## Index

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and other collaborators</td>
<td>2</td>
</tr>
<tr>
<td>Endorsing societies</td>
<td>3</td>
</tr>
<tr>
<td>Committees</td>
<td>4</td>
</tr>
<tr>
<td><strong>ABSTRACTS</strong></td>
<td></td>
</tr>
<tr>
<td>Joint plenary sessions</td>
<td>6</td>
</tr>
<tr>
<td>Oral sessions</td>
<td>14</td>
</tr>
<tr>
<td>Joint poster sessions</td>
<td>26</td>
</tr>
<tr>
<td>Index of authors</td>
<td>62</td>
</tr>
</tbody>
</table>
Sponsors

Platinum sponsors

Chiesi  NOVARTIS  ONE LAMBDA

Shire

Gold sponsor

astellas

Standard sponsors

Pfizer  SANOFI  Transplant

Other collaborators

Alexion  Biotest  Diagnóstica Longwood
The Organising Committee of the 2017 Banff-SCT Joint Scientific Meeting would like to thank sincerely the following societies for the support they have given to this meeting.

**SPECIAL RECOGNITION TO**
Organització Catalana de Transplantaments (OCATT)

**ENDORsing SOcieties**
Sociedad Española de Trasplante (SET)
Organización Nacional de Trasplantes (ONT)
Organització Catalana de Trasplantaments (OCATT)
European Society for Organ Transplantation (ESOT)
The Transplantation Society (TTS)

**ORGANISED BY**

---

BANFF-SCT JOINT SCIENTIFIC MEETING · BARCELONA · MARCH 2017
COMMITTEES

HONORARY PRESIDENCY
Hble. Mr. Antoni Comín i Oliveres
MINISTER OF HEALTH OF THE GENERALITAT DE CATALUNYA

ORGANISING COMMITTEE

BANFF BOARD
CHAIR
Kim Solez
TREASURER
Kim Solez
COUNCILLORS
Anthony J. Demetris
Denis Glotz
Alexandre Loupy
Michael Mihatsch
Brian Nankivell
Lorraine Racusen
Daniel Serón

SCT BOARD
PRESIDENT
Antonio Román
VICE PRESIDENT
Francesc J. Moreso
SECRETARY
Núria Masnou
COUNCILLORS
Gonzalo Crespo
Josep Maria Cruzado
Laura Lladó
Sonia Mirabert
Eduard Palou

SCIENTIFIC COMMITTEE

EXEcutIvE COMMITTEE
Mark Haas
Alexandre Loupy
Antonio Román
Daniel Serón

COUNCILLORS
Carlos Bravo
Patrick Bruneval
Lluís Castells
Linda Cendales
Gonzalo Crespo
Josep Maria Cruzado
Anthony J. Demetris
Cinthia Drachenberg
Constantino Fondevila
Josep Maria Grinyó
Lluís Guirado
David Hwang
Núria Masnou
Jaume Martorell
Michael Mengel
Michael Mihatsch
Sonia Mirabert
Francesc Moreso
Frederic Oppenheimer
Eduard Palou
Julio Pascual
Elizabeth Pavlisko
Llorain Racuse
Eulàlia Roig
Kim Solez

SCIENTIFIC AND TECHNICAL SECRETARIAT

BANFF·SCT 2017 Meeting – AOPC
Edif Colon, Av. Drassanes 6
E-08001 Barcelona
Tel 933 027 541
congress@aopc.es
Determinants of severe fibrosis in kidney allograft: major impact of circulating donor specific anti-HLA antibodies
Clement Gosset1, Denis Viglietti2, Marion Rabant3, Glotz Denis4, Christophe Legendre5, Jean Paul Duong Van-Huyen3, Alexandre Loupy2, Carmen Lefaucheur1
1: Pathology, Saint-Louis Hospital, Paris, France. 2: Paris Translational Research Center for Organ Transplantation, Paris, France. 3: Pathology, Necker Hospital, Paris, France. 4: Nephrology and Kidney Transplantation, Saint-Louis Hospital, Paris, France. 5: Nephrology and Kidney Transplantation, Necker Hospital, Paris, France

Background Interstitial fibrosis represents a major cause of kidney allograft loss. We investigated the role of circulating donor-specific anti-HLA antibodies (DSA) in the development of severe allograft fibrosis and the contribution of all traditional factors.

Methods We prospectively enrolled 1539 consecutive kidney recipients transplanted between 2004 and 2010 in two Paris centers with systematic assessment of allograft fibrosis using the IF/TA Banff score on biopsies performed at 1-year post-transplantation. We assessed DSA and all traditional determinants of allograft fibrosis recorded at transplantation and in the first year after transplantation, including all the histologic diagnoses (“for cause” biopsies; N=1804).

Results We identified 498 (32%) patients with severe fibrosis (IF/TA>1). DSA were associated with severe fibrosis (adjusted OR, 1.53; 95% CI, 1.16-2.01; P=0.002) after adjusting on traditional determinants including post-transplant injuries (TCMR, AMR, BKV AN, CNI toxicity, recurrent disease, pyelonephritis, acute tubular necrosis), donor factors and transplant characteristics. DSA were still associated with severe fibrosis in patients without AMR (OR, 1.47; 95% CI, 1.10-1.96; P=0.008). Patients with DSA-associated severe fibrosis (N=154) showed increased microvascular inflammation (P<0.001), transplant glomerulopathy (P<0.001), C4d deposition in capillaries (P<0.001), and a decreased allograft survival (P<0.001) as compared to patients with DSA-free severe fibrosis.

Among the modifiable risk factors for severe fibrosis, DSA was the first contributor, being involved in 11% of cases while TCMR, CNI toxicity, acute tubular necrosis, pyelonephritis and BKV AN were involved in 9%, 8%, 6%, 5%, and 4% of cases, respectively.

Conclusions Circulating anti-HLA DSA are major contributor to severe allograft fibrosis independent of traditional risk factors and of AMR.

BANFF v3 Arteritis: reappraisal of clinicopathologic characteristics under contemporary immunosuppression
Alton Farris, H. Sullivan, Thomas Rogers, Robert Bray, Howard Gebel, Carla Ellis
Department of Pathology, Emory University, Atlanta, United States

Background Banff v3 arteritis is defined as fibrinoid arterial change and/or transmural arteritis. Data have implicated antibody-mediated rejection in much v3 arteritis; however, clinicopathologic feature characterization is still needed, particularly with improved donor specific antibody (DSA) detection and immunosuppression.

Methods Rejection biopsies with v3 arteritis were retrieved during contemporary immunosuppression and human leukocyte antigen (HLA) DSA testing at our center (2012–2015); and clinicopathologic features were assessed, including Luminex® single antigen bead DSA assays.

Results Criteria for v3 arteritis (n=31) were fulfilled by fibrinoid necrosis (n=18), transmural arteritis (n=5), or both (n=8). Most (56%) were male with a mean age of 48±15 years (± standard deviation[SD]) and creatinine peaking at mean±SD=6.3±4.2 mg/dL (range=1.67-20.67). Treatment prevented graft failure in 56%; the remainder returned to dialysis. Immunosuppression included belatacept±tacrolimus, mycophenolate, and prednisone (n=20 patients) and tacrolimus, mycophenolate, and prednisone (n=11). DSAs were present in only 1 belatacept vs. 6 non-belatacept patients, a statistically significant relationship (Chi-square p=0.002). HLA DSAs included: class II (n=5 patients), class I (n=1), and class I+II (n=1). Banff criteria included mean±SD=t2.4±0.95, 1.2±2.08, g1.3±1.0, ptc1.4±1.1, cv0.84±1.0, c11.1±1.0, ct1.1±0.92, cg0.29±0.82, and immunohistochemistry C4d0.7±1.2 [C4d0 (negative) (n=21), C4d1 (n=3), C4d2 (n=2), and C4d3 (n=5)].

Conclusions This confirms that v3 arteritis occurs without DSA, possibly due to “pure” cellular rejection. Although formerly recognized, many prior v3 arteritis cohorts had more DSA. Immunosuppression apparently has a role, since DSAs occurred at a lower rate with belatacept. Overall, this prompts consideration of cellular rejection mechanisms as well as other possible rejection mechanisms (e.g. non-HLA antibodies); and larger v3 arteritis cohorts may yield novel insights.
Gene expression during development of chronic antibody mediated rejection in renal allografts from non-human primates: validation of markers used in humans and sequential changes in protocol biopsies

Benjamin Adam1, Rex Neal Smith2, Ivy Rosales2, Bahman Afzali1, Tetsu Oura3, Benedict Cosimi2, Tatsuo Kawai3, Robert Colvin2, Michael Mengel1

1: Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada. 2: Department of Pathology, Harvard Medical School and Massachusetts General Hospital, Boston, USA. 3: Department of Surgery, Harvard Medical School and Massachusetts General Hospital, Boston, USA

Background RNA transcript measurement is a promising adjunct for the diagnosis and classification of antibody-mediated rejection (AMR), however most technologies require specially processed biopsy samples. Here we assess a novel approach using the NanoString platform and routine formalin fixed paraffin embedded (FFPE) samples.

Methods We analyzed protocol renal allograft biopsies from non-human primates (NHP) with a custom Cynomolgus probe set corresponding to 67 genes selected from human studies. RNA was isolated from 105 archival FFPE renal allograft samples including 80 from animals that developed chronic AMR, 15 with other diagnoses, and 10 normal samples. NanoString gene expression data was correlated with pathologic features.

Results Expression of endothelial and inflammation-related genes correlated with diagnoses and histologic lesions of AMR and T-cell mediated rejection (TCMR), respectively. Six endothelial-associated transcripts (ENDATs) characteristic of AMR in humans exhibited strong association with AMR in NHP. This subset was significantly higher in AMR biopsies than normal and non-normal controls (p<0.001) and correlated with classic AMR histologic features (p<0.001). Principal component analysis highlighted the association of this subset with AMR as well as the ambiguity of v-lesions and peritubular capillaritis between AMR and TCMR (figure 1). Most animals with AMR demonstrated increasing expression with histologic progression. Some protocol biopsies showed increased expression of endothelial genes before histologic or immunopathologic evidence of AMR.

Conclusion These data validate in another species several molecular markers used in humans for AMR and TCMR, and suggest there may be sequential changes in protocol biopsies that correspond to the previously described stages of chronic AMR.

Tacrolimus and mycophenolate mofetil exposure and subclinical inflammation in low immunological risk renal transplants

Irina Torres1, Christina Dörje2, Francesc Moreso1, Anders Asberg2, Marta Vidal1, Clara Garcia Carro1, Finn P Reinholdt2, Eva Castella1, Maite Salcedo1, Joana Sellares1, Maria Antonieta Azancot1, Manel Perello1, Xavier Gun1, Hallvard Holdaas2, Anna Reisaeter6, Daniel Serón1

1: Nephrology, Hospital Universitari Vall d’Hebron, Barcelona. 2: Nephrology, Oslo University Hospital Rikshospitalet, Oslo Norway

The aim is to evaluate the relationship between maintenance immunosuppression, subclinical inflammation (i-score plus t-score) and interstitial fibrosis/tubular atrophy (ci-score plus ct-score) in paired surveillance biopsies performed in low immunological risk renal transplants treated with induction therapy, tacrolimus, mycophenolate mofetil (MMF) and steroids in two cohorts of patients. The Barcelona cohort consisted of 109 early (4 months) and 66 late (18 months) biopsies in patients receiving full tacrolimus exposure and reduced MMF dose. The Oslo cohort consisted of 308 early (1.5 months) and 284 late (12 months) biopsies performed in patients treated with low tacrolimus exposure and full MMF dose. Subclinical inflammation was associated with low tacrolimus trough levels (TAC0) in the early (OR: 0.75, 95% CI: 0.61-0.92; p=0.006) and late biopsies (OR: 0.69, 95% CI: 0.50-0.95; p=0.023) in the Barcelona cohort. In the Oslo cohort, subclinical inflammation was associated with low MMF daily dose in the early biopsy (OR: 0.91, 95% CI: 0.85-0.98; p=0.0162) and with low TAC0 in the late biopsy (OR: 0.80, 95% CI: 0.66-0.97; p=0.0258) after adjusting for confounding variables. IF/TA in the late biopsy was not associated with TAC0 or MMF in any of both cohorts. Our data suggest that concomitant minimization of TAC and MMF early after transplantation may favour the appearance of subclinical inflammation.

FIGURE 1: Principal component analysis

JPA1-3
JPA1-4
Noninvasive assessment of liver fibrosis and portal hypertension after viral eradication in post-transplant hepatitis C

Ezequiel Mauro¹, Gonzalo Crespo¹, María Carlota Londoño¹, Alba Díaz², Pablo Ruiz¹, Lydia Sastre¹, Julissa Lombardo¹, Jonathan Aguirre¹, Jordi Colmenero¹, Miquel Navasa¹

¹: Liver Transplant Unit, ²: Pathology Department, Hospital Clinic, IDIBAPS, CIBERehd, Barcelona

Background Most studies on the accuracy of Fibroscan have been performed in patients with active hepatitis C. With the use of direct antivirals a large part of this population will eradicate HCV, particularly after liver transplantation (LT). The accuracy of elastography after viral eradication has not been evaluated.

Methods All LT recipients with recurrent hepatitis C who achieved sustained virological response (SVR) between 2001 and 2015 were included. One year after SVR, patients underwent a liver biopsy (with or without HVPG measurement) and a liver stiffness measurement (LSM).

Results One-hundred-and-six patients were analyzed. One year after SVR, 15% of patients presented cirrhosis, and 21% of patients presented clinically significant portal hypertension (CSPH, HVPG ≥ 10 mmHg). The correlation between histology (Metavir Score) and fibroscan was significant (p<0.001). In addition, the correlation between HVPG and fibroscan was also significant (r=0.84, p<0.001). The AUROC of LSM for the diagnosis of CPH was 0.953 (p<0.001). Previously described cut-offs (non SVR patients) of 13.6 and 21 kPa presented high sensitivity and specificity (92% -91% and 58% -94%), PPV and NPV were 73% -98% and 70% -90% respectively. The AUROC for the diagnosis of cirrhosis was 0.977 (p<0.001). Best cut-off value was 14.2 kPa, which yielded sensitivity, specificity, NPV and PPV of 100%, 93%, 100% and 73%.

Conclusion LSM is a useful tool for the screening of cirrhosis and CPH in transplant recipients one year after SVR, and its accuracy seems to be at least as high as in patients with recurrent hepatitis C and active viral replication. Thus, LSM is useful for the screening of cirrhosis after SVR in transplant recipients, allowing the establishment of prognosis and surveillance strategies.

Outcomes of different cross-match techniques pre-transplantation among HLA-incompatible living kidney transplant patients

Edoardo Melilli¹, Maria Meneghini¹, Ignacio Revuelta², Fritz Diekmann², Omar Tacho¹, Josep Maria Cruzado¹, Elisabet Rigo³, Josep Maria Grinyó¹, Jaume Martorell³, Oriol Bestard¹

¹: Kidney Transplant Unit, Nephrology Department, Bellvitge University Hospital, IDIBELL, Barcelona. ²: Kidney Transplant Unit, Nephrology Department, Clinic University Hospital, Barcelona. ³: Immunology department. Clinic University Hospital. Barcelona

Background and aims It is still not determined the precise predictive value of all current different immune assays to assess the risk of transplant rejection before Living-donor kidney transplantation (LDKT). The aim of our study is to investigate the impact of the different cross-match techniques and their combination on the main clinical outcomes in a large cohort of LDKT.

Methods Retrospective study including 394 consecutive LDKT recipients from two Transplant Centres in Barcelona. All AB0 compatible, with negative CDC-crossmatch. Mean follow-up was 69 months. The different immune techniques evaluated were: CDC Panel reactive antibodies (PRA), B/T cells Flow-cytometry-crossmatch (FlowCM), Solid-phase assay: virtual crossmatch (Luminex®, Sp-DSA), Complement binding DSA (DSA-C3d+).

Results 27 Patients presented positive FlowCM; 22 Sp-DSA; 13 DSA-C3d+. DSA-C3d+ showed significantly higher MFI, the ROC curve identified a cut-off of 8192 to predict C3d binding capacity. The univariate analysis showed that FlowCM+, Sp-DSA+ and DSA-C3d+ were associated to high risk of acute rejection (AR) and to worse eGFR at 24 months; FlowCM+ and Sp-DSA+ were associates to graft loss. The multivariate analysis revealed that only previous AR and Sp-DSA+ independently predicted graft loss. Of note, only DSA-C3d+ or DSA with MFI≥6190 were associated to AR.

Conclusions Preformed DSA-C3d or those with high MFI are best predictors of AR prior to LDKT, which discriminates patients at higher risk of graft loss. Therefore pre-transplant virtual cross-match using Sp-DSA is the most accurate test to predict the risk of graft loss and should eventually be the main immune technique to be used before LDKT.
Differential profile of activated regulatory T cell subsets and microRNAs in tolerant liver transplant recipients

Alberto Baroja-Mazo1, Beatriz Revilla-Nuin1, Laura Martinez-Alarcon1, Jose Ignacio Herrero2, Carlos Martinez-Caceres1, Pablo Ramirez1, Jose Antonio Pons1

1: Digestive Surgery and Organ Solid Transplantation, Murcia’s Biohealth Research Institute, Virgen de la Arrixaca, El Palmar, Murcia.
2: Liver Unit, Clínica Universidad de Navarra, Pamplona

Introduction Regulatory T cells (Tregs) play a potential role in operational tolerance in liver transplant patients and microRNAs (miRNAs) are known to be involved in the immunological responses and tolerance.

Objectives Thus, we analyzed the implication of different peripheral blood Treg subsets and miRNAs in liver transplantation tolerance in 24 tolerant (To1) and 23 non-tolerant (non-To1) liver transplant recipients and 16 healthy individuals.

Methods 47 liver transplant patients and 16 healthy volunteers were analyzed and different types of samples were obtained, including PBMCs, DNA and total RNA. The study was performed by employing cellular (flow cytometry), genetic (RT-qPCR) and epigenetic (FOXP3 Treg-specific demethylated region (TSDR) demethylation rate) approximation.

Results Non-To1 patients had a lower demethylation rate of FOXP3 TSDR than To1 patients that correlated with frequency of circulating Tregs. To1 patients presented a different signature in Treg subset markers as compared with non-To1 patients with increased expression of HELIOS and FOXP3 and a higher proportion of LAP+ Tregs and CD45RA+HLA-DR+ activated effector-memory Tregs. The expression of 5 miRNAs (miR95, miR24, miR31, miR146a and miR155) was higher in To1 than in non-To1 patients. They had a positive correlation with activated Treg markers.

Conclusions These data suggest that activated effector-memory Tregs and a TSDR-demethylation state of Tregs may play a role in the complex system of regulation of LT tolerance. For the first time, a set of miRNAs differentially expressed in human liver transplant tolerant patients providing strong evidence that miRNAs are implicated in the preservation of self-tolerance as mediated by Tregs.

KL-6 as a potential biomarker to differentiate chronic allograft dysfunction phenotypes in lung transplantation

Cristina Berastegui Garcia1, Susana Gómez-Olles1, Thais Pereira-Vega1, Alberto Mendoza-Valderrey1, Berta Saez-Gimenez1, Manuel López-Meseguer2, Irene Bello Rodriguez, Carlos Bravo Masgoret3, Mario Culebras Amigo1, Victor Monforte Torres1, Antonio Roman Broto1

1: Pulmonology, 2: Thoracic Surgery, Hospital Universitari Vall d’Hebrón, Barcelona

Chronic allograft dysfunction (CLAD) is the main limitation for Lung Transplantation (LT) survival. Two phenotypes of CLAD had been defined: Bronchiolitis Obliterans Syndrome (BOS) and Restrictive Allograft Syndrome (RAS). We hypothesize that levels of glycoprotein KL-6 in serum in LT population may differ between phenotypes. Thus, the objective of the study was to analyze KL-6 levels in serum and bronchoalveolar lavage fluid (BALF) samples from LT patients in different situations: stable (ST), infection (LTI), and RAS.

Methods Seventy three patients with bilateral LT were included. The population was divided in 4 groups: 18 ST, 24 LTI, 20 BOS and 11 RAS patients. Samples were analyzed with the ELISA kit for KL-6 (Eidia Co., Japan). ROC analysis was used to evaluate the diagnostic accuracy of KL6 to identify RAS patients.

Results KL-6 levels in serum were higher in RAS patients being of 918 [IQR 487.8 to 1638]. Significant differences were shown between RAS vs ST, LTI and BOS groups (p<0.0001). No differences were found in BALF levels. Figure 1 y2. Diagnostic accuracy of KL6 to identify RAS vs BOS patients was AUC 0.93, 95% CI 0.83–1.02; p<0.0001. A cutoff value of 445.4 give a sensitivity of 100% (95% CI 71.51–100%) and a specificity of 75% (95% CI 50.9–91.34%).

Conclusion LT patients with RAS showed the highest values of serum KL-6. KL-6 in serum may act as a good biomarker to phenotype CLAD patients. BALF is not ideal for detecting KL-6.
Circulating donor-specific (D-SP) memory B cells (MBC) discriminates kidney transplant patients with histological lesions of ABMR in absence of circulating DSA

Sergi Luque1, Marc Lucia1, Marta Jarque1, Elena Crespo1, Edoardo Melilli2, Josep Maria Cruzado2, Joan Torras2, Josep Maria Grinyó2, Oriol Bestard2
1: Experimental Nephrology, IDIBELL, l’Hospitalet de Llobregat. 2: Kidney Transplant Unit, Nephrology Department, Bellvitge University Hospital, Barcelona. 3: Immunogenetics Laboratory, Hospital Clinic. Barcelona

Chronic (c) ABMR is a main cause of kidney allograft loss. For its diagnosis, specific histological lesions together with presence of circulating DSA must be reported. However, a significant number of patients with such lesions do not show detectable DSA, misunderstanding their diagnosis.

Methods In a cross-sectional group of (n=78) kidney transplant patients showing different histological phenotypes following Banff score classification: i) aABMR with DSA (n=16), ii) cABMR with DSA, (n=22) iii) cABMR without DSA (n=19), iv) IFTA lesions without inflammation and no DSA (n=6) and v) normal parenchyma (STA) (n=13); presence of d-sp mBc frequencies using a novel B-cell ELISPOT assay as well as main mBc and T follicular helper subsets were assessed in peripheral blood. Supernatants of d-sp mBc cultures were also assessed and correlated with circulating DSA.

Results Patients with cABMR with DSA and those with cABMR without DSA showed similar d-sp mBc frequencies (0.22±0.26 and 0.27±0.25, p=NS) but significantly higher to STA patients (0.04±0.05 and p=0.004 and p=0.001), whereas only 2 IFTA and none of STA individuals showed detectable d-sp mBc frequencies. Supernatants of stimulated mBc cultures illustrated the lower Ab production of mBc in cABMR patients compared to aABMR individuals, which was demonstrated by the higher detection sensitivity of the B–cell ELISPOT assay. No differences were detected in the number of the different mBc and TFH subsets in peripheral blood between groups.

Conclusion Assessment of circulating mBc frequencies may be useful to discriminate immune effector mechanisms of kidney allograft injury, regardless the presence of circulating DSA.

Immunopathological features of human chronic skin allograft rejection

Samuel Rotman1, Nathalie Koch1, Rosales Ivy2, Colvin Robert3, Aubert Vincent2, Raffoul Wassim2, Pascual Manuel2
1: Pathology, University Hospital of Lausanne, Lausanne, Switzerland. 2: University Hospital of Lausanne. 3: Pathology-MGH-Boston

A 65 year-old male suffered from extensive lower legs burns in 1991 at the age of 39. He was treated by coverage with non-vascularized and de-epithelialized, split-thickness allogeneic skin grafts (STSG) from a female donor. He received cyclosporine monotherapy during one month after the transplantation, but subsequently, the patient had no immunosuppressive regimen, with no biopsy-proven rejection, although superficial ulcers were noted at 1 year posttransplant.

23 years later, skin allograft ulcerations appeared and the STSG were surgically removed. Histological analysis showed grade IV rejection according to Banff CTA (Composite Tissue Allograft) 2007, with extensive fibrosis within the dermis and hypoderm, and a total loss of adnexa. Immunohistochemical analyses showed T cell endothelialitis with endothelial C4d deposition, associated with sparse T reg cells. Recipient HLA typing was identified by molecular analysis from DNA content within skin graft tissue. Serologic analysis showed high levels (5000-10'000 MFI) of circulating anti-HLA class II and class I antibodies by Luminex, with more than 10 HLA-DR specificities and 5 HLA-B specificities, respectively, in the recipient serum.

We thus report morphologic and histological evidence of chronic allograft injury, with antibody interaction with vascular endothelium (C4d deposits) and serologic evidence of donor-specific HLA-antibodies which all three together, may represent chronic active antibody-mediated rejection of the skin.

This unique case represents very long-term of chronic non vascularized skin allograft rejection in humans.
Digital image analysis in assessment of fibrosis in pediatric liver allografts

Alexander Kats1, Ryan Fischer2, Richard Hendrickson3, James Daniel2, Susan Foster4, Walter Andrews3

1: Department of Pathology and Laboratory Medicine, Children’s Mercy Hospital, Kansas City, MO, United States. 2: Department of Gastroenterology, Children’s Mercy Hospital, Kansas City, MO 64108. 3: Department of Surgery, Children’s Mercy Hospital, Kansas City, MO 64108. 4: Medical Student G2, Kansas University SOM, Kansas City, KS 66160

Background Serial biopsies demonstrate fibrosis in long-surviving pediatric liver allografts. The histologic grading of fibrosis in biopsies is subjective and may lead to delays in needed treatment interventions. We sought to compare standard fibrosis assessments of serial allograft biopsies with digital image analysis (DIA).

Methods The archived biopsies of patients who received liver transplants between 2007 and 2010 were retrospectively identified. Data through June 2015 was collected. Both “for cause” biopsies and bi-annual surveillance biopsies were analyzed. Rejection and fibrosis were scored using the Rejection Activity Index (RAI) and the METAVIR score. Trichrome stains of each biopsy sample were subject to DIA at 40X magnification. Red/magenta staining was “positive”. Fibrosis (blue) was “negative”. The selected image was analyzed by Aperio’s Positive Pixel Count Algorithm V 9.1 with ImageScope. Analysis included total “positive” and “negative” pixels and negative:positive ratios. ANOVA was performed to identify the relation of DIA fibrosis to METAVIR scoring and RAI.

Results Twenty patients and 131 biopsies were analyzed. DIA fibrosis ratios differed significantly among all METAVIR stages with the exception of stage 0 to stage 1. No stage 4 biopsies were available. Mean DIA fibrosis ratios increased with METAVIR stage (Stage 0: 0.029; Stage 1: 0.034 Stage 2: 0.060; Stage 3: 0.098). DIA fibrosis ratios did not differ significantly between RAI scores.

Conclusions DIA of biopsy specimens is a reproducible and reliable assessment of fibrosis in pediatric liver allografts.

Use of nanostring nCounter technology to assess C4d positive biopsies with no histological evidence of inflammation

Katherine Dominy1, Michelle Willicombe2, Tariq Al Johan1, Jack Galliford2, Adam McLean2, Terry Cook4, Candice Roufousse4

1: Centre for Complement & Inflammation Research (CCIR), Imperial College London, London, UK. 2: Imperial College Kidney and Transplant Institute, Hammersmith Hospital, London, UK. 3: King Saud University, Riyadh, Kingdom of Saudi Arabia. 4: Department of Cellular Pathology, Hammersmith Hospital, London, UK

Deposition of C4d is an established part of the Banff classification scheme for antibody mediated rejection (AbMR) and remains highly specific for AbMR despite a C4d-negative form being described. However, a small sub-set of patients with C4d-positive biopsies have no histological features of inflammation and donor specific antibodies are not always present. Our aim was to investigate these patients to understand the significance of C4d staining.

Gene expression analysis of 96 transcripts in 84 patients was carried out using the Nanostring nCounter system. Samples included diagnoses of AbMR, TCMR, Normal, stable ABO incompatible (ABOi) and the C4d-positive study group with no inflammation. Many genes showed widespread expression levels in the study group. Interferon-gamma induced C-X-C motif chemokines 10, 11 and 13 demonstrated reduced expression in normal, ABOi and C4d-positive study group samples, when compared to rejecting samples. However, IFNG itself was elevated in some C4d positive samples (Figure 1). Reduced expression in the study group was also observed for GNLY, PLA1A and TRD, all associated with AbMR, and EV12A and PTPRC. Expression levels were comparable to normal and ABOi samples.

A spread of expression levels within the C4d positive group indicates a heterogeneity that is not yet fully defined. Elevation of IFNG without chemokine elevation suggests in some cases rejection is initiated but subsequently halted, similar to accommodated grafts apparently blocking the complement cascade after C4d deposition.

Following up these patients to determine which develop AbMR is crucial to furthering our understanding of the rejection and accommodation processes.

Figure 1
SCIENTIFIC PROGRAMME

Oral Sessions
OS1-1

Monitoring miRNA-155-5p expression as biomarker of prognosis and diagnosis of acute rejection in liver and renal transplant recipients

Olga Millan1, Irene Aliart1, Klemens Budde2, Beatriz Bardaji3, Gonzalo Crespo4, Lluis Guirado2, Miquel Navasa4, Lara Orts4, Pablo Ruiz4, Claudia Sommerer4, Mercé Brunet1
1: Pharmacology and Toxicology Laboratory, CDB, IDIBAPS, CIBERehd, Hospital Clinic of Barcelona, University of Barcelona.
2: Medizinische Klinikum Schwerpunkt Nephrologie, Charité Universitätsmedizin Berlin, Germany.
3: Renal Transplant Unit, Nephrology Department, Fundació Puigvert, Barcelona.
4: Liver Unit, Hospital Clinic, IDIBAPS and CIBERehd, University of Barcelona.
5: Department of Nephrology, University of Heidelberg, Hospital University Heidelberg and Mannheim, Heidelberg, Germany

Background/Aims MicroRNAs (miRs) have been reported to play a role in immune system response. The results of several clinical trials have suggested that these molecules might be used as biomarkers to predict the risk of rejection. Our aim was to evaluate the clinical utility of monitoring miRs expression as prognostic and/or diagnostic biomarker of acute rejection (AR).

Methods 160 de novo transplant recipients were included: 80 liver patients from H. Clinic of Barcelona (single center) and 80 renal recipients (European multicenter). All patients were treated with Tacrolimus, Mycophenolic Acid and corticosteroids. For kidney recipients urinary miRs (miR-155-5p, miR-142-3p, miR-210-3p) and for liver recipients plasma miRs (miRNA-155-5p and miRNA-122-5p) expression was evaluated by quantitative RT-PCR pre-transplantation; 1st week, 1st, 2nd, 3rd and 6th month after transplantation.

Results Seventeen liver (21%) and eight renal (10%) recipients experienced biopsy-proven AR. Liver rejectors patients showed a significant increase of the plasmatic miRNA-155-5p, miRNA-122-3p before and during AR. Kidney rejectors showed also a significant gradual upregulation of the expression of miR-155-5p and miR-142-3p before and during AR and a significant decrease of miR-210-3p. Based on ROC curves, analysis of plasmatic and urinary miRNA-155-5p presents the best discriminatory capacity between rejectors and non-rejectors for both: Liver AUC =0.816 (P=0.05; 95% CI: 0.719-0.914; cut-off=0.22 sensitivity=71%, specificity=81%); Kidney: AUC=0.875 (P=0.046; 95%CI:0.784-0.966; cut-off=0.51 sensitivity=85% and specificity=86%).

Conclusions In summary, monitoring the expression of miRNA-155-5p in liver and kidney recipients has the potential to act as prognostic biomarker of AR risk. Prospective data from multicenter clinical trials are required to better qualify the clinical utility of this biomarker.

OS1-2

Bone marrow mesenchymal stem cells but not their extracellular vesicles improve kidney graft outcome in a model of chronic mixed cellular and humoral rejection in rat

Maria Jose Ramirez Bajo1, Jordi Rovira2, Marta Lazo-Rodriguez2, Elisenda Banon-Maneus1, Valeria Tubita2, Daniel Moya-Rull1, Natalia Hierro-Garcia2, Ignacio Revuelta2, Pedro Ventura2, Federico Oppenheimer2, Josep M. Campistol2, Fritz Diekmann3
1: Laboratori Experimental de Nefrologia i Trasplantament (LENIT), Fundació Clínic per la Recerca Biomèdica (FCRB), Barcelona.
2: Laboratori Experimental de Nefrologia i Trasplantament (LENIT), Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona.
3: Departament de Nefrologia i Transplantament Renal, Institut Clínic de Nefrologia i Urologia (ICNU), Hospital Clinic (HC), Barcelona

Background Bone Marrow Mesenchymal stem cells (BM-MSCs) have immunomodulatory properties and they secrete extracellular vesicles (EVs) than are mediators in interactions with immune cells. The aim of this study was to verify the immunomodulatory properties of BM-MSCs and their EVs from donor and recipient on kidney outcome in this chronic renal transplant.

Methods The heterotopic-kidney-transplant-rat Fisher-to-Lewis (F-L) model was performed to study chronic mixed cellular and humoral rejection. F and L-BM-MSCs and their EVs were administered: one dose of F-BM-MSCs and EVs after renal transplantation and 3 doses of L-BM-MSCs and EVs follow a preventive treatment (0, 4 and 8 weeks) and curative treatment (3, 6 and 9 weeks). Renal function and survival were monitored. The kidney graft was cut to assess infiltrating lymphocytes by flow cytometry and histological lesions.

Results F and L-BM-MSCs administration in all type of treatments significantly prolong survival and reduce the BUN levels and blood creatinine but it is not observed in the case of EVs. Renal tubulitis was decreased in all treatments with BM-MSCs and EVs showed statistical significance in preventive L-EVs and F-BM-MSC and curative in L-BM-MVs (* p<0.5 & ** p<0.05). The study of infiltrating lymphocytes by flow cytometry showed that only L-BM-MSCs significantly reduce T-cell filtration. Moreover, the T-cell population was increased in the case of curative L-EVs.

Conclusion BM-MSCs from donor and receptor but not their EVs, prolong graft and recipient survival. They improve graft function associated with diminution of both, tubular damage and of the T-cell infiltration.
MiRNA 181a and 148a plasma levels during acute cellular rejection in liver transplantation

Pablo Ruiz1, Olga Millan2, Lara Orts1, Irene Aliart2, Alba Diaz3, Lydia Sastre1, Jordi Collmenero1, Gonzalo Crespo1, Mercè Brunet2, Miquel Navasa1
1: Liver Transplant Unit, Hospital Clinic, IDIBAPS, CIBERehd, Barcelona. 2: Pharmacology and Toxicology, Hospital Clinic, IDIBAPS, CIBERehd, Barcelona. 3: Pathology Department, Hospital Clinic, Barcelona

Background and aims MicroRNAs (miRNAs) are small noncoding RNAs that regulate gene expression posttranscriptionally. In liver transplantation (LT), previous retrospective studies have suggested an association between miRNA 148a and acute cellular rejection (ACR). miRNA 181a expression in T cells is associated with an increased sensitivity to antigens. We aimed to assess the role of these miRNAs as biomarkers of ACR in LT.

Methods We performed a prospective, longitudinal study that included de novo LT recipients during 18 months. Plasma levels of miRNA 148a and 181a were measured 1 week, 1 month, and 3 months after LT, as well as at any time of graft dysfunction, which was predefined and studied with liver biopsy. A protocol liver biopsy was performed at month 3, and patients were followed for 12 months.

Results Sixty-six LT recipients were included. During follow-up, 19 patients (29%) presented graft dysfunction that led to liver biopsy, among them 12 episodes of ACR were diagnosed (18%), miRNAs plasma levels did not predict ACR; however, at ACR, there was a significant elevation of miRNA 181a (p=0.008) and 148a (p=0.001) with respect to previous levels. At the moment of graft dysfunction, a trend towards a difference in the levels of miRNAs between ACR and ischemia-reperfusion lesion was observed (p=0.06 and 0.11).

Conclusions miRNA 181a and 148a plasma levels significantly increase during ACR in LT, and they also may differentiate ACR from other causes of graft injury. Our data support further research in order to elucidate the potential role of miRNAs as biomarkers.

Impact of the new evaluation of glomerulitis according to Banff 2013 classification of antibody-mediated rejection

Javier Gimeno1, Dolores Redondo2, Maria Jose Pérez-Saez2, Dolores Naranjo-Hans1, Marisa Mir2, Julio Pascual2, Marta Crespo2
1: Department of Pathology, 2: Department of Nephrology, Hospital del Mar, Barcelona

Background Banff’13 classification introduced relevant changes in the criteria for antibody-mediated rejection (ABMR) in kidney allografts. We assessed the effects of these changes in glomerulitis.

Methods 73 kidney graft biopsies were evaluated according to Banff’09 and reassessed using Banff’13 by two pathologists, focused on the main changes introduced in ABMR.

Results With Banff’09, 34 samples (46.6%) showed glomerulitis (g1-n = 24, g2-n = 6, g3-n = 4), while Banff’13 reduced the presence of glomerulitis to 25 (34.2%) (g1-n =15, g2-n = 6, g3-n = 4). All biopsies previously identified as moderate-to-severe glomerulitis, showed variable occlusion of glomerular lumens, conserving the initial score. However, 9 biopsies initially g1 were reclassified to g0 with Banff’13 reassessment. At the time of the biopsy and based on Banff’09, HLA-DSAs were detected in 22 samples with glomerulitis (64.7%) and in 11 g0 (28.2%) (p=0.002*). With Banff’13, DSAs were detected in 68% and 33.3%, respectively (p=0.05). Two biopsies g0 (5.1%) and eleven with glomerulitis (32.3%) (p=0.002*) showed diffuse staining of C4d with Banff’09; the percentages were 12.5% and 28% (p=0.118), with Banff’13. Within the nine g1 reclassified as g0, diffuse positive C4d was present in three and DSA in five. Five of these g0 cases fall in Banff’09 Category 2 (three ABMR and two suspicious of ABMR); in absence of glomerulitis with 2013 definition, 4 samples remain in Category 2 (3 ABMR and 1 suspicious) and the other falls in Category 5 (IF/TA+DSAs).

Conclusion Banff’13 decreased the frequency of glomerulitis, the impact of this change in ABMR diagnostic accuracy remains uncertain, however, it may increase the specificity of glomerulitis as a marker of ABMR.
Complement-binding donor-specific antibodies, acute rejection and kidney graft loss: C3d better than C1q

Marta Crespo1, Dolores Redondo1, María José Pérez-Sáez1, Javier Gimeno2, Carme Garcia3, Marisa Mir1, Juan José Hernández3, Julio Pascual4
1: Department of Nephrology, 2: Department of Pathology, 3: Reference Laboratory, Hospital del Mar, Barcelona

Background Not all DSA produce the same consequences. Early complement-binding DSA have shown correlation with rejection (ABMR) and loss, but information late after KT is limited. We evaluated C3d and C1q-binding DSA long-term after KT.

Methods Prospective study of 425 active KT transplanted 1979-2012. C3d and C1q binding were assessed for samples with DSA. For analysis, we selected the first time point when the patient showed a C3d+DSA, first DSA when C3d- or first time tested in the absence of DSA (median time post-KT 31 months).

Results 382 had no DSA and 43 showed DSA-II: 32 C3d+ and 11 C3d-DSA. C3d+KT show ed worse graft survival and proteinuria than patients without DSA (p=0.001), but C3d-neg DSA-II did not (p=0.13). C3d+KT and C3d-KT were similar in age, transplant number, pretransplant DSA, acute rejection, immunosuppression and GFR. Most DSA were DQ. C3d+ were stronger than C3d- (MFI: 19300±11319 vs 4787±4728, p=0.001). C3d+DSA patients showed ABMR more frequently than C3d-DSA (81.3% vs 42.9%, p=0.006), higher microinflammation (p=0.01) but similar C4d+ or transplant glomerulopathy. The 43 KT DSA-II+ were tested for C1q: 28 were C1q+ and 15 negative. Unlike C3d+, C1q+ did not correlate with ABMR. Results were concordant in 81.4%. Seven patients had C3d+C1q-: 2 lost the graft, 4 had ABMR and only one had normal biopsy. The only patient with C3d-C1q+ DSA had not ABMR.

Conclusions Post-KT C3d binding DSA-II identifies recipients at higher risk of ABMR and graft-loss. C1q lacked to categorize a significant number of patients with DSA compared with C3d.

Outcomes of kidney transplantation in patients with preformed, cleared or persistent, HLA donor-specific antibodies

Dolores Redondo1, Marua José Pérez-Sáez1, Marisa Mir1, Javier Gimeno2, Carmen Garcia3, Juan José Hernández2, Jose Yélamos4, Julio Pascual1, Marta Crespo1
1: Department of Nephrology, 2: Department of Pathology, 3: Reference Laboratory, 4: Department of Immunology, Hospital del Mar, Barcelona

Background The presence of donor-specific antibodies (DSA) increase the risk of antibody-mediated rejection (ABMR) and graft failure in kidney transplant recipients (KTR). We aimed to analyze the evolution of preformed DSA after KT and their impact on graft survival.

Methods A prospective study was conducted in 370 KT recipients. DSA were assessed at baseline, 1-3-5 years after KT by Luminex® platform, considering a MFI>1000 as positive.

Results The 39 KTR (10.6%) who had preformed DSA (17 class-I/I&II and 22 class-II) presented with lower acute-ABMR-free survival [HR 10.6 (95% CI 5.5-20.4); p<0.001] and lower graft loss-free survival [HR 2.5 (1.3-4.7); p=0.003] than patients without antibodies. Early acute ABMR was more frequent among patients with preformed DSA class-I or I&II than class II alone (29.4% vs 4.5%, p=0.02). All patients with DSA class-I/I&II and acute ABMR lost their grafts but none of DSA class-II alone. At 1 year post-KT, 20 (58.8%) patients had persistent DSA. Preformed DSA class-II alone persisted more frequently than class-I/I&II [66.7% vs 33.3%; p=0.031]. The only risk factor associated with the persistence of DSA was pre-KT MFI [OR 1.01 (1.001-1.010); p=0.023]. Although in our overall population the highest risk of graft loss was found in patients with de novo DSA (HR 5.9[3.9-25.0]; p=0.016), graft loss was also very significant in KT recipients with either persistent preformed DSA (HR 4.8[2.27-10.38]; p=0.016) or those who cleared preformed DSA during follow-up [HR 3.7 (1.28-10.59); p=0.015].

Conclusions Preformed DSA are deleterious to graft survival, and the risk does not decrease significantly after post-KT DSA clearing.
Long-term evolution of living kidney donors in Catalonia

Enrique A. Flori1, Rebeca Jurado Tapiador1, Emma Arcos Fuster2, Jordi Comas Farnés3, Salvador Gil-Vernet3, Lluis Guirado Perich4, Ricardo Lauzurica5, Francesc Moreso6, Julio Pascual2, Jaume Tort Bardolet2, Fritz Diekmann1

1: ICNU, Hospital Clinic. 2: Organización Catalana de Trasplante. 3: Hospital Universitario de Bellvitge. 4: Fundación Puigvert. 5: Hospital Universitario Germans Trias i Pujol. 6: Hospital Vall d’Hebron. 7: Hospital del Mar, Barcelona

Facing the increased demand of organs, the selection criteria for living kidney donors have been expanded: hypertension, obesity, donor age over 60 years and/or history of nephrolithiasis. We conducted a retrospective analysis of donor evolution with or without expanded criteria.

Data was collected from the Catalan Transplant Organisation (OCATT) registry from 1969 to 2015. Two groups were created: A) standard criteria, and B) "expanded criteria" as defined above. We evaluated renal function, proteinuria, mortality and end stage kidney disease.

Among 1549 nephrectomies, we analysed 926 donors in group A and 463 in B. The ages at time of nephrectomy were 45.7±8.8 and 59.6±9.5 years respectively (p<0.0001). The CKD-EPI GFR (ml/min/1.73m²) in group A were 95.2±15.4 pre nephrectomy, 62±24.4 at one year, and 67.4±13.9 at 15 years, whereas in group B were 87.6±14.7, 55.3±15 and 56.9±13.9 respectively. The differences between the groups were statistically significant at any time. In contrast, there was no significant difference in proteinuria between the two groups at 15 years [60 (46-100) VS 70 (48-120) mg/24h]. 37 deaths (A=20 VS B=17) were registered; one death occurred within one month after nephrectomy. The age-adjusted mortality between the two groups was the same. Noticeably, one donor began dialysis at 72 y.o., 16 years after nephrectomy (unknown aetiology of CKD), and died at age 80 due to a myocardial infarction.

In conclusion, living donation is safe at short and long term. Renal function and health of donors does not seem to be seriously compromised, even when expanded criteria are applied.

Factors associated with infra-compensation of the remaining kidney after total nephrectomy after donation

Carla Burballa1, Marta Crespo1, Dolores Redondo-Pachón1, Maria José Pérez-Sáez1, Marisa Mir1, Lluis Fumadó2, Albert Francés2, Josep Maria Puig1, Lluis Cecchini2, Julio Pascual1

1: Department of Nephrology, 2: Department of Urology, Hospital del Mar, Barcelona

Introduction We aim to evaluate the factors associated to the infra-compensation of renal function by the remaining kidney in individuals who undergo nephrectomy for renal donation.

Methods In a series of consecutive living kidney donors at our institution, we studied the efficiency of compensatory mechanisms of the remaining kidney after donation. We also evaluated the potential factors associated by comparing patients included in either of the groups according to the rate of GFR compensation rate (Group A, infra-compensation [<70%]; Group B normal compensation [>70%]).

Results We included 64 donors (70, 6% women; median age 48, 34±11 years). Baseline serum creatinine was 0, 8±0, 1mg/dl and 1, 1±0, 2mg/dl one year after donation. We compared Group A (compensation<70%, n=38) and group B (compensation>70%, n=22). Predictors for compensation >70% were female gender (p=0.03) and a lower GFR both estimated by MDRD4 (A vs B 93, 73±19, 6 vs 78, 1±1 15, 3; 4p=0.001) or CKD-EPI (A vs B 97, 7±14, 7 vs 86, 1±1 15, 2; 17 p=0.005). Age, Body Mass Index, Hypertension or GFR measured by Tc99m-DTPA did not show significant association with remaining kidney rate of compensation. Multivariate analysis confirmed equation-estimated baseline GFR as a predictor of compensation: the higher baseline GFR, the lower the chance for compensation >70% of baseline renal function one year after donation (MDRD4 OR=0.50 [0.91-0.99], p=0.01; CKD-EPI OR=0.95 [0.91-0.99], p=0.02 respectivamente).

Conclusions The remaining kidney partially compensates renal function after living donor nephrectomy. A high baseline eGFR predicts limited compensation. A relatively low baseline eGFR is associated with a higher percentage of contralateral kidney function increase.
Survival comparison among kidney transplant recipients from deceased donors over 80 years and patients on dialysis awaiting transplantation

Emma Arcos1, María José Pérez Sáez2, Jordi Comas1, Julio Pascual2
1: Registre de Malalts Renals de Catalunya, Organització Catalana de Trasplantaments. 2: Dept Nephrology, Hospital del Mar, Barcelona

Background Patient survival with end-stage renal disease is longer after kidney transplantation (KT) compared with remaining in the waiting list on dialysis. We have questioned if this is true also using kidneys from donors ≥80 years-old.

Methods In a longitudinal mortality study in the Catalan Renal Registry, including 2098 patients on dialysis placed on waiting list, 293 of them received a first KT from a deceased donor 75-79 years-old and 94 from a deceased donor ≥80 years-old. The reference group included 2,040 patients who were placed on the waiting list (relative risk, 1.0). Patients in both groups had equal lengths of follow-up since placement on the waiting list. The adjusted risk of death and survival were calculated by non-proportional-hazard analysis taking the fact of being transplanted as a time dependent effect.

Results Compared with kidneys from donors <75y, graft survival was significantly lower for kidneys 75-79y (HR 1.28, 1.05-1.56) and ≥80 (HR 1.66, 1.18-2.34), but significance disappeared when including only recipients >70y. In comparison with those that remained on dialysis (HR 1), non-proportional adjusted risk of death after KT with a kidney 75-79yr was 0.38[95% CI 0.29-0.50; p<0.001] and with a kidney >80yr was 0.49[0.31-0.77; p<0.001] (see table). Projected years of life since placement on the waiting list was 6.5y without KT, 10.4y receiving a kidney 75-79 and 9.2y receiving a kidney >80.

Conclusion Despite KT from octogenarian deceased donors is associated with reduced graft survival, transplanted patients have lower mortality than those remaining on dialysis.

Relative’s perception about the tissue donation process: result of post donation phone survey

Rebeca Roque, Camino Rodríguez-Villar, David Paredes, Angel Ruiz, Rosana Gelpi, Javier Garcia, Samuel Rodriguez, Ramon Adalia
Sección de Donación y Coordinación de Trasplantes, Hospital Clinic, Universidad de Barcelona

Introduction Tissues donation (TD) requires to clearly explain the characteristic of TD that can affect the integrity of the body and delays in disposability of the body that can affect the funeral processes. The main objective was to evaluate global hospital care, care from Transplant Coordinators (TC), the correlation between information received and relative’s perception of the donation process including body integrity and funeral customs and intention to donate again.

Methodology Phone survey of 10 multiple-choice items was conducted one year after donation, to all TD relatives that agreed to donate tissues during 2014.

Results From 166 TD performed, all were included, the number of answered was 75 (45%). The hospital care evaluation was of 49% of cases as good and 40% very good. The TC care was rated as good by more than 50% of cases and very good in 40%. The information received about the donation process was considered good or very good in 90% of cases and the information received with the post donation experiences was considered very well correlated. Concerning TD global experience, the process did not cause problems with funeral services. The 40% of relatives didn’t expect to be requested for TD and the 10% did not know if they would donate again.

Conclusion The relative’s perception of care is a critical component of the quality evaluation of the TD process. The global evaluation results support our strategies for family approach for TD. However, it implies a permanent awareness and training to maintain the good quality of care and support the concept of continuous evaluation.
Strategy to assess extended donor criteria renal suitability: a paired kidney study comparing hypothermic pulsatile perfusion machine versus cold storage

David Paredes1, Anna Sánchez2, Angel Ruiz1, Camino Rodriguez-Villar1, Rebeca Roque1, Rosana Gelpi1, Javier Garcia1, Lluís Peri3, Fritz Diekmann2, Frederic Oppenheimer2, Ramon Adalia1
1: Donation and Transplant Coordination Unit, 2: Kidney Transplant Unit, 3: Urology Department, Hospital Clinic, University of Barcelona

Introduction
Extended Criteria Donors (ECD) after Brain Death represents 50% of donor activity. Since 2004, to assess kidney suitability a step-wise strategy combines Kidney Biopsy Score (KBS) and renal hemodynamic evaluation with Hypothermic Pulsatile Perfusion Machine (HPPM). Transplantation criteria are KBS<3, Renal Resistance (RR) <0.4 ml/mmHg/mL/min and Renal Flow (RF) >70ml/min.

Methods
Between June 2004 and December 2013, paired kidneys where one was preserved in Cold Storage (CS) and other with HPPM. End point: Primary Non Function (PNF), delayed graft function, hospital length, one year creatinine and graft survival. Data analyzed with SPSS.

Results
196 paired kidneys were randomly allocated to one preservation strategy. Comparing both strategies no differences in age, gender, cardiovascular risk factors, cause of death and KBS. Significant differences were Transplant Rate (TR) 73.3% in CS vs 90.6% in HPPM; PNF 7.2% vs 1% and hospital length over 10 days 64.2 vs 46.7%, comparing CS vs HPPM respectively. Additionally, a longer cold ischemia time 18, 3 vs 14, 9 hours, because CS kidney were grafted before HPPM kidney.

Conclusions
Although the significant amount of ECD kidneys, the systematic use of HPPM has allowed maintaining a high TR. When comparing both preservation methods, a tendency for a better preserved organ with less PNF and less hospital stay length, justify the use of the HPPM as an essential tool to evaluate kidney suitability in brain death ECD. Additional analysis of the evolution of grafted kidneys according with the stratification of HPPM selection criteria are undergoing and will be presented as well.

Effect of the lung allocate score in postoperative lung transplantation in a university hospital

Irene Bello1, María Deu1, Laura Romero1, Alberto Jauregui1, Javier Pérez1, Juan Manuel Ochoa1, Vanessa Díaz1, Leire Sánchez1, Fernando Ascano1, Cristina Berastequi1, Alberto Sandiumenge1, Dani Ruiz1, Cesar Laborda1, Juan Solé1
1: Thoracic Surgery, 2: Pneumology, 3: Transplant Coordination, 4: Anesthesiology, 5: Intensive Care, Vall d’Hebrón University Hospital, Barcelona

Background
On 2014 the system for allocation of lung donors for transplant in HU V.H changed from allocation based on waiting time to allocation based on Lung Allocate Score (LAS score). We have analyzed the postoperative impact of this change.

Methods
We retrospectively reviewed the cohort of 248 adult recipients of lung transplantation performed between 01/01/2012 and 12/31/2015. Patients were grouped by type of allocation: before LAS era (BLE) and after LAS era (ALE)

Results
We didn’t find differences in receptor’s age, gender or type of lung disease; the number of receptor who needed oxygen requirements for arterial blood gas test and walking-6-minutes-test before lung transplant was increased in ALE (Table 1). The donor’s characteristics didn’t change (Table 2). We performed an increased number of bilateral lung transplant and more recipients needed transfusion of packed red blood cells in ALE; an increased number of PRBC introduction and more time of cardiopulmonary by-pass was needed in ALE (Table 3). After implementation of the LAS score the incidence of primary graft dysfunction and the incidence of pulmonary allograft rejection were decreased; we found an increased ICU length of stay without changes in hospital length of stay (Table 4). We didn’t found changes in one year and two year survival.

Conclusions
Allocating lungs for transplant based on urgency and benefit instead of waiting time was associated with a greater severity of recipients and an improvement of postoperative outcomes without changes in survival.
Impact on the perception and attitudes of an on-line educative action about limitation of life sustaining treatment (LLST), donation after brain death (DBD) and donation after circulatory death (DCD) on Spanish critical care doctors

Alberto Sandiumente1, Xavier Montañá-Carreras2, Maria del Mar Lomeró3, Juan Domingo Molina2, Maria Bodi4, Nuria Masnou5, Teresa Pont1
1: Transplant Coordination, University Hospital Vall d’Hebron, Barcelona. 2: Magnone e-Health and e-learning Services, Tarragona.
3: PhD student, Nursing University Rovira i Virgili. 4: Intensive Care Dept, University Hospital Joan XXIII, Tarragona.
5: Transplant Coordination, University Hospital Josep Trueta, Girona

Objective To assess the impact of training on perception and attitude on end-of-life care and donation.

Methods In 2015, an online course on LLST, DBD and DCD was delivered to 338 Spanish doctors. Participants were asked to complete a survey on their perceptions and attitudes before and after the educational intervention. McNemar’s test was used to compare paired nominal data. Significance p<0.05, SPSSv21©.

Results 74% (n=253) of the course participants completed both surveys (36.9±8.1 years old, 64.8% female). 68.8% were specialists and 27.7% were trainees at Spanish centres with donation (96.4%) and transplantation (47%) activity. Primary specialization was intensive care (64.8%), anaesthesiology (13.4%) and emergency (6.3%). Training increased the number of participants considering appropriate to incorporate donation into the end-of-life care plan (90.5% vs 97.2%) (p=0.002). After the course, an increasing number of participants agreed on a more active involvement of nursing staff in LLST decisions (59.2% vs 66.6%) (p=0.001) while more of them believed that the responsibility of the family should consist in understanding a medical decision (72.2% vs 89.9%) (p<0.001). Post-course, more participants rated “withdrawal” and “withholding” measures as ethically similar actions within LLST (43.3% vs 56.7%) (p<0.001). Training increased the number of participants considering appropriate the use of pre-emptive sedation in all patients undergoing LLST (71.0% vs 79.8%) as opposed to providing sedation only when suffering was evident (p<0.001). Training improved perception of DBD and DCD as reflected by an increase in the number of positive terms (maximum of 5) selected by participants to describe such programs (4.09±0.9 vs 4.8±0.6) and (2.9±1.2 vs 4.2±1.0) (p<0.001).

Conclusions Training doctors in end-of-life care and organ donation helps to eliminate misperceptions and leads to a positive attitude contributing to the development of such programs.

Donor mannose-binding lectin (MBL) gene polymorphisms increases the risk of severe bacterial infections after liver transplantation

Julissa Lombardo1, Gemma Sanclemente2, Jordi Colmenero1, Marta Español3, Pablo Ruiz1, Gonzalo Crespo1, Lydia Sastre1, Asunción Moreno2, Francisco Lozano2, Miquel Navasa1
1: Liver Transplant Unit, Hospital Clinic, IDIBAPS, CIBERehd, Barcelona. 2: Infectious Diseases, Hospital Clinic, Barcelona. 3: IDIBAPS area 1, Hospital Clinic, Barcelona

Backgrounds Mannose-binding lectin (MBL) is a serum molecule that binds to bacterial and fungal antigens as a part of the innate immunity. Mutations in the MBL2-gene (A/O; O/O; XA/XA vs other alleles) behave different serum levels (“MBL-insufficient” vs “MBL-sufficient” producers, respectively). Since MBL is synthesized in the liver, its serum levels after liver transplantation (LT) depend on the donor MBL2 genotype.

Aims To evaluate the influence of the donor MBL2-genotype on the incidence of infections, cellular rejection, and patient and graft survival within 1-year after LT.

Methods 240 paired donors and LT recipients (2007-13) at Hospital Clinic, Barcelona.

Results Infections occurred in 146 (61%) recipients: 135 (56%) were bacterial, 14 (6%) fungal, 32 (13%) viral non-CMV, 47 (19%) CMV infection and 15 (6%) CMV disease. The most common bacterial infections were urinary tract infection (26%) and pneumonia (22%). Recipients of MBL-insufficient producer donors had higher incidence of bacterial infection episodes (OR=1.48; CI 1, 04-2, 09; p=0, 028), first episode of pneumonia (OR=2, 13; CI 1, 17-3, 86; p=0, 013) and septic shock (OR=5, 62; CI 1, 92-16, 44; p=0, 002) compared to recipients of MBL-sufficient producer donors. The incidence of CMV infection/disease, fungal infection, cellular rejection or patient/graft survival was similar in both groups.

Conclusions LT recipients of MBL-insufficient producer donor (genotype-A/O; O/O; XA/XA) have a higher risk of developing bacterial infection, first episode of pneumonia and septic shock after LT. Donor MBL2 genotyping could help identify LT recipients at a higher risk of severe bacterial infectious complications. Further studies are needed to evaluate the effect of antibiotic prophylaxis or recombinant MBL replacement for LT recipients of MBL-insufficient producer donors.
Short and long-term outcomes in liver transplantation of arterial reconstruction on the recipient’s splenic artery due to inadequacy of the hepatic artery. Experience in our center after 1500 liver transplants

Alejandro Bravo Salva, Laura Llado Garriga, Emilio Ramos Rubio, Juli Busquets Barensq, Lluis Secanella Medayo, Kristel Milis Julià, Nuria Peláez Serra, Emma Gonzalez Vilatsarana, Joan Fabregat Prous
Liver Transplant Unit, University Hospital of Bellvitge, Barcelona

In liver transplantation in case of inadequacy of hepatic artery anastomosis several technical options have been proposed. The aim of the study is to analyze our short and long-term outcomes of arterial reconstruction on the splenic artery.

Methods This study prospectively analyzes our experience with 54 patients in whom arterial anastomosis were performed on the recipient’s splenic artery (SA group) compared to the group of patients with standard HA anastomosis (HA group; n=1405) between 1984 to 2016. Patients with other type of anastomosis were excluded.

Results Patients in SA group were more frequently retransplantations (SA: 17 (31.5%) vs HA: 113 (8%); (p=0.001). SA group required transfusion more frequently (SA: 88% vs HA: 69%; p= 0.001), duration of surgery (SA: 424± 95 min Vs HA: 394 ± 102 min; p= 0.02) and hospital stay were longer (SA: 28.5± 29 days Vs HA: 20 ± 18 days; p= 0.04). There were no differences on arterial complications (SA: 8 Vs HA: 96; p=0.18), biliar tract complications (SA: 7 (12, 9%) Vs HA: 47 (10, 7%); p=0.61) nor postoperative mortality (SA: 13% SA vs HA 7% ; p=0.127).

Five year actuarial survival was similar between groups (59.2% SA vs 55.6% HA; p=0.593).

Conclusions Anastomosis with the recipient’s splenic artery is a safe alternative in liver transplantation with good short and long-term outcomes.

Endoscopy vs surgery for the treatment of anastomotic biliary stricture following deceased donor liver transplantation

Kristel Milis1, Laura Llado1, Carme Baliellas1, Joan B. Gornals2, Claudia Consiglieri2, Emma Gonzalez-Vilasartana1, Juli Busquets1, Emilio Ramos1, Joan Fabregat1
1: Unitat de Cirurgia Hepatobiliopancreatica i Trasplantament, 2: Aparell Digestiu, Hospital Universitari de Bellvitge, l’Hospitalet de Llobregat

Background and aims Nowadays endoscopy is considered the first line treatment for anastomotic biliary stricture (ABS) after liver transplantation (LT). Since 2012, we perform an endoscopic treatment in every patient who develops an ABS. The aim of this study is to compare de results of patients treated endoscopically to those before 2012, treated with surgery (hepatico-jejunostomy).

Methods We included all patients diagnosed with ABS after LT since 2012 (n=18). All of them were treated with endoscopic retrograde colangiography with maximal stent therapy. We compared these patient with a group of patients treated before 2012 with surgery (n=18).

Results A mean of 4, 7 procedures per patient were necessary in the endoscopic group, and 1, 5 procedures in the surgery group (p<0.05). 9 patients (50%) in the endoscopic group presented morbidity, without major complications. In the surgery group, 4 patients (22, 2%) presented morbidity (p=0, 08), 2 of them died (p=0, 15) and 1 required retransplantation (total of 3 graft loses, p=0, 07). Initial success was achieved in 94, 4% (n=17) in both groups. Final success was achieved in 66, 7% (n=12) in the endoscopic group, and 72, 2% (n=13) in the surgery group (p=0, 72). Recurrence appeared in 4 patients in the endoscopic group, and 4 patients in the surgery group (p=0, 92). The duration of treatment was significantly higher in the endoscopic group (326 days vs 90 days, p<0, 05).

Conclusions Endoscopic treatment of ABS after LT is safe and effective, and should be considered as the first line treatment for ABS. Hepatico-jejunostomy should be reserved for those patients in which the endoscopic treatment is not successful.
Impact of sustained virological response on liver fibrosis in recurrent hepatitis C after liver transplantation

Ezequiel Mauro¹, Gonzalo Crespo¹, Maria-Carlota Londoño¹, Alba Díaz², Lydia Sastre¹, Pablo Ruiz¹, Jordi Colmenero¹, Xavier Forns¹, Mercè Brunet³, Miquel Navasa¹

1: Liver Transplant Unit, 2: Pathology Department, 3: Pharmacology and Toxicology, Hospital Clinic, IDIBAPS, CIBerehd, Barcelona

Background  New direct-acting antivirals (DAAs) have revolutionized the prognosis of liver transplant (LT) recipients with recurrent hepatitis C, in which sustained virological response (SVR) has shown to improve survival. We aimed to describe the degree of fibrosis regression with SVR and its associated factors in a large cohort of LT recipients.

Methods  All LT recipients who underwent antiviral therapy between 2001 and 2015 and achieved SVR were included. A liver biopsy (with or without HVPG and LSM) was performed before treatment. One year after SVR, liver biopsy (if at least F1 before treatment), HVPG (if at least HVPG6 mmHg before treatment) and LSM were repeated. Fibrosis regression was defined as a decrease ≥1 stage in the METAVIR score one year after treatment.

Results  One-hundred-and-eight patients were included. Before treatment, significant fibrosis, cirrhosis and fibrosing cholestatic hepatitis (FCH) were present in 74%, 25% and 11%, while one year after SVR, respective categories included 53%, 14% and 0%; with 71% of the cohort presenting fibrosis regression. Fifty-six percent of recipients with cirrhosis presented regression, compared with 70-80% in the rest of stages (p=0.036). Changes in HVPG and elastography paralleled changes in fibrosis. Factors associated with fibrosis regression were pre-treatment HVPG and elastography, time between LT and treatment, a previous decompenation episode before therapy and elastography reduction during treatment.

Conclusion  Our results show that patients treated early after transplantation and without significant graft damage have a much higher chance to undergo regression of liver fibrosis, suggesting that antiviral treatment with new drugs should not be delayed in this population.

Incidence of de novo tumors after liver transplantation and influence on survival of conversion to mTOR inhibitors

Mónica Serrano, Laura Lladó, Carmen Ballellas, Xavier Vilaseca, Emilio Ramos, Juli Busquets, Emma González-Vilatarsana, Lluís Secanella, Núria Peláez, Joan Fabregat

Liver Transplant Unit, Hospital Universitario Bellvitge, l’Hospitalet de Llobregat

Background and aims  The most important long-term causes of death after liver transplantation are cardiovascular diseases and de novo tumors. Some evidence suggests that mTOR inhibitors could influence on the evolution of these patients. The objective is to evaluate the incidence of de novo tumors, risk factors and influence of mTOR inhibitors conversion on survival in patients diagnosed of de novo tumors at our institution.

Methods  Prospective evaluation of patients transplanted between 2005 and 2015. We compare patients with and without de novo tumors.

Results  The incidence of de novo tumors was 10% (63/620). The most frequent were cutaneous tumors (14/22%), followed by lymphoproliferative (10/16%), and gastrointestinal (12/10%). 32 patients died during follow-up (51%), most of them (80%) due to the tumor. Patients with de novo tumors were older (57.3±9 vs. 54.5±10, p=0.015) and more frequently previous alcohol consumers 79% (50) vs. 51% (319), p=0.008 compared to patients without de novo tumors. Patients with de novo tumors treated with mTOR inhibitor had similar survival compared to patients not converted to mTOR inhibitor (p=0.848). After splitting patients depending on the type of tumor (cutaneous vs other) there were neither no differences between patients converted or not to mTOR (cutaneous; p= 0.592; Non-cutaneous: p=0.698).

Conclusions  Age, male gender and enolism are risk factors of development of de novo tumors after liver transplantation. Conversion to mTOR inhibitors is not associated with improvement in survival.
Incidence of non-skin cancer after kidney transplantation: risk factors and long term impact

Anna Buxeda i Porras, Dolores Redondo, María Jose Pérez, Álvaro Bartolomé, Marisa Mir, Ana Pascual, Anna Sans, Marta Crespo, Julio Pascual
Department of Nephrology, Hospital Del Mar, Barcelona, Spain

Introduction Cancer after kidney transplant (KT) is the only cause of death that increases in large records. Its incidence is higher compared to the general population and the prognosis is worse. We analyzed incidence, risk factors and characteristics of cancers in a cohort of KT recipients with long term follow-up.

Methods Retrospective study of KT performed at our center 1979-2014 (n=942), followed until April-2016. Solid organ tumors and lymphomas were analyzed, excluding skin tumors.

Results 110 (11.7%) developed solid organ tumors (9%) or lymphoma (2.7%). The median postKT time to diagnosis was 6 years (IQR 3, 1-10, 7), estimated incidence 18.3 cases/year, or 2121 cases/100.000 inhab/year. The estimated incidence in general population in our community is 520/100.000 inhab/year: 4.1 times lower than in KT population. Solid organs affected were: lung (30%), bladder (11%), prostate (11%) and native kidney (7%). The prevalence of cancer in patients followed for a very long period is extremely high (25% of patients who reach 20 years after KT). Patients who developed cancer had received more thymoglobulin as induction therapy (31% vs. 18%, p=0.002) and cyclosporine (47.3 vs. 32.5%, p=0.003). In multivariate analysis, adjusted cancer risk factors: thymoglobulin induction [OR 1.752, 1.073-2.861; p=0.025] and time after KT [OR 1.061 (1.017-1.105)/year; p=0.005]. Cancer was associated with much lower patient survival.

Conclusions The incidence of non-skin cancer after KT is four times higher than in the general population. The prevalence in KT patients followed for longer time is high. Lung is the most common solid organ affected. Thymoglobulin induction could be a modifiable risk factor.

Adaptive NKG2C+ NK cell response and the risk of cytomegalovirus infection in kidney transplant recipients

Dolores Redondo1, Marta Crespo1, Jose Yélamos2, Aura Muntasel1, Maria José Pérez-Sáez1, Carlos Vilches3, Julio Pascual1, Miguel López-Bote2
1: Department of Nephrology, Hospital Del Mar, Barcelona.
2: Department of Immunology, Hospital Del Mar, Barcelona.
3: Department of Immunology, Hospital Puerta de Hierro, Madrid

Background Cytomegalovirus (CMV) infection in kidney transplant recipients (KTR) has been associated with an increased risk of graft loss and reduced host survival. CMV promotes persistent expansions of NK cells expressing the CD94/NKG2C receptor. The NKG2C (KLRC2) gene is frequently deleted and copy number influences the adaptive response of NKG2C+ NK cells.

Methods The distribution of NKG2C+ NK cells and NKG2C genotypes (NKG2C+/+, NKG2C+/del, NKG2Cdel/del) were studied in cross-sectional (N=253) and prospective (N=122) KTR cohorts. Assessment of CMV viremia was restricted to symptomatic cases in the retrospective study, but was regularly monitored in the prospective cohort.

Results Overall, the proportions of NKG2C+ NK cells were significantly higher in KTR who had suffered post-transplant symptomatic CMV infection in the cross-sectional study. Yet, along the prospective follow up (3, 6, 12 and 24 months), post-transplant NKG2C+ NK cell expansions were not observed in every patient with detectable viremia who received preemptive anti-viral therapy, suggesting that the adaptive NK cell response may be inversely related with the degree of CMV control. Remarkably, the incidence of post-transplant viremia was reduced among cases with high pre-transplant levels of NKG2C+ NK cells. The NKG2C genotypes distribution was comparable in KTR and healthy controls, and greater proportions of NKG2C+ cells were detected in NKG2C+/+ than in NKG2C+/del patients. Yet, a trend towards increased NKG2C+/del and reduced NKG2C+/+ frequencies associated to symptomatic infection was appreciated in both cohorts.

Conclusion Our results indirectly support that adaptive NKG2C+ NK cells are involved in the control of CMV in KTR.
Impact of rATG on CMV-specific memory T cell homeostatic proliferation and its implication in CMV infection

Marta Jarque¹, Sergi Luque¹, Elena Crespo¹, Edoardo Melilli², Joan Torras², Josep Maria Grinyó², Oriol Bestard²
¹: Experimental Nephrology Laboratory, IDIBELL, Barcelona. ²: Kidney Transplant Unit, Nephrology Department, Bellvitge University Hospital, Barcelona

Human CMV infection is the most common opportunistic infection in kidney transplantation, with impact on both graft and patient survival. T-cell responses are crucial for controlling viral replication. Transplant recipients are at risk of CMV infection, particularly when using T-cell depleting agents such as rabbit anti-thymocyte globulin (rATG). Whether CMV-specific memory T cells repopulate after rATG treatment and how they influence on infection has not been well documented.

Methods We evaluated CMV-specific memory T-cell responses using the IFN-γ ELISPOT assay (T-SPOT.CMV) in 70 kidney transplant recipients receiving either rATG (n=42) or anti-IL2R monoclonal antibodies (basiliximab®) (n=28) induction therapy followed by tacrolimus, MMF and steroids as maintenance treatment. We monitored the response against two dominant CMV antigens (IE-1 and pp65) at baseline, two weeks and at one, three and six months after transplantation and evaluated their impact on CMV infection.

Results RATG-treated patients showed a generalized abrogation of CMV-sp T-cell frequencies over the first 6 months as compared to Basiliximab-treated patients. RATG-treated patients showed lower CMV-sp T-cell frequencies at 2weeks (p<0.05) but fully recovered by month 3 for pp65 and month 6 for IE-1 compared to baseline frequencies (p=NS). No impact on CMV-sp T-cell responses was observed regarding the type of preventive strategy followed. Notably, patients not recovering sufficient CMV-sp T-cell responses did more likely develop CMV infection as compared to those that fully recovered their CMV-sp T-cell response.

Conclusions rATG induction significantly impacts on CMV-sp memory T-cell responses, although a rapid homeostatic proliferation might be observed in some patients driving protection against CMV infection.
Isolated crystalloid podocytopathy with focal segmental glomerulosclerosis in renal allograft: an unusual presentation of post-transplant monoclonal gammopathy of renal significance

An-Hang Yang¹, Che-Chuan Loong², Niang-Cheng Lin², Chih-Yu Yang³
¹: Department of Pathology and Laboratory Medicine, ²: Department of Transplantation Surgery, ³: Division of Nephrology, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Background Monoclonal gammopathy of renal significance (MGRS) denotes a spectrum of hematological disorders which cause direct or indirect renal damage. MGRS in allograft kidney, if not properly treated, may cause severe consequences resulting in morbidity or even graft loss.

Methods Renal pathology diagnosis included light microscopy, immunofluorescent and immunohistochemistry analysis, and electron microscopy.

Results A 51-year-old man had received living-donor kidney transplant from his wife in 2008. He was found to have gradual increased proteinuria four years later. His renal biopsy revealed cytoplasmic crystalloid inclusions in the podocytes. No crystalloid inclusion was found in other renal cells. Despite that immunofluorescent examination failed to show light chain deposition, the serum immunoelectrophoresis revealed monoclonal IgGκ. Bone marrow biopsy showed infiltration of plasma cells about 10%. A follow up renal biopsy was performed in 2016. Light microscopy showed focal segmental glomerulosclerosis. The immunofluorescent examination remained negative for light chain, but κ-light chain could be demonstrated after antigen retrieval. Similar to previous biopsy, cytoplasmic inclusions were found only in podocytes. The crystalloid inclusions frequently protruded to form cilia-like membrane spikes on cell surface of podocytes.

Conclusions As far as our knowledge, this is the first report of MGRS presents as isolated crystalloid podocytopathy in the allograft kidney. The mechanism of preferential podocyte deposition of crystalloid immunoglobulin remains unclear. The inherent features of crystalloid podocytopathy may mislead the pathological diagnosis.

Nephrotic range proteinuria in renal transplantation: clinical and histologic correlates in a 10-year retrospective study

Rita Leal¹, Helena Pinto¹, Ana Galvão¹, Lidia Santos¹, Catarina Romãozinho¹, Fernando Macário¹, Rui Alves¹, Vitor Sousa², Carol Marinho², Lia Prado e Castro³, Arnaldo Figueiredo⁴
¹: Nephrology, ²: Anatomic Pathology, ³: Urology and Renal Transplantation, Centro Hospitalar e Universitário de Coimbra, Portugal

Background and aims Proteinuria of more than 1g/day is an accurate predictor of graft loss and more than 10% of renal transplant recipients develop nephrotic range proteinuria. Despite the high incidence of nephrotic proteinuria, its histologic correlates and prognostic implications are not well characterized. We assessed the clinical and histologic correlates of renal transplant patients with nephrotic range proteinuria (> 3.5g/day).

Methods We have retrospectively analysed 55 kidney transplant biopsies of 44 recipients with nephrotic range proteinuria between 2006 and 2015. The mean time of follow up was 86 months.

Results Our cohort included 86% recipients of deceased donor grafts. The maintenance immunosuppressive regimen was calcineurin inhibitors in 70% and m-Tor inhibitors in 30% of patients. The average proteinuria was 6.9±3.8 g/day, with 52% of patients presenting with nephrotic syndrome. The time between the transplant and the biopsy was 44 months (range: 24-102). The histological findings were: transplant glomerulopathy (22%), de novo glomerular disease (22%); recurrence of primary disease (22%), acute rejection (10%), tubular atrophy and interstitial fibrosis (16%) and other findings (8%). Only 7 patients (14%) had proteinuria remission after 3 months while 31 patients (62%) lost the graft at follow-up. There was no statistically significant difference between the histologic findings and graft outcome or between the immunosuppressive regimen and proteinuria levels.

Conclusions Nephrotic range proteinuria in renal transplant patients is related to high rate of graft loss. The main causes of nephrotic range proteinuria in patients undergoing biopsy are transplant glomerulopathy, recurrence of the underlying disease and de novo glomerulonephritis.
Vasa recta hyalinosis reflects severe arteriopathy extending to efferent arteriole in the latter phase of allografted kidney biopsy

Hideyo Oguchi1, Ken Sakai1, Yutaka Yamaguchi2, Takeshi Kawamura3, Masaki Muramatsu1, Itabashi Toshihiro1, Hyoudou Youji1, Takahashi Yusuke1, Nihei Hiroshi1, Yonekura Takashi1, Ohashi Yasushi1, Hamasaki Yuko1, Shishido Seichiro1, Mikami Tetsuo3, Nemoto Tetsuo4, Shibuya Kazutoshi4, Aikawa Atushi1

1: Nephrology, Toho University School of Medicine, Tokyo, Japan. 2: Yamaguchi Pathology Institution. 3: Toho University School of Medicine, Pathology. 4: Toho University School of Medicine, Hospital Pathology

Background and aims According to the Banff classification 2007, arteriolar hyaline thickening due to calcinulin inhibitor (CNI) was defined as the aah score by the replacement of degenerated smooth muscle cells by hyaline deposits. Our aim of this study is to examine the clinicopathologic significance of a hyaline deposition in the vasa recta (Vasa recta hyalinosis: VRH) in the medulla (figure).

Method We analyzed the protocol or episode biopsies which include vasa recta for more than 8 year after living kidney transplantation between January, 2012 and December, 2015. We excluded the specimen of the patients who had diabetic nephropathy as original disease and who had diabetes mellitus after kidney transplantation.

Result In 31 biopsy specimens which include vasa recta from more than 8 year after kidney transplantation, 13 VRH lesions were identified. In the VRH group, aah3 was observed in the 9 cases, aah2 was observed in the 4 cases, aah1 and 0 were not, and 12 cases showed efferent arteriolar hyalinosis. In contrast, in the non-VRH group, aah3 score was not observed, aah2 score was observed in the 6 cases, aah1 score was observed in the 8 cases, aah0 score was observed in the 4 cases and efferent arteriolar hyalinosis was observed in 1 case.

Conclusion VRH in renal allografts in the later period after kidney transplantation might correlate with severe aah lesion extending to efferent arteriole, while severe aah was not observed in non- VRH. VRH may help the diagnosis of the CNI arteriopathy.

Vasa recta hyalinosis

HMGB1 increase the survival pathways to protect steatotic and non-steatotic liver transplantation from cadaveric donors

Elsa N. Negrete-Sánchez1, Cindy G. Avalos de León1, Mónica B. Jiménez-Castro2, Arani Casillas-Ramírez3, María Eugenia Cornejo-Petronio1, José Guifó4, Ana Isabel Álvarez-Mercado1, Esther Bujaldón4, Jordi Gracia-Sancho5, Juan Rodés1, Carmen Peralta1

1: Instituto de Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona. 2: Transplant Biomedical S.L, IDIBAPS, Barcelona. 3: Hospital Regional de Alta Especialidad de Ciudad Victoria, Facultad de Medicina e Ingeniería en Sistemas Computacionales de Matamoros, Universidad Autónoma de Tamaulipas, México. 4: Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERHD), Barcelona. 5: Barcelona Hepatic Hemodynamic Laboratory, IDIBAPS, CIBERHD, Barcelona

Background A high percent the liver grafts undergoing transplantation derive from brain dead (BD) donors, which may also show hepatic steatosis, being both characteristics risk factors in liver transplantation (LT). Nevertheless BD reduces the tolerance of liver grafts to the preservation/reperfusion injury and reduces graft survival. HMGB1 acts as an alarm initiating the inflammatory response. We examined the mechanisms of HMGB1 in steatotic and non-steatotic liver grafts undergoing transplantation from BD donors.

Methods Steatotic and non-steatotic liver grafts from non-BD and BD-donors were cold stored for 6h and then transplanted. HMGB1 was pharmacologically modulated and the underlying mechanisms was characterized. In addition, the involvement of PI3K/Akt pathways in the effect of HMGB1 on damage and inflammatory response was evaluated.

Results Herein we show that BD reduces HMGB1 expression which is associated with inflammation and damage. The treatment with HMGB1 increases the PI3K/Akt cell survival signaling pathway and this result in protection against neutrophil accumulation, oxidative stress, and hepatic damage, altogether increasing the survival of recipients. In addition, PI3K/Akt inhibition abolished the benefits of HMGB1 in steatotic and non-steatotic liver grafts from BD donors. Thus, PI3K/Akt activation was responsible for HMGB1 benefits.

Conclusions Our findings propose a pharmacological intervention to activate the HMGB1 signaling pathway as a protective strategy to reduce the adverse effects of BD and to ultimately improve liver graft quality.
Pathological assessment of allograft nephrectomy; an Iranian experience

Diana Taheri¹, Mojgan Ghavami¹, Shahaboddin Dolatkhah², Mehdi Fesharakizadeh³, Shahrriar Fesharizadeh⁴, Parvin Mahzouni¹, Abdolamir Alapour⁵, Mozaffar Hashemi⁶, Hamid Mazdak⁷, Roxana Salahegheh⁸

¹: Pathology, Isfahan University of Medical Sciences, Isfahan, Iran. ²: Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. ³: Department of Surgery, Najaf Abad branch of Islamic Azad University, Isfahan, Iran. ⁴: Department of Biochemistry, San Francisco State University, San Francisco, USA. ⁵: Department of Nephrology, Isfahan University of Medical Sciences, Isfahan, Iran. ⁶: Department of Thoracic Surgery, Isfahan University of Medical Sciences, Isfahan, Iran. ⁷: Department of Urology, Isfahan University of Medical Sciences, Isfahan, Iran. ⁸: Faculty of Medicine, Yazd University of Medical Sciences, Isfahan, Iran

Background The aim of this study was to determine the pathologic causes of renal allograft failure in transplant nephrectomy (TN) specimens divided in early and late period after transplantation.

Materials and methods Medical files of patients who underwent TN in the referral transplant center of Isfahan provinces from March 2008 to March 2013 were studied. In some cases, renal allograft failure was diagnosed by biopsy-proven pathological evaluation before TN.

Results Thirty-nine individuals were participated in this research study of which 22 (56.41%) were male and 17 (43.59%) were female. Most of the patients (64.1%) were nephrectomized in a time period of less than six months post-transplantation. Pathologic assessment of TN specimen extracted from the body less than 6 months post-transplantation showed renal vein thrombosis (RVT) in most cases. Chronic T-cell mediated rejection (TCMR) was the only pathologic finding for all of patients nephrectomized more than two years post-transplantation. There were two cases showing acute tubular necrosis (ATN) regarding pathologic assessment of allograft biopsy which further showed RVT in TN specimen. Another biopsy proven case of ATN also showed severe necrosis in background of T-cell mediated rejection in TN specimen.

Conclusion The most pathologic diagnoses of TN in a period of less than six months post-transplantation and more than six months post-transplantation were RVT and TCMR respectively. Early histopathologic assessment of allografts by protocol biopsy is suggested that lead to better prevention and management of chronic failure which may only present with non-specific pathologic appearance on late biopsies or TN specimens.

Benign clinical course and histological change of living-related renal transplant from the donor with membranous nephropathy

Satoshi Hara¹, Yoshinori Takahashi², Mitsuhiro Kawano¹

¹: Internal Medicine, Kanazawa University Graduate School of Medicine, Kanazawa, Japan. ²: Internal Medicine, Takaoka City Hospital, Takaoka, Japan

Background Clinical course and histological change of living-related renal transplant from membranous nephropathy (MN) remains unknown because of the scanty report so far. Here, we report a successful case of living-related kidney transplantation from a donor with MN.

Case description A 26-year-old Japanese man, who had received regular hemodialysis due to end-stage renal disease from X-linked Alport syndrome, underwent ABO-matched living-related kidney transplantation from his 63-year-old father with membranous nephropathy, mild proteinuria, and normal renal function after obtaining adequate informed consent. Both 0 and 1 hr allograft kidney biopsies revealed diffuse peripheral granular IgG deposition on the glomeruli. Although the recipient showed slow graft function soon after kidney transplantation, kidney function has been stable (serum creatinine 1.4 mg/dL) and urinary protein has maintained within a low grade range (<0.5 g/g creatinine) under usual immunosuppressive therapy (mycophenolate mofetil, tacrolimus, and prednisolone) and angiotensin receptor blocker. Six months after the transplantation, allograft kidney biopsy revealed the resolution of IgG deposition on the glomeruli. The donor has also maintained good kidney function (serum creatinine 1.3 mg/dL) with around 1g/gCr of proteinuria.

Conclusion The present case showed benign clinical course of renal transplant from the donor with MN. Of note is that peripheral granular IgG deposition on the glomeruli could resolve within 6 months in transplanted MN.
Incidence of infectious disease and malignancies after rituximab therapy in kidney transplant recipients - results from a cohort in Germany (GRAID)

Eva Schrezenmeier1, Fabian Halleck1, Oliver Staeck1, Michael Duerre1, Lukas Lehrmeier1, Dmitro Khadzhynov1, Klemens Budde1
1: Nephrology, Charité Universitätsmedizin Berlin.

Background Rituximab is frequently used in solid organ transplantation off-label, especially in patients with antibody-mediated rejections, in ABO-incompatible renal transplantation, in pre-sensitized organ recipients or the treatment of recurrence of focal segmental glomerulosclerosis in renal allografts. Only few data are available on the safety aspects of solid-organ transplant recipients receiving rituximab. There is a knowledge gap on long-term follow-up data, in particular on infectious complications.

Patients and methods A retrospective observational registry study (German Registry on Autoimmune Diseases/GRAID) comprising a total of 681 patients was conducted. The data of 63 adult kidney transplant recipients who have received rituximab between 2006 and 2013 were used in this analysis.

Results Median follow-up was 42 (1-109) months. At least one severe infection occurred in 57% of patients. The median time between the first rituximab infusion and the first infection was 4 (1-48) months. Of the overall 88 infections, 74 were severe bacterial infections, 5 were severe viral infections, 3 were severe fungal infections, 2 were combined severe bacterial and fungal infections and 4 were combined severe viral, fungal and bacterial infections. Seven patients died during the observational period, two of them due to infectious complications. In the observational period one case of squamous cell carcinoma, but no other malignancies were observed.

Conclusion Consistent with previous data a high incidence of infections was observed after rituximab in kidney transplant recipients. Most infections occurred within six months after rituximab initiation. With more than 3 years of follow-up we were able to document a low incidence of secondary malignancies after rituximab with only one case in our cohort.
**P-11**

Gene expression measurement during swine lung ex vivo perfusion: molecular quantification of donor lung injury and repair

Benjamin Adam¹, Peter Dromparis¹, Siegfried Wagner¹, Nader Aboelnazar², Sayed Himmat², Jessica Luc², Darren Freed², Jayan Nagenandra², Michael Mengel³

¹: Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada. ²: Department of Surgery, Division of Cardiac Surgery, University of Alberta, Edmonton, Canada.

**Background** Brain death, organ procurement and preservation cause acute lung injury (ALI). As a result, only about 20% of donated lungs are suitable for transplantation and a quarter of these develop primary dysfunction. With the recent development of ex vivo perfusion, previously inadequate donor lungs can now potentially be used for transplantation. However, mechanisms of ex vivo repair remain poorly understood. The aim of this large animal study is to define and validate a set of molecular markers for the quantification of ALI and monitoring of ex vivo repair.

**Methods** 41 samples were collected at different time points from swine lung donor organs in vivo (IV, n=4), after cold static preservation (CSP, n=13), and following ex vivo lung perfusion (EVLP, n=24). Functional parameters were recorded during EVLP. Samples were assessed by histology for features of ALI. RNA was isolated from FFPE samples and 53 genes previously shown to be up-regulated in different models of ALI were quantified with NanoString.

**Results** Heat map analysis highlighted two subsets of genes separating EVLP from IV and CSP: 28 “repair” genes with relative up-regulation in EVLP and 9 “injury” genes with relative down-regulation in EVLP. Expression of “repair” genes was inversely correlated with neutrophil infiltration by histology (r=-0.330, p=0.047) but showed a positive correlation with P/F-ratio (r=0.687, p=0.005) and compliance (r=0.738, p=0.002).

**Conclusion** We defined a gene set for quantification of ALI that can be used for molecular monitoring of tissue repair during EVLP and thus as a tool for tailoring ex vivo protocols in individual patients.

**FIGURE 1:** Relative expression of 53 acute lung injury-related genes in peripheral swine lung samples (n=29).

**P-12**

JAK3 inhibition prolongs renal allograft survival in a model of chronic mixed cellular and humoral rejection in rat

Jordi Rovira¹, Maria J Ramirez-Bajo¹, Elisenda Banon-Maneus¹, Marta Lazo-Rodriguez², Daniel Moya-Rull², Natalia Hierro-Garcia², Valeria Tubiita³, Ignacio Revuelta³, Pedro Ventura-Aguir³, Federico Oppenheimer³, Josep M Campistol³, Fritz Diekmann³

¹: Laboratori Experimental de Nefrologia i Trasplantament (LENT), Fundació Clinic per a la Recerca Biomèdica, Barcelona. ²: Laboratori Experimental de Nefrologia i Trasplantament (LENT), IDIBAPS, Barcelona. ³: Departament de Nefrologia i Trasplantament Renal, Hospital Clinic, Barcelona.

**Background** Chronic antibody-mediated response in renal transplantation is critical for graft dysfunction and loss. Our objective was investigated the utility of Tofacitinib, a JAK3 inhibitor, on an experimental chronic rejection model.

**Methods** The heterotopic kidney transplant Fisher-to-Lewis rat model was performed to study chronic mixed cellular and humoral rejection. Rapamycin (Rapa) and tofacitinib (Tofa) were administered in food from the third week after transplantation. Renal function was assessed at 1, 4, 8 and 12 weeks after transplantation. At 12 weeks, kidney grafts were harvested and cut into sections to analyze; infiltrating lymphocytes by flow cytometry and histological lesions and damage using several conventional and immunohistochemical stains.

**Results** Tofa treatment reduced BUN and serum creatinine levels from the first week of treatment until the end of the protocol. Meanwhile, Rapa was only able to control serum creatinine levels until week 8. Both immunosuppressive treatments significantly prolonged recipient survival. Histological analysis of kidney grafts showed that Tofa and Rapa were able to significantly reduce tubular atrophy, tubulitis, capillaritis and fibrosis. Rapa and Tofa treatments could reduce C4d depositions on peritubular capillaries. The study of infiltrating lymphocytes by flow cytometry showed that only Tofa can significantly reduce T cell infiltration, both CD4 and CD8 in the graft. However, Rapa and Tofa blocked to the same extent NK cell infiltration.

**Conclusion** The JAK3 inhibitor, tofacitinib, is able to reduce the immune response generated in renal transplant model allowing prolonged graft and recipient survival, better graft function and less histological damage.
Prophylaxis with enoxaparin for prevention of venous thromboembolism after lung transplantation

Berta Sáez-Giménez, Helena Sintes, Cristina Berastegui, Manuel López-Meseguer, Víctor Monforte, Carlos Bravo, Antonio Roman
Lung Transplant Unit, Hospital Universitari Vall Hebrón, Barcelona, Spain

Background Venous thromboembolism (VTE) is a frequent complication after solid organ transplantation (SOT) and, specifically, after lung transplantation (LT). The objectives of this study were to evaluate prophylaxis with enoxaparin and to describe risk factors for VTE after LT.

Methods We retrospectively reviewed the clinical records of 333 patients who underwent LT in our institution between 2009 and 2014 to determine the incidence of VTE during the first year after transplantation. We compared 2 consecutive cohorts, one that received enoxaparin only during post-transplant hospital admissions and a second cohort that received 90-day extended prophylaxis with enoxaparin. Risk factors were analyzed using a Cox proportional hazards regression model.

Results The incidence of VTE in our cohort was 15%. Median time from transplant to the event was 40 (p25-p75 14-112) days. Ninety-day extended prophylaxis did not seem able to prevent this complication. In the present study, the risk factors associated with VTE were population, male gender, and interstitial lung disease.

Conclusions VTE is a major complication after LT, and 90-day extended prophylaxis was not able to prevent it. Large, multicenter, randomized clinical trials should be performed to define the best strategy for preventing VTE in lung recipients.

Post-transplant IGA nephropathy: experience of 20 cases from a tertiary care center in India

Manoj Jain¹, Dharmendra Singh Bhaduaria², Raj Kumar Sharma², Vinita Agrawal¹, Narayan Prasad²
1: Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, India.
2: Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, India

IgA nephropathy (IgAN) is most common form of glomerulonephritis (GN) in native kidney biopsy. Literature on occurrence of IgAN after renal transplantation is scarce.

Authors describe 20 patients of biopsy proven IgAN occurring after live renal transplantation in last 12 years from a tertiary care center in north India, out of 1545 renal allograft biopsies. Mean post-transplant duration of occurrence of IgAN was 48.9 months (range 7-110 months). Mean age at the time of diagnosis of IgAN was 30.9 years (range 19-44 years) and male: female ratio was 17:3. Pre-transplant diagnoses were biopsy proven IgAN in 4, suspicion of chronic GN in 12 and suspicion of chronic interstitial nephritis in 4. Mean S. creatinine was 1.8 mg/dl (range 1.3-3.4 mg/dl). Nephrotic range proteinuria was in 5 and subnephrotic proteinuria in 13 patients. Oxford classification (MEST scoring) of IgAN had mesangial proliferation (M0) in 5, (M1) in 15; endothelial proliferation (E1) in none; segmental sclerosis (S0) in 13, (S1) in 7; and tubular atrophy (T0) in 7, (T1) in 9 and (T2) in 4 recipients’s biopsy. Biopsies had 2+ to 4+ mesangial IgA on immuno-fluorescence microscopy. Three patients had coexistent lesions acute antibody mediated rejection, chronic active antibody mediated rejection and calcineurin inhibitor (CNI) toxicity in one case each. Five patients became dialysis dependent on mean followup of 20.3 months (range 2 -72 months).

IgAN occurs late after transplantation in allograft biopsies. Complete immuno-fluorescence panel should be performed to diagnose IgAN in allograft biopsy.
Donor specific antibodies in long term survivors after double-lung transplant

Susana Gomez-Olles¹, Alberto Mendoza-Valderrey², Berta Saez², Roser Escobar², Thais Pereira², Cristina Berastegui³, Victor Monforte³, Manuel Lopez-Meseguer², Carlos Bravo¹, Amparo Sole³, Felipe Zurbano⁴, Mercedes de la Torre⁵, Rosalia Laporta⁶, Javier Redel⁷, Jaume Martorell⁷, Antonio Román¹

¹: Servicio de Neumología, Hospital Universitario Vall d’Hebrón, Universidad Autónoma de Barcelona, Barcelona. Ciber de enfermedades Respiratorias (CibeRes), Instituto de Salud Carlos III, Madrid. ²: Servicio de Neumología, Hospital Universitario Vall d’Hebrón, Barcelona. ³: Servicio de Neumología, Hospital Universitario La Fe, Valencia. ⁴: Servicio de Neumología, Hospital Universitario Marqués de Valdecilla, Santander. ⁵: Servicio de Cirugía Torácica, Hospital Juan Canalejo, A Coruña. ⁶: Servicio de Neumología, Hospital Universitario Puerta de Hierro, Madrid. ⁷: Unidades de Gestión Clínica de Neumología, Cirugía Torácica y Trasplante Pulmonar, Hospital Universitario Reina Sofia, Córdoba. ¹: Servicio de Inmunología, Centro de Diagnóstico Biomédico (CDB), Hospital Clínic Barcelona, Barcelona

Background and aim Long-term survival after lung transplantation (LT) is hindered by the development of chronic lung allograft dysfunction (CLAD). However, a small number of LT patients exists who are long-term survivors (LTS) and remain without CLAD. We want to know if both populations differ in terms of donor specific antibodies (DSA).

Methods This is a multicenter cross-section case-control study to determine circulating DSA in 62 double-LT patients. Thirty-one LTS (i.e. patients with stable lung function after 10 years from LT) and 31 CLAD patients. Screening for HLA-specific antibodies class I and II was done in serum samples using Lifecodes Lifescreen Deluxe kit. Samples with a positive or doubtful result were further studied by single-antigen flow bead assays on a Luminex platform.

Results Anti-HLA antibodies were detected in 6 out of 62 (9.7%) samples in the screening test against Class I and 26 out of 62 (41.9%) against class II. No significant differences were observed between groups for Class I and Class II (p=1 and P=0.797), respectively. Presence of DSA anti class I was only observed in one CLAD patient and none LTS. DSA anti-class II was observed in 5 (16.1%) CLAD patients and in 2 (6.5%) LTS patients, but difference was not statistically significant (p=0.425).

Conclusion Detection of DSAs was low, mostly of class II and there were no differences between CLAD and LTS patients. Study financed by Instituto Salud Carlos III (PI13/01076) (FEDER), FUCAP, Astellas, Novartis and Chiesi. *JM and AR equally contributed.

Is the immunosuppressant therapy altering the iron metabolism in graft kidney

Elisenda Banon-Maneus¹, Jordi Rovira¹, Ignacio Revuelta², Luis F. Quintana³, Marta Lazo-Rodriguez³, Maria Jose Ramirez-Bajo³, Daniel Moya-Rull³, Natalia Hierro-Garcia³, Valeria Tubita³, Pedro Ventura-Aguilar³, Federico Oppneheimer³, Fritz Diekmann³, Josep M. Campistol³

¹: Laboratori Experimental de Nefrologia i Trasplantament (LENIT), Fundació Clinic per a la Recerca Biomèdica, Barcelona. ²: Departament de Nefrologia i Trasplantament Renal, Institut Clinic de Nefrologia i Urologia (ICNU), Hospital Clinic (HC), Barcelona. ³: Laboratori Experimental de Nefrologia i Trasplantament (LENIT), IDIBAPS, Barcelona

In patients with kidney diseases, renal tubules are exposed to a high concentration of iron owing to increased its glomerular filtration and iron-containing proteins. Levels of intracellular catalytic iron may increase when glomerular and renal tubular cells are injured. Some preliminary results from our lab using urinary proteomic approach with renal transplant recipients, showed alteration of some proteins of the iron metabolism depending on the treatment. The aim of this study is elucidate the implication of the immunosuppressive therapy in iron metabolism in the graft kidney.

The heterotopic kidney transplant rat Fisher-to-Lewis model was performed to study chronic mixed cellular and humoral rejection under immunosuppressant therapy with mTOR inhibitors (mTORI) or calcineurin inhibitors (CNI). Renal biopsies and clinical data from renal transplant patients (RTP) with immunosuppressant therapy with mTORI or CNI, where collected.

Iron content from CNI treated animals had 3, 23 μg Fe/mg compared with the 1, 7 from the mTOR animals. This result where confirmed by the histological analysis, mainly localized in proximal tubules and some deposition in the interstitium. When those depositions were colocalized with macrophages we detected it mainly in CNI animals. Gene expression showed that mTORI animals have the samme profile than control animals and CNI animals had some dysregulation of iron metabolism.

All these results were confirmed in human samples. It seems to be a strong relationship between the immunosuppressant therapy and iron metabolism in kidney. These results open new ways to understand the CNI nephrotoxicity and its relation with ferroptosis.
**Diffuse extent of peritubular capillaritis in late antibody mediated rejection – association with transplant glomerulopathy and more severe chronic allograft damage**

Nicolas Kozakowski¹, Farsad Eskandary², Harald Herkner³, Gregor Bond², Daniel Dalos⁴, Heinz Regele¹, Rainer Oberbauer², Georg A. Böhmig², Željko Kikić²

¹: Department of Pathology, ²: Division of Nephrology and Dialysis, Department of Medicine III, ³: Department of Emergency Medicine, ⁴: Division of Cardiology, Department of Medicine II, Medical University of Vienna, Austria

**Introduction** Histologic scoring of peritubular capillaritis (ptc) is a tool for the diagnosis of antibody-mediated rejection (ABMR) in renal allografts, but the utility of a detailed subcharacterization of this lesion is under debate. Recently diffuse ptc (> 50% of the renal cortex) was highlighted as an independent risk factor for inferior outcomes and chronic ABMR.

**Methods** We characterized ptc by score, extent and leukocytic subpopulation in protocol biopsies of 85 recipients with donor-specific antibody (DSA) ≥6 months after transplantation in a secondary analysis of a large prospectively designed cross-sectional screening trial. We examined those characteristics in relation to the mean fluorescence intensity of the immunodominant DSA (MFI_max) and their impact on chronic allograft damage transplant glomerulopathy ([TG] and the chronic lesion score [CLS]).

**Results** Ptc (n=42) scores 1, 2, and 3 were present in 36%, 55% and 9%, focal vs. diffuse ptc in 36% vs. 64%. Mononuclear cells were dominating (76%). Recipients with diffuse ptc had higher DSA MFI_max [median: 4.407 vs. 2.419 (focal ptc; p=0.04) or 1.946 (no ptc; p=0.004)], more often cg [58% vs. no ptc 24% (p=0.02)] and higher CLS [mean: 6.81 vs. 4.67 (focal ptc, p=0.01) or 5.18 (no ptc, p=0.001)]. Ptc scores ≥2 were only associated to TG. In regression analysis, association of diffuse ptc with chronic injury was independent of DSA_MFI_max, ptc scores and leukocytic composition.

**Conclusions** Our results suggest diagnostic and prognostic relevance of reporting diffuse ptc as a risk factor for chronic damage in kidney allografts.

---

**IGG subclass of plasma cell-rich infiltrates in the kidney allograft**

Shigeo Hara, Tomoo Itoh

Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

**Backgrounds and aims** IgG subclass of plasma cell-rich infiltrates (PCI) in the kidney allograft has not been fully elucidated.

**Methods** PCI was defined by the presence of plasma cells that comprised >10% of the inflammatory cells irrespective of the status of functional or dysfunctional renal allograft. CD138 immunostaining was used to evaluate the degree of PCI. Among 434 biopsy cases for either dysfunctional renal allograft or protocol from April 2009 to October 2016, 4 cases were enrolled in the present study as PCI in the kidney allograft. IgG subclass was immunohistologically examined using formalin-fixed paraffin-embedded sections. Density (cell count/mm²) and percentage (%) of plasma cells harboring each IgG subclass was examined using digital microscopy software (NanoZoomer, Hamamatsu, Photonics, Hamamatsu, Japan).

**Results** Cases with PCI consists of borderline changes (BC) [n=1], BC with chronic antibody mediated rejection [n=1], and plasma cell-rich acute rejection (PCAR) [n=2]. In 3 cases including 2 BC cases and 1 PCAR case, the density of IgG1-positive plasma cells ranged from 24.5-70.4 cell count/mm² (54.2-74.2%). The other case of PCAR showed co-dominant distribution of IgG1 (24.3 cell count/mm²) and IgG3 (40.1 cell count/mm²)-positive plasma cells (34.6 % and 57.0 %, respectively). In all cases, IgG4-positive plasma cells were scarce (range 0.1-8.1%).

**Conclusions** In the present study with small cohort, IgG subclass of plasma cells did not differentiate PCAR and plasma cell-rich BC.
**P-20**

**Prolonged prophylaxis with valgancyclovir prevents CMV disease in CMV high risk kidney transplant recipients**

Fabian Halleck, Dmytro Khadzhynov, Klemens Budde, Oliver Staeck
Nephrology, Charité Berlin, Germany

**Background** Kidney transplant recipients (KTR) with high-risk CMV constellation (D+/R-) are at high risk to develop severe clinical manifestations of CMV disease. Long-term data about incidence and timing of CMV-seroconversion, CMV disease and the influence of prolonged Valgancyclovir (VGC) prophylaxis on the clinical course of CMV infection are missing.

**Methods** We conducted a retrospective long-term observational study of 89 consecutive KTR with high-risk CMV constellation (D+/R-) between 2003 and 2012. The majority of KTR received prolonged VGC prophylaxis after transplantation (median 187 days [range 126-261 days]). Long-term outcome was assessed over a maximum of 10 years post-transplant.

**Results** During the follow-up (median 62 months) 60 (67%) patients developed CMV seroconversion, 29 (33%) symptomatic CMV disease. In 43% of the patients seroconversion occurred during prophylaxis with Valgancyclovir (median 154 days after transplantation), 25% showed conversion after the end of prophylaxis with Valgancyclovir (median 320 days after transplantation). The baseline characteristics of the two groups did not differ significantly. Seroconversion during prophylaxis vs. after end of prophylaxis was associated with significantly less CMV disease (34% vs. 73%, p=0.007), less severe CMV disease (16% vs. 64%, p<0.001) and less organ manifestations (26% vs. 64%, p=0.006). Valgancyclovir resistance occurred in 1 case (1%).

**Conclusions** CMV seroconversion during prolonged prophylaxis with Valgancyclovir occurred after a median of 154 days and was associated with significantly lower incidence of CMV disease, severe CMV disease and CMV complications.

---

**P-21**

**The utility of oxford classification for IGA nephropathy in renal allograft recipients**

Vinita Agrawal, Aparna Singh, Anupma Kaul, Ritu Verma, Manoj Jain, Rakesh Pandey
Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS)

**Introduction** IgAN may present as recurrent or de-novo glomerulonephritis in renal allograft recipients. We studied the clinico-pathological features of post-transplant IgAN and re-classified graft biopsies according to Oxford classification.

**Material and methods** All graft biopsies during a ten-year period, from January 2005 to December 2014 with IgA deposits were evaluated. IgAN was diagnosed on presence of ≥2 dominant/codominant IgA deposits on IF and any degree of hematuria and/or proteinuria.

**Results** 915 graft biopsies were received; 61 showed IgA deposits (1 to 4+). 24 biopsies from 22 patients were diagnosed as IgAN. Mean duration for post-transplant IgAN was 69.6±46.1 months (range 6.8-194). Recurrent IgAN was seen in two (9%). 72.7% (16/22) presented with rise in s.creatinine. Associated rejection was present in four biopsies. 91% (20/22) presented with proteinuria and 31.8% (7/22) presented with hematuria. 24-hour proteinuria ranged from 0.32 to 11.7 gm/day (mean±S.D 2.56±2.7) with nephrotic proteinuria in four (21%) patients. The most frequent Haas class was III (n=7; 29.1%), followed by IV and I (n=5; 20.8% each). There was no significant correlation of Oxford MEST score M1, E1 and S1 with raised serum creatinine, low eGFR and nephrotic proteinuria. Tubular atrophy (T1) was associated with raised serum creatinine and low eGFR at presentation (p<0.05). S1 was associated with raised mean arterial pressure (p<0.05). The mean duration of follow-up (n=20) was 30.5±27.6 months (range 2.4-116; median 25.7).

**Conclusion** Post-transplant IgAN was seen in 2.6% biopsies. T-score of Oxford classification is associated with raised s.creatinine and low eGFR at diagnosis.
Kidney allograft histology in patients with transplantation vintage longer than 20 years: tremendous effects of donor age

Tomoko Namba1, Masahiro Kyo2, Takayuki Hamano3, Yutaka Yamaguchi4, Yoshitaka Isaka1, Shiro Takahara5
1: Nephrology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan. 2: Sakura-bashi Iselkai Clinic, Dialysis Center. 3: Osaka University Graduate School of Medicine, Comprehensive Kidney Disease Research. 4: Yamaguchi’s Pathology Laboratory. 5: Osaka University Graduate School of Medicine, Advanced Technology for Transplantation

Background and aim  Despite the improvement of graft survival, few studies evaluated long-term graft histology. The aims were to reveal the characteristics of histology in long-term graft survivors and to identify clinical manifestations associated with histological findings.

Methods  All allograft biopsies conducted between 2002 and 2014 in recipients with > 20-year transplantation vintage were included (25 biopsies, n=22). The histological findings were scored according to the revised Banff criteria. To explore clinical factors associated with each histological parameter, we employed receiver operating characteristic (ROC) analyses followed by multivariate logistic regression analyses.

Results  Median (IQR) transplantation vintage (year), recipient age at biopsy, and donor age were 23.0 (21.5, 25.0), 58.0 (44.5, 61.0), and 48.5 (31.0, 54.3). Mean eGFR and proteinuria at biopsy was 32.6±18.0 mL/min/1.73m2 and 0.91±1.03 g/day, respectively. No obvious acute or active lesion was found. Most cases presented mild interstitial fibrosis and tubular atrophy (Figure). As to glomerular findings, FSGS-like lesion was observed in 24% of the samples. The clinical characteristic associated with the presence of ci, ct, and FSGS lesion was found to be donor age by ROC analyses (AUC=0.89, 0.86, and 0.86, respectively). This was confirmed by multivariate logistic regression analyses (Odds ratio 4.3 (95% CI 1.3-43.3), 4.9 (1.4-54.0), and 24.6 (2.4-1755.3)) after adjusting for proteinuria. Transplantation vintage was not associated with any histological score.

Conclusions  Even after >20 years graft survival, still does donor age, but not transplantation vintage, affect tubulointerstitial damage and the prevalence of FSGS-like lesion.

Donor-specific anti-HLA antibodies accelerate the progression of interstitial fibrosis in the kidney allograft

Clément Gosset1, Denis Viglietti2, Marion Rabant3, Denis Glotz4, Christophe Legendre5, Jean Paul Duong Van-Huyen2, Alexandre Loupy2, Carmen Lefaucheur2
1: Pathology, Saint Louis Hospital. 2: Paris Translational Research Center for Organ Transplantation. 3: Pathology, Necker Hospital. 4: Nephrology and Kidney Transplantation, Saint Louis Hospital. 5: Nephrology and Kidney Transplantation, Necker Hospital, Paris, France

Background  Addressing the causes of accelerated ageing of kidney allografts represents an important challenge to improve long-term outcomes. We investigated the role of donor-specific anti-HLA antibodies (DSA) in allograft fibrosis progression.

Methods  We prospectively enrolled 913 kidney recipients transplanted between 2004 and 2010 with systematic assessment of DSA at Day-0 and at 1-year post-transplantation. Allograft fibrosis was assessed on biopsies performed at Day-0 and at 1-year using the IF/TA Banff score. We integrated all the “for cause” biopsies performed within (N=1035) and after (N=784) the first year. The progression of fibrosis was evaluated over the first year post-transplant using the difference between 1-year and Day-0 IF/TA scores (∆IF/TA), and over long term using mixed-effect models (median time of biopsies 18.4 months; IQR, 13.3-40.4).

Results  At Day-0, the distribution of fibrosis was: 726 (80%) IF/TA0, 145 (15%) IF/TA1, 36 (4%) IF/TA2, and 6 (1%) IF/TA3 as compared to 325 (35%), 263 (29%), 173 (19%), and 152 (17%) at 1-year, respectively (P<0.001). Over the first year, 507 (56%) patients presented progression of fibrosis (∆IF/TA>0). Patients with Day-0 DSAs showed an increased progression of fibrosis within the first year (∆IF/TA of 1.08±1.15) as compared to patients without Day-0 DSA (0.86±1.12) (P=0.016). After 1 year, by integrating the biopsies performed at 1-year and after, we showed that patients with DSA (preformed or de novo) exhibited accelerated progression of allograft fibrosis as compared to patients without DSA (P for interaction DSA-time=0.0078).

Conclusions  DSAs are associated with accelerated progression of interstitial fibrosis in the kidney allograft.
Long-term outcomes of kidney transplant recipients with primary idiopathic FSGS

Olivier Staecck, Fabian Halleck, Klemens Burdde, Dmytro Khadzhynov
Nephrology, Charité Universitätsmedizin, Berlin, Germany

Introduction Few data exists analyzing recurrence rates, treatment response and long-term outcomes in kidney transplant recipients (KTR) with primary FSGS.

Methods This retrospective observational study included 1218 consecutive KTR 2002-2016. All patients with primary idiopathic FSGS were identified applying strict diagnostic criteria. Outcomes were followed over an average of 70.4 months.

Results We identified 48 KTR (3.9%) with primary FSGS. 7-year death-censored graft survival was 81% (primary FSGS) vs. 85% (control), p=0.297 (Fig.1a). Among KTR with primary FSGS, 18 KTR experienced FSGS-recurrence (predicted incidence 50% after 7-years; Fig.1b). 7-year graft survival in KTR with FSGS-recurrence was significantly worse than in FSGS-KTR without recurrence (63% vs. 96%, p=0.015; Fig.1c).

In case of FSGS recurrence a multimodal treatment approach was applied, including: plasma exchange (PE) (100% of patients), cyclosporine i.v. (50%), rituximab (61%) and the ‘multiple target treatment’ according to Canaud (JAT 2009) (39%). The median number of PE-sessions was 27. Proteinuria decreased significantly and persistently during the course of treatment (Fig.1d). Complete remission of FSGS was observed in 7 patients (39%), another 7 patients (39%) developed partial remission (PE-dependence observed in 4 patients (22%). 4 patients (22%) with FSGS recurrence experienced early graft loss (< 6 months post-transplant) despite all treatment efforts.

Conclusions In KTR with primary FSGS a high proportion of recurrences occurred during the long-term follow-up and led to significantly worse graft survival. However, a multimodal treatment approach mostly resulted in resolving of proteinuria and full or partial remission. Graft survival in KTR with underlying primary FSGS was comparable with the control group.

Brain-dead donors terminal inflammation is associated to delayed graft function in kidney transplant recipients

David Cucchiari¹, Fritz Diekmann², Pedro Ventura-Aguilar², Jordi Rovira², David Paredes³, Ramon Adália³, Frederic Oppenheimer², Ignacio Revuelta²
¹: Renal Transplant Unit, Hospital Clinic, Barcelona. ²: Laboratori Experimental de Nefrologia I Trasplantament (LENIT), Fundació Clinic, IDIBAPS - Barcelona. ³: Transplant Coordination Unit, Hospital Clinic, Barcelona

Background In kidney transplantation recipients, increased biomarkers of systemic inflammation before and after the transplant are associated to worse short- and long-term renal outcomes. However, little is known about the role of systemic inflammation in the donor and if it is associated to worse graft outcomes.

Material & methods We retrospectively analyzed clinical and biochemical characteristics of all kidney brain-dead donors generated in the Hospital Clinic of Barcelona in the 2006-2015 period (n=194). Donors who were tested for C-Reactive Protein (CRP) in the 24 hours before BD declaration were included (n=97, 50%). Clinical and biochemical features of their respective recipients (n=165) were analyzed, comparing recipients who developed Delayed-Graft Function (DGF) (n=30) with recipients who did not (n=135).

Results In the univariate analysis, CRP and dialysis vintage were significantly associated to DGF (p=0.025 and p=0.002, respectively), while PRA, donor and recipients age/sex, ischemia time, ICU stay and terminal creatinine were not (see table). However, in logistic regression analysis, CRP proved to be significant only in non-Expanded Criteria Donors (ECO) (p=0.027), while it lost significance in the ECO group (p=0.76). Notably, DGF patients had worse 1-year creatinine (p=0.02) and more episodes of graft rejection in the first year (p<0.01).

Conclusions Donor inflammation assessed by terminal CRP was associated to DGF in non-ECO. It is worth mentioning that DGF was associated to worse renal outcome in the first year after transplantation.
Prolonged low-dose prophylaxis with valganciclovir in CMV D+/R- kidney transplant recipients allows seroconversion and prevents CMV disease

Fabian Halleck, Dmytro Khadzhynov, Olesja Rissling, Klemens Budde, Oliver Staeck
Nephrology, Charité Universitätsmedizin Berlin, Germany.

Background Kidney transplant recipients (KTR) with CMV D+/R- constellation are at high risk to develop severe clinical manifestations of CMV disease. Long-term data about incidence and timing of CMV-seroconversion, CMV disease and the influence of prolonged valganciclovir prophylaxis on the clinical course of CMV infection are missing.

Methods We conducted a retrospective long-term study of 89 consecutive KTR with CMV D+/R-constellation transplanted 2003-2012. The majority of KTR received prolonged valganciclovir prophylaxis after transplantation (median 187 (126-261) days) with a median dose of 213 (181-338) mg/day. Long-term outcome was assessed over a maximum of 10 years post-transplant.

Results During the follow-up (median 62 months) 60 (67%) patients developed CMV seroconversion, 29 (33%) symptomatic CMV disease. In 43% of the patients seroconversion occurred during prophylaxis with valganciclovir (median 154 days post-transplant), 25% showed conversion after the end of prophylaxis with valganciclovir (median 320 days after transplantation). The baseline characteristics of the two groups did not differ significantly. Seroconversion during prophylaxis vs. after end of prophylaxis was associated with significantly less CMV disease (34% vs. 73%, p=0.007), less severe CMV disease (16% vs. 64%, p<0.001) and less organ manifestations (26% vs. 64%, p=0.006). Valganciclovir resistance occurred in 1 case (1%). In this cohort risk of disease was limited to the first 475 days after transplantation (Fig.1).

Conclusions Prolonged prophylaxis with low-dose valganciclovir allowed CMV-seroconversion in a high proportion of D+/R- patients. Seroconversion occurred after a median of 154 days and was associated with significantly lower incidence of CMV disease, severe CMV disease and CMV complications.

The current Banff classification of BK polyomavirus-associated nephropathy does not accurately stratify patients at risk for progressive renal graft failure

Yassine Bouatou1, Joris Roelofs1, Frederike Bemelman2, Jesper Kers1, Sandrine Florquin1
1: Pathology, 2: Nephrology, AMC, Amsterdam, Netherlands

Background and aims With current immunosuppressive regimens, BK polyomavirus associated nephropathy (BKPyVAN) is still a concern in clinical practice. A reproducible grading system is of uttermost importance to assess prognosis and we therefore aimed at assessing the prognostic value of the Banff grading system, SV40 positive tubules (pvl score) and other components of the Banff classification to predict eGFR trajectories and death-censored graft survival.

Methods We retrospectively analyzed BKPyVAN cases in our center from 2002 to 2010 (n= 22) and searched clinical data for estimated glomerular filtration rate (eGFR, MDRD) and death censored graft survival (Kaplan-Meier plots). All patients had their immunosuppression weaned according to our protocol.

Results Among 22 patients, 11 lost their grafts. We observed that group B had more graft failure and had a more declining eGFR trajectories than group A and C (Figure), which could be explained by more infected tubules and more total inflammation in group B compared to C.

Conclusion Our findings are discordant with the current Banff BKPvVAN working proposal in terms of prediction of graft loss, most probably due to less infected tubules and less inflammation representing a more favorable follow-up in group C. Further subclassification on these features in group C should be given consideration.
**P-29**

**Donor-recipient relationship significantly influences the long-term immunologic outcome in living related kidney transplantation**

Dmytro Khadzhynov, Fabian Halleck, Lukas Lehner, Danilo Schmidt, Klemens Budde, Oliver Staeck

**Nephrology, Charité Universitätsmedizin Berlin, Germany**

**Background** The aim of the study was to analyze the long-term immunologic outcomes of living related kidney transplantations depending on the donor-recipient relationship.

**Methods** This retrospective single center study included adult kidney transplant recipients (KTR) transplanted 2000-2014. Among 1117 KTR 178 patients (15.9%) received living related donations. Those patients were categorized according to the donor-recipient relationship: 65 transplantations between siblings, 39 father-to-child (FtC) and 74 mother-to-child (MtC) donations. Allograft biopsies were performed for clinically suspected rejections. Data analysis included patient and graft survival, biopsy proven rejections (T-cell mediated (TCMR) or antibody mediated (ABMR)) and development of de novo DSA. Outcome data were assessed over a period of maximal 14 years.

**Results** There was no significant difference between the groups (siblings, FtC, MtC) with regards to HLA-mismatch, prior kidney transplantation, time on dialysis and cold ischemia time. Among KTR with related donors the type of relationship had no significant influence on graft survival (Fig. 1a). FtC- and MtC-pares showed comparable incidences of TCMR, both significantly exceeding the rate in sibling-to-sibling pares (Fig. 2b). A multivariate Cox regression analysis adjusted for recipient age, donor age and HLA (A, B, DR)-mismatch identified both MtC and FtC donation as important independent risk factors for TCMR (HR 8.13, p< 0.001 and HR 8.09, p=0.001, respectively). There was no significant difference between the groups in terms of ABMR (Fig. 1c) and development of de novo DSA (Fig. 1d).

**Conclusion** Our results point out that parent-to-child kidney donation is an independent risk factor for TCMR.

**FIGURE 1** Immunologic outcome according to donor-recipient relationship

**FIGURE 2** Influence of donor-recipient relationship on A aorta and B celiac artery wall-lumen ratio

---

**P-30**

**Evaluation of frozen and paraffin sections using the MAPI-score in kidneys donor’s biopsies of a Brazilian cohort**

Andre Costa Teixeira1, Victoria Sobreira Lacerda2, Carolina Costa Freire De Carvalho3, Gabriel Pinho Mororo2, Lucas Dourado Mapurunga Pereira2, Ronaldo Matos Esmeraldo4

1: Renal Pathology, Argos Pathology. 2: Faculty of Medicine, Unichristus. 3: Faculty of Medicine, University of Fortaleza. 4: Department of Transplantation, General Hospital of Fortaleza, Fortaleza, Brazil

**Background and aims** MAPI (Maryland Aggregate Pathology Index) score was developed to predict the suitability of donor's kidneys for transplantation. Biopsies are evaluated using frozen (FS) and/or paraffin sections (PS) based on a semi-quantitative score (low - 0 to 7, intermediate - 8 to 11, high - 12 to 15) according to the following criteria; periglomerular fibrosis (4 points), global glomerulosclerosis in more than 15% of glomeruli (2), arteriolar hyalinosis (4), wall-lumen ratio > 0, 5 in arteries (2) and scar (3). Kidneys with an intermediate or high score are considered inadequate. This study aimed to evaluate the agreement between FS and PS.

**Methods** a retrospective analysis of clinical and pathological data of 262 donors' biopsies done between July-2014 and July-2016 was carried out. The biopsies were examined by an on-call pathologist (FS) and then by an experienced renal pathologist (PS). The agreement was calculated by Kappa test and was considered the gold standard.

**Results** positive criteria were more frequent in PS and Kappa score was 0, 29 for global glomerulosclerosis, 0, 37 for periglomerular fibrosis, 0, 38 for wall-lumen ratio, 0, 45 for arteriolar hyalinosis and 0, 51 for scar. A kappa of 0, 59 was obtained for total MAPI score when the groups with prognostic significance were evaluated together (intermediate/high MAPI). FS had higher specificity than sensitivity for all criteria.

**Conclusion** MAPI can be useful to improve the agreement between FS and PS and has high specificity in FS. However, more effort should be emphasized to recognize some alterations during intraoperative pathology consultation.

**TABLE 1** Evaluation of number of glomeruli, MAPI criteria and total MAPI score in frozen sections and paraffin sections of kidney donor’s biopsies

**TABLE 2** Sensitivity, specificity, accuracy and kappa score of MAPI criteria and total MAPI score in frozen sections according to paraffin sections (gold standard)
Acute transplant arteritis resulting in sudden death in cardiac transplant patients
Joanna Dalland1, Sally Self2, Nicholas Batalis1, Omar Moussa1, Thomas Hulse3, Adrian Van Bakel4, Evelyn Bruner1
1: Pathology, University of Kentucky, Lexington, KY, USA. 2: Pathology, 3: Pediatrics, 4: Medicine, Medical University of South Carolina, Charleston, SC, USA

Cardiac allograft vasculopathy (CAV) is a well-recognized complication which accounts for a large number of cardiac transplant deaths; however, a clear consensus of the definition remains elusive. The variability in classifications found in the literature along with the observation that cardiac transplant patients who experienced a sudden death at our institution often had a component of vasculitis associated with the CAV, led us to perform a retrospective analysis of these patients. The clinical records and autopsy reports of heart transplant recipients at the Medical University of South Carolina were reviewed to evaluate the histologic vascular changes seen in this population and correlate these findings with the cause of death. We found that both an acute vasculitis and a vasculitis in the setting of cardiac allograft vasculopathy (concentric intimal fibrosis), what we termed as “chronic active vasculopathy”, correlated with a cardiac cause of sudden death. Furthermore, when present, a younger age at the time of transplant and at the time of death was noted. This data suggest that these two entities should be separated diagnostically from pure intimal fibrosis in an effort to standardize definitions of these various lesions, particularly in consideration of the observed associated clinical outcomes. Moreover, acute arteritis and chronic active vasculopathy are potentially treatable and it would be beneficial to these transplant patients to find a way to diagnose them pre-mortem to prevent this as a cause of sudden cardiac death.

Thrombotic microangiopathy in renal allograft biopsies: minimal histopathological criteria and spectrum
Marjan Afrouzian1, Jan Becker2, Seshan Seshan3, Helen Liapis4
1: Department of Pathology, University of Texas Medical Branch (UTMB), Galveston, USA. 2: Institute of Pathology, University Hospital of Cologne, Cologne, Germany. 3: Department of Pathology, Weill Cornell Medicine, New York, USA. 4: Department of Pathology, Washington University School of Medicine, St. Louis, USA

Introduction Thrombotic microangiopathy (TMA) is a microvascular (endothelial) injury that can be localized to the allograft kidney only, without systemic involvement. Focal distribution, lack of specific and reliable serological markers, and confounding factors affecting the allograft result in marked diagnostic heterogeneity. There are no minimal diagnostic criteria for allograft biopsies. A newly formed Banff Working Group is aiming to develop standardized criteria for the diagnosis of allograft TMA.

Design We employ the ‘Delphi’ methodology for consensus generation. Delphi is a structured process in which a panel of experts (the panelists) and facilitators (not involved in scoring) will reach a consensus through 9 repeat anonymous surveys, without bias from group dynamics, in an iterative fashion. We have assembled a panel of 61 experts (the panelist) based on strict inclusion and exclusion criteria. Thirty transplant biopsies composed of bonafide TMA and controls (non-TMA) and equivocal TMA were selected and will be circulated among the panelists. Through controlled survey feedbacks given by the facilitators, the panelists will be asked to come up with a core set of histopathological diagnostic criteria; at each iteration and to rank the criteria. The input from the panelists will be curated and re-distributed multiple times by the facilitators for further refinement of the criteria.

Results Preliminary data collected by the TMA-WG facilitators will be presented at the Banff meeting. This will be the introduction of the Delphi method to Banff classifications aiming to refine an unbiased consensus generation for Banff Working Groups.
Outcome assessment in kidney transplantation using different clinical pretransplant kidney donor variables: is KDPI useful?
Carlos Arias-Cabrales¹, María José Péres-Sáez¹, Dolores Redondo-Pachón¹, Anna Buxeda¹, Carla Burballa¹, Sheila Bermejo¹, Adriana Sierra¹, Marisa Mir¹, Andrea Burron², Ana Zapatero³, Marta Crespo¹, Pascual Julio¹
¹: Nefrología, ²: Epidemiology and Evaluation, ³: Intensive Care Medicine, Hospital del Mar, Barcelona

Introduction
Kidney donor shortage requires an expansion in donor selection criteria, as well as use of objective tools to minimize the percentage of discarded organs. Some easily available donor pretransplant variables such as age, definition of standard/expanded criteria donors (SCD/ECD) and calculation of the United States Kidney Donor Profile Index (KDPI), have demonstrated correlations with patient and graft outcomes. We aimed to establish the accuracy of the three models to determine the prognostic value on kidney transplantation (KT) major outcomes.

Material and methods
We performed a retrospective study in deceased donor KT at our institution. Unadjusted Cox and Kaplan-Meier survival, and multivariate Cox analyses were fitted to analyze the impact of the three predictor scores donor age, SCD/ECD and KDPI on outcomes.

Results
A total of 389 KT were included. Mean donor age was 53.6±15.2 years; 163 (41.9%) came from ECD; mean KDPI was 69.4±23.4%. Median follow-up was 51.9 months. The unadjusted Cox and Kaplan-Meier showed that the three prognostic variables of interest, namely donor age, ECD status and KDPI were related with increased risk of patient death, graft failure and death-censored graft failure. However, in the multivariate analysis only KDPI was related with higher risk of graft failure (HR 1.03 [95%CI 1.01-1.05]; p=0.014).

Conclusions
SCD/ECD classification did not provide significant prognostic information about patient and graft outcomes. KDPI was linearly related with higher risk of graft failure, providing a better assessment. More studies are needed before using KDPI as a tool to discard or accept kidneys for transplantation.

Effects of gamma irradiation on bacterial microflora associated with human amniotic membrane
Tahsin Ahmed Kazi
Department of Biochemistry and Microbiology, North South University Bangladesh, Dhaka, Bangladesh

Human amniotic membrane is considered a promising allograft material for the treatment of ocular surface reconstruction, burns, and other skin defects. In order to avoid the transmission of any diseases, grafts should be perfectly sterile. Twenty-five amniotic sacs were collected to determine the microbiological quality of human amniotic membrane, to analyze the radiation sensitivity pattern of the microorganism, and to detect the radiation decimal reduction dose ($D_{10}$) values. All the samples were found to be contaminated, and the bioburden was ranged from $3.4 \times 10^2$ to $1.2 \times 10^5$ cfu/g. Initially, a total fifty bacterial isolates were characterized according to their cultural, morphological, and biochemical characteristics and then tested for the radiation sensitivity in an incremental series of radiation doses from 1 to 10KGY. The results depict gradual decline in bioburden with incline of radiation doses. Staphylococcus spp. were the most frequently isolated bacterial contaminant in tissue samples (44%). The $D_{10}$ values of the bacterial isolates were ranged from 0.6 to 1.27 KGY. Streptococcus spp. were found to be the highest radioresistant strain with the radiation sterilization dose (RSD) of 11.4 KGY for a bioburden level of 1000. To compare the differences, $D_{10}$ values were also calculated by graphical evaluations of the data with two of the representative isolates of each bacterial species which showed no significant variations. Findings of this study indicate that lower radiation dose is quite satisfactory for the sterilization of amniotic membrane grafts. Therefore, these findings would be helpful to predict the efficacy of radiation doses for the processing of amniotic membrane for various purposes.
**The effects of MyD88 inhibitor local infusion in ischemia-reperfusion kidney injury**

Hye Jeong Kim¹, Hee Jung Cha², Jong Soo Lee³, Hong Rae Cho⁴, Byungsuk Kwon¹
¹: Biomedical Research Center, University of Ulsan, Ulsan, Korea (South). ²: Department of Pathology, University of Ulsan. ³: Department of Internal Medicine-Nephrology. ⁴: Department of Surgery-Transplantation, University of Ulsan, Ulsan, Korea

**Introduction** We have previously shown that tubular epithelial cells play a central role in regulating ischemia-reperfusion kidney injury (K-IRI). Tubular epithelial cells damaged by hypoxic insult release high levels of high-mobility group box 1 (HMGB1) protein, an endogenous damage-associated molecular pattern (DAMP), which in turn induces secretion of CCR5 ligands through TLR2 in an autocrine manner. NK cells are recruited to the kidney in response to CCR ligands and stimulate CD137L in tubular epithelial cell via their cell surface CD137. CD137L signalling results in production of CXCR2 ligands which are required for recruitment of neutrophils. These results suggest that the sequential signalling events occurring in tubular epithelial cells during K-IRI course are targets for therapeutic intervention of K-IRI.

**Method** We adopted mouse kidney ischemic reperfusion injury model. C57BL/6 mice were used between 7 and 8 weeks of age.

**Result** In this study, we showed that infusion of MyD88 peptide inhibitor through renal vein just before induction of K-IRI was highly effective in reducing K-IRI: it inhibits CCR2 ligands, preventing infiltration of NK cells into the kidney; subsequent recruitment of neutrophils was impaired and general renal inflammation induced by ischemia-reperfusion was markedly decreased. In vitro assays showed that MyD88 inhibitor effectively blocked secretion of CCR5 ligands promoted by TLR2 stimulation.

**Conclusion** Taken together, our results indicate that infusion of TLR2 inhibitor into the kidney before transplantation may contribute to reduce K-IRI that commonly occurs in transplanted kidneys.

---

**An accurate method for cell quantification of the inflammatory infiltrates in plasma cell-rich rejection liver transplant biopsies**

Elena Aguado-Dominguez¹, Lourdes Gomez², Jose Manuel Sousa³, Miguel Angel Gomez-Bravo⁴, Antonio Nuñez-Roldan¹, Isabel Aguilera¹
¹: Immunology, Instituto de Biomedicina de Sevilla IBiS. ²: Pathology, Instituto de Biomedicina de Sevilla. ³: Digestive Diseases, ⁴: Liver Transplant Unit, H.U. Virgen del Rocio, Sevilla

**Background and aims** Plasma cell-rich rejection is a dysfunction of the liver allograft characterized by the presence of plasma cells on the inflammatory infiltrates. Very little is known about the type or number of other immune cells on these infiltrates. The aim of this study is to complete the cellular profile and degree of representation of each cell type on the infiltrates found in liver diagnostic biopsies of patients with PC-rich rejection.

**Methods** A total of 6 liver biopsies from 6 patients with PC-rich rejection were included in the study. We performed immunohistochemistry experiments using the following markers: CD138, IgG4, CD3, CD20 and CD68. Immunostained slides were assessed using our protocol based on Visiopharm® computer-assisted stereology quantification method, which leads to the estimation of number of cells per area.

**Results** We have designed a novel protocol that provides an accurate, unbiased, and reproducible tool to support diagnosis of PC-rich rejection. Based on the median values, the cellular composition of the infiltrates is as follows: CD3+ T lymphocytes are the predominant cells infiltrating the portal areas (32.80%), followed by plasma cells CD138+ (24.90%), macrophages (22.68%) and CD20+ B lymphocytes (15.80%), being IgG4+ plasma cells present at lower number (3.83%).

**Conclusions** Knowledge of a characteristic cellular profile will contribute to a more reliable diagnosis of PC-rich rejection, mainly based on histologic findings that remains challenging. The methodology used here provides an important tool, not subjected to individual interpretation of the findings in biopsy.
**P-37**

Renal allograft biopsy computerized inflammatory cell quantitation for rejection assessment: comparison of commercial and open source image analysis algorithms

Andres Moon, Geoffrey Smith, Thomas Rogers, Carla Ellis, Alton Farris
Department of Pathology, Emory University, Atlanta, United States

**Background** Renal allograft rejection diagnosis depends on assessment of parameters such as the degree of interstitial inflammation; however, studies have shown interobserver variability. Image analysis and automated quantitative methods may prove more reproducible in assessing inflammation, with data suggesting correlation between CD3 staining density and severity of rejection. Commercial cell counting algorithms are available; however, other solutions such as ImageJ are open source and may provide more customization, which we investigated here.

**Design** Renal allograft biopsies including varying degrees of rejection were retrieved (n = 45), and CD3 immunohistochemistry slides were scanned to obtain whole slide images (WSIs). Inflammation was quantitated in the WSIs using pathologist visual assessment, commercial algorithms (Aperio nuclear algorithm to give CD3 cell count/mm2 and Aperio positive pixel count algorithm), and customized open source algorithms developed in ImageJ.

**Results** Custom ImageJ algorithms involving thresholding/positive pixel counting (Calculated CD3/mm2) and identification of pixels fulfilling ‘maxima’ criteria for CD3 expression (Custom CD3 count/mm2) qualitatively corresponded to visual assessment and commercial algorithms. CD3 quantitation algorithms correlated between each other and also with visual assessment in a statistically significant manner (r = 0.43 to 0.94, p = 0.004 to < 0.0001). Methods for assessing inflammation showed a progression through the grades of tubulointerstitial rejection.

**Conclusion** Assessment of CD3-stained slides using open source image analysis algorithms shows correlation with visual and commercial methods of CD3 quantitation. These analysis techniques are promising and highly customizable, providing a form of on-slide ‘flow cytometry’ that may facilitate diagnostic accuracy in pathology assessment.

---

**P-38**

Oxalate deposition in the renal allograft biopsy within 3 months after transplantation

Malou Snijders1, Joke Roodnat2, Dennis Hesseling2, Marian Claansen-van Groningen1
1: Department of Pathology, 2: Department of Nephrology and Transplantation, Erasmus MC, Rotterdam, The Netherlands

**Background and aims** Deposition of calcium oxalate (CaOx) may impair both native and transplant renal function. We analyzed the role of CaOx in postoperative transplant dysfunction.

**Methods** We retrospectively analyzed all preimplantation renal biopsies (t0) for CaOx obtained in 2000-2001 at ErasmusMC. Thereafter, we retrospectively investigated all for-cause renal allograft biopsies obtained within 3 months post-transplantation of patients transplanted in 2014-2015 in ErasmusMC for CaOx. Clinical data were collected. H&E stained slides were analyzed using polarized light.

**Results** A total of 106 t0 biopsies (56 living, 50 deceased donor) were available for analysis, 1 showed CaOx (0.94%) (living donor). 388 patients were transplanted in 2014 and 2015; 77 had DGF, 148 (38.4%) had at least one biopsy within the first 3 months after transplantation. Twenty-four (16%) patients showed CaOx in their biopsy. No diagnosis (ATN, rejection or other) prevailed in the CaOx. DGF was more frequent with CaOx (p=0.02). Significantly more patients with CaOx had been on dialysis before transplantation (p=0.023). Other clinical parameters investigated were not significantly different between the groups. In the CaOx population 3 grafts failed (12.5%) and 2 patients died (8.3%) versus 8 (6.5%) and 6 (4.8%) in controls (ns).

**Conclusion** One in 6 patients have CaOx in their renal allograft biopsy within 3 months after transplantation which can contribute to renal dysfunction. Prevalence was not significantly different between recipients of living or deceased donor kidney, but it significantly prevailed in patients that were on dialysis before transplantation. Patients with DGF significantly more often had CaOx.
**C reactive protein is modulated by subclinical inflammation in kidney allograft surveillance biopsies**

Clara García-Carro¹, Christina Dörje², Anders Åsberg³, Karsten Midttvedt², Hallvard Holdaas², Anna V. Reisæter², Daniel Serón¹

¹: Nephrology, Hospital Vall d’Hebron, Barcelona. ²: Trasplante Medicine, Oslo University Hospital Rikshospitalet, Oslo, Norway

C reactive protein (CRP) is an acute phase reactant and its levels also increase in chronic inflammation. It is associated with all-cause mortality, especially cardiovascular, in general population and in kidney transplant recipients. CKD constitutes a predictor of elevated CRP levels apart from classical cardiovascular risk factors, suggesting that renal function impairment contributes to systemic inflammation. It is not known if the presence of inflammation in stable grafts contributes to systemic inflammation. The aim of our study is to evaluate if the presence of subclinical tubulo-interstitial inflammation in surveillance biopsies at 1 year after transplantation is related to higher CRP levels.

We analyzed 544 standard immunological risk recipients with a stable clinical situation. Surveillance biopsies were performed at 1 year after transplantation and classified as normal (n=367), borderline (n=148) or subclinical rejection (SCR) (n=29). Patients were distributed into two groups according to high sensitive CRP (hsCRP) levels: low hsCRP (n=189) and high hsCRP (n=355). Univariate analysis showed that patients from high hsCRP group were older (55.98±13.67 vs 53.21±15.07), with a higher BMI (27.25±5.08 vs 25.09±4.03), a higher proportion of active and previous smokers (18.8% vs 16.1% and 37.9% vs 27.9%), a higher proportion of diabetes mellitus (20.5% vs 12.7%) and a higher rate of SCR at surveillance biopsy (6.8% vs 2.1%). Independent predictors of high hsCRP were BMI (1.055-1.152 95% CI, 1.103 OR) and SCR (1.002-9.209 95% CI, 3.037 OR) at 1 year surveillance biopsy.

The presence of severe subclinical inflammation in stable grafts at 1 year after transplantation contributes to higher levels of CRP.

**Clinical and pathological analyses of acute vascular rejection cases after kidney transplantation**

Tomokazu Shimizu¹, Ishida Hideki¹, Unagami Kohei¹, Okuni Masayoshi¹, Tanabe Kazunari¹, Honda Kazuho², Koike Junki³

¹: Department of Urology, Tokyo Women’s Medical University, Tokyo. ²: Department of Anatomy, Showa University, Tokyo. ³: Department of Pathology, Kawasaki Municipal Tama Hospital, Kanagawa, Japan

**Aim** We carried out a clinical and pathological analysis of cases presenting with acute vascular rejection (AVR), characterized by intimal arteritis and transmural arteritis (Banff ‘v’ score), after kidney transplantation in an attempt to clarify the mechanisms underlying the development and prognostic significance of AVR.

**Patients** AVR (Banff score: v>0) was diagnosed in 31 renal allograft biopsy specimens (BS) obtained from 31 renal transplant patients being followed up at the Department of Urology, Tokyo Women’s Medical University, between January 2010 and April 2016.

**Results** AVR was diagnosed at a median of 124.6 days post-transplant. Among the 31 BS showing evidence of AVR, the AVR was mild (v1 in Banff’s classification) in 25, moderate (v2) in 6, and severe (v3) in zero. We classified the 31 BS showing evidence of AVR by their overall histopathological features, as follows; isolated-v lesion (IVL) was seen in 6 (20%) BS, acute T-cell-mediated rejection (ATCR) in 11 (39%), acute antibody-mediated rejection (AAMR) in 8 (23%), and both ATCR and AAMR seen in 6 (20%). Loss of the renal allograft occurred during the observation period in three patients (10%), and of the remaining cases with functioning grafts, deterioration of the renal allograft function after the biopsies occurred in only two patients (7%).

**Conclusions** The results of our study suggests that ATCR contributes to AVR in 40%-60% of cases, AAMR in 20%-45% of cases, and IVL in 20% of cases. The prognosis of the graft exhibiting AVR was relatively good under the present immunosuppression and the current anti-rejection therapy.
Aged donors can produce graftable limbal stem cells

Núria Nieto-Nicolau1, Raquel Adela Martinez Gª de la Torre1, Ricardo Pedro Casaroli-Maranò2
1: Cell Biology, 2: Department of Surgery & Hospital Clinic de Barcelona, University of Barcelona

Background and aims Limbal stem cells (LSC) are stem cells responsible of the transparency and the integrity of the cornea. When they lack, due to congenital or acquired causes, corneal blindness occurs together with inflammation and corneal scarring. Current treatment includes LSC ex vivo expansion and transplantation to the damaged eye. Autologous treatment is not possible in bilateral LSC, where compatible donors of LSC need to be sought, being the cadaveric donors the most important source for tissue donation. To date, there has not been studied the potential of LSC from aged donors (>60 years) to generate grafts that could give rise to successful LSC transplantation (LSCT).

Methods We have classified 3 groups of donors according to their age (<60, 60-75, >75 years) and analyzed graft quality by percent p63-positive (p63+) cells by immunofluorescence, colony forming efficiency (CFE), and mRNA and protein expression of p63, PAX6, Wnt7a, E-cadherin, and cytokeratin (CK) 12, CK3, and CK19.

Results Results showed that LSC cultures from aged donors can express ≥3% of p63+ cells – the minimum value for predicting favorable clinical outcomes after LSCT. Younger donors presented a lower percentage of p63+ cells, data that were consistent with the lack of results in the CFE.

Conclusions Data showed that aged donors can give rise to graftable LSC and also remarked the need to analyze each donor for the percentage of p63. We also propose that the exclusion criteria for cornea donation - intraocular surgeries or associated pathologies - should not be the same than for LSC tissue donation.

Rejection phenotypes in the current era of immunosuppression

Helmut Hopfer1, Caroline Wehmeier2, Patrizia Amico3, Patricia Hirt-Minkowski2, Argyros Georgalis2, Gideon Hönger2, Thomas Menter4, Michael J. Mihatsch1, Felix Burkhalter2, Jürg Steiger2, Michael Dickemann2, Stefan Schaub2
1: Pathology, 2: Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland

Besides ‘definitive rejection’ the Banff-classification includes categories for ‘suspicious for rejection’ (SFR) phenotypes. The aim of this study was to determine the frequency and phenotypes of rejection episodes in 316 consecutive renal transplants from 2009-2014 grouped into patients without/with pre transplant HLA-DSA (ptDSAneg: n=251; ptDSApos: n=65). All adequate indication (n=125) and surveillance biopsies (n=538) performed within the first year post transplant were classified according to the current Banff-criteria. SFR phenotypes were 3-times more common than ‘definitive rejection’ phenotypes in biopsies from ptDSAneg patients (35% vs 11%) and equally common in biopsies from ptDSApos patients (25% vs 27%). In both groups, SFR-phenotypes were more frequent in surveillance than in indication biopsies (28% vs 16% in ptDSAneg patients, and 37% vs 29% in ptDSApos patients). ‘Borderline TCMR’ (91%) was the dominant SFR-phenotype in ptDSAneg patients, while ‘borderline TCMR’ (58%) and ‘suspicious for ABMR’ (42%) were equally frequent in biopsies from ptDSApos patients. Inclusion of SFR-phenotypes increased the one year incidence of clinical (ptDSAneg patients: 18% vs 8%, p=0.0005; ptDSApos patients: 24% vs 18%, p=0.31) and (sub) clinical rejection (ptDSAneg patients: 59% vs 22%, p<0.0001; ptDSApos patients: 68% vs 40%, p=0.004). In conclusion, SFR-phenotypes are very common in the current era and outnumber the frequency of ‘definitive rejection’.
A comparison of ultrastructural glomerular features in biopsies from patients with de novo donor specific antibodies with surveillance biopsies

Linda Moran¹, Jill Moss¹, Michelle Willicombe², Esma Diyenli³, Liam Rasch³, Paul Brookes⁴, Jack Galliford², Adam McLean², David Taube², Terry Cook⁵, Candice Roufossé⁵
¹: Electron Microscopy, ²: Renal Medicine, ³: Centre for Complement and Inflammation Research, Imperial College. ⁴: Tissue Typing, ⁵: Celluar Pathology, and Centre for Complement and Inflammation Research, Imperial College Healthcare NHS Trust, London, UK

Background and aims Patients with de novo donor specific anti-HLA antibody (de novo DSA) are at increased risk of antibody-mediated rejection and our aim is to compare biopsies from such patients with surveillance biopsies, to identify the effect of DSA on ultrastructural features of glomeruli.

Methods Ultrastructural features in 40 biopsies: 15 1-year surveillance biopsies from DSA-negative patients and 25 biopsies from patients with de novo DSA were recorded. Unpaired t tests were applied (Mann-Whitney) using GraphPad Prism 6.

Results There was a statistically significant difference between de novo DSA biopsies and surveillance biopsies for: mean loss of endothelial fenestration per loop (p=0.0001), mean endothelial swelling per loop (p=0.03), mean endothelial crenellation per loop (p=0.02), percentage of loops with new basement membrane (p=0.02), percentage of loops with double contours (p=0.006), and percentage of loops with extensive foot process effacement (p=0.02).

Conclusions Ultrastructural glomerular features are significantly different between biopsies from patients with de novo DSA and surveillance biopsies. Further investigations will be carried out on a wider range of biopsies, to validate the diagnostic value of these features.

Early loss of peritubular capillaries after kidney transplantation is associated with later renal function decline: a validation study in 121 patients

Anke Keijbeck¹, Floor Steegh¹, Marielle Gelens², Ernst van Heurn², Maarten Christiaans², Carine Peutz-Kootstra¹
¹: Pathology, Maastricht University Medical Centre, Maastricht, Netherlands. ²: Internal Medicine, Maastricht University Medical Centre, Maastricht, Netherlands.

Background and aims Chronic transplant dysfunction is a major cause of renal graft loss and is preceded by IF/TA. Previously we showed in a pilot study of 48 patients that IF/TA development is preceded by peritubular capillary (PTC) loss in the first 3 months after transplantation (Steegh et al. JASN 2011). The aim of this study is to validate these findings.

Methods The validation cohort consisted of 121 new patients, who had a kidney transplantation between 2003 and 2009 at the MUMC+ and of whom representative protocol biopsies were taken at transplantation, 3 and 12 months posttransplant. IF/TA, PTC number and eGFR were studied as described in the pilot study.

Results A significant loss of PTCs three months after transplantation was found in post-mortal donor kidneys (P<0.01). In univariate analyses, this PTC loss was associated with longer first warm and cold ischemia time, DGF and immunological events. When corrected for confounders, PTC loss is correlated with higher IF/TA score (P=0.02) and with lower eGFR (P=0.014) one year after transplantation. Although demographic and pre-transplant clinical variables were similar, PTC loss was less severe in the validation than in the pilot cohort, which may be related to lower incidence of DGF and shorter first WIT in DCDs.

Conclusion This study confirms that PTC loss occurs mainly in postmortal donor kidneys, in the first three months after transplantation and is associated with higher IF/TA scores and a decreased eGFR at year 1. Preserving microvascular integrity may aid in prevention of chronic transplant dysfunction.
Retrospective analysis of kidney transplant recipients with antibody-mediated rejection

Gastón Piñeiro 1, Erika De Sousa 1, Jesús Villarreal 1, Miguel Lozano 2, Joan Cid 2, Manel Solé 3, Mario Jimenez 2, Federico Oppenheimer 4, Fritz Dietmann 1

1: Nephrology and Renal Transplant, 2: Apheresis Unit, Department of Hemotherapy and Hemostasis, 3: Pathology, Hospital Clinic de Barcelona

Acute antibody mediated rejection (AMR) is a major cause of allograft loss. We retrospectively reviewed all kidney allograft recipients between 2002 and March of 2016 who received at least plasma exchange therapy (PE) and intravenous immunoglobulins (IVIG) for AMR. Investigated the variables associated with response to treatment and graft survival.

Table 1 summarizes the clinical and immunological characteristic of patients. The median follow-up was 43.5 months (range 0.5-141).

All patients received PE (mean number 6.4 +/-2.7, mean total volume 23.3 L) and IVIG (200 mg/kg after every two PE), and 88 (86.3%) rituximab (736mg SD 417). The response to treatment was better in early (less than 1 year) 72% vs late rejection 23%, OR 0.11 (p<0.001). The mean graft survival at two years was 72.4% +/- 7.9 and 46% +/-11.7 months in early and late rejection respectively. Tubulitis greater to 1 and presence of IFTA were associated with no response to treatment (OR 2.49 and 8.3, p 0.04 and 0.01) and graft loss during the first year (OR 4.06 and 2.8, p 0.039 and 0.047).

There were 43 (42.2%) graft loss, 24 in the first year after treatment.

In the next 2 years after treatment there were 84 episodes of infections in 49 patients that required hospital admission. A Charlson comorbidity index of 5 or greater was associated with more infections OR 3.5 (p<0.001), and mortality OR 35 (p<0.001).

In conclusion the response to treatment and outcomes depends of earliness of rejection, comorbidities and presence of IFTA and tubulitis greater 1.

MDRD or CKD-EPI for the estimation of living kidney donor’s renal function

Carla Burballa 1, Marta Crespo 1, Dolores Redondo-Pachón 2, María José Pérez-Sáez 2, Marisa Mir 3, Lluís Fumadó 2, Albert Frances 3, Josep Maria Puig 3, Lluís Cecchini 3, Julio Pascual 1

1: Department of Nephrology, 2: Department of Urology, Hospital del Mar, Barcelona

Introduction It remains uncertain which creatinine-based equation yield the most accurate estimation of Glomerular Filtration Rate (GFR) when evaluating individuals as potential kidney donors. Thus, we aim to study the correlation between renal function estimation equations and measure methods for assessing renal function.

Methods We analyzed the relationship between basal values of GFR measured by Tc-99m-DTPA (diethylene-triamine-pentaacetate) and those estimated by Modification Diet Renal Disease (MDRD4) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations in a series of consecutive kidney donors at our institution. The isotopic renogram was performed after intravenous Tc99m-DTPA bolus (5-10 mCi (370 Mbq)) which activity may be detected in the body.

Results We included 64 donors (70, 6% women; age 48, 34±11 years)

Baseline Scr was 0.8±0.1mg/dl and 1, 1±0, 2mg/dl one year after donation. Estimation equations under-rate GFR measured by Tc99m-DTPA (MDRD4 -9, 4±25 ml/min, p<0.05, and CKD-EPI -4, 4±21 ml/min). The correlation between estimation equations and the measure method was superior for CKD-EPI (r=0.41 p<0.004) than for MDRD4 (r=0.27; p=0.05). eGFR decreased to 59, 6±14 (MDRD4) and 66, 2 ± 14 ml/min (CKD-EPI at one year. This means a mean eGFR reduction of 28, 2±16, 7ml/min (MDRD4) and 27, 3±14, 4ml/min (CKD-EPI) at 1yr. No correlation was observed between baseline donor kidney function and the function achieved at one year of donation (r=0.24, p=0.084)Donor and Recipient GFR were similar at one year after renal transplantation (r= 0.1; p> 0.4).

Conclusions In our experience Fgm-Tc99m-DTPA correlates better with the estimation of GFR with CKD-EPI equation than with MDRD4 equation when assessing renal function for donor screening purposes.
**Determination of the culture time point to induce corneal epithelial differentiation in IPSC**

Raquel Adela Martínez¹, Núria Nieto-Nicolau¹, Adrián Morales-Pastor¹, Ricardo Pedro Casaroli-Marano²

1: Cell Biology, University of Barcelona. 2: Department of Surgery & Hospital Clinic de Barcelona, University of Barcelona

**Background and aims** Limbal Stem Cells (LSC) are progenitor cells which renew the corneal epithelium. Limbal Stem Cells Deficiency (LSCD) induces blindness by the loss of corneal transparency. Bilateral LSCD deficiency has not an accurate treatment due to the lack of an autologous source of stem cells. Current treatment is based on ex vivo expansion of LSC from healthy donors. Complications of this treatment are deleterious effects of immunosuppression and the risk of rejection. Induced Pluripotent Stem Cells (iPSC) are a promise to use in cell therapy, because will be an autologous source of cells that can be differentiated into corneal epithelial cells. However, there are not standardized protocols to achieve a complete corneal epithelial differentiation.

**Methods** By qPcR and Western blot, we examined the expression of several markers in an Episomal iPSC line (GibcoTM), after an induction period of the embryoid bodies. We evaluated progenitor LSC (p63, cytokeratin 19 and 15) and corneal epithelial differentiation markers (cytokeratin 12, 15, 19, E-cadherin and PAX6), extracellular matrix protein adhesion molecules (integrins α2, α6, α9 and β1) and wingless signaling pathway (Wnt7a).

**Results** Overall, differentiation and progenitor markers increased after maintaining the cell culture for 14 days in specific conditions. We also observed a decrease in pluripotency (SOX2, OCT 3/4, c-myc and Nanog) markers.

**Conclusion** We concluded that the optimal time point to initiate an iPSC differentiation into LSC phenotypes with specific substrates and medium is at 14 days after the corneal epithelial induction of the embryoid bodies.

---

**Adipose derived mesenchymal stem cells (ads) bioengineered grafts for ocular surface regeneration**

Ricardo Pedro Casaroli-Marano¹, Raquel Adela Martínez Gª de la Torre², Núria Nieto-Nicolau²

1: Department of Surgery & Hospital Clinic de Barcelona, University of Barcelona. 2: Cell Biology, University of Barcelona

**Background** Mesenchymal stem cells derived from adult human adipose tissue (ADS) manifest multilineage differentiation capacity. However, their plasticity to differentiate into epithelial characteristics still remains little well-known. The corneal epithelium is maintained by limbal stem cells (LSC). Transplantation of autologous LSC is not possible in several cases in which bilateral disease produces total LSC deficiency (LSCD). For that, the use of autologous ADS as a source of progenitor cells for the ocular surface reconstruction is being studied.

**Methods** The plasticity, cellular and molecular characterization and ADS in vitro behavior to assume epithelial-like characteristic were evaluated. LSC markers (p63, ABCG2, NGFr) and epithelial markers (cytokeratins 3 and 12, integrins, EGFr and E-cadherin) have been analyzed by q-PCR. After five days in epithelial-induced medium culture, ADS cells were seeded onto human amniotic membrane and applied in a rat model of LSCD. Histopathological and molecular analyses were carried-out after 30 days.

**Results** ADS cells can assume epithelial-like phenotypes when cultured into CnT-30 or SHEM media after 5 days. Expression of epithelial markers was more evident in SHEM between 3rd and 7th days in culture. Histopathological studies revealed restructuration of corneal surface, more evident with ADS cells cultured in SHEM. PCR experiments with sequencing methods demonstrated the presence of human ADS CK12 in corneas of murine in vivo model.

**Conclusion** Our in vitro and in vivo results showed that epithelial-induced ADS cells could be a potential cell source for ocular surface regenerative medicine.
Ductular reaction and hepatocyte ballooning indentify patients with fibrosing cholestatic hepatitis (FCH) after liver transplantation

Laura-Patricia Llovet1, Sergio Rodriguez-Tajes1, Maria-Carlotà Londoñò1, Carla Montironi2, Salvatore Sciarrone3, Claudia Mescoli3, Massimo Ruggè3, Patrizia Burra3, Xavier Forns1, Alba Diaz2, Gonzalo Crespo3
1: Liver Transplant Unit, Hospital Clinic, IDIBAPS, CIBERehd, Barcelona. 2: Pathology Department, Hospital Clinic, Barcelona. 3: Padova University Hospital

Background and aims  Fibrosing cholestatic hepatitis (FCH) is defined by ILTS criteria including clinical, analytical and histological variables. These criteria are not well validated and the information regarding the correlation between histological and analytical criteria in the diagnosis of FCH is scarce. We aimed to evaluate this correlation in the diagnosis of early severe recurrent hepatitis C.

Methods  Retrospective analysis of 70 patients with severe hepatitis C recurrence between 2000 and 2014 at 2 University hospitals. FCH was defined by bilirubin >6mg/dL, AP and/or GGT>5 times the upper normal limit (UNL), and HCV-RNA >107IU/mL. Cholestatic hepatitis (CH) was defined as AP and/or GGT>5 times UNL. The remaining patients were classified as acute hepatitis (AH).

Results  Most patients were male (66%), genotype 1b (71%), and mean time since LT to the diagnosis of the recurrence was 3.7 ± 2 months. According to laboratory parameters, 37, 21 and 12 patients were classified as FCH, CH and AH, respectively. Histological findings were: ballooning (mild n=30, moderate n=21, intense n=11), ductular reaction (focal n=27, diffuse n=22), lobular disarray (focal n=35, diffuse n=30), cholestasis (mild n=15, moderate n=17, severe n=9), and peri-sinusoidal fibrosis (n=33). Patients with FCH had more ductular reaction (FCH n=17, CH n=3, AH n=2; p=0.03) and a tendency towards a more intense hepatocyte ballooning (FCH n=10, CH n=0, AH n=1; p= 0.06). There were no differences in cholestasis, lobular disarray and peri-sinusoidal fibrosis.

Conclusion  The presence of ductular reaction and ballooning discriminate FCH from other forms of severe hepatitis C recurrence.

Dual kidney transplantation in the same recipient: a systematic review

Dolores Redondo1, Nuria Montero2, Maria José Pérez-Sáez2, Marta Crespo1, Julio Pascual1
1: Department of Nephrology, Hospital del Mar, Barcelona. 2: Department of Nephrology, Hospital de Bellvitge, Barcelona

Background  Dual KT has been proposed to increase KT with suboptimal kidneys. The transplant physician considers that a single kidney from a given donor will not be sufficient to add sustained stable kidney function. Although a common practice in some Spanish units in the past, dual KT represents less than 1% of all procedures.

Methods  We did a systematic literature search (OVID, Medline, Cochrane Database) and meta-analyses when possible, pooling data for calculating relative risks (RR) of major outcomes, comparing dual with single KT.

Results  Sixteen reports met inclusion criteria. DGF was lower performing dual (n=2564) vs single KT (n=23812, RR 0.81[0.68-0.98], p=0.03). Scr at one year was similar after dual or single KT (9 studies, difference -0.24 [-0.55, -0.07], p=0.13). One-year graft loss was similar (9 studies, RR 0.92[0.73-1.15], p=0.47) but 5-year graft loss was lower with dual (n=507) vs single (n=695) (RR 0.45[0.30-0.67], p<0.0001). One-year mortality was similar after dual (n=1135) or single KT (n=8583) (RR 0.94[0.52-1.69], p=0.83). Mortality at 5 years was lower after dual (n=443) vs single (n=680) (RR 0.61[0.41-0.90] p=0.01).

Conclusions  Systematic literature analysis shows better 5-year patient and graft survival in patients receiving dual KT vs single ECD-KT. However, in our opinion, these differences are based in few reports with a relatively low number of cases and the actual reported differences in survival are not enough to justify the investment of two kidneys in one recipient as a routine practice, given the shortage of organs and the mortality rates in the waiting list.
Analysing donation and transplantation of cardiovascular tissue

Maria Luisa Pérez, Elba Agusti, Anna Vilarrodona, Ricardo Pedro Casaroli-Marano, Esteve Trias
1. Barcelona Tissue Bank, Banc de Sang i Teixits, Barcelona. 2. Departamento de Cirugía Facultad de Medicina, Universidad de Barcelona

Background and aim After 25 years experience as Tissue Establishm ent, the m arge into a unique m ultitissue bank in Catalonia has implied an increase in tissue availability. A donor center was created to coordinate donor selection and tissue retrieval. The bank gives response to requests coming not only from Catalonia but also from other countries. The study aims to analyse the activity in the last two years, the sources of cardiovascular tissues and their final destination.

Methods The information related to cardiovascular bank activity has been check ed, in particular the numbers of received and sent tissues during 2014 and 2015 were analysed.

Results In this period, 259 hearts were donated to the bank for heart valves retrieval, as well as vascular segments from 180 donors. Between 2014 and 2015, the bank sent 444 cardiovascular homografts for transplantation, 226 of them (50.9.1% ) were valves (Table 1). The distribution to Catalanon hospitals represented the 23% of the total grafts shipped; 33% were implanted in the rest of Spain, and 44% went to hospitals in Europe (Figure 1). Moreover, 16 requests for arterial segments to be used in liver, kidney or pancreatic transplantation were satisfied, 9 of them for paediatric surgeries.

Conclusion To be highlighted the requests for vascular segments to be used during liver, kidney or pancreatic transplantation that are also one of the sources of tissue to the preserved in the bank. A close relationship between transplant coordinators, tissue banks and transplant surgeons is needed to give response to the increasing demand for cardiovascular tissues.

Table 1: Type of cardiovascular grafts distributed

<table>
<thead>
<tr>
<th>Type of cardiovascular segment</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>ortic</td>
<td>15</td>
</tr>
<tr>
<td>femoral artery</td>
<td>52</td>
</tr>
<tr>
<td>pulmonary artery</td>
<td>41</td>
</tr>
<tr>
<td>auricular artery</td>
<td>10</td>
</tr>
<tr>
<td>arterial</td>
<td>218</td>
</tr>
<tr>
<td>Type of heart valve</td>
<td>Total</td>
</tr>
<tr>
<td>ortic</td>
<td>89</td>
</tr>
<tr>
<td>pulmonary</td>
<td>126</td>
</tr>
</tbody>
</table>

FIGURE 1 Supplied cardiovascular grafts 2014-2015

P-52

Chronic infection by hepatitis C virus and the development of transplant glomerulopathy

Dabaiba Regidor, Miguel Angel Martínez, Natalia Polanco, Francisco Díaz-Crespo, Francisco Javier Ahijado, Rafael Díaz-Tejeiro, Maria Angeles Fernández, Marta Romero, Eugenio García, Jose Maria Morales
1. Nephrology, Hospital Virgen de la Salud de Toledo. 2. Pathology, Hospital Doce de Octubre, Madrid. 3. Nephrology, Hospital Doce de Octubre, Madrid. 4. Pathology, Hospital Virgen de la Salud de Toledo. 5. Investigation Institute, Hospital Doce de Octubre, Madrid

Objective To demonstrate that chronic infection with the hepatitis C virus (HCV) is a risk factor for the development of transplant glomerulopathy (TG) in a large sample of kidney biopsies analyzed by electron microscopy, and to demonstrate its negative impact on graft survival.

Methods Retrospective analysis, all biopsy samples of renal grafts with the diagnosis of chronic graft dysfunction (CGD), conducted between 2000 and 2014 in Madrid at 12 de Octubre Hospital were collected. 229 in total. Those in which histological study was carried out immunofluorescence (IF) and electron microscopy (EM) were selected. The work was divided in two phases: Case control study and Retrospective cohort.

Results HCV was a risk factor for developing TG with an OR=7.20 95% (2.47 to 21.01). The DSA was a risk factor for GT with an OR = 1.71 95% (1.06 to 2, 76). Patients with CGD and HCV + showed significantly worse graft survival than the HCV-.

All patients who presented ultrastructural diagnosis of TG (57) were divided into two cohorts based on status for HCV. Significant differences between HCV+ / HCV-patients concerning the presence of interstitial fibrosis and tubular atrophy degree of the samples were found, being higher in the HCV+ patients. TG+ HCV+ patients significantly showed worse graft survival.

Conclusions Chronic HCV infection is a risk factor for transplant glomerulopathy diagnosed by electron microscopy, showing a lower graft survival after diagnosis by biopsy, and even lower when associated with HCV+, being this the longest published series of renal grafts with TG diagnosed by ME. Time (months) since Bx to graft failure

P-53
**Intratubular calcification of renal allografts detected by protocol biopsies: a new classification.**

The purple study

Ana Coloma¹, Noa Díaz-Novo¹, Rosa Fornons¹, Manel Solé², Jose-Vicente Torregrosa³

¹ Renal Transplant Unit, ² Pathology Department, Hospital Clinic, Barcelona

**Background and aims** Intratubular calcification has been described in renal allograft though its clinical relevance remains to be established. The aims was to investigate mineral bone metabolism and graft function association to intratubular calcification of serial protocol biopsies done at 3 and 12 months after kidney transplantation (KT).

**Methods** 515 biopsies from 271 kidney recipients were included. Histological grouping was established according to intraluminal calcification findings: Grade 0 had none or one (P0), grade 1 had two (P1) and grade 2 more than two (P2). Laboratory data were evaluated at the moment of transplantation, 3, 6, 12, 24 and 36 months after KT.

**Results** More than one calcification was observed in 112 recipients (41.3%). Calcification was not related neither to age, gender, dialysis mode, nor immunosuppression treatment. Kidneys from donor after circulatory death (DCD) had an incidence of calcification (71.8%) higher than brain-dead (35.1%) and living ABO-compatible donor (30.5%) p<0.001. ABO-incompatible grafts revealed higher calcification incidence than ABO compatible (65% and 30.5%; p<0.001). Patients on P1 and P2 groups had significantly delayed renal graft function (DGF) (66.2%; p<0.001). Histology of grafts at 3 months with moderate interstitial fibrosis and tubular atrophy had more calcifications (p<0.05). In the first year of KT, patients with more calcifications had significantly higher serum PTH (p<0.05) and alkaline phosphate. Renal graft function was not related to calcification grade.

**Conclusions** Kidneys from DCD and living ABO-incompatible donor had higher intratubular calcification grade and it correlated with DGF in recipients. The association between mineral bone metabolism data and intratubular calcifications suggest considering an earlier treatment.

---

**Diagnostic value of peritubular capillary density in early renal allograft biopsies**

Vinita Agrawal, Narayan Prasad, Vikas Agarwal

Pathology, SGPGIMS, Lucknow, India

**Background and aims** Peritubular capillaries (PTC) are a target of microvascular injury in ABMR in renal allograft biopsies. PTC loss is seen in chronic ABMR. We performed this pilot study to analyse the diagnostic utility of peritubular capillary density in early transplant biopsies.

**Methods** Consecutive renal allograft indication biopsies from Jan to June 2016, within one year of transplantation were evaluated. Routine light microscopy and immunofluorescence including C4d was done. Immunohistochemistry for endothelial marker CD31 was performed and ten images of the cortex at 20x magnification were obtained in a serpentine manner. The medulla and the sub capsular cortex were excluded. The mean number of CD31-positive PTCs per tubule and the mean number of PTCs per 20x field were evaluated.

**Results** During this period, 37 early transplant biopsies were received, ten of which were diagnosed as rejection. Acute ABMR was diagnosed in eight; four of which were C4d negative. In ABMR, the mean PTCs per field (100.4±21) and the PTCs per tubule (1.8±0.33) were not significantly different from those with no evidence of rejection. The PTC numbers did not show significant association with age of recipient, time to transplant, C4d positivity and presence of DSA. PTC dilatation was seen in acute rejection and in biopsies with isolated acute tubular injury.

**Conclusion** This pilot study shows that PTC dilatation may suggest some allograft pathology warranting thorough evaluation. However, PTC density in early renal allograft biopsies does not appear to have diagnostic utility in determining the aetiology of acute renal allograft dysfunction.
Kidney graft evolution in hepatorenal transplant with immunological risk

Gastón Piñeiro, Anna Sánchez, Jordi Colmenero, Miquel Navasa, Jaume Martorell, Nuria Esforzado

1: Nephrology and Kidney Transplant, 2: Liver Transplantation Unit, 3: Immunology, Hospital Clinic de Barcelona

It has been suggested that liver graft provides immune protection to renal graft in context of hepatorenal transplant (HRT). We retrospectively reviewed the HRT in our hospital from May 1993 until December 2014 and identified patients with high immunological risk (HIR), defined by a positive pre-transplant citotoxicity crossmatch (CDC-CM), positive flow cytometry crossmatch (FCC) or donor specific antibodies (DSA) prior to transplantation.

Seventy-five HRT were performed, 17 (22.6%) were HIR. The mean follow-up was 79 ± 64 months. The prevalence of HCV infection, second renal transplant and time on dialysis was significantly higher in this group.

Graft survival at 1, 3 and 5 years was 63.3%, 57% and 50.7% respectively in the HIR group, and 91.3%, 87.5% and 77.7% respectively in the group without immunological risk. Graft survival censoring the patient's death was 100% in the HIR group throughout the follow-up.

Patients survival at 1, 3 and 5 was 63.3%, 57% and 50.7% respectively in the HIR group, and 93%, 91%, 88% respectively in the non HIR group.

Of the 75 patients 11 (14.6%) developed a kidney acute graft rejection, 5 (29.4%) in the HIR and 6 (10.3%) in the non HIR group. All the patients presented good response to treatment and two patients with antibody mediated rejection improved kidney function spontaneously.

Only three HIR patients had delayed graft function in context of acute humoral rejection immediately post transplant.

In our HRTs with HIR the prevalence of immunological complications was very low and the evolution of renal function was good.

Renal transplantation for patients with autosomal dominant polycystic kidney disease: long term follow-up and importance of intracranial aneurysms on outcomes

Carla Burballa, Maria José Pérez-Sáez, Dolores Redondo-Pachón, Marisa Mir, Laia Sans, Alfonso Califano, Anna Buxeda, Ana Marina Granados, Marta Crespo, Julio Pascual

Department of Nephrology, Hospital del Mar, Barcelona

Introduction ADPKD We evaluated long-term outcomes following kidney transplantation (KT) in Autosomal Dominant Polycystic Kidney Disease (ADPKD) patients. In particular, we focused on the prevalence of intracranial aneurysms (IA) and their consequent mortality rate.

Material and methods Retrospective study of 709 transplants performed in 1979-2013. Patient and graft survival 3-5-10 years post-KT were assessed. Brain imaging tests were employed when symptoms were present or when patients had familial history of IA. They were not used as screening tests in asymptomatic patients.

Results 98 KT recipients (13.8%) had ADPKD. When comparing ADPKD with non-ADPKD recipients, those with ADPKD were older (53, 5±10, 8 vs.47, 8±14, 6; p<0.0001), more women (50 vs.37.3%; p=0.004), 5-10-yr patient survival rates are greater in ADPKD-KT recipients.

5-year graft survival was higher in ADPKD recipients (72.9 vs 61.3%; p=0.04), but 10-yr survival was similar. Multivariate analysis showed association between ADPKD and graft survival HR 0.69[0.48-1.01], 54/98 recipients (47.3%) had imaging tests before KT. Twelve IA were detected (prevalence 22.2%). Three patients with IA died after IA rupture, three patients underwent surgery repair (microsurgical clipping or endovascular embolization) and the remaining six underwent surveillance. Amongst those who died of an aneurysmal hemorrhage, two patients did not have previous imaging test.

Conclusion Patients with ADPKD have better survival rates than non-ADPKD recipients. Haemorrhage due to ruptured brain aneurysms is an important cause of death in ADPKD KT recipients. Therefore, there may possibly be sufficient net benefit to screening these patients for IA.
**Modulation of leukocyte-endothelium interactions with RATGS after ischemia-reperfusion injury in an experimental human perfusion model**

Andres Beiras-Fernandez¹, Isabella Werner², Pengfei Wang², Anton Moritz², Christian Vahl¹

¹: Cardiothoracic and Vascular Surgery, Universitätsmedizin Mainz, Mainz, Germany. ²: Department of Experimental Surgery; University of Frankfurt, Frankfurt, Germany

**Purpose**
The failure of translating results obtained in animal models into humans is a pivotal problem of research in transplantation. We developed a model in the human placenta to study endothelial reactions after ischemia-reperfusion by means of intravital microscopy. We investigated the effect of ATG upon the reduction of leukocyte-endothelial interactions.

**Methods**
Human placentas (n=12) from elective caesarean deliveries were used after informed consent. All placentas were immediately connected to a monitored double perfusion system consisting of a two roller-pumps, reservoir, oxygenator, hemo-filter and bubble-trap. The placentas were reperfused with compatible human blood for 240 min after 60 minutes ischemia (perfusion with Ringer Lactate). ATG (1mg/kg; Thymoglobuline, Sanofi, USA) was applied to the human blood before reperfusion. Pressure, flow, and AVDO₂ were investigated. Intravital Microscopy was performed to analyse adherence and infiltration of leukocytes and recorded.

**Results**
Our human placenta model could be validated for the study of inflammatory and vascular-endothelial reactions. The hemodynamic measurements were consistent and the AVDO₂ showed a continuous vitality of the perfused tissues. Morphological analyses confirmed a normal configuration of placental tissue and its endothelium after 4 hours of reperfusion. Intravital microscopy was feasible and allowed quantification of adherent leukocytes. Immunomodulation with ATGs resulted in better microcirculation, increased blood flow velocity and reduction of leukocyte adherence.

**Conclusion**
Our results show that the placenta model is an adequate tool for the study of leukocyte-endothelial reactions after ischemia-reperfusion injury. Treatment with ATG before reperfusion showed an improvement of the microcirculation as well as reduction of leukocyte adherence.

**Ectopic lymphoid structures are present in type I T-cell mediated kidney transplant rejection**

Kitty de Leur¹, Marian Claesen-van Groningen², Gretchen de Graav¹, Dennis Hesselink², Janneke Samsom², Carla Baan¹, Karin Boer¹

¹: Department of Internal Medicine, Transplantation laboratory, ²: Department of Pathology, ³: Department of Pediatrics, Erasmus MC, Rotterdam, The Netherlands

**Background**
In renal transplantation, many allograft recipients develop donor-specific antibodies associated with an increased risk for graft rejection. Current immunosuppressive agents are principally aimed at T-cell-mediated alloimmunity, underestimating humoral effectors. Antibody responses are mainly mediated by BCL6⁺ T follicular helper (Tfh)-cells that activate B-cells predominantly via interleukin-21 (IL-21). Whether this reaction appears in the allograft is still being debated. Here, we investigated if ectopic lymphoid structures (ELSs) are present in T cell mediated rejection (type I and II) and antibody-mediated rejection after renal transplantation.

**Material & methods**
Fifteen renal transplant biopsies were studied. Primary diagnosis were C4d+ antibody-mediated rejection (ABMR, n=5), T-cell mediated rejection type I (TCMRI, n=5), and T-cell mediated rejection type II (TCMRRII, n=5). FFPE sections were stained for T-cells (CD3), B-cells (CD20), and follicular dendritic cells (FDCs, CD23). In addition, double immunofluorescent stainings for IL-21 and BCL6 were performed. Slides were analysed for the presence and composition of infiltrate.

**Results**
In all 15 biopsies, infiltrates of CD3⁺ T cells were detected. In TCMRI, CD20⁺ B-cells formed aggregates surrounded by T-cells in the tubulo-interstitial compartment. In these aggregates CD23⁺ FDCs were detected, suggesting the presence ELSs. In contrast, ABMR and TCMRRII showed diffuse spread of T cells and B cells and no CD23⁺ cell aggregates. IL-21 was present in all biopsies, however, co-localization with BCL6 was predominantly observed in TCMRII biopsies.

**Conclusions**
Nodal lymphoid proliferations with FDC networks and BCL6⁺IL-21⁺ cells are mainly found in TCMRI and may suggest a pivotal role for Tfh cell – B cell interaction.
Undetected lung cancer in candidates for lung transplantation with interstitial lung disease

Cristina Berastegui Garcia¹, Judit Sacanell², Jordi Riera², Irene Sansano³, Laura Romero⁴, Irene Bello⁴, Teresa Pont⁵, Carlos Bravo Masgoret¹, Victor Monforte¹, Helena Sintes¹, Manuel Lopez¹, Berta Saez¹, Antonio Roman¹

¹: Pulmonology, ²: intensive Care, ³: Pathology, ⁴: Thoracic Surgery, ⁵: Organ Procurement, Hospital Universitari Vall d’Hebron, Barcelona

Diagnosis of cancer in recipients of lung transplantation (LT) has some limitations, in particular regarding lung adenocarcinomas in patients with interstitial lung diseases (ILD). Most of these tumors are difficult to detect in thoracic computed tomography (CT) or PET scan. The aim of the study was to retrospectively review those cases in our institution.

From a total of 931 LT carried out between August 1990 and November 2016, 357 (38%) of them were performed in ILD patients. In this group, unexpected lung adenocarcinomas in explanted lungs were found in 5 (1.4%) of them. All patients were male, mean age was 59 (r: 48-66) years, with a previous smoking exposure of 40 (SD 13) packs/year. Preoperative diagnosis were UIP (2 cases), probable UIP (2 cases) and 1 chronic HP. In two of them one lung biopsy was carried out for diagnosis. Preoperative thoracic CT scan showed ground glass in 4 patients and typical UIP pattern in one patient. One single LT was performed in 4 patients and 1 died on the waiting list being kidney donor. Four were mucinous variants of adenocarcinoma and 1 was a small cell carcinoma. All were at least stage IIIA at the time of diagnosis. One explanted lung showed smoking related interstitial fibrosis and in the other 4, advanced fibrosis difficult to classify was observed. None of the adenocarcinomas harbored KRAS mutations. Two out of 4 LT patients dead because of cancer.

Lung cancer detected in explanted lungs with ILD are an unusual finding that may have an impact in outcomes. One better screening of potential recipients, in particular in the case of ILD with atypical CT scan, should be established.

Six-month surveillance biopsies with borderline changes are associated with worse allograft function irrespective of the severity of interstitial inflammation

Shiang-Cheng Kung¹, Mehdi Tavakoli², Dejan Dobi³, Flavio Vincenti¹, Sindhu Chandran¹, Zoltan Laszik³

¹: Medicine/Nephrology, ²: Surgery, ³: Pathology, University of California San Francisco, San Francisco, United States

Background and aim The clinical impact of subgroups of Banff borderline (BL) changes in transplant renal biopsies with variable severity of inflammation is unknown. Our study looked at a single center six-month surveillance renal transplant biopsy cohort with BL i0t1 and i1t1 changes with regard to their serum creatinine (Cr) and eGF R at 1 and 2 years post-transplant vs. those biopsies without inflammation (i0t0).

Method We conducted a single center retrospective cohort analysis of 1104 six-month surveillance kidney transplant biopsies performed at UCSF from 7/1/2009 – 1/31/2014. Two subsets of biopsies with BL changes, i0t1 (n=137); i1t1 (n=40) were studied. Biopsies without inflammation or tubulitis (i0t0) served as controls (normal) (n=543). Demographics and clinical variables were obtained via electronic medical records. GFR was estimated by CKD-EPI formula. Univariate linear regression was used for statistical analysis.

Result All demographic variables, diabetes incidence, death rate, etc were similar (p>0.05) in the groups. Serum Cr and eGF R at 1 and 2 years post-transplant were significantly different between the i0t1 subgroup and controls. eGF R was significantly lower in the i1t1 subgroup vs. controls at 1 year post-transplant.

Conclusion Subclinical BL changes in six-month surveillance transplant kidney biopsies are associated with significantly worse renal function at 1 and 2 years post-transplant. The impact of even subtle changes with minimal or no interstitial inflammation (i0) in the presence of mild tubulitis (t1) is comparable to that seen with i1t1 lesions. These observations suggest the need for novel therapies and strategies to better control low grade cell-mediated alloimmune injury.
A study of the relationship between peritubular capillary basement membrane multilayering and time post transplantation

Linda Moran¹, Jill Moss¹, Lavina Bellaramani², Esma Diyen³, Michelle Willicombe³, H Terry Cook¹, Candice Roufosse³

¹: EM Unit, Imperial College Healthcare NHS Trust. ²: Dept Complement and Inflammation Research, Imperial College. ³: Dept Renal Medicine, Imperial College Healthcare NHS Trust. 4: Cellular Pathology, Imperial College Healthcare NHS Trust, London, UK

Background: Severe peritubular capillary basement membrane multilayering (PTCBML) is a defining feature of chronic antibody-mediated rejection. We have also noted an increase in the mean number of basement membrane (BM) layers in early antibody-mediated rejection. However, it is not clear how time post-transplant affects BM layers in an unselected population of transplant biopsies.

Methods: We performed counts of numbers of BM layers in 25 cortical peritubular capillaries in 307 consecutive transplant biopsies for which EM was requested. Numbers with 1, 2, 3-4, 5-6 and 7 or more layers were recorded and expressed as a mean. Linear correlation was used to compare mean PTCBML with time post transplantation. Biopsies were also separated into groups: 0-6 months (n=64), 6-12 months (n=48), 1-2 years (n=56), 2-3 years (n=23), 3-5 years (n=54), and 5-10 years (n=62) post-transplantation. Median and interquartile range were compared between groups using Kruskal-Wallis. Statistics were performed with GraphPad Prism software.

Results: There was linear correlation between mean PTCBML and time post transplantation (p= 0.004, r²= 0.026) (Figure 1). When comparing samples grouped by post-transplant era, there was a significant difference between the median values (p=0.0057), related to a significant difference between samples from 6-12 months post-transplantation compared with 5-10 years post-transplantation (Figure 2).

Conclusion: The mean PTCBML slowly increases with time post transplantation, but remains low (<2) in the vast majority of samples.

P-65

Macrophage density in 6-week-surveillance biopsies predicts future renal transplant function at 4 years post transplantation

Jan Hinrich Bräsen¹, Abedalrazag Khalifa¹, Jessica Schmitz¹, Wei Dai¹, Gunilla Einecke², Anke Schwarz², Michael Hallensleben³, Bernhard M. W. Schmidt², Hans Heinrich Kreipe¹, Hermann Haller³, Sibylle von Vietinghoff³

¹: Nephropathology, Institute for Pathology, ²: Department of Internal Medicine, Division of Nephrology and Hypertension, ³: Institute for Transfusion Medicine, Hannover Medical School, Hannover, Germany

Inflammation is difficult to quantify by eye at low densities. We measured leukocyte abundance in early surveillance biopsies by digital image analysis to test for predictive value of leukocyte subsets.

In six-week surveillance biopsies (n=67), T cells (CD3), B cells (CD20), macrophages (CD68, clone PGM1) and dendritic cells (CD209) were stained and subsequently scanned (Leica). Leukocyte densities were assessed in whole slide images using a digital approach (Definiens Tissue Studio).

Renal cortical T cell, B cell and macrophage infiltration was significantly higher in histological rejection (n=11; borderline=8, cellular rejection=2, humoral rejection=1). Above median, macrophage density was associated with lower combined patient and graft survival (p<0.05). Both B cell and macrophage densities inversely correlated with estimated glomerular filtration rate (eGFR) four years after transplantation. In addition, macrophage infiltration correlated with eGFR loss. Among histological measurements (including a complete Banff classification), only macrophage density was a significant predictor of an eGFR<30ml/min after four years (p<0.01) and part of the best eGFR prediction set in multivariable linear regression analysis of multiple clinical and pathological parameters. The macrophage cutoff value retained its discriminative power for survival and eGFR in a second independent cohort (n=50).

In summary, digital high-resolution assessment of CD68+ macrophage infiltration shows prognostic value in early renal transplant biopsies.
Factors affecting kidney allograft outcome in transplant glomerulopathy
Clarissa Cassol¹, Juarez Braga², Joseph Kim³, Rohan John¹
¹: Laboratory Medicine and Pathobiology, University of Toronto, ²: Institute for Health Policy, Management and Evaluation, Faculty of Medicine, University of Toronto, ³: Division of Nephrology and the Kidney Transplant Program, Department of Medicine, Toronto General Hospital, University Health Network, University of Toronto. Toronto, Canada

Background Chronic antibody-mediated rejection, of which transplant glomerulopathy (TG) is a major morphologic expression, has been recognized as the leading cause of late renal allograft loss. We investigated clinical and histopathological characteristics of TG patients to determine factors associated with outcome.

Methods The cohort included for-cause renal allograft biopsies with a first diagnosis of TG between 2001 and 2015. Relevant clinical and Banff histopathologic parameters were analysed with regards to graft survival.

Results TG was mild in 80, moderate in 58, and severe in 134 cases. C4d was positive in 36%, Donor Specific Antibodies (DSAs) were present in 71% of tested patients, and 6% had hepatitis C. After median follow-up of 22.5 months, 170 patients lost grafts, 22 died and 80 were alive with functioning grafts. Severe TG showed greater glomerulitis and combined microvascular inflammation score (both p<0.0001). There was no difference in glomerulosclerosis or IF TA across TG grades. Graft survival was significantly decreased for TG grades 2/3 (p=0.04), and severe IF TA (p<.0001), but was not affected by DSA, C4d, or microvascular inflammation score. Multivariable Cox analysis showed fibrosis ≥ 50% and prior transplant to be associated with increased risk for graft loss, in addition to lower eGFR and greater proteinuria at biopsy.

Conclusion In a large cohort of TG patients over 15 years of study, clinical parameters of proteinuria, eGFR and prior transplant, and histologic parameters of TG grade ≥ 2 and IF TA>50% were the only factors impacting graft survival.
**P-68**

**High-speed mass spectrometry imaging identifies lipid degradation products in kidney donor tissue that are associated with severity of ischemic injury**

Tim van Smaalen¹, Shane Ellis², Nadine Mascini², Tiffany Porta², Berta Cillero-Pastor², Lisa Hillen³, Ernest van Heurn⁴, Carine Peutz-Kootstra⁵, Ron Heeren²

1: Department of Surgery, Maastricht University Medical Center, Maastricht, Netherlands. 2: M4I, The Maastricht Multimodal Molecular Imaging Institute. 3: Department of Pathology, Maastricht University Medical Center. 4: Department of Surgery, Amsterdam Medical Center, Amsterdam, The Netherlands

**Background and aims** There is a need for new tools to rapidly assess ischemic kidney injury and thus estimate graft viability and aid in graft selection. The aim of this study is to investigate the added value of mass spectrometry imaging (MSI) in viability assessment of ischemic donor kidney tissue. Furthermore, by identifying (novel) molecules that have discriminative capacity we aim to provide novel insights into the pathophysiologic processes of ischemic kidney injury.

**Methods** A perfusion model was developed where paired porcine kidneys received either warm or cold ischemia (n=8 per group). Ischemic tissue damage was assessed systematically by two blinded pathologists using HE and PAS stained sections. Secondly, we applied a new high-speed MALDI-ToF mass-spectrometer to study spatial distributions and compositions of lipids from kidney tissue with different types of ischemia.

**Results** Systematic histopathological examination revealed no significant differences in acute kidney injury parameters between kidneys with warm or cold ischemia. We were able to perform MSI on frozen tissue sections within two hours, making it a clinical useful tool for viability assessment. We identified that certain lipid degradation products, including those specific to mitochondria, were elevated in renal tissue of pigs with warm, more severe ischemia. MSI could discriminate in 100% of kidney pairs (Figure 1).

**Conclusions** MSI can differentiate and identify molecular patterns of ischemic kidney injury in a clinical acceptable time frame. Identified lipidomic patterns provide additional insights in the pathophysiologic processes of organ injury during the donation process and possibly provide new biomarkers for graft viability assessment and potential targets for therapeutics.

**FIGURE 1** MSI pictures of kidney biopsies

---

**P-69**

**Quantitative image analysis combined with tissue-based gene expression profiling has the potential to improve the diagnosis of Banff’s ‘Borderline Changes’ category**

Dejan Dobi¹, Sarah Bowman¹, Sindhu Chandran³, Flavio Vincenti², Qizhi Tang³, Zoltan Laszik¹

1: Department of Pathology, University of California, San Francisco, USA. 2: Department of Medicine, Division of Nephrology, University of California, San Francisco, USA. 3: Department of Surgery, Division of Transplant Surgery, Transplantation Research Laboratory, University of California, San Francisco, USA

**Background and aims** Although histologic reproducibility of Banff ‘Borderline Changes’ (‘BL’) is suboptimal, no alternative clinical diagnostic platforms are available to detect the low end of cell mediated alloimmune injury. To explore the potential of a multifaceted tissue-based approach to better define ‘BL’ category we applied gene expression analysis in combination with quantitative morphometry in biopsies with normal morphology, ‘BL’, and ‘Acute Cellular Rejection’ (‘ACR’).

**Methods** 12 cases from each group (‘Normal’, ‘BL’ and ‘ACR’) were selected. Gene expression analysis (GEA) and CD45 immunohistochemistry (IHC) were performed on sections from formalin-fixed paraffin-embedded tissues. For GEA, NanoString nCounter platform was used with a customized panel of 800 genes. CD45 IHC was followed by whole-slide digital image analysis to quantify the inflammatory cell count/mm² tissue (ICC). One-way ANOVA with post-hoc test, Pearson’s correlation, and multivariate regression were used, where applicable.

**Results** ICC was significantly different amongst different diagnostic groups (p < 0.0005), and it increased from ‘Normal’ (140±88) to ‘BL’ (360±274), and ‘ACR’ (1763±1047), in that order. There was an excellent correlation between ICC and CD45 mRNA level r=0.933, (p<0.0005). Based on the fold change comparison of the gene expression levels, the ‘cytotoxicity’ geneset proved to be the most discriminative for separating ‘BL’ both from ‘Normal’ and ‘ACR’ [Global significance score (GSS) ‘Normal’ vs. ‘BL’ = 2.267; GSS ‘BL’ vs. ‘ACR’ = 4.347].

**Conclusions** A multimodal tissue-based approach has the potential to better define BL category as an alternative to the current gold standard histopathological assessment and the gene expression-only strategies.
Size matters: kidney biopsy sample size has major impact on the diagnosis of Banff’s ‘Borderline Changes’ in cases with low inflammatory load

Dejan Dobić, Flavio Vincenti, Sindhu Chandran, Zoltan Laszik
1: Department of Pathology, University of California, San Francisco, USA. 2: Department of Medicine, Division of Nephrology, University of California, San Francisco, USA

Background and aims The i0t1 lesion – as part of the Banff ‘Borderline changes’ (‘BL’) category – represents the low-end of cell-mediated alloimmune injury. Since ‘BL’ may be one of the contributing factors to late allograft loss, identifying ‘BL’ cases with low inflammatory load (‘LIL-BL’) is essential. However, the impact of biopsy sample size on the diagnostic accuracy is understudied. Therefore, in a set of ‘LIL-BL’ cases we explored the within-sample consistency of Banff i, t, ti, ci, and ct lesions.

Methods Protocol biopsies 6-month post-transplant that had at least two adequate cores per case (≥7 glomeruli/core) with Banff-score of either i0t1 (n=35) or i1t1 (n=4) were enrolled. One PAS and two H&E digitized sections/case were used to assign Banff i, t, ti, ci, ct scores for the individual biopsy cores in a given sample.

Results κ-statistics showed moderate-strong correlation between the two cores of a given sample for i, ti, ci, ct (0.478, 0.640, 0.552, 0.728 respectively p<0.002 for all tests) but not for t (-0.111, p=0.485). Biopsies without i1 lesion in at least one tissue core had a 83% less chance (95% CI, 23% to 96%, p=0.021) to have t1 lesion in both cores compared to biopsies with i1 in at least one core.

Conclusions If the biopsy consists of only one adequate core and shows i0 lesion the detection rate of tubulitis is significantly hampered versus those biopsies with at least 14 glomeruli. To improve diagnostic accuracy of ‘BL’, Banff’s renal biopsy adequacy criteria need to be reconsidered.

Assessment of cytomegalovirus (CMV) specific immune response measured by Quantiferon and overall immune response measured by Immuknow® in lung transplant patients with positive CMV serology pre-transplantation

Helena Sintes, Victor Monforte, Piedad Ussetti, Virginia Pérez, Francisco Santos, Amparo Solé, Jose Maria Borro, Jose Cifrián
1: Pulmonology, Hospital Universitario Vall d’Hebron, Barcelona. 2: Pulmonology, Hospital Universitario Puerta de Hierro, Madrid. 3: Pulmonology, Hospital Universitario Doce de Octubre, Madrid. 4: Pulmonology, Hospital Universitario Reina Sofia, Córdoba. 5: Pulmonology, Hospital Universitario La Fe, Valencia. 6: Pulmonology, Hospital Universitario A Coruña. 7: Pulmonology, Hospital Universitario Marqués de Valdecilla, Santander

Background CMV seropositive patients are considered in risk to develop CMV infection in lung transplant recipients (LuTR). The aim of this study is to identify patients who will develop CMV infection by measuring CMV-specific immune response (Quantiferon®) and overall immune response (Immuknow®) in a group of CMV seropositive LuTRs.

Methods A prospective, observational, multicentre study including 92 patients at 3 months post-transplant. Both test (Quantiferon® and Immuknow®) were performed at 3, 6, 8, 10 and 12 months post-transplant. CMV prophylaxis length indication was 6 months. Cut off for quantiferon was 0, 2 UI of interferon gamma/mL and for immuknow 225 ng of ATP/mL.

Results CMV infection (>0 copies/mL) occurred in 43 (46, 74%) patients. Twenty (21, 74%) developed high level DNAemia (>1000 copies/mL) and 4, 3% (N=4) suffered CMV disease. Twenty-six (28, 26%) patients registered adverse reactions; in 9 (34%) withdrawal of prophylaxis was required. Quantiferon showed 80, 4% of specificity and 22, 2% of sensitivity to predict CMV infection from 6 to 12 months post-transplant. Positive and negative predictive values (PPV and NPV) were 47, 1% and 56, 9% respectively. Immuknow showed 14, 9% of specificity and 87, 5% of sensitivity. PPV and NPV were 46, 7% and 58, 3% respectively. Both in combination showed improved sensitivity (89%) and NPV (69, 2%).

Conclusions Quantiferon showed high specificity and immuknow high sensitivity to predict CMV replication (>0 copies/mL). Quantiferon and Immuknow in combination showed improved sensitivity and NPV to predict CMV infection.
Panel reactive antibodies is a debatable indicator of post-transplant function and survival
Meagan McCahery1, Ajda Rowshan1, Katya Mauff2, Judith Kal- van Gessel2, Marian Claesen- van Groningen1
1: Department of Pathology, 2: Department of Nephrology & Transplantation, 3: Department of Biostatistics, Erasmus Medical Centre Rotterdam, Rotterdam, The Netherlands

Background Panel reactive antibodies (PRA) estimation is widely used in determining sensitization status and severity. Currently there is no strong evidence supporting that PRA% is predictive as a prognostic measurement for renal allograft outcome. Here, we investigated the value of PRA% as a prognostic indicator of post-transplant function and renal allograft survival.

Methods All patients who received a renal allograft at our centre from 2010 through 2014 were included. We retrospectively analyzed the association of current-pretransplant PRA% (cPRA%) and highest measured PRA% (hPRA%) (cut-off value 6%) with the incidence of rejection and kidney function. Patients were divided into three groups. Group 1, control group, is negative for cPRA% and hPRA%. Group 2 is hPRA% positive and cPRA% negative. Group 3 is cPRA% positive and hPRA% positive. Clinical data were collected.

Results A total of 942 patients was included and 866 for cause renal biopsies were obtained from 471 patients. Strikingly, there is no significant relation between hPRA% and increased biopsy proven rejection rate (P=0.08) No significant difference in eGF R at 3 and 12 months post-transplant was found between groups. The hPRA% positive groups had a trend in developing more proteinuria at 3 and 12months post-transplant compared to the control group (P=0.05).

Conclusion We conclude that cPRA% and hPRA% values do not predict the occurrence of rejection and are not associated with graft function and proteinuria up to one year after transplantation. We therefore question the use of PRA% in this setting in prioritizing patients for eligibility for solid organ transplantation.

Enteric drainage of pancreas transplantation. Clinical impact of intra-abdominal complications
Joana Ferrer1, Brenda Cano-Vargas2, Lilia Martinez De La Maza1, Miguel Angel López-Boado1, Ramón Rull1, Maria Jose Ricart3, Pedro Ventura3, Esmatjes Enric4, Santiago Sánchez1, Josep Fuster1, Juan Carlos García-Valdecasas1
1: Hepato-bilio-pancreatic Surgery and Transplantation Department, Hospital Clinic, Barcelona. 2: Hospital General Centro Médico Nacional La Raza. México. 3: Renal Transplant Unit, Hospital Clinic, Barcelona. 4: Diabetes Unit, Hospital Clinic, Barcelona

Aim To analyze retrospectively the surgical complications associated with enteric drainage in a single center over a period of 15 years.

Methods From 2000 to 2015, 333 pancreas transplants were performed (SPK: 272, PAK: 23, PA: 3, Retransplantation: 35). Systemic vascular drainage was performed with porto-cava anastomosis and arterial anastomosis between superior mesenteric artery or iliac graft artery to right iliac primitive artery. For exocrine secretion, enteric drainage was performed by side-to-side with handsewn duodeno-jejunostomy anastomosis.

Results Nineteen patients were identified with intestinal complications: intestinal obstruction in 7 patients, paralytic ileus in 4 patients, ischemic graft duodenum in 2 patient, dehiscence of duodeno-jejunostomy in 2 patients, intestinal fistula without anastomatic dehiscence in 3 patients and anastomatic dehiscence in jejunum after transplantectomy in one case of retransplantation. According Clavien-Dindo, complications were: Grade I: 10.5%, Grade II: 10.5%, Grade IIb: 57.9% and Grade IVa: 21.1%. Fifteen patients required reoperation (lysis adhesions (n=7), pancreas transplantectomy (n=5), primary closure and intestinal bypass (n=1), simple suture (n=1), intestinal resection and anastomosis (n=1). Vascular thrombosis diagnosed by imaging assessment was related with ischemic process of enteric drainage on 15.8% of cases (n=3), with a significant correlation for graft loss in two of the cases.

Conclusions Enteric drainage for exocrine secretion of graft pancreas is a safe and feasible technique with a low rate of complications. Vascular thrombosis associated with intestinal complications is a risk factor for the viability of pancreatic graft, so early detection is important.
**Experimental porcine model in pancreas transplantation**

Joana Ferrer¹, Víctor Molina¹, Jimmy Nils Hidalgo¹, Roger Pujo³, Lidia Gómez², Pablo De La Calle³, Miguel Angel López-Boado¹, Josep Fuster¹, Laureano Fernández-Cruz¹, Juan Carlos García-Valdecasas³

¹: Hepato-bilio-pancreatic Surgery and Transplantation Department, Hospital Clinic, Barcelona. ²: Department of Anesthesiology, Hospital Clinic, Barcelona. ³: Universidad de Alcalá de Henares, Madrid

**Aim** Porcine model is one of the best since the anatomy and physiological similarities with human. The aim of this study is start up an experimental model valid, similar and comparable to humans in order to make it useful in future studies.

**Methods** Sixty-four pigs took part of this research, the half of them being pig-pancreas donor, and the other half being recipient. The group of recipient became diabetic with two methods, 10 with Streptozotocin (STZ) and 22 with total pancreatectomy. The technique used in donor was the extraction the whole pancreas with the duodenum, both fully vascularized. The abdominal aorta was dissected above the iliac bifurcation for cannulation. The duodenum-pancreas graft complete with aorta patch was excised. The venous anastomosis was done between the donor portal vein and vena cava. The arterial anastomosis was done between donor aorta-patch and recipient infrarrenal aorta. Satisfactory reperfusion was indicated by a progressive normalization of coloration of the pancreatic graft. It was done the anastomosis between the duodenum of the graft and the jejunum of the recipient.

**Results** Six out of ten pigs treated with STZ died, because of his toxicity in some cases. Nine out of twenty-two with total pancreatectomy died. Once became diabetics and after transplantation, three animals had surgical complications. The rest lived with a normalization of glucose levels until the euthanasia.

**Conclusions** This research allows establishing a large animal model in pancreas transplantation. STZ has a very high toxicity and mortality. Pancreatectomy seems an effective and safety procedure to make them diabetic.

---

**Glomerulocapillary miRNA signatures in three models of antibody-mediated rejection**

Georg Dieplinger², Veronika Grau³, Falko M. Heinemann⁴, Peter T. Jindra⁵, Ute Eisenberger⁶, Jan Ulrich Becker¹

¹: Institute of Pathology, University Hospital of Cologne, Cologne, Germany. ²: Department of General, Visceral and Cancer Surgery, Transplant Center Cologne, University of Cologne, Cologne, Germany. ³: Laboratory of Experimental Surgery, Department of General and Thoracic Surgery, Justus-Liebig-University Giessen, Giessen, Germany. ⁴: Institute for Transfusion Medicine, University Hospital Essen, University Duisburg-Essen, Essen, Germany. ⁵: Immune Evaluation Laboratory, Department of Surgery, Baylor College of Medicine, Houston, TX, USA. ⁶: Clinic for Nephrology, University Hospital Essen, University Duisburg-Essen, Germany

Antibody-mediated rejection (ABMR) is still a diagnostic problem in kidney transplantation and its pathophysiology incompletely understood. miRNAs that negatively regulate entire gene sets might be involved and can be quantified from minimal amounts of paraffin-embedded biopsy material. We examined a rat model, an in vitro model of ABMR and human biopsies with thrombotic microangiopathy (TMA) due to ABMR for glomerulocapillary miRNA expression signatures. Normal Lewis control kidneys, Fischer-F344 to Lewis and Lewis to Lewis rat renal allografts, glomerular endothelial cells treated with anti-HLA class I ABMR and microdissected glomeruli from paraffin-embedded human biopsies with TMA due to ABMR were investigated with low density qRT-PCR arrays for differentially regulated miRNAs. Candidate miRNAs were validated with single rRT-PCR runs. Two glomerular miRNAs were upregulated in rat allografts (miR-199a-3p, miR-125b-2-3p), one was upregulated only in isografts and remained at nontransplant control levels in allografts (miR-451-5p). In glomeruli of class I ABMR 10 miRNAs were upregulated (let-7c-5p, miR-28-3p, miR-30d-5p, miR-99b-5p, miR-125a-5p, miR-195-5p, miR-374b-3p, miR-484, miR-501-3p, miR-520e) and 2 downregulated (miR29b-3p, miR-885-5p). A random forest analysis based on glomerular miRNA quantification allowed identification of 80-90% of patients with class I ABMR vs. controls. In TMA due to ABMR glomerular miR-532-3p was upregulated, its target ADAMTS13 downregulated on the protein level.

Surprisingly, our three models exhibited a wide spectrum of deregulated glomerular miRNAs without any overlap. Glomerular miRNA quantification might be a promising diagnostic technique for ABMR, complementing conventional histology that should be prospectively validated in human biopsies. Moreover, our results could be translated into novel therapeutic approaches.
Prevalence of histopathological abnormalities detected at time pre-implantation renal biopsy among living kidney donors

Mona Abdelrahim, EhabWafa Dahab
Urology and Nephrology Center, Mansoura University, Egypt

To study histologic abnormalities at the pre-implantation biopsies of living kidney donors to evaluate their significance as a clinical and research tool. Also to compare with subsequent histopathological findings after transplantation either protocol or event biopsy. Pre-implantation biopsy was not previously studied in our patients. Through the period between Nov. 2009 and April 2012, 94 pre-implantation donor biopsy were performed by wedge biopsy. H&E, PAS, Masson-trichrome and Silver Methane-amine were carried out. Examination for specimen adequacy, chronic changes and others. CADI score were applied. Clinical and biochemical data at the time of transplantation were recorded. Continuous variables were expressed as mean values ± SD. Chi square analysis was used for categorical variables. Male were 37 (39.4%), females were 57 (60.6%). The mean age was 39.8 ±10.6 (range 22-66 years). Eighty five percent of biopsies were adequate (contained > 10 glomeruli & 2 arteries). Segmental sclerosis was detected in 9.6%, mesangial thickening in 29.8%, global sclerosis in 29.8% and Tubular atrophy in 7.4%. No cases have shown interstitial fibrosis. Interstitial inflammation was noticed in 2.1% and edema in 5.3%. ATI in 13.8%. Focal and diffuse nodular hyaline changes were seen in 7.4% and 1.1% respectively, intimal fibrosis was detected in 16%. Correlating age interval to number of glomeruli has no statistical significance. The mean body index was 29.3±6.5 (range 18.3-48.4) . The mean serum creatinine was 0.71± 1.6 mg% (range 0.4-1.1), creatinine clearance was 152.6± 52.7 (range 87-485) & FBG was 93.5± 10.6mg% (range 72-146).The mean serum cholesterol was 189± 35.3 and for uric acid was 4.7 ±1.2. There are histopathological abnormal findings at the pre-implantation biopsies. Protocol renal allograft biopsy is a potentially valuable diagnostic and research tool. The clinical useful information they provide justifies its importance as a reference tool in future pathology.
Envarsus®
Redefiniendo el tratamiento con tacrolimus

Chiesi
People and ideas for innovation in healthcare
We Invite you to One Lambda’s Symposium

Official Meeting Symposium of Banff-SCT 2017

Monday, 27th March
14:00-15:00
Paraninf Room
Universitat de Barcelona

Speakers

Ten Years Development of Antibody Characterization Assays: Progress, Clinical Relevance and Unmet Needs

Carmen Lefaucheur, MD, PhD
Paris Transplant Group
Paris, France

The Path Toward Next Generation Sequencing Application to Solid Organ Transplants

Peter Nickerson, MD, BSc (Med), FRCPC, FCAHS
University of Manitoba
Winnipeg, Canada