BELGIAN TRANSPLANTATION SOCIETY

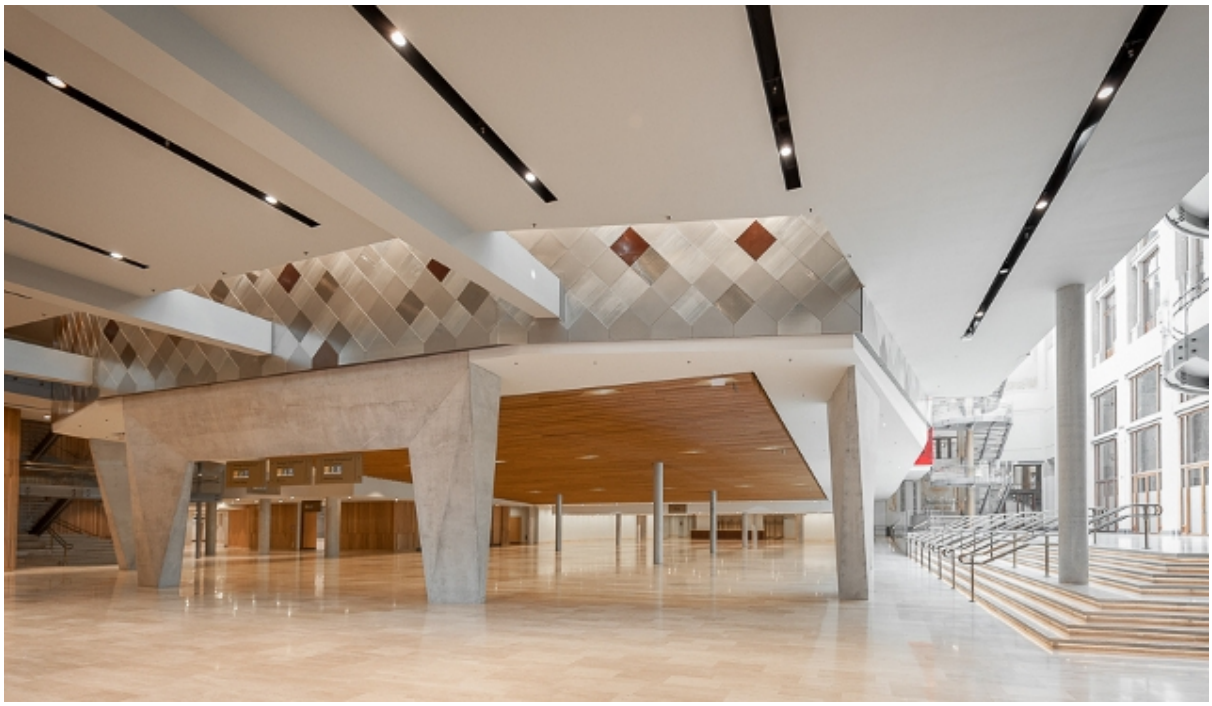
ANNUAL CONGRESS

14th March 2019

Flanders Meeting and Convention Centre, Antwerp.
Koningin Astridplein 20, 2018 Antwerpen

Infectious Diseases and Solid Organ Transplantation.

Programme and Abstract book.



Programme:

8.30 Registration and coffee.

9.00 **Oral abstract session**
Moderators : K.M. Wissing (Brussel) - J. Van Cleemput (Leuven)

An 8-Gene Expression Assay in Peripheral Blood for Diagnosis of Antibody-Mediated Rejection after Kidney Transplantation
Van Loon E., Gazut S.[1], Yazdani S., Lerut E., De Loor H., Coemans M., Noël L.-H.[1], Thorrez L., Van Lommel L., Schuit F., Lambrechts D., Van Brussel Th., Sprangers B., Kuypers D., Essig M.[1], Gwinner W.[2], Anglicheau D.[1], Marquet P. [3], Naesens M.[1] (Leuven, [1]Paris, Fr,[2]Hannover, D,[3]Limoges, Fr)

Recurrent diabetic nephropathy despite intensive glycemic control: an observational cohort study
Coemans M., Van Loon E., Lerut E., Kuypers D., Sprangers B., Gillard P., Mathieu Ch., Verbeke G., Naesens M. (Leuven)

The use of plasma donor-derived cell-free DNA to monitor acute rejection after kidney transplantation
Gielis E. [1], Ledeganck K. [1], Dendooven A. [1], Meysman P. [1], Beirnaert Ch. [1], Laukens K. [1], De Schrijver J. [1], Van Laecke S.[2], Van Biesen W.[2], Emonds M.-P.[3], De Winter B. [1], Bosmans J.-L. [1], Del Favero J. [1], Abramowicz D. [1] ([1]Antwerpen, [2] Gent, [3]Mechelen)

18F-FDG PET/CT imaging at 3 months post transplantation excludes subclinical rejection in kidney transplant recipients
Hanssen O., Weekers L, Lovinfosse P., Jadoul A., Bonvoisin C., Bouquegneau A., Huynen A., Hustinx R., Jouret F. (Liège)

Peripheral blood chemokine levels in kidney allograft rejection
Van Loon E., Claes S., Schols D., Naesens M. (Leuven)

The impact of eplet mismatches on kidney transplant outcome: a single-center cohort study
Senev A.[1], Coemans M.[2], Van Sandt V. [1], Sprangers B.[2], Kuypers D.[2], Emonds M.-P. [1], Naesens M.[2] ([1]Mechelen, [2]Leuven)

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Opt-out donor legislation, quo vadis Belgica?
Monbaliu D., Nys H., Schotsmans P., Ferdinande P. (Leuven)

Idarucizumab for the reversal of dabigatran in patients undergoing heart transplantation
Van Keer J., Vanassche Th., Droogne W., Rex S., Rega F., Van Cleemput J., Verhamme P. (Leuven)

Heart donation after circulatory death
Ledoux D., Massion P., Hans G., Amabili Ph., Joris J., Tchana-Sati V., Bruls S., Ancion A., D'Orio V., Detry O., Meurisse N., Schielke A., Pirard Ch., Amand Th., Lagny M., Blafart F., Delbouille M.-H., Monard J., Defraigne J.-O. (Liège)

Chest CT has Prognostic Value at BOS Diagnosis after Lung Transplantation
Van Herck A., Sacreas A., Heigi T., Kaes J., Vanstapel A., Verleden S., Vanaudenaerde B., De Weyer W., Verleden G. M., Vos R. (Leuven)

11.00 Coffee Break/Poster viewing/Sponsor interaction

11.30 **Infection and the transplant recipient**
Moderators : Y. Van Belleghem (Gent) – O. Detry (Liège)

Should we transplant HIV-positive recipients
L. Vandekerckhove (Gent)

HEV and solid organ transplantation
T. Vanwolleghem (Antwerpen)

Vaccination and the transplant recipient
S. Van Ierssel (Antwerpen)

13.00 Lunch/Poster viewing/Sponsor interaction

14.00 **Infection in the organ donor**
Moderators : O. Van Caenegem (Louvain-en-Woluwe) – D. Monbaliu (Leuven)

Donor-transmitted infections
P. Grossi (Varese, I.)

Hepatitis-C positive donors: to accept or to decline
Y. Horsmans (Louvain-en-Woluwe)

15.00 **Oral abstract session**
Moderators: J. Pirenne (Leuven) – L. Weekers (Liège)

Determination of creatinine and tacrolimus using Dry Blood Spot Monitoring in stable kidney, lung and heart transplant recipients - The DBSM Study
Van Caenegem O., Evrard P., Dumonceaux M., Goffin E., Wallemacq P. **(**Louvain-en-Woluwe)

Effects of allograft position during ex vivo lung perfusion in a porcine model.
Ordies S., Frick A., Martens A., Vanstapel A., Verschakelen J., Vanaudenaerde B., Verleden G., Vos R., Verleden S., Van Raemdonck D., Neyrinck A. (Leuven)

Portal vein thrombosis in patients on the waiting list for liver transplantation: a single center cohort study
Verhelst X., Bert J., Geerts A., Vanlander A., Abreu de Carvalho L., Berrevoet F., Troisi R., Rogiers X., Van Vlierberghe H. (Gent)

A single center experience with 157 controled dcd-liver transplantations
Schielke A., Paolucci M., Meurisse N., Vandermeulen M., Lamproye A., Delwaide J., Joris J., Kaba A., Honoré P., Detry O. (Liège)

Best abstract award winner:
Oxygenated Hypothermic Machine Perfusion Of Kidneys Donated After Circulatory Death: An International Randomised Controlled Trial
Jochmans I.[1], Hofker H.S.[2], Davies L.[3], Monbaliu D.[1], Darius T.[4], Mikhalski D.[5], Pipeleers L.[6], Weekers L.[7], Ysebaert D.[8], Randon C.[9], Knight S.[10], Ploeg R.J.[10], Pirenne J.[1] ([1]Leuven,[2] Groningen, G,[3]Devon, UK, [4]Louvain-en-Woluwe, [5]Bruxelles, [6]Brussel, [7]Liège, [8]Antwerpen, [9]Gent, [10]Oxford, UK)

16.00 Coffee Break/Poster viewing/Sponsor interaction

16.30 **Phd Session**
Moderators: C. Randon – D. Mikhalski.

Liver and systemic hemodynamics in cirrhotic children: contributions to the phyisiopathology and to the surgical algorithm in pediatric liver transplantation.
De Magnée C., Reding R. (Louvain-en-Woluwe)

The impact of mesenchymal stromal cells administration in renal ischemia-reperfusion injury and in kidney transplantation.
P. Erpicum (Liège)

17.15 **Annual 2019- BTS Donation Award**

17.30 **BTS General Assembly**
Report of the Transplant Coordinators Report of the BTS President
Report of the BTS Treasurer
Election of new BTS members.
Miscellaneous

18.00 **Congress closure.**

Oral Abstracts:

An 8-Gene Expression Assay in Peripheral Blood for Diagnosis of Antibody-Mediated Rejection after Kidney Transplantation

Van Loon E., Gazut S.[1], Yazdani S., Lerut E., De Loor H., Coemans M., Noël L.-H.[1], Thorrez L., Van Lommel L., Schuit F., Lambrechts D., Van Brussel Th., Sprangers B., Kuypers D., Essig M.[1], Gwinner W.[2], Anglicheau D.[1], Marquet P. [3], Naesens M.[1] (Leuven, [1]Paris, Fr,[2]Hannover, D,[3]Limoges, Fr)

BACKGROUND : Antibody-mediated rejection is a leading cause of graft failure after kidney transplantation. The diagnosis of antibody-mediated rejection is made by combining assessment of circulating antibodies with histological assessment of invasive allograft biopsies. Non-invasive biomarkers with sufficient diagnostic accuracy are not available. We sought to identify and validate a blood biomarker for non-invasive detection of antibody-mediated rejection.
METHODS : In the multicentre BIOMARGIN study, peripheral blood samples were prospectively collected from June 2011 to August 2016 at time of renal allograft biopsies, and then analysed in three phases, following a case-control design (discovery and derivation phase, N=117 and N=183 respectively) and a trans-sectional study for performance assessment (independent validation phase, N=387). Untargeted screening of whole genome transcriptomics was performed for the discovery phase and targeted mRNA expression analysis for the derivation and validation phases.
RESULTS : In the discovery and derivation phases, we developed and locked a multigene assay of 8 genes in peripheral blood that discriminated cases with (N=49) from cases without (N=134) antibody-mediated rejection (diagnostic accuracy in derivation cohort, 78.1% (95% CI, 70.7 to 85.6, p<0.001). In the independent validation cohort, this 8-gene marker discriminated cases with (N=41) from cases without antibody-mediated rejection (N=346) with similar accuracy (79.9%; 95% CI, 72.6 to 87.2, p<0.001). At the optimal cut-off the marker held a sensitivity of 80.5%, specificity of 71.4%, PPV of 25.0% and NPV of 96.9%.
CONCLUSION : We developed and validated a novel 8-gene expression assay in peripheral blood that can be used for non-invasive diagnosis of antibody-mediated rejection of kidney allografts.

Recurrent diabetic nephropathy despite intensive glycemic control: an observational cohort study

Coemans M., Van Loon E., Lerut E., Kuypers D., Sprangers B., Gillard P., Mathieu Ch., Verbeke G., Naesens M. (Leuven)

OBJECTIVE: After kidney transplantation, recurrence of diabetic nephropathy has been reported. The presentation and kinetics of recurrent diabetic nephropathy and its risk factors remain however unclear. This study investigated the recurrence of diabetic nephropathy after kidney transplantation in light of pre-transplant diabetes. Research Design and
METHODS: In this single-center prospective cohort study, 953 individual renal allograft recipients were included, with histological data of 3458 protocol-specified renal allograft biopsies, obtained at time of transplantation and during the first 5 years after transplantation. We studied the effect of pre-transplant diabetes on the post-transplant histological evolution.
RESULTS: Prior to transplantation, diabetes was present in 164 of 953 (17.2%) renal allograft recipients, primarily type 2 (N=146; 89.0%). Despite intensive glycemic control (glycated hemoglobin 7.00±1.34% [53±14.6 mmol/mol], 6.90±1.22% [52±13.3 mmol/mol] and 7.10±1.13% [54±12.4 mmol/mol], respectively at one, two and 5 years after transplantation), mesangial matrix expansion reached a cumulative incidence of 47.7% by 5 years after transplantation in patients with pre-transplant diabetes, vs. 27.2% in the absence of diabetes, corresponding to a hazard ratio of 1.55 (95% CI, 1.07 to 2.26; P=0.005). The divergence of cumulative incidences was noted already by two years after transplantation. Pre-transplant diabetes was not associated with other structural changes of the glomerular, vascular or tubulo-interstitial renal compartments. Pre-transplant diabetes was associated with post-transplant proteinuria, but not with estimated glomerular filtration rate or graft failure.
CONCLUSION: Mesangial matrix expansion, an early indication of diabetic nephropathy, can rapidly recur in patients with diabetes prior to transplantation.

The use of plasma donor-derived cell-free DNA to monitor acute rejection after kidney transplantation

Gielis E. [1], Ledeganck K. [1], Dendooven A. [1], Meysman P. [1], Beirnaert Ch. [1], Laukens K. [1], De Schrijver J. [1], Van Laecke S.[2], Van Biesen W.[2], Emonds M.-P.[3], De Winter B. [1], Bosmans J.-L. [1], Del Favero J. [1], Abramowicz D. [1] ([1]Antwerpen, [2] Gent, [3]Mechelen)

BACKGROUND: After transplantation, cell-free DNA derived from the donor organ (ddcfDNA) can be detected in the recipient's circulation. We aimed to investigate the role of plasma ddcfDNA as biomarker for acute kidney rejection.
METHODS: From 107 kidney transplant recipients, plasma samples were collected longitudinally after transplantation (day 1 – 3 months) within a multicenter set-up. Cell-free DNA from the donor was quantified in plasma as a fraction of the total cell-free DNA by next generation sequencing using a targeted, multiplex polymerase chain reaction (PCR)-based method for the analysis of single nucleotide polymorphisms.
RESULTS: In 42 stable transplant recipients, plasma ddcfDNA% decreased to a mean (SD) ddcfDNA% of 0.46% (± 0.21%) which was reached 9.85 (± 5.6) days after transplantation. A ddcfDNA threshold value of 0.88% (mean + 2SD) was determined in kidney transplant recipients. Increases of the ddcfDNA% above this threshold value were significantly associated with the occurrence of episodes of acute rejection (p = 0.017), acute tubular necrosis (p = 0.011) and acute pyelonephritis (p = 0.032). For the diagnosis of acute rejection, the measurement of ddcfDNA% (AUC 0.64; 90% CI: 0.501 – 0.779) did not outperform the serum creatinine (AUC of 0.64; 90% CI: 0.499-0.781) (p = 1.00).
CONCLUSION: Although increases in plasma ddcfDNA% are associated with graft injury, plasma ddcfDNA does not outperform the diagnostic capacity of the serum creatinine in the diagnosis of acute rejection.

18F-FDG PET/CT imaging at 3 months post transplantation excludes subclinical rejection in kidney transplant recipients

Hanssen O., Weekers L, Lovinfosse P., Jadoul A., Bonvoisin C., Bouquegneau A., Huynen A., Hustinx R., Jouret F. (Liège)

BACKGROUND : Subclinical rejection (SCR) of kidney allograft corresponds to "the histological documentation of unexpected evidence of acute rejection (AR) in a stable patient". SCR detection relies on surveillance biopsy. Still, non-invasive approaches may help avoid biopsy-associated complications and limitations. Positron emission tomography (PET) coupled with computed tomography (CT) after injection of 18F-fluorodeoxyglucose (18F-FDG) may be an option.
METHODS :From 11/2015 to 01/2018, we prospectively performed 18F-FDG-PET/CT in adult kidney transplant recipients (KTR) who underwent surveillance transplant biopsy at ~3 months post transplantation. Banff-2017 classification was used. Mean standard uptake value (mSUV) of kidney cortex was measured. Statistics were done via Python library SciPy. Our 95-patient cohort was categorized into 3 groups upon Banff-based histology: normal (n=70); borderline (n=16); AR (n=6). Three cases were excluded for PCR-proven BK nephropathy (n=2) or uninterpretable histology (n=1).
RESULTS : No clinical or biological difference was observed between groups. mSUV reached 1.49+/-0.32, 1.64+/-0.34 and 1.77+/-0.35 in normal, borderline and AR groups, respectively. A significant difference of mSUV was found among groups (ANOVA, p=0.05). Furthermore, mSUV was significantly higher in AR versus normal groups (t-test, p=0.04). The area under the ROC curve was 0.71, with 66% sensitivity and 62% specificity using mSUV threshold at 1.6. mSUV positively correlated with total inflammation score (r2=0.06, p=0.02) and with acute composite Banff (g+i+t+v+ptc) score (r2=0.05, p=0.03).
In CONCLUSION, our pilot study suggests that 18F-FDG-PET/CT helps non-invasively detect SCR, with a negative predictive value of 96% using 1.6 as mSUV threshold.

Peripheral blood chemokine levels in kidney allograft rejection

Van Loon E., Claes S., Schols D., Naesens M. (Leuven)

BACKGROUND: Cytokines and chemokines play a critical role in acute rejection after kidney transplantation and may be of importance in the quest for better diagnostic markers and new therapeutic strategies for rejection. In this study we evaluated 27 cytokines, chemokines and growth factors measured in peripheral blood for their associations with rejection types and specific histological lesions.

METHODS: All for-cause biopsies performed in University Hospitals Leuven between 07/08/2012 and 13/07/2016 (N=293 in 192 recipients) were included. In concomitant peripheral blood samples, 27 cytokines, chemokines and growth factors were measured through multiplex analysis. Expression differences in acute rejection types were evaluated using ANOVA and logistic regression analysis, corrected with mixed models for multiple sampling.

FINDINGS: Expression of CXCL-10 and the MIP-1 family of chemokines (MIP-1alfa, MIP-1beta and RANTES), ligands to the CXCR3 and CCR5 receptors were importantly associated with ABMR and its individual histological lesions. Higher levels of these chemokines reflect the interferon-gamma signature associated with T helper 1 cells, monocytes, macrophages and NK cells in rejection. These changes are not observed in TCMR and borderline changes. The diagnostic performance of peripheral blood cytokine profiles seems insufficient to help in non-invasive monitoring, reaching ROC AUC of 74.4% (95% CI 63.9%-84.9%, $p<0.0001$) when combining TNF-alfa, CXCL10/IP-10, MIP-1beta, RANTES and basic-FGF in a multivariate model for diagnosis of ABMR vs no ABMR.

INTERPRETATION: This study contributes to a better understanding of the roles of cytokines in renal allograft rejection and might aid the development of new therapeutic tools.

The impact of eplet mismatches on kidney transplant outcome: a single-center cohort study

Senev A.[1], Coemans M.[2], Van Sandt V. [1], Sprangers B.[2], Kuypers D.[2], Emonds M.-P. [1], Naesens M.[2] ([1]Mechelen, [2]Leuven)

BACKGROUND: Evaluating HLA eplet mismatches (MM) instead of antigen MM could theoretically enable better assessment of the donor-recipient HLA incompatibility and provide better risk assessment and outcome prediction. In this study, we aimed to evaluate the impact of the eplet MM on kidney transplant outcome in a large cohort of donor-recipient pairs with full HLA genotyping at high-resolution level.

METHODS : In total, 926 transplant pairs were retrospectively genotyped at high-resolution. HLAMatchmaker software was used to determinate the total number of HLA epitope/eplet MM for each transplant pair. Our study cohort comprised mainly first single-kidney transplant recipients (86.7%) with mean age of 53.8 ±13.2 years, male (59.8%) and mainly Caucasians (98.4%).

RESULTS : Pretransplant DSA were present in 10.2% of the recipients, all with a negative CDC crossmatch. Total HLA antigen MM ranged from 0 to 14, while the total number of HLA eplet MM ranged from 0 to 98. At the level of the individual HLA molecules, the highest mean of antigen MM was observed for B, while the highest number of eplet MM was observed for the DQ molecule. Univariate and multivariate Cox analyses confirmed that the classical HLA-A, -B and-DR antigen MM were significantly associated with graft failure. Considering the eplet MM, the total number of eplet MM was not associated with increased risk of graft failure, and only weak associations were found with class II antibody-verified epitope MM, likely explained exclusively by the antibody-verified eplet MM in the HLA-DQ locus. The subsequent adjusted multivariate Cox model confirmed that antibody-verified DQ epitope MM and classical HLA-A,-B and-DR antigen MM are both associated with the highest risk of graft failure.

In CONCLUSION, our results show that the total number of eplet MM will not offer better prediction of graft outcome compared to the classical antigen MM.

Opt-out donor legislation, quo vadis Belgica?

Monbaliu D., Nys H., Schotsmans P., Ferdinande P. (Leuven)

BACKGROUND AND INTRODUCTION: In 1986 Belgium introduced an opt-out law for organ donation. The effectiveness of this law resulted in a high number of organ donations and transplantations per million inhabitants in our country compared to countries with an opt-in legislation. Contra-intuitively to such an opt-out legislation, the option to explicitly consent was also made possible after legislative changes after 1986. Over the last decade, an increasing number of individual and political initiatives have been taken on a local and national level, not only to promote organ donation, but also to encourage residents to explicitly consent for organ donation which, by law, is not strictly necessary.

AIM: Firstly, to report on the evolution of the number of residents that oppose against or explicitly consent in favor or organ donation. Secondly, to make an estimation on the final number of explicit consents needed to equal the current number of organ donations in Belgium to adress the hypothetical introduction of an opt-in legislation.

RESULTS: In Belgium the number of residents that officially opposed against post-mortem organ donation remained quite stable over the last decade: 192,464 in 2008 vs. 195,464 in 2018, or 1.72% vs. 1.83%, respectively. In contrast, the number of residents that explicitly consented in favor of post-mortem donation increased from 83,755 in 2008 vs. 343,893 in 2018, representing 0.8% and 3% of the total Belgian population, respectively. However, to equal the number of ~30 donors pmp, we calculated that 6,800,000 explicit consents would be needed.

CONCLUSION: In Belgium, despite the relatively low number of residents (~5%) that either explicitly opposed against or consented in favor of post-mortem organ donation, the number of organ donors pmp is high. This is due to the opt-out legislation, installed in 1986. Following some legislative changes, there has been a steady increase of campaigns to persuade residents to explicitly consent in favor of organ donation. However, such campaigns are confusing and create the impression of an evolution towards an opt-in legislation. Despite the 3-fold increase of residents explicitey consented in favor of organ donation, this has not resulted in an equal increase of effective donors. We believe that information campaigns should not focus on explicit consent but on raising awareness and correct interpretation of the opt-out law installed in 1986.

Idarucizumab for the reversal of dabigatran in patients undergoing heart transplantation

Van Keer J., Vanassche Th., Droogne W., Rex S., Rega F., Van Cleemput J., Verhamme P. (Leuven)

BACKGROUND : Atrial fibrillation is common among patients with advanced heart failure who are listed for transplantation. Idarucizumab is a monoclonal antibody fragment that was developed to neutralize the activity of the direct thrombin inhibitor dabigatran. We describe the experience of dabigatran reversal with idarucizumab in 10 patients undergoing heart transplant surgery at the University Hospitals Leuven.

METHODS : At the time of listing for heart transplantation, patients requiring anticoagulation because of non-valvular atrial fibrillation, CHA2DS2VASc score ≥ 2 and without ventricular assist device or end-stage renal failure, were started on or switched to dabigatran. Upon availability of a donor organ, dabigatran was neutralized with 5 g of intravenous idarucizumab, immediately prior to induction of anaesthesia.

RESULTS : Ten patients have received a heart transplant using this protocol since its implementation at our centre on October 1st, 2015. Mean age was 57.9 years, 9 of the 10 patients were male, median CHA2DS2VASc score was 3 and mean eGFR at time of transplantation 53 mL/min. Mean time since last intake was 6.2 h. Evolution of dabigatran concentration (measured by a calibrated diluted thrombin time assay) and activated partial thromboplastin time (aPTT) in function of time after idarucizumab administration are represented in Figure 1. Mean dabigatran level before administration of idarucizumab was 117.8 ng/mL. All dabigatran concentrations post idarucizumab were unmeasurably low. Mean aPTT (reference range 25.1 - 36.5 s) was 55.8 s prior to idarucizumab and 35.4 s immediately post idarucizumab. During surgery, patients received on average 1.0 unit of packed cell transfusion, 4.1 units fresh frozen plasma, 0.9 pools platelets and 587 mL blood that was recovered via cell salvage. Two patients (20.0 %) needed re-intervention because of bleeding. No

adverse reactions or unexpected events that could potentially be related to idarucizumab administration were noted. There were no thrombotic complications. This is the largest report describing the use of idarucizumab to normalize coagulation in patients on dabigatran awaiting heart transplantation. Administration of 5 g of idarucizumab led to a sustained and complete biochemical reversal, without thrombotic complications, and without interfering with heparinization for cardiopulmonary bypass.
CONCLUSION : However, there still were some bleeding events. The availability of an immediately-acting complete reversal agent makes dabigatran an attractive choice for non-VAD patients with non-valvular atrial fibrillation who are listed for heart transplantation.

Heart donation after circulatory death

Ledoux D., Massion P., Hans G., Amabili Ph., Joris J., Tchana-Sati V., Bruls S., Ancion A., D'Orio V., Detry O., Meurisse N., Schielke A., Pirard Ch., Amand Th., Lagny M., Blafart F., Delbouille M.-H., Monard J., Defraigne J.-O. (Liège)

INTRODUCTION : The number of heart donation decreases over the time. This is related to fact that increase of donors is mainly due to increase of donation after circulatory death (DCD) while increase of donation after brain death is minimal. While for years heart procurement from DCD was deemed unrealistic, recent works showed that this was feasible and showed good results.
METHODS : In that context, we designed an adaptation of our protocol for DCD to enable heart donation (HDCD). The main features of the protocol are: insertion of ECMO cannulas in the right groin prior withdrawal of life sustaining therapies (WLS), thoracoabdominal normothermic regional perfusion (NRP), in situ heart resuscitation and cold storage heart preservation prior transplantation. That protocol was presented to our local ethics committee (EC) which found that it met the ethical requirement.
RESULTS : In 2018, three patients were detected as potential HDCD donors, resulting in 3 successful heart transplantations. Total donation warm ischemic time for the heart (time between WLS and NRP initiation) were 25, 26 and 18 minutes. The duration of NRP was 20, 20 and 17 minutes. After final physiological heart assessment, procurement and transplantation were successfully carried out in a similar fashion than in DBD heart procurement. Total ischemic time were 53, 81 and 150 minutes. Kidneys and liver were also retrieved except for one case (severe steatosis).
CONCLUSION: Authors developed a Heart Donation after Circulatory Death (HDCD) protocol that allowed successful heart transplant. Development of similar protocols could increase the pool of heart grafts.

Chest CT has Prognostic Value at BOS Diagnosis after Lung Transplantation

Van Herck A., Sacreas A., Heigi T., Kaes J., Vanstapel A., Verleden S., Vanaudenaerde B., De Weyer W., Verleden G. M., Vos R. (Leuven)

PURPOSE : Long-term survival after lung transplantation (LTx) is hampered by chronic lung allograft dysfunction, with bronchiolitis obliterans syndrome (BOS) as its most common phenotype. Bronchiectasis (BRECT), hyperinflation and airtrapping are considered the key features of BOS on chest CT. We investigated whether chest CT has prognostic value at BOS diagnosis after LTx.
METHODS : Patients transplanted between 2004-2015 who developed BOS (n=124) were included. BOS was defined as a persistent FEV1 decline of at least 20% compared to baseline, in absence of other conditions explaining FEV1 decline, restrictive pulmonary function tests or persistent infiltrates. Chest CT was scored at BOS diagnosis with an adapted Brody score and subscores (BRECT score, hyperinflation score, mucous plugging score, peribronchial thickening score and parenchyma score). Post-BOS survival of patients with a score higher than the median was compared with post-BOS survival of patients with a lower score.
RESULTS : Patients with a higher adapted Brody score (n=38), demonstrated worse survival compared to patients with a lower score (n=52, p=0.019). Patients with a higher mucous plugging score (n=19), peribronchial thickening score (n=32) and parenchyma score (n=70), had worse

survival compared to patients with lower mucous plugging score (n=99, p=0.0003), peribronchial thickening score (n=86, p=0.0046) and parenchyma score (n=48, p=0.016). There was no difference in survival between patients with a higher or lower BRECT score (p=0.34) and hyperinflation score (p=0.30).
CONCLUSION : Chest CT, and in particular the adapted Brody score, mucous plugging score, peribronchial thickening score and parenchyma score, has prognostic value at BOS diagnosis after LTx.

Determination of creatinine and tacrolimus using Dry Blood Spot Monitoring in stable kidney, lung and heart transplant recipients - The DBSM Study

Van Caenegem O., Evrard P., Dumonceaux M., Goffin E., Wallemacq P. **(**Louvain-en-Woluwe)

BACKGROUND : Tacrolimus (TAC) displays a narrow therapeutic window and an important inter- and intraindividual variability, requiring careful therapeutic drug monitoring (TDM). LC-MS/MS is considered as the reference method for TAC TDM. We aimed to compare LC-MS/MS TAC TDM in EDTA blood to capillary blood collected by fingerprick and stored as dry blood spot on sampling paper (DBSM). A disk punched out the paper allows liquid chromatography measurements similarly to liquid samples.
METHODS : Kidney (n=6), lung (n=11) and heart (n=11) transplant recipients were included in this prospective multicentre trial. TAC and creatinine measurements were performed both in EDTA blood after venipuncture or fingerprick DBSM before (T0), 90 min. (T1.5) and 180 min. (T3) after drug intake.
RESULTS : TAC venous levels measured by LC-MS/MS at T0, T1.5 and T3 are 8.2±0.5, 20.0±2.1 and 16.1±1.2 ng/mL respectively, whereas those measured through DBSM are 7.5 ± 0.3, 17.7±1.5 and 14.4±0.9 ng/mL (p=0.27 LC-MS/MS vs DBSM). The correlation coefficient for TAC levels is r = 0.89 (95% CI=0.84-0.93, p <0.001). The correlation coefficient for the area under the TAC curve is r = 0.90 (95% CI=0.77-0.96, p <0.001). Plasma creatinine levels are 121.9 ± 7.2 µmoL/mL in the venous samples and 138.1 ± 9.5 µmoL/mL by DBSM. The correlation coefficient for creatinine measurements is r = 0.98 (95% CI=0.98-0.99, p <0.001).
CONCLUSION :Correlations between creatinine and TAC TDM in venous samples and DBSM are excellent. DBSM offers to patients a less invasive method of TAC TDM, even allowing them to perform their home checks without moving to the hospital.

Effects of allograft position during ex vivo lung perfusion in a porcine model.

Ordies S., Frick A., Martens A., Vanstapel A., Verschakelen J., Vanaudenaerde B., Verleden G., Vos R., Verleden S., Van Raemdonck D., Neyrinck A. (Leuven)

BACKGROUND : Ex vivo lung perfusion (EVLP) allows preservation and evaluation of donor grafts prior to lung transplantation (LTx). Standard EVLP occurs in supine position. We previously demonstrated that prone positioning could redistribute edema accumulation in non-injured grafts. We hypothesize that alternating allograft position during EVLP will better preserve lung function compared to static positioning.
METHODS : Porcine lungs were procured after 90min warm ischemic time, flushed with cold LPDG and put on EVLP for 6 hours. The allografts were positioned in supine position [S] (n=6), prone position [P](n=7) or experimental position (3h supine and 3h prone [SP] (n=7). During EVLP, physiology was recorded. After EVLP, biopsies in ventral and dorsal areas were taken for wet-to-dry weight (W/D) ratios. The left lung was inflated, frozen and CT scanned.
RESULTS : Survival was similar between groups: 50% of [S], 57% of [P] and 71% of [SP] survived 6 hours. Physiology (compliance, PVR and oxygenation) did not differ between groups (p=0.82, p=0.36 and p=0.14 respectively). Dorsal W/D ratio was increased in [S] compared to [P] and [SP] (p=0.03). Similarly, CT densities of dorsal areas revealed a higher density in [S] compared with [P] and [SP] (p=0.051). Edema in ventral areas did not differ between groups (W/D ratio (p=0.54) and CT densitiesground (p=0.23)). Furthermore, lung weight increase was lowest in [SP] and highest in [S]

(p=0.06). Despite similar physiology between [S], [P] and [SP], edema accumulation was highest in [S].
CONCLUSION : These findings suggest that changing position during EVLP might be beneficial to reduce edema accumulation compared to static positioning.

Portal vein thrombosis in patients on the waiting list for liver transplantation: a single center cohort study

Verhelst X., Bert J., Geerts A., Vanlander A., Abreu de Carvalho L., Berrevoet F., Troisi R., Rogiers X., Van Vlierberghe H. (Gent)

BACKGROUND AND AIMS: Portal vein thrombosis (PVT) is a well-recognized complication of end-stage liver disease. However, current literature is still inconclusive about its impact on the clinical course in liver transplant candidates. The aim of this study was to identify the prevalence of and the risk factors for PVT, to assess the usefulness of anticoagulant therapy and to determine the impact of thrombosis as well as anticoagulation on postoperative outcomes, patient and graft survival.
METHODS : We performed a single center retrospective cohort study in an expert liver transplant unit. Patient receiving liver transplantation between January 2006 and June 2016 were included. Relevant demographic, clinical and outcome data were retrieved from the medical records. For analysis, patients were stratified in two groups according to presence of PVT. Univariate and multivariate logistic regression analysis and survival analysis were performed.
RESULTS : During the study period 390 adult patients underwent orthotopic liver transplantation. In 40 patients (10,26%) PVT was diagnosed. In respectively 10 (2,56%), 7 (1,79%) and 23 (5,9%) patients, the thrombus was identified at time of evaluation for transplantation, during waiting time and at time of transplantation. Among the 37 (9,49%) cases who still had PVT at the time of transplantation, 20 (54,05%) showed partial and 17 (45,05%) showed complete thrombosis. In a multivariate analysis, body mass index (p=0,006; OR 1,1; 95% CI:1,028-1,177), previous treatment of portal hypertension (p=0,001; OR 3,59; 95% CI:1,681-7,671) and a history of encephalopathy (p=0,007; OR 2,86; 95% CI=1,332-6,142) were independently associated with the occurrence of PVT. A beneficial trend was present favouring the use of anticoagulation towards the accomplishment of recanalization (n=3/7 versus 0/9; p=0,062). In the anticoagulated patients, only one mild bleeding episode (14,3%) occurred. Operation time was increased (p=0,001) in patients where the thrombus was discovered incidentally during surgery. Length of stay was increased (p=0,012) in the presence of PVT. Patient and graft survival rates were similar between the groups with and without portal vein thrombosis after 5 year of follow up. However, 1-year patient survival was significantly lower (p=0,031) in patients with PVT. Variables independently associated with the risk of 1-year and overall patient mortality included respectively the presence of portal vein thrombosis (p=0,032) and male gender (p=0,023).
CONCLUSION : PVT occurred in 10% of patients awaiting liver transplantation and had a deleterious effect on one year survival after liver transplantation. Anticoagulation is safe and showed a beneficial trend on recanalization of PVT and on the one year survival rate.

A single center experience with 157 controled dcd-liver transplantations

Schielke A., Paolucci M., Meurisse N., Vandermeulen M., Lamproye A., Delwaide J., Joris J., Kaba A., Honoré P., Detry O. (Liège)

INTRODUCTION: Donation after circulatory death (DCD) have been proposed to partially overcome the organ donor shortage. DCD-LT remains controversial, with reported increased risk of graft loss and retransplantation. The authors retrospectively reviewed a single centre experience with controlled DCD-LT in a 15-year period.
PATIENTS AND METHODS: 157 DCD-LT were consecutively performed between 2003 and 2017. All donation and procurement procedures were performed as controlled DCD in the operating theatre. Data are presented as median (ranges). Median donor age was 57 years (16-83). Median DRI was

2.242 (1.322-3.554). Allocation was centre-based. Median recipient MELD score at LT was 15 (6-40). Mean follow-up was 37 months. No patient was lost to follow-up.
RESULTS: Median total DCD warm ischemia was 19 min (7-39). Median total ischemia was 313 min (181-586). Patient survivals were 89.8%, 75.5% and 73.1% at 1,3 and 5 years, respectively. Graft survivals were 89%, 73.8% and 69.8% at 1,3 and 5 years, respectively. Biliary complications included mainly anastomotic strictures, that were managed either by endoscopy or hepatico-jejunostomy. Two patients were retransplanted due to intrahepatic ischemic lesions.
CONCLUSION: In this series, DCD LT provides results similar to classical LT. Short cold ischemia and recipient selection with low MELD score may be the keys to good results in DCD LT, in terms of graft survival and avoidance of ischemic cholangiopathy.

Best abstract award winner:

Oxygenated Hypothermic Machine Perfusion Of Kidneys Donated After Circulatory Death: An International Randomised Controlled Trial

Jochmans I. [1], Hofker H.S.[2], Davies L.[3], Monbaliu D. [1], Darius T. [4], Mikhalski D. [5], Pipeleers L. [6], Weekers L. [7], Ysebaert D. [8], Randon C. [9], Knight S. [10], Ploeg R.J. [10], Pirenne J. [1] ([1]Leuven,[2] Groningen, G,[3]Devon, UK, [4]Louvain-en-Woluwe, [5]Bruxelles, [6]Brussel, [7]Liège, [8]Antwerpen, [9]Gent, [10]Oxford, UK)

METHODS : An international, double-blinded, randomised, paired trial investigated the effect of oxygenated (HMPO) vs non-oxygenated hypothermic machine perfusion (HMP) on 1y graft function in cDCD kidneys 50 years of age or older. Kidneys were pumped from retrieval until transplantation. Primary endpoint was eGFR at 1y post-transplant (CKD-EPI) (90% power, alpha=0.05 to detect 8ml/min/1.73m² difference). A pre-specified sensitivity analysis accounted for cases where no 1y-eGFR was available due to graft loss (eGFR imputed as 10 mL/min/1.73m²) or patient death with functioning graft (last known eGFR carried forward).
RESULTS : 197 kidney pairs (median donor age 56y (range: 50-78)), of which 106 pairs were successfully transplanted (recipient age 61y (21-79)). Total donor warm ischemia time was 28.5min (8-114). Cold and pump times were 11h (4.6-27.6), 6.9h (1.7-24.3) in HMPO and 10.3h (3.5-27.1), 7.4h (1.3-23.8) in HMP. Of the 106 kidney pairs, there was no difference in delayed graft function (36% in both groups), primary nonfunction (2.8% in HMPO vs 4.7% in HMP, p=0.48) and patient death (6.6% in HMPO vs 7.5% in HMP, p=0.88). Graft loss was significantly lower in HMPO (2.8% vs 10.4%, p=0.021). 83 pairs were eligible for primary analysis (intention-to-treat) (23 all-cause graft failures of one or both kidneys excluded). 1y-eGFR was similar in HMPO and HMP (mean(SE): 50.5(2.1) vs 46.7(1.8) mL/min/1.73m², p=0.12). However, sensitivity analysis, accounting for all-cause graft failure, showed a higher 1y-eGFR in HMPO (47.6(1.9) vs 42.6(2.0) mL/min/1.73m², p=0.035).
CONCLUSION : This first randomised controlled trial suggests that HMPO improves 1-year kidney graft function when accounting for the beneficial effect on graft survival.

Posters:

Mucormycosis after kidney transplantation: a rare deadly infection

Anthonissen B., Gérard L., De Meyer M., Devressse A., Duprez Th., Kanaan N. (Louvain-en-Woluwe)

INTRODUCTION : Mucormycosis is a rare, opportunistic fungal infection caused by filamentous ubiquitous fungi belonging to the Mucorales family. It causes aggressive infections in immunocompromised and diabetic patients, most commonly rhino-orbital-cerebral disease and pulmonary syndromes.
CASE REPORT : A 42-year old woman was transplanted with a deceased-donor kidney in July 2018. Her past history was relevant for previous kidney transplantation in 2008 for end-stage renal disease secondary to abdominal metastatic neuroblastoma she had presented at age 10, successfully treated with unilateral nephrectomy, autologous hematopoietic transplantation and chemotherapy. She lost her first graft at 2015. She received plasma exchanges for hyperimmunization and tacrolimus, mycophenolate mofetil and corticosteroids. Her immediate post-transplant evolution was marked by an infection of the scar, complicated by abscess formation and sepsis treated with cefuroxime. One week after the septic episode, she complained of headaches and loss of vision of the right eye. Clinical examination revealed ophtalmoplegia of the right eye. Cerebral RMI showed sphenoid, ethmoid and maxillary sinusitis. Nasopharynx endoscopy displayed white filaments, evocative of mycotic infection. Intravenous liposomal amphotericin B was started and surgical debridement of sinuses was undergone. Mucor sp. grew on sinuses cultures. Her condition deteriorated rapidly. Control MRI showed an explosive pan-sinusitis, optic nerves edema and compression, and frontal and temporal cerebral damage. Despite surgical sinus debridement and transplantectomy, the outcome was fatal.
CONCLUSION : Early recognition of mucormycosis is crucial to improve chances of survival by instituting antifungals combined with surgical debridement. Mortality remains however very high in transplanted patients.

Kidney progenitor cells derived from urine of preterm neonates have immunomodulatory properties.

Arcolino F.O., Herman J., Reda A., van den Heuvel L., Levtchenko E. (Leuven)

BACKGROUND: Mesenchymal stromal cells (MSC) have immunomodulatory potential along with self-renewal and ability to differentiate towards cells of mesodermal origin. We recently described human kidney stem/progenitor cells (nKSPC) isolated from urine of preterm neonates, born before completing nephrogenesis1. nKSPCs have regenerative paracrine effects and differentiate into functional kidney epithelial cells. This study aimed to investigate whether nKSPCs can also convey impactful immunomodulatory effects.
METHODS: Mixed lymphocyte reaction (MLR) was performed to investigate the potential of nKSPCs to suppress T-cells proliferation. nKSPCs or MSCs were added to the MLR at different ratios. The release of immunomodulatory cytokines and indoleamine 2,3-dioxygenase (IDO), a known suppressor of T-cells proliferation, was measured during the 5 days of co-culture using a MSD U-plex. Expression of genes related to immunomodulatory effects were analysed by qPCR after priming nKSPCs with IFN-γ or poly I:C, a TLR3 stimulator, for 24h.
RESULTS: nKSPCs were as efficient as MSCs in suppressing T-cells proliferation. MSC suppressed release of IFN-γ, but nKSPCs did not. Consequently, IDO was only released by nKSPCs, as its activity is INF-γ-driven. Incubation of nKSPCs with IFN-γ drastically increased expression of IDO, while poly I:C had higher impact COX2-PGE2 pathway and it was only up regulated in MSC. These results suggest that although nKSPCs and MSC have similar immunosuppressive potential, the mechanism of action is different.

CONCLUSIONS: Besides their potential to differentiate into functional kidney cells and regenerative paracrine effects, nKSPCs present immunosuppressive properties, which shape them as ideal source of cells for kidney-targeted regenerative medicine.

1. Arcolino FO, et al. Urine of preterm neonates as potent source of kidney stem/progenitor cells. JASN. 2016.

Clinical relevance of mismatch in Toxoplasmosis serostatus in Hearttransplantation

Braaksma A., Van Cleemput J. (Leuven)

Early 2017 a 32-year old patient received an redo-hearttransplantation in the UZ Leuven, Belgium, after a clinic of graft failure and signs of chronical rejection. He had undergone a HLA-sensitisation in order to lower the donor-specific antibodies and thus the risk of a mismatch. However, this proved to be unsuccessful and left the patient immunocompromised. Initially, the intra- and postoperative process continued without complications, other than slow weaning and a postoperative delirium, but at day 12 postop, the patient started developing a raised body temperature eventually going as high as 40°C. Initially, no cause could be found, as the lab results, imaging and clinical signs were inconclusive. Eventually the patient started to develop a respiratory insufficiency with radiographical imaging of diffuse pulmonary atelectasis. Vancomycin and meropenem were started, but the patient continued to deteriorate, leading to an ARDS-clinic with signs of sepsis. Transfer to a Critical Care Unit was needed and a VV ECMO installed, to be later on converted to a VA ECMO. Unfortunately without clinical success. The progressive presence of multi-organ failure, including heart failure, led to the decision to stop the treatment, leading to the death of the patient. An autopsy was performed to try to figure out what had been the cause of this rapid clinical deterioration and showed a Toxoplasmosa gondii pneumonia in both lungs on microscopical examination. The patient had been seronegative for T. gondii pre-transplant, in contrast to the T-gondii seropositive donor.

ABO-incompatible living donor renal transplantation: Back to the future.

Buemi A., De Meyer M., Latinne D., Lambert C., Eeckhoudt St., Darius T., Goffin E., Devresse A., Kanaan N., Mourad M. (Louvain-en-Woluwe)

BACKGROUND: More than 30 years after the first world series of ABO-incompatible living donor renal transplantation (ABOi-LKT) described by G.P. Alexandre in our Institution, this transplantation procedure has achieved worldwide the same success rate as ABO-compatible LKT. Objective: The aim of this study is to highlight the evolution of the therapeutic strategy during the last three decades for ABOi-LKT and to report our results in three recent consecutive procedures. Comparison between current and historical approach and outcomes will be presented.
METHODS: ABO-LKT program started in 1982 until 1989 (n=39) and resumed from January 2018 (n=3). Our current desensitization before transplantation was obtained using rituximab and plasmapheresis to reach a titer less than 1/16, followed by triterapy immunosuppressive regimen, anti-CD25ab and according to the anti-A/B Ab titer, post-transplantation plasmapheresis. RESULTS: From the initial cohort graft survival reaches 41% at 20 years. In the recent series the maximum initial anti-A/B Ab titer was 1:256. One patient was HLA sensitized (PRA 38%). To obtain an acceptable anti-A/B Ab titer, 3-11 plasma exchange sessions were performed. All pairs underwent simultaneous uneventful kidney removal and transplantation surgeries and achieved immediate graft function recovery. No acute rejections occurred at follow up. Mean serum creatinine level at 116 days (median duration of follow-up) was 1.59 ± 0,16 mg/dl. No infection episodes or other surgical complications were observed.
CONCLUSION: ABOi-LKT is a reasonable modality to increase the donor pool and currently achieve worldwide excellent results. Compared to the initial experience, the evolution of modern knowledge in the field of ABOi-LKT has allowed an improvement in outcomes, however we would like to stress that the basic principle of treatment remained globally unchanged.

Orthotopic kidney transplantation: a single center "recent" experience of an "old" procedure in patients with severe iliac vessels impairments.

Buemi A., Darius T., De Meyer M., Goffin E., Devresse A., Kanaan N., Mourad M. (Louvain-en-Woluwe)

BACKGROUND: We previously described our single center experience of kidney implantation on vascular grafts in selected patients with severe aorto-iliac atheromatosis. Here we report retrospectively our results of a consecutive series of three orthotopic kidney transplantation in patients with poor accessibility of the renal artery implantation on the aorto-iliac trunk.
METHODS: Between 2017 and 2018 three orthotopic kidney transplantations were performed. The clinical data, indication for transplantation, surgical reports and complications were reviewed.
RESULTS: In all cases patients presented a massive aorto-iliac atheromatosis associated with a complete occlusion of the left iliac vein and the inferior vena cava under the renal veins level in one case and a previous SPK in a second case. Surgery was conducted throw a left sub-costal incision and an intraperitoneal approach. After a left nephrectomy the transplant vein was implanted to the native left vein and the transplant artery was implanted to the distal part of the splenic artery. Mean creatinine was 1,83 ± 0.36 mg/dl up to 6 months after grafting. Mean operative time was 4 ±0.09 hours and Mean hospital stay was 15±5,5 days One case of urinary leakage and one urinary infection were observed, no vascular complications occurred.
CONCLUSIONS: Orthotopic kidney transplantation is a feasible and safe procedure in selected patients with severe atheromatosis or no accessibility to iliac vessels. Moreover, it's a valuable alternative to the renal arterial grafting on a vascular prosthesis implanted simultaneously or before transplantation.

Timing and donor-specific antibodies, but not C4d deposition, determine leukocyte infiltration in renal allograft biopsies with the histological picture of antibody-mediated rejection.

Callemeyn J.[1], Senev A.[1], Lerut E.[1], Coemans M.[1], Kuypers D.[1], Gwinner W.[2], Essig M.,[3] Anglicheau D.[4], Marquet P.[3], Naessens M.[1] ([1]Leuven, [2]Hannover, [3]Limoges, [4]Paris)

BACKGROUND: Despite substantial improvement in detection of donor-specific antibodies (DSA), often no HLA-DSA can be demonstrated in patients with the histological picture of ABMR. It is unclear whether this DSA-negative phenotype reflects a distinct clinicopathological entity with different effector mechanisms.
METHODS: Microarray analysis was performed of renal allograft biopsies fulfilling the histological Banff 2017 criteria for ABMR (ABMRh). Concurrent TCMR, borderline changes, BKV nephropathy and glomerulonephritis were used as exclusion criteria to avoid time-dependent confounding. Deconvolution analysis of probesets was performed to estimate the absolute leukocyte subtypes within the graft.
RESULTS: In a cohort of 224 kidney transplant biopsies, a total of 32 ABMRh biopsies were found, of which 14/32 (43,8%) did not have detectable HLA-DSA (DSAnegABMRh). Individual genes were upregulated similarly in both DSAposABMRh and DSAnegABMRh compared to normal biopsies. Among 22 leukocyte subtypes, only monocyte infiltration was significantly larger in DSAposABMRh compared to DSAnegABMRh. Utilizing peritubular C4d deposition as proxy for DSA in DSAnegABMRh did not demonstrate monocyte infiltration difference. Additionally, no differences between C4dposABMRh (n=13) and C4dnegABMRh (n=19) were found. ABMRh cases that occurred within three months after transplantation (n=11) had a significant increase of infiltrating macrophages and CD8+ T cells compared to cases beyond one year (n=20).
CONCLUSION: Timing and DSA status, but not C4d deposition, appear to influence cellular infiltration in renal allograft biopsies with the histological picture of ABMR. Additional molecular studies are currently being performed to investigate the time-dependent cellular component of ABMR pathophysiology.

Hepatic artery thrombosis after pediatric liver transplantation

Channoui A., Tambucci R., Pire A., de Magnée C., Reding R. (Louvain-en-Woluwe)

The incidence/outcome of hepatic artery thrombosis (HAT) were reviewed with a particular focus on chronology and results of surgical redos regarding survival and biliary complications. Among 882 primary pediatrics liver transplantations (LT), each HAT case was retrospectively paired with an equivalent LT recipient according to diagnosis, age at LT, type of graft, and transplant era. Both groups were compared assessing patient/graft survival, retransplantation rate, and biliary complications. HAT could be fully documented in 35 cases (HAT group), and these children were paired to recipients without HAT (control group). 5 year patient survivals were 77% vs 84%, in HAT and control groups, respectively (NS). Corresponding graft survivals were 20% vs 81%, respectively ($p<0.0001$). Retransplantation rates were 78% vs 11% in HAT and control groups, respectively ($p<0.0001$). Corresponding 5 year biliary complication-free survivals were 12% vs 80% ($p<0.0001$). Regarding timing of HAT, early HAT (<14 days, n=28, 80% of HAT cases) were reoperated in 16/28 cases (57%). Among the reoperated HAT cases, 14 cases were reoperated within 7 days post-LT (revascularization obtained in 6/14, 43%), whereas no revascularization could be obtained in the 2 cases operated beyond 7 days post-LT. Only 6/16 cases (38%) were successfully revascularized. Results confirmed the pejorative prognosis of developing HAT in terms of graft survival. Patient survival in HAT cases could be partly preserved through retransplantation. This analysis suggested that HAT cases should be reoperated if occurring within 7 days post-LT.

Prevention of diabetic nephropathy after kidney transplantation requires more than pursuing low levels of glycated hemoglobin

Coemans M., Van Loon E., Lerut E., Kuypers D., Sprangers B., Gillard P., Mathieu Ch., Verbeke G., Naessens M. (Leuven)

BACKGROUND: Diabetic nephropathy is the leading cause of end-stage renal disease and progresses in five stages. During the second stage, morphologic lesions develop, without signs of clinical disease. The impact of diabetes on the evolution of this renal histology and the role of glycemic control (HbA1c) herein, remains insufficiently understood.
METHODS: We performed a cohort study based on a prospectively collected database at a single kidney transplant center. In total, 953 single kidney transplantations performed between 2004 and 2013 were included, with histological data on 3458 protocol biopsies, obtained up to 5 years after transplantation. We studied the effect of post-transplant HbA1c (median of 6 measurements per patient, in total 8750 measurements) on the occurrence of chronic lesions in kidney allografts using a joint longitudinal-survival model.
RESULTS : Pretransplant diabetes was present in 164 of 953 (17.2%) renal allograft recipients, primarily type 2 (N=146; 89.0%). Naturally, these patients showed higher levels of HbA1c post-transplantation. A linear mixed model for the individual HbA1c trajectories and an interval-censored, proportional hazards survival model were fitted simultaneously in order to test for a cumulative HbA1c effect on the hazard of first occurrence of certain histological lesions. Although HbA1c levels at the time of transplantation were significantly associated (P=0.03) with the occurrence of mesangial matrix expansion in the kidney allograft (HR 1.23; 95% CI, 1.02 to 1.48), no cumulative HbA1c effect was present (HR 1.03; 95% CI, 0.90 to 1.18; P=0.61).
CONCLUSION: We concluded that pre-transplant diabetes patients, on average, showed higher values of HbA1c after transplantation. However, our joint model illustrates that the susceptibility to diabetic nephropathy lesions was not associated with the individual, cumulative HbA1c trajectories. Prevention of diabetic nephropathy recurrence after transplantation thus requires more than pursuing low levels of glycated hemoglobin. The effects of novel antidiabetic agents on post-transplant recurrence of diabetic nephropathy need further evaluation.

Brief O2 uploading at the onset of continuous HMP results in comparable early graft function compared to continuous active oxygenated HMP and is significantly better than non-active oxygenated HMP or end ischemic O2 supply in a pig auto-transplant model.

Darius T., Vergauwen M., Gianello P., Buemi A., De Meyer M., Mourad M. (Louvain-en-Woluwe)

BACKGROUND: The aim of this study was to evaluate the impact of different perfusate oxygen concentrations and timing during continuous hypothermic machine perfusion (HMP) on early graft function in a porcine kidney ischemia-reperfusion auto-transplant model.
METHODS: The left kidney of ±40 kg landrace pig was exposed to 30 minutes of warm ischemia by vascular clamping and randomized out to one of 7 studied preservation strategies: 1) 22h static cold storage (SCS), 2) 22h (no active oxygen supply) HMP, 3) 22h oxygenated HMP (HMPO2low)(pO2=220-240mmHg), 4) 20h SCS + 2h HMPO2low, 5) 22h HMPO2high(pO2=700-800mmHg), 6) 2h HMPO2high+20hHMP, and 7) 20h HMP + 2h HMPO2high. The LifePort Kidney Transporter® was used for all machine perfusion strategies. The kidney was auto-transplanted in a right orthotopic position.
RESULTS: The overall effect of each treatment strategy on early graft function expressed as AUC of the serum creatinine of 46 auto-transplants from day 1 until day 13 post-transplantation demonstrated that 2h HMPO2high+20h HMP was comparable with 22h HMPO2high or 22h HMPO2low, but significantly lower than non-active oxygenated HMP ($p<0.0001$), 20h HMP+2hHMPO2high ($p=0.0349$) and end ischemic HMPO2 after SCS ($p<0.0001$). The serum creatinine was significantly lower from day 1 until day 4 after transplantation in the 2h HMPO2high+20h HMP group, the 22h HMPO2low or 22h HMPO2high group but no difference was observed in the 20h HMP+2h HMPO2high group compared to 22h non-active oxygenated HMP.
CONCLUSION: Brief O2 uploading at the start might be the best and most convenient oxygenation strategy for continuous HMP to improve early graft function.

Pancreatic Islet Isolation from Donors after Controlled Circulatory Death.

De Paep D.L.[1], Zhidong L.[1], Vanhoeij M.[1], Pirenne J.[2], Lamote J.[1], Pipeleers D.[1], Jacobs-Tulleneers-Thevissen D.[1] ([1]Brussel, [2]Leuven)

OBJECTIVE : Donors after controlled circulatory death (DCD-III) are considered a valuable source of organs to expand the donor pool but they are associated with a higher risk of graft dysfunction and post-transplant complications due to an initial period of warm ischemia. The present study evaluates outcome of pancreatic islet cell isolation from DCD-III in comparison with donors after brain death (DBD).
METHODS : A retrospective analysis of donor and procurement characteristics as well as quality control data of the isolates was performed using the database of our Beta Cell Bank. From 2007 till 2018, 578 DBD organs and 133 DCD-III organs were included.
RESULTS : Outcome of pancreatic islet isolation from DCD-III was significantly inferior to DBD in terms of beta cell yield on day of isolation (76±6.6x106 vs 97±2.8x106 beta cells; $p<0.01$) and after 2 days of culture (41±3.4x106 vs 61±2.1x106 beta cells; $p<0.01$). DCD-III were also associated to a lower utility rate for transplantation (35% vs 41%). In DCD-III, beta cell yield after isolation was correlated to the duration of acirculatory warm ischemia ($p<0.05$). Longer acirculatory ($p=0.05$) and total warm ischemia time ($p<0.05$), longer procurement time ($p<0.01$) and cold preservation time ($p<0.05$) correlated to beta cell number after culture.
CONCLUSIONS : DCD-III pancreases for islet cell isolation are more vulnerable to duration of procurement and cold preservation compared to DBD. Initial warm ischemia influences beta cell yield and clinical transplantation rate. DCD-III remain a valuable source of donor organs for islet cell preparation when procured and preserved under priority conditions.

Pancreatic Islet Isolation from Donors after Euthanasia

De Paep D.L.[1], Zhidong L.[1], Ysebaert D.[2], Poelaert J.[1], Vanhoeij M.[1], Lamote J.[1], Pipeleers D.[1], Jacobs-Tulleneers-Thevissen D.[1] ([1]Brussel, [2]Antwerp)

OBJECTIVE : Human donor pancreases can be processed to islet cell grafts but less than 50% of isolates reach criteria for clinical transplantation. Donor, procurement and processing conditions are considered to influence this utility rate. The subgroup of donors after circulatory death involving euthanasia (DCD-V) has been associated with excellent outcome of solid organ transplants. This study evaluates its outcome in the preparation of islet cell grafts. Methods We present a retrospective analysis using our database containing donor and procurement characteristics and quality control data of the isolates.
RESULTS : Eleven DCD-V pancreases were included for analysis and compared with our reference cohort of donors after brain death (DBD, n=578) and donors after controlled circulatory death (DCD-III, n=133). Isolation outcome from DCD-V was significantly superior to DCD-III in terms of beta cell yield (124±25.2 vs 76±6.6x106 beta cells; p<0.05) and insulin content of the preparation (21±3.1 vs 14±0.7 µg insulin/106 beta cells; p<0.05) and superior, albeit not significant, to DBD (97±2.8x106 beta cells; 16±0.4 µg insulin/106 beta cells) leading to higher clinical utility rate (91%, 35% and 41%; p<0.01). These better outcome parameters can at least partially be attributed to differences in donor profile (glycemia; p<0.01, glycosylated haemoglobin; p<0.01, liver enzymes; p<0.01, lipase; p<0.05, and serum sodium levels; p<0.01) and priority handling of these organs (shorter extraction; p<0.01, warm; p<0.01, and cold ischemia time; p<0.01).
CONCLUSIONS : The markedly higher clinical utility of islet cell preparations from post-euthanasia-donor pancreases underlines the importance of donor and procurement conditions for this type of graft.

SIMULTANEOUS AND SEQUENTIAL LIVER-HEART TRANSPLANTATION: SINGLE-CENTER EXPERIENCE AND REVIEW OF THE LITERATURE

Haentjes L., Ceulemans L. (Leuven)

OBJECTIVE : Combined liver-heart transplantation (cLiHTx) is a complex procedure for selected patients with end-stage cardiac and hepatic pathology. The aim was to analyze our single-center experience with simultaneous and sequential cLiHTx.
METHODS : This study is a single-center retrospective analysis of patients who received a simultaneous or sequential cLiHTx between 07/1990-11/2017. Three patients received a simultaneous cLiHTx and 1 patient a simultaneous cLiHLungTx. Four patients received sequential HTx followed by LiTx and 1 patient a LiTx followed by HTx. Demographics, indications and outcome are analyzed. Results are presented as median (range).
RESULTS : Patients with simultaneous transplantation had an age of 46 years (41-53). Indications were familial amyloidosis (n=2), cardiac myopathy and cirrhosis (n=1) and HCV cirrhosis with portopulmonary hypertension and right ventricular failure (n=1). One patient died 4 months post-transplant due to myocardial infarction. One-/5-year patient survival was 75%. Five sequential transplant recipients had an age of 47 years (46-65). Indications were cardiomyopathy in combination with hepatorenal polycystosis (n=2), cardiac cirrhosis (n=1), ethyl cirrhosis (n=1) and hepatocellular carcinoma (n=1). No patient died. During the same period, 1194 isolated LiTx and 638 isolated HTx were performed at our institution. One-/5-year patient survival was 89%/78% and 92%/88%, respectively.
CONCLUSION : Simultaneous and sequential cLiHTx is a rare but life-saving procedure with good outcome that should be offered in specialized centers to selected patients. Comparable results as for isolated HTx and LiTx could be achieved.

MYELOID-DERIVED SUPPRESSOR CELLS IN LUNG TRANSPLANT RECIPIENTS

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INTRODUCTION: Myeloid-derived suppressor cells (MDSC) are a heterogeneous group of immune cells from myeloid lineage. MDSC expand in pathological situations such as chronic infections, cancer and transplant rejection. Chronic lung allograft dysfunction (CLAD) is the single most important factor limiting long-term survival after lung transplantation (LTx), MDSCs may also play a role in its complex pathophysiology. We investigated the technical feasibility of quantifying granulocytic/polymorphonuclear MDSCs (G/PMN-MDSC) in peripheral blood from LTx recipients and assessed MDSC in post-transplant complications as infection and CLAD.
METHODS: Peripheral blood from healthy control subjects (n=4) and lung transplant recipients (n=21: stable n=6, infection n=6, BOS n=5, RAS n=4) was collected at the University Hospitals Leuven. Samples were shipped to Tübingen (Germany) on ice and analyzed the same day. Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood and MDSCs by Ficoll density gradient centrifugation. MDSC typing and counting was performed by flow cytometry to assess the percentage of G-MDSCs (CD11b+CD33b+CD66b+).
RESULTS: G-MDSC were increased in stable LTx recipients (52.1 (33.3-61.9)%) versus healthy subjects (9.4 (7.6-16.4)%) (p=0.0095). LTx recipients with an infection or CLAD had or tended to have lower % G-MDSC versus stable LTx recipients, respectively 28.2 (17.2-36.6)% (p=0.041) and 33.0 (25.6-38.1)% (p=0.088). Within CLAD % G-MDSC were comparable in BOS and RAS.
CONCLUSION: Circulating G-MDSCs are measurable in LTx recipients. Stable LTx recipients showed higher percentages of G-MDSCs, which decreased in post-transplant complications. These pilot data invites for more in depth analysis of the role of MDSC after LTx.

Orbital aspergillosis in a kidney transplant recipient – a case report and review of literature
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Orbital aspergillosis is an uncommon orbital infection, usually seen in immunocompromised individuals. Diagnosis may be challenging. Initial site of involvement is usually the paranasal sinuses with secondary involvement of the orbit. A 64-year-old man was transplanted with a kidney in 1999 for autosomal dominant polycystic kidney disease. He was admitted from March to June 2018 for hepatic cyst infection, treated with antibiotics for 3 months. In the end of the hospitalization, he complained of left hemicranial headache and orbital pain. Computerized tomography scan showed left sphenoidal sinusitis with mucosal thickening and hyperdense masses, suggesting aspergillosis sphenoiditis. A surgical left sphenoidotomy was performed. Orbital pain did not improve and he presented a gradual vision loss of his left eye. RMI showed a left optic neuritis secondary to contamination from the left sphenoid sinus. Pathological examination of the sinus material showed fungal hyphae morphologically consistent with Aspergillus. Treatment with voriconazole and short therapy of steroids allowed only partial improvement of vision. Currently, five months later, the patient is still under voriconazole with severe left visual defect. His last RMI showed a partial improvement of the optic neuritis but a persistent maxillary and sphenoidal sinusitis. Orbital aspergillosis is a rare, severe infection, potentially fatal if not diagnosed rapidly. Antifungal therapy with voriconazole is currently the standard treatment. Prolonged therapy is recommended; the duration is dependent upon the response to therapy. In addition, surgical debridement of the necrotic tissue may be needed in some cases.

Effect of temperature on cardiac metabolism during ex-vivo reperfusion of the allograft in an animal model of donation after circulatory death.

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BACKGROUND : Hearts from donation following circulatory death (DCD) have been recently introduced into clinical practice. Ex-vivo reperfusion following DCD and retrieval is deemed necessary in order to evaluate the recovery of cardiac viability after the period of warm ischemia. Lactate concentration in the perfusate is used as a marker of cardiac viability during ex-vivo perfusion. Aim of this study is to test the effect of 4 different temperatures on cardiac metabolism during ex-vivo reperfusion in a porcine model of DCD heart.
METHODS : We used an animal model of DCD heart with 20 adult Landrace pigs. After 20 minutes of Functional Warm Ischemic Time the heart was retrieved in standard fashion and put on ex-vivo reperfusion machine during 3 hours at 4 different temperatures (4° C - 18° C - 25° C - 34° C). Serial dosage of Lactate in the solution during ex-vivo perfusion and Weight of the allograft before and after perfusion to evaluate myocardial oedema.
RESULTS : We observed an increase of Lactate concentrations in the perfusate particularly during the 1st hour of reperfusion. However, the temperature of the solution does not seem to have an effect on lactate concentration. Further, all cardiac allografts exhibit a significant weight increase after 3h of ex-vivo reperfusion due to cardiac oedema, however the temperature of the solution does not seem to have an effect.
CONCLUSIONS : The temperature of the solution during ex-vivo reperfusion in a model of DCD heart does not seem to have an effect on cardiac metabolism nor oedema.

Continued improved outcome after simultaneous pancreas kidney transplantation despite low case load. A single center cohort.

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BACKGROUND: Simultaneous Pancreas Kidney Transplantation (SPK) is the treatment of choice in kidney transplant candidates with end stage renal failure and type 1 diabetes mellitus. With improvement of diabetes care, the number of pancreas transplantations has declined worldwide. This is worrying because reduced case load correlates with inferior outcome (Kopp et al. Transplantation 2017) and this might lead referring nephrologists/endocrinologists and patients to favor kidney transplantation alone instead of SPK. Aim: Patient and graft survival after SPK in our center were reviewed.
METHODS: Retrospective analysis on patients undergoing SPK between 01/1992-12/1996 (n=31); 01/1997-12/2006 (n=48); and 01/2007-11/2018 (n=44). 3-Year patient, pancreas graft and kidney graft survival were analyzed.
RESULTS: Patient and graft survival steadily improved over time within our center: 3-year patient survival was 90%, 92%, and 100%; 3-y pancreas graft survival was 74%; 87%, and 93%; and kidney graft survival was 90%, 92%, and 100% between 1992-‘96, 1997-’06, and 2007-’18, respectively. Pancreatectomy was performed in 6/31 (19%), 7/48 (15%), and 1/44 (2%) of patients between 1992-‘96, 1997-’06, and 2007-’18, respectively.
CONCLUSIONS: Despite a low case load (~5 SPK/year), excellent patient and graft survival continue to be achieved after SPK at our center and compare favorably with international standards. Results have even improved in more recent years with minimization of early surgical graft loss. Patients and referring physicians should be aware that SPK remains the best treatment of end stage renal failure and type 1 diabetes. Access to SPK should be guaranteed for these patients.

EARLY LISTERIOSIS AFTER LIVER TRANSPLANTATION: REPORT OF TWO CASES

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Listeria monocytogenes is a rare cause of potentially lethal infection and sepsis in transplant patients. Listeriosis is usually described after kidney or bone marrow transplant, and has rarely been reported after liver transplantation. Here, the authors present two cases of severe Listeria infection occurring within three months after complicated liver transplantation in patients still recovering on the ward. The patients were successfully treated by intravenous ampicillin. These cases should remind transplant physicians that listeriosis may develop in liver recipients, that food safety advice should be provided, and that intravenous ampicillin might be an effective treatment for systemic listeriosis in solid organ recipients.

Calcineurin inhibitors do not deregulate the subcellular reactive oxygen species content at physiological concentrations.

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INTRODUCTION: calcineurin inhibitors (CNI) are the basis of maintenance immunosuppressive regimes in solid organ transplantation, however, they are nephrotoxic and are associated with interstitial fibrosis. We previously confirmed a profibrotic response in human renal cells in response to "physiologic" CNI exposure, but the underlying mechanism for CNI-induced toxicity remains unknown. Other studies demonstrated excessive production of reactive oxygen species (ROS) in response to a supraphysiologic dose of CNIs, activating downstream (pro)fibrotic signals. Mitochondria and peroxisomes are the redox signaling hubs of the cells and important organelles in metabolizing and balancing ROS.

HYPOTHESIS AND METHODS: we hypothesized that CNIs at a "physiologic" dose can enhance ROS production and thus lead to increased production of (pro)fibrotic cytokines. To test this hypothesis, we measured glutathione redox couple and hydrogen peroxide in SV-40 transformed African green monkey kidney (COS-7) cells exposed to tacrolimus and cyclosporine using highly sensitive subcellular targeted Rho-GFP probes in real time.

RESULTS: We observed that tacrolimus at physiological concentrations corresponding to intracellular concentrations of this drug (200 ng/mL) found in kidney tissue in patients on tacrolimus treatment, does not alter glutathione or hydrogen peroxide content in the cytoplasm, mitochondria nor the peroxisomes after 1, 2 or 3 days of exposure. At supra-physiological concentrations of tacrolimus and cyclosporine (300 ng/mL and 15 μg/mL respectively), the same results were obtained after similar exposure time.

CONCLUSION: at physiological concentrations, CNIs do not deregulate the cellular ROS balance. Therefore, ROS does not seem to be the primary effector in activating (pro)fibrotic signals.

Intragraft IgG levels and donor-specific anti-HLA antibodies in different phenotypes of chronic lung allograft dysfunction.

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PURPOSE : Donor-specific antibodies in serum (sDSA) increase the risk of chronic lung allograft dysfunction (CLAD) and mortality after lung transplantation. Detection and interpretation of sDSA remains unstandardized and discrepancies between serological and pathological/clinical findings of antibody-mediated rejection are common. Therefore, we assessed the presence of intragraft DSA (gDSA) in different phenotypes of CLAD.

METHODS: Explanted lungs with bronchiolitis obliterans syndrome (BOS, n=18) and restrictive allograft syndrome (RAS, n=18) were inflated, frozen in liquid nitrogen fumes and processed into tissue cores. IgG antibodies were eluted and total IgG levels were measured via ELISA and anti-HLA Class I and II antibodies were identified via Luminex.

RESULTS: IgG levels were higher in RAS versus BOS (p<0.001). In general, there were more gDSA than sDSA, although not significant (13/36, 36% vs. 7/36, 19%; p=0.19). In BOS, 2 patients had both sDSA and gDSA and 2 had gDSA only (2/18 sDSA; 4/18 gDSA). In RAS, 4 patients had both sDSA and gDSA, while 1 patient had sDSA only and 5 patients gDSA only (5/18 sDSA; 9/18 gDSA). All results combined, DSA tended to be higher in RAS than BOS (p=0.086). IgG levels were higher in samples of gDSA+ versus gDSA- (p=0.0019), but not in sDSA+ versus sDSA- patients (p=0.48).
CONCLUSION: IgG levels were higher in RAS and in gDSA+ samples. DSA were more prevalent in RAS compared to BOS. We believe that the applications of gDSA need further investigation as this could provide complementary information to sDSA findings.

Extended spectrum betalactamases (ESBL) and carbapenemases producing enterobacteriacae perioperative acquisition in renal transplant recipients.

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BACKGROUND : Urinary tract infections (UTI) due to extended spectrum betalactamases (ESBL) or carbapenemases (C) producing enterobacteriacae (ESBL/C-E) in renal graft recipients are associated with higher hospitalizations and recurrences rates. We aimed to determine the timing of acquisition and risk factors associated to ESBL/C-E gut colonisation and bacteriuria as a preliminary effort to reduce carriage and infections.
METHOD : Between 1st May 2015 and 30th April 2017, we prospectively screened for ESBL/C-E (rectum and urine) all new kidney transplant recipients in a tertiary hospital at different perioperative times (admission, post-anesthetic unit and surgical ward).
RESULTS : 105 patients (406 samples) were screened at least one time: 100% post-surgery and 49,7% at the admission. 13 patients were positive: 5 ESBL-E at the admission and 8 subsequent acquisitions (2 ESBL-E and 2 C-E in the post-anesthetic unit and 4 ESBL-E in surgical ward) corresponding to a prevalence of 18,42% in 2015, 11,6% in 2016 and 0% in 2017 (until april). 4 patients had concomitant gut-colonization and bacteriuria, 5 bacteriuria alone and 4 gut-carriage alone. Neither previous antibiotherapy, recent hospitalization, urologic surgery, immunosuppression, corticosteroid, diabetes or type of extrarenal epuration was identified as a risk factor for ESBL/C-E colonization.
CONCLUSION : New acquisition of ESBL/C-E during hospitalization occurred but carriage was already present at the admission in nearly half of our ESBL/C-E patients. Further efforts to identify risk factors of colonization are needed to reduce ESBL/C-E carriage and diseases.

Kinetics of pretransplant HLA-DSA, post-transplant histology, and graft failure after kidney transplantation

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In this cohort study (N=924 patients with 4260 post-transplant biopsies), we investigated the evolution and clinical significance of pretransplant donor-specific antibodies (preDSA), positive with the single antigen beads assay but negative in CDC crossmatch. The donor specificity of the preDSA (N=107 patients) was determined by retrospective high-resolution genotyping of all donor-recipient pairs and evaluating all HLA loci. We found that in 52% of the patients with preDSA, the DSA spontaneously resolved within the first 3 months after transplantation, without receiving specific therapy for removal of DSA. PreDSA that persisted had higher pretransplant MFI values (6143±4565 vs. 2874±2391, p<.0001) and more specificity against class II (78.5%), especially against DQ (49%). Although patients with resolved (53.6%) and persistent preDSA (58.8%) both had a high incidence of histological picture of antibody-mediated rejection (ABMRh) with similar histological appearance, the patients with preDSA that persisted after transplantation had worse 10-year survival compared to resolved preDSA and DSA-negative patients (43.9% vs. 81.2% vs. 87.4%, p<.0001). Compared to cases without DSA, Cox modeling revealed an increased risk of graft failure in patients with persistent preDSA, in the presence (HR=8.3, p<.0001) but also in the absence (HR=4.3, p=0.001) of ABMRh. In contrast, no increased risk of graft failure was seen in patients with resolved preDSA

independent of ABMRh. We conclude that persistence of preDSA after transplantation has a negative impact on graft survival, beyond the diagnosis of ABMRh. Even in the absence of antibody-targeting therapy, low-MFI preDSA, and non-DQ preDSA often disappear early after transplantation.

Chronic Hepatitis E in the solid organ transplant setting of a Belgian tertiary care centre

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BACKGROUND: Limited data are available on chronic hepatitis E in Belgium.
METHODS: We describe a case series of 4 patients diagnosed with chronic hepatitis E in the solid organ transplant setting of a Belgian tertiary care centre.
RESULTS: A total of 4 patients were diagnosed with chronic hepatitis E between January 2014 and October 2018: one heart transplant, one combined heart-kidney transplant and two kidney transplant patients. All were asymptomatic and referred to the outpatient Hepatology clinic upon incidental finding of impaired liver function tests. At diagnosis, HEV IgM was positive in 3/4 patients, serum HEV RNA PCR was positive (mean viral load: 6.95±0.61 log IU/mL) and ALT levels were elevated (mean ALT=131±25 IU/mL) in all patients. All were genotype 3. Liver biopsy showed minimal liver fibrosis (Metavir F1 or lower). Ribavirin treatment was started in 3/4 patients: immediately after documentation of chronicity in the two heart transplant patients and after failure of immunosuppressant dose adjustment in patient 3. Immunosuppressant dose adjustment is ongoing in patient 4. HEV seroclearance was achieved in all treated patients. At treatment cessation, HEV RNA in stool remained positive in 2 patients, of which one showed a viral rebound 3 months later. Due to intolerance for ribavirin, close follow-up was performed for 1 year in this patient. HEV RNA remains positive and the patient now shows signs of progressive liver disease.
CONCLUSION: All transplant physicians must be aware of the occurrence of chronic Hepatitis E. Long-term viral replication can result in significant liver damage.

Pentraxin-3 Polymorphisms are Associated with Invasive Pulmonary Aspergillosis after Lung Transplantation.

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PURPOSE Pentraxin-3 (PTX3) polymorphisms influence the risk of invasive pulmonary aspergillosis (IPA) in chronic obstructive pulmonary disease patients, hematopoietic stem cell recipients and solid organs recipients. Therefore, we aimed to investigate this association in a large lung transplant population.
METHODS Patients who underwent lung transplantation (LTx) between 01/01/2011 and 31/12/2015 in the University Hospitals Leuven were included (n=292). Recipient DNA was successfully extracted from peripheral blood (n=268) or explanted lung tissue (n=24) and successfully genotyped for rs2120243 (n=229, 85.4%), rs2305619 (n=244, 91.0%) and rs3816527 (n=255, 95.1%) polymorphisms using TaqMan® OpenArray® genotyping plates. Cumulative IPA frequency, diagnosed according to EORTC/MSG guidelines, and CLAD-free survival were assessed for each polymorphism.
RESULTS Cumulative IPA frequency was higher in rs2120243 AC and AA haplotypes compared to the CC haplotype (15.5% vs 4.5% after 1 year and 28.0% vs 14.9% after 5 years, p=0.024). Cumulative IPA frequency was higher in rs2305619 AG and AA haplotypes compared to the GG haplotype (15.3% vs 4.8% after 1 year and 28.3% vs 12.0% after 5 years, p= 0.018). Cumulative IPA frequency was higher in rs3816527 AC and CC haplotypes compared to the AA haplotype (16.3% vs 3.6% after 1 year and 30.9% vs 10.3% after 5 years, p=0.0015). Chronic lung allograft dysfunction (CLAD) developed in 23% of patients (n=68) after a median time of 2.3 (1.0-3.6) years. There was no difference in CLAD-free survival between different PTX3 genotypes (p=0.53, p=0.50, p=0.50).
CONCLUSION PTX3 polymorphisms are associated with an increased risk for IPA after LTx.

Pilot Study on Pancreatic Islet Cell Implantation in Omentum of Type 1 Diabetes Patients.

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BACKGROUND : Intraportal injection of pancreatic islets in type 1 diabetes patients results in functional beta cell implants which can improve metabolic control and restore hypoglycemic awareness (1,2). Implant function declines over time (3) but little information exists on the underlying process. We examined in vivo and in situ correlations for omentum implants, first in rodents (4) and then in patients. Two cases of an implant in the omentum have been reported so far (5,6).

METHODS : Seven patients participated in a pilot study in which outcome of an omentum implant was monitored over three months, and followed, in case of absent metabolic effect, by an intraportal implant at which time an omental biopsy was taken. Omental access occurred under laparoscopy without adverse events. All recipients were under immune suppression (induction ATG, maintenance MMF/tacrolimus).

RESULTS : Omental implants resulted in a lower functional beta cell mass than intraportal implants. Histological analysis showed small endocrine cell aggregates, containing insulin- and glucagon-positive cells, with adjacent endothelial cells, lymphocyte clusters and sometimes ductal structures. A prior omentum implant did not negatively influence outcome of an intraportal implant compared to intraportal alone recipients (n=10): no differences at 6 and 12 months post-transplantation in hyperglycemic clamp values, BETA-2 score, HbA1c, insulin dose and glycemic variability.

CONCLUSIONS : A pancreatic islet cell implant in the omentum establishes functioning beta cells in type 1 diabetes patients but their metabolic outcome was lower than for intraportal implants. It allowed histopathologic analysis of the implant and did not interfere with outcome of a subsequent intraportal implant.

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Fibrin deposition and organizing pneumonia in transbronchial biopsies from lung transplant patients.

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Acute fibrinous organizing pneumonia (AFOP) may result in a rapid decline in respiratory function and death. We investigated the effect of intra-alveolar fibrin and OP in transbronchial biopsies (TBBs) from lung transplant patients on graft survival, chronic lung allograft dysfunction (CLAD)-free survival and restrictive allograft syndrome (RAS) development. We reviewed the TBBs from 468 patients who underwent lung transplantation between 2011 and 2017. The presence of fibrin or OP was defined as early (<3m) or late (>3m). Early and late fibrin/OP were detected in 23 (5%) and 28 (6%) patients. CLAD was diagnosed in 107 (22.9%) patients, in 4/23 patients (17.4%) with early fibrin/OP (1 RAS+), and in 16/28 patients (57.1%) with late fibrin/OP (12 RAS+). Donor-specific antibodies (DSAs) were present in 58 patients (12%), in 2/23 patients (9%) with early fibrin/OP, and in 9/28 patients (32%) with late fibrin/OP. The presence of late fibrin/OP significantly increased the risk of RAS (OR:13.31; CI [3.871 – 40.2], p<0.0001) and presence of DSAs (OR:3.729; CI [1.509 – 8.855], p=0.0043) whereas early fibrin/OP showed no correlation with RAS (p=0.57) or DSAs (p>0.99). CLAD-free survival was significantly lower in patients with late fibrin/OP (p<0.0001, median 2.64y) compared to patients without or with early fibrin/OP (median >7.68y and >7.64y). Similarly, graft survival was significantly lower in patients with late fibrin/OP (p=0.0008, median 4.46y) compared to patients without or with early fibrin/OP (median >7.81y and >7.77y). The pathologist should search for fibrin and OP in TBBs, as it is associated with worse prognosis and CLAD development, specifically RAS.

Acquired von Willebrand syndrome in patients on long-term left ventricular assist device support: results of a Belgian center.

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OBJECTIVES : Acquired von Willebrand syndrome (aVWS) in patients on left ventricular assist device (LVAD) support is characterized by the loss of high molecular weight (HMW) von Willebrand factor (VWF) multimers, often coinciding with a decreased binding of VWF to collagen (VWF:CB) or to GPIb (VWF:GPIbR). Short term follow-up of aVWS in LVAD patients has been well described, while little information on long-term follow-up is available. The aim of this study was to monitor VWF and ADAMTS13 parameters during a long-term follow up of LVAD patients and after heart transplantation.
METHODS : Plasma samples of 16 LVAD patients (long-term follow-up ranged from 1 month up to 2 years after device implantation) of which four patients underwent heart transplantation, were collected. LVAD and healthy donor (n=20) samples were analyzed for VWF antigen (VWF:Ag), VWF:CB, VWF:GPIbR and ADAMTS13 antigen (ADAMTS13:Ag) levels using ELISA, for ADAMTS13 activity (ADAMTS13:act) using FRETS (fluorescence resonance energy transfer) VWF73 substrate and for VWF multimers using SDS agarose gel electrophoresis.
RESULTS : All LVAD patients demonstrated a loss of HMW VWF multimers during the long-term course of LVAD support. This loss also resulted in decreased VWF:CB/VWF:Ag and VWF:GPIbR/VWF:Ag ratios (<0.7) in 78% and 71% of the samples respectively. ADAMTS13:Act/ADAMTS13:Ag ratio was decreased in 83% of the cases. Heart transplantation following LVAD support in 4 patients, resulted in aVWS reversal in 2 out of 4 patients after LVAD removal.
CONCLUSION : Long-term follow-up of LVAD patients shows that aVWS is detected during the entire period of LVAD implantation. Hence, bleeding complications in patients on long-term LVAD support should be treated accordingly.

Evaluation of compliance in young transplant patients.

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AIM: We studied the compliance after transplantation in young people in transition between the ages of 12 and 25. We aimed to identify the difficulties in the achievement of good compliance and define suggestions for improvement of compliance behaviour.
METHOD: Fifteen respondents from the University Hospital Ghent were interviewed in qualitative in-depth interviews.
RESULTS: The results are shown in three components. Adherence: All respondents had difficulties with the adjustments in lifestyle and 14 of them with medication-intake. Defining difficulties: Difficulties are dependent on the time after the transplant. The doctor-patient relationship and support from the parents have the greatest influence closely after the transplant surgery. After the adjustment period, the need for making own decisions and disease perception were more decisive factors. A factor found to have an important influence on patient adherence is self-image. Suggestions for improvement: Next to a personal connection with their doctor, patients want an open communication. A clear message in which the doctor tells them what is important and for what reasons. Finally, other recommendations to improve their compliance behaviour were the use of alarms, medication boxes and phone applications to reduce the practical influence.
CONCLUSION: First, compliance problems in transplant patients is a significant factor. Second, we conclude that based on qualitative in-depth interviews, adherence to therapy among young patients in transition, can be improved by investing in the personal relationship between patient and caregivers.
