FOCUS GROUP

FG01 – OPTIMISING ORGANS FOR TRANSPLANTATION

FG001 THE ROLE OF PULMONARY BLOOD FLOW AS A RISK FACTOR FOR PRIMARY GRAFT DYSFUNCTION IN A NOVEL EXPERIMENTAL MODEL OF UNILATERAL LUNG TRANSPLANTATION

Anna Elisabeth Frick[1], Michaela Orlitová[1], Sofie Ordies[1], Berta Sáez-Giménez[2], Tobias Heigl[3], Janne Kaes[3], Robin Vos[3], Geert M. Verleden[3], Bart Vanaudenaerde[3], Stijn E. Verleden[3], Dirk E. Van Raemdonck[4], Arne P. Neyrinck[1]

[1]Department of Cardiovascular Sciences, KU Leuven; [2]Pulmonology Service, Lung Transplant Program, Hospital Universitari Vall d'Hebrón, Universitat Autònoma de Barcelona; [3]Leuven Lung Transplant Unit, Department of Chronic Diseases, Metabolism and Ageing (Chrometa), KU Leuven; [4]Department of Thoracic Surgery, University Hospitals Leuven and Experimental Thoracic Surgery, KU Leuven

Background: Primary graft dysfunction (PGD) remains a major obstacle after lung transplantation. Large animal models of isolated left lung transplantation are essential to study PGD. However, most studies do not clamp the contralateral native lung in their models to avoid right heart failure. In this study, we developed an innovate approach to selectively assess reperfusion injury in the transplanted lung only and also investigated the impact of pulmonary flow.
Materials and Methods: We performed 12 left orthotopic lung transplants ($n = 6$ × donor + recipient in low and high flow group). Donor lungs were harvested, stored for 24 h on ice followed by a left lung transplantation in a recipient animal and were observed for 6 h after reperfusion. Invasive catheters for pulmonary artery (PAP) and left atrial pressure (LAP) monitoring were inserted. Cardiac output (CO) and flow to the transplanted left lung were measured with flowmeters (Transonic®) around left and main pulmonary artery (PA). In group 1 (high flow), the right PA was partially clamped to allow 50% of the CO towards the transplanted lung. In group 2, no vessels were clamped.
Results: Survival after 6 h was 100% in both groups. In table 1 the data are depicted. The pO_2/FiO_2 ratio of the transplanted lung was significantly lower and the mPAP was higher ($p < 0.05$) in the high flow versus low flow group. The wet/dry ratios of the right native lung and the left transplanted lung were not significantly different after 6 h of reperfusion.
Conclusions: Single-lung transplantation in a large animal setting is demanding, but feasible. High flow through the pulmonary artery leads to a lower P/F ratio, indicative of more severe PGD. The lack of difference in lung water accumulation may be related to too short reperfusion times. Our innovative approach to control the flow over the transplanted lung and to monitor the function of the right native lung allows to further study the physiology and treatment of PGD.

FG002 DEFERIPRONE MARKEDLY ATTENUATES BOTH KIDNEY GRAFT PRESERVATION AND ISCHEMIA/REPERFUSION INJURY IN A NOVEL AUTOTRANSPLANTATION MODEL IN PIGS

Vasileios Tatsis[1], Michail Mitsis[1], Vasiliki Galani[2], Evangeli Lampri[3], Dimitra Koumasi[3], Ioannis Sainis[3], Evangelia Dounousi[4], Dimitrios Nastos[1]

[1]Department of Surgery and Transplant Unit, University Hospital of Ioannina, Ioannina; [2]Laboratory of Anatomy-Histology-Embryology, University of Ioannina, Ioannina; [3]Cancer Biobank Center, University of Ioannina, Ioannina; [4]Department of Nephrology, University Hospital of Ioannina, Ioannina

Background: Iron, as transition ion, plays a crucial role during preservation of harvested kidney grafts and the post-operative period. It is implicated in the development of ischemia-reperfusion injury, which leads to significant non-immune graft damage. Using an experimental model of porcine kidney autotransplantation, we investigated the possible protective effects of the iron-chelating agent deferiprone (L1) on kidney graft function.
Methods/Materials: 14 large pigs were used. The left kidney was harvested and stored for a mean period of 17 h (4 h of Hypothermic Machine Perfusion + 13 h of static cold storage). Then, after right nephrectomy, the graft was implanted to the right renal vessels and native right ureter. 7 animals were used as controls (control group: CG), while L1 was administered to the rest 7 animals (L1 group). Laboratory and histopathological parameters were monitored up to 14th post-operative day.
Results: At the end of the storage period the mean weight of grafts and the preservation fluid concentrations of CK and LDH were significantly lower in L1 group compared to CG ($p = 0.001$, $p = 0.001$ and $p = 0.007$, respectively). At 30 min after reperfusion the mean concentration of 8-isoprostanes was lower in L1 group compared to CG ($p = 0.007$). Histopathology Index (HI) was significantly lower in L1 group compared to CG at 14th post-op day and at 30 min after reperfusion (both $p = 0.001$). Postoperatively, HI was increased in CG, while it remained stable in L1 group ($p = 0.042$ and $p = 0.862$, respectively). At 30 min, the expression of VCAM-1 was lower in L1 group compared to CG ($p = 0.02$) and the same result was apparent for the expression of ICAM-1 and VCAM-1 at 14th post-op day ($p = 0.029$ and $p = 0.04$, respectively). From 3rd up to 8th post-op day serum Urea and Creat concentrations were significantly lower in L1 group compared to CG (all $p < 0.05$).
Conclusions: L1 manifests a strong renoprotective effect on experimental kidney autotransplantation and leads to better graft function.

FG003 TOWARDS THE TEMPERATURE PARADIGM IN MACHINE PERFUSION PRESERVATION: A SYSTEMATIC REVIEW OF ANIMAL MODELS

Maria Irene Bellini[1], Mikhail Nozdrin[2], Janice Yiu[3], Vassilios Papalois[1]

[1]Imperial College NHS Trust; [2]Imperial College London; [3]University College London

Background: There is limited knowledge in the effects of perfusion temperature on intrinsic cell metabolism, which in turns governs the extent of injury and function of grafts in recipients. Molecular parameters of ischaemia-reperfusion injury include mRNA expression of pro-inflammatory cytokines, ATP and cellular injury.
Methods: A systematic search in databases (Embase, Medline, Cochrane Library, Transplant Library) generated 10,585 studies, with 134 studies included.

	Low flow	High flow	Time	Groups (low vs. high)
Number of pigs	6	6	*p*-value ($p < 0.05$)	*p*-value ($p < 0.05$)
Parameter				
CO, l/min	4 (3.78–4.03)	4.13 (4.02–4.18)	0.43	0.32
Flow left PA, l/min	0.52 (0.34–0.59)	1.68 (0.53–1.92)	<0.0001	0.0005
pO_2, mmHg	473.8 (463–479.2)	430.8 (394–458.2)	0.27	0.38
pO_2 (LPV), mmHg	290 (266.9–361.2)	207.7 (163.6–284.6)	0.014	0.09
pO_2 (RPV), mmHg	393.8 (362.8–418.5)	381.8 (340–398.7)	0.31	0.60
mPAP, mmHg	31.5 (27.83–31.5)	36.17 (27.33–39.33)	0.01	0.16
Lung compliance, ml/cm H_2O	36.67 (35.83–38.5)	34.17 (33.5–36.17)	0.40	0.66
PVR, dyn·s/cm^5	500.2 (428.6–535.3)	586.8 (402.6–592.5)	0.07	0.90
PVR left lung, dyn·s/cm^5	4,450 (3,897–6,783)	1,674 (1,452–3,213)	0.10	0.88
W/D ratios RLL	6.66 (±0.48)	6.81 (±0.28)		0.49
W/D ratios LLL	7.91 (±0.38)	8.26 (±0.78)		>0.99

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Results: A novel study demonstrated that a combined liver-kidney normothermic machine perfusion (NMP) is associated with an increase in graft tissue ATP and a decrease in liver injury enzyme levels, AST/ALT. Other NMP studies showed that a higher temperature could also be associated with increase in graft function. The impact of perfusion temperature on the increase in tissue graft ATP compared to conventional static cold storage (SCS) was analysed as a measure of metabolic recovery, cellular oxygen consumption and function. This association was demonstrated between hypothermic machine perfusion (HMP) versus SCS in 4 liver studies, with limited data in NMP. An analysis of 3 studies on the preservation temperature on pancreas graft function revealed a lack of consensus on the optimal temperature associated with lower rate of DGF and IRI. Two studies suggested that a range of (7–10°C) was superior to a hypothermic (0–4°C) one. Qualitative representation of novel findings was common in different studies, therefore, more quantitative studies are needed for further investigation of underlying physiological mechanisms behind differences in outcomes from SCS and MP.
Conclusions: There are emerging animal studies suggesting that different machine perfusion temperatures could influence intrinsic cellular and tissue metabolism, reflected by a reduction in delayed graft function. More studies are needed for further investigation of underlying physiological mechanisms behind differences in outcomes from SCS and MP.

FG004 COULD EXTRACELLULAR MATRIX MODIFICATION BE THE MISSING PIECE IN THE PRECONDITIONING PUZZLE?

Charlotte Brown, Usman Khalid, Emma Woods, Lucy Newbury, Irina Grigorieva, Donald Fraser, Gilda Pino-Chavez, Robert Steadman, Rafael Chavez, Soma Meran
University Hospital of Wales, Cardiff

Ischaemic preconditioning (IPC) reduces ischaemia-reperfusion injury (IRI) in-vivo, but mechanisms are not understood. Hyaluronan (HA) is a major polysaccharide of the extracellular matrix; usually limited to the renal medulla. In pathology, HA accumulates in the cortex and correlates with renal outcomes, possibly mediated through the CD44 receptor. HA synthesis occurs at the plasma membrane, dependent on HA synthases, HAS 1/2/3. Here we characterise the HA "profile" in a model of evolving injury, to identify a mechanism for IPC. We hypothesise that HA formation and/or assembly into a pro-inflammatory state is prevented through inhibition of the pro-fibrotic synthase HAS2 and CD44 expression.

A rat model of IRI was used, where both renal pedicles were clamped for 45 min. Lewis rats were assigned to IRI/SHAM/IPC. Preconditioned rats underwent 3 cycles of pulsatile IPC prior to IRI. Kidneys were retrieved at 48 h and day 14/28 and assessed histologically, including immunohistochemistry (IHC). Creatinine was measured at baseline and retrieval. RT-qPCR and RNA-sequencing was performed on whole kidney.

High creatinine and tubular necrosis typified IRI acutely. Chronic injury was evident at day 28 by interstitial and perivascular fibrosis. In response to IRI, expression of HAS1/2, TSG-6 (HA-binding protein), HYAL2 (hyaluronidase) and CD44 was increased at 48 h ($p < 0.001$). IHC demonstrated increased expression of HAS1/2 and CD44 in the cortex, which were mainly limited to the medulla in controls. IPC reduced serum creatinine and histology scores both acutely and at 28 days ($p < 0.0001$). IPC prevented overexpression of HAS2 and CD44 ($p < 0.0001$), an acute influence, which dissipated with progressive injury. This was confirmed through IHC demonstrating reduced expression of HAS2 and CD44.

The renoprotective effect seen in this model was associated with modification of the HA "profile"; preventing overexpression and relocation of key fibrotic mediators HAS2 and CD44.

FG005 BILE PRODUCTION AND BILE QUALITY DURING NORMOTHERMIC EX VIVO LIVER PERFUSION CORRELATES WITH GRAFT INJURY AND CAN BE IMPROVED WITH NOR-URSODEOXYCHOLIC ACID TREATMENT

Dagmar Kollmann[1], Ivan Linares[1], Sujani Ganesh[1], Roizar Rosales[1], Matyas Hamar[1], Peter Urbanellis[1], Aryn Wiebe[1], Paul Yip[2], Adeyi Oyedele[3], Markus Selzner[1], Nazia Selzner[1]
[1]Toronto Organ Preservation Laboratory, Multi Organ Transplant Program, Toronto; [2]Laboratory Medicine Program, Department of Laboratory Medicine and Pathobiology, University of Toronto; [3]Laboratory Medicine and Pathobiology, University of Toronto, University Health Network, Toronto

Background: The risk of biliary complications remains a major obstacle for liver transplantation (LT) of donation after circulatory death (DCD)-grafts. norUrsodeoxycholic acid (norUDCA) has been accredited anti-cholestatic and anti-inflammatory properties. In this study, bile production and the potential of norUDCA-treatment during normothermic *ex vivo* liver perfusion (NEVLP) and after LT were evaluated.
Methods: Pig-LT was performed after 5 h NEVLP using heart-beating-donor (HBD-group) and DCD grafts with 30 and 60 min warm ischemia (30'DCD-group, 60'DCD-group; $n = 5$ each). Additionally, 60'DCD grafts were treated with norUDCA during perfusion and after LT (60'DCD-norUDCA-group, $n = 3$). Bile was collected hourly during perfusion and daily during a 4-day survival-period. Markers of cholangiocyte function (pH, HCO_3^-) and injury (AST, GGT, LDH) were assessed in bile.
Results: All 18 pigs survived for 4 days. AST-levels were higher in perfusate from 60'DCD-livers vs. HBD- and 30'DCD-livers at baseline, 2 and 4 h of perfusion ($p = 0.003$, $p < 0.001$, $p < 0.001$, respectively). Bile production was higher in the HBD-group at 1 and 2 h of perfusion ($p < 0.001$, $p = 0.002$, respectively) and bile cholesterol levels were lower in DCD-groups with the biggest difference at 2 h of perfusion. After LT, bile AST, GGT and LDH were higher in the 60'DCD-group reaching significant differences on POD3 ($p = 0.031$, $p = 0.011$ and $p = 0.031$, respectively). Treating the 60'DCD group with norUDCA led to markedly higher bile production during perfusion and significantly higher HCO_3^- levels at 2 h of perfusion. Furthermore, after LT, lower serum ALP levels and lower bile AST, GGT and LDH levels were detected in the 60'DCD-norUDCA-group.
Conclusion: We determined significant differences in bile production and quality during NEVLP of liver grafts with different grades of injury. NorUDCA treatment during perfusion and after LT improves the quantity and quality of bile production and thus might protect the bile ducts.

FG006 ORGAN-SPECIFIC METABOLIC PROFILES OF THE LIVER AND KIDNEY DURING BRAIN DEATH AND AFTERWARDS DURING RENAL NORMOTHERMIC MACHINE PERFUSION

Anne C. van Erp[1], Haiyun Qi[2], Nichlas R. Jespersen[2], Marie V. Hjortbak[2], Petra J. Ottens[1], Janneke Wiersema-Buist[1], Christoffer Laustsen[2], Henri G.D. Leuvenink[1], Bente Jespersen[2]
[1]UMCG; [2]Aarhus University

Metabolic assessment of brain-dead donors is a potentially novel strategy to assess and target graft quality prior to transplantation. We investigated metabolic changes during brain death (BD) using hyperpolarised MR spectroscopy and ex vivo graft glucose metabolism during normothermic kidney machine perfusion.

BD was induced in mechanically-ventilated rats by inflation of an epidurally-placed Fogarty catheter; sham-operated rats served as controls. Hyperpolarized [1-13C] pyruvate MR spectroscopy in a 9.4 T preclinical system was performed to quantify pyruvate metabolism in the liver and kidneys at three different timepoints during BD, each preceded by an injection of hyperpolarized 1-13Cpyruvate, polarized in a SpinLab. Following BD, glucose oxidation was measured using tritium labelled glucose isotope (D-6-3H-glucose) in an isolated perfused kidney device. qPCR and biochemistry was performed on stored tissue/plasma.

At 4 h after BD compared to sham, alanine production increased in the liver ($p < 0.001$) and lactate production at the kidney ($p < 0.05$). Immediately following BD, lactate production increased in both organs ($p < 0.001$). Following BD, renal glucose oxidation was reduced compared to sham animals ($p < 0.001$). No differences in enzyme activities were found in the liver or kidney. Gene expression of lactate transporter MCT4 increased in the kidney following BD ($p < 0.01$).

In conclusion, metabolic processes during BD in the liver and kidney can be visualised non-invasively using hyperpolarised MRI and during ex vivo renal machine perfusion with assessment of glucose oxidation. With these techniques, we showed that the liver and kidney of brain-dead animals showed a distinctly different metabolic profile compared to sham animals.

FG02 – CARDIOVASCULAR COMPLICATIONS AFTER KIDNEY AND LIVER TRANSPLANTATION

FG007 CARDIAC OUTPUT OPTIMISATION FOLLOWING LIVER TRANSPLANTATION (COLT) TRIAL: A FEASIBILITY RANDOMISED CONTROLLED TRIAL

Farid Froghi[1], Rahul Koti[1], Daniel Martin[1], Kurinchi Gurusamy[1], Louise Longworth[2], Jeshika Singh[2], Fiammetta Soggiu[1], Susan Mallett[1], Nick Schofield[3], Linda Selves[4], Douglas Thorburn[5], Christine Eastgate[3], Helder Filipe[3], Margaret McNeil[3], Zacharias Anastasiou[6], Brian Davidson[1]
[1]UCL Division of Surgery & Interventional Sciences; [2]PHMR Limited; [3]Royal Free Perioperative Research Group; [4]Royal Free Hospital HPB Surgery & Liver Transplantation Unit; [5]Royal Free Hospital Sheila Sherlock Liver Centre; [6]UCL Department of Statistical Science

Background: Goal-directed fluid therapy (GDFT) reduces morbidity following major surgery but has not been robustly assessed in liver transplantation. We therefore conducted a prospective trial to assess the feasibility of delivering GDFT following liver transplantation.

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Methods: Patients with liver cirrhosis were recruited to either 12 h of GDFT using non-invasive cardiac output monitoring (Fig. 1) or standard care (SC) guided by attending clinicians. The primary outcome measure of the study was feasibility. Secondary outcomes included postoperative complications (scored on the Clavien-Dindo (CD) scale), quality of life (using EQ-5D-5L) and an assessment of resource use. Trial specific follow up occurred at 90 and 180 days after surgery.

Figure 1. GDFT Protocol.

Results: During the 16 month recruitment period 224 patients were identified as eligible for the trial; of these, 122 were formally approached of whom 114 (93.4%) consented to participate. 60 patients were enrolled into the trial, stratification by organ donor characteristics occurred prior to randomisation. No patients were removed from the study by the clinical teams. Median crystalloid administered during the 12 h intervention period was 3,500 ml in the GDFT group versus 2,225 ml in the SC group. There were an increased number of CD grade 3 complications in the GDFT group at discharge from hospital (63.3%) versus the SC group (20.0%). There was no statistically significant difference in quality of life scores and resource use between the groups.

Conclusions: This feasibility study has demonstrated it is possible to recruit patients into a study of GDFT following liver transplantation and deliver the intervention in an ICU setting. The study was not powered to show differences in outcomes but has shown higher rates of grade 3 complications in the GDFT group.

FG008 CLINICAL OUTCOME OF KIDNEY TRANSPLANTATION AFTER BARIATRIC SURGERY: A SINGLE-CENTER RETROSPECTIVE COHORT STUDY

L. Outmani, H.J.A.N. Kimenai, R.C. Minnee
Erasmus MC University Medical Center Rotterdam

Introduction: Morbidly obese patients with end-stage renal disease are often found ineligible for kidney transplantation (KTx) due to an increased risk of postoperative complications and technically challenging surgery. Bariatric surgery (BS) has proven to be the most effective method of weight loss and became recently an option for KTx candidates who were initially considered inoperable. The aim of this study is to evaluate the clinical outcomes of KTx in patients who became eligible after successful BS and compare the outcomes with morbidly obese KTx recipients (BMI > 35) without BS.

Method: This retrospective, single-center study included patients who received a kidney transplant between January 1, 1994 and December 31, 2018. Patients who became eligible for kidney transplantation after BS were included. The control group consisted of patients who were morbidly obese at the time of KTx. The primary outcome was incidence of postoperative complications. As secondary outcomes, we investigated uncensored and death-censored graft survival, and patient survival.

Results: A total number of 156 patients were included in this study of which 23 underwent BS prior to KTx. Baseline characteristics were similar between both groups. There was no difference in postoperative complications, except for urinary tract infections which were more frequent in the BS group ($p = 0.008$). After a median follow-up of 4.0 years, death-censored graft survival, uncensored graft-survival and patient survival was similar to the controls (log-rank test $p = 0.800$, 0.789 and 0.488 respectively). In univariable analysis, having undergone BS was not an independant risk factor for patient death.

Conclusion: Patients who became suitable for KTx due toBS after initial rejection have similar complication rates, graft- and patient survival as patients who were transplanted despite being morbidly obese.

FG009 VALVULAR LESIONS FROM ROUTINE PRE-OPERATIVE ECHOCARDIOGRAMS AND POST KIDNEY TRANSPLANT COMPLICATIONS: A SINGLE-CENTRE ANALYSIS

Zahrah Goolam-Mahomed[1], Georgia Morgan[1], Felicity Evison[2], Suzy Gallier[2], Jay Nath[3], Rick Steeds[4], Charles Ferro[3], Adnan Sharif[3]
[1]University of Birmingham; [2]Department of Health Informatics, University Hospitals Birmingham; [3]Department of Nephrology and Transplantation, University Hospitals Birmingham; [4]Department of Cardiology, University Hospitals Birmingham

Introduction: Guidelines for pre-operative cardiovascular assessment for low-risk kidney transplant candidates differ. 45% of respondents stated an echocardiogram should be part of the work-up in a European survey (Maggiore et al. NDT 2019). At our centre, echocardiograms are repeated every three years before transplantation. This study aimed to investigate the association between pre-operative valvular lesions found on echocardiogram and post-transplant complications.

Methods: Data from hospital informatics for all transplant recipients between 2007 and 2018 was linked with recipients' latest pre-operative echocardiogram data for valvular lesions. Mortality, graft loss and delayed graft function data were crosschecked with the UK Transplant Registry.

Results: We analysed 761 transplant recipients. Baseline demographics were; median age 48 years (IQR 38–58 years), male gender 57.8% and white ethnicity 58.6%. Certain valvular lesions were more commonly observed than others as shown in the table.

Valve lesion	None (%)	Trivial (%)	Mild (%)	Moderate (%)	Severe (%)
Mitral regurgitation (MR)	30.9	38.6	26.9	3.6	0.0
Mitral stenosis (MS)	98.0	0.2	1.5	0.4	0.0
Aortic stenosis (AS)	96.6	2.9	0.5	0.0	0.0
Aortic regurgitation (AR)	76.5	9.0	10.7	3.7	0.1
Tricuspid regurgitation (TR)	26.7	44.8	25.5	2.9	0.1

Excluding TR, all valve lesions were significantly more common in recipients aged 50 and over. Worsening grades of MR was associated with increased risk for emergency re-admission within 90-days post-transplantation; moderate MR (70.4%) versus mild MR (38.7%), trivial MR (41.3%) and no MR (41.9%). There was no association between severity of valve lesion and risk for re-admission due to a cardiovascular event.

Discussion: This data supports the recommendation from the ERA-EDTA to minimise diagnostic tests in asymptomatic candidates aged under 50. Our cohort only includes candidates who proceeded to transplantation leading to selection bias as some candidates may have been excluded due to significant valvular lesions.

FG011 TIME TO OPTIMIZE BLOOD PRESSURE AFTER KIDNEY TRANSPLANTATION?

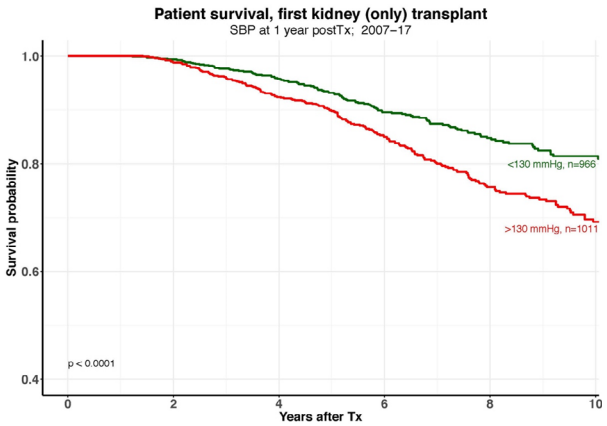
Anders Åsberg, Karsten Midtvedt, Anna Varberg Reisæter
Oslo University Hospital-Rikshospitalet

Background: In kidney transplant (KTx) recipients, inadequate treatment of hypertension is associated with reduced graft and patient survival. International guidelines advocate a target blood pressure of < 130/80 mmHg. The aim of the present study was to assess blood pressure treatment in KTx in Norway.

Methods: We addressed first time, adult KTx patients engrafted between 2007 and 2017 analyzing data from the Norwegian Renal Registry (NRR) which collects annual data from all KTx recipients in Norway. Annual follow-up data of blood pressure (BP) target and patient survival was retrieved.

Results: A total of 2,385 first kidney transplantations were performed in the time period (mean age 54 ± 17 years, 68% male, 31% living donor KTx). The annual percentage of recipients that achieved the BP target was 41 ± 5%, ranging yearly from 37% to 56%. The target achievement tended to be better in younger patients (<40 years: 52 ± 4% vs. >70 years: 32 ± 5%) and negatively associated with number of antihypertensive drugs (0 drugs: 59 ± 7% vs. 3 + drugs: 31 ± 10%). Patient survival was significantly improved for recipients reaching the BP treatment goal by 1 year ($p = 0.0062$) and highly significant for those with a 1-year systolic blood pressure (SBP) below 130 mmHg (Figure 1, Kaplan-Meier plot, $p < 0.0001$).

Conclusion: Target achievement of BP was low in all age categories of KTx recipients, also in patients without treatment-resistant hypertension (i.e. use of <4 antihypertensive drugs). Long-term survival was significantly better in patients reaching the BP goal by 1 year and SBP < 130 mmHg one year posttransplant seems to be the driving factor. The present data underline the need for a more aggressive antihypertensive approach.



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FG012 IMPLEMENTATION OF A NOVEL ALGORITHM TO OPTIMISE FLUID THERAPY IN RENAL TRANSPLANTATION

Jeremy Fabes, Ammar Al Midani, Amanpreet Sarna, Dina Hadi, Neal Banga, Gareth Jones, Peter Berry, Marc Wittenberg
Royal Free NHS Foundation Trust

Background: Renal transplant graft function depends on optimised perioperative fluid status and haemodynamics. Evidence in major surgery supports the use of goal-directed intravenous fluid therapy, guided by markers of cardiac output, to optimise outcomes.

Our centre employs intermittent blood pressure measurement with central venous pressure-guided fluid titration. This risks supra-normal intravascular volume status and slow recognition of hypotension particularly around induction of anaesthesia and graft perfusion.

The Edwards ClearSight™ device provides continuous non-invasive blood pressure measurement and a marker of intravascular filling, stroke volume variation. We implemented an intraoperative ClearSight™-based algorithm for administration of fluid and cardioactive agents to optimise intravascular fluid and haemodynamic status.

Methods: 41 transplant procedures performed using the standard of care were compared to 20 cases managed using the ClearSight™ algorithm.

Results: There were no differences in demographics or comorbidities between the two groups. Mean intraoperative crystalloid administration was reduced from 4,200 to 2,300 ml ($p < 0.001$) with non-significant reductions in normal saline (22–5%, $p = 0.096$) and blood product exposure (9.8–0%, $p = 0.152$). Perioperative cardiac complications were reduced from 14.6% to 0% ($p = 0.099$). There was no change in the use of vasoactive agents ($p = 0.531$), the rate of delayed graft function or percentage decrease in serum creatinine at 24 h, nor in the estimated GFR at 90 days post-transplant.

Conclusion: A ClearSight™-based algorithm to titrate fluid and cardioactive agent therapy is safe and reduces the administered fluid volume. This is associated with reduced post-operative cardiac complications, iatrogenic haemodilution and blood product transfusion. This supports the need for clinical trials assessing goal-directed approaches to cardiovascular optimisation in renal transplantation.

FG03 – KIDNEY ALLOCATION REVISITED

FG013 LEVERAGING TECHNOLOGY TO IMPROVE WAITLIST MANAGEMENT PERFORMANCE

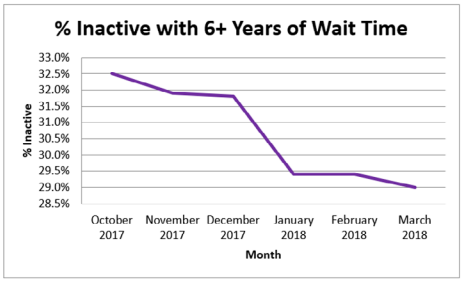
Wade Liu
Transplant Connect

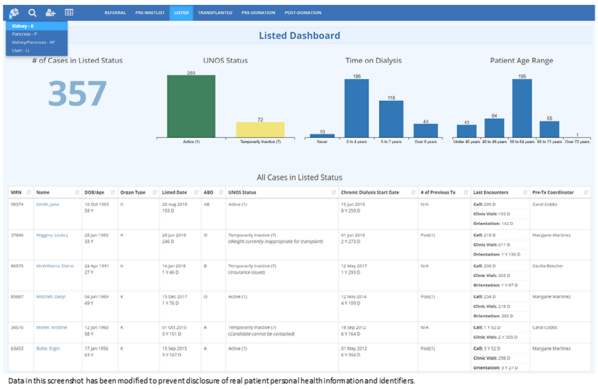
Background: A US transplant center established a goal to maintain a transplant waitlist that is 75% active (UNOS Status 1). An intensive PI project to achieve this goal and target subgroups of patients with increased waitlist inactivity began as a formal QAPI project. This PI project was executed alongside the design and deployment of a new electronic transplant patient management system to maximize real-time, data-driven decision making.

Methods: The center embarked on the development of a new electronic patient management system to improve patient care, regulatory compliance, waitlist management performance, and operational efficiency. The development began by identifying current deficiencies and goals, including maximizing technology to improve management of waitlisted patients. The center partnered with a software team who gained intimate knowledge of the key clinical and operational workflows before delivering a comprehensive new electronic solution for the unique needs of transplant centers.

Results: Since the launch of the new electronic patient management system, the center's listed patients with active status improved to 80% – a figure surpassing the center's 75% goal as well as both regional and national performance of the same measurement. Additionally, a 3.5% change in the subgroup of patients with 6+ years of qualifying wait time was observed, improving from 32.5% to 29% inactive in less than a year. Via use of the new system, data is now easily accessed for regulatory, reporting, and QAPI purposes. Patient reasons for hold-up in the workup process or inactivity on the waiting list are easily visualized in real-time to all members of the team.

Conclusion: Manual report generation and analysis of the center's critical patient waitlist has been replaced by user-friendly, live dashboards that provide staff with real-time metrics to continually and easily manage the program waitlist as part of their standard workflow and day-to-day activity.





Data in this screenshot has been modified to prevent disclosure of real patient personal health information and identifiers.

FG014 DECEASED-DONOR INITIATED KIDNEY PAIRED DONATION (KPD): FIRST REPORT OF A SERIES OF CHAINS

Lucrezia Furian[1], Antonio Nicolò[2], Emanuele Cozzi[3], Massimo Cardillo[4], Cristina Silvestre[1], Pamela Fiaschetti[5], Alessandro Nanni Costa[5], Paolo Rigotti[1]
[1]Kidney and Pancreas Transplantation Unit, Hospital University of Padova; [2]Department of Economics and Management, University of Padova; [3]Transplant Immunology Unit, Padova University-Hospital; [4]IRCCS Policlinico Hospital Milan; [5]Italian national Transplant Center, Rome

HLA and AB0 incompatibility (AB0i, HLAi) among living donors (LD) and their intended recipients can be addressed by KPD programs. In addition to KPD started with altruistic donors, the option of initiating chains of LD with a deceased donor (DD) kidney has been successfully explored.

Starting from March 2018 to January 2019, 4 kidneys from a DD were used to initiate chains allowing to perform 12 kidney transplants, and enabling 8 incompatible pairs (1 AB0i and 7 HLAi) to receive and donate a kidney with no need for desensitization. Recipients of incompatible pairs were given priority in the allocation of chain initiating kidneys from DD only in the absence of urgent, highly sensitized or candidates to combined transplants.

Seven Italian centers were involved either in procurement or transplant procedures. All patients are alive, no graft losses occurred, no cases of DGF are reported, mean cold ischemia time was 350 ± 145 min, and serum creatinine at discharge was 1.23 ± 0.52 mg/dl.

After appropriate management of the ethical, allocation and logistic issues, KPD starting with DD kidneys turned out to be feasible, consenting short cold ischemia time, no occurrence of DGF, and optimal renal function.

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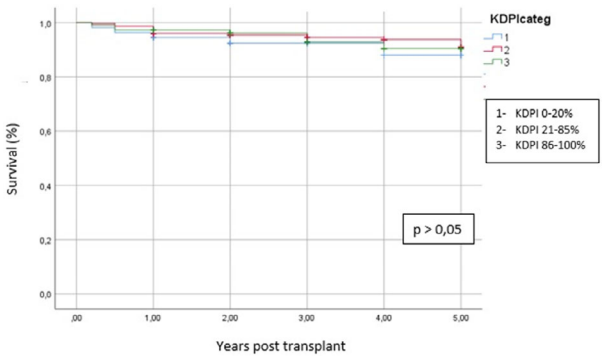
FG015 INTERNATIONAL KIDNEY EXCHANGES PROVIDING LIVING DONOR KIDNEY TRANSPLANTS FOR 38 PATIENTS INVOLVING 18 TRANSPLANT CENTERS FROM SIX COUNTRIES

Michael Rees[1], Obi Ekwenna[1], Siegfredo Paloyo[2], Ty Dunn[3], Kimberly Krawiec[4], Susan Rees[5], Alvin Roth[6], Itai Ashlagi[6], Michael Zimmerman[7], Jeffery Punch[8], Rachel Forbes[9], Christopher Marsh[10], Christian Kuhr[11], Jeffrey Rogers[12], Miguel Tan[13], Mark Boelkins[14], Laura Basagoitia[15], Ricardo Correa[16], Jorge Ortiz[1], Puneet Sindhwani[1], Ian Thomas[17], Jacopo Romagnoli[18], Ignazio Marino[19], Franco Citterio[18]
[1]University of Toledo; [2]Philippine General Hospital; [3]University of Pennsylvania; [4]Duke University; [5]Alliance for Paired Donation; [6]Stanford University; [7]Medical College of Wisconsin; [8]University of Michigan; [9]Vanderbilt University; [10]Scripps Health; [11]Virginia Mason Medical Center; [12]Wake Forrest; [13]Piedmont Hospital; [14]St. Mary's Hospital Grand Rapids; [15]Social Securtity Mexican Institute; [16]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; [17]Mount St John Medical Center; [18]Catholic University of Rome – Gemelli Hospital; [19]Thomas Jefferson University

Introduction: Kidney exchange (KE) is a widely adopted strategy to increase living donor kidney transplants (KTs) for patients with willing but immunologically incompatible donors. KE could be expanded to help more patients if the genetic diversity encountered across international borders allows matching for more highly sensitized patients. Regulatory, logistical, legal and financial impediments currently limit international KE (iKE).
Methods: From June 2014 to February 2019, a United States (US)-based non-profit organization began to include pairs from non-US countries to increase KE transplants for US and non-US patients.
Results: iKE has produced 6 chains and 2 cycles that has allowed 8 non-US patients (3 from The Philippines, 3 from Mexico, 1 from Denmark and 1 from Italy) and 30 patients in the US to receive KTs. The lengths of each chain were 12, 7, 6, 2, 4, 2 and cycle lengths were 3 and 2; coordination of these KTs involved 18 transplant centers. Five US recipients had blood type (BT)-A, 21 BT-0, 3 BT-B, and 1 BT-AB; 6 non-US recipients had BT-A and 2 had BT-O. The PRA was 0–20% for 14 patients, 21–79% for 13 and >80% for 11 (5 non-US); 39.5% of recipients were non-white. Non-US recipients have 100% graft survival to date (longest 4.25 years) and all non-US donors have normal creatinine and blood pressure. Five non-US patients faced financial barriers that prevented travel to the US for transplantation including three with financial barriers to transplantation in their home country. A combination of philanthropy and donor travel helped overcome financial barriers. Shipping kidneys was legally or logistically not possible, requiring six non-US donors to travel to the US and two US donors to travel outside the US.
Conclusion: iKE appears to be a mechanism to increase opportunities for hard to match blood type O and highly sensitized patients. Further work is needed to develop scalable mechanisms to overcome regulatory, logistical, legal and financial barriers.

FG016 ADEQUACY OF KDPI TO EVALUATE KIDNEY DONORS IN A LARGE PORTUGUESE COHORT

Sofia Cerqueira[1], Natalia Silva[1], Ciria Sousa[1], Pedro Pereira[1], Rui Castro[1], Catarina Romaozinho[2], Teresa Morgado[1], Arnaldo Figueiredo[2]
[1]Vila Real Hospital; [2]CHUC



The population of donors and receptors of kidney transplant is continuously changing. The gap between offer and need for kidney transplant has been increasing. Evaluation of suboptimal donors has become frequent practice. Kidney Donor Profile Index was designed based on the population of USA.

FG017 HIGH VOLUME SINGLE CENTER KIDNEY PAIRED DONATION (KPD) PROGRAM: A REPORT OF 100 KPD PATIENTS OVER TWO YEARS

Khalid Almeshari, Dieter Broering, Ibrahim Alahmadi, Syed Raza, Tariq Ali, Hani Alahdal, Amira Al Abassi, Fadi Alzayer, Amalnaji Algharabli
King Faisal Specialist Hospital & Research Center

Purpose: Matching rates of very highly sensitized patients with cPRA of 91–100% (VHSP) and blood type O recipients of ABO incompatible donors (ABO I → O) remain relatively low in all reported single center and national KPD registries. We report our experience in matching and transplanting such difficult to match KPD recipients.
Methods: The key features of our single center KPD program include:

1. Inclusion of HLA and ABO compatible pairs (CP) with poor HLA match.
2. As one of the matching goals, a qualified ABO Incompatible (ABO I) matching and/or low risk desensitization in the context of KPD for HLA incompatible (HLA I) VHSP.
3. As one of the matching goals, a downgrade of high risk ABO I in ABO I → O to low risk ABO I (A2 → O or B → O with low iso-agglutinin titer).
4. Emphasis on HLA class II matching for all KPD candidates.
5. High frequency match run utilizing Biologic Tx Matchgrid™ software.

Results: After implementing the program in May 2016, and as of May 2018, our KPD pool consisted of 193 pairs; 124 (64%) were HLA I; 34 (17%) were ABO I; and 35 (19%) were CP. Match rates are presented in the following table:

Number	Match rate	Percentage
Total (N = 193)	140/193	73
HLA I (N = 124)	80/124	64
VHSP: cPRA 91–94 (N = 8)	7/8	87
cPRA 95–97 (N = 12)	9/12	75
cPRA 98–100 (N = 66)	31/66	47
ABO I (N = 34)	26/34	76
ABO I → O (N = 21)	13/21	62
CP (N = 35)	34/35	97

Out of those matched, 100 patients (57 HLA I, 15 ABO I and 28 CP) were transplanted over the two-year period. The modalities of KPD were traditional 2–5 way paired exchanges in 93 patients and one closed chain in seven patients. 28/57 (49%) of the transplanted HLA I were VHSP and 10/15 (66%) of transplanted ABO I were ABO I → O. Over an average follow-up period of 300 days, patient survival was 100%; graft survival was 99%; incidence of AMR was 0%; and incidence of ACR was 13% (Banff IA-IIB). Average serum creatinine was 90 μmol/l (range: 55–169).
Conclusion: Our single center KPD transplant volume and matching rates of difficult to match KPD candidates compare favorably to the best of those reported by other high volume single center and national KPD programs.

FG018 RETHINK THE USE OF EXPANDED CRITERIA DONORS AFTER CONTROLLED CIRCULATORY DEATH: A MULTICENTRIC RESTROSPECTIVE COHORTS STUDY

Nuria Montero[1], Nestor Toapanta[2], Rafael Alvarez[1], Lluís Guirado[3], Carme Facundo[3], Fritz Diekman[4], Ignacio Revuelta[4], Maria Meneghini[1], Francesc Moreso[2], Oriol Bestard[1]
[1]Hospital universitari de Bellvitge; [2]Hospital Universitari de Vall d' Hebrón; [3]Fundació Puigvert; [4]Hospital Clínic

Background: The increasing kidney transplant waiting lists and organ shortage has led to an expansion of the deceased donor transplant pool by the use of kidney organs from expanded criteria donors (ECD) and after controlled donation after circulatory death (cDCD). While previous reports have shown excellent graft and patient results using cDCD from young donors (<65), robust data supporting the same outcomes among ECD-cDCD is still lacking. The aim of this study was to evaluate patient and kidney transplant outcomes of cDCD and brain death donors (DBD) stratified according to donor characteristics (standard (SCD) or expanded donors).
Methods/Materials: Multicentric (4 transplant Units in Barcelona), retrospective cohort study from January 2013 until July 2017 (n = 1,023). Donors were classified in 4 categories: DBD-SCD, DBD-ECD, DCD-SCD; DCD-ECD.
Results: Of 1,023 kidney transplants, 279 (27.3%) were classified as DCD transplants. Mean follow-up was 33.6 ± 13.32 months. Donors and recipients' characteristics are described in Table 1. Patient and graft survival (Figure 1) were worse in DCD-ECD compared to DBD-SCD, DBD-ECD or DCD-SCD (Log Rank $p < 0.001$). In ECD-DCD compared to SCD-DBD, the HR of graft loss was 3.5 (95% CI 2.2–5.5) and HR of patient death was 6.8 (95% CI 2.8–16.1). Cold ischemia time was longer in DBD-ECD ($p < 0.001$), delayed graft function was higher in DCD-ECD ($p < 0.001$) and eGFR at 1 year was lower in ECD ($p < 0.001$) (see Table 1).
Conclusion: In this large multicentric cohort of kidney transplant recipients, the use of ECD-DCD kidneys entails poorer results in terms of graft function and patient and graft survival compared with those obtained with kidneys from standard donors or ECD after brain death. However, it is necessary to evaluate if this approach provides better patient survival than remaining on dialysis waiting for a better quality kidney.

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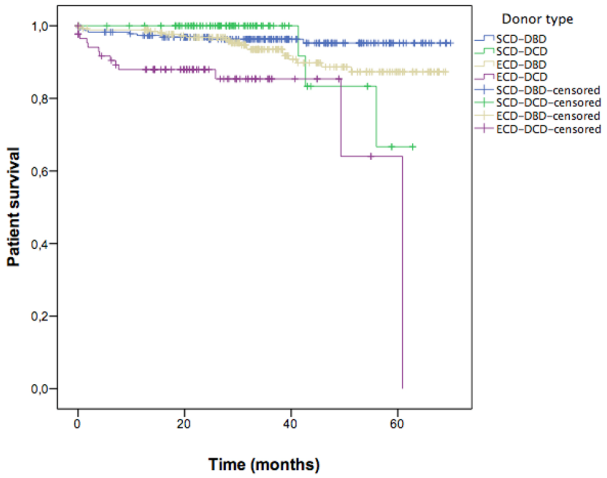
	DBD-SCD (n = 314)	DBD-ECD (n = 430)	DCD-SCD (n = 126)	DCD-ECD (n = 153)	p-Value
Donor					
Age (mean ± SD)	47 ± 10.4	72 ± 7.7	50.1 ± 9.7	70 ± 7.1	<0.001
Gender (m/f)	177/137	198/232	82/44	99/54	<0.001
Arterial hypertension (%)	18	56.1	8.4	17.6	<0.001
Diabetes mellitus (%)	20.5	61.4	1.8	16.4	<0.001
KDRI (mean ± SD)	1.16 ± 0.5	2.13 ± 0.93	1.17 ± 0.31	2.09 ± 0.77	<0.001
Recipient					
Age (mean ± SD)	49.2 ± 10.7	66.9 ± 8.8	53 ± 9	65.8 ± 10	<0.001
Gender (m/f)	220/94	275/155	72/54	109/44	0.024
cPRA (%) (mean ± SD)	13.9 ± 32.2	11.4 ± 27.8	13.43 ± 30.5	12.74 ± 29.7	ns
Outcomes					
Cold ischemia time (h) (mean ± SD)	17.1 ± 5.4	18.1 ± 6.1	11.8 ± 7.5	14.1 ± 6.1	<0.001
Delayed graft function (%)	28	30.9	42.9	52.3	<0.001
eGFR (MDRD-4) 1 year (ml/m/1.73 m^2)	57.4 ± 20.5	41.83 ± 15.13	55.2 ± 21.7	40.1 ± 13.1	<0.001



FG04 – KIDNEY REJECTION AND HISTOLOGY

FG019 IMPACT OF FCGR3A POLYMORPHISMS ON AMR OUTCOME IN KIDNEY TRANSPLANTATION

Alice Koenig[1], Virginie Mathias[2], Maud Rabeyrin[3], Antoine Sicard[1], Emmanuel Morelon[3], Véronique Frémeaux-Bacchi[4], Valérie Dubois[2], Olivier Thaunat[1]

[1]INSERM; [2]EFS; [3]HCL; [4]APHP

Background: Antibody-mediated rejection (AMR) is widely recognized as the first cause of allograft failure. AMR outcome is however heterogeneous at the individual level, making difficult the assessment of the individual risk of graft loss at the time of diagnosis.

During AMR, the binding of donor specific antibodies (DSA) on graft endothelial cells triggers the recruitment of innate immune cells (in particular NK cells), which in return damage graft vasculature by antibody-dependent cell-mediated cytotoxicity (ADCC). NK cells interact with Fc Fragment of DSA by a unique receptor: FcγR3A (CD16A). A SNP (FcγRIIIa*559A > C, rs396991) has been shown to modulate FcγR3A binding capacity to Fc of IgG but its impact in AMR has never been assessed so far.

Method and Results: Among the renal transplant patients followed in Lyon University Hospital that had a graft biopsy between 2004 and 2015, 118 presented an AMR as defined by Banff: (i) presence of microvascular inflammation on biopsy, and (ii) circulating DSA. The 15.9% of patients that were homozygous for the "high-binding" FcγR3A allele had an inferior allograft survival as compared with patients with a "low-binding" FcγR3A (p = 0.03).

An in vitro model of ADCC, in which purified human NKs were co-cultured with endothelial cells coated with DSA, confirmed that NKs with a high-binding FcγR3A displayed stronger activation and promoted more endothelial damages.

Conclusion: Our work demonstrates that FcγR3A polymorphisms impact AMR outcome and suggest that this genetic biomarker could be useful to stratify the risk of graft loss at diagnosis of AMR.

FG020 COMPARISON OF LONG-TERM OUTCOMES BETWEEN ALEMTUZUMAB AND RABBIT ANTI-THYMOCYTE GLOBULIN FOR ACUTE KIDNEY ALLOGRAFT REJECTION

Marieke van der Zwan[1], Marian C. Clahsen-van Groningen[1], Dave L. Roelen[2], Martijn W.F. van den Hoogen[1], Madelon Van Agteren[1], Joke I. Roodnat[1], Carla C. Baan[1], Dennis A. Hesselink[1]

[1]Erasmus MC; [2]Leiden University Medical Center

Introduction: T cell-depleting antibody therapy with rabbit anti-thymocyte globulin (rATG) is the treatment of choice for glucocorticoid-resistant, recurrent and/or severe acute kidney allograft rejection (AR), however rATG is associated with serious infusion-related side effects. Alemtuzumab, a humanized rat monoclonal antibody against CD52, is incidentally used as off-label treatment for AR. Following satisfactory results in a pilot study, alemtuzumab has become the first line T-cell depleting agent in our center. Here, the long-term outcomes were compared of patients treated with either alemtuzumab or rATG for AR.

Materials and Methods: Between 2012 and 2017, we identified 113 patients, treated with alemtuzumab for biopsy-proven glucocorticoid-resistant, recurrent or severe AR. Long-term outcome was compared with the outcome of a retrospective cohort of 108 patients treated with rATG for AR between 2002 and 2012.

Results: Patient survival between patients treated with alemtuzumab or rATG was similar (p = 0.05, hazard ratio (HR) 2.08, 95%-confidence interval (CI) 0.99–4.34). Death-censored allograft survival after AR was comparable between both groups (p = 0.87, HR 0.96, 95%-CI 0.62–1.50). A multivariate Cox regression analysis of alemtuzumab-treated patients showed 4 variables that influenced allograft survival negatively: no maintenance immunosuppressive therapy with glucocorticoids, actual panel reactive antibodies above 6%, eGFR drop of more than 50% between baseline eGFR and eGFR at time of AR, and a lower HLA mismatch. Infusion-related adverse events occurred less often after alemtuzumab treatment. Infection-free survival in the first year after alemtuzumab treatment was superior compared with the infection-free survival of rATG-treated patients (p = 0.002, HR 0.54, 95%-CI 0.37–0.84).

Conclusion: Alemtuzumab therapy is a good alternative therapy for glucocorticoid-resistant, recurrent and/or severe AR.

FG021 WHAT IS THE ROLE OF ENDOTHELIAL-TO-MESENCHYMAL TRANSITION (ENDOMT) OF RENAL CAPILLARIES ON THE RENAL OUTCOME BOTH IN ISOLATED TRANSPLANT GLOMERULOPATHY AND CHRONIC ANTIBODY-MEDIATED REJECTION (CAMR)

B. Handan Ozdemir[1], F. Nurhan Ozdemir[2], Aydincan Akdur[3], Mahir Kirnap[3], Gokhan Moray[3], Mehmet Haberal[3]

[1]The Department of Pathology, Faculty of Medicine, Baskent University, Ankara; [2]The Department of Nephrology, Faculty of Medicine, Baskent University, Ankara; [3]The Department of Transplantation, Faculty of Medicine, Baskent University, Ankara

Introduction: Although transplant glomerulopathy (TG) is the component of CAMR, a substantial number of patients with TG did not have C4d or DSA, indicating that a non-alloantibody-mediated process may be involved in the development of TG and called isolated TG. We compared the renal outcome and the development of EndoMT among patients displaying TG with or without C4d expression and DSA.

Methods: Among 156 recipients 76 had isolated TG (Group 1), and 80 had CAMR (Group 2). Glomerular and peritubular capillary (PTC) leukocyte and macrophage infiltration graded. To show the development of EndoMT, CD31, VEGF, paxillin, α-SMA, and Smad2 studied. Tubulointerstitial TNF- α and TGF-β expression examined. Follow-up biopsies analyzed for the development of interstitial fibrosis (IF), and glomerulosclerosis (GS) (>30% of glomeruli).

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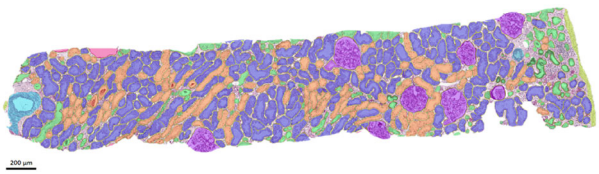
Results: Group 1 displayed a lower degree of leukocyte and macrophage infiltration in the interstitium, glomeruli, and PTCs compared to Group 2 patients ($p < 0.001$). Both in glomeruli and PTCs, the expression of α-SMA, paxillin, and Smad2 were found higher, and VEGF and CD31 were found lower in Group 2 than Group 1 ($p < 0.001$), that means the development of EndoMT found to be higher in Group 2 than Group 1. The degree of both PTC and glomerular α-SMA, paxillin and Smad2 expression increases with the increasing degree of tubulointerstitial TGF-β and TNF-α expression ($p < 0.001$). The development of diffuse IF and GS during follow-up was found to be higher in Group 2 than Group 1 ($p < 0.001$). Overall 5-year graft survival was 82% and 45% for Group 1 and Group 2 respectively ($p < 0.001$).
Conclusion: Compared to CAMR, patients with isolated TG associated with a lesser degree of allograft inflammation, a lower incidence of EndoMT with the lower development of fibrosis. The EndoMT process plays an essential role in the fibrosis process through the TGF-β/Smad signaling pathways in allografts with an endothelial injury which explains the higher rates of fibrosis in CAMR.

FG022 DEEP-LEARNING BASED HISTOPATHOLOGICAL ASSESSMENT OF RENAL TISSUE AS AN AID FOR KIDNEY TRANSPLANT RESEARCH

Meyke Hermsen[1], Thomas de Bel[1], Marjolijn den Boer[1], Eric Steenbergen[1], Jesper Kers[2], Sandrine Florquin[2], Joris Roelofs[2], Mark Stegall[3], Mariam Priya Alexander[3], Byron Smith[3], Bart Smeets[1], Luuk Hilbrands[1], Jeroen van der Laak[1]
[1]Radboudumc; [2]Amsterdam UMC; [3]The Mayo Clinic

Background: Quantitative measures are often used for histopathological kidney allograft assessment. Currently, these are obtained through manual scoring or classical image processing techniques. These methods possess limited reproducibility and are time-consuming. We trained a convolutional neural network (CNN) for the multi-class segmentation of digitized Periodic acid-Schiff (PAS) stained renal tissue sections.
Methods: The CNN was trained using multi-class annotations from 40 whole-slide images (WSIs) of PAS-stained renal transplant biopsies. We applied the CNN on 4 unseen data sets. Segmentation performance was assessed by calculating Dice coefficients (DC) for 10 tissue classes on 10 transplant biopsies from Radboudumc and on 10 transplant biopsies from an external center for validation. Additionally, we fully segmented 15 nephrectomy samples. Lastly, glomerular counts and Banff ci and ct scores of 3 pathologists were compared with CNN quantifications in 82 kidney transplant biopsies.
Results: The weighted mean DCs of all classes were 0.80 and 0.84 in 10 kidney transplant biopsies from Radboudumc and Mayo Clinic, respectively. An example of a fully segmented transplant biopsy is depicted in the figure below. The best segmented class was "glomeruli" in both data sets (DC 0.95 and DC 0.94). The CNN detected 92.7% of all glomeruli in nephrectomy samples, with 10.4% false positives. The mean intraclass correlation coefficient for glomerular counting performed by pathologists versus the CNN was 0.83. A significant correlation was observed for Banff ci and ct lesion scores and the percentage of interstitium and atrophic tubuli calculated by the CNN.
Conclusions: This study presents the first CNN for multi-class segmentation of PAS-stained nephrectomy samples and transplant biopsies. Our CNN can be of aid for quantitative studies concerning renal histopathology across



centers and provides opportunities for deep learning applications in routine diagnostics.

FG05 – LOOKING FOR THE LIVER TRANSPLANT BENEFIT: A DISCUSSION ON DONATION, ALLOCATION AND ISCHEMIA-REPERFUSION INJURY

FG025 RECURRENCE OF PRIMARY SCLEROSING CHOLANGITIS DETERIORATES GRAFT SURVIVAL: AN INTERNATIONAL MULTICENTER STUDY

Thijmen Visseren[1], Nicole S. Erler[2], Julie K. Heimbach[3], Nazia Selzner[4], Aliya Gulamhusein[4], Frans Van der Heide[5], Robert J. Porte[6], Bart Van Hoek[7], Ian P.J. Alwayn[8,9], Mark Walsh[9], Herold J. Metselaar[10], Jan N.M. IJzermans[11], Sarwa Darwish Murad[10]
[1]Department of Gastroenterology & Hepatology, Department of Surgery, Erasmus MC University Medical Center Rotterdam, Rotterdam; [2]Department of Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam; [3]Division of Transplant Surgery, Mayo Clinic College of Medicine, Rochester, MN; [4]Multiorgan Transplant Program, University Health Network, University of Toronto, Toronto, Ontario; [5]Department of Gastroenterology and Hepatology, University of Groningen, University Medical Centre Groningen, Groningen; [6]HPB and Liver Transplant Surgery, University of Groningen, University Medical Centre Groningen, Groningen; [7]Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden; [8]LUMC Transplant Center, Leiden, The Netherlands; [9]Atlantic Multi Organ Transplant Program, Dalhousie Univ., Halifax, Nova Scotia; [10]Department of Gastroenterology & Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam; [11]Department of Surgery, Division of HPB and Transplant Surgery, Erasmus MC University Medical Center Rotterdam, Rotterdam

B/Patients who receive a liver transplant (LT) due to Primary Sclerosing Cholangitis (PSC) have a risk of 8.6–27% for recurrence of PSC (rPSC). Single center studies and national registry studies have shown conflicting results regarding the impact on graft and patient survival. We provide the first transatlantic international multicenter study on rPSC using original, non-registry data.

M/We included patients who received their first LT for PSC between 1990 and 2005 in six large-volume LT centers in Europe and Northern America. All centers were visited to collect data in a standardized fashion. A detailed dataset was constructed with a focus on pre-LT course of PSC, LT characteristics, rPSC (defined according to the Mayo criteria), and graft and patient survival. Data are shown as *N* (%) or median (25–75%). Survival was analyzed in a Cox model with rPSC included as a time-dependent covariate.

R/In total 544 patients were included of whom 371(68%) were male, 373 (69%) had IBD at time of LT. Type of donor was in 44 patients (8%) living donation, 466 (86%) DBD, and 34 (6%) DCD. Median MELD at LT was 16 (12–20.5), median warm ischemia time was 56 (43–73) min, and median age at LT was 45 (36–54). The median follow-up was 155 (109–220) months and survival at 1, 5, 10, and 15 years was 87%, 78%, 66%, and 50% (graft) and 94%, 86%, 76%, and 65% (patient). A total of 114 (21%) patients were diagnosed with rPSC after a median of 79 (39–121) months after LT. In total 224 (41%) died during follow-up, of whom 37 (17%) had rPSC. A total of 120 (22%) patients received a second LT, of whom 41 (36%) had been diagnosed with rPSC. Patients with rPSC had significantly more often a reLT (36% vs. 18%, $p < 0.001$). The time dependent Cox model showed that rPSC has a significant negative effect on graft survival (HR 2.8; $p < 0.001$).

C/We showed a negative effect of rPSC on LT outcome with graft survival being severely reduced, and significant more reLT. Studies examining risk factors for rPSC are warranted.

FG026 SIGNIFICANT SURVIVAL ADVANTAGE FROM ACCEPTING A CIRCULATORY DEATH LIVER TRANSPLANT OFFER

James Richards[1], Rhiannon Taylor[2], Elisa Allen[2], Aaron Goh[1], James Neuberger[3], David Collett[2], Gavin Pettigrew[1]
[1]University of Cambridge; [2]Statistics and Clinical Studies, NHS Blood and Transplant; [3]University Hospital Birmingham NHS Foundation Trust

Background & Aims: Over the last decade, donation after circulatory death (DCD) liver transplantation has significantly increased in the UK in an attempt to tackle waiting list mortality. However, DCD liver transplantation outcomes are poorer than those from brain-stem death donors (DBD).

This study examines whether a recipient to should accept a "poorer quality" DCD organ or wait longer for a "better" DBD organ.
Methods: Survival was modelled using Cox regression to evaluate the impact on patient survival of accepting a DCD liver offer compared to deferring for a potential DBD transplant in all patients listed for deceased donor liver transplantation between 2008 and 2015 in the United Kingdom.
Results: 953 (23%) of the 3,949 liver transplantations performed utilised DCD donors. Five-year transplant survival was poorer following DCD than DBD transplantation (69.1% (DCD) vs. 78.3% (DBD); $p < 0.0001$: adjusted hazard ratio [HR] = 1.65, 1.40–1.94).

Of the 5,798 patients on the transplant list, 1,325 (23%) died or were removed from the list without receiving a transplant. Patients who received DCD livers had a lower risk-adjusted hazard of death than those who remained on the waiting list for a potential DBD organ (adjusted HR 0.55, 0.47–0.65). The greatest survival benefit was in those with the most advanced liver disease (adjusted HR 0.19 (0.07, 0.50).
Conclusions: Although DCD liver transplantation has poorer transplant outcomes, the individual's survival is enhanced by accepting a DCD offer, particularly in those with more severe liver disease.

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FG027 IMPACT OF MELD-NA COURSE (DELTA MELD-NA) ON OUTCOME AFTER LIVER TRANSPLANTATION

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 institutional data and confirmed by an Eurotransplant 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 risk prediction of posttransplant survival by adding recipient Sodium values to Delta MELD (Delta MELD-Na).
Method: More than 22,000 patients of the UNOS data base were analyzed, who were transplanted in the US from 2012 to 5/2016.

MELD-Na was calculated according to this formula

MELD − Na − [0.025 × MELD × (140 − Na)] + 140 (na ranges from 125 to 140)

Delta MELD-Na was defined as MELD-Na at listing minus MELD-Na at transplantation: Delta MELD = MELD-Na (ON) − MELD-Na (TX)

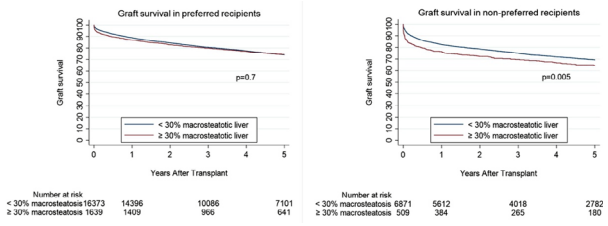
Delta MAX was the highest MELD-Na deterioration between two observation time points.

Delta LAST was the alteration between forelast and last observation before transplantation.
Results: 69.7% of patients showed a stable MELD Na during waiting time for transplantation with a maximum increase of 4 points. In 15.4% of patients an increase of 5–9 points was observed. Further 14.8% of patients showed an increase of 10 and more points. Statistical significant factors for posttransplant survival were MELD Na ON ($p = 0.007$), MELD Na TX ($p = <0.001$) and Delta MELD-Na and Delta MELD-Na MAX (both $p = <0.001$). Delta MELD-Na LAST did not show statistical significance ($p = 0.35$).
Conclusion: A severe deterioration of MELD- Na during waiting time results in significantly poor posttransplant survival in liver transplantation. Also temporary deterioration during waiting time showed similar risk.

FG028 MINIMIZING RISKS ASSOCIATED WITH STEATOTIC DONOR LIVERS BY MATCHING TO PREFERRED RECIPIENTS

Kyle Jackson, Jennifer Motter, Christine Haugen, Betsy King, Luckmini Liyanage, Allan Massie, Benjamin Philosophe, Andrew Cameron, Jacqueline Garonzik-Wang, Dorry Segev
Johns Hopkins Hospital

Introduction: Donor livers with ≥ 30% macrosteatosis represent a possible expansion to the donor pool, but are frequently discarded as they are associated with an increased risk of graft loss. We hypothesized that there are certain patient phenotypes that would tolerate donor macrosteatosis well, and are therefore best suited to receive these grafts.
Methods: Using US national registry data from the SRTR between 2005 and 2017, we compared 2,148 recipients of ≥ 30% macrosteatotic grafts to 23,244 recipients of < 30% macrosteatotic grafts. We defined donor steatosis as any liver with ≥ 30% macrosteatotic on biopsy, and other livers were considered non-steatotic. We then identified recipient factors that amplified the effect of donor steatosis on graft loss using interaction analysis. Recipients without these factors (i.e. without risk factors that amplified the negative effect of steatotic donor livers) were classified as preferred recipients. We used Kaplan-Meier analysis to compare outcomes between preferred and non-preferred recipients.
Results: Preferred recipients of steatotic livers were determined to be first-time recipients with a MELD < 35, without primary biliary cirrhosis or peritonitis, and not on life support prior to transplant. Preferred recipients had similar graft survival when using steatotic donor livers, compared to using non-steatotic livers (3-year graft survival: 80.6% vs. 79.8%, $p = 0.7$). In contrast, non-preferred recipients had worse graft survival when using steatotic donor livers, compared to non-steatotic livers (3-year graft survival: 69.5% vs. 75.1%, $p = 0.005$). Similarly, preferred recipients had equivalent patient survival when using steatotic donor livers (3-year survival 82.6% vs. 83.1%, $p = 0.5$), whereas non-preferred recipients had worse patient survival when using steatotic donor livers (3-year survival 72.8% vs. 77.9%, $p = 0.005$).
Conclusion: The risks of steatotic donor livers could be minimized by appropriate recipient matching.



FG029 CLINICAL OUTCOMES OF DCD TYPE V LIVER TRANSPLANTATION: DONATION AFTER EUTHANASIA

M. van Reeven[1], Nicholas Gilbo[2], D. Monbaliu[2], O.B. van Leeuwen[3], J. Blokzijl[4], R.J. Porte[3], N. Meurisse[5], O. Detry[5], D. van der Helm[6], B. van Hoek[6], I.P.J. Alwayn[7], Olga Ciccarelli[8], X. Rogiers[9], Sarwa Darwish Murad[10], J.N.M. IJzermans[1], W.G. Polak[1]
[1]Division of Hepatopancreatobiliary and Transplant Surgery, Department of Surgery, Erasmus University Medical Center Rotterdam; [2]Department of Surgery, Division of Abdominal Transplant Surgery, University Hospitals Leuven; [3]Department of Surgery, Section of Hepatobiliary Surgery & Liver Transplantation, University Medical Center Groningen; [4]Department of Gastroenterology and Hepatology, University Medical Center Groningen; [5]Department of Surgery, Section of Abdominal Surgery and Transplantation, CHU Liege; ; [6]Department of Gastroenterology and Hepatology, Leiden University Medical Center; [7]Department of Surgery, Division of Hepatopancreatobiliary and Transplant Surgery, Leiden University Medical Center; [8]Department of Surgery, Division of Abdominal Transplantation, University Hospital Saint-Luc Brussels; [9]Department of Surgery, Division of General & Hepatobiliary Surgery, Liver Transplantation Service, Ghent University Hospital; [10]Department of Gastroenterology and Hepatology, Erasmus University Medical Center Rotterdam

Introduction: Due to shortage of donor organs, physicians and surgeons are forced to accept livers from donation after circulatory death (DCD) donors. One special group of DCD organs are those obtained after euthanasia (DCD type V). To create more awareness on the possibility of organ donation after euthanasia, it is important to evaluate the results of transplantation with this type of graft. The aim of our study was to evaluate the outcome of DCD type V liver transplantation (LT) in the Netherlands and Belgium.
Methods: All DCD type V LT performed until 2018 in all three Dutch LT centers and four out of six Belgian LT centers, were included in this study. Grafts that have been preserved with machine perfusion were excluded. Continuous data are expressed as median (IQR), categorical data as number (percentage).
Results: Until 2018, 44 DCD type V LT have been performed. Five cases in which the liver was preserved by machine perfusion were excluded. Median age of donor and recipient was 51 years (42–58) and 56 years (48–64), respectively. A neurological disease was the most common underlying disease in donors requesting euthanasia, followed by psychiatric disorders. Median time between administration of the euthanatics and cold perfusion was 19 min (14–25). Peak AST and ALT levels in the recipients were 904 U/l (586–2,478) and 709 U/l (448–1,841) respectively. One-, three- and five-year patient survival was 90%, 83% and 83%, respectively (figure 1). Five patients (13%) required a retransplantation, due to PNF ($n = 1$), HAT ($n = 1$) or post-transplant cholangiopathy ($n = 3$), the majority within the first year after the prior LT.
Conclusion: Liver transplantations with grafts from donors who underwent euthanasia yield satisfying results during the relatively short follow up period that is currently available. Comparison of these results with DCD type III LT and donation after brain death (DBD) LT is currently ongoing.

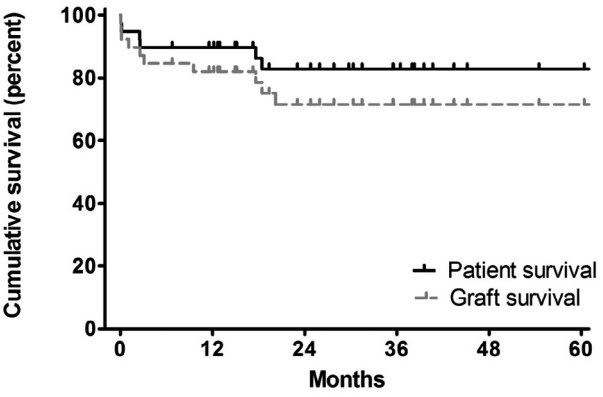


Figure 1: patient and graft survival after DCD-V LT

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FG06 – UNDERSTANDING AND MANIPULATING POST-TRANSPLANT IMMUNE RESPONSES

FG030 BTLA SUPPRESSED ACUTE REJECTION BY REGULATING T CELL RECEPTOR DOWNSTREAM SIGNAL PATHWAYS AND CYTOKINE PRODUCTION IN RENAL TRANSPLANT AND CONTRIBUTED TO PROLONGATION OF ALLOGRAFT SURVIVAL

Zijie Wang, Shuang Fei, Hao Chen, Li Sun, Zhijian Han, Jun Tao, Xiaobin Ju, Ruoyun Tan, Min Gu

The First Affiliated Hospital of Nanjing Medical University

The present study aimed to investigate the role of B and T lymphocyte attenuator (BTLA) in the progress of acute rejection after kidney transplantation. In human allograft renal transplanted recipients with biopsy-proven acute rejection (BPAR) or stable allograft function, the expression of BTLA was measured by flow cytometry, and immunohistochemistry (IHC) staining. In rat allograft renal transplant model, HE staining, IHC, western blot and qRT-PCR were performed to detect the BTLA expression in rat allograft renal samples. Mixed lymphocyte reaction (MLR) was also conducted. Finally, western blot was adopted to explore the function of the transcription factors of T cell receptor (TCR) downstream signal pathways in acute rejection. Flow cytometry showed BTLA expression on peripheral CD3 + T lymphocytes of BPAR recipients was significantly decreased compared with the stable group. In rat allogeneic renal transplant model, acute rejection was observed obviously from 3 to 7 days after transplantation, and the BTLA expression in grafts decreased at the early stage in acute rejection. Remarkably, overexpression of BTLA was found to significantly inhibit the progress of acute rejection, and regulate post-operative immune status, and prolong renal allograft survival. Besides, BTLA overexpression could directly suppress T cells proliferation in MLR culture. Moreover, BTLA overexpression has significantly suppressed interleukin (IL)-2 and IFN-γ production, and increased IL-4 and IL-10 production in vivo and in vitro. In addition, vital factors of signal pathways including mitogen-activated protein kinase (MAPK), NF-κB and the nuclear factor of activated T cells (NFAT) have been significantly repressed by BTLA overexpression. In conclusion, BTLA overexpression could suppress acute rejection and regulate allogeneic responses of kidney transplant through regulating TCR downstream signaling pathways and inflammatory cytokines production, and improve long-term graft outcomes.

FG032 RAPAMYCIN PROLONGS SKIN ALLOGRAFT SURVIVAL IN OBESE MICE THROUGH MYELOID-DERIVED SUPPRESSOR CELLS

Astrid Deißler[1], Andrea Della Penna[1], Chiel Van Geffen[2], Bernd Nürnberg[2], Alfred Königsrainer[1], Saeed Kolahian[2], Markus Quante[1]

[1]Department of General, Visceral and Transplant Surgery, University Hospital Tübingen, Tübingen, Germany; [2]Department of Pharmacology and Experimental Therapy, Institute of Experimental and Clinical Pharmacology and Toxicology and I

Background: Obesity has become a relevant problem in transplantation medicine with steadily increasing numbers of obese transplant candidates and graft recipients. However, the role of immunomodulatory drugs on transplant-related outcomes among obese patients is unknown. Here, we studied the effect of Rapamycin which has been shown to implicate robust immunosuppressive properties via various immune cells in a murine model of obesity and skin allograft transplantation.
Methods/Materials: Diet-induced obese mice underwent fully-mismatched skin transplantation (DBA/2 onto C57BL/6). Graft recipients were injected daily with Rapamycin (i.p., 2 mg/kg) starting at day of transplantation. We evaluated graft survival and performed immunophenotyping of myeloid-derived suppressor cells (MDSCs), T cells and macrophages using flow cytometry. Immunosuppressive activity of MDSCs was evaluated using MDSC – T cells co-culture suppression assay (CFSE) for 72 h.
Results: Rapamycin significantly prolonged allograft survival in obese mice compared to Rapamycin-treated lean controls. Rapamycin treatment in obese mice significantly increased the percentage of MDSCs (both Granulocytic-MDSCs and Monocytic-MDSCs) and their anti-proliferative activity on T cells compared to obese untreated animals. The number of anti-inflammatory M2-like macrophages was increased in obese recipients treated with Rapamycin compared to lean Rapamycin-treated animals.
Conclusion: Our results show that Rapamycin treatment increases not only the number of MDSCs but also the T cell-suppressive activity of MDSCs in obese recipients. In addition to MDSCs generation and activation, increase in the number of M2-like macrophages may support allograft survival in obese mice. The more profound understanding of the immunomodulatory role of the Rapamycin in obesity will facilitate the clinical application of this drug in transplantation medicine in the future.

FG033 THE FUNCTIONAL ALLOREACTIVITY IN VIVO OF GRAFT INFILTRATING LYMPHOCYTES IN EARLY PHASE POST-TRANSPLANTATION IN MICE

Yoshikazu Ganchiku, Ryoichi Goto, Rumi Igarashi, Ryo Kanazawa, Kazuaki Shibuya, Yasutomo Fukasaku, Norio Kawamura, Masaaki Zaitsu, Masaaki Watanabe, Moto Fukai, Akinobu Taketomi

Department of Gastroenterological Surgery I, Hokkaido University

Background: Immunological behavior leading to a graft rejection or acceptance depends on the local immune activity of graft infiltrating lymphocytes (GILs). However, the transition of immune balance of GILs that determines graft fate remains unclear. Herein, we examined the immunological behavior of early GILs itself against alloantigen by applying lymphocyte reconstitution method in immunodeficient mice.
Methods: C57BL/6 (B6, H-2K^b) cardiac allografts were transplanted into Balb/c (H-2K^d) mice. At 72/120 h posttransplantation, GILs were procured from the allografts and transferred into Balb/c Rag2$^{-/-}$?c$^{-/-}$ (BRG) mice intraperitoneally. 70 days after adoptive transfer, the immune function was examined.
Results: A few CD3$^+$GILs ($1.0 \pm 0.2 \times 10^4$, $n = 11$) were obtained from cardiac allograft 72 h posttransplantation, almost all of which expressed H-2K^d ($96.5 \pm 1.2\%$); recipient derived. When compared lymphocytes subset between 72 and 120 h posttransplantation, significant increase numbers of CD3$^+$GILs expressed on CD69 (21.8 ± 2.3 to $58.4 \pm 7.9\%$, $n = 4$, $p = 0.005$) and a TCR specific activation marker Nur77 (8.4 ± 1.3 to $31.0 \pm 2.8\%$, $n = 4$, $p = 0.003$), T-bet$^+$CD4$^+$GILs (34.7 ± 5.9 to $63.2 \pm 3.7\%$, $n = 4$, $p = 0.007$) and CD8$^+$GILs producing Perforin (3.5 ± 1.7 to $27.3 \pm 3.7\%$) and Granzyme B (7.6 ± 1.1 to $37.7 \pm 5.9\%$) were observed. Further, the alloantigen specific IFN? production was noted in BRG mice adoptively transferred with 120 h GILs (Fig. 1). Of note, transplanted B6 cardiac allografts were rapidly rejected in 120 h but not 72 h GILs-reconstituted BRG mice (Fig. 2). These unresponsiveness of 72 h GILs were confirmed by re-transplantation of B6 allografts at 72 h posttransplantation into BRG mice, which did not reject these allografts over 100 days ($n = 4$).
Conclusion: GILs 72 h posttransplantation did not participate an allograft rejection in vivo, while GILs 120 h did. To understand the precise function of the GILs may allow elucidating the mechanism of graft rejection and acceptance.

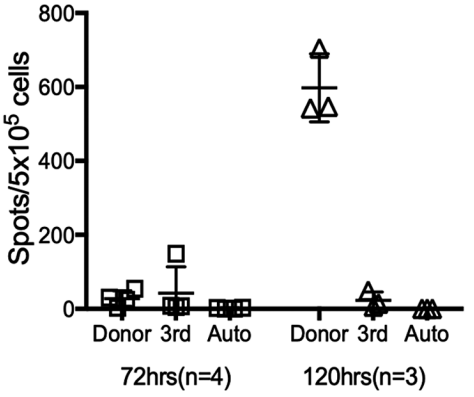

Fig 1. 70 days after adoptive transfer of GILs, ELIspot assay of spleen cells of GILs-reconstituted BRG mice were performed. Donor: B6, 3rd: C3H, Auto: Balb/c

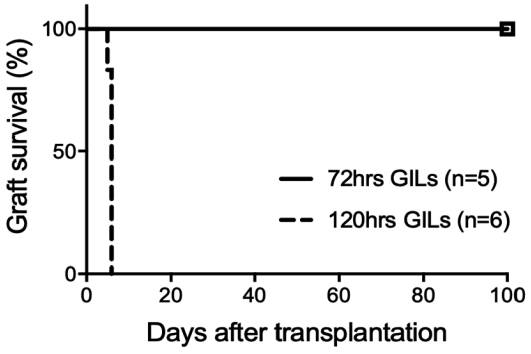

Fig 2. B6 cardiac graft survival of GILs-reconstituted BRG mice 70 days after adoptive transfer

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FG034 MODULATION OF THE IL-33/ST2 AXIS FOR REGULATORY T CELL THERAPY IN TRANSPLANTATION

Kento Kawai, Joanna Hester, Fadi Issa
University of Oxford

Background: Regulatory T cells (Tregs) are crucial mediators of immune homeostasis, with the ability to modulate alloreactive T cell responses and control transplant rejection. The interleukin-33 (IL-33)/ST2 axis has recently been demonstrated to have a role in the modulation of Tregs. Here we present novel data that demonstrate the ability of exogenous IL-33 administration to expand a highly suppressive population of Tregs in mice in vivo that can promote the survival of MHC-mismatched skin grafts.
Materials/Methods: $CD4^+FoxP3^+$ Tregs from groups of mice receiving either saline (control) or recombinant IL-33 injections were isolated and adoptively transferred together with effector T cells (Teffs) into syngeneic immunodeficient mice ($n = 8$ for Teff, $n = 11$ naive Treg, $n = 11$ for IL-33 Treg). Mice were then transplanted with an allogeneic skin graft where survival was monitored until allograft rejection and their organs were harvested for phenotypic analysis. Nanostring gene expression data analysis was performed on splenocytes from nontreated and IL-33 treated mice.
Results: Nanostring gene expression analysis showed that IL-33 in vivo treatment resulted in increased relative abundance of Tregs, reduced relative abundance of DCs, $CD8^+$ T cells, NK cells and Th1 cells, and reduced adaptive, cell cycle, chemokine and cytokine receptors, among others. Recombinant IL-33 administration expanded a $CD4^+FoxP3^+ST2^{hi}CD73^{hi}$ Treg population with an effector phenotype ($CD44^{hi}CD62L^-$). Mice treated with sorted IL-33-expanded Tregs demonstrated an enhanced ability to modulate Teff responses and suppress allograft rejection. Naïve Tregs extended allograft median survival time (MST) from 14 to 40 days, whereas IL-33 Tregs promoted long term survival (>100 days, $p = 0.03$).
Conclusion: Administration of IL-33 in vivo can significantly expand effector ST2hiCD73hi Tregs, which demonstrate an enhanced ability to prolong allogeneic skin graft survival.

FG035 ROLE OF CATS/PAR2 FOR THE REJECTION PROCESS IN MURINE RENAL TRANSPLANTATION

Benjamin Ehle[1], Yutian Lei[2], Santosh Kumar[2], Susanna Mueller[3], Julian Bucher[4], Hans-Joachim Anders[2], Joachim Andrassy[1]
[1]University of Munich, Surgery, Klinikum Grosshadern; [2]University of Munich, Nephrology, Klinikum Innenstadt; [3]University of Munich, Pathology; [4]University of Munich, Klinikum Großhadern

Background: Cathepsin S is involved in peptide loading to the MHC class II and thus important for antigen presentation. CatS can also be secreted by activated macrophages and neutrophils and activates protease-activated receptor-(PAR)-2 on the endothelial cells. We hypothesized that targeting CatS/Par2 would have a dual suppressive effect on kidney allograft rejection by limiting alloantigen presentation as well as vascular damage.
Methods: Murine kidney transplantation was performed in the syngeneic (B6 to B6) and allogeneic setting (Balb/c to B6). Mice were either treated with CatS inhibitor or vehicle. To study the effects of Par2 deficiency, we performed kidney transplantation using C57BL/6.Par2-/-. Therapeutic effects were assessed by histopathology, immunohistochemistry and RT-PCR.
Results: At 10 days allografts showed severe acute rejection with strongly induced mRNA levels of CatS and numerous inflammatory genes. CatS inhibition significantly ameliorated the acute rejection process. Immunostaining showed suppressed $CD8^+$ cell infiltration into grafts, reduced mRNA expression levels of inflammatory genes. Allografts from Par2-deficient mice showed less histological damage and less graft infiltrating $CD8^+$ cells as compared to their wildtype controls.
Conclusions: These data show that CatS/Par2 is critically involved in the pathogenesis of allograft rejection.

FG07 – ADVANCES IN CELL THERAPIES, REGENERATIVE MEDICINE AND TISSUE ENGINEERING

FG036 BIO ARTIFICIAL ENDOCRINE PANCREAS GENERATED FROM ACELLULAR HUMAN PLACENTA FOR TYPE-1 DIABETES TREATMENT

Kevin Bellofatto[1], Andrea Peloso[2], Charles-Henri Wassmer[1], Fanny Lebreton[1], Vanessa Lavallard[1], Estelle Brioudes[1], David Cottet-Dumouli[1], Géraldine Parnaud[1], Domenico Bosco[1], Christian Toso[2], Thierry Berney[1], Ekaterine Berishvili[1]
[1]Cell Isolation and Transplantation Center, University of Geneva; [2]Hepato-Pancreato-Biliary Centre, Geneva University Hospitals

Background: Development of vascularized biological scaffolds providing mechanical protection for islets is a challenging objective of modern regenerative medicine. Human placenta comprises cotyledons with rich pancreas specific extracellular matrix (ECM) and abundant vessel arborescence that makes it perfect candidate for the bioartificial pancreas engineering. The aim of our study was to develop vascularized endocrine pancreas using decellularized placental cotyledon.
Methods/Materials: Human placenta was decellularized by perfusion, using 0.5% sodium dodecyl sulfate. Decellularization was assessed by histological analyses, scanning electron microscopy (SEM) and residual DNA quantification. Glucosaminoglycans (GAG) and hydroxyproline were analyzed. Placental cotyledons were recellularized by a intravascular perfusion of human umbilical vein endothelial cells (HUVECs) during the 24 h HUVECs perfusion, followed by intraparenchimal injection of INS-1E cells. Recellularization was assessed by hystological and immunohistochemical methods, and endocrine function was confirmed by glucose stimulated insulin secretion tests performed at different time points.
Results: Histological staining and SEM showed complete decellularization and well preserved ECM structure. This was confirmed by the absence of residual DNA. GAG and collagen content was similar in decellularized cotyledons and in native placentas. Immunostainings of recellularized cotyedons showed insulin expressing islet like structures with intense vascularization confirmed by CD31 staining. Adequate insulin secretion in response to high glucose stimulation was also observed, confirming the functional activity of INS-1E cells.
Conclusion: These data demonstrate that acellular placental cotyledons seeded with endocrine pancreatic tissue and endothelial cells could be used for functional pancreas bioengineering.

FG037 DETAILED CHARACTERISATION OF HEALTHY AND CIRRHOTIC LIVER ORGANOIDS

Foad Rouhan, Olivia Tysoe, Kourosh Saeb-Parsy, Fotios Sampaziotis, Ludovic Vallier
University of Cambridge

Introduction: Organoids are three dimensional cellular structures, composed of multiple cell types and which may enable in vitro disease modelling. Non-alcoholic fatty liver disease (NAFLD) is increasing in prevalence and is projected to become the most common indication for liver transplantation in the future. The mechanisms behind how liver damage occurs during NAFLD and the implications for genetic stability in the liver are largely unknown. As a proof of principle, we generated biliary organoids from normal and cirrhotic liver biopsies and compared cellular composition, differentiation capabilities and transcriptional profiles. We then assessed each type of organoid for genetic stability and mutations.
Methods: Organoids were derived from needle biopsies of declined organ donor livers and cirrhotic NAFLD patients at time of explant during liver transplantation. The tissues were processed both as whole specimens as well as single cells and plated in culture media promoting intra-hepatic biliary cells self-renewal in Matrigel. Organoids were then individually picked and expanded. Further assessments included single cell clonal expansion, expression of hepatocyte and cholangiocyte markers and proliferation capabilities. Each organoid subclonal line was then sequenced to look for novel single nucleotide variants.
Results: Organoids were generated successfully from both healthy and cirrhotic biliary tissue with established organoids forming after 5 days in culture. All organoids showed similar cell compositions on immunohistochemistry and flow cytometry. The gene expression patterns were also similar in healthy and cirrhotic liver organoids. Cirrhotic organoids showed more genetic aberrations compared to healthy liver organoids.
Discussion: The derivation system used to generate organoids from liver biopsies is reliable, robust and efficient. These organoids could be useful to model NAFLD in vitro and also to understand the mechanisms leading to disease progression.

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FG038 NON-CULTURED ADIPOSE-DERIVED REGENERATIVE CELLS LIMIT EARLY INFLAMMATION AND FIBROSIS IN RENAL ISCHEMIA REPERFUSION INJURY

Rashida Lathan[1], Ryan Ghita[1], Rhian Touyz[1], Patrick Mark[1], Marc Clancy[2]
[1]University of Glasgow; [2]Queen Elizabeth University Hospital

Background: Studies in our rat model of ischemic reperfusion injury (IRI) demonstrate improved kidney function post injection of adipose-derived regenerative cells (ADRC). The mechanism on how these cells induce reparative effects during IRI remains elusive. We investigated ADRC-derived effects on fibrosis and inflammation within the injured kidney at early timepoints.
Methods/Materials: Inguinal rat ADRC or vehicle control were injected via the renal artery of the IRI rat model. At 48 h and 1-week post-ischemia injury, kidney was evaluated for fibrotic and inflammatory markers through qPCR and western blotting of (n = 6–8). Leukocyte quantity was assessed by flow cytometry (n = 4–5). Histology was used to measure infiltrative lesions and Masson Trichrome stained collagen accumulation (n = 8–20).
Results: ADRC-treated kidneys expressed lower levels of inflammatory gene CXCL12 and significantly lower protein levels of granulocyte macrophage colony-stimulating factor (both $p < 0.05$). In addition, a consistent increase in cytotoxic T-lymphocyte-associated protein 4 transcript was characteristic of ADRC treated kidneys. At 48 h post-IRI, half of vehicle controls contained higher levels of $CD45^+$ leukocytes. Assessment of leukocyte infiltrate indicated a trend of higher infiltrate in vehicle control kidneys compared to ADRC kidneys at 48 h with significant apparent differences by 1-week post IRI ($p < 0.05$).

Early accumulation of interstitial factors: tissue inhibitor of metalloproteinase-1 ($p < 0.05$) and collagen type 1, alpha 2 ($p < 0.001$) in vehicle control kidneys indicated early fibrotic development. This was mirrored by significantly high levels of collagen staining in control compared to ADRC treated kidneys at 1-week post IRI ($p < 0.001$).
Conclusion: Collectively, gene, protein expression and histological evidence suggest that ADRC treated IRI kidneys experience early anti-inflammatory changes conducive to the inhibition of fibrogenesis.

FG040 ISLETS LOADED IN HYDROGEL DERIVED FROM HUMAN AMNIOTIC MEMBRANE REVERSE DIABETES IN SCID MICE

Kevin Bellofatto, Fanny Lebreton, Charles-Henri Wassmer, Lisa Perez, Vanessa Lavallard, Géraldine Parnaud, David Cottet-Dumoulin, Domenico Bosco, Thierry Berney, Ekaterine Berishvili
Cell isolation and Transplantation Center, Geneva University Hospital

Background: Human amniotic membrane (HAM) is inexpensive and attractive as a biomaterial due to its structural similarities to islet extracellular matrix (ECM), and its immunomodulatory, anti-inflammatory and antifibrotic properties.

The aim of our study was to develop hydrogel derived from HAM and assess whether it could support islet function in vitro and in vivo.
Methods/Materials: The hydrogels were generated from HAM and accessed for porosity and ECM content.

To assess hydrogel impact on islet viability and function isolated rat islets were incorporated into the hydrogels and cultured for one week. The cell viability was evaluated by FDA/PI staining. To demonstrate islet function the glucose stimulated insulin secretion (GSIS) tests were performed using standard ELISA.

Next, we assessed whether incorporation of islets into hydrogel could enhance engraftment and lead to better glycemic control in diabetic SCID mice. For this purpose 350 rat islets (IEQ) loaded into the hydrogels or islets alone were transplanted into the epididymal fat of diabetic SCID mice. Blood glucose levels were monitored daily and intraperitoneal glucose tolerance tests (IPGTTs) were carried out. Grafts and serum were harvested to assess outcome.
Results: ECM concentration in the hydrogel affected the pore size. Insulin and glucagon expression and viability of islets incorporated into hydrogel was significantly higher than that of islets in free-floating culture. In addition, significant enhancement of GSIS was observed from islets embedded in hydrogel as compared to controls. In vivo experiments showed that, transplantation of 350 IEQ embedded in hydrogel lead to enhanced engraftment, vascularization, viability and better glycaemic control compared to control mice transplanted with islets alone.
Conclusions: Incorporation of pancreatic islet into amnion-derived hydrogels enhances islet engraftment and is a valuable approach to improve islet transplantation outcomes.

FG041 FEASIBILITY OF ALLOGENEIC MSC ADMINISTRATION IN THE RENAL GRAFT ARTERY IN A DCD AUTOTRANSPLANTATION PIG MODEL

Stine Lohmann[1], Marco Eijken[2], Ulla Moeldrup[3], Bjarne K. Moeller[4], James Hunter[5], Cyril Moers[6], Henri Leuvenink[6], Rutger Ploeg[5], Martin Hoogduijn[7], Carla C. Baan[7], Anna K. Keller[8], Bente Jespersen[9]
[1]Aarhus University; [2]Department of Renal Medicine and Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark; [3]Department of Urology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Clinical Medicine and Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark; [5]Nuffield Department of Surgical Sciences, Oxford Biomedical Research Centre, University of Oxford, Oxford, UK; [6]Department of Surgery–Organ Donation and Transplantation, University of Medical Center Groningen, Groningen, the Netherlands; [7]Department of Internal Medicine, Nephrology and Transplantation, Erasmus MC, University Medical Center, Rotterdam, the Netherlands; [8]Department of Clinical Medicine, Department of Renal Medicine and Department of Urology, Aarhus University Hospital, Aarhus, Denmark; [9]Department of Clinical Medicine and Department of Renal Medicine, Aarhus University Hospit

Background: Mesenchymal stromal cells (MSC) therapy may improve renal function after ischemia reperfusion injury in transplantation due to release of anti-inflammatory and regenerative factors. Renal intra-arterial ex-vivo injection before transplantation is a targeted way to deliver MSC. We tested feasibility, tolerability and effectiveness of this in a pig model simulating donation after circulatory death (DCD).
Materials and Methods: Left kidneys from female 50 kg pigs were exposed to 75 min of warm ischemia and 16 h of static cold storage in University of Wisconsin Solution (UW). Next, kidneys were infused with 10 m male porcine MSC suspended in 50 ml cold UW solution (n = 8) versus controls with UW alone (n = 8). Kidneys were autotransplanted after contralateral nephrectomy and animals observed for 14 days. MSC were adipose tissue-derived, grown to third passage, and thawed after cryopreservation.
Results: Labeled MSC were distributed in the graft cortex. A PCR based method to detect male cells in a cortex biopsy taken 1 h and 14 days after reperfusion confirmed the presence of MSC in all grafts at 1 h, while only 2–5% of the injected MSC were detected at 14 days.

Postoperatively, mean peak levels of P-creatinine were 1.27 vs. 1.23 (MSC vs. Control) mmol/l (p = 0.69). Peak U-NGAL/creatinine ratio was 1.45 vs. 1.10 mg/mmol (p = 0.16). One pig in the MSC group was terminated because it did not regain urine production, and then P-creatinine decreased similarly in the two groups with GFR (51Cr-EDTA-clearance) of 44 vs. 40 ml/min at 14 days (p = 0.66). Tubular function estimated by Tc99-MAG3 clearance was also similar. Histological assessment displayed mild tubular injury and fibrosis, unaffected by MSC treatment.
Conclusion: In conclusion, intra-arterial MSC therapy in donor kidneys before transplantation is easy and clinically feasible, potentially offering benefits. MSC can be tracked in the kidneys and do not compromise function. Within 14 days of follow up renal function was unaffected.

FG08 – INFECTIONS

FG042 FAILURE OF VALGANCICLOVIR PROPHYLAXIS IN PATIENTS WITH DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

Teun Van Gelder[1], Wieteke Kleinherenbrink[2], Marije Baas[3], Dennis Hesselink[3], Luuk Hilbrands[3]
[1]Erasmus MC, University Medical Center Rotterdam; [2]Erasmus MC Rotterdam; [3]Radboud UMC

Background: Valganciclovir is the first choice for prophylactic treatment of CMV-infection after solid organ transplantation. Dose adjustments are made if renal function is impaired. Based on a number of cases with CMV disease during low dose valganciclovir prophylaxis we suspected that in some patients with poor renal function valganciclovir is underdosed.
Methods: In a large population of renal transplant recipients (n = 1,300) the incidence of CMV disease within the first 3 months was compared between patients with Delayed Graft Function (DGF) and patients with immediate function.
Results: The incidence of CMV disease within the first 3 months was higher in patients with DGF (15/274 = 5.5%), compared to patients with immediate function (16/1,026 = 1.6%). (p = 0.0002). In 281 CMV seronegative patients with a seropositive donor treated prophylactically with valganciclovir 51 (18.1%) patients suffered from DGF and 230 (81.9%) had immediate graft function. CMV disease within the first 3 months after transplantation occurred significantly more often in 6/51 (11.8%) of the patients with DGF than in 2/230 (0.9%) of the patients with immediate graft function. (p = 0.0006).

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Conclusion: The higher incidence of breakthrough CMV disease in patients with DGF may be the result of underdosing of valganciclovir. In this population of patients dose adjustment based on ganciclovir plasma concentrations may lead to improved outcome. Prospective studies evaluating the added value of therapeutic drug monitoring are needed.

FG043 THE ANTI-CD40 MAB ISCALIMAB (CFZ533) DOES NOT IMPAIR IMMUNE EBV CONTROL

Tina Rubic-Schneider, Deborah Garcia, Martine Marchant, Brigitte Christen, Nathalie Runser-Loll, James Rush, Elisabetta Traggiai, Peter Ulrich
Novartis Institutes for Biomedical Research

Epstein Barr Virus (EBV)-associated post-transplant lymphoproliferative disorders (PTLD) is linked to EBV primary infection or reactivation. In an immunocompetent individual, the anti-viral T cell response controls the infection but EBV remains latent in B cells and some other cell types. In transplanted patients, immunosuppression could dampen the anti-EBV T cell response, leaving EBV-induced B cell proliferation uncontrolled. The goal of this study was to examine the effects of an anti-CD40 mAb on T cell-driven control of EBV-B cells and consequently B cell outgrowth. To do so we performed an EBV regression assay using peripheral blood mononuclear cells incubated with Cyclosporine A (CsA), CTLA4-Ig fusion protein (Belatacept) in comparison to the anti-CD40 mAb (CFZ533/Iscalimab). In addition, we evaluate the effect of blocking CD40 or CTLA-4 on T cell proliferation and IFNg production by using autologous co-cultures of T cells with EBV-B cells (sero-positive and sero-negative) or primary B cells. Belatacept and CsA but not anti-CD40 mAb Iscalimab reduced T cell activity resulting in over-growth of in vitro immortalized cells. Furthermore, Belatacept but not Iscalimab reduced EBV-mediated T cell proliferation and IFNg secretion in presence of EBV-B cells using the co-culture system. In conclusion, Iscalimab does not impair EBV control in vitro, in contrast to CsA and Belatacept, suggesting that transplant patients dosed with Iscalimab may have a reduced risk of PTLD.

FG044 PROPHYLACTIC STRATEGY AGAINST CYTOMEGALOVIRUS IS ASSOCIATED WITH INFERIOR KIDNEY FUNCTION IN TRANSPLANT PATIENTS

Arturo Blázquez-Navarro[1], Chris Bauer[2], Birgit Sawitzki[1], Timm Westhoff[3], Richard Viebahn[3], Petra Reinke[1], Oliver Thomusch[4], Christian Hugo[5], Michal Or-Guil[6], Nina Babel[3]
[1]Charité; [2]MicroDiscovery; [3]Ruhr University Bochum; [4]University Clinic Freiburg; [5]University Clinic Dresden; [6]Humboldt University

Background: Prevention of Cytomegalovirus (CMV) complications includes the prophylactic (universal drug administration) or the pre-emptive strategy (early treatment in case of reactivation). While the pre-emptive approach is advantageous with respect to the appearance of side effects and ganciclovir resistances, the prophylactic strategy is known to prevent CMV reactivations more efficiently. However, which strategy is superior with respect to transplantation outcome, including renal function, viral reactivations and other adverse events is not clear so far.
Methods: We have retrospectively analysed 540 patients from the multicentre Harmony study: 308 patients followed a prophylactic strategy, 232 a pre-emptive strategy. Patients were analysed for clinical markers along eight visits during the first posttransplant year. The effects of prevention strategy on transplantation outcomes were assessed employing the multivariate method stepwise backwards regression.
Results: Prophylaxis had a higher protective effect against CMV, leading to lower incidence of syndrome and lower viral loads, and to a delay in the appearance of reactivation compared to the pre-emptive strategy. However, the prophylactic strategy was associated with significantly reduced glomerular filtration rate (eGFR) one year posttransplant (difference: 4.8 ml/min/1.73 m^2) and higher incidence of acute rejection ($p = 0.002$); these effects were independent from demographic factors. Additionally, the prophylactic strategy led to increased incidence of severe BK virus reactivation, while no evidence of a protective effect against Epstein-Barr virus was observed.
Conclusions: Our results show for the first time that the prophylactic strategy might lead to inferior transplantation outcomes: While prophylaxis prevents CMV complications more effectively, it is associated with lower eGFR and higher incidence of acute rejection and severe BK virus infection.

FG045 HOSPITALIZATION AND DRG-COSTS IN GERMAN KIDNEY TRANSPLANT RECIPIENTS

Wiebke Duettmann, Fabian Halleck, Danilo Schmidt, Petra Glander
Charité – Universitätsmedizin Berlin

Introduction: Kidney transplant recipients (KTR) have frequent and unscheduled hospitalizations but detailed information on reasons and costs are scarce. Here we performed a detailed analysis of the health care costs of KTR with regards to specific causes of hospital admission.
Methods: Retrospective analysis of hospital data from all hospitalizations of KTR with ICD code Z.94.0 in our tertiary care hospital between 01.01.2015 and 31.12.2015. Main diagnoses were clustered and evaluated for DRG-costs. Costs for the initial transplantation (operation costs) were excluded.
Results: We care over 2.596 KTR. 1.861 hospital cases were recorded in 1,042 patients in 2015. Out of this 891 (47.83%) were unscheduled emergency hospitalizations. Main reasons for hospitalization were suspected rejection or treated rejection, infections, and the treatment of cardiological complications. Importantly, patients were hospitalized on average 1.79 times. Total DRG-costs were 4.591.008€ for all KTR with large variability between patients, maximum was 329.786€, median was 4.531€ ± 28.617€, and minimum 638€. Costs per case are presented in Table 1.

Reasons for admission	Number of cases	DRG-costs in ?	Costs per case in ?
AKI, suspected rejection/rejection	570 (26.43)	48.313	84,75
Infections	351 (18.86%)	186.977	532,69
Other	192 (10.3%)	453.067	8.162,74
Cardiological CC	137 (7.36%)	394.095	2.876,61
Gastrology and hepatology CC	130 (6.98%)	317.714	2.444
Urological CC	99 (5.31%)	142.390	1.438,28
Pneumological CC (incl ventilation)	84 (4.51%)	2.041.677	24.305,68
Oncology	77 (4.13%)	229.101	2.975,33
Angiological CC	70 (3.75%)	31.874	455,34
Dermatological CC	58 (3.11%)	79.842	1.376,58
Neurological CC	32 (1.71%)	182.021	5.688,17
Ophtalmological CC	17 (0.91%)	19.809	1.165,26
Nephrological CC	17 (0.91%)	28.495	1.676,14
Diabetes mellitus II	13 (0.69%)	15.538	1.195,2
Intensive care stay	9 (0.48%)	408.483	45.387,02
Thrombosis	3 (0.16%)	1.543	514,33
Evaluation for Tx other than kidney	2 (0.1%)	2.930	1.465,1

Conclusion: This analysis demonstrates the high rate of hospitalizations and emergency hospitalizations resulting in high costs to the health care system for KTR during follow-up. Preemptive identification of complications and timely intervention might lead to relevant cost savings within the health care system. However, strategies to reduce hospitalizations and costs are urgently needed.

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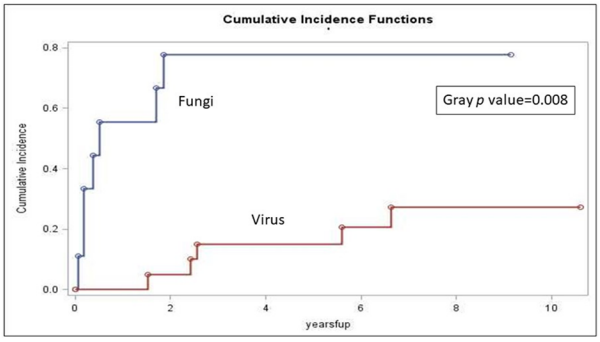
FG046 CENTRAL NERVOUS SYSTEM INFECTIONS IN SOLID-ORGAN TRANSPLANTATION: RESULTS FROM A NATIONWIDE COHORT STUDY

Lorena Van den Bogaart[1], Simona Rossi[2], Dionysios Neofytos[3], Katia Boggian[4], Laura Walti[5], Karine Hadaya[6], Nina Khanna[7], Christian Garzoni[8], Nicolas Mueller[9], Matteo Mombelli[1], Oriol Manuel[1]
[1]Service of Infectious Diseases and Transplantation Center, University Hospital of Lausanne; [2]University Hospital of Basel; [3]Transplant Infectious Diseases Unit, University Hospital of Geneva; [4]Division of Infectious Diseases and Hospital Hygiene, Cantonal Hospital St Gallen; [5]Department of Infectious Diseases, University Hospital of Bern; [6]Division of Nephrology, University Hospital of Geneva; [7]Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Basel; [8]Clinic of Internal Medicine and Infectious Diseases, Clinica Luganese; [9]Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zurich

Background: The incidence of central nervous system (CNS) infections after solid-organ transplantation has been estimated to be 5–10%. However, the burden of CNS infections has not been systematically assessed in the current era.
Methods/Materials: Patients from the Swiss Transplant Cohort Study (STCS) transplanted between 2008 and 2017 with a CNS infection were included in this study. Epidemiological and clinical data were extracted from the STCS database. Descriptive statistics were used to characterize the patients' population. We analyze the incidence rate of CNS infections, and patient and graft survival at 90 days and at the end of follow-up.
Results: 40 cases of CNS infection in 38/4,568 (0.8%) transplant recipients were included in the study [21/2,637 kidney (0.8%), 8/952 liver (0.8%), 6/425 lung (1.4%), 3/333 heart (0.9%), 0/173 combined, 0/48 other]. Mean age was 49 years (SD 17) and median time from transplant was 17 months (0.3–96). Overall incidence rate of CNS infection was 1.8 per 1,000 patient-years. There were 4/40 (10.0%) cases of bacterial infections (2 nocardiosis, 1 neuroborreliosis, 1 *E. coli*/*Enterococcus* meningitis), 21/40 (52.5%) of viral infections (8 VZV infections, 5 EBV-related PTLD, 3 progressive multifocal leukoencephalopathy, 2 HSV infections, 2 enterovirus meningitis and 1 tick-borne encephalitis), 9/40 (22.5%) of fungal infections (6 aspergillosis, 3 cryptococcosis) and 6/40 (15.0%) cases of meningitis without microbiological documentation. 90-day mortality and graft loss was 29% and 37%, respectively. CNS fungal infections were associated with a higher long-term mortality compared to CNS viral infections (Fig. 1).
Conclusion: In this contemporary nationwide cohort of transplant recipients, we observed a low incidence of CNS infections, probably due to successful antimicrobial prophylactic strategies. However, CNS infections remain associated with significant mortality, in particular for fungal infections.

Fig. 1 Mortality rate stratified by pathogen



FG047 HEPATITIS B VIRUS INFECTION IS ASSOCIATED WITH RECURRENT NEPHROPATHY AFTER KIDNEY TRANSPLANTATION

Guodong Chen, Zixuan Wu, Chang Wang, Xiaomian Liu
The First Affiliated Hospital of Sun-Yat sen University

Background: Hepatitis B virus (HBV) infection can cause HBV associated nephropathy, and is one of the major reasons for secondary nephropathy. We carried out a retrospective cohort study to investigate whether HBV infection is associated with recurrent nephropathy after kidney transplantation.
Methods: We retrospectively collected data of 1,130 patients who received kidney transplantation in our hospital from January 2000 to December 2005. The patients were divided into HBV infection group and control group according to whether their HBsAg test was positive or not before transplantation. The patients were followed up until November 2016, and the following data were recorded including recurrent nephropathy, the recurrent time, proteinuria, hematuria, acute rejection and serum creatinine levels.
Results: Among 1,130 patients, 149 (13.2%) patients were HBsAg positive before kidney transplantation and belonged to HBV infection group, and the other 981 patients belonged to control group. The recurrent nephropathy rate was significantly higher in HBV infection group compared to control group (25.5% vs. 13.7%, $p < 0.001$). The median recurrent time for recurrent nephropathy was much shorter in HBV infection group (4.6 years vs. 6.8 years, $p < 0.001$). The proteinuria rate was higher in HBV infection group (48.3% vs. 34.8%, $p = 0.001$), and hematuria rate was also higher in HBV infection group (56.4% vs. 42.0%, $p = 0.001$). Acute rejection rate was similar in two groups (12.1% vs. 12.5%). The 3-, 5- and 10-year serum creatinine levels were significantly higher in HBV infection group compared to control group ($p < 0.01$). Logistic multivariate regression showed that HBV infection was an independent risk factor for recurrent nephropathy after kidney transplantation (OR 2.35, $p < 0.01$).
Conclusion: HBV infection may increase the risk of recurrent nephropathy and cause chronic allograft injury after kidney transplantation.

FG09 – FG09: HOW DO WE FEEL ABOUT MTORI TODAY?

FG048 COST-EFFECTIVENESS ANALYSIS OF M-TOR VERSUS MYCOPHENOLATE IN KIDNEY TRANSPLANT RECIPIENTS RECEIVING NO PHARMACOLOGICAL PROPHYLAXIS FOR CYTOMEGALOVIRUS INFECTION: A PHARMACOECONOMIC EVALUATION

Gustavo Ferreira[1], Flavia Lícia Rodrigues Magacho[1], Juliana Bastos Campos Tassi[1], Vinicius Sardão Colares[1], Alfredo Chaoubah[2]
[1]Santa Casa De Juiz de Fora; [2]Universiade Federal de Juiz de Fora

Introduction: Standards of immunosuppression in renal transplantation have changed dynamically in recent years. The aim of our study was to determine cost-effectiveness of everolimus (EVR) versus mycophenolate sodium (MPS) in kidney transplant recipients receiving induction therapy, tacrolimus, prednisone, and no prophylaxis for cytomegalovirus infection.
Material and Methods: Data from a single-center prospective trial were used along with data from the center's medical bills database. The target population comprised adults with low immunological risk submitted to first ABO-compatible transplantation with kidneys recovered from living or deceased donors. The interventions included tacrolimus and prednisone plus a single dose of rabbit antithymocyte globulin (ATG) and EVR (Group 1 = 91 patients) versus tacrolimus and prednisone plus two doses of basiliximab (BAS) and MPS (Group 2 = 93 patients). The clinical outcomes considered for this analysis were cytomegalovirus disease, acute rejection, graft dysfunction, surgical complications, graft loss, and death. We used for the pharmacoeconomic analysis of the immunosuppressive regimens, the static model, of the decision tree type, was used.
Results: Group 1 was cost-effective in relation to Group 2 in the analysis made from the incidence of adverse effects, as well as in the significant reduction of events related to cytomegalovirus, which is responsible the greatest cause of morbidity and mortality in transplant patients.
Conclusion: A regimen comprising induction with ATG, followed by maintenance therapy with tacrolimus, prednisone and everolimus, is likely to be effective for low immunological risk adult kidney transplant patients and a cost-effective.

FG049 TREATMENT OF NK MEDIATED REJECTIONS BY MTOR INHIBITORS: A TRANSLATIONAL STUDY

Alice Koenig[1], Chien-Chia Chen[1], Antoine Marçais[1], Virginie Mathias[2], Antoine Sicard[1], Maud Rabeyrin[3], Maud Racapé[4], Jean Paul Duong Van Huyen[5], Patrick Bruneval[6], Alexandre Loupy[4], Sébastien Dussurgey[6], Stéphanie Ducreux[2], Helena Paidaissi[1], Romain Guillemain[5], Jean Luc Taupin[5], Jasper Callemeyn[7], Emmanuel Morelon[3], Antonino Nicoletti[1], Béatrice Charreau[1], Valérie Dubois[2], Maarten Naesens[7], Thierry Walzer[1], Thierry Defrance[1], Olivier Thaunat[1]
[1]INSERM; [2]EFS; [3]HCL; [4]Paris Descartes University; [5]APHP; [6]SFR Biosciences; [7]University of Leuven

Background: Our group recently demonstrated that Natural Killer (NK) lymphocytes, can perceive the absence of expression of self HLA class I molecules ("missing self") on graft endothelial cells and cause antibody-independent microvascular inflammation. Missing self-induced NK cell-mediated rejections have the same detrimental impact on graft survival as chronic humoral rejections and probably explain ~half of late graft losses.
This translational study aimed at identifying the molecular pathway involved in missing self-induced NK cell activation in order to guide future personalized therapy.
Methods and Results: Purified human NK cells were cocultured with K562 cells, which lack the expression of HLA class I molecules. Imaging flow cytometry analyses demonstrated that missing self-induced NK cell activation

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depends upon the mTORC1 pathway, which can be blocked with rapamycin. A murine heterotopic heart transplant model was used to validate that rapamycine (but not cyclosporin) efficiently suppressed the development of graft microvascular lesions in vivo. Finally, we retrospectively identified 2 transplant patients (1 heart and 1 kidney recipient), in whom the introduction of mTOR inhibitor reduced missing self-induced NK cell-mediated rejection lesions.
Conclusion: Our work demonstrates that the mTORC1 pathway is critical for missing self-induced NK cell-activation and suggests that mTOR inhibitors is a valid therapeutic option for this new type of rejection. A prospective pilot study has been launched to confirm these promising results.

FG050 COMBINATION OF EXTENDED-RELEASE TACROLIMUS PLUS EVEROLIMUS ONCE-DAILY IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: ER-TAC VERSUS LCPT

Gionata Spagnoletti, Maria Paola Salerno, Flavia De Gennaro, Jacopo Romagnoli, Franco Citterio
Fondazione Policlinico Universitario A. Gemelli, IRCCS, Roma, Italy

Introduction: Combination of Everolimus (EVR) with Tacrolimus (Tac) permits reduced calcineurin inhibitors exposure and, recently, has been demonstrated safe and effective.

Two different once-daily Tacrolimus formulations, with different pharmacokinetic profiles are now available: ER-Tac and LCPT.

Aim of this study was to compare in kidney transplant recipients (KTx), the short-term efficacy and safety of ER-Tac versus LCPT, both in combination with EVR, administered concomitantly once a day.
Methods: Fifty-seven KTx were openrandomized to once-daily maintenance immunosuppressive regimen based on ER-Tac + EVR + Steroids (ER-Tac + EVR, $n = 30$) or LCPT + EVR + Steroids (LCPT + EVR, $n = 27$). All patients received induction therapy with Thymoglobuline (total dose 200 mg).
Results: Median follow-up was 10 months (range 3–18). Here we present the intention-to-treat analysis at 6 months. There were no differences in patients as well as in graft survival. Moreover, we found no differences in renal function, acute rejection rate, CMV infection. According to the Concentration/Dose ratio of Tacrolimus, there was a significantly higher number of slow metabolizers 1-month after transplant in the LCPT + EVR group. Data are detailed below (Table 1).

6 Month	ER-Tac + EVR	LCPT + EVR	*p*
Patients survival (%)	95	100	0.355
Graft survival death-censored (%)	100	89	0.169
Serum creatinine (mg/dl)	1.97 ± 0.99	1.72 ± 0.65	0.346
Acute rejection *N* (%)	1 (3.3)	0 (0)	0.526
Cytomegalovirus viremia (%)	23.3	33.3	0.293
Drop-out *N* (%)	6 (20)	3 (11)	0.292
EVEROLIMUS trough blood levels (ng/ml)	4.0 ± 0.8	3.8 ± 0.6	0.440
TACROLIMUS trough blood levels (ng/ml)	5.0 ± 1.3	5.3 ± 1.4	0.407
1-month tacrolimus C/D [fast/intermediate/slow] (%)	62/21/17	29/17/54	0.015

Conclusions: Our data show that the two extended release Tac formulations, when administered with EVR once-daily, have comparable 6-month safety and efficacy.

We can speculate that the higher number of slow metabolizers in the LCPT group may be an advantage to reach target exposure early after transplantation.

FG051 MTOR INHIBITOR-BASED IMMUNOSUPPRESSION IS ASSOCIATED WITH A HIGHER FREQUENCY OF IFNγ-PRODUCING EBV-SPECIFIC CD4⁺ T CELLS AS COMPARED TO MTOR INHIBITOR-FREE THERAPY IN KIDNEY TRANSPLANT PATIENTS

Moritz Anft[1], Toralf Roch[2], Patrizia Wehler[2], Ulrik Stervbo[1], Richard Viebahn[3], Timm Westhoff[1], Mira Choi[2], Nina Babel[1]
[1]Marien Hospital Herne; [2]Charite Berlin; [3]Knappschaftkrankenhaus Bochum

About 80–90% of adults are infected with Epstein-Barr-Virus (EBV), which persists in a latent stage. The immunosuppressive regime after organ transplantations can cause reactivation of EBV and thereby complications such as Post-transplant lymphoproliferative disorder (PTLD), a life-threatening malignant lymphoma. Cellular immunity is known to control viral proliferation and reconstitution of EBV-specific T cell immunity under immunosuppression (IS) is crucial for prevention of EBV replication. IS drugs are known to impact the functionality of cellular immunity at different extent. Previously, we demonstrated advantageous effect of mTORi on the efficacy of BKV-specific T-cell immunity as compared to other IS drugs. However, the effect of mTORi on EBV-specific cellular immunity has been not analysed in details. The aim of this study is to elicit the effect of mTORi on the quantity and functionality of EBV-specific T-cell response in kidney transplant patients.

We conducted an explorative cross-sectional analysis on characterisation of EBV-specific T-cells in patients treated with mTORi-based triple IS; $n = 20$) in comparison to pair-matched controls treated by mTORi-free triple IS ($n = 20$). PBMCs were challenged with EBV overlapping peptides and EBV-specific T cells were analysed by multi-parameter flow cytometry.

Our data revealed a significantly higher number of EBV-specific T cells in patients treated with mTORi as compared to mTORi-free group. Within EBV-specific T cells, the number of $CD4^+CD154^+IFN\gamma^+$ T cells was significantly higher in mTORi therapy group as compared to mTORi-free regimen.

Our study provides evident for advantageous impact of mTORi therapy on the magnitude and functionality of EBV-specific $CD4^+$ T cells This might lead to a better EBV control and prevention of of EBV-associated complications in transplant patients. Further studies are required to confirm our observation.

FG052 COMBINATION OF CALCINEURIN AND MTOR INHIBITORS IN KIDNEY TRANSPLANTATION: A PROPENSITY SCORE ANALYSIS BASED ON CURRENT CLINICAL PRACTICE

David Cucchiari[1], Alicia Molina-Andujar[1], Enrique Montagud-Marrahi[1], José Ríos[2], Ignacio Revuelta[1], Gastón Piñeiro[1], Jessica Ugalde-Altamirano[1], Pedro Ventura-Aguiar[1], Erika De Sousa-Amorim[1], Nuria Esforzado[1], Frederic Cofán[1], Jose-Vicente Torregrosa[1], Frederic Oppenheimer[1], Fritz Diekmann[1]
[1]Hospital Clínic de Barcelona; [2]Universidad Autonoma de Barcelona

Background: The TRANSFORM study suggests that the best way to exploit the beneficial effects of mTOR inhibitors (mTORi) in kidney transplant recipients consists in reaching trough levels of 3–8 ng/ml in association with a calcineurin inhibitor. As the same protocol is carried out in our Unit since 2013, we present herein the results of such a combination in everyday clinical practice.
Methods: Analysis of 401 kidney transplant recipients transplanted from June 2013 to December 2016 in our Unit. All patients received tacrolimus with prednisone in combination with either mycophenolate (MPA, $n = 186$) or an mTORi (either sirolimus or everolimus) ($n = 215$). A propensity score (Inverse Probability of Treatment Weighting, IPTW) to receive mTORi was calculated based on the following parameters: age and sex of donor and recipient, BMI, number of previous transplants, diabetes, cPRA, dialysis before transplantation, dialysis vintage, type of donor, ABO incompatibility, HLA-mismatches, induction and ischemia time. Median follow-up was 963 (748–1,451) days.
Results: Cox-regression analysis demonstrated good results for mTORi versus MPA in terms of 1-year Biopsy-Proven Acute Rejection (BPAR, $p = 0.063$), 1-year graft loss ($p = 0.025$) and patient survival ($p < 0.001$). Curiously, the better results observed for BPAR and graft failure were largely attributed to those patients that would have been excluded by the TRANSFORM because of some exclusion criteria (52.9% of the initial population, $p = 0.003$ for 1-year BPAR and $p = 0.040$ for graft loss). On the other side, patients who would have been included in the trial had similar results for acute rejection and graft failure in comparison with MPA, while the beneficial effect on overall survival persisted.
Conclusions: In a real-life setting, a protocol based on optimal-dose mTORi with tacrolimus and prednisone could be employed as a standard immunosuppressive regimen and was associated with good patient and graft outcomes.

FG053 A CLINICAL PHARMACOGENETIC MODEL TO PREDICT THE EFFICACY OF SIROLIMUS DURING THE EARLY ADMINISTRATION IN RENAL TRANSPLANT RECIPIENTS

Shuang Fei, Zijie Wang, Hao Chen, Li Sun, Zhijian Han, Jun Tao, Xiaobin Ju, Ruoyun Tan, Min Gu
The First Affiliated Hospital of Nanjing Medical University

This study was to develop a clinical pharmacogenetic model to predict the efficacy of sirolimus during the early administration in renal transplant recipients. 70 recipients were enrolled according to the inclusion and exclusion criteria. Target sequencing based on next-generation sequencing was used to detect all single nucleotide polymorphisms (SNPs) in 9 genes related to the sirolimus metabolism in vivo (*CYP3A4, CYP3A5, CYP2C8, CYP2C19, ABCB1, POR, PPARA, UGT1A8, UGT1A9, UGT2B7*). Logistic regression analysis adjusted by the confounding factors was conducted to identify the potential associations of all detected SNPs with the sirolimus concentrations on 7 days and 1 month after the administration of sirolimus within the first 3 months after kidney transplantation. A clinical score was designed by simplifying regression coefficients of the independent variables. Cutoff levels were chosen based on the clinical score, and positive and negative response rates were calculated. An evaluation of the model was performed in a second group of recipients containing 100 recipients. The model for sirolimus efficacy consisted of gender, body mass index, immunosuppressive protocols, the incidence of delayed graft function and acute rejection, as well as 5 SNPs in the *CYP3A4, CYP3A5, ABCB1* and *UGT1A8* genes. This prediction model was transformed into a scoring system ranging from 0 to 11.5. Scores of ≤ 3.5 had a true positive

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response rate of 95%, while scores of ≥ 8 categorized as either responders or non-responders, whereas 18.6% of the patients were categorized using a non-genetic model. Evaluations of the model in second group supported the results. In conclusion, our study established a clinical pharmacogenetics model to predict the efficacy of sirolimus administration in recipients during early phase following renal transplantation, leading to the better-tailored initial treatment decision of sirolimus within the first 3 months.

FG10 – METABOLIC SYNDROME – A THREAT TO OUR TRANSPLANT PATIENTS?

FG054 OCCURRENCE AND RECURRENCE OF NAFLD AFTER LIVER TRANSPLANTATION

Tajana Filipec Kanizaj[1], Nikola Sobocan[1], Maja Mijic[1], Milos Lalovac[2], Tina Borcic[2], Ivan Bogadi[2], Zrinka Misetic Dolic[2], Nino Kunac[2], Diana Ilic[2], Ana Ostojic[2], Petra Dinjar Kujundžić[2], Slavko Gasparov[1], Anita Skrtic[1], Helena Jerkic[1], Branislav Kocman[2]

[1]University Hospital Merkur, Medical School University of Zagreb, Croatia; [2]University Hospital Merkur

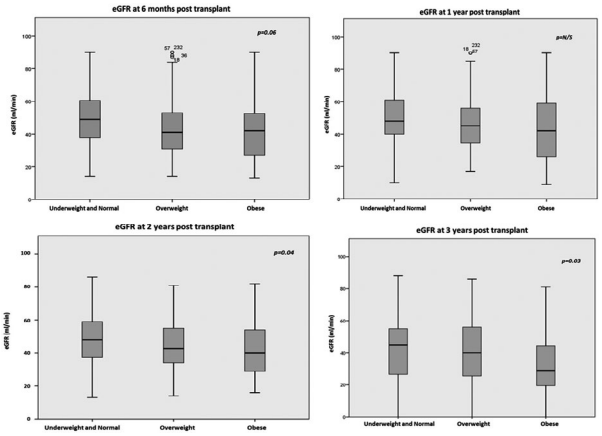
Introduction: Recurrence or de novo occurrence of NALFD after LT is possibly very common but not well studied.
Aim: In this retrospective study we aimed to evaluate time trends in LT for NAFLD, recipient and graft survival and rate of recurrence and de novo occurrence of NAFLD in adult LT recipients in University hospital Merkur, Zagreb, Croatia in 5 years (2012–2017).
Materials and Methods: Data included in analysis were: indication for LT, 5-year's recipient and graft survival, pre-implantation bioptic finding of donor liver, bioptic finding of last liver biopsy performed at least 6 months after LT.
Results: In last 5 years 503 first LT from cadaveric donors were performed. ESLD due to NAFLD cirrhosis represents 7.4% of all indications and is stable in last 5 years. HCC is fastest growing indication especially due to NAFLD (7.1–41.7% in 5 years for NAFLD recipients). Twenty percent of all donors had steatosis before implantation (14% grade 5–29%, 6% grade 30–60%). Overall 5-year graft and recipient survival were 90.1% and 80.9%, respectively. Primary indication (NAFLD vs. non-NAFLD) and donor steatosis had no impact on recipient or graft survival. Comparison of basal donor bioptic sample and post-LT finding revealed that 9.5% NAFLD recipients and 11.4% with non-NAFLD indications had stable stage of liver steatosis, 4.8% and 24.7% regression or disappearance of steatosis and 23.8% and 12.4% recurrence/de novo occurrence of steatosis, respectively (p: 0.08).
Conclusions: LT recipients transplanted due to NAFLD or usage of liver grafts with steatosis had no impact on recipient and graft survival. Regression of graft steatosis is possible in up to 4.8% and 24.7% NAFLD and non-NAFLD recipients. Recurrence or de novo occurrence of NAFLD was detected in 23.8% and 12.4% recipients. This underlies higher rate and more rapid course of NAFLD recurrence than occurrence after LT.

FG055 THE EFFECT OF BODY MASS INDEX IN GRAFT FUNCTION AFTER KIDNEY TRANSPLANTATION

Maria Irene Bellini[1], Kostantinos Koutroutsos[2], Hannah Nanapragasam[1], Jack Galliford[3], Paul Elliot Herbert[1]

[1]Renal Transplant Directorate, Hammersmith Hospital, Imperial College NHS Trust; [2]Department of Nephrology, Brighton and Sussex University Hospital NHS Trust; [3]Department of Nephrology, Queen Alexandra Hospital

Background: There is an ongoing debate regarding the suitability for transplantation of the high Body Mass Index (BMI) kidney transplant recipients (KTRs), given the limited organ pool.
Methods: Retrospective analysis of 370 consecutive KTRs stratified as following: underweight/normal (n = 164, 41.3%), overweight (n = 152, 38.3%), obese (n = 72, 18.1%). As a measure of allograft function eGFR was used at 3, 6 and 12, 24 and 36 months post-transplant.
Results: Mean BMI was 26.2: 148 (40%) preobese, 47 (12.7%) class I obese, 11 (3%) class II obese, 9 (2.4%) class III obese. A linear trend from the normal BMI group moving through the progressively higher groups was observed for male sex and younger age. Overweight and obese KTRs had higher incidence of pre-transplant diabetes (p = 0.021), but there was no difference in new-onset hyperglycemia post-transplant (p = 0.35). Obesity was a significant risk factor for lower eGFR at 3 and 6 months, but this did not persist at 1 year follow-up. It was instead significant at 2 and 3 years follow up. No statistical difference in DGF and hospital length of stay was observed. Overall, 28 patients lost their grafts, and 25 patients died during follow-up. 45 allografts were lost in total, with 9 patients dying after allograft failure. Kaplan-Meier analysis showed no difference in all-cause allograft loss between the different BMI groups (log rank p = 0.8) in a mean follow-up of 42 months (0–58).
Conclusion: Obesity affects eGFR in the long-term. The allograft survival was lower but not significant.



FG056 ROLE OF SEX IN POST-TRANSPLANT DIABETES MELLITUS DEVELOPMENT: ARE MEN AND WOMEN EQUAL?

Ivana Dedinska, Petra Skálová, Karol Graňák, Matej Vnučák, Juraj Miklusica, Ľudovít Laca

University Hospital Martin and Jessenius Faculty of Medicine

Sex differences with regard to PTDM have not yet been published in any available study and therefore the objective of our multicentre prospective 12-month analysis was to determine whether risk factors for PTDM in patients after kidney transplantation (KT) are the same for women and men.

This prospective multicentre analysis with 12-month follow-up included 417 patients without a diagnosis diabetes mellitus type 1 or 2 or prediabetes at the time of KT were engaged in the analysis. We divided the patients into four groups as follows: men – control group, men – PTDM, women – control group, and women – PTDM. PTDM was diagnosed according to the ADA criteria. oGTT was performed in 10–12 weeks after KT and 12 monthsafter KT.

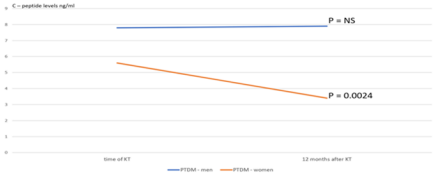
A total of 417 patients (271 men and 146 women) were included in the monitored group. Age at the time of KT more than 60 years [HR 2.2737; (p = 0.0268) – for men, HR 16.6250; (p = 0.0042) – for women] and hypovitaminosis D at the time of KT (<20 μg/l) [HR 4.7500; (p = 0.0005) – for men, HR 2.2500; (p = 0.0021) – for women] were identified as independent risk factors for PTDM in both men and women. We further confirmed as an independent risk factor for men a waist circumference at the time of KT > 94 cm [HR 1.6842; (p = 0.0146)], C-peptide at the time of KT > 5 ng/ml [HR 3.2995; (p = 0.0356)], HOMA-IR > 2 [HR 3.3503; (p = 0.0358)] and triacylglycerols at the time of KT > 1.7 mmol/l [HR 4.1386; (p = 0.0308)]. In case of women, the dominant factor was BMI at the time of KT more than 30 kg/m^2 [HR 4.1667; (p = 0.0001)] and menopause at the time of KT [HR 4.1386; (p = 0.0308)].

Men with PTDM had significantly the worst graft survival, followed by women with PTDM. We recorded a significant decrease in the value of C-peptide in the group of women with PTDM, which is one of the most important findings in our analysis.
Conclusion: Women show pancreas? cell dysfunction, whereas insulin resistance and metabolic syndrome are dominant in men in PTDM development.

PTDM	input - M n = 106	12 months after KT - M n = 106	P-value	input - W n = 46	12 months after KT – W n = 46	P-value
waist circumference (cm)	95.9 ± 12.2	101.5 ± 10.8	**0.0005**	90.6 ± 15.7	92.5 ± 15.4	0.5594
BMI (kg/m²)	26.8 ± 3.8	28.3 ± 4.3	**0.0077**	28.2 ± 4.4	29.8 ± 4.8	0.0991
C-peptide (ng/ml)	7.8 ± 6	7.9 ± 5.8	0.9019	5.6 ± 4.7	3.4 ± 0.9	**0.0024**
IRI (μIU/ml)	14.2 ± 7.5	21.5 ± 11.8	**<0.0001**	10.2 ± 7	12.6 ± 8.2	0.1346
HOMA-IR	4.0 ± 0.6	5.5 ± 0.5	**<0.0001**	2.3 ± 1.3	3.4 ± 2.5	**0.0096**
triacylglycerols (mmol/l)	3.3 ± 2.8	2.1 ± 1.0	**<0.0001**	2.2 ± 0.5	1.8 ± 0.8	**0.0050**
cholesterol (mmol/l)	5.2 ± 1.2	4.9 ± 1.9	0.1708	5.5 ± 1.7	5.4 ± 0.8	0.7190
magnesaemia (mmol/l)	0.7 ± 0.1	0.7 ± 0.1	1.0000	0.7 ± 0.1	0.7 ± 0.1	1.0000
vitamin D (μg/l)	23.6 ± 3.5	25.9 ± 3.3	**<0.0001**	19.5 ± 2	23.9 ± 1.8	**<0.0001**

M – men; W – women; KT – kidney transplantation; BMI – body mass index; IRI – immunoreactive insulin; HOMA-IR – homeostatic model assessment for insulin resistance; HbA1c – glycated haemoglobin

Table 1. Development of monitored parameters – PTDM



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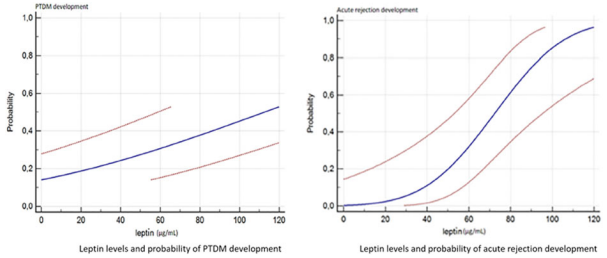
FG058 LEPTIN – NEW MARKER FOR REJECTION OF KIDNEY TRANSPLANT?

Ivana Dedinska, Petra Skálová, Karol Graňák, Matej Vnučák, Juraj Miklušica, Ľudovít Laca

University Hospital Martin and Jessenius Faculty of Medicine

Obese patients have increased production of leptin and selective resistance to its central anti-adipogenic effects, yet its pro-inflammatory immunostimulating effect persists. The aim of the analysis was to determine the impact of immunosuppression to levels of hormones in fat tissue – leptin and adiponectin. In the group of 72 patients who underwent primary kidney transplantation (TK) without diabetes mellitus type 1 or type 2 at the time of TK we examined the level of adiponectin and leptin before TK and subsequently 6 months after TK. We have found that the level of adiponectin has significantly reduced ($p = 0.0009$), whereas the level of leptin has significantly increased in the monitored period ($p = 0.0065$). Adiponectin level 6 months after TK correlated with the waist circumference [$r = -0.5479$; ($p = 0.0101$)], body mass index (BMI) [$r = -0.4847$; ($p = 0.0266$)] and HOMA-IR index [$r = -0.7729$; ($p < 0.0001$)]. The level of leptin correlated with the value of triacylglycerols [$r = 0.3834$; ($p = 0.0008$)], development of post-transplant diabetes mellitus (PTDM) [$r = 0.6794$; ($p = 0.0005$)] and acute rejection (AR) [$r = 0.7559$; ($p < 0.0001$)]. Applying the multivariate analysis we found out that high level of leptin is a risk factor for the development of AR [HR 2.1273; 95%CI 1.0130–4.4671 ($p = 0.0461$)] and PTDM [HR 7.200; 95%CI 1.0310–50.2836 ($p = 0.0465$)]. On the contrary, low levels of adiponectin represent a risk factor for the development of insulin resistance [HR 38.6135; 95%CI 13.3844–67.7699 ($p < 0.0001$)] and obesity (BMI more than 30 kg/m^2) [HR 3.0821; 95% CI 0.8700–10.9192 ($p = 0.0053$)].

We did not observe effect of immunosuppression on concentrations of monitored hormones in the serum in our analysis. However, we found that high concentration of leptin in serum constitutes an independent risk factor for the development of acute rejection and requires further monitoring.



FG059 POST-TRANSPLANT OBESITY IS ASSOCIATED WITH POOR LONG-TERM SURVIVAL AFTER LIVER TRANSPLANTATION

Jeffrey van Son, Suzanne Stam, Antonio Gomes Neto, Maryse Osté, Hans Blokzijl, Aad van den Berg, Robert Porte, Stephan Bakker, Vincent de Meijer

University Medical Center Groningen

Background: Short-term survival after liver transplantation (LT) has improved over the past decades, but long-term survival remains impaired. The effects of obesity on long-term survival after LT are controversial. Because pre-transplant body mass index (BMI) can be confounded by ascites, we hypothesized that post-transplant BMI at 1 year could predict long-term survival.

Methods: A post-hoc analysis was performed of a prospective cohort consisting of all adult recipients of a first LT between 1993 and 2010. Baseline BMI was measured at 1 year post-transplantation to represent a stable condition. Patients were stratified into normal weight (BMI < 25 kg/m^2), overweight ($25 \leq$ BMI ≤ 30 kg/m^2), and obese (BMI > 30 kg/m^2). Kaplan-Meier survival analyses were performed with log-rank testing, followed by Cox proportional-hazards regression analyses.

Results: Out of 370 included recipients, 184 had normal weight, 136 had overweight, and 50 were obese. After a median follow-up of 12.3 years, 107 (28.9%) recipients deceased. Obese LT recipients had a significantly decreased 15 years survival of 56% when compared to a 75% survival of normal weight LT recipients (HR 2.00, 95% CI 1.08–3.68, $p = 0.03$; Figure 1a). BMI was inversely associated with 15 years survival (HR 1.08, 95% CI 1.03–1.14, $p = 0.001$ per 1 BMI point), independent of age, gender, muscle mass, transplant characteristics, cardiovascular risk factors, kidney, and liver function (Figure 1b).

Conclusion: Post-transplant BMI is inversely associated with long-term survival after LT. Obesity at 1 year post-transplantation conveys a 2-fold higher mortality risk, which may offer potential for interventional strategies (i.e. dietary advice and lifestyle modification) to improve long-term survival of obese LT recipients.

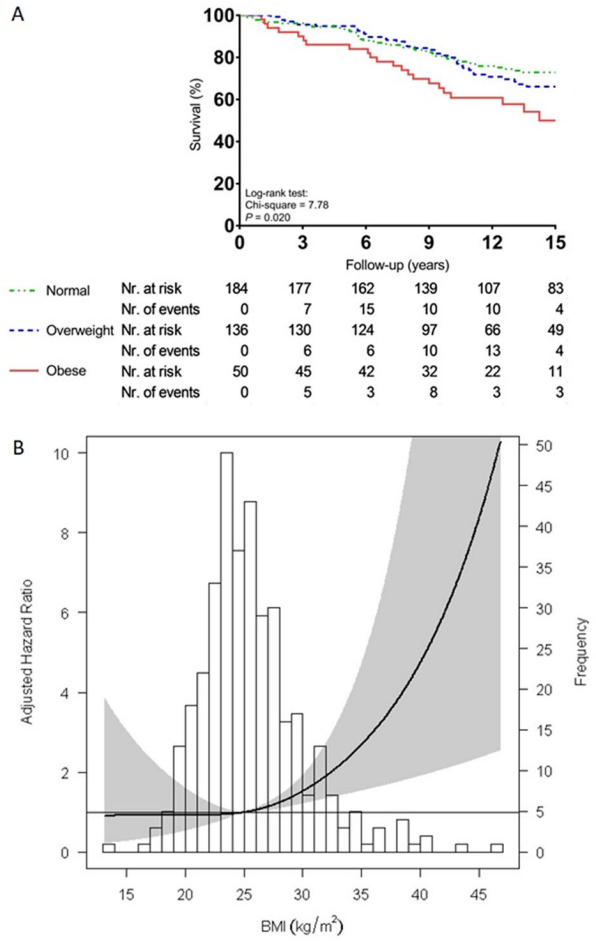


Figure 1. Actuarial survival for all-cause mortality according to BMI-stratified groups (a), and restricted cubic spline visualizing adjusted hazards ratio for BMI on all-cause mortality (b).

FG11 – INNOVATIONS IN TRANSPLANT BIOMARKER DEVELOPMENT

FG060 DISTINCTIVE ENDOTHELIAL AND INFLAMMATORY PROFILES CHARACTERIZE KIDNEY TRANSPLANTS FROM EXTENDED CRITERIA DONORS

Romain Boissier[1], Pauline François[2], Maité Meunier[3], Bastien Gondran Tellier[2], Luc Lyonnet[4], Stéphanie Simoncini[2], Tristan Legris[3], Jeremy Magalon[2], Francoise Dignat-George[2], Eric Lechevallier[1], Florence Sabatier[2], Pascale Paul[2]

[1]Urology and Transplantation department, Assistance Publique Hopitaux de Marseille, Marseille; [2]INSERM 1263, INRA, C2VN, Aix Marseille Univ, INSERM, Marseille; [3]Nephrology and transplantion Department, Assistance Publique Hopitaux de Marseille, Aix Marseille Univ; [4]Hematology Department, Assistance Publique Hopitaux de Marseille, Marseille

Background: The shortage of transplants leads to the use of kidneys taken from older donors with co-morbidities. Use of organs from extended criteria donors (ECD) has been associated with poorer kidney allograft outcome. Aging of the kidney is associated with senescent profiles of cells that secrete pro-inflammatory cytokines that impact its regenerative function. Our study aimed to identify factors of the donor microenvironment that may influence the "quality" and early outcome of aging kidney transplants.

Methods: Perirenal (PR) adipose tissue was obtained from 40 kidney donors (10 living and 30 deceased donors with various comorbidities factors). Collagenase digestion allowed isolation of the Stromal Vascular Fraction (SVF). Leucocyte, endothelial, pericyte and stromal cell subsets were analyzed within PR-SVF. RNAseq transcriptomic analysis was performed on PR-SVF from 5 ECD and 5 non-ECD donors. The SVF-dependent formation of capillary-like structures was evaluated in an in vitro MatrigelTM assay. We also

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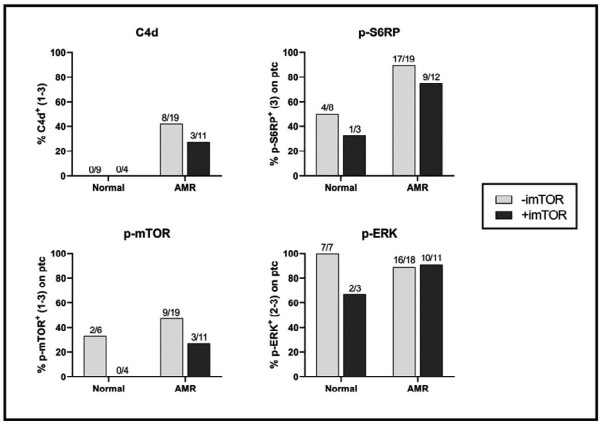
evaluated whether paracrine factors found in the perfusion fluid of ECD kidneys could induce endothelial senescence in vitro.
Results: The angiogenic function and quantitative distribution of the stromal and endothelial cell compartments within the perirenal stromal vascular fraction exhibited high inter-individual variability among donors. SVF from ECD donors displayed a differential signature characterized by over-expression of CD144 and inflammatory transcripts. In vitro exposure of endothelial cells derived from the PR-SVF of young donors to machine perfusion fluid of ECD donors was shown to induce endothelial senescence.
Conclusions: Our study shows that PR-SVF allows an individualized assessment of donor-related parameters that associate to the dysfunction of kidney allografts. Such appraisal of biomarkers that reflect the quality of transplants may open perspectives for targeted approaches aimed at preserving the regenerative function of aging kidneys.

FG061 PHOSPHORYLATION OF S6RP IN PERITUBULAR CAPILLARIES IS ASSOCIATED WITH ANTIBODY-MEDIATED REJECTION IN KIDNEY ALLOGRAFTS

Dalia Raïch-Regué, Javier Gimeno, Silvia Menendez, David Benito, Dolores Redondo, M. Jose Pérez-Sáez, Laura Llinás, Carlos Arias, Marta Riera, Julio Pascual, Marta Crespo
IMIM/Hospital del Mar

Background: Antibody mediated rejection (AMR) in the presence of donor-specific HLA antibodies (DSA) is recognized as key factor in late renal allograft loss. DSA have been reported to activate microvascular endothelial cells through the mTOR pathway. The phosphorylation of the mTOR pathway proteins S6RP and 70S6K have been proposed as new markers of AMR on transplanted hearts. Our aims were (1) to evaluate the mTOR pathway activation because of HLA DSA in kidney grafts with AMR compared to normal biopsies, and (2) to evaluate the potential modulation of the mTOR pathway by immunosuppression with mTOR inhibitors (mTORi).
Methods: We included 45 kidney transplant patients with graft-biopsies (RB) performed in 2011–15: 34 with AMR diagnosis (Banff 2015), all with HLA-DSA, and 11 age-matched recipients with normal biopsies. 17 had received mTORi (13 AMR) and 28 had not (21 AMR). RB were stained for C4d and phosphorylation of the mTOR pathway proteins S6RP (Ser235/236), ERK (Thr202/204) and mTOR (Ser2448) in peritubular capillaries (PTC) by immunohistochemistry in paraffin sections. PTC labelling was graded according to the scale: 0, no staining; 1, rare staining of single cells; 2, focal staining; 3, multifocal to diffuse staining.
Results: Staining of RB with AMR showed a significant increase in C4d staining ($p = 0.006$) and expression of pS6RP in PTC compared to controls ($p = 0.012$). No association was found between AMR and pERK or pmTOR staining. The presence of circulating HLA-DSA associated with pS6RP ($p = 0.034$) in PTC. There was no correlation between C4d and staining of the studied mTOR phosphoproteins. Treatment with mTORi had no significant impact neither on C4d, pERK, pmTOR, pS6RP staining in PTC, or chronicity.
Conclusion: Our findings support that S6RP phosphorylation in PTC is associated with AMR in RB. Consequently, pS6RP staining may be useful for AMR diagnosis. Treatment with mTORi does not seem to modify pS6RP, pERK or mTOR in kidney allografts.



FG062 A URINARY METABOLITE CONSTELLATION TO DETECT ACUTE REJECTION IN KIDNEY ALLOGRAFTS

Miriam Banas[1], Sindy Neumann[2], Philipp Pagel[2], Franz Josef Putz[1], Bernhard K. Krämer[3], Petra Rümmele[4], Johannes Eiglsperger[2], Eric Schiffer[2], Bernhard Banas[1]
[1]Department of Nephrology, University Hospital Regensburg; [2]Numares AG; [3]Fifth Department of Medicine, University Medical Center Mannheim; [4]Department of Pathology, University Hospital Erlangen

Background: Post-transplant surveillance for acute rejection is mainly based on regular monitoring of serum creatinine levels and transplant biopsies upon functional renal impairment. Recently, we developed a novel method to detect kidney allograft rejection via a characteristic constellation of the urine metabolites alanine, citrate, lactate, and urea investigated by nuclear magnetic resonance (NMR) spectroscopy (Banas M et al. Metabolomics 2018).
Methods: Within the prospective, observational UMBRELLA study 986 urine specimens were collected from 109 consecutively enrolled renal transplant recipients and metabolite constellations were analyzed by NMR spectroscopy. A metabolite rejection score was calculated and compared to histopathological results of corresponding allograft biopsies ($n = 206$).
Results: The metabolite constellation was found to be a useful biomarker to non-invasively detect acute allograft rejection (AUC = 0.75; 95% confidence interval (CI) 0.68–0.83; based on 46 cases with biopsy-proven rejection and 520 controls). A combination of the metabolite rejection score and the estimated glomerular filtration rate (eGFR) at the time of urine sampling further improved the overall test performance significantly (AUC = 0.84; 95% CI 0.76–0.91; based on 42 cases and 468 controls). In a subgroup of patients without rejection episodes the test results remained well below a diagnostic threshold associated with high risk of acute rejection. In other cases a marked increase above this threshold indicated an acute allograft rejection already 6–10 days before diagnostic renal biopsies were performed.
Conclusions: In conclusion, a combination of a NMR-based urine metabolite analysis and glomerular filtration rate is promising as a non-invasive test for post-transplant surveillance and to support decision making whether renal allografts need histopathological evaluation.

FG063 EXPRESSION PROFILING OF EXOSOMAL MIRNAS DERIVED FROM THE PERIPHERAL BLOOD OF KIDNEY RECIPIENTS WITH DGF USING HIGH-THROUGHPUT SEQUENCING

Junpeng Wang[1], Xin Li[2], Xiaoqiang Wu[1], Zhiwei Wang[1], Chan Zhang[1], Guanghui Cao[1], Tianzhong Yan[1]
[1]Henan Provincial People's Hospital; [2]Zhengzhou University

Background: Delayed graft function (DGF) is one of the major obstacles for graft survival for kidney recipients. It is profound to reduce the incidence of DGF for maintaining long-term graft survival. However, the molecular regulation of DGF is still not adequately explained and the biomarkers for DGF are limited. Exosome-derived proteomic and RNA signature profiles are often used to account for the molecular regulation of diseases or reflect the conditional state of their tissue as biomarkers. Few researches have been done to demonstrate the function of exosomes associated with DGF.
Methods: In this study, high-throughput sequencing was used to explore the miRNA expression profiling of exosomes in the peripheral blood of kidney recipients with or without DGF. Two algorithms miRanda, and Targetscan were used to predict the target genes of exosomal miRNAs which were differentially expressed between DGF and control groups. Subsequently, the gene ontology terms (http://www.geneontology.org/) and KEGG pathway terms (http://www.genome.jp/kegg) enriched in predicted target genes were determined to explore the function and related pathway of the targets.
Results: We identified 52 known and 5 conserved exosomal miRNAs specifically expressed in recipients with DGF. Three co-expressed miRNAs, hsa-miR-33a-5p_R-1, hsa-miR-98-5p and hsa-miR-151a-5p, were observed significantly up-regulated in kidney recipients with DGF. Moreover, hsa-miR-151a-5p was positively correlated with the first-week serum CR, BUN and UA levels of the kidney recipients after transplantation. Furthermore, we also analyzed functions and signaling pathways of the three up-regulated miRNAs target genes to uncover putative mechanism that how these exosomal miRNAs functioned in DGF.
Conclusions: Overall, these findings identified biomarker candidates for DGF and provided new insights into the important role of the exosomal miRNAs regulation in DGF.

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FG064 DOES ALLOGRAFT MITOCHONDRIAL COPY NUMBER IMPACT ON RENAL TRANSPLANT OUTCOMES?

Oliver Shapter[1], Dagmara McGuinness[2], Karen Stevenson[1], David Kingsmore[1], Paul Shiels[2]
[1]Renal Surgery and Transplant Unit, Queen Elizabeth University Hospital, Glasgow; [2]University of Glasgow, College of Medical, Veterinary and Life Sciences, Institute of Cancer Sciences, Glasgow

Background: Dysregulation of mitochondrial biogenesis is a hallmark of ageing and disease. Donor age is a significant determinant of post-transplant renal outcomes. Collectively, these imply that pre-transplant mitochondrial content delineates a renal allograft with inherent IRI resilience and improved allograft function attributable to the preservation of basal cellular energetics underpinned by the mitochondrial-telomere-ribosome (MTR) theory.
Methods and Materials: Mitochondrial expression, evaluated by mitochondrial DNA (mtDNA) content, was determined using real time quantitative polymerase chain reaction (qPCR) for 78 pre-perfusion biopsies. Associations with donor characteristics (age, sex, donor type), cold ischaemic time (CIT), anastomosis (AT) and specific post-transplant outcomes (renal function at 3, 6 & 12 months, rapid or delayed graft function (DGF)) and graft loss were analysed.
Results: Greater mtDNA copy numbers was associated with a lower serum creatinine (Cr) and a greater modified diet in renal disease (MDRD4) eGFR at 3 months ($p = 0.005$ & $p = 0.005$ respectively). This extended to 12 months with serum Cr ($p = 0.015$). MtDNA content exceeding mean and median values was associated with higher MDRD4 at 3 and 12 months with ECD DCD organs ($p = 0.041$) and longer CITs ($p = 0.001$ & $p = 0.015$) being associated with below mean and median values. Negative correlation was found between mtDNA content and p14ARF expression ($p = 0.014$) with p14ARF expression negatively impacting on MDRD at 3 months ($p = 0.046$). Donor characteristics, operative parameters or immediate functional outcomes did not correlate to mtDNA expression.
Conclusion: Resilient renal allografts express elevated mtDNA content and demonstrate improved allograft functional outcomes. These organs have increased ribosomal biogenesis with a higher energy potential and thus instigate restorative processes using the elements postulated in the MTR theory.

FG065 CIRCULATING CELL-FREE NUCLEOSOMES AS MARKER OF GRAFT INTEGRITY IN KIDNEY TRANSPLANTATION PATIENTS

Jeroen Verhoeven[1], Carla Baan[1], Marielle Herzog[2], Dennis Hesselink[1], Karin Boer[1]
[1]Erasmus MC, University Medical Center Rotterdam; [2]Belgian Volition SPRL

Introduction: There is an unmet need for non-invasive markers, specific for graft rejection and early identify graft injury, which eventually could overcome the need for a transplant biopsy. Here, we evaluated the potential of circulating cell free nucleosomes (ccfn) to serve as a marker for graft injury and rejection in serum samples from kidney transplantation recipients.
Material and Methods: Forty kidney transplant recipients after de novo kidney transplantation were evaluated for ccfn. Per patient 4 fixed time points were studied: before transplantation, day 3–6, 1 and 6 months after transplantation. In addition, serum collected at times of allograft rejection ($n = 13$) were also analysed. The global amount of ccfn was measured with a Nu.Q™ Total Assay kit (VolitionRx), an ELISA-based assay with antibodies directed against nucleosomes.
Results: At 3–6 days after transplantation the concentration of ccfn was significantly higher than the values measured before transplantation [median and interquartile range: 4.9 μg/ml (4.4–5.3) vs. 4.2 μg/ml (3.1–4.7), $p < 0.01$, respectively]. During rejection the values of ccfn were significantly higher than in patients without rejection (non-rejectors) at month 6 [4.6 μg/ml (3.7–5.4) vs. 3.7 μg/ml (2.2–4.2), $p < 0.01$, respectively]. In patients without any clinical problems, the values did not change significantly between pre transplant, month 1 and month 6 after transplantation.
Conclusion: For the first time, we demonstrate that ccfn are significantly increased in the first period after transplantation and at times of rejection. This likely reflects tissue injury resulting from ischemia-reperfusion injury during transplantation and from alloreactivity. Ccfn could serve as non-invasive markers for the detection of graft injury and rejection, nevertheless the release of ccfn in other pathological conditions needs to be elucidated.

FG12 – HEART TRANSPLANTATION

FG067 TACROLIMUS FOR PREVENTION OF HEMODYNAMICS AND INFLAMMATION CHANGES IN EXPERIMENTAL BRAIN DEATH-INDUCED RIGHT VENTRICULAR FAILURE

Asmae Belhaj[1], Laurence Dewachter[2], Robert Naeije[2], Kathleen Mc Entee[2], Benoit Rondelet[1]
[1]CHU UCL Namur; [2]Université Libre de Bruxelles

Background: Right ventricular (RV) dysfunction remains the leading cause of early death after cardiac transplantation. Tacrolimimus was reported to improve ventricular function in experimental infarction however physiopathologic explanation for that remains unexplained. We sought to determine whether tacrolimus, acting on hemodynamic physiology and inflammation, might prevent brain death-induced RV dysfunction.
Methods: After randomization to placebo ($n = 9$) or to methylprednisolone ($n = 7$; 0.1 mg/kg/J), 18 pigs were assigned to a brain-death procedure. The animals underwent hemodynamic evaluation at 2, 4 and 6 h after Cushing reflex (i.e., hypertension and bradycardia). The animals euthanized, and myocardial tissue was sampled. This was repeated in a control group ($n = 8$).
Results: At 6 h after the Cushing reflex, brain death resulted in increased pulmonary artery pressure (27 ± 2 vs. 19 ± 1 mmHg) and in a one-third decreased ratio of RV end-systolic to pulmonary arterial elastances (Ees/Ea) Cardiac output and right atrial pressure did not change.

Brain death-induced RV dysfunction was associated with increased RV expression of interleukin (IL)-6, IL-10, IL-1β, and tumor necrosis factor (TNF)-α.

Tacrolimus pre-treatment prevented RV-arterial uncoupling and decreased RV expression of cytokins and neutrophil infiltration.
Conclusions: Brain death-induced RV dysfunction is associated with RV activation of inflammation and is partly limited by tacrolimus.

FG068 OUTCOME AND MORTALITY OF HEART TRANSPLANTATION FOR BIVENTRICULAR FAILURE

Denise Galbiati[1], Francesco Cacciatore[2], Vittorio Palmieri[3], Irene Mattucci[4], Roberto Andini[4], Emanuele Durante Mangoni[1], Ciro Maiello[3], Cristiano Amarelli[3]
[1]Vanvitelli University; [2]Federico II; [3]Monaldi, Azienda dei Colli; [4]Azienda Dei Colli

Many institutional reports and registries report BI-Ventricular Assist Devices and Total Artificial Heart to be associated with higher mortality respect to Left Ventricular Assist Devices (LVAD). Few data are reported regarding the impact of biventricular failure on the outcome of Heart Transplantation (HTx). The aim of the study is to analyze the impact of the "milieu" of the biventricular failure recipient on the outcome of HTx.

108 consecutive HTx performed in a single institution during a six years period were evaluated and categorized on the basis of the pathophysiology of the disease. The study population comprised 82 males (75.9%) and 26 females undergoing HTx due to ischemic cardiomyopathy (29 pts), valvular (8 pts), Idiopathic (40 pts) and in 31 cases due to other causes. 29 Patients were acknowledged as biventricular failures and 79 mono-ventricular failures.

Clinical features are shown in Table 1.

Variables	Monoventricular	Biventricular	Total	*p*
Age	49.3 ± 15.3	36.8 ± 19.9		0.001
Female sex	17 (20.7%)	9 (34.6%)	26 (24.1%)	0.12
Etiology (non ischemic nor idiopatic)	19 (23.2%)	12 (46.2%)	31 (28.7%)	0.019
TAPSE	16,3 ± 3	7.8 ± 3.2		<0.0001
Pro-BNP	4,008 ± 5,062	9,239 ± 7,319.9		0.048
Creatinine	1.2 ± 0.5	1.2 ± 0.5		0.863
ECMO	2 (2.4%)	3 (11.5%)	5 (4.6%)	0.08
Hospitalization	37 (45.1%)	18 (69.2%)	55 (50.9%)	0.027
Donor age	36.1 ± 13.1	28.4 ± 15.9		0.015
Total ischemic time (Warm+Cold)	193.5 ± 57.8	203.1 ± 55.9		0.478
1-Year Mortality	14 (34.7%)	25 (58.3%)	39 (40.6%)	0.037

These clinical features account for two different footprints of recipients experiencing significantly different outcomes that appear suboptimal despite the usage of ideal donors.

Biventricular failure acts as a risk factor on the outcome of HTx despite the allocation of ideal donors. The outcomes appear dramatically unfavorable and similar to the outcomes reported by international registries on Mechanical Circulatory Support devices. Due to the donor shortage, the choice between a device and Htx should be carefully weighed to avoid the waste of ideal donors.

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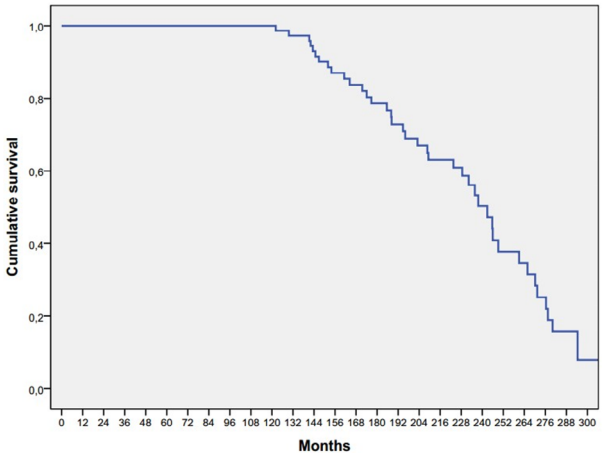
FG069 AGING WITH A NEW HEART

Sandro Sponga, Concetta Di Nora, Veronica Ferrara, Andrea Lechiancole, Vincenzo Tursi, Chiara Nalli, Giorgio Guzzi, Ugolino Livi
Azienda Sanitaria Universitaria Integrata di Udine

Background: Although patients with a transplanted heart and long-term follow-up are steadily increasing, little is known about late functional status, complications and quality of life of recipients approaching the eighth decade.
Methods: Among 640 transplanted patients, 74 reached an age ≥75 years and a follow-up ≥10 years and were revaluated for mortality, morbidity and quality of life.
Results: At a mean follow-up of 17 ± 4 years, renal failure occurred in 38 (51%), tumors in 35 (47%), infections in 30 (41%), and allograft vasculopathy in 41 (55%); only 10 patients (14%) developed acute rejection ≥2R. Echocardiographic data were stable during follow-up: mean left ventricular ejection fraction was 64 ± 6% and pulmonary arterial pressure 28 ± 6 mmHg. At 10-year follow-up, 72 (97%) were treated with cyclosporine, 18 (24%) with purine-antimetabolite drugs and 17 (23%) with prednisone. There were 40 (54%) late deaths. At univariate and multivariate analysis, risk factors for mortality were renal failure (OR = 2.4, 1.3–4.4, $p < 0.01$) and higher systolic pulmonary pressure (sPAP) (OR = 1.1, 1–1.2, $p = 0.03$). Scores of SF36 test showed a physical health of 44 ± 11 (−0.6 SD from general population) and mental health 53 ± 8 (+0.3 SD from general population). Causes of death were immunesuppression related (such as neoplasia, renal failure and infections) in 17 patients (43%), cardiac related in 7 cases (18%), other or unknown in 15 (37%).
Conclusions: Transplanted patients approaching at long-term follow-up the eighth decade have an acceptable outcome. Quality of life post-transplant is similar to general population. Acute rejection episodes are uncommon, while renal failure correlates with mortality. Therefore, a lower level of immunosuppression should be considered in this subset of heart transplanted patients.

Variables	
Complications at follow up	
Renal failure	38 (51%)
10-year blood creatinine level, mean ± SD	1.5 ± 0.6
Infections	30 (41%)
Allograft vasculopathy	41 (55%)
Acute rejection ≥2R	10 (14%)
10-year echocardiographic data	
LVEF, mean ± SD	64 ± 6
sPAP, mean ± SD	28 ± 6
10-year immune-suppressive therapy	
Cyclosporine	72 (97%)
Cyclosporinemia	121 ± 54
Prednisone	17 (23%)
Purine-antimetabolite drugs	18 (24%)



FG070 ECG IN PREDICTING CARDIOVASCULAR EVENTS AFTER HEART TRANSPLANTATION: AN OLD BUT STILL GOOD ASSAY?

Marco Masetti, Elvira Presta, Nicolina Conti, Laura Giovannini, Silvia Boschi, Francesca Corazza, Antonio Russo, Emanuela Bertolino, Paola Prestinenzi, Luciano Potena
Bologna University Hospital

Background: Little is known about the role of ECG after heart transplantation (HT). In this study, we sought to identify ECG parameters that could help to identify graft dysfunction and to stratify prognosis.
Methods: Patients (pts) enrolled in a prospective study aimed to test a novel immune monitoring test (Quantiferon monitor, QFM), consecutively coming at our Clinic (2014–17) were divided into 3 groups: (A) normal graft function (HT < 2 years); (B) normal graft function (HT > 5 years); (C) LVEF < 50% or symptoms of heart failure. ECG data collected at the enrolling visit were: PQ, QRS width, QTc (Bazett's formula), heart rate, rhythm, conduction disorders. The endpoint was the 3-years combined survival from cardiovascular death and MACE.
Results: Among 153 pts (58 ± 14 years, 75% M), 79% had normal graft function (51% A, 28% B). Pts with graft dysfunction had a different distance from HT (1.2 ± 1.6 vs. 15.7 ± 5.7 vs. 12.9 ± 7.4 years), more frequently CAV (8.8% vs. 14.9% vs. 64%), longer PQ (148 ± 25 ms vs. 163 ± 38 vs. 181 ± 53), wider QRS (101 ± 18 vs. 105 ± 18 vs. 131 ± 34 ms), longer QTc (445 ± 4 vs. 453 ± 3 vs. 473 ± 5 ms), more conduction disorders (39.2% vs. 51.2% vs. 75%) and Afib (0 vs. 4.6% vs. 9.1%); comparisons A versus B versus C, $p < 0.01$ for all. Pts at >5 years from HT and, similarly, those with CAV, had longer PQ, wider QRS, more conduction disturbances ($p < 0.01$ all), similar QTc. CAV pts had lower voltages. MACE occurrence was higher in group C, similar in the other two groups (62.8 ± 8.7% vs. 94.8 ± 2.5% vs. 90.3 ± 4.6%, $p < 0.001$). At multivariate analysis, QTc ≥ 470 msec (HR:2.9, $p = 0.03$) and CAV (HR:5.5, $p < 0.01$) independently predicted MACE, even after adjusting for distance from HT(Figure).
Conclusions: ECG parameters in HT are influenced by many factors, reflecting multiple pathways involved in graft dysfunction. The finding of a long QT, being a marker of subclinical systolic dysfunction (i.e. microvascular disease, chronic rejection) may help in identifying patients at high risk of MACE.

FG071 COLD ANTEGRADE MYOCARDIAL PERFUSION TO REDUCE PRIMARY GRAFT DYSFUNCTION AFTER HEART TRANSPLANTATION

Sanjeet Singh Avtaar Singh, Sudeep Das De, Jonathan Dalzell, Karim Morcos, Yasser Hegazy, Hazim Al-Haideri, Sukumaran Nair, Harikrishna Doshi, Nawwar Al-Attar, Philip Curry
Golden Jubilee National Hospital

Background: Primary Graft Dysfunction (PGD) is the leading cause of early mortality after heart transplantation and affects around 1 in 3 transplants. The pathophysiology of PGD is thought to be ischaemic-reperfusion injury (IRI). Several risk factors have been identified, including prolonged warm ischaemic time, donor age, gender mismatch and recipient diabetes mellitus. We therefore adopted a novel method of implantation using antegrade myocardial perfusion (AMP) during implantation to augment IRI. We looked at our experience using this method compared to a historical cohort of patients at our centre.
Methodology: For the AMP cohort, an antegrade infusion of 600 ml of cold blood cardioplegia followed by cold oxygenated blood (4–6°C) is infused to achieve a mean aortic root pressure of 60–70 mmHg employing a constant pressure-variable CPB flow pump with an in-situ leucocyte depleting filter. This continuous antegrade perfusion is maintained throughout the left atrium and aortic anastomosis with a left ventricular vent in situ. Upon completion of the aortic anastomosis, a warm cardioplegia hotshot is infused into the aortic root followed by removal of the recipient aortic cross-clamp.

Systemic perfusion is initiated with continued aortic root and LV venting. The remaining anastomoses are carried out in the usual fashion sequentially.

We compared our experience with this method to a historical cohort of patients (2012–2014). We performed multivariable logistic regression with moderate/severe PGD as the outcome measure. Confounders adjusted for include recipient age, total ischaemic time, bypass time, predicted left ventricular (LV) mass mismatch, recipient diabetes mellitus and donor age.
Results:
Conclusion: The new implantation technique utilising antegrade myocardial perfusion significantly lowers the rate of moderate and severe PGD when compared to the standard implantation technique employed by the historical cohort.

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Details	AMP cohort(n=33)	Historical control(n=42)	p-value
Recipient Age(years)	48.2±11.9	45.9±11.8	0.400
Recipient M:F ratio	25:8	30:12	0.674
Pre-transplant Recipient Creatinine (μmolL^{-1})	90.0±28.7	97.3±25.1	0.259
Recipient Diabetes Mellitus (%)	1(3)	6(14.2)	0.101
Recipient Resternotomy (%)	12(36.3)	11(26.2)	0.343
Recipient Aetiology			
• Dilated Cardiomyopathy • Restrictive/Hypertrophic obstructive cardiomyopathy • Ischaemic cardiomyopathy • Other	22(66.7) 4(12.1) 6(18.2) 1(3.0)	17(40.5) 5(11.9) 13(30.9) 7(16.7)	0.077
Total Ischaemic time(mins)	154±50.2	181±47.1	**0.018**
Explant Time(mins)	20.1±9.3	19.0±10.3	0.647
Implant Time(mins)	50.4±18.9	54.5±18.6	0.117
Cold ischaemic time(mins)	120.9±48.7	111.4±46.0	0.390
Warm Ischaemic time(mins)	10.6±8.6	71.7±20.2	**<0.001**
Bypass time(mins)	217.1±65.3	247.2±92.0	0.104
Donor Age(years)	36.6±11.1	41.9±12.3	0.056
Donor-Recipient LV mass mismatch (%)	-7.7±24.9	4.4±23.2	**0.032**
Post-operative Inotrope score	15.0±8.0	18.6±9.9	0.086
Donor-Recipient Gender mismatch (%)	7(21.2)	16(38.1)	0.115
Pre-operative inotrope dependence (%)	14(42)	13(31)	0.304
Pre-operative MCS (%)	8(24.2)	7(16.7)	0.416
Pre-operative IABP (%)	14(42.4)	13(31.0)	0.304
Post-operative IABP (%)	19(57.6)	27(64.3)	0.554
Post-operative ECMO (%)	5(15.2)	23(54.8)	**<0.001**
Moderate/Severe Primary Graft Dysfunction (%)	7(21.2)	26(61.9)	**<0.001**
Multivariable analysis	**Odds ratio**	**95% Confidence intervals**	**p-value**
Continuous Variables			
Bypass time (mins)	1.013	1.0042, 1.0224	**<0.002**
Donor Age (years)	1.1053	1.0434, 1.1707	**<0.001**
Categorical Variable			
Antegrade myocardial perfusion	1(reference category)	N/A	N/A
Historical Cohort	4.15	1.2096, 14.2403	**0.02**

FG13 – KIDNEY TRANSPLANT OUTCOMES: PREDICTIONS, PREDICTIONS!

FG072 DEVELOPMENT OF NOVEL EUROPEAN PREDICTION MODELS FOR DELAYED GRAFT FUNCTION AND UNACCEPTABLE OUTCOME AFTER KIDNEY TRANSPLANTATION FROM 50+ DECEASED DONORS

Cyril Moers[1], Mostafa El Moumni[1], Nichon Jansen[2], Andries Hoitsma[2]
[1]University Medical Center Groningen; [2]Dutch Transplantation Foundation

Background: An abundance of prediction models for delayed graft function (DGF) and the relative risk of graft failure after kidney transplantation are around. However, many are validated on a Northern American population and often not specifically focused on renal grafts at risk for unacceptable outcome. In addition, "unacceptable outcome" does not only comprise graft failure, but also very poor function post-transplant. We have developed new prediction models for the *absolute* risk of DGF and unacceptable outcome, on a large cohort of European elevated-risk renal transplants.
Methods: All kidney transplants from 50+ deceased donors, carried out in The Netherlands between 2000 and 2015 were identified. Non-linear, spline based multivariable prediction models were constructed, one for the risk of DGF and one for the risk of "unacceptable outcome", defined as graft failure or death within the first year, or an eGFR < 30 ml/min at one year post-transplant. Models were internally validated by means of bootstrapping and externally validated on a separate cohort of more recent transplants (2016–2017), to obtain discrimination (c-statistic) and calibration (HL test).
Results: We included 3,305 renal transplants and an additional 551 for external validation. Twenty-one donor and recipient variables were utilized to construct prediction models. After internal validation, the model for DGF had a c-statistic of 0.75, the HL-test showed $p = 0.9993$. Internal validation of the unacceptable outcome model yielded a c-statistic of 0.67 and an HL-test $p = 0.4044$. External validation showed a c-statistic of 0.70 and HL-test $p = 0.2172$ for the DGF model and a c-statistic of 0.61 and HL-test $p = 0.0567$ for the unacceptable outcome model.
Conclusion: The model for DGF had reasonable discrimination and good calibration. The model for unacceptable outcome had moderate discrimination and calibration. These European models may help clinicians to make more objective decisions on acceptance or discard of higher-risk organs.

FG073 ZERO-BIOPSY AND KIDNEY TRANSPLANT FUNCTION OF DONOR KIDNEYS FROM ACCELERATED ORGAN ALLOCATION PROCEDURE (AOAP): REAL, RESCUE, CENTER OFFER COMPARED TO STANDARD EUROTRANSPLANT KIDNEY ALLOCATION SYSTEM (ETKAS) – SINGLE CENTER ANALYSIS 12/2013–12/2017

Katharina M. Heller[1], Apel Hendrik[1], Sven Wach[2]
[1]Transplant Centre Erlangen – Nürnberg; [2]Urology, University Hospital Erlangen

Background: In December 2013, only in Germany AOAP were supplemented by a web-based system "recipient oriented extended allocation" (REAL). AOAP accounts 19% of ET kidney allocation.

Donor kidney that is repeatedly rejected as non-transplantable in standard ET allocation process go into AOAP. ET offers donor kidney concurrently to several transplant centers, according to the motto "first come, first served". Hence, donor kidney may be judged being of inferior quality due to previous offer rejections.
Material/Method:

1. Is there a potential quality difference in pre-implant biopsy (0-Bx) of AOAP versus ETKAS kidney?
2. Is there a possible quality difference in primary function (<2 dialyses post transplantat (ktx)), creatinine at discharge, at month (mo) 6, 12, 24.

12/2013–12/2017, $n = 216$ ET realised ktx at our center, 50 (23%) AOAP/166 ETKAS.

In 211 cases (97.7%) 0-Bx was obtained, 23% AOAP ($n = 48$).
Results: AOAP/ETKAS: Interstitial fibrosis, tubular atrophy (IFTA): 66.7/58.9%. Arterial hyalinosis (AAH): 50.0%/35.0%. Glomerulosclerosis (gs): 45.8/44.8%. Acute tubular necrosis (ATN): 93.8/97.5%. Delayed graft function (DGF, >1 dialysis post ktx): 48.2/26.0%. Mean creatinine (mg/dL) at discharge: 2.94/1.88; 6th mo: 1.75/1.49; 12th mo: 1.67/1.45; 24th mo: 1.68/1.5.
Conclusion: Our analysis shows that kidneys of AOAP perform poorer compared to ETKAS in preimplantation phase as well as in early phase of ktx, given clearly higher proportion of IFTA, AAH in 0-Bx and higher risk for DGF. These early quality differences level out with 6th month after ktx. 2-year observation does not show significant functional difference between AOAP and ETKAS. This effect may be due to free choice of recipients that transplant center can make in AOAP. Then, donor-recipient match is independent of ET allocation criteria and allows to use center-specific matching criteria (biometric, immunologic, age-related). Our analysis calls for a multicenter study to confirm our results in general and also in longterm monitoring.

FG074 PRE -TRANSPLANT IN SITU KIDNEY BIOPSY TO REDUCE COLD ISCHEMIA TIME AND TO IMPROVE TRANSPLANT OUTCOME: MONOCENTRIC RETROSPECTIVE ANALYSIS

Federica Odaldi, Matteo Serenari, Giorgia Comai, Raffaele Bova, Giacomo Frascaroli, Deborah Malvi, Lorenzo Maroni, Francesco Vasuri, Valeria Corradetti, Irene Capelli, Vania Cuna, Antonio Siniscalchi, Antonietta D'Errico, Massimo Del Gaudio, Valentina Rosa Bertuzzo, Chiara Zanfi, Gaetano La Manna, Matteo Ravaioli
Sant'Orsola-Malpighi Hospital, Bologna, Italy

Background: Kidney biopsy is usually obtained to assess if an extended criteria graft can be used for transplantation or must be discarded. Performing biopsy may lead to an increased cold ischemia time (CIT). CIT has been associated with delayed graft function (DGF) and reduced graft survival. Since 2012, we perform kidney biopsy before the aortic cross clamping of the donor, sending the biopsy immediately to pathologist. We evaluated if this strategy reduces CIT and improves graft outcome.
Methods: Kidney transplants performed in our centre from January 2007 to December 2017 were retrospectively analysed. Grafts with pre-implantation kidney biopsy were included. Biopsies were performed during surgical back table (ESKB, ex-situ kidney biopsy) or in situ (ISKB, in situ kidney biopsy) before the aortic cross clamping. To overcome biases owing to different distribution of covariates among patients, a propensity score model was developed using the nearest neighbour method. Primary endpoint of the study was a lower CIT and secondary endpoints were lower DGF and better graft survival.
Results: Population consists in 322 patients, 116 ESKB and 206 ISKB. Groups (ESKB vs. ISKB) were significantly different concerning recipient age that was significantly higher in the ISKB: median 70 vs. 64 years, $p < 0.001$. Propensity score matching led to a population of 134 patients, 67 ESKB and 67 ISKB. Groups were not significantly different for donor features (age, gender, BMI, KDPI), Karpinski score, recipient features (age, gender, BMI, percentage of diabetes and cardiovascular disease), rate of dual kidney transplants. Median CIT was 900 min in ESKB vs. 720 min in ISKB, $p < 0.001$ 52.2% patients in ESKB group developed DGF vs. 34.3% in ISKB group, ($p < 0.001$). Graft survival at 5-year was 88.8% in ISKB vs. 80.8% in ESKB, $p = 0.041$.

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Conclusion: Our strategy of performing pre-implantation kidney biopsy during the retrieval was effective to reduce significantly CIT and to improve graft outcome.

FG075 SHORT-TERM RENAL FUNCTIONAL RESERVE PREDICTS LONG-TERM RENAL OUTCOME AFTER LIVING KIDNEY DONATION

Jessica van der Weijden, Marco van Londen, Stephan Bakker, Gerjan Navis, Stefan Berger, Martin de Borst

University Medical Center Groningen

Introduction: After a reduction in renal mass, the remaining kidney tissue is able to compensate: the renal functional reserve (RFR). After living kidney donation, the RFR leads to a glomerular filtration rate (GFR) >50% of the pre-donation value. Here, we investigated whether the short-term RFR is associated with long-term renal outcome in living kidney donors.
Methods: We measured pre- and post-donation mGFR (125-Iothalamate) in 408 living kidney donors between 1984 and 2018. The RFR was defined as the mGFR 3 months after donation minus 50% of the pre-donation mGFR. We used linear regression analysis to investigate the association between RFR and mGFR at 5 (n = 408) and 10 years (n = 132) after donation. Furthermore, we investigated the pre-donation determinants of the RFR.
Results: Mean age at donation was 53 ± 11 years (54% female). Mean pre-donation mGFR was 111 ± 23 ml/min and mean mGFR 3 months post-donation was 72 ± 15 ml/min. equalling 64 ± 8% of pre-donation mGFR, resulting in an RFR of 15 ± 9 ml/min (range [−28;72] ml/min]). Backward linear regression revealed that age (st. β = −0.37), pre-donation mGFR (st. β = −0.17) and body weight (st. β = 0.14) were independent determinants of the RFR (all $p < 0.001$, R^2 = 12%). In a multivariable linear regression model the RFR (st. β = 0.25, $p < 0.001$), pre-donation mGFR (st. β = 0.64, $p < 0.001$), age (st. β = −0.20, $p < 0.001$) and body weight (st. β = 0.11, $p < 0.001$) were all independently associated with mGFR 5 years post-donation (R^2 = 75%). In a similar analysis RFR was also independently associated with 10-year mGFR (st. β 0.24, $p < 0.001$).
Conclusion: RFR is associated with long-term mGFR after living kidney donation, independent of known determinants of renal outcome including pre-donation mGFR, age and weight. Our data indicate that the RFR can serve as an early marker of renal resilience that could identify donors at risk for GFR loss on the long term.

FG076 EXPANDING THE DONOR POOL: RECIPIENT OUTCOMES FOLLOWING RENAL TRANSPLANT FROM DECEASED AKI DONORS. A 24-MONTH RETROSPECTIVE ANALYSIS

Lucy Hare, John Black, Mayar Ghazal-Aswad, Rose Johns, Mohamed Morsy, Anna Rizzello, Tahir Doughman, Atul Bagul

Leicester General Hospital, University Hospitals of Leicester

Aims: Acute Kidney Injury (AKI) is defined as an abrupt reduction in kidney function, measured through an increase in serum creatinine and/or decreased urine output. This study looks at kidney donation in the context of donor AKI, with a particular focus on recipient outcomes (graft function, transplant rejection, and mortality).
Methods: 23 recipients of kidney transplant from a donor with AKI (stages 1–3) were identified over a 24 month period (01/06/15–01/06/17). 16 recipients were included in this study; 7 were not included based on exclusion criteria. Donor forms were used to obtain donor specifics. Local electronic records were used to assess recipient outcomes.
Results: Salient donor details and recipient outcomes from our study are summarised in the table below. Mean (±SD) is used unless otherwise specified.

Donor details		Recipient outcomes	
Age (years)	51.9	Age (years)	51.3
Sex (M:F)	1:1	Primary non-function (PNF)	0%
BMI	27.1(±4.03)	Delayed graft function (DGF)	31.3%
Donor type (DBD:DCD)	5:2	Episode of rejection	6.3%
Admission creatinine (μmol/L)	98.1(±36.9)	Creatinine 7 days (μmol/l)	525(±254)
Retrieval creatinine (μmol/L)	204(±101.4)	Creatinine 1 month (μmol/l)	195(±91.6)
Urine output in last hour (ml)	120	Creatinine 3 months (μmol/l)	174(±85.9)
History of hypertension	28.6%	Creatinine 6 months (μmol/l)	170(±89.2)
History of diabetes	0%	Creatinine 12 months (μmol/l)	157(±85.9)
Proteinuria >30 mg/dL (+)	35.7%	Mortality	0%
Haematuria	57.1%	Length of stay (days)	11.2(±5.88)

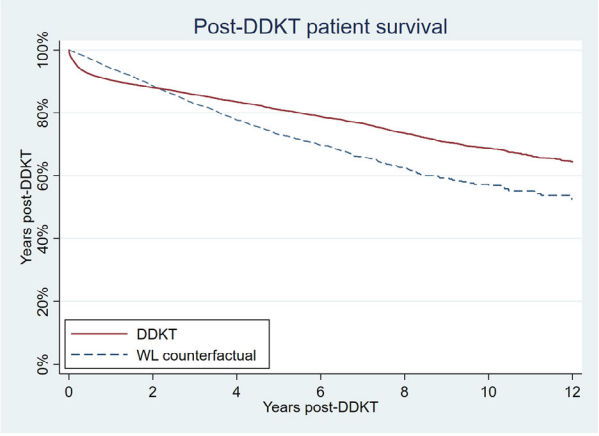
Mean donor age was 51.9 years (range 11–76 years). 71.4% were DBD donors. 28.6% were DCD. The mean donor serum creatinine on admission was 98.1 μmol/L, and 204 μmol/L at retrieval. 28.6% had a history of hypertension. Mean recipient age was 51.3 years (range 29–68 years). The mean serum creatinine at 7 days post-transplant was 525 μmol/L. Mean serum creatinine at 1, 3, and 6 months were 195, 174 and 170 μmol/L respectively. One year mean serum creatinine was 157 μmol/L. Average length of stay was 11.2 days. 31.3% of recipients had DGF. 1 recipient had an episode of rejection, which was successfully treated. 12 month graft survival was 100%. 1 recipient was treated for acute CMV infection at 5 months post-transplant. 1 recipient developed adenocarcinoma of the colon at 12 months. There were no mortalities.
Conclusions: This study suggests that AKI donor outcomes are acceptable. Whilst extreme offer variables are often declined, this study suggests that AKI donors should be considered as a feasible way of expanding the deceased donor pool. However, further larger scale studies are required to fully evaluate, particularly of AKI stage 3 donors.

FG077 TRENDS IN MORTALITY AND SURVIVAL BENEFIT OF DECEASED-DONOR KIDNEY TRANSPLANTATION IN BRAZIL

Allan Massie[1], Macey Henderson[2], Amrita Saha[2], Vinicius Colares[3], Juliana Bastos[3], Marcelo Perosa de Miranda[4], Dorry Segev[2], Gustavo Ferreira[3]

[1]Johns Hopkins School of Medicine; [2]Johns Hopkins University; [3]Santa Casa de Misericordia de Juiz de Fora; [4]Hospital Alemão Oswaldo Cruz

Most transplant research has occurred in high-income countries (HICs) and may not generalize to lower and middle-income countries (LMICs) in the context of differing demographics, comorbidity profiles, infectious disease risks, and standards of waitlist/post-transplant care. We drew on state transplant registry data to quantify waitlist mortality, post-transplant mortality, and the survival benefit of deceased-donor kidney transplantation (DDKT) in Brazil, a middle-income country with the third highest volume of transplants worldwide.
Methods: Using Sao Paulo state registry data on 54,019 waitlist registrants and 14,771 DDKT recipients 2000–2018, we studied temporal trends in waitlist (WL) and post-DDKT mortality adjusting for candidate age, sex, race/ethnicity (white/black/mixed/Asian), dialysis time at listing, and PRA. We calculated survival benefit by matching transplant recipients to a counterfactual WL population with the same WL followup time, using inverse probability of treatment weights to address covariate imbalance (Table).
Results: 5-year WL survival increased from 71.4% 2000–2004 to 78.7% 2013–2018; 5-year post-DDKT survival increased from 74.8% to 85.9%. In adjusted models, WL mortality was 21% higher among black registrants (aHR = $_{1.13}1.21_{1.30}$, $p < 0.001$) and 16% higher among mixed-race (aHR = $_{1.10}1.17_{1.23}$, $p < 0.001$), but race/ethnicity was not associated with post-DDKT mortality (all $p > 0.7$). Later era was associated with reduced WL mortality (aHR 2015–2018 vs. 2000–2004=$_{0.79}$ 0.88 $_{0.99}$, $p = 0.02$) and sharply reduced post-DDKT mortality (aHR = $_{0.38}0.45_{0.53}$, $p < 0.001$). Patient survival was lower among DDKT recipients in the first 2.2 year post-DDKT, and higher thereafter, e.g. 68.8% vs. 57.2% at 10 years post-DDKT ($p < 0.001$, Figure).
Conclusions: Post-DDKT survival has improved over time in Brazil. Despite lower post-DDKT survival compared to HICs, DDKT can confer substantial survival benefit in LMICs.



FG14 – PANCREAS/ISLET

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FG078 ASSESSMENT OF INSULIN SENSITIVITY IN PANCREAS AND ISLET TRANSPLANT RECIPIENTS

Charles-Henri Wassmer, Giulio Cesare Vitali, Axel Andres, Thierry Berney
University of Geneva Hospitals

In this study, we have evaluated the validity of several indices of insulin sensitivity in patients with type 1 diabetes successfully treated with various types of beta cell replacement therapies.

Thirty recipients of pancreas transplantation with systemic venous drainage (SYS; $N = 10$), pancreas transplantation with portal venous drainage (POR; $N = 10$) or islet of Langerhans transplantation (ISL; $N = 10$) were included. All patients had a successful transplant, as defined by insulin independence fasting blood glucose (FBG) < 6 mmol/L and HbA1c <6.5%. A 75-g oral glucose tolerance test (OGTT) was administered to all patients in the second year after transplantation, and parameters of response to glucose and insulin sensitivity were computed from OGTT results.

Highly significant differences were observed between the POR, SYS and ISL groups on several OGTT-derived values and are summarized on the Table.

Group	FBG	Glucose T 120'	AUC glucose	AUC insulin	HOMA-R	QUICKI	Gutt index	Matsuda index
POR	5.1	5.6	127	2,942	1.65	0.36	83.7	4.64
SYS	4.7	6.7	125	5,022**	3.36**	0.34	71.1**	3.13**
ISL	5.5	7.8**	156**	3,636**	1.92*	0.36	65.9**	3.82**

*$p < 0.05$ vs. POR.
**$p < 0.01$ vs. POR.

Overall, OGTT data confirmed that the average ISL patient displays impaired glucose tolerance characteristics even with perfect metabolic control. The area under the curve (AUC) of insulin response differed significantly between groups. Most indices appeared to show diminished insulin sensitivity in the SYS and ISL groups in comparison to the POR group, but not consistently in the same relative way. The QUICKI index was remarkably similar in all 3 groups.

The differences between groups in the insulin AUC is arguably a reflection of the location of the graft with respect to portal flow and its impact on first passage of insulin in the liver. It is likely that sensitivity indices, based on glucose and insulin blood levels, will be affected by this, as shown by the marked differences observed between patients with identical excellent metabolic control C.

FG079 FUNCTIONAL AND METABOLIC EFFECTS OF PANCREAS TRANSPLANTATION ALONE WITH PORTAL OR SYSTEMIC INSULIN DRAINAGE IN TYPE 1 DIABETIC PATIENTS

Walter Baronti, Vittorio Grazio Perrone, F. S. Indovina, Chiara Terrenzio, Elena Gianetti, Fabio Vistoli, Ugo Boggi, Piero Marchetti
Pancreas and Kidney Transplantation Center, Pisa City and University Hospital, Pisa, Italy

Background: Pancreas transplantation (PTx) restores normoglycemia in diabetic patients by replenishment of beta cell mass and function. Delivery of insulin release from the pancreatic graft may be accomplished by portal (PD) or systemic (SD) drainage. Little information is available on whether PD or SD have different impact on glycemic control in PTx recipients.
Methods: In the present study we report on the functional and metabolic outcomes of PTx alone drained by PD or SD in type 1 diabetic patients (re-transplants excluded), followed for 3 years. The pre-transplant main clinical characteristics of the PD and SD groups are reported in the table 1. Both groups received the same immunosuppressive therapy.

	N	Age (years)	M/F	BMI (kg/m^2)	DD (years)	Insulin (U/day)	HbA1c (%)	C-peptide (ng/ml)
PD	58	38 ± 9	27/31	23 ± 3	25 ± 10	44 ± 4	9.0 ± 1	0.13 ± 0.04
SD	28	40 ± 7	15/13	23 ± 3	26 ± 9	41 ± 12	8.5 ± 2	0.06 ± 0.08

Results: At the 3-year time point, no significant difference between PD and SD occurred in terms of patient survival (57/58, 98.3% vs. 27/28, 96.4%). However, 3-year pancreas graft survival (insulin-independence) was higher ($p = 0.027$ by the chi-square test) in the PD (46/58, 79.3%) than in the SD group (15/28, 53.6%). At the end of the follow-up, fasting plasma glucose levels were superimposable in the two groups (PD: 84 ± 7 mg/dL; SD: vs. 84 ± 12 mg/dL), and the same was observed as for HbA1c values (PD: 5.42 ± 0.19%; SD: 5.28 ± 0.48%). Whereas fasting C-peptide concentrations were similar in the two series (2.7 ± 1.5 ng/ml in PD and 2.6 ± 0.6 ng/ml in SD), insulin levels were significantly lower ($p < 0.001$) in the PD (10.8 ± 1.9 μU/ml) than SD (17.1 ± 6.1 μU/ml) patients.
Conclusion: This study shows that the PD drainage of insulin secretion in PTx alone may have functional (pancreas survival) advantages and is associated with lower insulin levels, conceivably due to the first pass liver extraction of the hormone.

FG080 PROPENSITY SCORE MATCHING ANALYSIS OF PORTAL VS SYSTEMIC VENOUS DRAINAGE IN PANCREAS TRANSPLANTATION ALONE

Fabio Vistoli, Niccolò Napoli, Francesca Palumbo, Vittorio Grazio Perrone, Emanuele Kauffmann, Sara Iacopi, Carlo Lombardo, Francesca Menonna, Gabriella Amorese, Piero Marchetti, Ugo Boggi
Pancreas and Kidney Transplantation Center, Pisa City and University Hospital, Pisa, Italy

Background: Portal drainage (PD) of pancreas grafts has been associated with improved metabolic profile and fewer rejections than systemic drainage (SD). These advantages would be especially useful in pancreas transplant alone (PTA) recipients due to higher risk of rejection and metabolic disarrangements.
Methods: Between December 2000 and May 2017 the venous effluent of 101 PTA was managed by PD ($n = 65$) or SD ($n = 36$). The groups were well matched for all baseline characteristics and received equivalent maintenance immunosuppression. Basiliximab (41 PD vs. 14 SD) or thymoglobuline (24 PD vs. 22 SD) was used as induction. The comparison was performed applying the Propensity Score Matching (PSM) on a 1(SD):2(PD) basis, in order to obtain greater homogeneity. Data were analyzed in terms of graft survival, complete thrombosis of the graft, acute 6-month rejection rate, overall acute rejection rate and chronic rejection.
Results: Six grafts were lost in the early post-PTA course due to vascular thrombosis (2 SD vs. 1 PD) and humoral rejection (0 SD vs. 3 PD). Relaparotomy rate was 19.4% in SD and 15.4% in PD group. PSM selected 57 PD vs. 26 SD. No differences in terms of graft survival (OR = 0.67, $p = 0.33$), overall acute rejection (OR = 0.40, $p = 0.07$) and chronic rejection (OR = 0.44, $p = 0.17$) were recorded. Six-month acute rejection rate (OR = $5.16*10^{-9}$, $p < 0.0001$) was significantly lower in PD group. No difference was seen in thrombosis onset (OR = 0.44, $p = 0.43$). Glycemic control was excellent in both groups, but fasting serum insulin levels were significantly lower in PD. Patient survival at 1 and 5 years was 100% (SD) vs. 98.2% (PD) at either time points. Equivalent figures for insulin independence were 78.9% and 61.3% (SD) vs. 87.9% and 80.1% (PD).
Conclusion: Either routes of venous drainage are suitable for PTA, although more recipients experience rejection with SD as compared with PD in the early post-PTA period. This difference could become even wider with larger randomized series.

FG081 ISLET AUTO TRANSPLANTATION AFTER TOTAL PANCREATECTOMY FOR CANCER

Carlo Lombardo[1], Fabio Vistoli[1], Domenico Bosco[2], Emanuele Kauffmann[1], Vittorio Grazio Perrone[1], Francesca Menonna[1], Niccolò Napoli[1], Gabriella Amorese[1], Piero Marchetti[1], Thierry Berney[2], Ugo Boggi[1]
[1]Pancreas and Kidney Transplantation Center, Pisa City and University Hospital, Pisa, Italy; [2]Cell Isolation and Transplantation Center, Department of Surgery, Geneva University Hospitals and University of Geneva, Geneva

Background: Limited experience is available for Islet autotransplantation (IAT) after pancreatic surgery due to other indications than chronic pancreatitis. Aim of the study is assessing short-term metabolic and oncologic outcomes of IAT in patients who received total pancreatectomy (TP) with vascular resection (venous combined or not, with arterial) after induction therapy for locally advanced pancreatic ductal adenocarcinoma (PDAC) or pancreatic neuroendocrine tumor (NET).
Methods: From December 2016 to August 2018, 7 non diabetic patients (3 females; median age 57 years: from 44 to 81 years; median BMI 24.4: from 20.1 to 26.3) received IAT to prevent brittle post-surgical diabetes after TP, for PDAC ($n = 6$) or NET ($n = 1$). Islets were prepared by enzymatic digestion and density gradient purification (median IEq $n = 178,083$: range 14,097–405,133; median IEq/Kg $n = 2,968$: range 224–5,331; median purity 40%: range 20–85%). Intraportal, ultrasound guided, IAT was performed the day after surgery without complications.
Results: Overall, according Clavien-Dindo, 4 grade 1, 1 grade 2 and 1 grade 3a complications were recorded, no reintervention were required and no complication, IAT procedure related, occurred. According to Igls criteria, after a median follow-up of 438 days (ranging from 170 to 685 days), 3 patients (42.9%) obtained optimal beta-cell function and 3 patients (42.9%) obtained good beta-cell function. At last follow-up, median C-peptide value is 1.28 ng/ml, ranging between 0.11 and 1.86 ng/ml. Five patients (71.4%) are alive and disease free at last follow-up. Two patients died (28.6%) at 4 and 15 months from TP+IAT due to cancer metastases but with insulin independence.
Conclusion: This early experience shows that IAT after TP is able to obtain an insulin-independence and/or improved metabolic control. The oncologic safety of this procedure remains to be established in a larger series with longer follow-up.

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FG082 EARLY PANCREAS GRAFTS LOSS, TRENDS OVER THE THREE DECADES OF PANCREAS TRANSPLANTATION IN THE UNITED STATES

Anna Adamusiak, Scott Jackson, Arthur Matas, Erik Finger, Raja Kandaswamy, Vanessa Humphreville, Samy Riad
University of Minnesota

Background: Long-term pancreas transplant (PTx) outcomes continue to improve. However, data for early graft loss (EGL) trends are limited. We studied the historical change in incidence and risk factors for EGL.
Methods: Using data from the Scientific Registry of Transplant Recipient (SRTR), we analyzed all PTx performed in the US between 1987 and 2015 for incidence and risk factors for EGF (i.e., within 30 days from PTx). Recipients were grouped and compared by eras: 1987–1998, 1999–2005, and 2006–2015. A generalized linear mixed model was used to assess risk factors for EGL within 30 days of PTx, adjusted for era, PTx type (simultaneous kidney and pancreas [SPK], pancreas after kidney [PAK], pancreas transplant alone [PTA]), recipient and donor gender, recipient and donor BMI, diabetes type and number of HLA mismatches.
Results: Of 28,029 PTx, 2,419 (8.6%) had EGL. The EGL rates significantly improved by era: 10.3% vs. 9.3% vs. 7.7% ($p < 0.001$). Thrombosis accounted for more than half of the EGL in each era (55% vs. 51% vs. 58%). EGL due to rejection (8.7% vs. 3.1% vs. 0.9%) represented fewer losses over time.

Before 1999 the rate of EGL was 9.5% for type 1 diabetes and 12.5% for type 2 diabetes. In the 2nd and 3rd eras the rate of EGL was similar for both types of diabetes.

EGL after SPK decreased from 9% in the first two eras to 7% in the 3rd era. Similarly, EGL in PAK and PTA declined from 15% and 14%, respectively to 9% after the 1st era.

Recipient BMI > 25 (vs. 18.5–25) was associated with increased risk of EGL, as was donor BMI > 35. Grafts from older donors were more likely to be lost. Compared to donors aged 19–29 the odds ratio for EGL were 1.64 (95% CI 1.40–1.92), 2.30 (95% CI 1.94–2.72), and 2.90 (95% CI 2.20–3.84) for those aged 29–39, 39–49, and 50+ years, respectively ($p < 0.001$).
Conclusion: EGL after PTx has decreased since 1999. The improvement is most noticeable for PAK and PTA. Donor age and BMI remains a significant predictor for pancreatic EGL.

FG083 PROTOCOL DUODENAL GRAFT BIOPSIES AID PANCREAS GRAFT SURVEILLANCE

Jens G. Brockmann[1], Amir Butt[2], Hussa F. Al Hussaini[2], Hadeel AlMana [2], Khaled AlSaad[2], Moheeb Al-Awwami[2], Dieter C. Broering[2], Tariq Ali[2]
[1]Department of General, Visceral and Transplant Surgery, University Hospital Münster; [2]King Faisal Specialist Hospital and Research Centre, Riyadh

Background: Histological evaluation of the pancreas graft is usually done on demand resulting in significant delays. This analysis reports on endoscopic protocol duodenal graft biopsies at regular intervals to determine feasibility, safety and monitoring benefits.
Methods: Protocol duodenal graft biopsies in 27 18 consecutive pancreas transplants (10 simultaneous pancreas kidney [SPK], 17 pancreas after kidney [PAK]) with a follow-up of a minimum of 12 months were performed at days 14, 30, 90, 180, 360, 430. UPMC classification for intestinal rejection was used. C4d staining was performed when antibody mediated rejection was suspected.
Results: Overall patient and pancreas graft survival was 100% and 93% at a mean follow-up of 2.8 years. 167 endoscopic biopsy procedures were performed in 27 grafts without any complication. Biopsies revealed rejection in 3 (30%) SPK recipients and in 15 (82%) of PAK recipients as early as 14 days post-transplant. Two patients underwent PAK re-transplantation diagnosed with acute rejection at day 180. All except one recipient being treated for rejection, showed histological improvement following anti-rejection treatment. Following transient treatment success, a total of 3 pancreas grafts were lost for immunological reason. One loss was immediate despite anti-rejection treatment, one secondary to non-resolving rejection at 7 months and the third due to recurrent rejection 15 months post-transplantation. Additionally, biopsies detected vascular (venous thrombosis) and over-immunosuppression (CMV infection) complications.
Conclusions: Protocol graft duodenal biopsies detect complications following whole organ pancreas transplantation, are useful in guiding therapy and carry potential for improving outcome.

FG15 – FOCUS GROUP 15 SURGICAL TECHNIQUE KIDNEY

FG084 ROBOTIC ASSISTED KIDNEY TRANSPLANTATION IN OBESE RECIPIENTS COMPARED TO NON-OBESE RECIPIENTS: THE EUROPEAN EXPERIENCE

Thomas Prudhomme[1], Jean Baptiste Beauval[1], Marine Lesourd[1], Mathieu Roumiguié[1], Karel Decaestecker[2], Giampaolo Siena[3], Sergio Serni[3], Angelo Territo[4], Luis Gausa[4], Volkan Tugcu[5], Selcuk Sahin[5], Antonio Alcaraz[6], Mireia Musquera[6], Michael Stockle[7], Martin Janssen[7], Paolo Fornara[8], Nasreldin Mohammed[8], Nassim Kamar[9], Federico Sallusto[1], Alberto Breda[4], Nicolas Doumerc[1]
[1]Department of Urology and Kidney Transplantation, University Hospital of Rangueil, Toulouse, France; [2]Department of Urology, Ghent University Hospital, Ghent, Belgium; [3]Department of Urology, University of Florence, Careggi Hospital, Florence, Italy; [4]Department of Urology, Fundaciò Puigvert, Autonoma University of Barcelona, Barcelona, Spain; [5]Department of Urology, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey; [6]Department of Urology, Hospital Clinic, Barcelona, Spain; [7]Department of Urology, University Saarland, Homburg/Saar, Germany; [8]Department of Urology, University Hospital Halle (Saale), Halle, Germany; [9]Department of Nephrology and Organ Transplantation, University Hospital of Rangueil, Toulouse

Introduction and Objectives: Kidney transplantation (KT) in obese patients (body mass index – BMI > 30 kg/m^2) presents several challenges, related to the access to the external iliac vessels and the increased risk of surgical site infection. We present the results from the European Robotic Urological Section (ERUS) group, with the objective of evaluate perioperative and early postoperative surgical outcomes of RAKT in obese versus non-obese recipients
Methods: An ERUS group was created in March 2016 with the aim to collect common prospective data on RAKT from living donor performed at 8 different European Centers. Functional outcomes, surgical data, intra- and post-operative complications were compared between obese (BMI ≥ 30 kg/m^2) and non-obese (BMI < 30 kg/m^2) recipients.
Results: A total of 169 RAKTs from living donor were performed from 1th July 2015 to September 30th 2018. 32 patients had BMI > 30.

Operative time was statistically shorter in ≥30 BMI group (214.5 ± 12.6 vs. 282.3 ± 8 min in ≥30 BMI and <30 BMI groups respectively, $p < 0.0001$). There were no major intraoperative complications in both study groups. Serum creatinine values at POD 1, 3 and 7 showed no significant differences between the study groups. Concerning postoperative complications, pulmonary embolism was statistically more frequent in obese recipients. Others postoperative complications were equivalent in both groups. At univariate analysis, age, BMI, BMI > 30 kg/m^2 patient rate and grafts arteries numbers were significant predictor of suboptimal renal function on POD 30. Only the number of arteries was an independent predictive factor of suboptimal renal function (eGFR <45 ml/min/1.73 m^2), on POD 30, in multivariate analysis.
Conclusion: In obese population, RAKT provides excellent graft function and similar intra- and post-operative complication rate compared to the conventional open technique.

FG085 EN BLOC KIDNEY TRANSPLANT FROM INFANT DONORS WEIGHING LESS THAN 2.5 KG

Zhendi Wang[1], Qiuxiang Xia[1], Heng Li[1], Jian Liu[1], Jiali Liu[1], Jing Liu[1]
[1]Huazhong Science and Technology University, Union Hospital

Background: To explore the feasibility of en bloc kidney transplantation from infant donors less than 2.5 kg.
Methods: A retrospective analysis was conducted of 6 recipients of en bloc kidney transplant from cardiac death infant donors less than 2.5 kg between October 2015 and January 2019 in our center. Demographic characteristics of donors and recipients, graft and patient outcomes, and complications were analyzed with a follow up of 1–40 months.
Results: Among 6 infant donors, the age ranged from 6 to 31 days with body weight ranging from 1.3 kg to 2.3 kg. Recipients' age ranged from 23 to 47 years with body weight ranging from 39 to 52 kg. The graft and patient survival rate were 83.3% and 100% respectively during the follow up. All 6 cases were free of surgical complications including hemorrhage, renal artery/vein thrombosis/stenosis and urinary complications. 1 paired renal grafts lose function with normal perfusion detected under ultrasound. 1 recipient had satisfactory serum creatinine decline within follow up of only 1 month, and the remaining 4 recipients had normal serum creatinine level within follow up of at least 7 months. Among the 4 cases with follow up more than 7 months, all suffered from asymptomatic microscopic hematuria, but no proteinuria. Compared with transplant cases from donors weighing more than 2.5 kg in our center, the 5 pairs of working grafts in this study had significant higher serum creatinine level at 1 month after transplant.
Conclusion: Our results showed that en bloc kidney transplant from infant donors less than 2.5 kg had slower recovery of renal function, but still have promising outcomes. Improving surgical techniques and careful postoperative care make it possible for using donors with very low body weight, however information including long term outcome should be needed in the future.

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FG086 OBESITY DOES NOT AFFECT EARLY POSTOPERATIVE COMPLICATIONS OF KIDNEY TRANSPLANTATION

Karola Warzyszyńska[1], Edyta Karpeta[2], Agata Ostaszewska[1], Maciej Kosieradzki[1]

[1]Department of General and Transplant Surgery, Infant Jesus Teaching Hospital, Warsaw; [2]Department of Surgical and Transplantation Nursing and Extracorporeal Therapies of Warsaw, Medical University of Warsaw

Background: Kidney transplant recipients often have significant comorbidities, which increase perioperative risk and significantly affect transplantation results. Obese patients with BMI $\geq$ 30 kg/m^2 are at risk of delayed graft function and surgical complications, such as infections or delayed wound healing. There is also a trend to exclude extremely obese patients from transplantation (KTx). On the other hand, no association between obesity and either graft loss or death was noted.

The aim of the study is to evaluate the effect of BMI on the most common surgical complications after KTx.

Methods/Materials: We conducted an observational study on 872 patients transplanted in years 2010–2017. Median BMI was 24.4 kg/m^2 (13.9–34.3); 8.3% of the study group were obese (BMI $\geq$ 30 kg/m^2) and 4.2% had underweight (<18.5 kg/m^2). Patient records were searched for early surgical complications: lymphocele more than 7 days following transplantation, hematoma adjacent to transplant (at least 33 ml) more than 7 days following transplantation, urinary leakage or urinary tract infection [UTI].

An effect of BMI on these complications was assessed with multiple regression, logistic regression and chi-square test. p-value <0.05 was considered as statistically significant.

Results: Surgical complications occurred in 460 (52.8%) patients. Lymphocele was observed in 143 (16.4%; $p = 0.86$) patients, hematoma in 168 (19.3%; $p = 0.27$) patients, urinary leakage in 39 (4.5%; $p = 0.28$) patients and UTI in 287 (32.9%; $p = 0.82$) patients. No correlation between BMI and surgical complication rate was noted.

	Non-obese, % (n = 800)	Obesity, % (n = 72)	p	OR (95% CI)
Lymphocoele	16.5 (132)	15.3 (11)	0.86	0.94 (0.48–1.84)
Hematoma	19 (152)	22.2 (16)	0.50	1.23 (0.68–2.2)
Urinary leakage	4.8 (38)	1.4 (1)	0.22	0.28 (0.04–2.14)
UTI	33 (264)	31.9 (23)	0.99	1 (0.6–1.7)

Conclusions: Recipient's BMI has no influence on the most common surgical complications after KTx. There is no need to delay KTx in moderately.

FG087 A NEW INNOVATIVE MODEL OF EXPERIMENTAL PORCINE KIDNEY AUTOTRANSPLANTATION THROUGH TOTALLY EXTRAPERITONEAL APPROACH

Michail Mitsis, Vasileios Tatsis

Department of Surgery and Transplant Unit, University Hospital of Ioannina, Ioannina

Background: Porcine models of experimental kidney autotransplantation have been widely used, so far. Although, many technical variations have been described, all of them show several drawbacks (e.g. ileus, laparotomy etc).

In our study, we describe a novel, innovative model through totally extraperitoneal approach. This model combines all the advantages of the previous ones, while simultaneously it avoids their severe technical problems.

Methods/Materials: 8 large pigs were used to record advantages and drawbacks of the already described models.

Then, we tested our new model in 7 large animals (weighted 65–75 kg). The main surgical steps were as follows: 1. Left nephrectomy through a flank incision, 2. Graft preservation for 17 h with a combination of Hypothermic Machine Perfusion (4 h) and simple cold storage (1 h), 3. Right nephrectomy through a pararectus incision, 4. End to end arterial and venous anastomoses of the graft vessels to the right renal vessels after their appropriate figuration, if necessary, 5. End to end anastomosis of the graft ureter to the transected native right ureter, 6. Stabilization of the kidney graft by suturing the peritoneum to the right lateral abdominal wall.

The animals were monitored for 14 days. Biochemical parameters (Urea and Creat serum concentrations) of their graft function were calculated daily.

Results: All the animals survived the experiment. Urea and Creat consecrations were significantly increased during the first 8 postoperative days compared to the preoperative concentrations ($p \leq 0.002$). From 9th post-op day until the end of the follow-up period (14th post-op day) both were compared to the preoperative values.

Conclusion: This innovative model does not demand a long learning curve and it is easily replicated with excellent results. It avoids laparotomy for graft retrieval and implantation and its consequences. Thus, we believe that the above described technique represents a novel and very promising model.

FG088 SPEEDING ALLOWED: SHORT ANASTOMOSIS TIME IS ASSOCIATED WITH A LOWER INCIDENCE OF DGF IN DCD RENAL TRANSPLANTS

Natalie Vallant[1], Sami Dost[2], Basir Kunduzi[2], Kostas Stamatis[2], Benedict Phillips[2], Christopher Callaghan[2], Jonathon Olsburgh[2], Nicos Kessaris[2], Ioannis Loukopoulus[2], Ioannis Loukopoulus[2], Nikolaos Karydis[2]

[1]Guy's and St Thomas NHS Foundation Trust; [2]Guy's Hospital, London

Introduction: Delayed graft function (DGF) in renal transplantation prolongs hospital stay and leads to higher rejection and graft failure rates. Increasing use of marginal organs is expected to result in higher DGF rates. DCD kidneys are more commonly affected than DBD kidneys. Previous reports suggested anastomotic time (AT) as a risk factor for DGF in DBD kidneys. We explored the role of AT in DGF for both DBD and DCD kidney transplants in our centre over the last decade.

Methods: Our analysis included 579 deceased donor kidney transplants (352 DBD, 227 DCD) performed between 2007 and 2016. Recipients were older than 18 years of age, dependent on dialysis at the time, and receiving their first single kidney transplant. Primary non-function cases were excluded.

Results: The DGF rate was significantly higher in DCD compared to DBD transplants (50.2% vs. 26.9%, $p < 0.0001$). The static cold storage time was similar between both groups (834.9 $\pm$ 286.1 vs. 823.1 $\pm$ 296.9 min, $p = 0.65$). AT was significantly higher in the DGF group (42.2 $\pm$ 14.8 vs. 38.9 $\pm$ 10.6 min, $p = 0.0057$) and a mutlivariate regression analysis highlighted AT and DCD donor type as independent risk factors for DGF ($p < 0.0001$) (OR 1.02 and 2.9, respectively). Interestingly, a subgroup analysis showed that, in DBD transplants, the incidence of DGF was not associated with donor age, recipient age, or AT in the multivariate model ($p = 0.13$; 0.18; 0.27, respectively). In DCD transplants, AT remained a strong independent predictor of DGF in the multivariate analysis (OR 1.03, $p = 0.0071$), unlike donor ($p = 0.20$) and recipient age ($p = 0.73$). Overall, donor and recipient age were significantly higher in the DGF group (54.0 $\pm$ 14.0 vs. 49.4 $\pm$ 15.6 and 53.2 $\pm$ 11.6 vs. 49.6 $\pm$ 12.8; $p = 0.0003$ and $p = 0.0007$, respectively).

Discussion: Our data suggests that DGF in deceased donor kidneys is influenced by different factors, depending on the donor type. In DCD kidneys, a shorter anastomotic time may reduce the incidence of DGF.

FG089 PRELIMINARY RESULTS OF LAPAROSCOPIC SURGERY IN TREATMENT OF URETERAL STRICTURE AFTER KIDNEY TRANSPLANTATATION

Igor Miloserdov[1], Rafael Biktimirov[2], Dzhabrail Saidulaev[1], Vasiliy Bogdanov[1], Sergey Gautier[1]

[1]Shumakovs V. I. National Medical Research Center of Transplantology and Artificial Organs; [2]Federal Clinical Center of High-tech Medical Care, Clinical Hospital #119

Background: Urological complications are frequent technical adverse event following renal transplantation. The most frequent urological complication is ureteral stenosis. Laparoscopic ureteral reconstructive surgery is routinely performed, because it demonstrated efficacy, safety and low frequency of recurrence.

Objective: To evaluate results of laparoscopic ureteroplastic in patients with ureteral stenosis after kidney transplantation.

Methods: Clinical trial of patients who underwent laparoscopic ureteroplastic after kidney transplantation from 2017 to 2018. All the patients had ureteral stenosis.

Results: 7 patients aged from 34 to 57 (median = 48 years). 3 patients with ureterovesical anastomosis stenosis underwent Lich-Gregoire laparoscopic ureteral reimplantations, median operation time was 250 min (230–310). 3 patients with extensive ureteral stenosis in the middle segment of ureter underwent nephrectomy with ureter-ureter anastomosis, median operation time was 280 min (245–330). 1 patient that had stenosis between pelvis renalis and ureter underwent non-amputational pyeloureterplastic, operation time was 305 min. In all 7 cases ureteral stents were used. Median blood loss was 150 ml (100–300), median time of intensive care unit treatment was 18 h. Median postoperative hospital stay was 7 days (5–10). Within 6 month of observation no complication or recurrence of stenosis were discovered.

Conclusion: Laparoscopic ureteroplastic is a safe and effective treatment for ureteral stricture after renal transplantation. In case of ureterovesical anastomosis stenosis Lich-Gregoire laparoscopic ureteral reimplantation is recommended, in case of extensive ureteral stenosis nephrectomy with ureter-ureter anastomosis is recommended and in case of stenosis in upper segment of ureter non-amputational pyeloureterplastic is recommended.

FG16 – CANCER AND LIVER TRANSPLANTATION

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FG090 IMPROVED OUTCOMES OF LIVE DONOR LIVER TRANSPLANTATION COMPARED TO RADIOFREQUENCY ABLATION FOR HEPATOCELLULAR CARCINOMA LESS THAN 3 CM: AN INTENTION-TO-TREAT AND PROPENSITY SCORE MATCHING ANALYSIS

Phillipe Abreu, Andre Gorgen, Hala Muaddi, Walter Nelson, Adam Doyle, Robert Beecroft, John Kachura, Bettina Hansen, Anand Ghanekar, Les Lilly, Mark Cattral, Zita Galvin, Markus Selzner, Mamatha Bhat, Nazia Selzner, Ian McGilvray, Paul D. Greig, David R. Grant, Gonzalo Sapisochin
University of Toronto

Background: Radiofrequency ablation (RFA) and liver transplantation (LT) are considered curative therapies for small single hepatocellular carcinoma (HCC). We aimed to compare the long-term outcomes of patients treated with RFA with those that received a live donor liver transplant (LDLT) as their first treatment.
Methods: Patients with single HCC ?3 cm treated between 2000 and 2017 were included in an intention-to-treat analysis (ITT). Patients were divided according to the initial treatment intended: RFA or LDLT. Study outcomes were overall survival (OS) and disease-free survival (DFS). Outcomes were assessed by the Kaplan-Meier method and compared using the log-rank test. Multivariable Cox regression was applied to account for a priori selected clinical confounders. A propensity score matching was performed to reduce potential selection bias by equating groups based on initial MELD score and Child-Pugh-Turcotte (CPT) classification.
Results: We included 340 patients: 296 (87.10%) patients underwent RFA with curative intent and 44 (12.90%) patients were listed for LDLT. Median follow up time was 3.68 (IQR 2.21–5.96) years. At baseline, differences were observed in MELD [8.18 (IQR 6.86–10.10) vs. 12.00 (IQR 9.00–13.75), $p < 0.001$], CPT ($p < 0.001$) and etiology of liver disease ($p < 0.001$) at time of diagnosis. After a multivariable regression, the hazard ratio for HCC recurrence was 0.11 (95% CI 0.04–0.33) for LDLT over RFA. The propensity matched cohort was composed of 18 RFA and 18 LDLT patients.

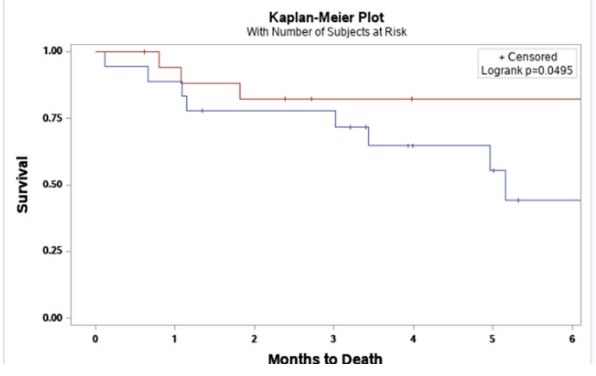
The median follow up time was 3.98 (IQR 1.95–8.81) years. The actuarial 1-, 3- and 5-year OS was 88.9%, 77.4%, 54.3% for RFA and 94.3%, 82.5%, 82.5% for LDLT ($p = 0.04$), while the 1-, 3- and 5-year DFS was 50%, 17%, 17% for RFA and 88.6%, 88.7%, 82.7% for LDLT, $p < 0.001$.
Conclusion: This study suggests that LDLT may be a better treatment option for patients with single HCC ?3 cm. LDLT should be considered and offered as a treatment modality to patients if available.

Table 1: Patient Characteristics before and after propensity score matching

	Before Propensity Score Matching					After Propensity Score Matching				
Variable	Total n=340	RFA ITT n=296	LDLT ITT n=44	p	d	Total n=36	RFA ITT n=18	LDLT ITT n=18	p	d
Sex, male (%)	250 (73.5)	217 (73.3)	33 (75.0)	0.81	0.03	24 (66.70)	12 (66.70)	12 (66.70)	1.00	0
Age, year median (IQR)	59.00 (53.00-64.00)	59.00 (53.00-64.00)	58.00 (52.00-62.00)	0.32	0.13	59.00 (53.25-64.00)	59.50 (55.75-64.25)	58.00 (52.75-63.00)	0.26	0.34
Child-Pugh, number (%)				<0.001	2.70				1.00	0
A	260 (76.50)	256 (86.50)	4 (9.10)			8 (22.20)	4 (22.20)	4 (22.20)		
B	54 (15.90)	40 (13.50)	14 (31.80)			28 (77.80)	14 (77.80)	14 (77.80)		
C	26 (7.60)	-	26 (59.10)							
MELD, median score (IQR)	8.47 (6.97-10.84)	8.18 (6.86-10.10)	12.00 (9.00-13.75)	<0.001	0.95	12.00 (11.00-12.60)	12.34 (11.09-14.33)	11.89 (9.75-13.00)	0.14	0.40
Etiology, number (%)				<0.001	0.96				0.72	0.49
HCV	163 (47.90)	131 (44.30)	32 (72.70)			21 (58.30)	10 (55.60)	11 (61.10)		
HBV	106 (31.20)	105 (35.50)	1 (2.30)			4 (11.10)	3 (16.70)	1 (5.60)		
ETOH	29 (8.50)	24 (8.10)	5 (11.40)			6 (16.70)	2 (11.10)	4 (22.20)		
NASH	20 (5.90)	18 (6.10)	2 (4.50)			3 (8.30)	2 (11.10)	1 (5.60)		
Other	22 (6.50)	18 (6.10)	4 (9.10)			2 (5.60)	1 (5.60)	1 (5.60)		
Tumour median size, cm (IQR)	2 (1.50-2.50)	2 (1.60-2.47)	1.60 (1.42-2.50)	0.12	0.21	1.90 (1.32-2.57)	2.10 (1.37-2.52)	1.75 (1.27-2.72)	0.78	0.07
AFP, number (%)				0.10	0.51				0.34	0.64
<20	205 (60.30)	181 (61.10)	24 (54.50)			21 (60.00)	10 (58.80)	11 (61.10)		
20-99	64 (18.80)	54 (18.20)	10 (22.70)			8 (22.90)	5 (29.40)	3 (16.70)		
100-999	35 (10.30)	27 (9.10)	8 (18.20)			5 (14.30)	1 (5.90)	4 (22.20)		
>1000	11 (3.20)	9 (3.00)	2 (4.50)			1 (2.90)	1 (5.90)	-		
Tumor differentiation, number (%)				0.80	0.15				0.33	0.62
Well	42 (12.30)	37 (12.50)	5 (11.40)			5 (20.00)	3 (25.00)	2 (15.40)		
Mod	148 (43.40)	131 (44.30)	17 (38.60)			18 (72.00)	9 (75.00)	9 (69.20)		
Poor	10 (2.90)	8 (2.70)	2 (4.50)			2 (8.00)	-	2 (15.40)		
Microvascular invasion, yes (%)	32 (9.40)	30 (10.20)	2 (4.50)	0.42	0.15	2 (5.60)	1 (5.60)	1 (5.60)	1.00	0

Table 1. Patient characteristics before and after propensity score matching. Categorical data are presented as absolute numbers with percentages while continuous variables are presented as median with IQR. p-values and absolute standardized mean difference (d) were calculated for variables of interest. RFA: radiofrequency ablation, LDLT: living donor liver transplantation, ITT: intention to treat, IQR: inter-quartile range, MELD: model for end-stage liver disease, HCV: hepatitis C, HBV: hepatitis B, ETOH: alcoholic, NASH: non-alcoholic steato-hepatitis, AFP: alfa-feto-protein.

Figure 1: Overall survival by groups
Years (Median), IQR
LDLT: 7.99 (2.40-10.80)
RFA: 3.70 (1.40-5.20)
p=0.04



FG091 SINGLE HEPATOCELLULAR CARCINOMA <50 MM ON CIRRHOTIC LIVER: RESECTION, RADIOFREQUENCY OR LIVER TRANSPLANTATION A SINGLE CENTER INTENTION TO TREAT ANALYSIS

Brice Ngaessi[1], Julie Navez[1], Desislava Germanova[1], Gontran Verset[1], Thierry Gustot[1], Vincent Donckier[2], Valerio Lucidi[1]
[1]Erasme University Hospital ULB; [2]Institut Jules Bordet

Background: Hepatocellular carcinoma (HCC) on cirrhosis may be treated with curative intent by liver resection (LR), radiofrequency (RF) or liver transplantation (LT). The choice of treatment depends on many variables but LT has the best oncological outcomes by treating simultaneously the underlying cirrhosis. This difference is less evident regarding early stage HCC. We aimed to compare long-term outcomes of early stage HCC according to the surgical treatment on an intention to treat analysis (ITT).
Methods: All patients undergoing surgical treatment for HCC on cirrhosis were retrospectively reviewed from a prospectively maintained database. An ITT analysis of patients with a single nodule ≤50 mm listed for LT or undergoing LR or RF, was performed.
Results: Between 2007 and 2018, 377 patients were surgically treated for HCC on cirrhosis, including 222 with a single nodule ≤50 mm. Among these patients, 78 were listed for LT, 66 underwent LR and 78 RF. LR and RF groups had more compensated cirrhosis and were older compared to LT group ($p < 0.001$). The 90-day postoperative mortality was similar between groups. Seven LT patients were removed from the waiting list because of tumor progression or non-compliance. Fourteen LR or RF patients were listed for LT after HCC recurrence, and 12 underwent salvage LT. On ITT progression-free survival at 1-, 3- and 5-year was higher in LT (93%/87%/79%) than LR (84%/49%/29%) or RF (72%/41%/23%) groups ($p < 0.001$). One and 3-year overall survivals (OS) were similar in RF, LR and LT groups (96%/68%,87%/72% and 92%/81%, $p > 0.05$) whereas 5-year OS was higher following LT than LR/RF (74%/36%/47%, $p < 0.001$), respectively.
Conclusions: Early stage HCC on compensated cirrhosis can be safely treated by LR or RF as ITT-OS was similar to LT until 3 years. In these patients, salvage LT could be a good option in case of HCC recurrence instead of primary LT, to save liver grafts.

FG092 AN INTENTION-TO-TREAT COMPETING-RISK MODEL FOR CANDIDATES WITH HEPATOCELLULAR CANCER AWAITING LIVER TRANSPLANTATION

Quirino Lai[1], Alessandro Cucchetti[2], Umberto Cillo[3], Karim Halazun[4], Samuele Iesari[5], Armin Finkenstedt[6], Arvinder Singh Soin[7], Massimo Rossi[8], Chung Mau Lo[9], Shinji Uemoto[10], Chao-Long Chen[11], Maria Hoppe-Lotichius[12], Yuji Soejima[13], Shu-Sen Zheng[14], Jan Lerut[5]
[1]Sapienza University of Rome; [2]Bologna; [3]Padua; [4]New York; [5]Brussels; [6]Innsbruck; [7]New Delhi; [8]Rome; [9]Hong Kong; [10]Kyoto; [11]Taiwan; [12]Mainz; [13]Fukuoka; [14]Hangzhou

Since the introduction of the Milan Criteria (MC), all systems focused on post-transplant prognosis of patients with hepatocellular cancer (HCC) are exclusively based on characteristics available at surgery, and neglect the intention-to-treat (ITT) principles. This study, based on a large international cohort, aimed to develop comprehensive ITT models through a competing-risk analysis. We used data available at first referral to predict the risk of delisting and HCC-related death after liver transplant (LT).

Twelve centres in the United States, Europe and Asia created a Derivation ($n = 2,318$) and an external Validation Set ($n = 773$) of HCC patients listed for LT between January 2000–March 2017. The study was registered at http://www.ClinicalTrials.gov (ID:NCT03595345).

In the Derivation Set, the competing-risk analysis identified three independent covariates predicting delisting (Model#1): age (SHR = 1.049; $p = 0.001$), MELD (SHR = 1.033; $p = 0.002$) and living donation availability (SHR = 0.422; p-value = 0.001). The risk of post-transplant HCC-related death (Model#2) was predicted by the combination of Metroticket2.0 (SHR = 1.724; $p = 0.001$) and MELD (SHR = 0.970; $p = 0.045$), both at first referral. In the external validation, both the Models exhibited the highest diagnostic performances (c-statistic = 63.3% and 67.7%, respectively). The identified upper limit of post-transplant HCC-related death was 13%, corresponding to the different combinations of alpha-fetoprotein (AFP) and morphological indicators: AFP ≤ 20 ng/ml and up-to-twelve as sum of diameter/number of lesions; AFP = 21–200 and up-to-ten; AFP = 201–500 and up-to-seven; AFP = 501–1,000 and up-to-five.

This study presents a scoring system based on a large international cohort of HCC patients awaiting LT. A freely accessible web calculator has been created to estimate the individual risks of delisting and HCC-related death after LT. Furthermore, a risk "recalculation" after neo-adjuvant treatments can improve patient selection and indications.

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FG093 PROGNOSIS AFTER TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA IN CIRRHOTIC VERSUS NON-CIRRHOTIC LIVERS USING PROPENSITY SCORE CALIBRATION TO ADJUST FOR UNMEASURED CONFOUNDING: A STUDY FROM THE EUROPEAN LIVER TRANSPLANT REGISTRY

Hans-Christian Pommergaard[1], Andreas Arendtsen Rostved[1], René Adam[2], Allan Rasmussen[1], Mauro Salizzoni[3], Miguel Angel Gómez Bravo[4], Daniel Cherqui[2], Paolo De Simone[5], Pauline Houssel-Debry[6], Vincenzo Mazzaferro[7], Olivier Soubrane[8], Juan Carlos García-Valdecasas[9], Joan Fabregat Prous[10], Antonio D. Pinna[11], John O'Grady[12], Vincent Karam[2], Christophe Duvoux[13], Lau Caspar Thygesen[14]

[1]Department of Surgery and Transplantation Rigshospitalet; [2]Department of Hepatobiliary Surgery, Cancer and Transplantation, AP-HP, Hôpital Universitaire Paul Brousse, Inserm U 935, Univ P; [3]Liver Transplant Center and General Surgery, A.O.U. Città della Salute e della Scienza di Torino, Molinette Hospital, Turin, Italy; [4]Department of Surgery – Liver Transplant Unit, Hospital Virgen del Rocio, Sevilla, Spain; [5]Hepatobiliary Surgery and Liver Transplantation Unit, University of Pisa Medical School Hospital, Pisa, Italy; [6]Service de Chirurgie Hépatobiliaire et Digestive, Hôpital Pontchaillou, Centre Hospitalier Université de Rennes 1, Rennes, France; [7]University of Milan and Division of Gastrointestinal Surgery and Liver Transplantataion, Istituto Nazionale Tumori, Fondazione I; [8]Department of HPB Surgery and Liver Transplant, Beaujon Hospital, Clichy, University Denis Diderot, Paris, France; [9]Hepatobiliopancreatic & Transplant Surgery, ICMDiM, Hospital Clínic, Barcelona, Spain; [10]Unitat de Cirurgia Hepato-bilio-pancreàtica, Hospital Universitari de Bellvitge, Barcelona, Spain; [11]General Surgery and Transplant Division, S. Orsola Hospital, University of Bologna, Bologna, Italy; [12]Institute of Liver Studies, King's College Hospital, London, UK; [13]Department of Hepatology and Liver Transplant Unit Henri Mondor Hospital, Paris Est University (UPEC), Créteil, France; [14]National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

Background: Prognosis differ between hepatocellular carcinoma (HCC) arising in cirrhotic and non-cirrhotic livers. Whether this results from tumor stage upon diagnosis or two separate tumor biologies is poorly understood. The aim was to investigate survival and HCC-specific survival after liver transplantation between patients with HCC in cirrhotic and non-cirrhotic livers.
Methods: We included patients registered in the European Liver Transplant Registry (ELTR) database transplanted due to HCC 1990-November 2016. We compared overall and HCC-specific mortality between cirrhotic and non-cirrhotic patients using propensity score (PS) calibration of Cox regression estimates to adjust for unmeasured confounding.
Results: We included 22,787 patients, of whom 21,995 (96.5%) had cirrhosis. Median survival was 10.7 years (65.5% five-year survival) for cirrhotic patients and 6.8 years (56.4% five-year survival) for non-cirrhotic patients. In the unadjusted analysis, non-cirrhotic patients had an increased risk of overall mortality with a hazard ratio (HR) of 1.37 (95% CI: 1.23–1.52). However, the HR approached unity with increasing adjustment and was 1.11 (0.99–1.25) when adjusted for unmeasured confounding. In unadjusted analysis, non-cirrhotic patients had an increased risk of HCC-specific mortality with a HR of 2.62 (2.21–3.12). After adjustment for unmeasured confound, the risk decreased but remained significantly increased (HR 1.62, 1.31–2.00).
Conclusion: Using PS-calibration to account for unmeasured confounding in the ELTR database, we show that HCC in non-cirrhotic livers have similar overall mortality, but higher HCC-specific mortality. This may be a results of a more aggressive cancer form in the non-cirrhotic liver. Thus, differences in HCC-specific mortality could not be explained by tumor characteristics and other prognostic variables.

FG094 IMPROVED SURVIVAL AFTER LIVER TRANSPLANTATION IN COLORECTALCANCER PATIENTS WITH LOW LIVER UPTAKE ON PET EXAMINATION

Svein Dueland[1], Harald Grut[2], Morten Hagness[2], Pål-Dag Line[2]

[1]Oslo University Hospital Rikshospitalet; [2]Oslo University Hospital

Background: Colorectal cancer (CRC) patients with non-resectable liver only metastases receiving liver transplantation (LT) have Kaplan-Meier estimated 5 years overall survival (OS) of about 60%, compared to less than 10% in a similar cohort of patients starting first line chemotherapy. To be able to establish LT as a treatment option in selected CRC with non-resectable liver only metastases it is important to be able to select patients with 5-year OS comparable to patients with hepatocellular carcinoma having LT.
Methods: All included CRC patients had a PET-scan to exclude extra hepatic disease at time of LT. The PET-uptake values in liver representing total tumor liver activity were determined. Patients were divided into two groups with activity with more than and less than liver metabolic tumor volume (MTV) of 70 cm^3. All patients with MTV > 70 were observed until death and median follow-up of patients alive having MTV < 70 was 85 months.
Results: Patients having MTV < 70 had a 5- year OS survival of 78% compared to 22% in patients with MTV > 70 ($p = 0.001$). Patients with MTV < 70 also had significant increased disease-free survival (DFS) median 23.0 months compared to 3.5 months ($p = 0.000$) as well as increased survival after time of relapse (median not reached vs. 23.2 months, $p = 0.014$) compared to patients with MTV > 70. Patients with MTV < 70 had significant lower number of liver metastases, smaller largest liver lesion, CEA levels and Fong Clinical Risk Score at time of LT.
Conclusion: Total liver uptake values determined by PET/CT scans may be used to select CRC with liver only metastases that will obtain long OS after LT. CRC patients with high MTV-values determined by pre-transplant PET-CT scan should be excluded from LT.

FG095 ROLE OF GENDER AND AGE OF LIVER DONOR IN DE NOVO NEOPLASMS OCCURRENCE AFTER LIVER TRANSPLANTATION

Sarah Shalaby[1], Martina Taborelli[2], Alberto Zanetto[1], Alberto Ferrarese[1], Chiara Becchetti[1], Salvatore Stefano Sciarrone[1], Monica Pellone[1], Francesca D'Arcangelo[1], Martina Gambato[1], Giacomo Germani[1], Marco Senzolo[1], Francesco Paolo Russo[1], Patrizia Boccagni[3], Giacomo Zanus[3], Umberto Cillo[3], Pierluca Piselli[4], Diego Serraino[2], Patrizia Burra[1], Immunosoppressione e Tumori, For Gruppo di Studio[5]

[1]Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital; [2]Cancer Epidemiology Unit, CRO National Cancer Institute, IRCCS; [3]Hepatobiliary Surgery and Liver Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital; [4]Department of Epidemiology, National Institute for Infectious Diseases L. Spallanzani; [5]Italian Transplant and Cancer Cohort Study

Background: De novo neoplasms(DNN) are one of the major causes of late-mortality after liver transplantation(LT). Current post-transplant surveillance strategies are largely based on general population guidelines but should be customized in the light of LT-recipients specific risk factors. The influence of donor-recipient sex and age matching on long-term survival after LT is controversial, and data on the possible effect on DNN-risk are lacking.
Material & Methods: All patients transplanted among 9 Italian centres between 1985 and 2014 were enrolled (excluded if: ≤18 years-old, follow-up shorter than 90 days or cancer diagnosis within 90 days after LT). Competing risk approach was applied to estimate 5-year cumulative cancer incidence by time since LT. Hazard-ratios for DNN and 95% CIs were obtained using Cox-models adjusted for recipient gender, age and calendar-year at transplant, and liver disease etiology.
Results: A total of 1,927 patients were enrolled. Cumulative DNN-incidence at 5 years after LT was 5.4%, with no differences when stratified by donor gender ($p = 0.45$). Considering both donor gender and age, among male-patients receiving a graft from a male-donor, the 5-year cumulative incidence was higher when donor was ≥60 years-old ($p = 0.03$). At multivariate-analysis, donor age or gender were not associated with DNN-risk. However, considering their joint effect, at elevated donor age (≥60 years), the DNN-risk increased for recipients from male-donors (HR = 2.00). When the associations were examined in strata of recipient-gender, a similar pattern emerged among male only (HR = 2.26) for those receiving an organ from male-donors ≥60 vs. <35 years).
Conclusions: In our cohort the risk of DNN occurrence was increased in male-patients receiving a liver graft from older male-donors, irrespectively from recipient age at transplant. Gender and age differences in liver-donors could influence DNN risk due to both donors and recipients biologic and lifestyle factors.

FG17 – RECRUITMENT OF LIVING AND DECEASED DONORS

FG096 IMPLEMENTATION OF A SUSTAINABLE NORMOTHERMIC REGIONAL PERFUSION (NRP) CLINICAL SERVICE

Hunt Fiona, Ian Currie, Andrew Sutherland, John Terrace, Sorina Cornateanu, Sharlene Philp, Gabriel Oniscu

Edinburgh Transplant Centre, Edinburgh

Background: Normothermic Regional Perfusion (NRP) has shown encouraging clinical results. However, translation from an experimental to routine procedure poses several challenges. Herein we describe a model that led to the implementation of NRP into standard clinical practice within 12 months of development.

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Methods: A novel role of Practitioner in Novel Technologies was created to lead and coordinate the implementation of NRP. A four-step process (recruitment, education and training, implementation and review for evaluation) included all stakeholders involved in the donation and retrieval process. A week-long bespoke competency based training and education programme supported by practical hands-on sessions and a simulation circuit for troubleshooting was developed. Team de-brief was used to streamline of service delivery of the service.
Results: Using this approach we achieved a four-fold increase in trained surgical staff and a 6-fold increase in competent senior organ preservation practitioners in 12 months. This process has now been extended to include junior members of the team, scrub team and Specialist Nurse in Organ Donation (SNOD) to allow NRP to be performed in any donor hospital throughout the UK.

The combination of focused sessions allowed the staff to prepare for actual donor attendance. The competency-based training ensured clear accountability and safety whilst performing NRP tasks.

Within 12 months of development, the NRP rota cover increased from 76% in January 2018 to 93% in December 2018.
Conclusion: The introduction of NRP into clinical practicepresents significant challenges. Developing a specific role of Practitioner in Novel Technologies has been key to delivering a structured and methodical approach to education, training and service delivery. This approach could be used for the development of other novel technologies in transplantation.

FG097 GENERATION Z ARE WILLING TO BUY ORGANS. DOES THIS REQUIRE A DRAMATIC POLICY CHANGE?

Veena Surendrakumar[1], John Ayorinde[1], Mohammad Hossain[2]
[1]University of Cambridge; [2]Addenbrooke's Hospital

Background: The Declaration of Istanbul states that organ donation should be a financially neutral act, and although this is the accepted dogma of the transplant community, the opinions of the general population are not as clear. Generation Z, born after the mid-1990s, encompass those who will soon join the voting populace. Their opinions will shape future government policy. As such, we have started an educational programme engaging senior secondary school students in discussion regarding the key ethical dilemmas faced in organ transplantation.
Methods: An ethics and case-based interactive presentation was delivered to small groups of 16–18 year olds in various secondary schools in the south of England. Using both pre- and post-session questionnaires, qualitative data was collected on the attitudes surrounding important transplantation issues.
Results: A total of 143 students participated in the school sessions. Only 17% reported current registration on the UK Organ Donor Register, however a further 96 would consider signing up. All participants were happy to accept a donated organ if they required one, with 65% stating they would use social media to find an organ donor. 71% of students would consider buying an organ if necessary. Following the session, 55% reported a change in views, with many students expressing a better appreciation of the decision-making process in transplantation. In some cases, qualitative feedback specifically referred to discussions regarding the monetary procurement of organs, voicing opinions on the black market and organ trafficking.
Conclusion: Our programme has shown a willingness by this key demographic to attach a monetary value to organ donation. Given that these young adults may become the future policymakers of society, we ask whether it is now time to open the discussion on procuring organs under such circumstances.

FG098 PARTICIPATION OF COMPATIBLE KIDNEY DONOR-RECIPIENT PAIRS IN THE DUTCH KIDNEY EXCHANGE PROGRAM (KEP): EXPLORATION OF DECISION-MAKING

Marry de Klerk, Willij Zuidema, Emma Massey, Jacqueline van de Wetering
Erasmus MC

Introduction: Participation of compatible pairs in KEP would increase the chances for the incompatible pairs. For compatible pairs, too, it can offer advantages by e.g. finding a donor with a better HLA match. Which factors influence the decision of compatible pairs to participate in our voluntary (v) KEP? How do they experience the education about vKEP?
Methods: During June 2016–September 2017, all new recipients and donors who visit our outpatient clinic for the first time were informed orally and by means of a leaflet about vKEP. If during the next visit they were compatible, we discussed the willingness to participate in our vKEP and gave them a questionnaire.
Results: Of the 93 approached, 62 completed the questionnaire. 12 (6 pairs) intended to participate in vKEP and 50 did not. Among those who did not want to participate, common reasons were: "My kidney fits well with my recipient" (32/50), and "it doesn't feel good" (19/50). A longer waiting time (29/38) and that the donor would donate in another hospital (23/39) were seen as barriers. Among those who intended to participate in vKEP, the most important motivation was that it felt good (8/10), hope for a better kidney (7/10) and altruism (4/10). A longer waiting time (6/10) and that the donor would donate in another hospital (7/10) were seen as obstacles. In both groups, anonymity was not seen as a barrier (40/52), they were very satisfied with the verbal explanation (50/55) and the leaflet (45/53). There was little objection to being informed about vKEP (49/54). Ultimately 4 compatible pairs underwent transplantation which resulted in 11 transplants instead of 4.
Conclusion: The decision whether or not to participate as a compatible pair in our vKEP is based on emotions, logistical and medical factors. Donors and recipients were open to education about and consideration of this program. Insights into barriers and facilitators will be incorporated into our vKEP policy and processes.

FG099 INAPPROPRIATE DONOR IDENTIFCATION: AN AVOIDABLE PROBLEM?

Patrick Evrard[1], Daniel Jacobs-Tulleneers-Thevissen[2], Patrick Ferdinande[3], Diethard Monbaliu[3]
[1]CHU Namur, Université Catholique de Louvain; [2]Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel; [3]University Hospitals Leuven

Introduction: Controlled donation after circulatory death (cDCD) steadily increased during the last decades, now representing ~25% of all deceased donors in Belgium. However, premature or inadequate identification of cDCD may erode the donation after brain dead (DBD) donor pool. Some donors, initially referred as cDCD to Eurotransplant (ET) with planned withdrawal of life sustaining therapy (WLST) and scheduled for organ procurement, ultimately evolved towards brain death. The aim of this retrospective study was to analyze the incidence and possible reasons for such a "donor category switch" in Belgium.
Methods: All donor category switches between 1/1/2011 and 31/12/2016, as registered by ET, were reported to the Belgian organ procurement committee and data were collected through an inquiry to their respective transplant centers.
Results: Out of 1866 effective DBD and cDCD donors reported, there were 18 donor category switches from cDCD to DBD, representing 3.4% of all cDCD, or 0.9% of all deceased donors. All these 18 misidentified donors were under mechanical ventilation related to trauma (7/18), ischemia (4/18), bleeding (3/18), post-anoxemic (3/18) and cerebral edema (1/18). The mean interval between hospital admission and 1st ET (cDCD) referral was 3.2d (range 1–5.6 h), between first ET referral and brain dead diagnosis 7.2 h (range 1.16–12.4 h), and between brain dead diagnosis and 2nd ET referral (DBD) 1.15 h (range 0.9–1.5 h).
Conclusion: Donor category switch (cDCD → DBD) is rare but it confirms that the WLST decision may be taken too early and that not enough time is given to recognize an ongoing evolution of intracranial hypertension leading to brain death. Correct identification of a donor that will or will not evolve towards brain death is important because cDCD is still associated with inferior outcomes and with less organs transplanted per donor versus DBD.

FG100 IMPACT OF AN EDUCATIONAL INTERVENTION ON ORGAN DONATION AND TRANSPLANTATION ON HIGH SCHOOL STUDENTS' KNOWLEDGE AND INTENTION TO DECIDE TO DONATE OR NOT

Olivier Giannini[1], Ottavio Beretta[2], Martine Bouvier Gallacchi[2], Daniela Garzoni[3], Andreina Bocchi[4], Paolo Merlani[4]
[1]Department of Internal Medicine and Service of Nephrology, Ospedale Regionale di Mendrisio; [2]Health Promotion and Evaluation Office (SPVS), Department of Health and Social Welfare (DSS), Bellinzona; [3]Service of Nephrology, Ospedale Regionale di Mendrisio; [4]Department of Intensive Care Medicine, Ospedale Regionale di Lugano

Background: Switzerland has one of the lowest rate of organ donation. Insufficient knowledge and lack of decision-making are barriers to the intention to decide to donate or not. The aims of this study were to understand knowledge and beliefs of an high school student population concerning organ donation and transplantation (ODT), and to evaluate the impact that an educational intervention had on the students.
Methods: Independent sample pretest-posttest design, relying on the *Theory of Planned Behaviour* (TPB) model. High school students attended an intervention on ODT organized in 5-hour lecture sessions. They were asked to fill a 44-item online questionnaire 3 months before, at the end of and 6 months after the intervention day. These items were based on knowledge about ODT as well as outcome, normative and efficacy beliefs.
Results: 142 students (average age 18-years) attended the program. Before the intervention, students declared that they had little knowledge about ODT; 85.6% of them thought that they did not have enough information about how to obtain a donor card and only 6.7% had one. The percentage of students that did not have enough information decreased to 13.2% at the end of the intervention and to 4.8% after 6 months. The rate of students who had a donor card increased to 30.2% few days after the intervention and to 56.5% after 6 months. The TPB model allowed us to identify the beliefs contributing to the intention to decide to donate or not, the outcome belief being the most

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important predictor that showed a strong increase in attitude at the end of the intervention and even six months later.
Conclusions: The educational intervention increased students' knowledge and awareness about ODT, and showed an effective and long lasting impact on the intention to decide about donation. An educational intervention can induce an effect on the intention to decide to donate or not and should be considered as a useful approach to improve knowledge about ODT.

FG101 INELIGIBLE: ATTITUDES AND FOLLOW-UP OF INDIVIDUALS RULED OUT OF LIVING KIDNEY DONATION

Carrie Thiessen[1], Danielle Dobosz[1], Jacqueline Gannon[1], Sienna Li[1], Kristie Kennedy[2], Daniel Gray[3], Adam Mussell[3], Peter Reese[3], Elisa Gordon[2], Sanjay Kulkarni[1]
[1]Yale School of Medicine; [2]Northwestern University Feinberg School of Medicine; [3]Perelman School of Medicine, University of Pennsylvania

Background: Little is known about the experiences of individuals who begin living kidney donor (LKD) evaluation but are ineligible to donate.
Methods: We conducted a prospective, longitudinal study of potential LKDs at 3 centers. Exclusion reasons were obtained via EMR review. Participants were interviewed at evaluation, two weeks post-notification of non-eligibility, and 6 months later. We thematically coded the interviews to elucidate responses to being turned down as donors.
Results: 53 of 307 potential LKDs (17%) who began in-person evaluation were ineligible. Table 1 lists the reasons for ineligibility. 6 participants were excluded from further analysis: 3 did not understand they were ineligible and 3 did not complete at least one follow-up interview. 6% did not know why they were ineligible; another 15% had only partial understanding of the exclusion reason. 60% were disappointed with the decision. A minority (9%) felt "devastated," "guilty," or "worthless." 25% were not sure the center's decision was appropriate: 2 appealed, 2 debated re-evaluation elsewhere, 2 underwent evaluation at another center, and 1 donated at another center. 76% learned something new about their health. 36% sought follow-up care, 23% planned follow-up. 6% (including a participant with suspected renal cell carcinoma) did not obtain subsequent care due to financial concerns.
Conclusion: 17% of potential LKDs who began in-person evaluation were medically ineligible. Most appreciated the new health information but a minority experienced severe emotional distress after being declined. Transplant teams should contact ineligible donors to ensure their understanding, provide support, and offer referrals for further care.

Table 1: Reasons for being declined as a living kidney donor

	n (% all potential donors)
Renal calculi	9 (3%)
Low GFR	8 (3%)
Positive crossmatch	6 (2%)
Pre-diabetes	5 (2%)
Renal cell or urothelial cell carcinoma	4 (1%)
Hypertension	3 (1%)
Renal artery abnormalities	3 (1%)
Psychiatric issues	3 (1%)
Proteinuria	2 (0.6%)
Renal cysts	2 (0.6%)
Hematuria	2 (0.6%)
Concern about voluntariness	2 (0.6%)
Liver disease	2 (0.6%)
Atherosclerosis	2 (0.6%)
Obesity	2 (0.6%)
Other	14 (5%)

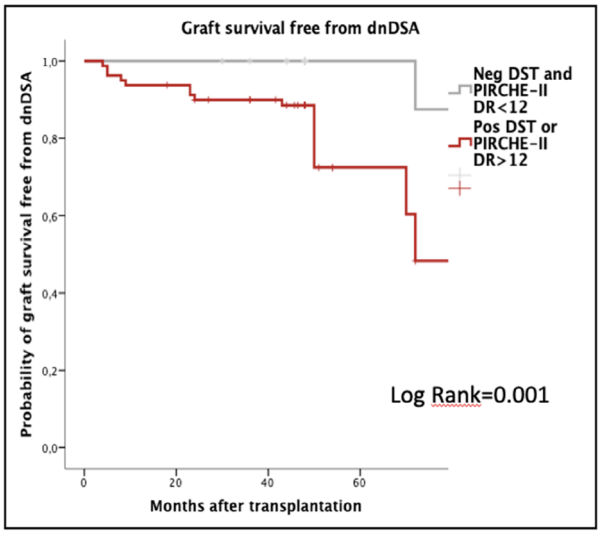
* When relevant, multiple reasons listed for a single participant

FG18 – HOW TO MAKE HLA MATCHING WORK?

FG102 DONOR-RECIPIENT HLA MISMATCHED PEPTIDES CALCULATED BY PIRCHE ALGORITHM ASSOCIATE WITH DE NOVO DONOR-SPECIFIC CELLULAR AND HUMORAL ALLOREACTIVITY AND PREDICT WORSE GRAFT OUTCOME

Maria Meneghini[1], Elena Crespo[2], Matthias Niemann[3], Alba Torija[2], Edoardo Melilli[4], Marta Jarque[2], Anna Manonelles[4], Nuria Montero[4], Josep Maria Cruzado[1], Josep Maria Grinyo[1], Oriol Bestard[1]
[1]Bellvitge University Hospital-IDIBELL; [2]Experimental Nephrology Laboratory-IDIBELL; [3]PIRCHE AG; [4]Bellvitge University Hospital

Background: Donor-recipient (D/R) HLA eplet mismatch (MM) algorithms have shown to predict Humoral alloimmune activation and kidney transplant (KT) outcomes. Among them, PIRCHE-II calculates donor-derived HLA peptides presented by HLA classII molecules to recipient Tcells, inferring the likelihood of anti-donor T-cell priming. Whether high PIRCHE-II MM may identify de novo donor-specific T-cell activation (dnDST) as an early immune process for subsequent donor-specific antibody (DSA) formation has not been evaluated.
Methods: 121 consecutives KT, without pre-KT DSA, were investigated for D/R MM by PIRCHE-II score and its prediction of KT outcomes as well as dnDSA and DST using an IFN-γ ELISPOT pre-KT and 6, 12, 24, 36 months after KT; with at least 36 months follow-up (mean 65 ± 15, range 41–120).
Results: Mean DR, DQ and total classII PIRCHE-II MM were 11.7 ± 10, 17.7 ± 14 and 29.3 ± 22. Despite no pre-TX DSA, 75/121(62%) patients showed preformed DST, whereas 46/121(38%) did not. ClassII dnDSA was observed in 16/121(13.2%) and dnDST in 11/46(24%). Mean time to dnDST and dnDSA was 10 ± 8 and 32 ± 7 months. 10/16(62.5%) dnDSA+ showed pre-TX DST whereas 37.5% did not. Interestingly, 4/11(36%) dnDST+ developed dnDSA, whereas only 2/35(6%) dnDST− ($p = 0.03$). dnDST+ and dnDSA+ patients displayed significantly higher DR and classII PIRCHE-II than DST- and DSA- (dnDST: 20 ± 14 vs. 10 ± 9, $p = 0.01$; 41 ± 24 vs. 27 ± 18, $p = 0.06$. dnDSA: 17 ± 15 vs. 11 ± 10, $p = 0.05$; 36 ± 24 vs. 28 ± 21, $p = 0.2$). A ROC analysis revealed a sensitive and specific PIRCHE-II DR cut-off predicting development dnDST and dnDSA (log-rank = 0.009 and 0.04, respectively). Combination of the 2 variables predicted dnDSA formation.
Finally, at multivariate analysis, a high classII PIRCHE-IIMM independently predicted death-censored graft loss (HR = 1.025, 95% IC = 1.002–1.105, $p = 0.03$).
Conclusion: A poor D/R HLA matching assessed by PIRCHE-II score predicts KT at higher risk of dn anti-donor T-cell priming which precedes the development of dnDSA and inferior graft outcome.



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FG103 MULTIPLE NON-HLA ANTIBODIES ARE SIGNIFICANTLY INCREASED IN CHRONIC-ACTIVE ANTIBODY-MEDIATED REJECTION

Kasia Sablik[1], Elena Kamburova[2], Dave Roelen[3], Henny Otten[2], Michiel Betjes[1]
[1]Erasmus MC; [2]University Medical Center Utrecht; [3]Leiden UMB

Background: Donor-specific anti-HLA antibodies play an important role in chronic-active antibody mediated rejection (c-aABMR). However, in many cases these antibodies cannot be detected. In recent years non-HLA antibodies have emerged as a possible prominent contributing factor in c-aABMR. We therefore investigated whether specific non-HLA antibodies are increased in patients with c-aABMR.
Methods: Fifty-six patients with a for-cause renal biopsy showing c-aABMR ($n = 35$) or interstitial fibrosis and tubular atrophy (IFTA) ($n = 21$) were included. Pre-transplantation sera ($t = 0$) and sera at time of biopsy ($t = 1$) of these patients were tested against 14 proteins highly expressed in the kidney using a multiplex non-HLA assay. The assay tested for the presence of autoantibodies against agrin, APMAP, ARHGDIB, ARHGEF6, endorepelin, AT1R, ETAR, LMNB1, LPLUNC1, PECR, Pla2R1, PRKCZ, Tubb4B, and vimentin.
Results: A significant increase in signal-to-background-ratios (STBR) was detected over time ($t = 0$ vs. $t = 1$) against autoantibodies against agrin ($p = 0.002$), ARHGEF6 ($p = 0.015$), AT1R ($p < 0.001$), ETAR ($p = 0.031$), PECR ($p = 0.027$), Tubb4B ($p = 0.032$), vimentin ($p = 0.018$) and ARHGDIB ($p = 0.011$) in patients with c-aABMR. Similarly, patients with IFTA also demonstrated a significant increase in STBR for agrin, AT1R, PECR, Pla2R, Vimentin, ARHGDIB and Tubb4B autoantibodies between $t = 0$ and $t = 1$. However, autoantibodies against ARHGDIB, APMAP, endorepelin and Tubb4B were significantly increased at $t = 1$ in patients with c-aABMR compared to the IFTA group. The STBR in patients with c-aABMR vs. IFTA was 3.40 vs. 1.46 ($p = 0.006$) for anti-ARHGDIB, 1.50 vs. 1.06 ($p = 0.007$) for anti-APMAP, 1.30 vs. 1.06 ($p = 0.033$) for anti-endorepelin and 1.71 vs. 1.15 ($p = 0.007$) for anti-Tubb4B.
Conclusion: After transplantation, renal transplant patients showed a significant increase in various autoantibodies. STBR for autoantibodies against ARHGDIB, APMAP, endorepelin and Tubb4B were significantly increased in patients with c-aABMR.

FG104 PREFORMED DSA ARE ASSOCIATED WITH INFERIOR LONG TERM RENAL TRANSPLANT OUTCOMES BUT RISK ASSESSMENT REQUIRES CONSIDERATION OF OTHER PROGNOSTIC INDICATORS

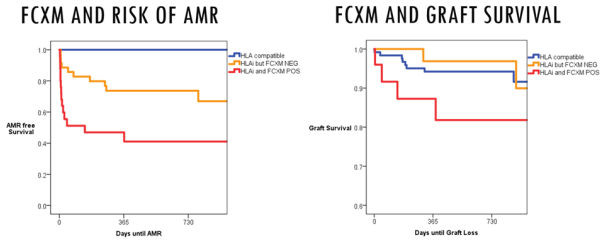
Eva Santos, Paul Brookes, Frank Dor, David Taube, Michelle Willicombe
Imperial College Renal and Transplant Centre, Imperial College Healthcare NHS Trust

Background: The immunological risk imposed by the presence of low level DSA detected by luminex alone pre-renal transplantation remains an area of controversy. In this study we report the long-term outcomes of patients transplanted with a low level preformed DSA, and consider independent risk factors associated with inferior allograft outcomes to aid risk assessment in the clinic.
Methods: 1,783 renal transplant recipients were analysed, of which 109 (6.1%) had preformed DSA. All patients received monoclonal antibody induction with a steroid sparing, tacrolimus based maintenance immunosuppression regimen. All patients were CDC:XM- and T-cell:FCXM- at the time of transplantation. A MFI of >500 was considered positive. Median follow up in the DSA+ group was 8.79 ± 3.27 years.
Results: Preformed DSA were associated with inferior allograft survival, HR: 1.62 (1.01–2.60), $p = 0.045$; rejection, HR: 3.23 (2.14–4.80), $p < 0.001$ and AMR, HR: 6.98 (3.87–12.61), $p < 0.001$. Immunodominant MFI did not predict AMR, $p = 0.19$; however, the presence of both class I and II DSA did, $p = 0.026$.
On multivariate analysis of all patients, allograft survival was associated with increasing donor age; HR: 1.03 (1.02–1.04), $p < 0.0001$ and preformed DSA; HR: 1.64 (1.10–2.45) $p = 0.016$, whilst pre-emptive transplantation was protective; HR: 0.66 (0.46–0.93), $p = 0.018$. AMR was associated with younger age HR: 0.98 (0.97–0.99), $p = 0.0018$ and preformed DSA HR: 3.10 (2.13–4.52), $p < 0.0001$; whilst receiving a preferentially matched transplant (NHSBT level 1 or 2, 0.25 (0.10–0.60), $p = 0.002$ and 0.43 (0.26–0.70), $p = 0.0006$ respectively) reduced the risk of AMR.
Conclusions: Preformed DSA are associated with inferior long term renal allograft outcomes in patients receiving a steroid sparing immunosuppression regimen. However independent variables associated with outcome such as pre-emptive transplantation, donor age and overall HLA mismatch should be scrutinised if considering alternate transplant options.

FG105 OUTCOMES FOLLOWING HLA-INCOMPATIBLE KIDNEY TRANSPLANTATION IN SCOTLAND

Trijntje Rennie[1], Richard Battle[1], Paul Phelan[1], Ann-Margaret Little[2], Marc Clancy[2], Neal Padmanabhan[2], Colin Geddes[2], David Turner[1]
[1]Royal Infirmary of Edinburgh; [2]Queen Elizabeth University Hospital

Background: Kidney transplantation in the presence of donor-specific HLA antibodies (DSA) is an option for difficult to match patients. Predicting the risk of rejection and worse outcomes is challenging.
Methods: National multi-centre case-control study of HLA incompatible (HLAi) kidney only transplants (2011–2018) matched with HLA compatible (non-HLAi) controls (2015–2016). Match criteria: gender, age, donor source. HLAi defined as the presence of DSA (DSA POS) by Luminex at time of transplantation irrespective of flow cytometry crossmatch (FCXM) status.
Results: Sixty-one patients received an HLAi transplant, 122 a non-HLAi transplant; mean age 46 years; 59% female, 25% received a live donor organ. Median cumulative MFI was 3,316 (IQR 1,277–6,661) and resulted in a positive FCXM in 25 (41%) recipients. Forty-six (75%) HLAi recipients received lymphocyte depleting (LDa) induction and 15 (25%) received an IL-2R antagonist (IL2Ra). Non-HLAi controls received IL2Ra. Mean follow up was 2.0 (SD ± 1.0) and 2.2 (SD ± 0.6) years for HLAi and non-HLAi. DSA POS/FCXM POS transplantation carried an increased risk of AMR (54%) compared to DSA POS/FCXM NEG transplants (27%) and non-HLAi transplants (0%). In the presence of a negative FCXM, DSA positivity alone did not reduce graft survival at 1 year (94% and 96% for non-HLAi and FCXM NEG transplants), whereas FCXM POS did reduce graft survival (87%). Mortality risk at 2 years was 17% and 2% for HLAi and non-HLAi recipients; 63% and 0% of deaths were infection-related.
Conclusion: HLA incompatibility increases the risk of AMR but not graft loss at 1 year compared to HLA compatible kidney transplantation. Transplantation in the presence of DSA and FCXM POS carries the greatest risk of both AMR and graft loss at 1 year. Mortality rates, in particular infection-related deaths, are significantly increased in HLAi transplant recipients.



FG106 THE CLINICAL SIGNIFICANCE OF HLA-DP MISMATCHES IN KIDNEY TRANSPLANTATIONS

Liesbeth Daniëls[1], Frans Claas[2], Aleksandar Senev[1], Leen Vanden Driessche[1], Marie-Paule Emonds[1], Steven Van Laecke[3], Rachel Hellemans[4], Daniel Abramowicz[4], Maarten Naesens[5]
[1]Histocompatibility and Immunogenetics Laboratory (HILA), Red Cross-Flanders; [2]Eurotransplant Reference Laboratory; [3]Department of Nephrology, Ghent University Hospital; [4]Department of Nephrology, Antwerp University Hospital; [5]Department of Nephrology and Renal Transplantation, University Hospitals Leuven

Background: HLA–DP is considered to be less immunogenic than other HLA antigens because of low expression on renal endothelium. The evidence for this is however scarce.
Methods: We evaluated the clinical significance of HLA-DP MM in kidney transplantations in 3 multicentre cohorts. In the 1st large cohort, we evaluated the prevalence of HLA-DP antibodies (Abs) in patients (pts) who experienced 1 or more graft failures (2008–2018; $N = 497$). A 2nd cohort was composed of pts with only HLA-DP DSA (2008–2018; $N = 14$). In this optimally selected cohort (no interference by other DSA) clinical outcome was evaluated, including histologic evaluation of biopsies by the Banff criteria. In the 3rd cohort ($N = 100$), the role of CDC-XM/FCXM in clinical decision-making was examined by collecting XM data from donor-patient pairs with only HLA-DP DSA.
Results: In the 1st cohort, DP Abs were detected in 99 pts (20%) and DQ Abs in 266 pts (54%). In 80%, DP Abs appeared only after graft failure. In the cohort of pts who had only DP DSA, AMR occurred in 5/14 pts (36%). In all 5 cases, DSA MFI was ≥3,141 but with negative CDC-XM. None of the pts with lower MFI DP-DSA experienced AMR. Epitope analysis showed an association with immunodominant eplets 84DEAV/85GPM-56AE/EE. In the non-AMR group (9/14) these eplets were also present as a MM but only in the presence of DSA with low MFI. Interestingly, we also observed high MFI (MFI > 20.000) DSA against the DPA locus (not DPB) in the non-AMR group. When we evaluated the XM results of cases with only DP DSA, a positive XM was only observed in

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case immunodominant eplets were present and MFI was ≥14.050 (CDC-XM) or ≥3,616 (FCXM). DSA against the DPA locus only, even up to MFI 14.233, never led to positive FCXM results.
Conclusion: AMR was observed in all cases with HLA-DP DSA when MFI ≥ 3,141 and directed towards immunodominant eplets. This illustrates that when HLA-DP Abs are found, HLA-DP typing, epitope analysis and FCXM are indicated for optimal decision-making.

FG107 EPITOPE MATCHING PREDICTS IMMUNIZATION AFTER RENAL ALLOGRAFT FAILURE LEADING TO WORSE OUTCOMES

Fabian Halleck[1], Marina Merkel[1], Paul Bach[2], Danilo Schmidt[1], Matthias Niemann[3], Nils Lachmann[4], Klemens Budde[1]
[1]Department of Nephrology, Charité Universitätsmedizin Berlin; [2]Institute of Biometry and Clinical Epidemiology, Charité – Universitätsmedizin Berlin; [3]PIRCHE AG, Berlin; [4]Institute for Transfusion Medicine, H&I Laboratory, Charité – Universitätsmedizin Berlin

Introduction: The number of immunized patients on the waitlist is increasing worldwide. There is a lack of data about the impact of immunization after transplantation on re-transplantation. The aim of this study was to examine the timing, epitope triggers and long-term effects of HLA immunization, graft failure or re-listing on re-transplantation.
Methods: From 1997 to 2017, 267 kidney graft failures of adults were detected and retrospectively analyzed. DnDSA were detected by solid-phase assays. Epitope matching was performed to predict development of dnDSA using the PIRCHE algorithm. Furthermore, the waiting time between re-listing at Eurotransplant and re-transplantation as well as graft survival and patient mortality depending on immunization were analyzed by means of Cox proportional hazards regression. Landmark analysis was used to avoid immortal time bias when assessing the effect of immunization on graft survival.
Results: In total, the risk for graft failure was highest in the first two years after transplantation and then moderately decreased (Fig. 1). DnDSA were detected in 137 allograft failures (51.3%). The occurrence of dnDSA was associated with a higher PIRCHE score (Fig. 2). When immunization was diagnosed within one year or within three years (Fig. 3 + 4) after transplantation, the patients had a significantly higher risk of graft loss. The waiting time for re-transplantation was longer when patients were immunized before relisting at Eurotransplant (Fig. 5). Surprisingly, when dnDSA were diagnosed before the first graft failure (66 patients), their mortality was lower, especially within the first two years after graft failure (18.8% vs. 34.4%), (Fig. 6).
Conclusions: Immunization seems to have a great impact on waiting time for re-transplantation and kidney allograft survival. The PIRCHE algorithm may help to reduce the risk of dnDSA. The relationship between immunization and mortality needs further evaluation.

FG19 – KIDNEY ISCHEMIA AND REPERFUSION

FG108 REMOTE ISCHAEMIC CONDITIONING AND EARLY CHANGES IN PLASMA CREATININE AS MARKERS OF ONE YEAR KIDNEY GRAFT FUNCTION – A FOLLOW-UP OF THE CONTEXT STUDY

Marie Bodilsen Nielsen[1], Nicoline Valentina Krogstrup[2], Mihai Oltean[3], Gertrude J. Nieuwenhuijs-Moeke[4], Frank J.M.F. Dor[5], Henrik Birn[2], Bente Jespersen[2]
[1]1987; [2]Aarhus University Hospital; [3]Sahlgrenska University Hospital; [4]University Medical Center Groningen; [5]Imperial College

Background: Ischaemia-reperfusion injury in kidney transplantation leads to delayed graft function (DGF), which is associated with reduced long term graft function. Remote ischaemic conditioning (RIC) improved early kidney graft function in a porcine model of donation after brain death and was associated with improved long-term cardiac outcome after myocardial ischaemia. This randomised, double-blinded trial evaluated the effect of RIC on kidney graft outcome in the first year, and examined the predictive value of a new measure of initial kidney graft function, i.e. the estimated time to a 50% reduction in plasma creatinine post-transplantation (tCr50).
Methods: A total of 225 patients undergoing deceased donor kidney transplantation were randomised to RIC or a sham procedure performed prior to kidney reperfusion. Up to four repetitive cycles of five minutes of leg ischaemia and five minutes of reperfusion were given. GFR, plasma creatinine, cystatin C and neutrophil gelatinase associated lipocalin (NGAL) were measured at three and twelve months and estimated GFR was calculated using four different equations. Other secondary outcomes were identified from patient files.
Results: RIC did not affect GFR or other outcomes when compared to the sham procedure at three or twelve months. tCr50 correlated with one year graft function ($p < 0.0001$ for both mGFR and eGFR estimates). In contrast, DGF i.e. "need of dialysis the first week" did not correlate significantly with one year GFR.
Conclusion: RIC during deceased donor kidney transplantation did not improve one year outcome. However, tCr50 may be a relevant marker for studies aiming to improve graft onset.

FG109 WHOLE ORGAN TOMOGRAPHIC IMAGING TO ASSESS VIABILITY AND RESPONSE TO THERAPY DURING EX VIVO PERFUSION

Matthew Harris[1], Jenna Dirito[2], Susann Spindler[1], Nabil Boutagy[1], Attila Feher[1], Hui Liu[1], Sarah Hosgood[2], Chi Liu[1], David Mulligan[1], Michael Nicholson[2], Albert Sinusas[1], Danielle Haakinson[1], Gregory T. Tietjen[1]
[1]Yale University; [2]University of Cambridge

Introduction: Thousands of "marginal" donor kidneys are discarded each year despite a severe organ shortage. This has motivated development of new technologies (e.g. ex vivo organ perfusion) to improve use of these organs without sacrificing patient outcome. However, we currently lack sophisticated diagnostic tools to assess organ function ex vivo. This presents a critical barrier to the development of therapeutic regimens for ex vivo organ repair. Here, we address this barrier by adapting computed tomography (CT) to enable quantitative whole organ assessment of human kidneys ex vivo. Our methods can facilitate quantitative evaluation of kidney viability ex vivo and thereby enable rational design of therapeutic repair strategies.
Methods and Results: CT imaging was developed and performed at the Yale Translational Research Imaging Center on a GE Medical Systems CT scanner. DICOM images were analyzed using custom MATLAB code. 25 Pig kidneys obtained under approved animal protocols were used to establish our imaging protocol. We then assessed a series of 6 transplant-declined human organs obtained in partnership with New England Donor Services under an approved ethical protocol.

Contrast enhanced CT was performed ex vivo using a constant pressure infusion with a crystalloid solution. Fig 1A shows 3D renderings of a 22 year old DCD donor kidney declined for a suspected air embolism (but otherwise transplantable) compared compared to a 39 year old DCD kidney with fibrosis. These organs, representing opposite ends of the marginal quality spectrum, displayed stark differences in the normalized volume of contrast enhancement (Fig 1B). Fig 1C shows a comparison of contrast volumes for all 6 human kidneys. Dynamic analysis was further performed by assessing iohexol washout rates as a quality measure of glomerular fitration (Fig 1D).
Conclusion: We have demonstrated that whole-organ-imaging is feasible and can enable dynamic assessment of human organ viability ex vivo.

FG110 KIDNEY TEMPERATURE DURING LIVING DONOR KIDNEY TRANSPLANTATION IS ASSOCIATED WITH 3 MONTHS GFR

Stan Benjamens, Tamar A.J. van den Berg, Thomas G.J. Kuipers, Mostafa El Moumni, Christina Krikke, Jan Willem Haveman, Stefan P. Berger, Henri G.D. Leuvenink, Robert A. Pol
University Medical Center Groningen

Background: The duration of cold (CIT) and warm (WIT) ischemia time are associated with both short and long-term kidney transplant function. In addition, a quick rise in kidney graft temperature is reported during the vascular anastomosis. This study was initiated, to gain insight in the effect of the kidney graft temperature on short-term transplant function.
Methods/Materials: From 2013 to 2015, patients receiving a living donor kidney transplant were prospectively analyzed. At set time intervals during transplantation, the graft temperature was measured using a noncontact infrared thermometer. Primary endpoint was the measured glomerular filtration rate (measured with 125I-iothalamate, mGFR) at 3 and 6-months after transplantation. Uni- and multivariable associations were identified using linear regression analyses. Multivariable analysis included donor gender and age, WIT and CIT, recipient gender and age at moment of transplantation.
Results: We evaluated 152 patients. Of these, 83 (55%) were male, mean (SD) age at time of transplantation was 50.3 (13.4) years and 79 (52%) were pre-emptively transplanted. In univariable analysis graft temperature, at 10 min after start of the vascular anastomosis, was associated with 3 and 6-months mGFR, b −0.21 (95% CI −2.32 to −0.28, $p = 0.013$) and b −0.22 (−2.53 to −0.06, $p = 0.040$) respectively. The associations with 3 months mGFR remained significant upon multivariable analysis, b −0.24 (−2.5 to −0.39, $p = 0.008$), while the association with mGFR after 6 months did not, b −0.19 (−2.37 to 0.15, $p = 0.08$).
Conclusion: A significant association between kidney graft temperature and 3-months post-transplant mGFR was identified. This independent association with short-term transplant function, urges for strategies to reduce warm ischemia time, but more specifically the kidney graft temperature during the vascular anastomosis.

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FG111 NEAR-INFRARED FLUORESCENCE IMAGING WITH ZW800-1 DYE TO ASSESS DONOR KIDNEYS WHILE ON EX-VIVO NORMOTHERMIC MACHINE PERFUSION

A.S. Arykbaeva[1], K.M. Rozenberg[2], M.L. Lo Faro[2], J. Hunter[2], J.B. Doppenberg[1], A.R.P.M. Valentijn[3], A.G.T. Terwisscha van Scheltin[3], H. Putter[4], I.P.J. Alwayn[5], J.V. Frangioni[6], K. Burggraaf[7], A.L. Vahrmeijer[1], R.J. Ploeg[2], V.A.L. Huurman[1]

[1]Department of Surgery, Leiden University Medical Center; [2]Nuffield Department of Surgical Sciences, University of Oxford; [3]Department of Clinical Pharmacy and Toxicology, Leiden University Medical Center; [4]Department of Biomedical Data Sciences, Leiden University Medical Center; [5]Department of Surgery, Leiden University Medical Center; [6]Curadel, LLC, Marlborough, MA; [7]Centre for Human Drug Research, Leiden

To increase organ utilisation without compromising outcomes, assessment of real-time perfusion using near-infrared fluorescence (NIRF) imaging prior to transplantation may assist in the decision making. ZW800-1 is a clinical applied non-toxic NIRF dye, which is rapidly and efficiently cleared by the kidney. Its ability to visualise (cortical) kidney perfusion may be more reliable than the experienced "surgical eye". In this pilot, we studied the feasibility of NIRF imaging as a technique to measure perfusion and kidney function during normothermic machine perfusion (NMP).

Slaughterhouse pig kidneys were placed on NMP at 37°C for 7 h with oxygenated, leukocyte-depleted autologous whole blood. Dose-escalation experiments (0.125; 0.25; 1.0; 4.0 mg/kg per kidney weight) were conducted to obtain robust and reproducible images. Following a ZW800-1 injection fluorescent images of kidneys were quantified as signal-to-background ratios (SBRs) using the FLARE imaging system. Urine and perfusate samples were collected to measure ZW800-1 concentration and calculate excretion as a reflection of kidney function.

A series of dosage experiments showed that 1.0 mg/kg of the compound was optimal, allowing reliable assessment of perfusion with a clear differentiation between well perfused and marginally perfused areas of the kidneys. The average SBR ($n = 5$) in the 1.0 mg/kg group decreased from 3.42 $\pm$ 1.09 to 2.28 $\pm$ 0.73, corresponding with a ZW800-1 concentration in the perfusate decreasing from 100 $\pm$ 51 μg/ml up to 6.4 $\pm$ 36.5 μg/ml, whilst increasing in the urine up to 8.7 $\pm$ 14.4 μg/ml throughout the perfusion. The clearance of dye per kidney (median 17% $\pm$ 24%) was directly associated with diminished fluorescence intensity.

This pilot study shows that NIRF imaging is feasible during NMP. By assessing the fluorescent intensity of different areas of the kidney and the urine dye excretion, the application of NIRF imaging could provide clinically relevant information concerning perfusion and function.

FG112 NORMOTHERMIC MACHINE PERFUSION OF KIDNEYS ALLOWS ASSESSMENT OF MITOCHONDRIAL RESPIRATION AND FACILITATES RECOVERY FOLLOWING KIDNEY INJURY

Kaithlyn Rozenberg[1], Laura Knijff[1], Letizia LoFaro[1], Fungai Dengu[1], Ann Ogbemudia[1], Annemarie Weissenbacher[2], Rutger Ploeg[1], James Hunter[1]

[1]University of Oxford; [2]Medical University of Innsbruck

Introduction: Normothermic Machine Perfusion (NMP) is a preservation strategy that may allow viability assessment of organs prior to transplant. 1 h of Kidney NMP is currently being assessed in a clinical trial in the UK and recent work showed that 24 h NMP is feasible in discarded human kidneys. The mechanism of action is unclear and we aimed to assess mitochondrial function during NMP.

Methods: Anaesthetised pigs ($n = 5$) had the vascular pedicle to one kidney clamped for 60 min. The healthy contralateral kidney was removed and placed on NMP for 8 h (healthy control (HC), $n = 5$). Following 60 min warm ischaemia the injured kidney was removed and placed on HMP for 24 h. After 24 h the injured kidney underwent NMP for 8 h ($n = 5$). An autologous red-cell based perfusate with albumin was used as a perfusion solution. Urine was recirculated to avoid volume depletion and maintain electrolyte balance. Mitochondria were extracted from fresh tissue biopsies and a Clark electrode was used to assess oxygen consumption and mitochondrial function.

Results: Interestingly, renal blood flow was significantly higher in injured kidneys compared with healthy controls (67 vs. 93 ml/min/100 g: $p = 0.0039$, figure 1). Intrarenal resistance was stable throughout perfusion and similar between groups (0.47 vs. 0.39 ru: $p = 0.17$). Median cumulative urine output was similar in both groups (107 vs. 58 ml: $p = 0.16$). Injured kidneys were more acidotic (median pH; 7.61 vs. 7.28: $p = 0.0021$). HC showed no difference in mitochondrial respiration throughout perfusion, however in injured kidneys at 8 h (52.07 $\pm$ 36.24 nmol O2/min/mg, mean $\pm$ SD) respiration was significantly increased compared to other time points (1 h 15.49 $\pm$ 7.7, $p = 0.0356$), (2 h 12.16 $\pm$ 3.6, $p = 0.0282$) and (4 h 9.6 $\pm$ 2.8, $p = 0.0180$), figure 2.

Discussion: Healthy kidneys were able to consume oxygen immediately and there was no change during 8 h NMP. Injured kidneys showed an increase in oxygen consumption over 8 h NMP, suggestive of mitochondrial recovery.

FG20 – SOMETHING NEW IN LIVER TRANSPLANT SURGERY: A DISCUSSION ON TECHNICAL ASPECTS

FG113 CLINICAL OUTCOMES OF LAPAROSCOPIC LIVING DONOR RIGHT HEPATECTOMY WITHOUT PRINGLE'S AND HANGING MANEUVER

Jaryung Han, Young Seok Han, Jae Min Chun, Sung Hoon Cho, Heon Tak Ha

Kyungpook National University, School of Medicie, Kyungpook National University Hospital

Careful preparation and blood-saving surgery will significantly lower the postoperative morbidity in laparoscopic liver resection (LLR). To reduce bleeding during hepatectomy, it is significant to decrease central venous pressure (CVP) and apply Pringle's & hanging maneuver (P&H). However, P&H are cumbersome and has the potential for further injury by excessive mobilization and dissection of inferior vena cava and right lobe of liver, especially in living liver donors. We would like to present the experience and outcomes of laparoscopic living donor right hepatectomy (LDRH) performed without P&H.

Between December 2014 and October 2018, among 97 cases of living donor right hepatectomy, 50 donors underwent LDRH. During LDRH, mean pneumoperitoneal pressure was 12 mmHg and CVP was less than 5 mmHg. The right liver was mobilized to the inferior half portion of retrohepatic IVC and large right inferior hepatic veins were preserved. The caudal approach without P&H was applied for liver parenchymal transection. The V5 and V8 for reconstruction were also preserved until just before the right hepatic duct transection.

Mean total operation time was 367 min and the warm ischemic time was 9.2 min. No donors required blood transfusion, conversion to open surgery, and re-operation. The postoperative course was uneventful except one donor with bile leakage from the cutting edge of the right hepatic duct stump. All donors' liver function was recovered to normal range within 2 weeks and mean postoperative hospital stay was 8 days.

Conclusively, although P&H is not used in LDRH, LLR under low CVP and constant pneumoperitoneal pressure without P&H can help reduce blood loss and prevent further liver graft injury by excessive mobilization of liver. However, because of the donor safety which is the most important issue in living donor hepatectomy, LDRH shou

FG114 RESCUE CAVO-PORTAL HEMITRANSPOSITION IN LIVER TRANSPLANTATION WITH PORTAL VEIN THROMBOSIS AFTER INEFFECTIVE THROMBECTOMY

Jacopo Lanari[1], Domenico Bassi[2], Francesco Enrico D'Amico[2], Riccardo Boetto[2], Alessandra Bertacco[2], Alessandro Vitale[2], Marina Polacco[2], Enrico Gringeri[2], Umberto Cillo[2], Elisa Fasolo[2]

[1]Padova University Hospital; [2]Hospital University of Padova

Back Ground: Intraoperative management of portal vein thrombosis (PVT) is one of the challenges of liver transplantation (LT). After LT, mortality in patients with PVT is reported to be higher than in patient without (13.5% vs. 9.9 after 1 year). The grade of occlusion and extension of the thrombosis also affect the outcome. Thrombectomy and thromboendovenectomy (TT) are used in presence of PVT in around 75% of patients. When this procedure is not feasible or ineffective, cavo-portal hemitransposition (CPH) is a potential option to rescue the portal flow.

Methods: Patient treated with LT between 2010 and 2018 at a single center were retrospectively analyzed. During this period 604 LT were performed with 1- and 5-year survival of 85.6% and 74.1%. Patients transplanted in the presence of PVT were 83 (13.7%). PVT was classified according to the Yerdel classification. CPH was attempted only after failure of TT.

Results: The 1.3- and 5-year survival of patients with PVT were respectively 78.4%, 69.5%, 67.3%. Of the 83 patients who underwent LT with PVT, 41 had grade 1 PVT, 17 grade 2, 9 grade 3, 17 grade 4. TT was utilized in all the 41 cases of PVT grade 1, in 15 over 17 cases of grade 2, in 8 over 9 of grade 3 and in 10 over 17 of grade 4. Survival at 1 and 3 year in grade 1 PVT was 87.6% and 77.9%. In grade 2 PVT treated with TT survival at 1 and 3 year were 86% and 80%. The 2 patients treated with CPH were lost perioperatively. In grade 3 PVT patients treated with TT had a 1- and 3-year survival of 75% and 60%. The only case treated with CPH is alive at 2 year. In PVT grade 4 patients treated with TT had a survival at 1- and 3-year of 60% while patients treated with CPH of 42%.

Conclusions: In patient with PVT classified with Yerdel grade of 2, 3, or 4, in case of ineffective TT, CPH is a possible rescue procedure with high mortality.

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FG115 HOW TO SELECT WHICH ANTERIOR SECTOR DRAINAGE VEINS TO RECONSTRUCT IN RIGHT LOBE LIVING DONOR LIVER TRANSPLANTATION?

Gokhan Ertugrul, Mehmet Seker, Onur Yaprak, Murat Dayangac
Medipol University Hospital

In right lobe (RL) living donor liver transplantation (LDLT), a good hepatic venous outflow is one of the basic principles of a technically successful procedure. However, the issue of whether all anterior sector (AS) drainage veins need reconstruction has been controversial. This study investigates the early outcome of reconstructed AS veins using polyester (Dacron®) grafts.

Between January 2018 and January 2019, of 48 adult patients who underwent RL LDLT in our institution, 37 (77.0%) received a RL graft with AS venous reconstruction including isolated segment 5 ($n = 19$), isolated segment 8 ($n = 2$), or combined segment 5 and 8 ($n = 16$) drainage. All reconstructed veins were ≥5 mm in size. Median donor age was 32.0 and median graft-to-recipient-weight ratio (GRWR) was 1.1%.

All patients underwent contrast enhanced CT or MRI within 2 weeks after the transplant. The 2-week graft patency rate was 54.1%. The rate of graft thrombosis was significantly higher in patients with a GRWR of ≥1.2% (80% vs. 20%, $p = 0.001$). The patency rate showed a significant negative correlation with the GRWR (Pearson coefficient = −0.380, $p = 0.02$). The patent Segment 5 and 8 veins were significantly larger than the thrombosed veins (Segment 5: 7.6 ± 1.7 mm vs. 5.1 ± 1.6 mm, $p = 0.003$; Segment 8: 6.3 ± 0.8 mm vs. 5.1 ± 0.3 mm, $p = 0.002$). The patency rate showed a significant positive correlation with the size of Segment 5 (Pearson coefficient = 0.490, $p = 0.003$) and 8 veins (Pearson coefficient = 0.684, $p = 0.002$). There was only one 90-day mortality (2.0%) and graft thrombosis was not associated with either lower liver graft regeneration or an increased risk of graft dysfunction.

After two of our recipients developed infection in the thrombosed polyester grafts, we questioned our policy of routine drainage for all sizable (≥5 mm) AS veins. Considering the low early patency rate and the risk of graft infection, RL grafts with GRWR ≥ 1.2% and AS veins <7 mm in diameter may not need reconstruction.

FG116 NOVEL INTRAOPERATIVE STRATEGIES SIGNIFICANTLY REDUCE TRANSFUSION REQUIREMENTS IN LIVER TRANSPLANTATION

Tumay Yanaral, Gokhan Ertugrul, Pelin Karaaslan, Onur Yaprak, Murat Dayangac
Medipol University Hospital

Introduction: Blood loss and transfusion has been shown to be independent predictors of outcome after liver transplantation (LT). Minimizing bleeding and reducing transfusion requirements are therefore key goals in LT surgery. In this retrospective single-center cohort study, we performed a comparative analysis of the impact of novel intraoperative strategies on transfusion requirements during adult living donor LT (LDLT).

Material/Methods: We analyzed 119 patients who underwent right lobe LDLT between November 2015 and November 2018. While the anesthesiology team remained the same, the first 77 (Era 1) and the last 42 (Era 2) cases were performed by two different surgical teams. In Era 2, a number of novel intraoperative strategies were introduced concomitantly. These strategies included routine use of somatostatin infusion and early portal clamping during recipient hepatectomy, an "intent-to-drain" policy for anterior sector venous drainage, routine intraoperative measurement of portal flow volume, goal-directed use of splenic artery ligation for portal flow modulation, abandonment of intraoperative cell salvage, and minimization of fresh frozen plasma (FFP) transfusion. Thromboelastography and Pulse index Contour Continuous Cardiac Output monitorization were routinely used during the study period.

Results: Intraoperative transfusion volume of both RBC and FFP showed significant correlation with post-transplant 90-day mortality (Spearman's rho = 0.282 and 0.287, respectively; $p < 0.001$). In Era 2, there was a significant reduction in both red blood cell (RBC) and FFP transfusions. The 90-day mortality also decreased significantly, which resulted in a significant improvement in post-transplant survival.

Conclusion: In LDLT, a number of intraoperative strategies are available to significantly decrease transfusion requirements and improve early outcomes.

	Era 1 ($n = 77$)	Era 2 ($n = 42$)	p
MELD-Na score	17.1 ± 7.4	16.0 ± 6.3	0.4
Donor age	34.5 ± 10.2	31.3 ± 7.8	0.1
Graft-to-recipient weight ratio (%)	1.1 ± 0.2	1.1 ± 0.2	0.5
Intraoperative cell salvage (%)	31 (40.3%)	0	<0.001
Anterior sector venous drainage (%)	14 (18.2%)	34 (81.0%)	<0.001
Splenic artery ligation (%)	5 (6.5%)	10 (23.8%)	0.009
RBC (units)	5.7 ± 7.6	3.5 ± 3.4	0.03
FFP (units)	6.8 ± 3.7	4.5 ± 3.3	0.001
90-day mortality	13 (16.9%)	1 (2.4%)	0.01
1-year patient survival	84.3%	97.6%	0.04

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