $403,000 ($485,000) for patients on C and $232,000 ($290,000) for patients on M.
Conclusions: Pre-emptive KT generates significant cost savings compared to dialysis with similar or better patient and graft survival.

OS392 RED CELL DISTRIBUTION WIDTH: A BIOMARKER OF AGEING IN RENAL TRANSPLANT RECIPIENTS?

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Introduction: Red cell distribution width (RDW) is a measure of erythrocyte size variability, calculated as part of a standard full blood count test. High RDW is associated with risk and severity of age-related diseases. Premature ageing is prevalent in chronic kidney disease patients but difficult to quantify objectively. We aimed to determine whether RDW could act as a biomarker of premature aging and better determine the risk of transplantation in a cohort of renal transplant recipients.
Methods: We retrospectively analysed 723 records of patients who received kidney transplants in Addenbrooke's Hospital between 2014-2018. Patients were stratified according to high or normal RDW levels before transplantation. Primary endpoint was patient survival time from transplant. Secondary outcome was association of high RDW with age-related diseases. Groups were compared using Chi-squared, Fisher's exact test or Wilcoxon rank sum test. Survival outcomes were analysed using the log rank test and cox-proportional hazards using a step-wise variable selection method.
Results: 701 patients were suitable for analysis. High RDW before transplant was associated with cerebrovascular disease, coronary artery disease, hypertension and multimorbidity for age related diseases.

Pre-transplant high RDW was associated with increased mortality (HR 3.19, 95% CI 1.40–7·25, p = 0·0.0058). This carried a greater effect than raised pre-transplant CRP (HR 2.74, 95% CI 1.07-7.00, 0.0351) and age at transplant (HR (per ten years) 1.33, 95% CI 0.97-1.84, 0.0792).
Conclusion: The new UK kidney allocation scheme aims to balance the risk of donors to recipients so it is increasing important that we can objectively assess the risk of transplantation for potential recipients. RDW shows great promise as a simple, cheap biomarker of recipient risk that may inform future organ allocation.

OS393 IMPROVED KIDNEY AND SIMULTANEOUS PANCREAS KIDNEY TRANSPLANT OUTCOMES FROM CDCD DONORS USING NORMOTHERMIC REGIONAL PERFUSION (NRP)

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Background: Normothermic regional perfusion improves the outcomes of liver transplantation from cDCD donors. Herein we report the effect of NRP on the outcome of kidney transplants and simultaneous pancreas-kidney transplants (SPK) in the UK.
Methods: First adult (≥18) transplants from UK DCD donors aged ≥ 16 between 01/01/2011 and 31/12/2017 with a one-year follow-up were included in the analysis. One-year graft survival was determined using Cox proportional hazard models adjusted for donor age and cause of death, recipient age, time on the waiting list, diabetic status, ethnicity and length of cold ischemia time and HLA matching for kidney graft survival; and donor age, BMI and recipient waiting time for pancreas survival. eGFR was calculated using the MDRD equation and the effect of NRP was determined using a general linear model adjusted for the factors that affect graft function in the UK (donor age, height, diabetes, hypertension, cold ischaemic time, recipient sex, ethnicity, age and waiting time).
Results: The rate of graft failure for NRP kidney transplants was comparable with non-NRP kidneys [5/120 (4%) vs 290/4605 (6%)]. There was no difference in SPK graft failures between NRP [1/15 (7%)] and non-NRP transplants [29/239 (12%)]. There was no difference between the function of the pancreas or kidney in the SPK transplants.

Table 1 shows the DGF rate and the mean eGFR at 12 months for the kidney transplants alone in the abdominal NRP group compared with the non-NRP group.

	No. Transplants	DGF rate (%)	Mean eGFR (ml/min/1.73 m2)
Abdominal NRP	100	27%	52.8
No abdominal NRP	4231	35%	45.3

When risk adjusting for the factors in the general linear model, there appeared to be a statistically significant difference between kidney transplants from NRP donors and non-NRP donors with an expected increase in the 12-months eGFR of 4 ml/min/1.73 m2($p = 0.04$) if abdominal NRP was used.
Conclusions: The use of NRP at the time of organ procurement in cDCD leads to increased kidney utilisation with a significantly better one-year kidney transplant function with a low graft loss.

OS46 - KIDNEY REJECTION AND HISTOLOGY: THE ROLE OF DSAS IN KIDNEY GRAFT REJECTION

OS394 RISK FACTOR AND CLINICAL COURSE OF ANTIBODY-MEDIATED REJECTION BY DE NOVO DSA AFTER RENAL TRANSPLANTATION

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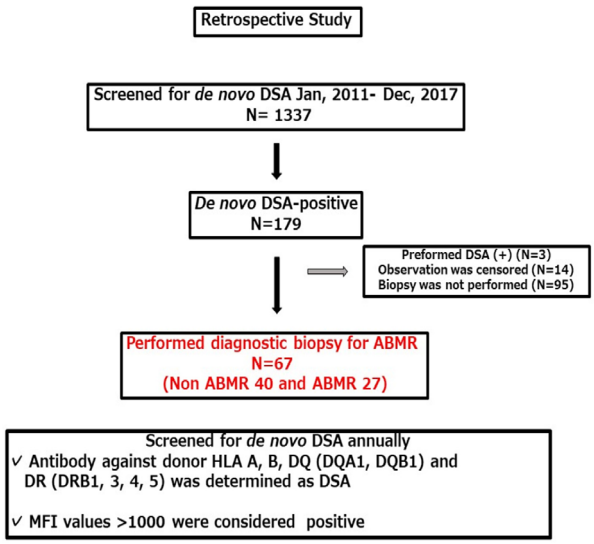
Nagoya Daini Red Cross Hospital

Background: Antibody-mediated rejection (ABMR) by *de novo* donor specific antibody (DSA) is one of main causes leading to poor outcomes after renal transplantation. However, incidence and risk factors of ABMR in cases with *de novo* DSA are still unclear. In addition, poor prognostic factors after development of ABMR haven't been clarified either.
Method: For the purpose of investigating incidence and treatment progress of ABMR, retrospective study was conducted on 67 renal transplant recipients with *de novo* DSA in whom diagnostic biopsy for ABMR was performed.
Result: Twenty seven of 67 (40.3%) were diagnosed as ABMR. In cases with ABMR, number, MFI of DSA and incidence of T cell-mediated rejection were higher than in cases without ABMR (1[1, 1] vs 1[1, 2], $P = 0.002$, 5016[1717, 13801] vs 13538[5757, 20017], $P = 0.006$ and 2/40 vs 7/27, $P = 0.027$). In addition, the former was younger than the latter (39.0[29.0, 48.5] vs 53.5[39.0, 62.3], $P = 0.006$). Although treatment including rituximab and apheresis was performed in cases with ABMR, estimated glomerular filtration (GFR) decreased > 30% in 15 of 27 cases a few years after diagnostic biopsy. Cases with overt proteinuria or a declining trend of GFR at the time point of diagnosis of ABMR had poor outcomes. On the other hand, renal function was stable in most cases that were diagnosed ABMR-negative in first diagnostic biopsy.
Conclusion: ABMR with a GFR decline tendency or overt proteinuria at diagnosis is resistant to treatment with rituximab and results in poor outcomes. Therapeutic effect on subclinical ABMR should be clarified in future.



OS395 CLINICAL RELEVANCE OF DONOR SPECIFIC ANTIBODIES DIRECTED AGAINST HLA DR51/52/53 IN KIDNEY TRANSPLANTATION

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Background: The monitoring of anti-HLA antibodies after kidney transplantation(KT) is essential to prevent antibody mediated rejections(ABMR) which influence graft survival. As reported in literature, de novo donor specific antibodies(DSA) are mostly directed against HLA class II antigens, with the predominance of the HLA-DQ specificity. If DSA directed against HLA-DR appear to be less dangerous than their HLA-DQ counterparts, only few studies reported the clinical relevance of HLA class II DSA to non-HLA DRB1 antigens, namely HLA-DR51/52/53, after KT.Our work aims to study the involvement of DSA directed against HLA-DR51/52/53 in KT.
Methods/Materials: Our study included 11 kidney transplant patients which developed de novo DSA to HLA DR51/52/53, alone or associated with DSA to HLA-DQ, after KT. The mean age of patients was 34.5 ± 4.95 years and the sex-ratio(M/F) was 0,5. All KT were from living related donors. Anti-HLA antibodies were detected using the solid-phase assay Luminex technology (Lifecodes LMX Immucor®). HLA class II specificities were identified using the Luminex single antigen assay(Lifecodes LSA2, Immucor®).
Results: Among patients, 45.45% developed an association of DSA against HLA-DR 51/52/53 and HLA-DQ. HLA-DR53 specificity was the most frequent (63%), while HLA-DR52 and DR51 specificities were found in only 25% and 12% of cases, respectively. Almost all patients(88%) did not develop anti-HLA-DRB1 antibodies. Furthermore, 87.5% of patients had impaired renal function, two of whom returned to dialysis, and half of them had features of acute or chronic ABMR in renal biopsies. The median of mean fluorescence intensities (MFI) of DSA was 8700 ± 5441. Moreover, patients with DSA to HLA-DR+DQ had significantly higher MFI than patients with DSA to HLA-DR51/52/53 alone.
Conclusion: Although the clinical relevance of DSA directed against HLA DR51/52/53 has not be clearly established in KT, their association with a poor clinical outcome was noted in our study.

OS396 HIGH PERCENTAGE OF MIXED GRAFT INJURIES IN KIDNEY TRANSPLANT RECIPIENTTS REVEALED DE NOVO DSA AND NON DSA ANTI HLA ANTIBODIES- 12 MONTHS PROTOCOL BIOPSY STUDY

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[1]University Clinic od Nephrology Skopje; [2]Univrsity "Sts Cyril and Methodius", RN Macedonia

Single antigen bead technology enabled detection of DSA and Non-DSA anti HLA antibodies(HLA-abs) who are responsible for acute and chronic antibody mediated rejection.
Methods: 50 pts with living (42) and deceased donor (8) were included in a 12 months prospective study. HLA-abs were analyzed using LAB Screen mixed kit in the 1st, 6th and 12th months after transplantation, divided in group 1 (HLA+) and 2 (HLA-). A total of 48 protocol biopsies were performed exactly on the 12th month after the surgery Histological findings were classified according to BANFF 13 modified and uploaded system. Mixed injuries were defined when ABMR, TCMR, BL or IF/TA are present.
Results: 17 of 50 revealed de novo HLA-abs (5 DSA and 12 non-DSA). The biopsies were categorized as normal (cat) in 15 pts, pure ABMR (cat 2) and pure TCMR (cat 4) in 2, 4 pts as Borderline (cat 3), IF/TA (cat 5) in 5 pts and other 5 pts (cat 6). 17 biopsies were classified as mixed injuries,

In the group of 17 HLA+ recipients 4 biopsies (23%) were classified as normal compared with 11 (33%) in HLA- group. 12 biopsies in HLA+ group (70%) were classified as a mixed rejections compared with 8 (21%) in HLA- group. Most of the mixed injuries reached the criteria for ABMR or "suspicious" ABMR combined with BL(7), IF/TA (8 case) or TCMR (4). The presence of ABMR and mixed rejections in HLA- group od patients relativizes the role of antibodies a as single factor in the processus of rejection.

Conclusion: Our data confirm that enlarging the criteria for ABMR and other graft injuries, we are facing a big confusion when we have to decide what is going on. Therefore it is probably time for providing a system for molecular assessment of graft biopsies.

OS397 MHC CLASS I MASKING AS A PRECONDITIONING STRATEGY TO MINIMIZE THE DELETERIOUS EFFECTS OF DONOR SPECIFIC ANTIBODIES TO THE KIDNEY TRANSPLANT

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Background: Patients immunized against major histocompatibility complex (MHC) have a lower access to transplantation and the presence of donor specific antibodies (DSA) strongly impacts kidney graft survival. We hypothesized that masking MHC on the graft endothelium could be an early first step to protect the graft against DSA.
Methods/Materials: In a porcine model of alloimmunisation, we tested in vitro the complement-dependent cytotoxicity (CDC) of DSA on endothelial cells (EC), with or without a monoclonal antibody anti- porcine class I MHC (JM1E3) preincubation, by MTT assay or FACS. We assessed JM1E3 and DSA fixation on EC in vitro by FACS and then perfused porcine kidney grafts on a hypothermic perfusion machine with JM1E3 and assessed its binding by immunofluorescence on sequential biopsies.
Results: In vitro, JM1E3 was saturating the endothelial cell surface at 1 μg/mL. After incubating EC with JM1E3 1 μg/mL in vitro from one hour (up to 24 h), complement dependent cytotoxicity of DSA was significantly lower than without preincubation, with a reduction of median cytotoxicity of 80% ($p = 0.0286$). DSA fixation at EC surface was lower after saturating doses of JM1E3 preincubation, but not totally inhibited. In the ex vivo hypothermic kidney perfusion on Waves machine with 1 μg/mL JM1E3 in IGL perfusion solution®, we were able to detect JM1E3 in the glomeruli and peritubular capillaries at 30 minutes and one hour.
Conclusion: MHC class I masking with the monoclonal antibody JM1E3 protect EC against DSA complement dependent cytotoxicity in vitro and binds to the graft endothelium during graft perfusion ex vivo. MHC class I masking ex vivo during transplant conservation may be part of a global preconditioning strategy to lower DSA damages to the kidney transplant.

OS398 MONITORING PATIENT DSA LEVELS AT SPECIFIC DAYS WITHIN EARLY STAGE POST HLA-I KIDNEY TRANSPLANT CAN INDICATE LIKELIHOOD OF GRAFT FAILURE

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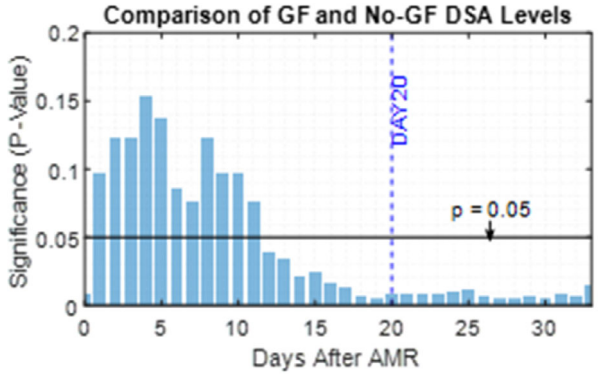
Background: Donor specific antibodies (DSA) following HLA-incompatible kidney transplantation have been shown to be of value in determining the long term graft survival. For example, Higgins et al. observed that an early fast rise and subsequent steep fall of DSAs within the first few months is associated with acute antibody mediated rejection (AMR) - which in turn may reduce graft function. Though incredibly insightful its value has not been fully appreciated in practice owing to the costly nature of measuring DSA on a daily basis. This research seeks to identify key periods of time which are of most prognostic value to measure – such as risk of graft failure (GF).
Method: DSA levels were collected up to daily in 90 patients who underwent HLAi kidney transplantation. 50 patients underwent early AMR were assessed for relation to GF. Daily accumulative DSA levels were compared for groups based on DSA against Class 1, 2 or both using the Wilcoxon rank sum test.



Results: The left figure presents the calculated p-values along the day of AMR comparing GF and no-GF groups for the patients with C1&2 DSA. A significant period is shown for days 12-33 ($p < 0.05$). Looking in detail on day 20 after AMR allowed for identification of a threshold DSA value of 10,000. Using this to split the cohort a clear distinction between groups is shown on the right-hand graph with a log rank test yielding 0.01. Observations show a nine-fold increase in chance of GF if DSA threshold exceeded.
Conclusion: This study has found a reliable method of predicting GF in HLAi kidney transplant patients who possess C1&C2 DSA and have had an AMR episode. Testing of antibodies, an expensive process, need not be done on a daily basis but could effectively be done only once in the range 12-33 days post AMR. If the DSA value exceeds 10,000 the patient is nine times as likely to experience GF.

OS399 INCREASED RISK OF ACUTE ANTIBODY-MEDIATED REJECTION IN CDC-NEGATIVE MALE TO FEMALE SPOUSAL KIDNEY TRANSPLANTATIONS WITH PREFORMED DONOR SPECIFIC ANTIBODIES

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Background: Shortage of deceased donor kidneys has led to an increase in the number of living unrelated kidney donors, in particular spousal donors. Female recipients of a spousal kidney have an increased risk for pre-immunization and acute antibody-mediated rejection (ABMR). The aim of this study is to assess the incidence of ABMR and preformed donor specific antibodies (pDSA) in living unrelated donors (LURD) and to identify risk factors for acute ABMR.
Methods/Materials: We identified all 349 ABO compatible, CDC-crossmatch negative, LURD transplants performed at our transplant center between 1997 and 2015. All for-cause biopsies were classified according to the BANFF 2018 classification. All patients with ABMR were retrospectively tested for the presence of pDSA with multiplex and single antigen tests (Luminex®). Risk factors for immunization were extracted from personal health records and questionnaires.
Results: The overall incidence of biopsy-proven acute rejection in the first 6 months was 20% (TCMR: 85%; ABMR: 15%); median time to onset of ABMR was 8 days (range 5-75 days). Outcome was poor in ABMR as compared to patients with TCMR or those w/o rejection (kidney graft loss or eGFR < 30 ml/min at month-6: 36%, 12% and 2% respectively). Eight patients with ABMR were female (73%) and six (75%) of these were recipients of a spousal kidney. Of these spouses 4 gave birth to children of the kidney donor and 2 received blood transfusions prior to transplantation. Retrospectively 80% of spousal recipients with ABMR had pDSA in the multiplex or single antigen test.
Conclusion: Female spousal kidney recipients have a relative high risk of ABMR. Traditional methods for detecting pDSA are not sensitive enough to rule out pDSA. Multiplex and single antigen should be included in the standard work-up of potential female spousal kidney transplant recipients to prevent ABMR and guide the option of indirect (cross-over) donation.

OS400 A HUMAN EX VIVO MODEL OF ANTIBODY MEDIATED REJECTION IN THE KIDNEY USING NORMOTHERMIC PERFUSION AND HLA & ABO ANTIBODIES

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Background: Currently, no human experimental model of antibody mediated rejection (AMR) exists. Such a model would be vital to investigate mechanisms and therapeutic interventions. The aim of our work is to establish the first human kidney model of AMR using ex-vivo normothermic perfusion (EVNP).
Methods/Materials: We developed AMR models caused by HLA incompatible antibodies (HLAi) and ABO antibodies (ABOi). 10 discarded human kidneys (via NHSBT) were used (including 3 pairs). All kidneys underwent standard pre-experimental EVNP stabilization. For each experiment, we injected fresh frozen plasma as a source of complement/coagulation factors & either 6 mg/ml of W6/32 anti-class 1 HLA antibody (for HLAi model) or (pre-tested) high blood group antibody-titre FFP alone (for ABOi model). EVNP renal blood flow index (RBFi ml/min/100 g), C3 desArg were taken with tissue biopsies. Our endpoints were: haemodynamic changes, thrombosis and biopsy proven complement fixation.

Results: A total of: 3 HLAi, 5 controls and 2 ABOi experiments were performed. Between 30-45 minutes post-antibody injection, all 3 HLAi (Fig 1) and one high-titre ABOi kidney showed a catastrophic collapse in RBFi with perfusion time (change in RBFi ranging from 0 to -122 ml/min/100 g and 0 to -93.6 ml/min/100 g for HLAi and ABOi kidneys, respectively) compared to controls. There was evidence of complement activation: mean C3 desArg % change from baseline = +115% HLAi; +199% controls; +103% ABOi, kidneys. All HLAi kidneys fixed C4d on biopsy but controls and ABOi kidneys did not. Histological microvascular thrombi were present in one HLAi and one ABOi kidney. Fig 1 shows drastic RBFi reduction in 3 HLAi kidneys after adding W6/32 antibody.
Conclusion: We have established the first human model of AMR. We induced hyperacute AMR in both HLAi and ABOi models, with evidence of complement activation & renal thrombosis. This model offers a unique platform for testing localised therapeutic agents.

OS401 CLINICAL IMPACT OF PREFORMED AND DE NOVO DONOR SPECIFIC ANTI-HUMAN LEUKOCYTE ANTIGEN ANTIBODIES IN KIDNEY TRANSPLANTATION

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Background: Donor specific anti-HLA antibody (DSA) is an important factor in short and long-term allograft outcomes after kidney transplantation (KT). However, the clinical impact of preformed and de novo DSAs on the post-transplant clinical outcome in kidney transplant recipients (KTRs) is still uncertain. The aim of this study was to evaluate the impact of preformed or de novo DSAs on graft survival, and incidence of antibody-mediated acute rejection (AMR).
Methods/Materials: We retrospectively analyzed the medical records of 254 patients performed KT between January 2013 and November 2017. The examined times of DSA were at pre-transplant, 3, 6, 12 months and annually post-transplant. We divided KTRs into three groups; noDSA group, group with preformed DSA (pDSA group), and group with de novo DSA (dnDSA group). We investigated the incidence of antibody-mediated rejection (AMR), graft and patient survivals according to DSAs, and risk factors related with graft failure.
Results: Among the study population, pDSA group was 21 patients (8.3%), and dnDSA group, 39 patients (15.4%). The incidence of AMR was significantly higher in pDSA and dnDSA groups compared to noDSA group (28.6%, 22.9%, and 6.4%, $P < 0.001$), but, there was no significant difference between pDSA and dnDSA groups. Death-censored graft survival rate was significantly lower in pDSA group in comparison with dnDSA group until 3 years after KT, but lower in dnDSA group in comparison with pDSA group since 3 years after KT ($P = 0.05$). In multivariate analysis, biopsy-proven acute rejection and tacrolimus trough level at 3 months after KT was an independent risk factor for graft failure. Patient survival rate showed no difference among them.
Conclusion: Adequate desensitization in KTRs with preformed DSA should be performed for short-term clinical outcome at the early period after KT, and de novo DSA should be screened for long-term outcome to prevent AMR and graft loss.

OS47 - INFECTIONS IN LIVER AND RENAL TRANSPLANT RECIPIENTS

OS402 LONG-TERM FOLLOW-UP AFTER LIVER TRANSPLANTATION FOR HEPATITIS B RELATED CIRRHOSIS: A SINGLE CENTER COHORT

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Introduction: Hepatitis B virus (HBV) related cirrhosis represents one of the most common indications for liver transplantation (LT), both for decompensated liver disease and for hepatocellular carcinoma. Introduction of combined prophylaxis of high barrier nucleo(s)tide analogues together with Hepatitis B immunoglobulins (HBIG) has significantly changed the rate of post-transplant disease recurrence. This study aimed to assess long-term graft and patient survival of patients who underwent LT for HBV related cirrhosis, focusing on prevalence of post-LT HBV recurrence.
Methods: All adults with HBV related cirrhosis listed for LT at Padua University Hospital between 01.2006-12.2016 were retrospectively evaluated. Patients without cirrhosis, with hepatitis delta coinfection and with acute liver failure were excluded. For each patient, clinical characteristics at time of waitlist registration and at time of LT were collected. Hepatitis B re-infection was defined by positive HBV DNA serum levels. Graft and patient survival was analyzed using Kaplan-Meier function.
Results: A total of 138 patients with HBV related cirrhosis (M/F 121/17, mean $\pm$ SD age 56.3 $\pm$ 8 years, hepatocellular carcinoma 63%) were wait-listed in the study period, and 78 (56.5%, M/F 68/10, mean MELD score at LT 17 $\pm$ 8) underwent LT after a mean time of 11.3 $\pm$ 16 months. Only two patients underwent early re-LT. All patients received combined prophylaxis with high barrier NUCs and HBIG; in particular 57% received i.m. administration and 43% s.c. administration. One- and 5-yr patient survival was 84% and 80%, respectively, without any episode of HBV recurrence defined as positive HBV DNA serum level.
Conclusions: Hepatitis B related cirrhosis has remained a stable indication to LT overtime in Italy, with optimal rates of graft and patient survival. Combined prophylaxis represents a highly effective strategy in preventing disease recurrence after liver transplantation.

OS403 LONG-TERM OUTCOME IN KIDNEY TRANSPLANT RECIPIENTS WITH HCV INFECTION WITH OR WITHOUT SUSTAINED VIROLOGIC RESPONSE

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Background: Treatment of HCV-infected kidney transplant recipients (KTRs) had been recommended only when the benefits of treatment clearly outweigh the risk of allograft rejection due to interferon-based therapy. The recent IDSA guideline provides treatment of HCV-infected persons is recommended for all patients with chronic HCV infection except those with a short life expectancy. The approval of new DAAs (direct-acting antivirals) has made it possible to treat almost all HCV-infected KTRs regardless of any genotypes or impaired graft function.
Purpose: From January 1972 to January 2019, more than 2800 kidney transplantations were performed at Nagoya Daini Red Cross Hospital. HCV PCR has been available since 2007 in Japan. HCV-infected recipient was defined as that with HCV PCR positive more than once during the follow-up period, allowing 54 HCV-infected KTRs to be included in this study. We investigated long-term outcome in HCV-infected KTRs with or without SVR (sustained virologic response).
Result: By the end of January 2019, 20 have achieved SVR, whereas 34 have been infected with HCV. During the follow-up period, 1 (5%) died due to rupture of abdominal aortic aneurysm in achieved SVR group, whereas 14 (41%) died in HCV infected group. The causes of death were liver failure, hepatocellular carcinoma, malignant cancer except liver, sepsis, myocardial infarction, cerebral hemorrhage, suicide, and sudden death. Twelve in achieved SVR group compared to 1 in HCV infected group lost their grafts. Kaplan-Meier estimates shows long-term patient and graft survival were significantly lower in HCV infected group than in achieved SVR group ($p = 0.001$ and $p = 0.00014$, respectively).
Conclusion: Achieved SVR in KTRs is associated with better long-term patient and graft survival. HCV infected KTRs without liver failure, included treatment failure by previous interferon-based therapy, should be treated by using recent DAAs as soon as possible.

OS404 LIVER TRANSPLANTATION FOR HEPATITIS DELTA RELATED CIRRHOSIS: A SINGLE CENTER COHORT

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Hepatitis D virus (HDV) related cirrhosis has been a stable indication for liver transplantation in the last decades, both for decompensated disease and hepatocellular carcinoma (HCC). Post-transplant graft and patient survival has significantly improved due to lowering rate of viral recurrence. This study aimed at assessing the evolution of indications in wait-listings and transplantation for HDV related liver disease, as post-LT graft and patient survival. All patients with HDV related cirrhosis who were listed for LT at Padua University Hospital between 2006-2017 were retrospectively evaluated. Patients with acute liver failure were not included. For each patient, indication for LT (decompensated cirrhosis vs HCC), severity of liver disease, outcome in the waiting list were assessed. For patients who underwent LT, long-term graft and patient survival, post-LT medical and surgical complications and rate of viral recurrence was assessed. Sixty-five (male/female 40/25, median age $\pm$ IQR 52.9 $\pm$ 13.4 years, 43.1% HCC) patients with definite diagnosis of HDV related cirrhosis were registered in the waiting list (WL) between 2006-2017. Overall prevalence of HDV cirrhosis as indication to wait-listing was 5.4%, remaining stable over time. Median $\pm$ IQR Model for end-stage liver disease (MELD) score was 17 $\pm$ 10. Thirty-eight (58.5%) patients experienced at least one decompensating event in the WL, mainly bacterial infection or hepatocellular carcinoma (20% and 18.5%, respectively). Mortality in the WL was 20%, whereas 42 (63%) patients underwent LT. One- and 5-year post-LT survival was 85% and 77% for patient and 76,9% e 71,1% for the graft. All but two patients received post-LT combined prophylaxis with HBV immunoglobulins

and nucleos(t)ide analogues, without any episode of viral recurrence. HDV related cirrhosis remained a stable indication to LT in the last decade, displaying optimal graft and patient survival and absence of post-LT viral recurrence.

OS405 DAA TREATMENT IN PATIENTS UNDERGOING LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: DOES TREATMENT TIMING CHANGE HCC RECURRENCE RISK?

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Introduction: Since the widespread adoption of new direct antiviral agents (DAA), the approach to HCV infection has deeply changed, as almost all the patients can be cured regardless the stage of liver disease. However, conflicting evidences have been reported regarding the risk of recurrence of hepatocellular carcinoma (HCC) in patients undergoing liver transplantation (LT). In particular, data on the impact that the timing of DAA treatement could have in terms of risk of tumoral recurrence after LT, are still scarce.
Materials and methods:: All HCV patients transplanted for HCC and treated with DAAs at Multivisceral Transplant Unit, were retrospectively evaluated. For each patient clinical, serological and virological data were collected. HCC characteristics ware retrieved from pathological assessment of liver explants and recurrence-rates were calculated. Patients treated with DAA while waitlisted were compared with those treated in the post-LT setting.
Results: Fifty patients were enrolled, 18 of which were treated while awaiting LT and 32 afterwards, achieving sustained viral response (SVR) in 94% of cases in both groups (p=NS). Histopathological analysis showed no differences in terms of median number and total tumor volume of HCC nodules, tumor differentiation or microvascular invasion. Median follow-up after LT was 21 and 36,5 months, for patients treated in the pre- and post-LT setting, respectively. During the follow-up 2/18 (11%) and 3/32 (9.3%) patients experienced HCC recurrence (p=NS), respectively. All of these patients did achieve SVR after first DAA course, except for one patient treated after LT, which relapsed after both SOF/RBV and DCV/SOF-based regimens.
Conclusions: Post-transplant HCC recurrence rates in both our cohorts were similar to the internationally reported ranges, with no higher risk. Furthermore, the timing of antiviral treatment did not seem to modify the risk of recurrence, either if started in the pre or post-LT setting.

OS406 HEPATITIS C VIRUS CAN BE ELIMINATED FROM A PREVALENT KIDNEY TRANSPLANT RECIPIENT POPULATION: A SINGLE-CENTRE STUDY IN THE DIRECT-ACTING ANTIVIRALS ERA

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Background: Direct-acting antivirals (DAAs) have recently revolutionized the treatment of hepatitis C (HCV) infection. Although previous studies have reported positive results with DAAs after kidney transplantation (KT), its impact on the real-world prevalence of HCV viremia in prevalent kidney transplant recipients (KTR) remains ill-defined.
Methods: We retrospectively reviewed the HCV status (serology, polymerase chain reaction) of all KTR followed at our outpatient KT clinic between 01/2014 and 12/2018 ($n = 1451$). We calculated the evolution of the prevalence of HCV viremia (HCVv) over this period and reviewed the clinical features of KTR treated with DAAs while having a functioning graft.
Results: Out of 1451 KTR, 22 (1.52%) had HCVv while having a functioning graft in 2014-18. From 2014 to 2018, annual prevalence of HCVv dropped from 1.97% to 1.81%, 1.77%, 1.79% and 0.43%, respectively ($p < 0.001$). Fourteen KTR were treated with DAAs (sofosbuvir/velpatasvir, $n = 4$; elbasvir/grazoprevir, $n = 5$; sofosbuvir/daclatasvir, $n = 2$; sofosbuvir/ledipasvir, $n = 2$; ombitasvir/paritaprevir/dasabuvir, $n = 1$), a median of 197 months (ranges: 5-374) after KT, mostly (79%) in 2017 after reimbursement of DAAs for KTR in Belgium. None of the treated KTR experienced graft loss, acute rejection, *de novo* donor specific antibody occurrence or allograft dysfunction during or after DAAs treatment; however, 2 patients died 14 months (B-cell lymphoma, despite sustained virological response (SVR) at 12 weeks after treatment) and 7 months (metastatic hepatocarcinoma, no SVR12) after DAAs initiation, respectively. SVR12 rate was 93%. Among HCVv KTR not treated with DAAs ($n = 8$), 2 lost their graft and 5 died. The current prevalence of HCVv in our cohort is 0.08% with a single patient to treat (ongoing).
Conclusion: The increased use of DAAs led to a dramatic decrease of HCVv prevalence in our cohort of KTR. DAAs use was safe and effective. The elimination of HCV in prevalent KTR is now possible.

OS408 PREVALENCE OF ACTIVE HEPATITIS E VIRUS INFECTION AND EFFICACY OF RIBAVIRIN TREATMENT IN RENAL ALLOGRAFT RECIPIENTS

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Hepatitis E virus (HEV) genotype 3 infection frequently progresses to chronic disease with persisting HEV viremia in immunocompromised patients. Here, we evaluated the prevalence of HEV infection in renal allograft recipients and investigated the efficacy and tolerability of ribavirin monotherapy.

A total of 947 recipients on average 8.7 years posttransplant were screened for anti-HEV IgG, IgM and HEV-RNA. Sixteen HEV-viremic renal allograft recipients were treated with ribavirin for 12 weeks. HEV-RNA concentration, laboratory and clinical parameters were assessed at baseline, during therapy and 12 weeks after treatment cessation. HEV-genotyping was performed in all HEV-viremic patients.

Past HEV infection was detected serologically in 18% of the renal allograft recipients. Ongoing HEV replication was found in 16 recipients (all genotype 3). Unanimously, distinct HEV-sequences were revealed in all HEV-viremic patients. At start of ribavirin treatment, median HEV-RNA viral load was 4.3x106 (8000-5.0x106) IU/mL. 94% of HEV-infected allograft recipients showed a sustained virological response 12 weeks after treatment cessation. Ribavirin treatment was associated with rapid decrease in liver enzymes and rare occurrence of anemia.

Prevalence of active HEV infection is important in renal transplant patients without signs of nosocomial infection. Ribavirin treatment was safe and effective.

OS409 THE ROLE OF BK POLYOMAVIRUS GENOTYPES IN POSTTRANSPLANT OUTCOME: PROSPECTIVE STUDY

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Background: BK polyomavirus (BKPyV) reactivates in 20–40% after kidney transplantation and causes BK virus-associated nephropathy (BKVN) in 1–10% cases with potential detrimental effect on allograft survival. Four genotypes of BKPyV have been recognized so far according to variations of viral protein 1 (VP1), however their biological implication is not fully understood.
Methods/Materials: In total, plasma and urine samples from 223 kidney transplant recipients and theirs 173 donors were screened by PCR for BKPyV presence during the first year after kidney transplantation. The VP1 (372 bp long region) epitope of BKPyV isolates from urine were genotyped by direct sequencing and phylogenetic analysis with known published sequences was performed. BKPyV serology was assessed in all plasma samples by ELISA assay with virus-like particles as an antigen.
Results: PCR screening showed positive BKPyV viremia (>10^4) in 14 (6.3%) and viruria (>10^7) in 47 (21%) patients during the first 6 months after kidney transplantation. All BKPyV urine isolates were either genotype Ib-2 (69%), IVc-2 (27%) or genotype Ib-1 (4%). 9 patients developed BK virus-associated nephropathy during follow-up. 6 months renal function was comparable between patients with and without BKVN [S-Cr 125 μmol/ (IQR 99; 169) vs. 116 μmol/L (IQR 99; 146), respectively, p = 0.57]. Most of the patients (89%) with BKVN were genotyped as Ib-2 and in none of them was BK nephropathy accompanied by rejection or associated with previous episode of rejection.
Conclusion: In this study, we identified polyomavirus BK genotypes in large set of kidney transplant recipients. Ongoing research will help to elucidate the impact of of recipients' and donors' BKPyV genotypes and other clinical parameters on dynamics of active infection later on.

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OS48 - BIOLOGICAL MARKERS IN SOLID ORGAN TRANSPLANTATION

OS410 PROFIBROTIC TGF-Β IN DECEASED DONOR KIDNEYS REGULATES CATABOLIC PATHWAYS AND LONG-TERM FUNCTION AFTER TRANSPLANTATION

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Background: We have previously shown that subclinical proteomic changes with increased expression of profibrotic proteins in preimplantation biopsies of deceased donor kidneys are associated with inferior function posttransplant. In this study, we tested the hypothesis that the profibrotic mediator TGF-β activates catabolic pathways including expression of cysteine protease Calpain-1 that may disrupt the donor kidney cytoskeleton and affect long-term allograft function.
Methods: Preimplantation biopsies were analysed from DBD and DCD kidneys with either good or poor functional outcomes post-transplant. First, we profiled proteolytic events in tissue of donor kidneys with poor allograft function (eGFR < 35 ml/min at 1y posttransplant) using protein Topography and migration analysis platform. Next, we confirmed the generation of distinct proteolytic profiles using immunoblotting. Finally, we studied the relationship between TGF-β and Calpain-1 in initiating endogenous proteolysis using an *in-vitro* model of human kidney immortalised proximal tubular cells (PTECs).
Results: Enhanced degradation with generation of protein fragment profiles, was found in donor kidneys with poor compared to good posttransplant outcomes. Due to endogenous proteases, key cytoskeletal protein families, including Collagens, Laminins and Talins, underwent proteolysis, generating fragment intermediates of lower molecular weight than the intact proteins(F1). Following treatment with TGF-β, PTECs showed a profound activation of Calpain-1 and development of fibrosis. This was illustrated by increased expression in a-smooth muscle in addition to degradation profiles of cytoskeletal proteins, matching those observed in deceased donor kidneys with poor post-transplant outcomes.
Conclusion: Profiling the deceased donor kidney degradome creates new opportunities to find new markers of kidney injury and to better understand key catabolic pathways that may affect long-term function in kidney transplantation.

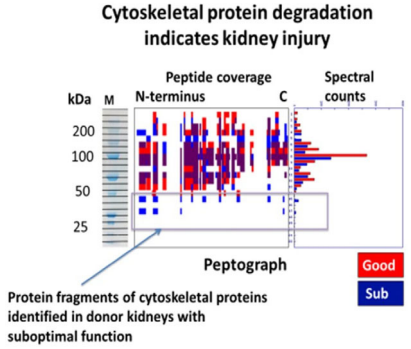

Figure 1. Application of PROtein TOpography and Migration Analysis Platform (PROTOMAP) combines 1-D gel electrophoresis and mass spectrometry to map the intact protein and protein fragment intermediates generated due to endogenous proteolysis

OS411 EVALUATION OF THE ENDOTHELIAL FUNCTION OF KIDNEY TRANSPLANTS IN A FEW MINUTES AFTER REPERFUSION TO COMPARE ORGAN STORAGE TECHNIQUES (SIMPLE HYPOTHERMIA AND CONTINUOUS PULSATILE PERFUSION)

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Department of General Surgery and Transplantation

Aim: In the study concentrations of ET-1, ET-2, ET-3 endothelin, proinflammatory interleukin 18 (IL-18), and potentially nephroprotective neutrophil-associated gelatinase (NGAL) were analyzed according to the renal transplant storage method: 1 / pulsatile perfusion and 2 / simple hypothermia.
Material and Methods: 176 blood samples taken from 44 renal recipients – patients with end stage renal disease. The recipients were divided into 2 groups: 22 patients were randomly assigned to group I – renal graft stored in pulsatile perfusion pump and group II - 22 patients – renal graft stored in simple hypothermia. Blood concentrations of ET-1, ET-2, ET-3, IL-18, and NGAL were determined with ELISA tests.
Results: Comparative analysis of ET-1, ET-2, ET-3, IL-18, and NGAL concentrations showed that there is a statistically significantly lower ET-2 concentration in blood plasma taken from renal graft vein in 30 minutes after reperfusion in group I compared to group II (108.86 ± 52.37 vs. 133.79 ± 38.73; p = 0.017). In group of kidneys stored in simple hypothermia, a statistically significant increase in ET-1 concentration was observed in 30 min after reperfusion (p = 0.033). In group of kidneys stored in pulsatile perfusion pump significant decrease in IL-18 concentration was noted (p = 0.026). Analysis of the correlation between the concentration of measured substances and the parameters of renal graft function showed a statistically significant positive correlation between ET-2 and urea and creatinine levels, and negative correlation with estimated glomerular filtration rate (e-GFR) in both groups.
Conclusions: Renal storage in pulsatile perfusion pump has an advantage over simple hypothermia, since use of the former is associated with inhibition of vasoconstrictor activity and a decrease in the activity of proinflammatory factors in the kidney. Nephroprotective effect of these phenomena is associated with improved transplanted organ function, measured by creatinine and e-GFR levels.

OS412 THE RENAL EPIGENETIC CLOCK IS A BETTER SURROGATE FOR AGING THAN TELOMERE ATTRITION

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[1]University Hospitals Leuven; [2]KU Leuven; [3]VIB

Introduction: Advanced donor age is a major risk factor for kidney transplant survival, but the underlying molecular and cellular alterations of aging have been proven difficult to dissect. One of the hallmarks of aging is telomere attrition. Recently, the epigenetic clock, that predicts age based on DNA methylation, was discovered. We evaluated for the first time both the epigenetic clock and telomere length in 162 kidney biopsies performed at the time of transplantation.
Methods: DNA methylation was measured genome-wide in two cohorts of renal transplant biopsies (n = 95 at implantation, and n = 67 post-reperfusion). Donor age ranged from 16 to 79 years. The epigenetic clock was calculated using the Horvath formula. Telomere length was measured in 79% of biopsies. Epigenetic age acceleration (older epigenetic age in comparison to chronological age) was defined by the residuals to the linear regression curve of donor age to the epigenetic clock. Protocol biopsies were performed at 3 and 12 months after transplant.
Results: Telomere length correlated with donor age, although the correlation was relatively weak (r = -0.37, p = 0.001 and r = -0.25, p = 0.07). In contrast,

the epigenetic clock correlated strongly with age, at $r = 0.93$, $r = 0.94$, respectively and $p<10^{-15}$ for both cohorts. Epigenetic age acceleration did not correlate with telomere length. Interestingly, in both cohorts the epigenetic clock overestimated the age of young donors. The epigenetic clock behaved also as chronological age in its correlation to several histological hallmarks of renal aging, in contrast to telomere length, which was less correlated to aging-associated histopathological lesions.
Conclusion: The renal epigenetic clock acts as a surrogate for chronological age with high accuracy. Accelerated epigenetic aging does however not correlate to telomere length, suggesting that renal epigenetic aging and replicative aging are seperate entities driven by different factors, ticking at different clocks.

OS413 INCREASED TOTAL URINARY CELL-FREE DNA PREDICTS RENAL TRANSPLANT REJECTION

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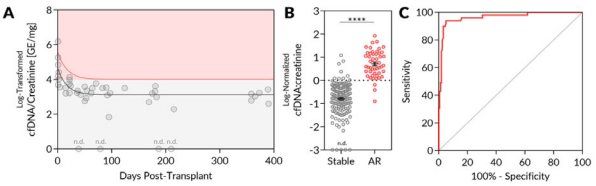
Purpose: While sequencing or SNP-based methods of quantifying donor-derived cell-free DNA (dd-cfDNA) from plasma have been used to detect allograft rejection, they remain expensive and inconvenient for patients and physicians. We assessed a novel urinary assay to quantify total cell-free DNA (tcfDNA) and detect kidney transplant (KT) rejection in a cohort of biopsy-matched KT samples.
Methods: 206 urine samples from KT patients were collected and categorized as stable ($n = 157$) or acute rejection (AR, $n = 49$). Samples were processed for quantification of urinary tcfDNA (genomic equivalents (GE)/mL) and creatinine (mg/mL). The cfDNA to creatinine ratio from longitudinally collected samples ($n = 47$) from 8 KT patients who were stable and had no evidence of subclinical rejection was correlated with days post-transplant to generate a 95% prediction curve for stable phenotypes.
Results: Urinary tcfDNA is significantly increased immediately post-transplant and decreases to a steady baseline (1298 GE of cfDNA/mg creatinine) by 3 months post-transplant (**Figure 1A**). The median level of 95% prediction interval-normalized tcfDNA was significantly higher in AR as compared with stable samples (0.64 vs. -0.71, $P < 0.0001$) (**Figure 1B**). Urinary tcfDNA showed high performance in discriminating stable and AR samples, with an AUC of 0.9649 ($P < 0.0001$). The sensitivity and specificity of the assay was 93.88% and 94.90% respectively (**Figure 1C**), suggesting that the assay could be used to screen patients at risk of rejection to avoid unnecessary biopsies in the clinical setting.
Conclusions: This novel urinary tcfDNA assay enables rapid and accurate discrimination of AR from stable patients. As collection of urine requires no training and can be performed as often as needed, this assay can provide inexpensive, accurate, and longitudinal assessment of AR in KT patients in a format amenable to use in transplant clinics.



OS414 AN 8-GENE EXPRESSION ASSAY FOR ANTIBODY-MEDIATED KIDNEY ALLOGRAFT REJECTION

Elisabet Van Loon[1], Stéphane Gazut[2], Saleh Yazdani[1], Evelyne Lerut[3], Henriette deLoor[1],Maarten Coemans[1], Laure-Hélène Noël[4], Lieven Thorrez[5], Leentje Van Lommel[6], Frans Schuit[6], Ben Sprangers[1], Dirk Kuypers[1], Marie Essig[7], Wilfried Gwinner[8], Dany Anglicheau[9], Pierre Marquet[7], Maarten Naesens[1]
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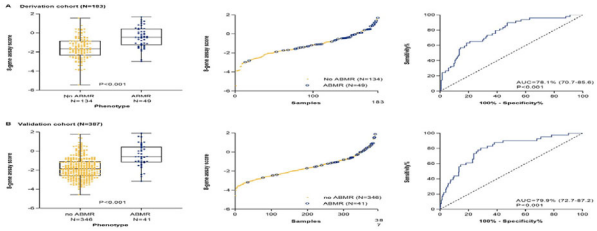
Background: Antibody-mediated rejection is a leading cause of graft failure after kidney transplantation. The diagnosis of antibody-mediated rejection is made by combining assessment of circulating antibodies with histological assessment of invasive allograft biopsies. Non-invasive biomarkers with sufficient diagnostic accuracy are not available. We sought to identify and validate a blood biomarker for non-invasive detection of antibody-mediated rejection.
Methods: In this multicentre study, peripheral blood samples were prospectively collected from June 2011 to August 2016 at time of renal allograft biopsies, and then analysed in three phases, following a case-control design (discovery and derivation phase, N = 117 and N = 183 respectively) and a trans-sectional study for performance assessment (independent validation phase, N = 387). Untargeted screening of whole genome transcriptomics was performed for the discovery phase and targeted mRNA expression analysis for the derivation and validation phases.
Results: In the discovery and derivation phases, we developed and locked a multigene assay of 8 genes in peripheral blood that discriminated cases with (N = 49) from cases without (N = 134) antibody-mediated rejection (diagnostic accuracy in derivation cohort, 78.1% (95% CI, 70.7 to 85.6, $p < 0.001$). In the independent validation cohort, this 8-gene marker discriminated cases with (N = 41) from cases without antibody-mediated rejection (N = 346) with similar accuracy (79.9%; 95% CI, 72.6 to 87.2, $p < 0.001$). At the optimal cut-off the marker held a sensitivity of 80.5%, specificity of 71.4%, PPV of 25.0% and NPV of 96.9%.
Conclusion: We developed and validated a novel 8-gene expression assay in peripheral blood that can be used for non-invasive diagnosis of antibody-mediated rejection of kidney allografts.



OS415 THE EPIGENETIC SIGNATURE OF OLD DONOR KIDNEYS MIGHT BE EXPLAINED BY CHRONIC HYPOXIA

Line Heylen[1], Ben Sprangers[1], Bernard Thienpont[2], Dirk Kuypers[1], Diether Lambrechts[3], Maarten Naesens[1]
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Introduction: Advanced donor age as well as prolonged ischemia time can lead to fibrosis of the renal transplant. DNA methylation is one of the key mechanisms driving cellular phenotype changes in tissues, and has been implicated in both aging as well as ischemia. We sought to evaluate whether both aging-associated and ischemia-induced DNA methylation changes share a common mechanism, potentially explaining why they might reinforce each other.
Methods: We measured DNA methylation genome-wide in 82 kidney transplant implantation biopsies. In addition, we determined both DNA methylation as hydroxymethylation genome-wide in 6 paired pre-and post-ischemia biopsies and 6 implantation biopsies from 3 old (>65y) and 3 young (<25y) donors. Findings were correlated to cold ischemia time as well as donor age, and the overlap was determined.
Results: As we described recently, DNA methylation increased after ischemia, through a decrease in hydroxymethylation. Interestingly, DNA hydroxymethylation levels were also lower in the old donor kidneys compared to young donor kidneys, together with an increase in DNA methylation. In the implantation cohort, DNA methylation increased both with prolonged cold ischemia time as well as with increased donor age ($p < 0.001$). Strikingly, these modifications were interdependent to some extent, as more CpGs of the ischemia-hypermethylated CpG islands were modified by donor age than would be expected by chance (543/1782 (30%) versus 92,778/803,663 (11,5%), $p < 0.001$).
Conclusion: We demonstrate unique similarities between epigenetic modifications induced by ischemia and aging in the kidney. These findings suggest that chronic cellular hypoxia or oxidative stress in the aged kidney might explain how aging modifies the kidney's DNA methylome.

OS416 SERUM GLYCOMICS ON POSTOPERATIVE DAY 7 ARE ASSOCIATED WITH GRAFT LOSS 3 MONTHS AFTER LIVER TRANSPLANTATION

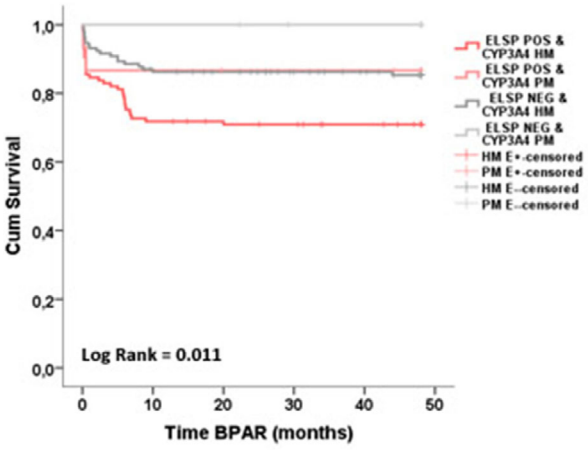
Xavier Verhelst[1], Anja Geerts[1], Roos Colman[2], Aude Vanlander[3], Luis Abreu deCarvalho[3],Frederik Berrevoet[3], Roberto Troisi[3], Xavier Rogiers[3], Nico Callewaert[4], Hans Van Vlierberghe[1]
[1]Ghent University Hospital, Dept of Gastroenterology and Hepatology; [2]Ghent University - Biostatistical Unit; [3]Ghent University Hospital, Dept of Hepatobiliary and Transplant Surgery; [4]Ghent University - VIB Center for Medical Biotechnology

Background: Graft loss during the first year after liver transplantation (LT) affects up to 15% of liver grafts, mainly in the first 3 months. Prediction of outcome early after LT is limited by the lack of robust clinical predictors.
Goal: Define a serum glycomic signature early after LT that is associated with graft loss at 3 months after LT.
Methods: A prospective study in an experienced liver transplant center was performed between 1/1/2011 and 21/12/2015. Glycomic analysis using DSA-FACE was applied to serum samples on postoperative day 7. Using Lasso regression, an optimal serum glycomic signature was identified, associated with 3 months graft survival.
Results: 117 patients were included. Graft loss at 3 months occurred in 14 patients (11.9%). The cohort was split in a training (82 without, 9 with graft loss) and a validation set (35 without, 5 with graft loss). The glycomic signature contains 13 glycans, using Lasso regression an optimal model was fitted yielding an AUC of respectively 0.95 and 0.94 in these sets for graft loss at 3 months ($p < 0.001$). Based on the Youden index an uptimal cutoff of this biomarker was defined at 0.773. In the complete sample, this showed a sensitivity of 94% (95% CI: 0.891-0.981) and a specificity of 93% (95% CI 0.661-0.998). PPV and NPV were respectively 99.1% (95% CI 0.943-0.997) and 68% (95% CI : 0.491-0.989). Graft loss was associated with increased undergalactosylation (a marker of inflammation) and an increased presence of fucosylated and triantennary glycans, both signs of liver regeneration. Cox regression analysis showed a hazard ratio of 6.4 (95%CI: 2.2 - 18.6) for graft loss ($p < 0.001$) at 3 months.
Conclusion: A serum glycomic signature obtained on postoperative day 7 a after LT is highly associated with graft loss at 3 months after LT. It could guide the clinician in the decision for early retransplantation and thus increase the quality of life and outcome of the patient. It can be applied on routine lab equipment.

OS417 COMBINED PRE-TRANSPLANT ANTI-DONOR T-CELL SENSITIZATION WITH SINGLE NUCLEOTID POLIMORPHISMS (SNPS) FOR CYP3A4 TACROLIMUS METABOLISM IDENTIFIES KIDNEY TRANSPLANT PATIENTS AT HIGH RISK OF ALLOGRAFT REJECTION

Elena Crespo[1], Anna Vidal[1], Sefrin Anett[2], Pere Fontova[1], Maik Stein[2], Volk Hans-Dieter[2], Grinyo Josep Maria[1], Reinke Petra[2], Lloberas Nuria[1], Bestard Oriol[1]
[1]IDIBELL; [2]Charité University Medicine Berlin

Background: Donor-specific (d-sp) T cell alloimmunity has a negative impact on allograft outcome and is associated with acute rejection (BPAR). Since the individual susceptibility related to specific single nucleotide polymorphisms (SNPs) of enzymes involved in TAC metabolism leads to different drug exposures, assessing pre-transplant d-sp T-cell alloreactivity according to TAC pharmacogenetic phenotypes would improve the discrimination accuracy of at-risk patients of BPAR.
Methods: We evaluated pre-transplant d-sp T-cell alloimmunity using an IFN-γ ELISPOT assay, and CYP3A4*22 SNPs in 274 consecutive kidney transplants from 2 different centers receiving TAC immediate release formulation, MMF and steroids, either with basiliximab (n = 170;62%) or Thymoglobulin (n = 104;38%).
Results: 56/274 patients (20.4%) displayed BPAR (36 TCMR, 8 ABMR, 1 mixed BPAR). Alloreactivity was observed in 132(48.2%) patients. 249(90.9%) patients were high metabolizers for CYP3A4 (HM;*1/*1 genotype) and 25 (9.1%) were poor metabolizers (PM;*22 expressers). While pre-transplant d-sp T-cell alloreactivity (E+) was associated with BPAR (OR = 2.191, p = 0.006), the pharmacogenetic phenotype was not. HM required higher TAC doses to reach the same trough levels as PM (trough levels/dose ratios: 1.58 ± 1.08 vs 1.99 ± 1.32, p = 0.07; 1.76 ± 1.04 vs 2.18 ± 1.28, p = 0.06 and 1.88 ± 1.26 vs 2.46 ± 1.93, p = 0.05 in HM vs PM, at 1, 3 and 6 months). When stratifying patients according to both factors, 117(42.7%) were HM/E+, 132(48.2%) HM/E-, 15(5.5%) PM/E+ and 10(3.6%) PM/E-. HM/E+ patients showed the highest BPAR risk (HR = 2.342, p = 0.002). When patients receiving Thymoglobulin were excluded, HM/E+ were at higher risk (HR = 2.833, p = 0.002). The combination of both variables and DGF independently predicted BPAR (HR = 2.442, p = 0.001; HR = 2.072, p = 0.007)
Conclusion: Assessment of pre-transplant d-sp T-cell alloimmunity together with CYP3A4 SNPs may help to better recognize patients at risk of BPAR, despite the use of TAC regimens.



OS18 LUNG TRANSPLANTATION

OS418 QUALITY OF DONOR LUNGS: A COMPARATIVE STUDY BETWEEN FAST AND SLOW BRAIN DEATH INDUCTION MODELS IN RATS

Judith vanZanden[1],Rolando Rebolledo[2], Dane Hoeksma[1], Jeske Bubberman[1], Hans Burgerhof[1], Annette Breedijk[3], Benito Yard[3], Michiel Erasmus[1], Henri Leuvenink[1], Maximilia Hottenrott[1]
[1]University Medical Center Groningen; [2]University of Chile; [3]University Medical Center Mannheim

Background:
Lung transplantations are commonly performed with lungs derived from brain-dead donors. Brain death (BD) is initiated by an intracranial pressure (ICP) increase, which damages the peripheral donor organs. In this study we aimed to elucidate whether the speed of ICP increase affects quality of the brain-dead donor lung, investigated in a rat model.
Materials & Methods:
Rats were randomly assigned to 3 donor groups: group 1) no intervention (control: immediate sacrifice), group 2) fast ICP increase (ICP rise over 1 min) or group 3) slow ICP increase (ICP rise over 30 min). In group 2 and 3 BD was induced by inflating a balloon catheter in the subdural space. Rats subjected to BD were sacrificed at different time points: 30 min, 1 h, 2 h and 4 h after BD induction to study time dependent changes. Hemodynamic stability, lung injury and inflammatory status were investigated.
Results:
Hemodynamic stability was more compromised in rats subjected to fast ICP increase than rats subjected to slow ICP increase. This was reflected by higher mean arterial pressures during the initial phase of the BD stabilization period and more need for fluid administration and inotropic support. Furthermore, 6 rats were lost as a consequence of fulminant edema after BD induction compared to no mortality in the slow BD model. On a histological level, higher total lung injury scores were observed in the fast BD model. Inflammatory status did not differ between the two BD models as reflected by pro-inflammatory gene expressions and infiltration of activated neutrophils.
Conclusion:
We conclude that donor lungs subjected to fast ICP increase have deteriorated quality compared to lungs subjected to slow ICP increase. Our observations reflect the human setting, in which traumatic brain injury resulting in fast occurrence of BD is associated with worse donor lung quality as compared to BD induced by haemorrhagic stroke.

OS08 IS WARM WINNING THE COLD WAR IN MACHINE PERFUSION?

OS419 NORMOTHERMIC REGIONAL PERFUSION (NRP) INCREASES ABDOMINAL ORGAN UTILISATION FROM CDCD DONORS

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Background: Normothermic regional perfusion is increasingly being used in controlled donation after circulatory death (cDCD). We analysed the impact of NRP on organ utilisation in the UK.
Methods: First adult (≥16) transplants from UK DCD donors between 01/01/2011 and 6/9/2018, were stratified by individual organ donor risk scores and the impact of NRP on utilisation was assessed in multi-variate models.
Results: A mean of 3.4 organs were transplanted from a cDCD donor when NRP was used as compared to 1.8 organs per donor when NRP was not used. Table 1 shows the offering outcomes for the abdominal organs in the analysis.

		Abdominal NRP	No abdominal NRP
Liver	No. offered	112	4739
	No. transplanted (% offered)	94 (84%)	2000 (42%)
	No. transplanted (% offered)	72 (64%)	1206 (25%)
Kidney (at least one)	No. offered	112	5116
	No. transplanted (% offered)	109 (97%)	3550 (69%)
	No. transplanted (% offered)	100 (89%)	3121 (61%)
Pancreas (includes those offered for islets)	No. offered	67	1939
	No. transplanted (% offered)	50 (75%)	749 (39%)
	No. transplanted (% offered)	23 (34%)	327 (17%)

There were 4,872 donors in the cohort where the liver was offered. After adjusting for the UK liver donor index, a liver transplant was over 4 times more likely to result from donors that underwent abdominal NRP compared to those that did not undergo abdominal NRP (OR = 4.5, 95% CI: 3.0-6.8).

At least one kidney was offered from 5,245 donors in the cohort. The 2017 Mumford UK Kidney Offering Scheme Donor Risk Index was applied to each of these donors. After adjusting for kidney donor risk profile, abdominal NRP significantly increased the odds of a kidney transplant resulting from a donor where at least one kidney was offered. Specifically, a kidney transplant was 4.5 times (95% CI: 2.5-8.3) more likely to result from donors that experienced abdominal NRP.

There were 2,060 donors in the cohort where the pancreas was offered. When adjusting for the Axelrod PDRI, a pancreas was two times more likely to be transplanted (p = 0.007) when NRP was used at the time of procurement.
Conclusions: The use of NRP at the time of organ procurement in cDCD donors significantly increases the utilisation of the abdominal organs offered for transplantation.

OS07 DETERMINANTS OF OUTCOMES IN DECEASED DONOR KIDNEY TRANSPLANTATION

OS420 BRIEF INITIAL AND END-ISCHEMIC O_2 SUPPLY VIA BUBBLE AND PERFUSATE SURFACE OXYGENATION DURING STANDARD HMP DEMONSTRATED TO BE SIMPLE YET EFFECTIVE FOR IMPROVING EARLY RECOVERY OF RENAL FUNCTION IN AN ISCHEMIA-REPERFUSION PORCINE AUTOTRANSPLANT MODEL

Tom Darius[1], Martial Vergauwen[2], Thomas Smith[3], Jay Nath[4], Kamlesh Patel[4], Selda Aydin[5], Antoine Buemi[6], Martine De Meyer[6], Christian Ludwig[3], Pierre Gianello[2], Michel Mourad[7]
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Background: Static cold storage (SCS) and hypothermic machine perfusion (HMP) are today the gold standard for kidney preservation. The aim of this study was to determine the ideal start time and least complicated method for adding oxygen during HMP to improve early graft function in a porcine kidney ischemia-reperfusion autotransplant model.
Methods: The left kidney of ± 40 kg Landrace pig was exposed to 30 minutes of warm ischemia by vascular clamping and randomized after ex vivo cold flush. The LifePort Kidney Transporter® modified to *include an external oxygenator* was used in the following study groups: 1) 22 h oxygenated HMP ($HMPO_2$(FiO_2 90%), *n* = 8), 2) 2 h HMPO2 + 20 h HMP(*n* = 6), and 3) 20 h HMP + 2 h $HMPO_2$(*n* = 5). The LifePort kidney Transporter *without external oxygenator* but direct perfusate oxygenation via bubble and perfusate surface (FiO_2=95%) oxygenation was used in a 4th study group, 22 h standard HMP including 30 min at start and 1 h end-ischemic O_2 uploading ($HMPO_2$uploading). SCS and standard HMP (no active oxygen supply) for 22 h served as control groups.
Results: The perfusate pO_2 at the start and the end of HMP is shown in Figure 1 according to the study group. Graft recovery measured by serum creatine levels was superior in the 22 h $HMPO_2$, the 2 h $HMPO_2$+20 h HMP and the HMPO2uploading groups compared with 22 h SCS ($p < 0.0001$), standard 22 h HMP ($p < 0.0001$) and 20 h HMP + 2h$HMPO_2$ ($p = 0.0288$) (Figure 2).
Conclusion: Our data suggest that during cold perfusion continuous oxygenation might not be required. Brief O_2 uploading via bubble and perfusate surface oxygenation was shown to be as effective as continuous oxygenation via an external oxygenator to obtain supraphysiological pO_2 and similar superior early graft function compared with standard HMP or SCS alone. Such simple but effective oxygenation method might easily get adopted in the clinic since it would hardly complicate handling or logistics during organ sharing.

OS421

EARLY EXPANSION OF TEMRA CD8 WITH INNATE-LIKE FUNCTION IDENTIFIES KIDNEY TRANSPLANT RECIPIENTS AT HIGH-RISK OF GRAFT FAILURE

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[1]CRTI UMR1064; [2]CRTI; [3]CHU de Nantes - ITUN; [4]EFS de Nantes; [5]SPHERE UMR1246

As CD8 TEMRA cells are associated with higher risk of long-term graft dysfunction, in this study, we evaluate if the monitoring of CD8-related biomarkers could improve the prognostic capacities of a clinical-based scoring system (Kidney Transplant Failure Score; KTFS). We also characterizethe functionality of TEMRA and especially their reactivity upon donor-specific stimulation. 286 kidney-transplant recipients prospectively enrolled were followed for more than 8-years. 51 return in dialysis. We demonstrate that the frequency of early memory CD8 cells (EM) and TEMRA measured at 1-year post-transplantation is correlated with the risk to return in dialysis during time. For patients at high-risk of long-term graft dysfunction (according to KTFS), the use of one-year TEMRA frequency allows the discrimination of patients that will lose their graft from those that will not. Donor-specific reactivities from TEMRA and EM were similar with an early expression of $CD25^+CD69^+CD107a^+$ and the high secretion of pro-inflammatory and cytotoxic molecules. Importantly, we identify an innate-like signature of TEMRA, with more than 5-fold higher expression of FCGR3A (CD16) by TEMRA as compared to NAIVE and EM. Cross-linking of CD16 triggers the secretion of TNFa and IFNg by TEMRA and their cytotoxic function and was further enhanced by the provision of IL-15. Finally, we demonstrate TEMRA and not EM display *in vitro* Antibody Dependent Cell Cytotoxicity conferring to TEMRA features of both adaptive and innate-like immunity and showing that anti-HLA antibodies, a major risk factor for long-term allograft outcome, could activate TEMRA.