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Transplant International

Abstracts of the 31st Annual Meeting of the German Transplantation Society, Erlangen, Germany, 29 September–1 October 2022

Transplant International

frontiers

ABSTRACTS OF THE 31ST ANNUAL MEETING OF THE GERMAN TRANSPLANTATION SOCIETY, ERLANGEN, GERMANY, 29 SEPTEMBER–1 OCTOBER 2022

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Welcome to the 31st Annual Meeting of the German Transplantation Society

Dear colleagues,

We are pleased to welcome you to the 31st Annual Meeting of the German Transplantation Society from 29 September to 1 October 2022 in Erlangen, Germany. It is the two-year anniversary of the Corona pandemic and last year we held a very successful hybrid congress in Stuttgart. To make it possible for everyone, who cannot travel to Erlangen this year because of worry, responsibility or work commitments, we will make large parts of the event available live via internet channels.

The motto of this year's congress is: "The holistic approach to transplantation". This does not only mean that organ transplantation is an interdisciplinary challenge for the treating colleagues, but also that, in addition to internal and surgical findings, the patient's overall situation, his/her disease history, his/her nutrition and fitness as well as his/her psyche and mental health must be integrated into the treatment process to achieve optimal transplantation success. Therefore, we have chosen the special features and interdisciplinary challenges of "young" and "old" patients as special topics for this year's congress and would also like to address the special features and interdisciplinary challenges of patients with "special" pre-existing conditions.

We are pleased that the abstracts of this meeting will be published in the current issue of Transplant International and are happy to welcome you personally to Erlangen.

On behalf of the Universitätsklinikum Erlangen, the organising committee and the board of the DTG

Mario Schiffer Michael Wiesener Mirian Opgenoorth

Programme

Thursday, 29 September 2022

08:00-09:30	Poster Session 01 (until 09:15)	Poster Session 02	Mentoring breakfast	Poster Session 03
09:30-09:45	Break			
09:45-11:00	Opening Ceremony and Lecture			
11:00-11:15	Break			
11:15-12:15		Satellite Symposium	Satellite Symposium	Satellite Symposium
12:15-12:30	Break			
12:30-13:45	Plenary Session I: Xeno-transplantation			
13:45-14:00	Break			
14:00-15:30	Allocation, who is prioritised?	Patient perspectives in the context of the holistic transplant approach	Commission: Kidney	CV risk after transplantation
15:30-16:00	Break			
16:00-17:30	Master Class I	Basic Science I: Approaches to overcoming immunologi-cal barriers	Commission: Pancreas	Commission: Psychology/ Psychosomatics
17:30-18:00	Get Together in the exhibition area - networking time			
18:00-20:00	DTG General Meeting			

Friday, 30 September 2022

08:00-09:30	Pre- and aftercare concepts/ prehabilitation/ rehabilitation	Thoracic organs (internal/ surgical)	Commission: Ethics	Commission: Liver/ Intestine
09:30-09:45	Break			
09:45-10:30		Breakfast Symposium	Breakfast Symposium (until 10:15)	Breakfast Symposium (until 10:15)
10:15-11:45	Plenary Session II: COVID-19			
11:45-12:00	Break			
12:00-13:00	Satellite Symposium	Satellite Symposium	Satellite Symposium	
13:00-13:30	Break			
13:30-15:00	Master Class II	AI - Opportunities and risks in the care of transplanted patients	Commission: Organ removal	Commission: Heart/ Lungs
15:00-15:30	Break			
15:30-16:45	Organ donation in Germany - is anything happening?	Clinical management: The transplant fails...now what?	Commission: Immunology	Poster Session 04
16:45-17:00	Break			
17:00-18:00	Interdisciplinary perioperative care	Transplantation of the "special" organs	Abdominal organs (internal/ surgical)	Poster Session 05

Saturday, 01 October 2022

08:30-09:45	Innovative processes: Machine perfusion	Psychoso-matics	Poster Session 06	Poster Session 07
09:45-10:15	Break			
10:15-11:30	Master Class III	Tumours before and after trans-plantation	Register studies	Poster Session 08
11:30-12:30	Break			
12:30-13:00	Award presentations			
13:00-14:00	Plenary Session III: Transplanta-tion concerns the "whole" person - Who am I helping? Who am I harming?			
14:00-14:30	Break			
14:30-15:45	News from the DTG Commissions and the work on guidelines	Basic Science II: Immunology	Living donation with "special" patients	Poster Session 09
15:45-16:15	Closing and invitation DTG 2023			

Oral Presentations

CV risk after transplantation

S03-03 Iptacopan#, a Novel oral complement Factor B (FB) inhibitor, significantly reduces proteinuria and C3 deposit scores in native and transplanted kidneys in C3 Glomerulopathy (C3G) patients

E. Wong[1], C.M. Nester[2], T. Cavero Escribano[3], A. Karras[4], M. Lequintrec-Donnette[5], L. Lightstone[6], U. Eisenberger[7], M.J. Soler[8], A. Biondani[9], F. Chaperon[9], K. Kulmatycki[9], J.M. Milojevic[9], P.K. Nidamarthy[10], N. Webb[9], G. Junge[9], G. Remuzzi[11]

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INTRODUCTION

C3G is a rare, inflammatory kidney disease caused by genetic mutations or auto-antibodies that dysregulate the complement system. With no approved therapies, progression to end stage renal disease is frequent. Iptacopan is a new, highly selective oral low molecular weight inhibitor of Factor B, a key complement alternative pathway (AP) protease. We report final Ph2 data [NCT03832114] for iptacopan in patients with native or recurrent C3G post kidney transplant.

#Iptacopan is not approved and part of a clinical research program

METHODS

Adults with biopsy-proven, native (CoA) or recurrent C3G post kidney transplant (CoB) received iptacopan for 12 weeks. CoA had proteinuria >1g/24h despite ACEi/ARB, and all had low C3 levels. Primary endpoints were reduction in UPCR from baseline to week 12 for native and change in C3 Deposit Score for post-transplant C3G patients. Patients were invited to continue iptacopan in a long-term extension trial [NCT03955445].

RESULTS

All patients (N=16/11 in CoA/B) completed the trial. Baseline mean age was 26.1/34.5 years; geo-mean UPCR (24h) was 401.9/36.2 g/mol; mean eGFR was 70.1/52.2 mL/min in CoA/B; median C3 deposit score was 3.0 in CoB. Iptacopan was well tolerated without any drug-related serious adverse events. Primary endpoint in CoA was met with -45% in UPCR from baseline to week 12 (p=0.0003). In CoB primary endpoint was met with significant reduction in C3 deposit score in kidney biopsies from baseline to week 12 (p=0.0313). A profound and sustained inhibition of the AP and normalization of C3 levels were observed. eGFR was stable with mean change from baseline to week 12 of +1.04 mL/min.

CONCLUSION

Treatment with iptacopan 200 mg (b.i.d) in patients with native or recurrent C3G was well tolerated and resulted in statistically significant and clinically important reduction of UPCR, normalization of C3 levels, stabilization of eGFR, and significant reduction in histologic C3 deposit score in follow-up kidney biopsies. Iptacopan is now tested in a pivotal Phase 3 trial APPEAR-C3G [NCT04817618].

Basic science I: Approaches to overcoming immunological barriers

S04-03 Risk of cellular and/or antibody-mediated transplant rejection in pediatric kidney transplant recipients with BK polyomavirus DNAemia - A multicenter CERTAIN analysis

B. Höcker[1,2], J. Schmidt[1,2], C. Süsal[2], A. Carraro[2], J. Oh[2], M. Zirngibl[2], S. König[2], L. Dello Strologo[2], L.T. Weber[2], A. Awan[2], K. Krupka[1,2], T. Bruckner[2], P. Schnitzler[2], H.H. Hirsch[2], A. Fichtner[1,2], B. Tönshoff[1,2]

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INTRODUCTION

To determine the risk of alloimmune responses (T cell-mediated rejection (TCMR) including borderline changes and *de novo* HLA donor-specific antibodies (dnDSA) and/or antibody-mediated rejection (ABMR)) as a consequence of reduced immunosuppression for management of BK polyomavirus (BKPyV) DNAemia in pediatric kidney transplant recipients.

METHODS

In the framework of the *Cooperative European Paediatric Renal Transplant Initiative* (CERTAIN), we studied 195 pediatric kidney transplant recipients (10.5 ± 5.5 years) in whom plasma BKPyV-DNAemia and dnDSA were measured regularly over a period of up to 5 years post-transplant. Risk factors for the development of dnDSA and transplant rejection were analyzed using univariate and multivariable Cox regression.

RESULTS

BKPyV-DNAemia was observed in 65 (33.3%), and biopsy-proven BKPyV associated nephropathy in 13 (6.7%) patients. Ninety (46.2%) patients developed

TCMR/borderline rejection, and 56 (28.7%) recipients developed dnDSA/ABMR during the 5-year period. The overall TCMR/borderline rate was comparable in patients with (20 (37.0%)) or without BKPyV-DNAemia (70 (49.3%), p=0.150) but recipients with BKPyV-DNAemia developed TCMR/borderline rejection significantly (p=0.004) later than those without, presumably due to reduced immunosuppression for BKPyV management. No independent risk factors for TCMR development were identified. The overall dnDSA/ABMR rate was also similar in patients with (16 (28.1%)) or without BKPyV-DNAemia (40 (29.0%), p=0.898). Independent risk factors for dnDSA/ABMR development in patients with BKPyV-DNAemia were re-transplantation (OR 10.8, p=0.004), a higher HLA-DR mismatch (OR 3.1, p=0.018) and a CSA-based immunosuppression compared to TAC (OR 3.7, p=0.031). eGFR loss was significantly (p=0.005) higher in pediatric kidney allograft recipients with BKPyV-DNAemia (13/53, 25.0%) than in those without (7/101, 6.9%). An independent risk factor for eGFR loss in low immunologic-risk patients with BKPyV-DNAemia was the occurrence of TCMR (OR 10.1, p=0.004).

CONCLUSION

Reduced immunosuppression as BKPyV management is not an independent risk factor for TCMR/borderline rejection and/or dnDSA/ABMR in pediatric kidney transplant recipients.

Pre- and aftercare concepts/prehabilitation/ rehabilitation

S05-03 Long-term outcome of pediatric liver transplant recipients who have reached adulthood – A single center experience

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INTRODUCTION

As long-term survival of pediatric liver transplant recipients increases, the assessment of physical, psychological and social well-being becomes more important.

METHODS

In this retrospective analysis 120 young adult patients (age ≥18 years) who underwent liver transplantation (LT) in childhood were studied. Patients with ideal outcome were defined as patients with a perfect graft function, with no complications from the immunosuppressive medication, no late re-transplantation, and no steroid treatment. Also, the patients' drug adherence and their psychosocial situation were assessed.

RESULTS

After a median follow-up of 19 years, only 16.7% of the patients (mean age: 26.5 years) were considered patients with ideal outcome. The main reasons precluding ideal outcome were chronic kidney disease (38.3%), elevated liver enzymes (33.3%) and arterial hypertension (31.7%). Ideal outcome decreased over time from 54% to 42%, 26% and 8% at 10-, 15-, 20-, and 25-year follow-up, respectively.

Reduced drug adherence was noted in 24.8% of patients and associated with a significantly higher prevalence of donor specific antibodies class II ($p = 0.015$), elevated transaminases ($p = 0.010$) and chronic rejection ($p < 0.001$). Also, 15% of patients suffered from a psychiatric disease, mainly depression.

CONCLUSION

The morbidity of young adults who underwent LT as children was high and increased over time. The majority developed complications from the immunosuppression or chronic graft dysfunction. More than 1 in 7 patients had a psychiatric disease and 1 in 4 was not perfectly drug adherent. Therefore, immunosuppressive treatment and psychological care should be optimized for these particularly vulnerable patients.

ACKNOWLEDGEMENT

The authors thank Eik Vettorazzi (M.Sc., Institute of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf) for his advice on the statistical analysis and Mareike Krull, a transplant nurse and office administrator at the University Transplant Center, for her support in collecting patient data.

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Thoracic organs (internal/surgical)

S06-03 Engineered T cells overcoming rejection by antibodies (CORA-T cells) through selective targeting of alloreactive B cells in solid organ transplantation

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INTRODUCTION

One major complication after solid organ transplantation (SOT) is antibody-mediated rejection (AMR) of the graft by anti-donor HLA antibodies. Modern immunosuppression mainly addresses T cell-mediated rejection, affecting the B-cell alloimmune response only indirectly. B-cell depletion protocols are inefficient in preventing AMR and associated with an increased infection risk, emphasizing the need for a more precise targeting of alloreactive B cells.

METHODS

B cells with anti-donor HLA specificity are uniquely characterized by expression of respective B-cell receptors (BCRs). Using the anti-HLA BCR as target molecule, we redirected T cells towards alloreactive B cells by introducing a novel chimeric receptor (CAR) comprising an HLA molecule fused to intracellular 4-1BB/CD3ξ signalling domains in order to generate T cells overcoming rejection by antibodies (CORA-T cells). As a proof of concept, CORA-T cells harbouring a receptor with an extracellular truncated HLA-A*02:01 molecule were designed, in which amino acid variations were introduced to abrogate CD8 binding. Their ability to recognize and selectively eliminate HLA-A*02:01 specific B cells to limit antibody release was tested.

RESULTS

Upon co-cultivation with a B-cell line expressing and releasing anti-HLA-A*02:01 antibodies, CORA-T cells showed specific upregulation of activation marker (CD69, CD137) and pro-inflammatory cytokine secretion (IL-2, TNF-α). They exhibited cytotoxicity towards the target B-cell line, secreted cytotoxic mediators and effectively reduced the amount of released anti-HLA-A*02:01 antibody. An optimized linker in the CORA receptor allowed for ideal HLA presentation and selective modification of the HLA-A*02:01 α3-domain was shown to abrogate CD8 binding and T-cell sensitization towards the HLA domain of the CORA receptor.

CONCLUSION

Our results demonstrate that CORA-T cells are able to specifically recognize and eliminate alloreactive B cells, having the potential to selectively prevent the formation of anti-HLA antibodies. This suggests application of CORA-T cells as an innovative approach to specifically combat AMR and to improve long-term graft survival in SOT while preserving general B-cell immunity.

ACKNOWLEDGEMENT

The authors would like to thank Sarina Lukis and Elvira Schulde for technical support.

AI – Opportunities and risks in the care of transplanted patients

S07-03 Importance of HLA fullhouse match in kidney transplantation with current immunosuppressive protocols

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INTRODUCTION

Kidneys with zero mismatch at HLA-A, -B, and -DR locus (0MM) are given high preference in Eurotransplant kidney allocation. However, the benefit of 0MM with advanced immunosuppression protocols and immunologic diagnostic techniques in the current era is unknown.

METHODS

We analysed the impact of 0MM in isolated cadaveric kidney transplant patients at our centre between 2000-2019. Patients with 0MM (n = 434) were younger than ≥1MM (n = 1704) ($p < 0.001$), had younger donor age ($p < 0.001$), shorter time on dialysis before tx ($p < 0.001$), and fewer comorbidities ($p < 0.001$).

RESULTS

Initial immunosuppression changed over time but did not differ between 0MM and ≥1MM. In 2000-2004, 66% of patients received dual immunosuppression. Since 2015, triple therapy with Tac/MMMF/Predni has been standard therapy.

0MM patients had a lower rate of primary non-function (5% vs 9%, $p = 0.0098$) or delayed graft function (16% vs 24%, $p < 0.001$). This difference was mainly observed in 2000-2004 ($p = 0.0081$) and was not significant thereafter.

Rejection rates in the first year post Tx were lower in 0MM vs ≥1MM until 2014 (27% vs 39%, p = 0.01 (2000-2004); 19% vs 33%, p = 0.005 (2005-2009); 23% vs 38%, p = 0.01 (2010-2014)) but comparable after 2015 (15% vs 19%, p = 0.43).

0MM kidneys had better eGFR: 49.3 vs 44.7 ml/min/1.73m2 at 1 year post Tx (p <0.001); 47.7 vs 43.2 at 3 yrs (p < 0.001); 46.4 vs 43.5 at 5 yrs (p = 0.034). However, the GFR slope was comparable (-1.1 vs -0.96 ml/min/1.73m2/yr; p = 0.77).

Graft survival was better in 0MM vs ≥1MM until 2014 (2000-2004: p = 0.009; 2005-2009: p = 0.047; 2010-2014: p = 0.006), but after 2015 no difference in graft survival was observed (p = 0.44). In ≥1MM, the main cause for graft loss was rejection (29%), followed by non-specific injury (20%). In 0MM, rejection was less often the cause of graft loss (13%, p = 0.014), while recurrent disease (17%) was more common.

CONCLUSION

In our single centre cohort, the impact of 0MM on early graft function and graft survival has decreased over time. An analysis in multicenter cohorts is warranted to assess whether it is still justified to give 0MM such high preference in the allocation system in the current era.

Organ donation in Germany – is anything happening?

S08-03 Regional differences in waiting time prior to kidney transplantation in Germany

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INTRODUCTION

Organ allocation algorithms promote regional allocation to keep ischemia times short. Whereas in the common Eurotransplant (ET) kidney allocation scheme (ETKAS), a regional bonus is integrated into a complex algorithm, the ET senior program (ESP) is primarily based on regional allocation. Little is known, however, how these algorithms influence regional waiting times prior to kidney transplantation (KTX) in Germany.

METHODS

We performed a retrospective cohort study including all patients that received a kidney-only graft under standard circumstances during 24 months in Germany (n=2053). We used simple and multiple linear regression to study regional differences in waiting time prior to KTX between the seven organ procurement regions in ETKAS and the 15 ESP subregions established by the *Deutsche Stiftung Organtransplantation* (DSO). The impact of the number of regionally procured kidneys on waiting time was also investigated.

RESULTS

In both exploratory analyses and multiple linear regression models, we found significant regional differences in median waiting time of up to 1.7 years in ETKAS and 4.4 years in the ESP. The ratio of the number of patients waitlisted in a certain region to the number of kidneys procured in that region correlated

with waiting time in ETKAS (R^2 0.70). In the ESP, the ratio of the number of patients listed in a subregion to the number of subregionally procured and transplanted kidneys also correlated with waiting time, albeit to a lower degree (R^2 0.62).

CONCLUSION

In Germany, waiting time is profoundly influenced by where a patient is listed for KTX. These results question the equity of the current allocation algorithms.

Transplant International

Tumours before and after transplantation

S15-03 Humoral response to SARS-CoV-2 mRNA vaccination in previous non-responder kidney transplant recipients after short-term withdrawal of mycophenolic acid one and three months post vaccination

T. Kühn[1], M. Schaier[1], C. Morath[1], M. Bartenschlager[2], H. Kim[2], S. Parthé[3], J. Beimler[1], M. Buylaert[1], C. Nußhag[1], F. Kälble[1], M. Reineke[1], M. Töllner[1], K. Klein[1], A. Blank[4,5], P. Schnitzler[3], M. Zeier[1], C. Süsal[6], R. Bartenschlager[2,5], T.H. Tran[7], C. Speer[1,8], L. Benning[1]

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INTRODUCTION

Kidney transplant recipients (KTR) are at high risk for severe COVID-19 disease and immune response to SARS-CoV-2 vaccination is impaired in most KTR. Especially KTR on mycophenolic acid (MPA) show lower seroconversion rates to mRNA vaccines.

METHODS

This study investigates the impact of short-term MPA withdrawal on humoral response of previous non-responder KTR after at least 3 COVID-19 vaccinations, both 1 and 3 months after an additional vaccination. 76 KTR with no seroconversion received a full mRNA-1273 dose in January or February 2022. 43 KTR with stable graft function and no rejection in the past year underwent MPA withdrawal for 5 weeks starting 1 week before vaccination. Humoral response to SARS-CoV-2 vaccination was analyzed by determining

anti-S1 IgG and cross-neutralization of the delta and omicron variants via live-virus assay. Graft function, donor-specific anti-HLA antibodies (DSA) and donor-derived cell-free DNA (dd-cfDNA) were analyzed for KTR with MPA withdrawal. SARS-CoV-2 specific T cellular response was analyzed in 52 KTR 3 months post vaccination via Interferon y release assay.

RESULTS

KTR with MPA withdrawal showed significantly higher anti-S1 IgG levels 1 month post vaccination compared to KTR on continued immunosuppression ($P<0.001$). Equally, neutralization titers against delta and omicron were significantly higher in KTR with MPA withdrawal compared to those without ($P=0.04$ and $P=0.02$, respectively). While s-creatinine and proteinuria were stable, DSA resurgence with MFI>500 was detected in 7/43 (16%) KTR with MPA withdrawal, and dd-cfDNA rose in 1 KTR above a 0.5% threshold to 0.65%. 3 months post vaccination, anti-S1 IgG levels declined significantly compared to 1 month post vaccination ($P<0.001$). T-cell response was noted in 6/23 (26%) KTR without seroconversion, with no significant difference between KTR with and without MPA withdrawal. Graft function was stable. During the study, 22 KTR had breakthrough infections with no hospitalization required, and 7 dropped out.

CONCLUSION

The study shows that MPA withdrawal increases immunogenicity to SARS-CoV-2 vaccination in previous non-responder KTR, yet withdrawal should only be applied in KTR without previous DSA.

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Transplant International

Register studies

S16-03 Mental health of living kidney donors before donation - First data from the German living donation register SOLKID-GNR (Safety of the Living Kidney Donor-German National Register)

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www.lebendspenderegister.de

INTRODUCTION

The aim of the SOLKID-GNR is to provide a prospective data collection for the scientific evaluation of long-term effects of living kidney donation (LD) on the physical and mental health of living kidney donors (LKD).

METHODS

Since 2020, SOLKID-GNR prospectively collects demographic, medical and psychosocial data of LKD at German transplant centers (Tx-centers). Amongst other things, the register captures established psychosomatic self-assessment questionnaires for health-related quality of life (SF-12), depression (PHQ-9), somatization (PHQ-15), psychosocial stress factors (PHQ-stress), anxiety (GAD-7), resilience (RS-13), fatigue (MFI-20) and ambivalence (Simmons's Ambivalence Scale) in the population of LKD before and at regular intervals after LD.

The ascertained scores before LD were compared with published German normative data using one-tailed t-tests.

RESULTS

As of March 2nd, 2022, complete data of the first measure point (0-4 weeks before LD) of 335 LKD from 28 Tx-centers are available. 66.1% of the LKD are female and the mean age is 54.3 (SD±10.2) years. 43.5% donate to their life partner, 34.5% to their child.

Across the entire population, LKD significantly showed scores in a more favorable range (higher or lower, depending on the polarity), compared to values of the German normative data, with predominantly medium and strong effect sizes. Deviating from this pattern, the group of <40-year-old female LKD (n=15) showed significantly increased scores in the MFI-20-subscales "Reduced Motivation" and "Physical Fatigue".

CONCLUSION

The group of LKD included in this survey, showed a disproportionally good mental health before donation. In the group of <40-year-old female LKD the MFI-20-subscales "General fatigue", "Reduced Activity" and "Mental Fatigue" revealed no significant differences compared to the normative data. An increased everyday stress in this group (e.g. high workload/child care) could have lead to increased fatigue scores of the MFI-20-subscales "Reduced Motivation" and "Physical Fatigue", especially considering the data collection during the Covid-19 pandemic. The small number of cases should be regarded when interpreting these findings.

ACKNOWLEDGEMENT

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Basic science II: Immunology

S19-03 Five-year follow-up of a phase I trial of donor-derived modified immune cell infusion in kidney transplantation

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INTRODUCTION

The administration of modified immune cells (MIC) prior to kidney transplantation led to specific immunosuppression against the allogeneic donor and a significant increase in regulatory B lymphocytes (Breg). We now wanted to investigate how this approach affects the clinical course of treated patients.

METHODS

Ten patients from a phase I clinical trial who had received MIC infusions before kidney transplantation were compared to 15 matched standard-risk recipients. Follow-up was until year five after surgery.

RESULTS

The 10 MIC patients had an excellent clinical course with stable kidney graft function and showed no donor-specific human leukocyte antigen antibodies (DSA) or acute rejections during follow-up. In contrast, 1 of 15 controls died and 5 of 15 controls developed DSA (log rank $P = 0.046$). While the number of patients with a non-opportunistic infection did not differ significantly between

groups (P = 0.36), opportunistic infections were reported more frequently in controls (log rank P = 0.033). Compared to controls, MIC patients were found to have a trend towards a higher COVID-19 anti-S1 IgG index after vaccination with a median of 53 vs. 2 (P = 0.16). Importantly, the four MIC patients who had received the highest MIC cell dose 7 days before surgery and were on low immunosuppression during follow-up, continued to show absent anti-donor T lymphocyte reactivity in vitro and high $CD19^{+}CD24^{hi}CD38^{hi}$ transitional Breg as well as $CD19^{+}CD24^{hi}CD27^{+}$ memory Breg.

CONCLUSION

MIC infusions together with reduced conventional immunosuppression were associated with lower de novo DSA development and lower rates of opportunistic infections. In the future, MIC infusions could contribute to graft protection while reducing the side effects of immunosuppressive therapy.

Living donation with "special" patients

S20-03 Transplantation of old organs accelerates aging in young recipients

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INTRODUCTION

In organ transplantation, donor and recipient age may differ substantially. The aging process of donor organs, in turn, leads to the accumulation of senescent cells that secrete a variety of inflammatory molecules[1], termed the senescence-associated secretory phenotype (SASP). We hypothesized that transplantation of old organs induces senescence in young recipients.

METHODS

Hearts from young and old (3 and 18 months) C57Bl/6 and p16-EGFP reporter mice were transplanted into young recipient mice. 30 days after transplantation, the number of senescent cells in recipient organs was quantified by IHC. Physical performance of recipient mice was tested using Rotarod and grip strength tests; cognitive function was assessed using Novelty-Y maze. Locomotor and metabolic activities were determined using metabolic cages. Abundancy of senescent donor cells in recipients was evaluated by EGFP-qPCR and SASP factors quantified by qPCR. Senolytics for the depletion of senescent cells were administered to donor mice one day before transplantation.

RESULTS

Young recipient mice of old donor hearts showed increased numbers of senescent cells in various tissues compared with recipients of a young donor heart. Recipients of old hearts showed impaired physical performance and limited locomotor activity. Furthermore, transplantation of old donor organs impaired spatial learning ability and memory performance of young recipients and decreased metabolic activity in these animals. Mechanistically, we did not observe donor derived senescent cells in recipient organs indicating that passenger leukocytes had not been involved in the transfer of senescence. In contrast, SASP factors, as critical drivers of cellular senescence, were significantly increased in recipients of old donor organs. Single treatment of old donor animals with senolytics prior transplantation prevented the induction of physical frailty in young recipients.

CONCLUSION

Transplantation of older organs transfers cellular senescence to young recipients resulting in compromised physical and cognitive performance. Treatment with senolytics represents a therapeutic approach to prevent the spread of senescence in recipients while improving organ function.

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Poster Presentations

Poster Session 01: Infections/complications after transplantation

P01-01 High similarity of T cell-receptor repertoires in Epstein-Barr-reactive T cell cultures despite immunosuppressive treatment

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INTRODUCTION

Epstein-Barr virus infection can cause serious complications in transplant patients due to suppression of T cells by immunosuppressive medication. One important determinator of successful viral control is the T-cell-receptor (TCR) repertoire diversity. However, the influence of different immunosuppressants on the phenotype of EBV-reactive T cells and their TCR repertoire diversity has not been well defined thus far.

METHODS

EBV-antigen-specific T cells of six healthy donors were isolated using FACS and then expanded in absence or presence of tacrolimus (TAC), cyclosporin A (CSA), prednisolone (PRED), rapamycin (RAPA), and mycophenolic acid (MPA).

Proliferation, viability, and phenotypes of T cells were assessed by flow cytometry. TCR repertoires were analyzed by next-generation sequencing.

RESULTS

Proliferation of EBV-reactive T cells was strongly decreased by MPA and also by RAPA-treatment, but not other immunosuppressants. Viability of T cell cultures, however, was increased by RAPA and strongly decreased by MPA. EBV-reactive $CD8^+$ T cells were slightly more frequent than $CD4^+$ T cells *ex vivo*, but $CD4^+$ T cells dominated most cultures after three-weeks. The majority of *ex vivo* EBV-reactive T cells were terminally differentiated T_{EMRA} or effector memory T_{EM} cells. However, after three weeks T_{EM} dominated the cultures of all donors. The reduced proliferative capacity of $CD8^+$ T_{EMRA} could explain this shift. RAPA treatment maintained $CD8^+$ T cells in culture, possibly benefiting cytotoxicity. The Morisita-Horn-indices for T cell cultures with and without immunosuppressants was relatively high, indicating that immunosuppression did not significantly impact T cell clonality.

CONCLUSION

Different immunosuppressants have diverse effects on EBV-reactive T cell proliferation, viability, and phenotype. MPA strongly impaired proliferation and viability, while RAPA reduced proliferation but increased viability and cytotoxicity. Of interest, immunosuppression did not affect the diversity of TCR repertoires in our cell-culture model. Thus, the immunosuppressants studied here impair the functionality of T cells, but do not seem to specifically target certain clones and nor lead to a shift in TCR repertoires.

P01-02 Herpes and polyoma virus infections in a German transplant cohort (DZIF)

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INTRODUCTION

Herpes and polyoma virus infections are the most common infections after renal transplantation. Incidence-rates and timelines of posttransplant infection episodes have not been comprehensively documented in a German transplant cohort.

METHODS

In this prospective multicenter study of the German Center of Infectious Diseases (DZIF), all herpes and polyoma virus infectious events observed during first year after renal transplantation were evaluated. Our cohort comprised all adult renal transplant recipients included in DZIF-Cohort from April 2011 to February 2021 (n=1035).

RESULTS

1035 renal transplant recipients (64.6% male, mean age: 51±14) were enrolled. Nearly all (99.7%) received the present standard immunosuppression consisting of an CNI, MPA and low-dose steroids. CMV prophylaxis was administered to 76.3% of recipients for at least 3 months. Within the first 12 months, 268 patients suffered 380 herpes- and polyomavirus infections, demonstrating a cumulative incidence rate of 26.4%, 95%CI=[23.8;29.2]. CMV accounted for the highest viral incidence-rate, affecting 14.2% [12.2;16.5] of patients. Replication mainly occurred between month 4 and 6 at a median of 138 days (IQR=77-219)

after transplantation. The incidence rate of the high-risk group (D+/R-) was 28.3% [22.7; 35.3] compared to 1.8 [0.7; 4.8] in the low-risk group (D-/R-). Other herpes virus infections were rare (incidence-rates: HSV-1:1.4% [0.8;2.3]; VZV: 0.9% [0.5;1.7]; EBV: 0.7% [0.3;1.4]; HSV-2: 0.6% [0.3;1.3]; HHV-6: 0.1% [-]). BKV incidence rate accounted for 13.1% [11.2;15.4]). JC-Virus was rare (n=3); exclusively occurring in the final quarter of the first year.

CONCLUSION

In the current era of immunosuppression and prophylaxis, renal allograft recipients in Germany experience a high burden of Herpes-and polyomavirus infections. CMV and BKV are predominating. Early CMV infections might be better prevented by prolonged prophylaxis.

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P01-03 Risk factors for multiple infections in the first year after renal transplantation

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INTRODUCTION

An analysis of the German transplant cohort (DZIF) revealed renal allograft recipients in Germany experience a high burden of infectious events throughout the first posttransplant year. In-depth analysis of the occurrence of multiple infectious events may detect surrogates for an exceptionally high infection vulnerability.

METHODS

In this prospective multicenter study of the German Center of Infectious Diseases (DZIF), all infectious events observed during first year after renal transplantation were evaluated and risk factors for multiple infectious (>2 infections/year) events analyzed. Our cohort comprised all adult renal transplant recipients included in the DZIF-Cohort from April 2011 to November 2019 (n=804).

RESULTS

Multiple infections were detected in 17.0% (137/804) of recipients. Prevalence increased with age (25.5% in recipients in >65 years vs. 10.5% in recipients <55 years, p<0.001). Univariate analysis revealed that recipient age, deceased donor, donor age, delayed graft function and the number of postoperative inpatient days were significantly associated with their occurrence.

Multivariate analysis confirmed that recipient age (OR=1.02 per year, 95%CI=[1.00;1.04], p=0.038) and number of postoperative inpatient days (OR=1.25 per week, 95%CI[1.10;1.43], p<0.001) were independent risk factors. Recipients infected with Candida albicans were frequently affected by multiple infections (mean: 5.0 infections/patient, range 1–10), but also by bacterial resistance (66.7%[12/18]). Incidence rates of nosocomial pathogens (e.g. Enterococcus spp.) were significantly higher in recipients suffering multiple infections compared to recipients suffering 1-2 infections. Bacterial infection increased the risk of fungal infection (HR=6.45, 95%CI=[3.23;12.90], p<0.001) and fungal infection increased the risk for bacterial infection (HR=3.50, 95%CI=[1.44;8.49], p=0.006).

CONCLUSION

Depending on age about 10.5 to 25.5% of all transplant recipients suffer from more than two infections per year. Among them, nosocomial pathogens are highly prevalent, especially in recipients with Candida spp. infection. Age and number of postoperative inpatient days were identified as independent risk factors.

P01-04 Daratumumab as a rescue treatment option in a challenging antibody-mediated heart allograft rejection

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INTRODUCTION

Antibody-mediated rejection (AMR) is a major cause of graft failure and affects long-term survival. Possible therapeutic targets are plasma cells and natural killer cells expressing CD38. Daratumumab, a human IgG1κ monoclonal antibody, binds and inhibits CD38, indirectly leading to cell apoptosis. It has been an approved therapy for multiple myeloma and lymphoma since 2013. So far, only a few case reports describe a successful AMR therapy after kidney and heart transplantation. We report on a 21-year-old heart transplant patient who suffered her third graft rejection (ISHLT 2R) associated with a marked increase in donor-specific antibodies (DSA) and clinical deterioration. The fulminant AMR occurred despite the patient had been receiving continuous photopheresis for the last two years. In our case daratumumab was used as a rescue therapy.

METHODS

After graft rejection, the patient was initially treated with plasmapheresis for 5 consecutive days. Then a weekly dose of 16 mg/kg daratumumab was administered for 8 cycles, followed by two further doses every fortnight. Premedication included prednisolone (2 mg/kg KG). After the 10th dose, the patient lost compliance and discontinued therapy. Monitoring of the patient included HLA antibody tests, determination of NT-pro-BNP levels, Electrocardiography and echocardiography in addition to clinical parameters.

RESULTS

After daratumumab therapy the level of DSA decreased or at least stagnated. In addition, there was a decline in NT-pro-BNP levels, a decrease in heart rate and a clinical improvement. No side effects were reported.

CONCLUSION

During a therapy with daratumumab for AMR we found decreasing or stagnant DSA titers, an echocardiographic improvement in myocardial strain imaging, a significant decrease in NT-pro-BNP levels and a clinical improvement of the patient. Even though therapy with daratumumab was preceded by plasmapheresis and prednisolone was administered concomitantly at low doses, we attribute the long-lasting effect to daratumumab. Thus, targeted therapy of CD38 can be a promising strategy for the treatment of AMR.

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P01-05 CC genotype of *GNAS* c.393C>T (rs7121) polymorphism has a protective impact on development of BKV viremia and BKV-associated nephropathy after renal transplantation

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INTRODUCTION

The *GNAS* gene encodes alpha-subunit of the stimulatory G-protein (Gsα) which is ubiquitously expressed in various tissues. The single-nucleotide polymorphism (rs7121) of *GNAS*, c.393C>T, is associated with occurrence of a splice variant leading to elevated production of Gsα and subsequent increase of the second messenger cAMP. In the current study, we analyzed the prevalence of this *GNAS* polymophism in renal allograft recipients and its effect on renal allograft outome.

METHODS

We screened for the *GNAS* c.393C>T polymorphism in a cohort of 436 renal allograft recipients and retrospectively studied its relationship with *de novo* formation of donor-specific antibodies (DSA), rejection events, allograft survival and appearance of viral infection in particular BKV viremia up to 5 years after transplant. *GNAS* polymorphism was determined using restriction fragment length polymorphism (RFLP)-PCR.

RESULTS

While *GNAS* c.393C>T polymorphism was prevalent in 319 (73%) recipients, 117 recipients (27%) were negative. The lack of *GNAS* polymorphism correlated with significantly lower postransplant frequency of BK polyomavirus

(BKV) viremia and BKV-associated nephropathy (17 (15%) vs. 84 (26%), p=0.01; 3(3%) vs. 27 (8%), p=0.03). BKV- associated nephropathy- free survival was significantly improved in noncarriers compared with *GNAS* polymorphism carriers (p=0.043). Multivariate analysis indicated an independent protective effect of CC genotype on development of BKV viremia and BKV-associated nephropathy after renal transplantation (relative risk 0.54, p=0.04; relative risk 0.27, p=0.036). High dose BKV viremia with $\geq 10^4$ copies/mL was linked to significantly reduced allograft survival and rapid progression to BKV-associated nephropathy compared to low dose viremia ($<10^4$ copies/mL). However, low dose BKV viremia was more prevalent in *GNAS* polymorphism noncarriers than in carriers. On the other hand, we found a trend towards lower portion of *de novo* DSA in recipients without evidence of the *GNAS* c.393C>T polymorphism than in polymorphism carriers.

CONCLUSION

Lack of *GNAS* c.393C>T polymorphism corresponding to the CC genotype seems to represent a protective factor in terms of development BKV- viremia and BKV-associated nephropathy in renal allograft recipients.

P01-06 *GNB3* c.825C>T (rs5443) polymorphism is associated with increased risk for acute cardiovascular events after transplantation in renal allograft recipients

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INTRODUCTION

The c.825C>T single-nucleotide polymorphism (rs5443) of the Guanine Nucleotide-Binding protein subunit β3 (*GNB3*) results in generation of a splice variant of *GNB3* leading to essential hypertension, atherosclerosis, coronary diseases and cerebrovascular events. The present study was aimed to investigate the effect of *GNB3* c.825C>T polymorphism on cardiovascular events appearing in renal allograft recipients posttransplant.

METHODS

Our retrospective study included 436 renal allograft recipients in which *GNB3* c.825C>T polymorphism as well as frequency of cardiovascular events, *de novo* formation of donor-specific antibodies (DSA), and clinical outcome up to 8 years after transplant were analyzed. *GNB3* c.825C>T polymorphism was detected restriction fragment length polymorphism-PCR.

RESULTS

The TT genotype of *GNB3* was identified in 43 (10%) of 436 recipients. Death due to acute cardiovascular event occurred more frequently in recipients having TT genotype (4 (9%) vs. 7 (2%), p=0.003). The frequency of myocardial infarction and acute peripheral artery occlusive disease (PAOD) posttransplant was significantly higher among TT genotype carriers than noncarriers

(8 (19%) vs. 27 (7%), p=0.007; 7 (16%) vs. 21 (5%), p=0.006). Myocardial infraction-free survival (p=0.003) and acute PAOD-free survival (p=0.004) rates significantly decreased in T homozygous patients. There was no difference regarding chronic cardiovascular diseases occurring pretransplant between TT geno-type carriers and noncarriers. Pretransplant diabetic nephropathy based on preexisting diabetes mellitus type II appeared more frequently in TT genotype than CT/CC genotypes. Adjusting for covariables in a multivariate analysis revealed only a mild effect of homozygous *GNB3* c.825C>T polymorphism as a heritable risk factor for occurrence of myocardial infarction and acute PAOD after renal transplantation relative risk 2,2 p=0.065; relative risk 2,4 p=0.05).

CONCLUSION

Our results suggest thathomozygous *GNB3* c.825C>T T allele has a slight impact on the risk for myocardial infarction and acute PAOD in renal allograft recipients after transplantation displaying noticeable effects only in presence of additional nonheritable risk factors.

P01-07 New lateral flow assays for CXCL9 and CXCL10 to detect polyoma-nephropathy or rejection

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INTRODUCTION

Success of kidney transplantation is threatened by infections and rejections. For diagnosis, biopsies are required; therefore, reliable noninvasive tests for specific biomarkers are urgently needed. Interferon-γ-induced CXCL9/10 are chemokines expressed at a certain level within the kidney during immune responses. They are released into the urine as a medium suitable for point-of-care-tests such as lateral flow assays (LFA).

METHODS

Urine samples derived from kidney transplant recipients (KTRs) of Hannover Medical School were analyzed by ELISA, to determine CXCL9/10 levels, and creatinine was additionally measured. For CXCL9, an aptamer- and antibody-based-hybrid- LFA[1] was built up and for CXCL10, an antibody-based-LFA was established. LFAs were validated with urine samples from 10-30 patients for each diagnostic category, antibody-mediated rejection (AMR), T-cell mediated rejection (TCMR), borderline-TCMR, or polyoma nephropathy in comparison with 10-30 samples of patients with biopsy-proven unsuspicious grafts as a negative control.

RESULTS

According to Wilcoxon test results, urinary CXCL9 concentrations of KTRs with AMR (N=24, 282.1 $\pm$ 286.2 pg/ml, $p<0.004$), TCMR (N=22, 555.5 $\pm$ 788.9 pg/mL, $p<0.01$), borderline-TCMR (N=25, 422.8 $\pm$ 636.8 pg/mL, $p<0.07$) or polyoma nephropathy (N=23, 426.4 $\pm$ 607.2 pg/mL, $p<0.0001$) were significantly higher compared to negative controls without such pathologies

(N=41, 125.0 ± 160.9 pg/mL). Patients suffering from TCMR (N=22, 62.4 ± 97.0 pg/mL, p<0.01) or polyoma infection (N=23, 110.4 ± 178.5 pg/mL, p<0.0001) additionally had significantly higher CXCL10 urine levels than patients with an unsuspicious graft biopsy (N=41, 18.8 ± 39.9 pg/mL). Fractional excretion rates for these chemokines per urinary creatinine revealed the same differences. LFAs were successfully used for diagnosis and performed independent from urine concentration.

CONCLUSION

LFAs for CXCL9/10 are helpful to identify polyoma nephropathy or TCMR in KTRs. In addition, the CXCL9-LFA can be used in AMR. Tests for CXCL9/10 have a sensitivity of 71%/91% and a specificity of 71%/85%, respectively.

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P01-08 Non-antigen-specific immunoadsorption is a risk factor for severe postoperative infections and increased mortality in ABO-incompatible kidney transplant recipients

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INTRODUCTION

To address the demand for kidney transplants, ABO-incompatible (ABOi) living kidney transplantation (KTx) has been an established procedure with long-term outcomes similar to ABO-compatible KTx. Desensitization protocols involve the use of immunoadsorption (IA) to eliminate preformed antibodies against the allograft. This study compares single-use antigen-specific Glycosorb® ABO columns to reusable non-antigen-specific Immunosorba® immunoglobulin adsorption columns regarding infectious complications and long-term outcome.

METHODS

All 138 ABOi KTx performed at the Freiburg Transplant Center from 2004 to 2020 were included in this monocentric retrospective study with a mean follow-up of 7.4 years. 81 patients received IA using Glycosorb® ABO columns, whereas 57 patients received IA using Immunosorba® immunoglobulin adsorption columns. The two groups were compared regarding long-term patient and graft survival as well as infectious complications.

RESULTS

Patient survival was significantly impaired in the group receiving non-antigen-specific IA during the first two years post KTx ($p = 0.048$, log-rank $P = 0.032$), mainly due to infections. Patients desensitized with non-antigen-specific IA suffered from significantly more recurring (6.2% vs. 21.4%; $p = 0.016$)

and severe infections (18.5% vs. 37.5%; p = 0.018) with significantly more urosepticemias, accounting for 61.9% of septicemias in this group (vs. 26.7%; p = 0.049). Regarding BK virus and cytomegalovirus infections, there was no difference in recipient positivity, however, the duration of BK viremia was significantly longer in the non-antigen-specific IA group (197.7 $\pm$ 114.1 d vs. 397.2 $\pm$ 272.2 d; p = 0.024). Contrariily, a significantly higher number of patients receiving antigen-specific IA suffered from graft rejection (29.6% vs. 14.0%; p = 0.041), although overall as well as death-censored graft survival were comparable between the two groups.

CONCLUSION

The outcome of patients after ABOi KTx regarding graft function was not influenced by the modality of immunoadsorption. However, non-antigen-specific IA was found to be a risk factor for severe postoperative infections as well as an increased mortality during the first two years post KTx.

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P01-09 Antiviral T-cell frequencies in a healthy population: Reference values for evaluating antiviral immune cell profiles in immunocompromised patients after transplantation

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INTRODUCTION

Viral infections and reactivations are a major cause of morbidity and mortality after solid organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT). Latent herpesviruses (e.g., CMV, EBV), lytic viruses (e.g., ADV) and polyomaviruses (e.g., BKV, JCV) can cause severe complications. Antiviral drugs form the mainstay of treatment; but their use is limited by side effects, and viral clearance usually depends on reconstitution of functional antiviral T-cell immunity.

METHODS

The aim of this study was to establish guiding values for virus-specific T-cell (VST) frequencies in healthy seropositive donors for more precise interpretation of VST frequencies observed in immunocompromised patients. We measured the frequencies of VSTs against 23 antigens from 11 clinically relevant human viruses in blood from healthy donors (n=151) by interferon-gamma enzyme-linked immunospot (ELISpot) assay. Moreover, previous exposure to the viruses of interest was determined by serological analyses. VST frequencies were correlated to serology, memory T-cell subset distributions and the number of total $CD3^+$ T cells within whole blood. Specifically,

we determined the VST frequencies and classified their distribution according to age and gender to allow for a more specific evaluation and prediction of antiviral immune responses.

RESULTS

In the total cohort, a small fraction of donors had T cells against BKV and JCV while more donors responded to EBV, ADV, HHV6, and Varicella-Zoster Virus (VZV). All CMV-seropositive donors had T-cell responses to CMV_pp65. Furthermore, most donors had T cells against EBV and HHV6. CMV- and EBV-specific T-cell frequencies appeared to increase with age, while ADV-specific T-cell frequencies decreased, regardless of gender. Serological correlations between CMV, EBV and Herpes Simplex Virus (HSV) were partly also reflected at the T-cell level.

CONCLUSION

The reference values established here provide an invaluable tool for immune response evaluation, intensity of therapeutic drugs and treatment decision-making in immunosuppressed patients. This data should make an important contribution to improving the assessment of immune responses in immunocompromised patients.

ACKNOWLEDGEMENT

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P01-10 The alloCELL program: Patient monitoring, donor selection and GMP-compliant manufacturing of virus-specific T cells for immunocompromised patients with and without transplantation history

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INTRODUCTION

Intensive immunosuppression leads to impaired T-cell immunity in transplanted patients. Infections with and reactivations of opportunistic pathogens (e.g., CMV, EBV, BKV) are frequent and associated with significant morbidity and mortality. EBV infections can lead to malignant complications, such as post-transplant lymphoproliferative disorder (PTLD). In addition, polyomaviruses BKV and JCV can cause serious opportunistic viral diseases such as virus-associated transplant nephropathy and progressive multifocal leukoencephalopathy (PML). The shortcomings of conventional therapies have increased interest in T-cell immunotherapy. Here, timely T-cell donor recruitment and rapid production of antiviral T cells are required.

METHODS

To facilitate the recruitment of T-cell donors, the alloCELL registry was established, which currently has >3,500 HLA-typed donors with an extensively characterized antiviral T-cell repertoire. The alloCELL lab established protocols to address clinical needs of high-risk patients or patients who have failed conventional therapy. T-cell donors are considered eligible if ≥0.01% IFN-γ^+ T cells are detectable. A related haploidentical or ≥5/10 HLA-matched alloCELL donor is recommended for patients whose graft donor is not suitable.

RESULTS

As of May 2022, >410 multi-/monovirus-specific clinical-grade T-cell products have been generated using the CliniMACS Prodigy and the majority was administered to patients after stem cell transplantation. However, 15% of the products have been generated for patients after SOT (kidney, lung and heart Tx) and 15% for patients without or before Tx. For patients in need of an unrelated third-party donor, suitable donors were found and T-cell products were provided within 1.5 weeks after request. Patients did not show severe adverse effects. Antiviral T cells were detected in 80% and monitored to determine frequency, chimerism and TCR repertoire. Of note, there is evidence that adoptive T-cell transfer induces endogenous T-cell responses.

CONCLUSION

Success of antiviral T-cell transfer benefits from (i) accurate monitoring of viral load and antiviral T-cell frequencies in patients, and (ii) early and fast selection of suitable T-cell donors.

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P01-11 No association between pre-transplant anti-BK virus antibodies and post-transplant reactivation

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INTRODUCTION

BK virus (BKV) reactivation is a very common complication after renal transplantation, which can lead to graft loss in 1-10% of the cases. While occurrence of reactivation seems to be associated with certain immunosuppressive regimes, particularly the use of calcineurin inhibitors, risk factors have not been sufficiently defined yet. Particularly, it is still unclear whether pre-transplant serostatus is associated with protection from BKV reactivation.

METHODS

Therefore, we characterized a large, multi-centre cohort (N=397) for the presence of IgG antibodies against the structural BKV protein VP1, using an ELISA assay. In parallel, BKV viral load in serum was monitored two weeks and one, two, three, six, nine and twelve months post renal transplantation. A total of 2092 samples were analysed for BKV viral load.

RESULTS

395 (99.5%) patients had detectable pre-transplant anti-BKV antibodies, with a median [IQR] IgG concentration of 23 [13-38] µg/ml. BKV load over the detection limit (>250 copies/mL) was observed in 196 (49.4%) patients. Importantly, no association between anti-BKV IgG concentrations and the occurrence of detectable BKV was observed (no reactivation: 22 [14-38] µg/ml, reactivation: 25 [13-38] µg/ml; P=0.886). Similarly, no significant difference was found when comparing patients without reactivation with those demonstrating a viral load > 10,000 copies/mL (24 [16-35] µg/ml; P=0.764). Finally, we evaluated whether the peak viral load during the first post-transplant year correlates with the anti-BKV concentration; no correlation was found (ρ=0.00, P=0.955). Similarly, no correlation was observed between pre-transplant anti-BKV IgG concentration and renal function one year post-transplant (ρ=0.00, P=0.950).

CONCLUSION

Our results support a lack of protection against BKV reactivation through pre-existing antibodies, as patients were similarly affected by BKV reactivation regardless of their pre-transplant serostatus. Further characterization efforts – including the donor – are needed to better understand the risk constellation of BKV reactivation.

P01-12 High incidence and viral load of HHV-6A in a multi-centre kidney transplant cohort

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INTRODUCTION

Human herpesvirus 6 (HHV-6) is a common opportunistic pathogen in kidney transplant recipients. HHV-6 reinfections and reactivations of a latent infection are common in the early post-transplant period. Especially reactivations are associated with symptoms ranging from fever to life-threatening hepatitis and bone marrow suppression. Two different variants of HHV-6, HHV-6A and HHV-6B, have been identified, of which the latter seems to be dominant. However, it is unclear whether they increase the likelihood of other viral reactivations.

METHODS

We characterized a multi-centre cohort of 93 patients along nine study visits for viral load in peripheral blood; the study visits were scheduled pre-transplant, one and two weeks post-transplant and one, two, three, six, nine and twelve months post-transplant. We tested for the following viruses: HHV-6A and HHV-6B, the herpesviruses cytomegalovirus (CMV) and Epstein-Barr virus (EBV) and the polyomavirus BK (BKV), with a detection limit of 250 copies/mL.

RESULTS

We detected HHV-6A viral load in 48 (51.6%) patients; the incidence of HHV-6B was much lower, being detected in 7 (7.5%) patients. Median peak viral load among HHV-6A positive patients was 13,600 [1484-2,378,4040] copies/mL; for HHV-6B it was 1350 [419-31,280] copies/mL. As a comparison, incidence of CMV was 27.7%, 7.7% for EBV and 29.2% for BKV. There was a strong association between HHV-6A and HHV-6B (P=0.066, OR=6.2), the lack of significance can be explained by the low incidence of HHV-6B. Importantly, we did not find any evidence of increased incidence of other viruses among patients with HHV-6A reactivation (CMV: P=0.386, OR: 1.4; EBV: P=0.882, OR=0.5; BKV: P=0.297, OR: 1.6). No negative effect of high HHV-6A load (10000 copies/mL) on markers of graft renal and hepatic function or blood count six months post-transplant.

CONCLUSION

Our results show a clear dominance of HHV-6A in peripheral blood when compared to HHV-6B, with higher incidence and viral loads. Despite the high HHV-6A loads observed, we did not identify any negative effects on graft renal function, hepatic function or in the haematopoiesis.

Poster Session 02: Basic science, COVID-19 and transplantation

P02-01 Urine derived renal tubular epithelial cells have immunomodulatory capacities and can directly induce BKV-specific T cell response

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INTRODUCTION

Reactivation of the BK virus (BKV) is a critical adverse event after kidney transplantation and can lead to transplant loss. Control of BKV and its clearance after reactivation that can be facilitated by decreasing the immunosuppression, is mediated by BKV-reactive T cells. However, the exact mechanism underlying the T cell-mediate BKV clearance in the kidney transplant is not clear. Here, we used urine derived renal tubular epithelial cell (udTEC) as model system to investigate the immunomodulatory capacity of udTEC and their potential to induce T cell responses against BKV with the aim to phenotypically characterize the BKV-reactive T cell response.

METHODS

UdTEC were generated by culturing urine-derived cell pellets and their identity was established by morphology and expression of surface molecules. To assess the inflammatory potential of udTEC, the cells were treated with Poly I:C or TNFα/IFNγ to mimic viral DNA challenge or inflammation, respectively.

Cytokine/chemokine secretion and expression of co-stimulatory molecules was evaluated using multiplex assays and flow cytometry (FC). To investigate udTEC-induced T cell responses, autologous T cells, isolated from blood were co-cultured with udTEC, in the presence of BKV protein-derived peptides and PolyI:C or TNFα/IFNγ. BKV-reactive T cells were quantified and phenotypically characterized by multi parameter FC.

RESULTS

UdTEC phenotypically match renal tubular epithelial cells since they express CD13, EPCAM, cytokeratin and the myo-inositol oxygenase. After stimulation with PolyI:C, udTEC show increased levels of CD40 and HLA-ABC, whereas TNFα/IFNγ only induced HLA-DR/ABC expression. PolyI:C and TNFα/IFNγ stimulation of udTEC induced a district pattern of inflammatory mediators. Interestingly, udTEC can present BKV peptides thereby inducing a functional BKV-reactive CD4 and CD8 T cells response.

CONCLUSION

udTEC express immunomodulatory molecules, and induce BKV-directed T cell reactivity, indicating that renal epithelial cells serve as non-conventional antigen presenting cells in the kidney facilitating BKV clearance.

P02-02 Performance of aged liver grafts in a rat model of normothermic ex vivo liver machine perfusion

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INTRODUCTION

Organ shortage is an increasing problem in most parts of the Eurotransplant region. This is in part due to the number of organ donations, which have decreased by 23% in Germany in the last ten years, but also due to the lack of suitable grafts. As liver machine perfusion has recently been proposed as a tool for graft assessment, we here aimed to characterize old and young liver grafts in a in a standardized rat model of normothermic ex vivo liver machine perfusion (NEVLP).

METHODS

A total of 24 livers from Sprague Dawley rats aged 3 months or 12 months were either perfused for 6 hours using a proprietary dual vessel NEVLP system or used as a reference group of non-perfused livers for each age (n=6/group). Tissue and perfusate samples were taken for histological and biochemical analyses.

RESULTS

Arterial and portal venous pressure, bile production as well as perfusate electrolytes did not differ between groups and remained in between the respective reference ranges throughout the perfusion. However, livers of older animals were heavier (20.2 g vs. 17.2 g; p=0.002). All perfused livers cleared

lactate during perfusion from a peak of 6.9 mmol/l at the start of perfusion to 1.6 mmol/l at the end of perfusion. Bile production remained high after 6 hours of perfusion (614 mg/h IQR 228mg) and Bile pH remained stable (median 8.17 IQR 0.11). LDH levels measured in the bile were significantly higher in 12-month-old animals (295 mU/m vs. 65 mU/ml; p=0.009). Peak transaminase levels in 12-month-old animals were nominally higher (ALT: 200 U/l vs. 272 U/l; p=0.2). Urea levels increased throughout the perfusion and were significantly higher in older animals (12.7 mmol/l vs. 16.3 mmol/l; p=0.04). H&E staining showed vital liver tissue and no significant differences between age groups.

CONCLUSION

In summary, liver grafts from 3- and 12-month-old Sprague Dawley rats performed equally well on NEVLP. Future studies should address the outcome after transplantation of aged and young rat livers with static cold storage compared to NEVLP.

P02-03 The effects of Treg and stem cell mobilization on transplant vasculopathy in a murine aortic transplant model

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INTRODUCTION

Effector and regulatory T cells (Tregs) are cell populations of interest in cardiac allograft vasculopathy (CAV).[1] Plerixafor mobilizes hematopoietic stem cells and may boost T cells.[2,3] The aim of this study was to evaluate if a single, repeated or continuous treatment with plerixafor induces graft tolerance through stem cell and Treg mobilization in a mouse allograft transplant model.

METHODS

CBA mice ($H2^k$) received fully allogenic abdominal aortas from C57BL/6 mice ($H2^b$). Continuous plerixafor application [1mg/kg/d] was carried out for 14 days using implanted osmotic pumps. Single dose (s.c.) injection of 1mg/kg/d or 5mg/kg/d were done at day 1 after transplantation (Tx.) and pulsed injections [1mg/kg/d] on days 1, 7, 14, and 21 post Tx. The control allograft group received vehicle loaded osmotic pumps. Stem cell mobilization was monitored by FACS. Recipients were sacrificed on day 14 for intragraft gene expression or on day 30 for histological analysis.

RESULTS

Murine aortic graftswith pulsed plerixafor injections showed significantly reduced neointima proliferation compared to control allografts (33.65%$\pm$8.84% vs.53.13% $\pm$12.41%; $p<0.05$). Single shot and continuous treatment groups exhibited no redcution of neointima formation vs. the untreated group.

FACS analysis revealed significantly less hematopoietic stem cells (HSC) in the bone marrow of plerixafor treated mice vs. the control at day 14 after Tx. Though, there were significantly more HSCs in the peripheral blood on day 30 after Tx, with the pulsed injection even doubling HSCs [0.0152%±0.008; $p < 0.005$ (pulsed); 0.0046%±0.002%; $p < 0.01$ (pump); 0.0076%±0.001%; $p < 0.01$ (single dose of 1mg/kg); 0.0039%±0.0017%; $p < 0.1$ (single dose of 5mg/kg) vs. 0.0018%±0.0016% (control)]. Preliminary intragraft gene expression results showed clearly reduced IFNγ, as well as E-Selectin and ICAM-1 expression and a significantly increase of IL-4, IL-10 and TGFβ.

CONCLUSION

The data suggests that pulsed, continued and single dose application of plerixafor leads to potent stem cell mobilization. Repeated treatment with plerixafor reduces neointima formation in our transplant model. Further analysis concerning immunohistochemistry are under progress.

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P02-04 Extrahepatic bile duct organoids as model to study ischemia/reperfusion injury during liver transplantation

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INTRODUCTION

Biliary complications are still a major cause for morbidity and mortality after liver transplantation (LT). Ischemia/reperfusions injury (IRI) leads to disruption of the biliary epithelium. Yet little is known about the underlying molecular mechanism. Here we introduce a novel model to study the effect of IRI on human cholangiocytes using extrahepatic cholangiocyte organoids (ECOs).

METHODS

Extrahepatic bile duct tissue was collected during LT (n = 10) and were stained for ACSL4 (marker of ferroptosis) using *in-situ*-hybridization. Further, using the extrahepatic bile duct tissue ECOs were expanded and cultured as described before Sampaziotis et al., 2017. Multiplex immunofluorescence and in-situ hybridization and qRT-PCR was performed to identify cholangiocyte phenotype of cultured organoids (Albumin, EPCAM, Sox9, LGR5 & CK19). IRI was induced by culturing cells in a hypoxic chamber for 48h, followed by reoxygenation. In-situ-hybridization and qRT-PCR were performed to study markers of programmed cell death induced by IRI.

RESULTS

After ECO expansion and culturing, ECOs formed circular structures recreating a tubular structure as the extrahepatic bile duct. qRT-PCR & mIFISH analysis revealed a cholangiocyte phenotype with high expression of EPCAM, Sox9, LGR5 & CK19 and low expression of albumin & AHH. After hypoxia and more pronounced after re-oxygenation, ECOs showed increased expression

of markers of programmed cell death, e.g. ACSL4. This expression pattern was comparable to the increase of ACSL4 expression during static cold storage and after reperfusion during LT. HIF1a, a marker for angiogenesis, was increased after hypoxia and re-oxygenation in ECOs and comparable in bile duct tissue during static cold storage and after reperfusion.

CONCLUSION

Organoids (ECOs) are *in vitro* cellular systems that self-organize through mechanisms like *in vivo*, they recapitulate the structure and show the same function, in terms of cell death induction and also angiogenesis induction as the extrahepatic bile duct during liver transplantation and thus are model to study IRI in cholangiocytes after LT.

P02-07 CD28 Superagonist D665-mediated activation of mouse regulatory T cells maintains their phenotype without loss of suppressive quality

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INTRODUCTION

Regulatory T cells (Tregs) maintain immune homeostasis by regulating the activation of other immune cells. In preclinical models of autoimmune diseases Treg infusion has been shown to prevent and even reverse the disease [1]. In the setting of transplantation, preclinical studies have shown that Treg infusion can control the alloimmune response and promote immunological tolerance to allografts [2,3]. Thus, Treg therapy in transplantation is promising, however, it is limited by the high number of cells needed to induce immunomodulatory effects. In this study, we aimed at improving the in vitro expansion of mouse Tregs using the CD28 Superagonist (CD28-SA) D665 [4] and comparing it to the conventional expansion using anti-CD3/anti-CD28 Dynabeads®.

METHODS

Lymphocytes were extracted from pooled lymph nodes from naïve C57BL/6 mice, stained with anti-CD4, anti-CD25 and anti-CD62L and sorted for CD4+CD62L+CD25+ for Tregs and CD25- for Tconv. Tregs were stimulated and with anti-CD3/anti-CD28 Dynabeads® or 10 µg/ml CD28-superagonist D665 and expanded for 14 days. Flow cytometry was used to characterize the cell phenotype. To determine the Treg function, cytokine ELISA as well as suppression assays were preformed.

RESULTS

CD28-SA—stimulated Tregs showed a slightly higher fold expansion compared to anti-CD3/CD28 bead-stimulated Tregs (52- vs 38-fold after 14 days, p=0.42). When comparing the two expansion methods, the Foxp3- and CD25-MFI (mean fluorescence intensity) of CD28-SA—stimulated Tregs were slightly higher (non-significant trend). In comparison to anti-CD3/CD28 bead-stimulated Tregs, Tregs expanded with the CD28-SA had a significantly lower percentage of CD62L-positive Tregs 5 and 7 days after activation (day 5: p=0.0487; day 7: p=0.0187). Both expansion methods led to Tregs producing comparable amounts of IL-10 and TGFβ. Tregs expanded with CD28-SA maintained their suppressive function and, non-significantly exceeded that of Tregs expanded with anti-CD3/CD28 beads (p=0.0538).

CONCLUSION

Thus, stimulating murine Tregs with the CD28-SA is a promising alternative since it maintains their suppressive capacity without altering their phenotype and yields a higher fold expansion within 14 days [5].

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P02-08 Metabolic characteristics of CMV-specific T-cells in renal transplant patients

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INTRODUCTION

Cytomegalovirus (CMV) infections occur frequently in renal transplant patients due to immunosuppressive therapy inhibiting CMV-specific T-cell immunity. It was the aim of this study to investigate the metabolic characteristics of CMV specific T-helper-cells in renal transplant patients.

METHODS

37 renal transplant patients and 10 healthy controls were recruited. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood. PBMC were labelled with TagIt tracking dye and cultured in presence of CMV lysate. Divided T-cells were defined as CMV-specific T-cells. CMV-specific T-cells were then assayed for uptake of fluorescently labelled glucose (2-NBDG) and fatty acids (Bodipy). Glucose and fatty acid uptake was quantified by flow cytometry. Unstimulated T-cells and T-cells treated with a polyclonal stimulus (SEB and anti-CD3/CD28) served as controls.

RESULTS

Independent of the stimulus used for T-cell activation, uptake of glucose and fatty acids was significantly higher in divided versus undivided T-cells. Interestingly, glucose uptake of SEB and anti-CD3/CD28 stimulated T-cells was significantly lower in patients than in HC. In contrast, CMV-specific T-cells were not different with respect to glucose uptake comparing HC and patients. In patients, CMV-specific CD25 expressing effector memory T-helper-cells were far more potent in taking up glucose and fatty acids

than SEB or anti-CD3/CD28 stimulated CD25 expressing effector memory T-helper-cells. Uptake of glucose and fatty acids by CMV-specific CD25 expressing effector memory T-helper-cells was efficiently suppressed by rapamycin and FK506 in vitro.

CONCLUSION

CMV-specific effector memory T-helper-cells utilize glucose and fatty acids upon activation. Immunosuppressive agents reduce uptake of glucose and fatty acids by CMV-specific T-cells and thereby hamper immunological control of CMV.

P02-11 Additional boost with NVX-CoV2373 (Nuvaxovid®) protein vaccine does not lead to an improvement of humoral or cellular immunity against SARS-CoV-2 in immunosuppressed renal transplant non-responder

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INTRODUCTION

Immunosuppression is essential to prevent graft rejection in post-transplant patients. However, immunosuppression is also known to alter the development of an effective response to vaccines. Significantly lower rate of seroconversion following COVID-19 mRNA/vector vaccination has been found in transplant patients as compared to non-immunosuppressed patients. Despite additional boosts, there is a significant number of humoral non-responders suggesting that other vaccination strategies are required to improve the vaccination response.

METHODS

We analyzed immunogenicity of COVID-19 protein-based vaccine (NVX-CoV2373) in 6 renal transplant patients with lack of seroconversion despite 4-5 doses of SARS-CoV-2 mRNA vaccination applied before. Patients were analysed before the first dose of NVX-CoV2373 and four weeks later. Titers of binding antibodies were estimated by ELISA. T cell immunity reactive against wild-type S-protein was analyzed by multiparameter flow cytometry.

RESULTS

We could not detect SARS-CoV-2 specific IgG antibodies four weeks after the first dose of NVX-CoV2373. Analysing the cellular immune response against SARS-CoV-2 S-protein overlapping peptides, no increase in the magnitude of SARS-COV-2 reactiveT cells could be found in the peripheral blood.

CONCLUSION

Application of the first dose of protein-based vaccine NVX-CoV2373 did not improve vaccination specific cellular and humoral immunity in our small cohort of vaccination non-responders. Evaluation of the response to the second NVX-CoV2373 dose as scheduled by the regular vaccination protocol in a larger patient cohort is required to evaluate the real immunogenicity of the protein-based vaccine in transplant population.

P02-12 Improvement of HBV seroconversion rate following COVID-19 boost in hemodialysis patients with initial lack of HBV vaccination response

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INTRODUCTION

Hemodialysis patients (HD) are known to be immunocompromised and a high degree of vaccination non-responders is observed in this population. The aim of this study was to assess the effect of heterologous immunity in context of HBV and COVID-19 vaccination in HD.

METHODS

We analyzed the adaptive immunity against SARS-CoV-2 and HBsAg in 16 hemodialysis patients (HD) following consecutive HBV and COVID-19 vaccination boosts applied 3 weeks apart each other. All patients were HBV vaccination non-responders (following 4 doses of Engerix), and no- or low-responder following prime-boost vaccination with Comirnaty. Titers of binding antibodies as well as neutralizing antibodies against HBV, SARS-CoV-2 WT, delta and omicron were estimated in follow up by ELISA and SARS-CoV-2 spike-protein (S-protein) pseudovirus assays, respectively. T cell immunity reactive against SARS-CoV-2 and HBV was analyzed by multiparameter flow cytometry. T cell receptor (TCR) repertoires of HBsAg- and S-protein-reactive T cells were analyzed by NGS.

RESULTS

3 weeks after the third SARS-CoV-2 vaccination, all 16 HD were able to develop a protective humoral immunity against SARS-CoV-2 wild-type, delta VOC and omicron VOC. Interestingly, while no HBsAg seroconversion could be observed 4 weeks following an HBV vaccination boost, 6 out of 16 initial HBV vaccination non-responders demonstrated seroconversion with median Ab titers of 123.5 IU/mL [53.5-129]. Three weeks after the SARS-CoV-2 boost, HBsAg- T cells were detectable in all vaccinated patients without differences between humoral responders and non-responders. Additionally, we found no overlapping TCR repertoire in HBsAg- and S-protein-reactive T cells.

CONCLUSION

6 out of 16 HBV vaccination non-responders on HD therapy were able to generate antibodies against HBV after COVID-19 vaccination. Since no TCR overlap could be detected between S-protein- and HBsAg-reactive T cells, unspecific activation following COVID-19 immunization rather than cross-reactivity appears to contribute to the development heterologous HBV immunity. Our data might have important implication for the vaccination regime for immuncompromized patienst such as hemodialysis and transplant patients.

P02-13 Variances in humoral response to different spike protein domains after SARS-CoV-2 vaccination in lung and heart transplant recipients

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INTRODUCTION

Immunocompromised recipients of organ transplants are at risk for severe courses of COVID-19 and were shown to exhibit an impaired humoral response to SARS-CoV-2 vaccination. Hence, additional studies on the degree of protection through SARS-CoV-2 vaccination in lung (LTx) and heart transplant (HTx) recipients are needed.

METHODS

Plasma obtained 4-6 weeks after the second dose of SARS-CoV-2 vaccination (80% mRNA) of n=404 LTx and n=89 HTx patients was analyzed for SARS-CoV-2 RBD-, S1- and S2 spike-specific IgG antibodies using Luminex-based multiplex assays. Threshold for seroconversion and high responders was set separately for each antigen based on the median MFI + 2σ in an unexposed pre-pandemic control group.

RESULTS

46.3% of LTx and 75.3% of HTx recipients developed IgG to at least one of the three spike domains. The superior IgG response of HTx compared to LTx recipients was also seen for every individual spike domain as well as in

relative BAU units for the S1 domain. The intensity of the domain-specific IgG responses varied within Tx entities, with both LTx and HTx recipients developing the significantly highest IgG concentrations against the S2 domain.

Associations of spike-specific IgG responses were identified with patient age, time after transplantation, type of immunosuppression and primary disease.

CONCLUSION

Large proportions of LTx and less HTx recipients failed to mount spike-specific IgG responses following two vaccinations. Even in responders, IgG levels remained below IgG levels of immunocompetent controls.

Additionally, spike vaccination stimulated a strong S2-specific responses to conserved regions, which indicates that pre-existing memory may improve humoral response in immunosuppressed LTx and HTx recipients.

Although S2-specific IgG may not be neutralizing, an influence on COVID-19 severity is likely. Furthermore, our data suggest that humoral immunity of Tx patients may be underestimated when only considering anti-RBD or S1 IgG as diagnostic marker.

P02-15 COVID-19 and transplant rejection: A case study of two patients and literature research

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INTRODUCTION

Due to their immunosuppression transplant patients are at high risk for COVID-19. In the past short studies have addressed the question whether reducing the immunosuppressive therapy in SARS-COV-2-positive transplant patients hightens the risk of rejection. We present a case study of two patients with COVID-associated organ rejection from our centre which underline along with results from other studies the risk for organ rejection during COVID-19 as a disease-specific risk.

METHODS

Case Study and Literature Review.

RESULTS

Patient 1 presented with acute kidney failure after pancreas-kidney transplant (2018). He had received his second vaccine against SARS-COV-2 one month previous to admission to our centre. A kidney biopsy showed a cellular rejection (Banff 1A) along with donor specific antibodies. He was treated with high dosed cortisone as well as thymoglobuline and underwent plasmapheresis. Patient 2 presented with elevated glucose levels after pancreas-kidney-transplantion (2003). She tested herself positive for COVID two weeks before presenting at our centre and was still positive for SARS-COV-2 at hospitalisation. CT-angiography of the abdomen revealed a good perfusion of the transplanted organs. The patient received high dosed cortisone for three days while being isolated for COVID. A biopsy of the pancreas showed a severe CD-4-positive cellular rejection which was treated with thymoglobuline.

CONCLUSION

It has been shown that SARS-COV-2 causes a massive immune response with rising neutrophile and diminished lymphocyte counts in serum. We confirmed these findings in our patients, even though the rejection observed was primarily T-cell-mediated. Both patients responded to the rejection therapy and had an overall good outcome up to this point, which is consistent with the findings of the group around Barros et al.[1] While Asti et al.[2] could not find a correlation between higher rejection rates and COVID-19 among their patients, Kudose et al[3] showed that COVID-19 is associated with glomerulopathy, tubular injury and T-cell-mediated rejection. We therefore suggest that transplant rejection is triggered by COVID-19 and pausing the immunosuppression should be a case-to-case-decision.

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Poster Session 03: Kidney transplantation

P03-02 Predictive value of HAS-BLED Score regarding bleeding events and graft survival following renal transplantation

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INTRODUCTION

Due to a high incidence of cardio- and cerebrovascular diseases among patients with end-stage renal disease (ERSD) scheduled for kidney transplantation (KT), use of antiplatelet (APT) and/or anticoagulant drugs in this population is common. However, these patients share high risk of complications either due to thromboembolic or bleeding events, which makes adequate peri- and post-transplant anticoagulation management challenging. Predictive clinical models, such as the HAS-BLED score, could be a helpful tool for optimization of antithrombotic management and reduce morbidity and mortality.

METHODS

Data of 204 patients undergoing KT between 2011-2018 at the University Hospital Leipzig were retrospectively analyzed. Patients were stratified into the "prophylaxis group" (without pre-transplant antithrombotic therapy and postoperative prophylactic heparin) and the "(sub) therapeutical group" (those with postoperative continued use of pre-transplant used (sub)therapeutically antithrombotic medication). Outcome analyses were conducted for associations of potential risk factors on bleeding events and allograft outcome.

RESULTS

94 of 204 (47%) patients received (sub) therapeutic antithrombotic therapy after transplantation, 108 (53%) prophylactic antithrombotic therapy. Incidence and timepoint of bleeding varied significantly between both groups. HAS-BLED risk model demonstrated a good calibration (bleeding and graft failure: HLT: $p = 0.802$ versus $p = 0.18$) and predictive performance (bleeding AUC: 0.72; graft failure: AUC: 0.7). In multivariate analyses, pre-existing cardiovascular disease (CVD) (OR 2.89; $p = 0.04$), HAS-BLED score > 3 (OR 1.49; $p = 0.018$), Vit K antagonists (VKA) (OR 5.89; $p = 0.037$), the combination of APT and therapeutic heparin (OR 5.4; $p = 0.018$) as well as postoperative therapeutic heparin (OR 3.37; $p < 0.01$) were independently associated with increased risk for bleeding.

CONCLUSION

HAS-BLED risk score showed a good predictive accuracy regarding bleeding events and graft failure in our KT population. The associated negative effect on allograft survival underscores the need to reduce any risk factors for post-operative bleeding to optimize outcome after kidney transplantation.

P03-03 Bubble and subsequent intermittent surface oxygenation is a simple and effective alternative for membrane oxygenation to maintain aerobic metabolism in kidneys during HMP

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INTRODUCTION

Brief bubble, and subsequent surface oxygenation is an alternative oxygenation technique for membrane-oxygenated kidneys during HMP. The aim of this study was to evaluate the metabolic effect of interruption of surface oxygenation (mimicking organ transport) during HMP as compared to continuous surface and membrane oxygenation in a pig kidney ex vivo preservation model.

METHODS

A kidney of a ±40 kg pig was exposed to 30 minutes of warm ischemia and preserved according to one of the following study groups: 1) 22h HMP+intermittent surface oxygenation (30 min at start, 4h interruption followed by 17h30 surface oxygenation) during 22h HMP (n=12), 2) 22h HMP+continuous membrane oxygenation (n=6), and 3) 22h HMP+continuous surface oxygenation (n=7). Brief O_2 uploading of the perfusion fluid before kidney perfusion was obtained either by a hollow fiber membrane oxygenator (study group 2) or by direct bubble oxygenation (study group 1 and 3).

RESULTS

O_2 uploading of the perfusion fluid by minimum 15 minutes of direct bubble oxygenation was as efficient as membrane oxygenation to achieve pO_2 levels above 450-500 mmHg (at 4°C) before connecting the kidney to the perfusion device. Metabolic analysis (i.e. lactate, succinate, glutamate, ATP, ADP, AMP, NADH, NAD+ and Flavin Mononucleotide (FMN)) on end-preservation cortical and medullar tissue biopsies demonstrated a similar mitochondrial protection/preservation in all study groups. FMN measurement by fluorescence demonstrated no difference between all study groups during the first 270 minutes of preservation, however perfusate FMN levels were significantly higher at the end of the preservation period in the membrane-oxygenated groups as compared by both surface-oxygenated HMP groups.

CONCLUSION

Brief bubble and intermittent surface oxygenation of the perfusate during standard HMP at procurement site might be an effective, user-friendly, and less expensive preservation strategy to protect mitochondria when compared with membrane-oxygenated kidneys eliminating the need for a membrane oxygenator and oxygen source during transport.

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P03-04 Belatacept in kidney transplant patients with severe BK-Polyomavirus (BKPyV) infection

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INTRODUCTION

In order to avoid allograft rejection on the one hand and infectious complications on the other, it is essential to balance the immune system in kidney transplant recipients by choosing the appropriate immunosuppressive treatment. BKPyV-associated nephropathy (BKPyVAN) is a viral complication of immunosuppression that seriously threatens kidney allograft survival. Until now, the main treatment strategy of BKPyVAN is to reduce immunosuppression, but this is associated with an increased risk of rejection. Belatacept is an immunosuppressant that blocks the CD80/86-CD28 co-stimulatory pathway of effector T-cells with marked effects on the humoral response but increased risk of acute T-cell mediated rejection. There are limited data to date on the use of belatacept in BKPyV infection.

METHODS

We evaluated the outcomes of nine kidney transplanted patients who were switched from a standard immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil or everolimus and prednisone to a belatacept-based regimen after the development of severe BKV-associated complications (five of them with biopsy proven BKPyVAN).

RESULTS

After conversion, all patients showed significantly improved control of BKPyV DNAemia and stabilized or improved graft function, with no allo-immunologic complications, despite increased immunologic risk in 4/9 patients (3x pre-existing donor-specific antibodies, 1x severe T-cell-mediated rejection).

CONCLUSION

The presented cases suggest that a switch to a belatacept-based immunosuppressive regimen is a save treatment option in patients with severe BKPyV infection without exposing them to increased immunological risk.

P03-09 Hyperspectral imaging for evaluating the perfusion in porcine kidney transplantation

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INTRODUCTION

Kidney transplantation is the gold standard in the therapy of terminal renal failure. Although the intraoperative evaluation of kidney perfusion is essential in kidney transplantation, there is no real-time imaging technique which is capable of visualizing kidney perfusion and its change over time during surgery. Hyperspectral Imaging (HSI) is a novel imaging technique that addresses these issues and makes it possible to differentiate pathological states of perfusion and reveal characteristic perfusion kinetics.

METHODS

For this experimental animal study in a porcine model, the TIVITA™ HSI Camera (Diaspective Vision GmbH) was used. HSI works by projecting white light of a wide spectrum from 500 to 1000 nm and then receives the reflected light for generating a continuous reflectance spectrum of each pixel (hypercube).

After laparotomy the kidney was prepared and explanted. On the back table the kidney was perfused with and stored in 4°C cold preservation solution (HTK). After 2 hours of cold ischemia the kidney was implanted and perfused in the sense of an autologous kidney transplantation. During all steps the HSI camera device recorded the reflectance spectra of the different stages.

The coding language Python enables to calculate state- and time-specific indices beyond conventional HSI. Furthermore, the intraoperative measurements of vital parameters and blood flow were correlated to the obtained graphical data from HSI.

RESULTS

The recorded data shows significant differences in the reflectance spectra between different states of renal perfusion and between the several stages during kidney transplantation. These conditions can be differentiated by machine learning algorithms due to respective spectral signatures.

Moreover, the saturation (StO_2) and perfusion (NIR) values – which were generated out of the continuous spectrum – correlate with the measured flow and clinical parameters in unmanipulated as well as in transplanted kidneys.

CONCLUSION

HSI is a ready-to-use system for intraoperative real-time evaluation of kidney perfusion also during the transplantation process. It can differentiate and predict various states of renal perfusion through the characteristic spectral reflectance.

P03-10 Synchronous papillary renal cell carcinomas in a native kidney and a kidney allograft

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INTRODUCTION

Chronic kidney disease and immunosuppressive therapy are risk factors for the development of renal cell cancer (RCC) in kidney transplant recipients. RCC typically occurs in the patient's native kidneys whereas RCC in kidney allografts has been reported only sporadically. We describe a rare case of a 73-year old patient who developed synchronous papillary RCC in the native kidney as well as in the renal allograft.

METHODS

The patient presented with abdominal pain and a CT scan was performed for suspected pancreatitis. This scan revealed the presence of suspicious masses in the left native kidney (4.5 cm) and the allograft (3 cm). Tumor nephrectomy of the native kidney was conducted and histopathological examination of the lesion revealed a papillary RCC. Analysis of a biopsy of the renal mass in the kidney graft also unveiled a papillary RCC. In order to differentiate between the presence of two independent tumors or a metastasis in one of the organs, DNA was isolated from the blood of the recipient as well as from the tumor samples. In order to gain non-tumor DNA from the donor, primary tubular cells were isolated from the patient's urine.

Short tandem repeat (STR) analysis was performed on these samples to compare the genetic background of the tumors.

RESULTS

STR analysis demonstrated that the papillary tumors arouse independently from each other from the respective kidney tissues, proving the coexistence of two primary malignant lesions. Hence, nephrectomy of the native kidney presented the curative therapy for the first RCC. Balancing graft function against the need for cancer control, the second RCC was removed by radio-frequency ablation.

CONCLUSION

The differentiation between primary tumor and metastasis is relevant for the selection of the adequate therapy, which may include tumor nephrectomy, local ablative procedures or a systemic therapy. As there are no specific guidelines for the treatment of renal tumors in kidney allografts, it is essential to weigh up the oncogenic risks and the consequences of graft failure determined by the choice of the individualised therapeutic concept.

P03-11 Emulation of the control cohort of a randomized controlled trial in pediatric kidney transplantation with Real-World Data from the CERTAIN Registry

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INTRODUCTION

Randomized controlled trials in pediatric kidney transplantation are hampered by low incidence and prevalence of renal failure in children. Real-World Data from patient registries could facilitate the conduct of clinical trials by substituting a control cohort.[1,2] However, the emulation of a control cohort by registry data in pediatric kidney transplantation has not been investigated so far.

METHODS

In this multicenter comparative analysis, we emulated the control cohort (n=54) of an RCT in pediatric kidney transplant patients (CRADLE trial;

ClinicalTrials.gov NCT01544491) with data derived from the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) registry, using the same inclusion and exclusion criteria (CERTAIN cohort, n=554).

RESULTS

Most baseline patient and transplant characteristics were well comparable between both cohorts. At year 1 posttransplant, a composite efficacy failure end point comprising biopsy-proven acute rejection, graft loss, or death (5.8% ± 3.3% vs. 7.5% ± 1.1%, P=0.33) as well as renal function (72.5 ± 24.9 vs. 77.3 ± 24.2 mL/min/1.73 m^2 P=0.19) did not differ significantly between CRADLE and CERTAIN. Further, the incidence and severity of BPAR (5.6% vs. 7.8%), the degree of proteinuria (20.2 ± 13.9 vs. 30.6 ± 58.4 g/mol, P=0.15) as well as key safety parameters such as occurrence of urinary tract infections (24.1% vs. 15.1%, P=0.10) were well comparable.

CONCLUSION

In conclusion, usage of Real-World Data from patient registries such as CERTAIN to emulate the control cohort of an RCT is feasible and could facilitate the conduct of clinical trials in pediatric kidney transplantation.

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P03-12 Neutrophil gelatinase-associated lipocalin (NGAL) and N-acetyl-β-d-glucosaminidase (NAG) reflect macroscopic injury during normothermic machine perfusion with whole blood

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INTRODUCTION

Normothermic machine perfusion (NMP) is a novel preservation tool currently investigated as a method to assess and recondition marginal donor kidneys. Due to the dire shortage of kidneys eligible for transplantation, the need to utilize marginal kidneys is rising. Those kidneys are currently often discarded based on concerns over their functionality. Biomarkers able to assess kidney injury would be needed to identify kidneys suitable for transplantation under the physiological conditions of NMP.

METHODS

33 porcine slaughterhouse kidneys underwent NMP for 4 h with autologous whole blood. Four physicians independently evaluated the kidneys' macroscopic perfusion quality (homogenous; <50% inhomogeneous; ≥50% inhomogenous). This evaluation was incorporated into a semiquantitative macroscopic score (MS), which also assessed the occurrence of urinary output and the extent of organ lesions. Kidneys were grouped according to a majority decision based on the MS into "transplantable" (T) and "not transplantable" (NT). The concentrations of the potential markers NAG and NGAL within the perfusate were determined via ELISA at 0 h, 1 h, 2 h and 4 h of NMP. Obtained concentrations were normalized to the total protein concentration.

RESULTS

17 kidneys were classified as T, 10 kidneys as NT. 6 kidneys could not be grouped. NAG concentrations in NT kidneys increased steadily over the duration of NMP and significantly differed from group T at 4 h ($p<0.005$). NGAL concentrations were also increased in NT kidneys, differing significantly after 1 h, 2 h and 4 h of NMP ($p<0.05$).

CONCLUSION

NT kidneys released higher levels of NGAL and NAG into the perfusing blood than good ones. Both molecules are released from the injured tubules. This shows that the biomarker for otherwise invisible damage within the kidney correlate with the macroscopic evaluation and could be used to support the subjective macroscopic evaluation with more quantifiable data. Further investigations of other laboratory and biochemical parameters are required to achieve an accurate prediction of not only the kidney injury, but also the potential functional capacity.

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P03-13 Recovered renal allograft function after indication-related conversion from IR-Tac to LCP-Tac

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INTRODUCTION

Tacrolimus (Tac) is the cornerstone of the first-line immunosuppression after renal transplantation (RTx), but may have nephrotoxic side effects[1]. Given the different pharmacokinetics of the available Tac formulations, we hypothesize that the renal function of RTx recipients will benefit better from an indication-based conversion from immediate-release Tac (IR-Tac) to LCP-Tac (LCP-Tac)[2,3].

METHODS

Eighty RTx patients receiving de novo immunosuppression with IR-Tac, mycophenolate, and prednisolone were included. All patients were switched from IR-Tac to LCP-Tac one month after RTx or later. Renal function and complications were monitored in a 36-month follow-up after conversion.

RESULTS

The main reason for a switch to LCP-Tac was trough level variation/avoidance of adverse effects in 67 patients (84%). The estimated glomerular filtration rate (CKD-EPI eGFR in mL/min/1.73 m^2) increased ten days after conversion from 41.7 to 44.8 ($p=0.001$), to 46.6 after 12 months ($p<0.001$, $n=78$) and to 47.4 ($p=0.065$, $n=60$) after 36 months. Complications occurred only in rare

cases after the switch: CMV infection: 5 (6.3%), BKV infections: 1 (1.3%), no posttransplant diabetes mellitus, acute rejections: 10 (12.5%).

CONCLUSION

Our data shows that RTx recipients can benefit from an indication-related conversion from IR-Tac to LCP-Tac with respect to to their renal function. Prospective multicenter trials including pharmacokinetic aspects are needed to confirm and further explain these findings.

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P03-14 A Luminex-based algorithm for the definition of unacceptable HLA prior to kidney transplantation. First results from the prospective, multicenter NAHA Study

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INTRODUCTION

There are no uniform criteria for the integration of Luminex single antigen bead (SAB) test results into algorithms for the definition of unacceptable HLA antigen mismatches (UAM) prior to kidney transplantation (KTX).

METHODS

We implemented a standardized UAM algorithm at three German transplant centers and prospectively studied its consequences on the incidence of early antibody-mediated rejection (ABMR) as well as kidney function (eGFR) and graft loss during follow-up in patients receiving a KTX or a combined kidney-pancreas transplant. HLA were defined as UAM if antibodies were found in cellular cytotoxicity (CDC) assays. If antibodies directed at HLA from previous transplantations were found in SAB but not CDC testing, the respective HLA were defined as UAM above a mean fluorescence intensity (MFI) of 500. Without a known sensitizing event, an MFI threshold of 5000 (for antibodies against HLA A, B, C, DR and DP) and 10,000 (for anti-HLA DQ) was

used as cutoff for UAM. KTX required a negative CDC-T and B-cell crossmatch. DSA-positive patients (MFI > 1000) were treated with thymoglobulin in case MFI was > 1500 with all other patients receiving basiliximab induction.

RESULTS

Between 01.01.2019 and 31.12.2021, 232 patients were included. 19.8 % were UAM-positive with median virtual panel reactivity (vPRA) of 66%. 33/232 (14.2%) patients had DSA at the time of KTX. The incidence of ABMR in the first six months after KTX was 12.1% (4/33) in DSA-positive compared to 4.0% (8/199) in DSA-negative patients (p=0.05). After a median follow up of 12 months, eGFR was comparable between the groups (49 vs. 48 ml/min). There were two (6%) and five (2.5%) graft losses in DSA-positive and DSA-negative patients, respectively (p=0.27).

CONCLUSION

A standardized UAM algorithm integrating sensitization history and MFI reduced the incidence of early ABMR compared to earlier observational studies. Long-term follow will reveal the impact on graft survival.

P03-15 Assessment of the American KDPI in a German cohort and establishment of a new KDPI based on German single centre data

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INTRODUCTION

The Kidney Donor Profile Index (KDPI) was established in the US in 2014 to improve the prognostic assessment of donor kidneys and thereby optimize the organ allocation.

METHODS

We aimed to investigate the utility of the KDPI in our German transplant centre by conducting a retrospective single-centre cohort study of 671 patients who received a deceased donor renal transplantation at the University Hospital of Erlangen between 2005 and 2015. Multivariate cox regression analysis was performed for the donor and recipient data and the outcome after one year and after five years.

RESULTS

In our cohort the mean donor age was 53 (±17) and the graft survival after one year 90.1%. When applying the American KDRI/KDPI the median KDRI_Median was 1,30 (KDPI 76%), with a higher proportion of >85% KDPI organs compared with the US transplantations of 2018 (33% vs. 7.8%). However, graft survival seemed acceptable even in > 85% KDPI organs (95.4%), which reflects the limited prognostic value of the American KDPI in our donor pool. Thus our goal was the creation of a new German European KDPI system based on our cohort of 671 deceased donors, using the American donor characteristics (except DCD status and ethnicity) and the graft survival. We found a correlation between our KDPI score and the graft survival ($p = 0.0009$).

In order to compare the American KDPI system and the KDPI model of Erlangen, we calculated the KDRI_Median of both models for each kidney (KDRI_Amerikaner and KDRI_Erlangen). The American KDPI system evaluated predominantly higher KDPIs with worse prognosis for our cohort, compared to our own Erlanger KDPI model.

CONCLUSION

Our KDPI system might be a better tool to assist German clinicians in differentiating marginal donor kidneys and deciding about decline and acceptance of these offers.

Poster Session 04: Thoracic organ transplantation, Pancreas transplantation, challenges of "young" transplant recipients

P04-01 Antibacterial effect of inhaled Sphingosine in *ex vivo* lung perfusion

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INTRODUCTION

Ex vivo lung perfusion (EVLP) is used to expand the donor pool for lung transplantation allowing for standardized evaluation of the donor's lungs. In addition, EVLP might be used as a platform to treat and restore donor lungs for various pathologies, for example, edema or infections. Sphingosine, a lipid and a natural compound of the cell membrane, exhibits a solid broad-spectrum antibacterial activity, including *P. aeruginosa*, *S. aureus*, and *A. baumannii*. Here, we aimed to evaluate the effects of sphingosine inhalation during EVLP on infected donor lungs.

METHODS

After standardized procurement, lungs from domestic mini pigs were connected to EVLP. *S. aureus* was inhaled through a nebulizer, followed 1 hr later by inhalation of sphingosine or control, i.e., NaCl 0.9% (each n=6). Bronchoalveolar lavage and biopsy were obtained through fiberoptic bronchoscopy, and a colony-forming assay was used to determine the number of bacteria. Hämatoxylin-Eosin (HE) and immunofluorescence staining were used to evaluate lung and bronchus morphology and sphingosine content.

Functional lung parameters, hemodynamics, and biomarker during EVLP were recorded.

RESULTS

In bronchial epithelial cells, bacteria were significantly reduced after sphingosine inhalation compared to the control group (Colony-forming units: Sphingosine group: 110 ± 60; NaCl group: 557 ± 213, $p<0.001$). The concentration of sphingosine in bronchia was higher after sphingosine inhalation. Lung edema (wet/dry ratio), histology results (HE staining), LDH levels in the perfusate, PO_2/FiO_2 ratio, pulmonary vascular resistance (PVR), and pulmonary artery pressure (PAP) did not significantly differ between the groups.

CONCLUSION

EVLP allows for the treatment of compromised donor lungs. Inhalation of sphingosine effectively eliminated S. aureus at the epithelial layer of tracheal and bronchial cells without side effects in isolated perfused and ventilated pig lungs.

ACKNOWLEDGEMENT

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P04-02 COVID-19 and viral co-infections in heart transplant patients

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INTRODUCTION

Transplant patients are at high risk for SARS-CoV-2 infections due to immunosuppression. Besides respiratory complications, transplanted COVID-19 patients may also suffer from concomitant cytomegalovirus (CMV) and Epstein-Barr virus (EBV) DNAemia. We aimed to analyse the clinical impact of COVID-19 infections in heart transplant (HTx) patients with particular focus on viral co-infections.

METHODS

Between March 2020 and April 2022 a total of n=36 patients were treated for PCR-confirmed SARS-CoV-2 infection after HTx in our center. Relevant data of all patients was retrospectively reviewed as an observational study regime.

RESULTS

SARS-CoV-2 infections were observed after a minimum of two months and up to a maximum of about 10 years after HTx. Most patients contracted BA.1 or BA.2 subvariant. In general, patients had received three or four doses of Comirnaty vaccine. About 80% of patients developed symptomatic COVID-19 disease, with fever, cough and sore throat as most common symptoms. Only three patients were treated on the intensive care unit. COVID-19 pharmacotherapy consists of remdesivir and casirivimab/imdevimab or sotrovimab. In 30% of patients with performed PCR for CMV, DNAemia was detected (maximum of 195 CMV-DNA copies/µg-DNA). In patients with examination of EBV-DNAemia, positive results were found in about 40% (maximum of 1230 EBV-DNA

copies/µg-DNA). In one patient both CMV- and EBV-DNAemia was detected. No patient suffered from symptomatic CMV- or EBV infections. We did not observe in-hospital death in any patient, however, in one patient cardiac arrest of unknown origin occurred a few days after discharge. During the following course, the patient developed reactivation of SARS-CoV-2 and died due to cardiac arrest-related cerebral hypoxemia.

CONCLUSION

Symptomatic COVID-19 infections are common in after HTx, however, due to vaccination and improved pharmaceutical treatment options, clinical impact remains relatively low. In addition, co-infections with CMV or EBV are frequent but without major clinical relevance. Future studies are necessary to further evaluate the correlation between COVID-19 and reactivation of neurotropic viruses after HTX.

P04-03 Combined heart and kidney transplantation: Early insights of five consecutive cases

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INTRODUCTION

End-stage heart failure patients often also suffer from concomitant kidney failure with need for haemodialysis. Combined heart and kidney transplant (HKTx) may offer a feasible approach for these patients. However, due to the complexity and the relatively small numbers of performed procedures, outcomes of HKTx, especially compared to kidney transplant after heart transplant are discussed controversially with a consensus guideline still missing.

METHODS

Between 2018 and 2021 a total of n=137 patients underwent heart transplant in our department. Of those, n=5 patients underwent HKTx. All patients received single-donor allografts. Initially orthotopic heart transplant procedure was performed. After a following short period of cardiopulmonary stabilization on the intensive care unit, patient returned to the operating room and heterotopic kidney transplant was carried out.

RESULTS

Patients were most likely male with a mean age of 53 years. No patient underwent previous open-heart surgery or kidney transplant. Cardiac graft function was good in all patients at any time after HKTx with no patient suffering from primary graft dysfunction. In contrast, late onset of kidney function with temporary haemodialysis was observed in all five patients. No patient developed postoperative stroke, wound infections or bacterial sepsis. CMV-DNAemia

or even disease could also be avoided in all patients with application of our usual prophylaxis in combined transplantations. Unfortunately, P4 died from septic shock due to fulminant candida infection 100 days after HKTx. All other patients are in stable conditions with no signs of heart failure and no patient dependent on haemodialysis until today.

CONCLUSION

HKTx can offer a feasible therapy option for patients suffering from both end-stage heart and kidney failure. Although we report only early results of a small cohort, we were able to show good clinical conditions for four of the patients after up to three years of follow-up with good cardiac and kidney allograft function. However, late on-set of kidney graft function was commonly observed.

P04-04 Impact of COVID-19 pandemic on donors, recipients and outcome of heart transplantation

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INTRODUCTION

Orthotopic heart transplantation (HTx) is the gold standard of care for end-stage heart failure. Since March 2020, COVID-19 pandemic has tremendously impacted health care all around the globe. However, impact of the pandemic on HTx remains unclear. We aimed to analyse the impact of the pandemic on donors, recipients and outcome of HTx.

METHODS

Between 2010 and 2022 a total of n=240 patients underwent HTx in our department. Relevant data of all patients and their corresponding donors was prospectively collected and retrospectively reviewed. Patients were assigned to two different study group regarding the date of the performed HTx. Group 1 (09/2010 to 02/2020): n=160, Group 2 (03/2020 to 04/2022): n=81.

RESULTS

Since beginning of the pandemic, leading aetiology of heart failure of the recipients has shifted from dilated (Group 1: 53.8%, Group 2: 33.3%) to ischemic cardiomyopathy (Group 1: 39.4%, Group 2: 50.6%, p<0.01). Portion of high urgency status of transplanted recipients dropped from 50.0% to 34.6% (p=0.03) and prevalence of previous left ventricular assist (LVAD) support from 56.9% to just 38.3% (p<0.01). Meanwhile mean waiting time of recipients also significantly decreased by about 40% (p=0.02). Since the pandemic, donors were 2-times more likely previously resuscitated (Group 1: 21.3%, Group 2: 43.2% (p<0.01) and drug abuse increased by more than 3-times (p<0.01) indicating

acceptance of more so-called marginal donors. Surprisingly, incidence of postoperative severe primary graft dysfunction requiring extracorporeal life support decreased from 33.1% to 19.5% (p=0.03) since the pandemic and 1-year survival numerically increased from 77.5% to 86.0%(p=0.29).

CONCLUSION

COVID-19 pandemic significantly affected both donors and recipients of HTX but not the postoperative outcome. Donors nowadays are more likely suffering from ischemic heart disease and are less likely on high urgency wait list status and LVAD support. Simultaneously, an increasing number of marginal donors are accepted leading to shorter waiting times with by trend even increased short-term survival of patients.

P04-05 Intravenous immunoglobulins (IVIG) in subclinical antibody mediated rejection after lung transplantation are leading in elimination of de-novo donor specific antibodies (dnDSA)

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INTRODUCTION

De novo DSA have been associated with reduced survival and worse outcome after lung transplantation (LuTx). However, there are no generally accepted therapeutical guidelines and a variety of protocols has been used, making any conclusion about treatment efficacy difficult. The aim of this study was to identify prognostically important factors for the treatment with IVIG.

METHODS

We identified 47 patients between 2015 and 2019 with dnDSA after LuTx who received IVIG (initial dose 1 g/kg/bw followed by 0.5 g/kg/bw at four weeks interval not more than three times). We classified the patients in two groups: 1) Responders with elimination of dnDSA (n=23) and 2) non-responders without elimination of dnDSA (n=24). The presence of HLA-antibodies was analysed by Luminex Single Antigen Bead assay prior to and frequently after transplantation, as well as after treatment. We used Chi^2-test and Fisher's exact test to compare categorical variables and t-test to compare mean values of metric variables between groups. We used multivariate logistic regression models to determine factors associated with elimination of dnDSA.

RESULTS

In 49% (n=23) of patients treated with IVIG, dnDSA could no longer be detected (responders). While age and gender did not differ significantly (p=0.28 and p=1.00, respectively), the group of non-responders was significantly more likely to have HLA class II dnDSA (92% versus 48% in responders, p=0.03). Furthermore, the mean maximum MFI value (11683 versus 7152 in responders, p=0.02) as well as the time to the first dnDSA differed significantly (226d versus 61d in responders, p=0.005).

In the multivariate analysis we found that a treatment before appearance of any clinical symptoms or deterioration of lung-function (subclinical AMR) had a significant impact on the elimination of dnDSA (OR = 28.33, 95%CI 2.25 – 357.27, $p < 0.01$).

CONCLUSION

Therapeutical consequences for patients with dnDSA after LuTx is still a matter of debate. Our results indicate that an early treatment of dnDSA could have a positive impact on the elimination of dnDSA.

P04-06 Frequency, risk factors, and outcomes of late-onset atrial flutter in patients after heart transplantation

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INTRODUCTION

Atrial flutter (AFL) is a common late-onset atrial arrhythmia after heart transplantation (HTX) and has been associated with worse clinical outcomes.

METHODS

This study investigated the frequency, risk factors, and outcomes of late-onset AFL in patients after HTX. We analyzed 639 adult HTX recipients who underwent HTX at Heidelberg Heart Center between 1989 and 2019. Patients were stratified by diagnosis and type of late-onset post-transplant AFL (> 90 days after HTX). Analysis included donor and recipient characteristics, medications including immunosuppressive drugs, echocardiographic features, graft rejections, and mortality after diagnosis of AFL.

RESULTS

Fifty-five patients (8.6%) were diagnosed with late-onset post-transplant AFL. HTX recipients with late-onset post-transplant AFL were significantly younger (48.8±11.2 years versus 52.4±10.2 years, difference: 3.6 years, 95% confidence interval: 0.5–6.7 years, $P = 0.028$) and had a higher percentage on biatrial anastomosis (24 of 55 [43.6%] versus 140 of 584 [24.0%]; difference: 19.6%, 95% confidence interval: 6.1–33.1%; $P = 0.001$). Mean time from HTX until diagnosis of AFL was 10.7±7.6 years. Clinical findings of HTX recipients with late-onset AFL included presence of graft rejection, cardiac ischemia, severe

tricuspid regurgitation, infection, and hemodialysis. More than a quarter of HTX recipients with late-onset AFL died within two years after diagnosis (14 of 55 [25.5%]).

CONCLUSION

HTX recipients with late-onset AFL were younger and more often received biatrial anastomosis. Clinical findings comprised graft rejection, cardiac ischemia, severe tricuspid regurgitation, infection, and hemodialysis. Mortality after diagnosis of late-onset post-transplant AFL was markedly increased highlighting the vulnerability of these patients.

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P04-07 Influence of dental status on survival after lung transplantation

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INTRODUCTION

Poor dental status is considered to play a potential role as a focus for infections and inflammatory diseases. Up to this date, data on the impact of dental status on patients' survival after lung transplantation (LuTX) is scarce. The majority of transplant centers have their own standards regarding preoperative dental care as there is currently no general clinical guideline. The objective of this retrospective study was to assess the dental status of patients listed for LuTX. By analyzing survival data and patients' dental status, we aimed to determine factors that could have an impact on postoperative care, survival and outcome.

METHODS

200 patients having undergone LuTX from 2014 – 2019 were selected. Collected data comprised information about the indication for TX, periodontal status, number of carious teeth and fillings and, if applicable, cause of death. Only patients with a preoperative panoramic dental x-ray and consultative clarification by a dentist were included.

RESULTS

63.5 % had carious dental status, differing significantly regarding the underlying condition leading to TX ($p > 0.001$). Patients with ILD and COPD had the worst dental status, accounting for up to 41.7 % (ILD) of all patients with

carious teeth, compared to cystic fibrosis patients that only made up 3.1 %. The influence of age within these groups has to be noted, as mean age at the time of LuTX differed significantly. Performing survival analysis, it became apparent that neither preoperative carious dental status, nor periodontitis or signs of bone decay deteriorated survival after LuTx significantly. There was no evidence that either resulted in a greater number of deaths related to an infectious etiology such as sepsis or multi organ failure.

CONCLUSION

This study shows that carious dental status, periodontitis and bone decay do not affect post-TX survival. However, literature states that oral hygiene and dental status can lead to systemic and pulmonary infections, which again can deteriorate survival after LuTX due to immunosuppressive medication. As there are currently no standardized procedures regarding dental care and LuTX, further studies should be conducted and clinical guidelines established.

P04-09 6 Years experience in ex vivo lung perfusion for lung transplantation

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INTRODUCTION

Ex vivo lung perfusion (EVLP) is increasingly used to evaluate and optimize donor lungs to prevent donor organ rejection. Aim of the study was to compare mid-term results in LuTx recipients with or without the use of EVLP.

METHODS

Prospectively collected data of 262 consecutively transplanted patients (2016-2021) were analyzed in a retrospective single-centre study. Extended criteria donor lungs were evaluated by EVLP (n=29), out of them 19 were afterwards transplanted (EVLP group, n=19). The non EVLP group (n=19) consisted of conventional LuTx recipients matched for age and pulmonary disease. Both groups were compared for the endpoints survival, primary graft dysfunction, rejection episodes and chronic allograft dysfunction.

RESULTS

Recipient age was 56 $\pm$ 6 years in EVLP group and 58 $\pm$ 4 years non EVLP group (n.s.). Female gender was present in 42 % EVLP patients and 52% non EVLP (n.s.) The rate PGD grade 1 at 72h post-LTx was 11% in both groups (each2/19) as well as for PGD 2 (11%). PGD3 was present only in the EVLP group 11% (2/19) vs. 0% in control. At last visit, post-LTx, forced expiratory volume in 1s (FEV1%) as percentage of predicted best was similar in the EVLP and non-EVLP group (80% vs. 81%). Chronic lung allograft dysfunction was diagnosed in one non EVLP patient and one EVLP patient during follow up post-LTx. One recipient in the EVLP group received a redo LTx after 944 days.

In the EVLP group 2 patients had rejection episodes subjected to treatment and 8 patients in the non EVLP group (n.s.). Survival at 6 years was 74% for the EVLP group and 94% in non EVLP group (p<0,07).

CONCLUSION

EVLP increased the number of transplantable donor lungs. Recipients transplanted with extended criteria donor lungs, thouroghly evaluated by EVLP show simlar mid term outcomes as conventionaly transplanted lungs from standard donors. EVLP seems to be a valuable tool to increase the number of acceptable donor lungs.

P04-10 Analysis of volatile anesthetic-induced organ protection in simultaneous pancreas–kidney transplantation

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INTRODUCTION

Despite recent advances, early pancreatic graft dysfunction, mainly specified as ischemia reperfusion injury (IRI) - remains a common cause of pancreas graft failure with potentially worse outcome in Simultaneous Pancreas-Kidney Transplantation (SPKT). Anesthetic conditioning is a widely described strategy to attenuate IRI and facilitate graft protection. Here, we investigate the effects of different volatile anesthetics (VA) on early IRI-associated posttransplant clinical outcome and graft function/ outcome in SPKT recipients.

METHODS

Medical data of 105 patients undergoing SPKT between 1998-2018 were retrospectively analyzed and stratified according to the used VA. Primary study endpoint was the association of VA on pancreas allograft failure following SPKT, secondary endpoint analyses included "IRI- associated posttransplant clinical outcome" as well as long-term graft function and outcome. Typical clinico-pathological characteristics, postoperative outcome such as early graft outcome and long-term function were analyzed.

RESULTS

Of the included patients three VA were used: isoflurane (n = 58 patients; 55%), sevoflurane (n = 22 patients; 21%) and desflurane (n = 25 patients, 24%). Donor- and recipient characteristics were comparable between both groups. Early graft loss within 3 months (24% versus 5% versus 8%, p = 0.04) and

IRI- associated postoperative clinical complications (pancreatitis: 21% versus 5% versus 5%, p = 0.04; vascular thrombosis: 13% versus 0% versus 5%; p = 0.09) occurred more frequently in the isoflurane group compared to the sevoflurane and desflurane group. No difference with regard to 10-year pancreas graft survival as well as metabolic function among all three VA groups was observed. Multivariate analysis revealed the choice of VA as an independent predictor for graft failure three months after SPKT.

CONCLUSION

In our study, Sevoflurane and Desflurane were associated with significantly increased early graft survival as well as decreased IRI-associated posttransplant clinical outcome compared to the isoflurane group and should be the focus of future clinical studies evaluating positive effects of different VA agents in patients receiving SPKT.

P04-11 Successful pregnancy in a kidney-pancreas transplanted patient on LifeCycle Pharma tacrolimus (LCPT) - based immunosuppression: A case report

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INTRODUCTION

As no experiences concerning LifeCycle Pharma tacrolimus (LCPT) in pregnancy after simultaneous pancreas kidney transplantation (SPK) are published so farwe retrospectively analyzed the long-term graft function, obstetric/neonatal course, LCPT dosage, tacrolimus (TAC) levels, concomitant medication and complications in a 25-year-old female SPK recipient at our center, who gave birth to a child in posttransplant month 32.

METHODS

Due to TAC fast metabolism she was converted from a standard TAC formulation to LCPT in the first month posttransplant. Her long-term immunosuppression including the obstetric and peripartal course consisted of LCPT, prednisolone, azathioprine.

RESULTS

She kept an excellent function of both grafts at the observation time of 48 months posttransplant. All (mostly infectious) complications were reversible and no relapse of her pretransplant episode of atypical haemolytic uremic syndrome with critical deterioration of her general condition (requiring clinically indicated early termination of her first pregnancy prior to SPK) occurred posttransplant. Her child is in good health at the age of 12 months without any malformations.

CONCLUSION

We conclude from this single case experience that pregnancy in SPK under LCPT is feasible. Further experiences on this subject are of interest in order to expand the empirical knowledge surrounding tacrolimus.

P04-12 Severe acute Non-A-E hepatitis (NAEH) of unknown origin: A 13-year single-center retrospective analysis in children

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INTRODUCTION

Pediatric acute liver failure (PALF) is a rare, but potentially life-threating condition. 30-50% of PALF remains without detectable cause, especially in children under 4 years even up to 60%. NAEH (known as indeterminate) refers to hepatitis of unknown origin. Many of the pediatric patients with NAEH develop bone marrow hypoplasia-aplasia.

METHODS

We retrospectively collected all pediatric patients with presentation of acute NAEH between 2009-2022. The patients enrolled in the study met the following criteria: 1) 3months-18years old, 2) no prior evidence of chronic liver disease, 3) GOT/GPT>500IU/l, 4) acute hepatitis causes as viral-bacterial infections, drugs, metabolic diseases, toxins, ischemia, rare miscellaneous causes have been excluded.

RESULTS

A total of 40 children with acute NAEH were included in our study. Median age was 7,9 years. In 19 (48%) patients a potentially triggering unspecific viral respiratory/gastrointestinal infection was found. 21/40 (53%) patients had developed by the time of the presentation a PALF, whereas the rest with an acute hepatitis did not fulfill the criteria for PALF. 8/21 (38%) patients with PALF underwent liver transplantation. 27/40 (68%) patients with NAEH presented with icterus. 12/40 (30%) children developed an hepatitis associated aplastic anemia (HAAA). Patients who later developed HAAA had a slight low count

of lymphocytes upon presentation and over time they developed a severe lymphopenia (minimal mean lymphocyte-count 340\µl) in contrast to the other ones that had a normal lymphocytes count. 1/12 patients with HAAA underwent a liver transplantation, 9/12 received steroid treatment, and 2/12 received neither steroids nor liver transplantation. 11/28 patients with NAEH (incl. NAEH with PALF) without HAAA were also treated with steroids. 7/28 patients underwent liver transplantation, and 10/28 patients received neither steroids nor liver transplantation. In comparison to patients who received steroid treatment, patients without steroid treatment nor liver transplantation showed a similar hepatic recovery.

CONCLUSION

Acute NAEH makes up a big proportion of fulminant hepatitis and ALF in children. Furthermore, HAAA could develop 0-3 months after NAEH. Low lymphocytes could be an early marker for HAAA.

Poster Session 05: Liver and visceral transplantations

P05-01 Hypothermic oxygenated machine perfusion (HOPE) in liver transplantation - Influences on physiological responses, vasopressor demands, and electrolyte shifts during reperfusion

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INTRODUCTION

Due to the persisting organ-shortage novel technologies such as ex vivo perfusion have been implemented, expanding the donor pool towards marginal organs.

Beside graft availability, the operative period remains critical for patient survival. Following reperfusion, hemodynamic stress and electrolyte shifts are often observed, resulting in part in a post-reperfusion-syndrome.

METHODS

50 hypothermic oxygenated perfused (HOPE) liver grafts were compared with 50 organs kept in static cold storage (SCS). Portal venous perfusion was carried out by the LiverAssist® - device. Mean arterial blood pressure was monitored by invasive catheterization and vasopressor administration tracked. Potassium levels were measured using sequential blood gas analyses and serum transaminase levels determined.

RESULTS

Transaminase levels were lower in the HOPE group compared to SCS (AST 1169 vs 1809, p = 0,0017; ALT 529 vs 1086, p = 0,0004). After reperfusion median immediate drop in mean arterial pressure was 13% in the HOPE group compared to 28% in the SCS group (p<0.0001), resulting in lower vasopressor demand for norepinephrine (750µg vs 960µg, n.s.) and epinephrine (96µg vs 199µg, p= 0,0184). Post-reperfusion syndrome occurred in 12% of cases in the HOPE group versus 42% in the SCS group (p=0.0013).

Blood potassium concentration decreased by 16,4% vs 4,9% in controls (p< 0,0001) after reperfusion, requiring substitution in 40% of cases, compared to 16% after cold storage respectively (p=0.0135).

CONCLUSION

HOPE provides a number of long term benefits, such as improved hepatic integrity. In this study, we also show a positive impact during the operative period. HOPE results in higher hemodynamic stability during reperfusion, lower incidence of post-reperfusion syndrome and lower vasopressor demand compared to SCS. Furthermore, a decrease in potassium levels after reperfusion was seen in the HOPE group, potentially reducing the risk for hyperkalemic arrhythmias. Whereas in the past preemptive shifting via insulin administration was often required, this should be omitted in HOPE-perfused livers and possible potassium substitution anticipated to avoid hypokalemia.

P05-04 Deep learning as a donor-recipient matching model for liver transplantation

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INTRODUCTION

The world around us is changing. The "digital era" in the field of medicine is the new "here and now". Deep learning has entered many fields of medicine and as of late is emerging in the field of organ transplantation. Being able to predict the outcome after liver transplantation for a donor recipient match must be desired. Solid organs remain a scarce resource, living in a time where the utilization of such a scarce resource appears to be more vital than ever novel organ allocation system need to be evaluated. Within this work we developed and validated a novel deep learning-based donor-recipient allocation system for liver transplantation.

METHODS

In this study we used data collected from all liver transplant patients between 2004 and 2019 at the university clinic, Munich. We aimed to design a transparent, interpretable, and partly supervised deep learning framework to predict the outcome after liver transplantation. An individually designed neural network was developed to meet the unique requirements of transplantation data. The metrics used to determine the model quality and its level of performance are accuracy, cross-entropy loss, F1 score as well as AUC score.

RESULTS

A total of 529 patients were included. Total of 1058 matching donor and recipient observations were added into the database. The combined prediction of all outcome parameters is 95.8% in accuracy (cross-entropy loss of 0.042). The prediction of Death within the hospital was 94.3% in accuracy

(cross-entropy loss of 0.057). The overall F1 score displayed 0.899 in average whereas the overall AUC score was 0.940.

CONCLUSION

With the achieved results, the network reflects a high potential in predictive capacity. It adds new inside to the potential of Deep Learning to assist medical decisions. Especially in the field of transplantation, an AUC Score of 94% is very valuable. This neuronal network is unique as it utilizes transparent and easily interpretable data to predict the outcome after liver transplantation.

P05-05 Noninvasive prediction of subclinical graft injury after liver transplantation using peripheral blood microparticles

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INTRODUCTION

Graft biopsies (Lbx) are still the gold standard for identifying graft injury such as acute or chronic rejection. However, Lbx come with a risk of bleeding due to their invasiveness, as well as causing high costs and requiring patients to visit a transplant center. The detection of specific biomarkers could therefore be helpful in diagnosing (subclinical) rejection.

METHODS

This study aimed at comparing peripheral blood levels of microparticles (MP) in patients with clinical overt T cell-mediated rejection (clinTCMR; n=16) in comparison to stable liver transplant recipients (LTR) (liver enzymes < 2x upper limit of normal (ULN)) with various degrees of subclinical graft injury (n=37) ranging from subclinical TCMR (subTCMR; n=25) to patients without graft injury (n=12). Nineteen of the 37 stable patients had no relevant graft injury according to 2016 BANFF criteria for the minimization of immunosuppression (BANFFMini), leaving 34 patients with graft injury beyond BANFFMini. MP were isolated by ultracentrifugation from cryo-conserved plasma samples and analyzed by FACS using 10 different markers.

RESULTS

Frequencies of MP with positivity for CD4, CD39, ASGPR, Cx43, HLA class I, CD39+Annexin V, CD31+Annexin V or Cx43+Annexin V were significantly

associated with clinTCMR in comparison to stable LTR. However, only MP with positivity for CD31+Annexin V (AUC .797), HLA class I (AUC .703) or CD31 (AUC .760) were significantly associated with the presence of subclinical TCMR within stable LTR. In addition, only $CD4^+$ MP were significantly associated with the presence of relevant subclinical graft injury according to the 2016 BANFF criteria for immunosuppression reduction (AUC .676) within stable LTR.

CONCLUSION

These results match previous studies, indicating that quantification of peripheral blood MP can be useful but is not yet a reliable diagnostic tool for a non-invasive detection of subclinical graft rejection in surveillance biopsies in a cross-sectional approach.

P05-06 Validation of risk scores for allograft dysfunction after liver transplantation: A retrospective cohort analysis

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INTRODUCTION

Several clinical risk scores have been proposed to predict allograft dysfunction and outcome after liver transplantation. We aimed to validate nine clinically relevant donor and recipient risk scores on a large German liver transplantation dataset.

METHODS

Single center retrospective cohort analysis of all de novo liver transplantations performed in adult patients at the Charité – Universitätsmedizin Berlin from January 2007 until December 2021 with organs from donation after brain death.

RESULTS

906 liver transplantations were analyzed based on nine previously published risk scores (Eurotransplant donor risk index [ET-DRI/DRI], donor age and model for end stage liver disease [D-MELD], balance of risk [BAR], early allograft dysfunction [EAD], model for early allograft function [MEAF], liver graft assessment following transplantation [L-GrAFT$_7$], early allograft failure simplified

estimation [EASE], and a score by *Rhu et al.)*. The EASE score provided the best prediction of 3-, 6-, and 12-month graft survival, with a c-statistic of 0.8, 0.77, and 0.78 respectively. In male recipients with a high MELD (>25) and transplantation of an extended criteria donor organ, the EASE score was suited best. Scores only factoring in pre-transplant data predicted outcome less reliably compared to scores including postoperative laboratory values data (e.g., ET-DRI vs. EAD, $p<0.001$ at 3-month graft survival). Out of these, the BAR score performed best with a c-statistic of 0.6 for 3-month graft survival.

CONCLUSION

In our comprehensive comparison of the clinical utility of risk scores for the outcome after liver transplantation, the EASE score had the highest overall c-statistic of 0.8. Furthermore, the EASE score was the only score sufficiently predicting 12-month graft and patient survival. Despite a relatively complex calculation, the EASE score provides significant prognostic value for patients and health care professionals in Germany.

P05-07 Prevention of Large-for-Size Syndrome after liver transplantation by *ex-vivo* liver graft reduction through right posterior sectionectomy – single center experience

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INTRODUCTION

Transplantation of an excessively large liver into a small recipient cavity leads to graft compression, impaired perfusion, and intra-abdominal compartment syndrome (i.e. Large for Size Syndrome, LFS). LFS is a life-threatening situation associated with graft loss. The reduction of the whole liver grafts may represent a way out of this problem. In particular, reduction of the graft right lobe could be an alternative to avoid LFS in cases, where an extreme size mismatch can be expected. In this regard, Pu et al. recently published an *ex-vivo* technique of right posterior sectionectomy (RPS) to prevent LFS, with good short and long-term results in 5 patients. Herein we present our experience with this technique in the setting of small young and pediatric recipients.

METHODS

Retrospective review of deceased donor liver transplantation performed during the period January 2018 to April 2022 using the *ex-vivo* RPS technique for the reduction of the graft at our institution.

RESULTS

In the study period, 7 patients were transplanted with reduced-size grafts through *ex-vivo* RPS. The median age of recipients was 8 years (range 2-18), M/F ratio was 1/6, with a median weight of 36 kg (range 11-73), a median

height of 141 cm (range 89-163), and a median BMI of 18 (range 13-27). Six patients were transplanted as high urgency and received grafts through primary allocation. The grafts had a median ET-DRI score of 1,17 (range 1,09-1,89) considered as whole liver, and of 1,99 (range 1,64-2,84) as partial liver. The median Graft-to-Recipient Weight Ratio (GWRW) was 4,7 (range 2,2-10,9) before, and 2,2 (range 1,1-5,5) after RPS. A delayed fascial closure was necessary only in one case. No postoperative LFS occurred. One recipient died 34 days after transplantation with a functioning graft due to brain edema and herniation, and one patient was re-transplanted 22 days after LT due to severe ITBL and graft failure. All other patients presented at the last follow-up with a normal function of the graft.

CONCLUSION

We confirm that the *ex-vivo* RPS-technique represents a feasible surgical strategy to prevent LFS, in particular in small recipients and in the setting of high urgency or impossibility to split the graft.

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P05-09 Long-term follow-up of renal function after liver transplantation for polycystic liver disease in autosomal dominant polycystic kidney disease: Results of a retrospective multicentric cohort study

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INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is associated with polycystic liver disease in 83% of patients. In cases with a dominant and symptomatic liver phenotype and preserved renal function isolated orthotopic liver transplantation (OLT) improves patients' quality of life. Liver transplant patients are susceptible to chronic kidney disease (CKD). However, the specific risk of CKD after OLT in ADPKD has not been studied sufficiently.

METHODS

A retrospective multicentric data analysis of patients was performed for patients with ADPKD and isolated OLT (n=37) during 2008-2021. Patients with combined liver and kidney transplantation (KT), kidney before liver

transplantation, OLT due to isolated polycystic liver disease and a follow-up time < 12 months were excluded. Patients were longitudinally assessed for estimated glomerular filtration rate (eGFR). Baseline parameters such as height adjusted total kidney volume (HtTKV), diabetes mellitus and arterial hypertension as well as post OLT parameters were analyzed.

RESULTS

The median observation period after OLT consisted of 50 months (IQR 28 - 73). Age at the time of OLT was 50 years (IQR 53 - 45). Women were more frequently affected (86.5 %, n = 32). Median eGFR at the time of OLT was 55 ml/min (IQR 39 - 73). 29.7% (n = 11) required permanent dialysis after a median time interval from OLT to dialysis requirement of 40 months (IQR 18 - 63). HtTKV was significantly higher in the group of patients requiring dialysis (1006.2 ml/m vs. 777.9 ml/m, p = 0.031). Six patients (16.2 %) received a KT after OLT. Median time interval to KT was 51.5 months (IQR 7.7 – 115.7). The median percentage of decline of eGFR one year after OLT was 82.8% from baseline eGFR (IQR 67.5 – 101.1) and 62.2% (IQR 24.9 – 99.6) after 5 years.

CONCLUSION

Patients with ADPKD receiving OLT appear to have a high risk of progressive deterioration of kidney function. HtTKV seems to be associated with the risk of permanent hemodialysis in our cohort. Our study might improve selection of optimal candidates for combined liver and kidney transplantation which is important to avoid secondary kidney after OLT.

Poster Session 06: Kidney transplantation, living donation, psyche und transplantation

P06-01 A Machine learning approach to the prediction of serum creatinine of kidney transplant patients

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INTRODUCTION

Many prediction models that were developed in the past focused on the prediction of graft loss. The ambition in the daily work of a clinician is usually to maintain an as good as possible renal function rather than just kidney survival. In an effort to detect harmful events to the graft at an early stage, a large number of follow-up appointments are made. Unfortunately, some patients lose kidney function rather quickly. Identifying patients at high risk of losing renal function could improve the follow-up strategy.

METHODS

Our single-centre study cohort consists of 472 patients who received a kidney transplantation between 2007 and 2017 and were followed for five years. The patients were divided randomly into two groups (80 % training data and 20 % validation data). Each patient was labelled depending on whether his serum creatinine at one, two, and five years after transplantation was above or below the mean value of all patients at this time. Random Forest (RF) classifier models were trained to predict those labels with multiple donor and recipient properties up to a certain time in the follow-up period. An optimisation by a grid search with multiple hyperparameters and a 5-fold cross-validation resulted in 15000 RF classifiers in each set. All calculations were performed using Python 3 (Python Software Foundation).

RESULTS

The mean serum creatinine levels were 1.48 mg/dl (1 year), 1.48 mg/dl (2 years), and 1.60 mg/dl (5 years). Prediction accuracies of 0.7 to 0.98 were achieved with the training data, and 0.7 to 0.8 with the validation data. The prediction accuracy could be confirmed for most models by testing the best RF classifier with the validation data. Only when predicting the 5-year serum creatinine with the 3-month data, there was a large difference in prediction accuracy, indicating overfitting.

CONCLUSION

RF classifiers can be used at various times in the follow-up with satisfying accuracy. The accuracy of the prediction is better when given more data and with short-term predictions. A confirmation of the accuracy by testing on unseen data is essential to prevent overfitting. It is expected that further models trained on larger cohorts will provide better predictions.

P06-06 Automating the HLA matching process: Finding the most suitable recipient with python

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INTRODUCTION

In kidney transplantation, HLA matching is crucial for graft and patient survival. HLA matching is linked to a lower incidence of acute rejection and opportunistic infection after pancreas transplantation. Microsoft Excel is one of the most extensively used tools in clinical and research settings. Many transplant programs use Excel lists to administrate their waiting list, even in search for "best matched" recipients in case of competitive or extended criteria organ offers. Despite the fact that Microsoft Excel provides built-in features, the software lacks a feature that allows the user to search, filter, or perform operations that methodically process each input. Thus a time consuming manual selection has to be performed in urgent situations, mainly at night. In the digital era, individual solutions that are compatible with existing softwares should be simple to design and use. Python, for example, is a widely used programming language that is a high-level scripting language that is designed to be highly readable, and it can assist practitioners and researchers not only in the fields of data science, statistics, and machine learning, but also in the automation of time-consuming and error-prone tasks.

METHODS

We designed and implemented a python algorithm to predict the best recipient for pancreatic transplantation, kidney transplantation, and pancreas-kidney transplantation by providing the donor phenotype. The algorithm goes through the excel list and compares each recipient's phenotype to that of the donor, while also taking into account any unacceptable antigens the recipient may have.

RESULTS

After integrating this python script into our clinical workflow, we were able to save resources, eliminate errors in the HLA-Matching process, and react to transplantation offers much faster and more efficiently.

CONCLUSION

We believe that by sharing our strategy, clinicians will be motivated to employ, integrate, and adopt technology (particularly programming) in transplantation.

P06-07 Minimally invasive video-assisted parathyroidectomy (MIVAP) versus conventional parathyroidectomy for renal hyperparathyroidism

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INTRODUCTION

The purpose of this study was to compare minimally invasive video-assisted parathyroidectomy (MIVAP) versus conventional surgery for renal hyperparathyroidism (rHPT).

METHODS

Between 2006 and 2020, 53 patients underwent MIVAP and 182 underwent conventional parathyroidectomy for rHPT at the Kliniken Essen-Mitte and Knappschaftskrankenhaus Bochum, respectively. Two propensity score-matched groups were retrospectively analyzed: the MIVAP group (VG; n=53) and the conventional group (CG; n=53). To assess long-term results, the patients were questioned prospectively (VG; n = 17, and CG; n = 26).

RESULTS

The VG had a smaller incision (2,8 vs. 4,8 cm), shorter operation duration (81,0 vs. 133,9 min), and shorter duration of stay (2,4 vs. 5,7 days) ($p < 0,0001$) but a smaller drop in parathyroid hormone (PTH) postoperatively (81,3 vs. 85,5%, $p = 0,022$) than the CG. The conversion rate was 9,4% (n=5). The VG had better Patient Scar Assessment Scale (PSAS) scores (10,8 vs. 11,7 $p = 0,001$) but worse SF-12 health survey scores (38,7 vs. 45,8 for physical health and 46,7 vs. 53,4 for mental health) ($p < 0,0001$). The PTH level at follow-up was higher in the VG (162,7 vs. 59,1 ng/l, $p < 0,0001$). There were no differences

in morbidity, number of removed parathyroid glands, disease persistence, late rHPT relapse and need for repeat surgery between groups.

CONCLUSION

MIVAP was superior to conventional parathyroidectomy regarding aesthetic outcomes and cost effectiveness. Conventional surgery showed better control of PTH levels and health scores on follow-up than MIVAP, without any impact on rHPT relapse and need for repeat surgery.

P06-09 Characterization of living kidney donors in Germany – First results from the German Living Donation Register SOLKID-GNR (Safety of the Living Kidney Donor-German National Register)

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INTRODUCTION

Living kidney donation (LKD) represents the optimal treatment for patients with endstage renal failure. There is a lack of prospective multicenter studies evaluating the physical and psycho-social outcome of living kidney donors (LD) in Germany. Since 2020 german transplant centers can participate at the prospective National Living Donation Register SOLKID-GNR.

METHODS

28 of 38 transplant centers in Germany evaluated LD in an interdisciplinary approach (01/2020 to 01/2022). Clinical baseline data collected prior and 8-14 weeks after LKD were summarized to characterize LD in Germany.

RESULTS

305 LD were enrolled (33% male, mean age 55±10 years, range 29-83 years) representing 84% of the recruitable LDs in Germany. Pre-emptive LKD was performed in 30%, AB0-incompatible LKD in 27.3%, and 8.6% immunized LKD with donor-specific antibodies.

Prior LKD S-creatinine was 0.8±0.14 mg/dl and CKDepi eGFR was 91±13 ml/min. Alb/Crea ratio was 11+28mg/g; microalbuminuria showed 6.6% of the LD and 3 LDs with an BMI>35kg/m^2 (mean BMI 25.9 ± 3.6 kg/m^2, range 17-39 kg/m^2). Most of the LDs (82.4%) reported to be completely healthy. Medical history revealed 26.6% hypertension, 1.0% diabetes, 3.6% cardiovascular diseases, 9.0% hyperlipidemia, 4.3% autoimmune/immunological diseases and 3.3% former malignancies. 3.6% of LD reported about chronic pain, 3.7% sleeping disorders, 1.7% restlessness, 4.0% psychological/psychosomatic diseases and 0.7% depressive symptoms. 26.8% of LDs without any medical history revealed to take medication.

8 to 14 weeks after LKD S-creatinine increased to 1.2±0.26 mg/dl and CKDepi decreased to 59±12 ml/min. 42.1% of the LDs were in CKD stage 2, 57.0% in CKD stage 3 and one LD in CKD stage 4. There was no significant increase of microalbuminuria, or blood pressure after LKD.

CONCLUSION

LDs in Germany are not only healthy young persons but also persons with pre-existing medical problems. About 35% reduction of renal function after LKD was confirmed. To evaluate any negative effect on biological and physical influence due to the nephrectomy all LDs need a regular follow-up at the transplant center. Especially LDs with a medical history should have close and comprehensive check-up visits.

ACKNOWLEDGEMENT

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P06-12 STEP^{LTX}: Stigmatization experiences of patients after liver transplantation in Germany

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INTRODUCTION

Patients after liver transplantation face several psychosocial challenges. Besides the diversity of these patients regarding their psychosocial functioning and severity of medical problems, they share the commonality of being ill in a social context. Taking this social perspective on having undergone a liver transplantation, the experience of stigma may be a potential consequence of the liver transplantation and the causing disease. However, literature regarding the experience of stigmatization after liver transplantation is scarce. This study aimed to investigate the extent to which people after a liver transplantation experience stigma in different settings of life and care.

METHODS

Using participatory research principles, all parts of the study were guided by a advisory board consisting of patient representatives. Ten problem-centered interviews were conducted and recorded. After transcription, the text material was analyzed using content-structured qualitative content analysis. Findings were embedded in the Health Stigma and Discrimination Framework.

RESULTS

The experience of stigmatization was reported by all participants in all relevant life and care settings and described in detail in terms of serious consequences. Whereas none of the interviewees had an alcohol-associated liver disease, the most frequent stigmatization experiences were based on the stereotype that people with liver disease are alcoholics. Further experiences of stigmatization

were described, which included that those affected self-inflicted their disease, that they represent a burden on the care and the insurance system and that they are highly unlikely to give truthful statements about the cause of their illness. Psychological, physical, and structural consequences were elaborated.

CONCLUSION

This qualitative study emphasize that the experience of stigma is significant challenge for patients after liver transplantation. Further studies are needed to corroborate our results using quantitative designs and larger sample sizes.

Poster Session 07: Infections / complications after transplantation, ethics in transplantation medicine, aftercare concepts / prehabilitation / rehabilitation

P07-03 A restrictive immunosuppression after recurrence of HCC/CCC may prolong survival in liver transplant patients

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INTRODUCTION

Recurrence of hepatocellular (HCC) or cholangiocellular (CCC) carcinoma after curative liver transplantation (LT) remains the most feared complication with significant impact on survival. Oncological treatment strategies include resection, radioablation and chemotherapy, but still, median survival is about 12 months. Optimal management of the life-long administered immunosuppressive (IS) management after liver transplantation in these patients remains unclear.

METHODS

Patients transplanted for HCC or CCC in our transplant center were analyzed over a course of 30 years in this retrospective study. Clinical course and oncological parameters were analyzed. IS at time of diagnosis and after where evaluated. Impact on survival of reduction of IS in case of recurrence was analyzed.

RESULTS

112 patients suffering from recurrence of HCC and 44 patients with recurrent CCC or mixed HCC/CCC after LT were identified. In both groups, a cohort was found, where IS was reduced in an individualized approach (group HCC: n=69; group CCC: n=23) and another, were IS remained unaltered upon diagnosis of recurrence. For both entities, a restrictive IS-regimen improved survival after diagnosis with statistical significance: In group HCC median survival was 13.2 months vs 7.0 months, p = 0.001) and in group CCC median survival was 16.7 (0.53-72.8) months vs 5.3 (0.13-42.5) months (p=0.01).

CONCLUSION

In this retrospective analysis, we found significant impact of reduction of IS towards improved survival after recurrence of primary liver tumors after LT and a restrictive IS management after diagnosis might be an additional oncological strategy in these patients.

ACKNOWLEDGEMENT

Data for recurrent HCC from this manuscript have been published previously but were now supplemented with the course of CCC patients and thus, an analysis for the effect if IS for recurrence of all primary liver tumors after LT was conducted.

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P07-04 Anal HPV prevalence exceeds genital detection in female transplant recipients

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INTRODUCTION

Transplant recipients are at increased risk of developing anogenital (pre) malignancies related to HPV-infections. Previous studies on the prevalence of high risk (hr)HPV-infection among female transplant recipients have been contradictory.

METHODS

Women who had undergone kidney or liver transplantation received anal (Anyplex™ II HPV28 (Seegene)) and cervical HPV testing (Cobas® HPV Test (Roche Diagnostics)). In cases of cervical HPV positivity further genotyping was performed via Anyplex™ II HPV28 (Seegene). All participants completed a questionnaire regarding medication, sexual behaviour and medical history.

RESULTS

201 patients were included in the study. 32 had a cervical hrHPV infection resulting in a prevalence of 15.9%. The most common type detected was HPV 16 (31%). There were no significant differences in HPV prevalence between liver and kidney transplant recipients. Increased hrHPV prevalence was not attributable to transplant specific risk factors like type and duration of immunosuppressive therapy. Anal hrHPV showed an overall prevalence of 20.3% (40/197), HPV16 was detected in 17.5% (7/40). The co-prevalence of anal hrHPV in the cervical hrHPV group was 68.8%. 28/32 patients with cervical

hrHPV infection attended follow-up: Intraepithelial neoplasia was detected in 3 women. The overall HPV vaccination rate was only 12.4% (25/201).

CONCLUSION

Data indicate that cervical HPV prevalence is almost tripled among female transplant recipients. In comparison the overall anal hrHPV detection rate is even higher, suggesting that screening should be discussed, at least in high-risk groups.

P07-06 Reduction of calcineurin inhibitors after diagnosis of solid visceral de novo neoplasms may further improve oncological outcome in liver transplant patients

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INTRODUCTION

Liver transplantation (LT) has become an established treatment procedure for selected patients with end-stage liver diseases. However, one of the most severe complications of LT and its subsequent long-term immunosuppressive (IS) therapy is the increased risk for the development of de novo malignancies. Even though the contributing effect of IS on oncogenesis is well established, standardized regimens for IS after tumor diagnosis are still missing. In this retrospective study, we investigated the effect of reduction of calcineurin inhibitors (CNI) on oncological outcome in patients with posttransplant colorectal (CRC) or lung carcinoma.

METHODS

Patients with de novo colorectal (CRC) or lung cancer after LT were included in this study over a course of 30 years in a retrospective manner. Oncological parameters, treatment regimens, patients´ course as well as graft function and handling of IS were analyzed.

RESULTS

From 1989 to 2019, 33 patients with de novo CRC and 62 patients with lung cancer after LT were identified. Median time from initial LT was 12.0 years (0.9-27) and 9.7 years (0.7 – 27.0 years), respectively.

Regarding handling of IS upon diagnosis, for each entitiy, two groups were identified: In 20 (CRC-group) and 33 (lung cancer group) patients, IS consisting of backbone therapy with CNI was significantly reduced and in 13 (CRC-group) and 29 (lung cancer group) IS was not altered or increased further.

Kaplan-Meier analysis revealed significant improved survival for patients with reduced IS in both tumor entities. In CRC patients, median survival was 83.46 (8.4-193.1) months for patients with reduction of IS vs 24.8 (0.5-298.9) months; (Breslow<0.01 and Log rank=0.02). In lung cancer patients, median survival was 38.6 months (12.1-65.1) and 6.7 months (0.0-17.5), respectively (log rank= 0.02, Breslow<0.01). No loss of graft function was recorded.

CONCLUSION

Reduction of CNI in new onset of oncological diseases after LT may exhibit additional benefit for these patients without compromising graft function when under close surveillance. In regard of optimization of individual patient´s course, a restrictive IS management seems justified with biological plausibility.

P07-07 Fearful complication after pancreas kidney transplantation

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INTRODUCTION

We present the case of a 60-year-old Caucasian man, who received a simultaneous pancreas-kidney transplantation a few months ago due to end stage renal disease because of diabetic nephropathy. He was on peritoneal dialysis for 6 months at the time of transplantation.

METHODS

On day 14 posttransplantation the patient developed out of nowhere a fasting hyperglycaemia of circa 300 mg/dl, although at this time the previous blood sugar profiles were maximum 120 mg/dl for fasting blood sugar and 140 mg/dl for postprandial values and insulin was not needed since day 4 postttranplant.

RESULTS

The CT with contrast agent showed no blood perfusion of the pancreas transplant. The diagnosis of complete thrombosis of the main artery of the pancreas transplant was made. The endovascular intervention was not sufficient to remove all the thrombi in the arterial system. Because of remaining thrombi in the distal vessels (arteries and veins) of the pancreas, we were forced to remove the pancreas transplant on the same day. The kidney transplant function remained normal. It needs to be mentioned, that the pacient was haematologically evaluated before the transplantation (Protein C, S, thrombocyte aggregation and adherence assays, was screened for Factor V and MTHFR (methylenetetrafolate reductase) mutations), all of the above indicating no high risk of thrombosis. We noticed that on the same day the

thrombocytes were for the first time under the normal range (100000/mcl) and fell with 50% after day 1 post transplantation. An ELISA assay was positive for antibodies against PF4-heparin complex and a few days afterwards a functional assay (HIPA) confirmed the presence of platelet activation through heparin-dependent antibodies. A non-heparin anticoagulant was started and no other signs of arterial or venous thrombosis were noted afterwards.

CONCLUSION

We were faced with a typical diagnosis of heparin-induced thrombocytopenia typ 2 in an atypical environment, leading to the loss of one transplant organ. Due to the serious consequences, it might be useful to screen for heparin-induced thrombocytopenia when evaluating the patients for organ transplantation.

P07-09 Fit for kidney transplantation through comprehensive rehabilitation - a clinical trial of an interdisciplinary treatment approach in elderly dialysis patients

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INTRODUCTION

The decrease in physical performance and the associated increase in the risk of frailty jeopardize the transplantability status in the long-term course, especially in older patients on the waiting list for a kidney transplant. The project "Fit for kidney transplantation through comprehensive rehabilitation" aims to reduce this risk and enable an optimal preparation for a transplantation through an interdisciplinary sustainable program.

METHODS

Approximately 100 patients (> 65 years, waiting or pre-waiting list) are to be included by the end of the year. In addition to a 3-week inpatient rehabilitation, patients receive individual sports and nutritional care in addition to standard care. To monitor the effects of the project, patients undergo biannual assessments of physical performance, body composition, quality of life, bone density, and general health (e.g., blood values). Data are initially analysed descriptively using comparisons of means over the long-term.

RESULTS

Data before and after rehabilitation showed significant improvements in 6 min walk test (+49.7m; $p<0.001$), Berg Balance Scale (BBS) (+1.9P, $p<0.001$),

abdominal circumference (-2.1cm, p=0.09), body fat (-1.7kg, p=0.033), and Barthel-Index (+5.7P, p=0.003). Important for the success of the project is a sustainable improvement in physical and mental health. In this context, the first analyses of the assessments six months after inclusion compared to baseline show significant improvements in 1-min sit-to-stand test (+1.7x, p=0.33), BBS (+2.3P, p=0.004), abdominal circumference (-3.2cm, p=0.02), BMI (-0.9kg/m^2, p=0.07), body fat (-2.2kg, p=0.049) and Barthel-Index (+4.7P, p=0.008).

CONCLUSION

The high demand for interdisciplinary care of older dialysis patients highlights the need for sustainable approaches to improve and maintain physical resources of patients on the waiting list for a kidney transplant. The difficulty is to maintain the activity and motivation toward a healthier and active lifestyle over the waiting period for a kidney transplant. By integrating this additional supply of care, the project can make an important contribution to the permanent improvement of the physical performance of this patient group.

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P07-11 Effects and safety of a 3-week rehabilitation program on physical performance and symptom burden in kidney transplant recipients and patients with ESRD: An observational study

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INTRODUCTION

Patients with CKD are at increased risk for cardiovascular morbidity and mortality, have an impaired quality of life and physical performance. The latter is well established to be predictive of relevant outcomes like transplant survival. Despite CKD being a chronic condition often accompanied by multiple comorbidities, only limited data exist on the safety and effects of rehabilitation programs in nephrology.

METHODS

In this retrospective analysis 220 patients after kidney transplantation were included. At the beginning and the end of our 3-week rehabilitation program physical performance status and symptom burden was measured. Assessments included the 6 minute walking test (6MWD), a rowing test, the short physical performance battery (SPPB), the ESRD-SCL-questionnaire and eGFR (calculated by CKD-EPI formula).

Furthermore, 76 patients with ESRD were assessed before and after our rehabilitation program in terms of symptom burden as well as their physical performance status as measured by the 6MWD, the rowing test, the SPPB and the ESRD-SCL-questionnaire.

Data was stratified by age group, dialysis vintage and time since transplantation. Statistical analysis was performed using paired wilcoxon-rank tests.

RESULTS

In the transplant group, patients showed significant improvement in all categories: The 6MWD, the rowing test, the SPPB and the ESRD-SCL-questionnaire. Additionally, eGFR showed a slight increase after completion of rehabilitation. This effect was consistent for different time points since transplantation.

Similar results were obtained in the transplant group where patients significantly improved both their physical performance as represented by the 6MWD, the rowing test, the SPPB test and the symptom burden as measured by ESRD-SCL.

CONCLUSION

To our knowledge, this is the largest observational study on the effects of a specialized rehabilitation program for both patients with ESRD and after kidney transplantation.

In both patients groups, rehabiliation is associated with significant improvement in physical performance and symptom-burden.

In terms of eGFR, our multimodal rehabilitation program is safe in all stages after transplantation.

P07-12 Vaccination status in renal transplant recipients

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INTRODUCTION

Patients after renal transplantation are at higher risk of serious infections due to their immunosuppressive therapy and should therefore undergo extensive vaccination procedures.

The aim of this study was to examine the frequencies and titers of documented vaccinations in a cohort of renal transplant patients.

METHODS

Patients were recruited from the outpatient renal transplantation unit of the university hospital Essen. In addition to their yearly check- up at the outpatient renal transplantation unit patients are regularly seen by their nephrologist and/or family doctor. 105 renal transplant patients were included into this cross-sectional study (63% male, 37% female). Vaccination cards were evaluated at check-up. Patients were asked to answer a questionnaire and blood samples were taken to determine vaccination titers.

RESULTS

18 of the 105 patients (17%) had no vaccination card. With respect to the upcoming option of vaccination against SARS-CoV-2 patients were asked whether they wanted to get vaccinated if an approved vaccine would be available. 22% were against vaccination, 66% were in favor and 12% were unsure. 44% of the patients with vaccination cards had no valid registered tetanus

vaccination and 15% had no valid registered measles vaccination. 53% of the patients with vaccination cards lacked vaccination against pneumococci, 18% lacked proof of vaccination against hepatitis B virus (HBV) and 44% against poliomyelitis.

Only 52% of the patients had protective antibody titers against diphtheria and 89% had protective antibody titers against tetanus. 3% of the patients had no protective antibody titers against measles. 82% of the patients had three documented HBV vaccinations but only 25% thereof had titers above 100 lU/l.

CONCLUSION

Renal transplanted patients were not sufficiently vaccinated in a cross-sectional cohort of the year 2020. Missing vaccination cards, incomplete vaccinations and failure to check titers of immunity add up to this result. Even though the vaccination rates measured in this study are still below the set goals they all surpass the general population vaccination rates of Nordrhein measured in the epidemiological bulletin 50/2021 by the Robert Koch Institute.

Poster Session 08: Transplantation immunology, immunosuppression

P08-01 Correlation of the Fc gamma receptor IIIa polymorphism V158F with pneumococcal antibodies in vaccinated kidney transplant recipients

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INTRODUCTION

Antibodies against microorganisms and allografts bind to Fc receptors and can thereby lead to immune activation. Several polymorphisms within Fc receptors (FCR) have been described, of which some correlate with allograft function [1]. We observed that kidney transplant recipients showed a significant increase in their pneumococcal antibodies after vaccination, however at a lower level than healthy controls [2]. We furthermore found that in females but not in males non-specific HLA antibodies (i.e., without donor-specificity) increased after vaccination [3].

METHODS

In the current study we determined three Fcγ receptor and five Fcα receptor dimorphisms in 47 kidney transplant recipients, who have been vaccinated against *Streptococcus pneumoniae*. We analyzed if FCR genotypes correlated with pneumococcal antibodies and their serotype-specific opsonophagocytic function, tested prior to and at month 1 and 12 post vaccination. In parallel, we assessed antibodies against HLA and MICA and determined kidney function.

RESULTS

We observed that IgG2 antibodies against pneumococci at month 1 and 12 after vaccination and IgA antibodies at month 1 differed significantly between carriers of the three genotypes of FCGR3A rs396991 (V158F, p = 0.02, 0.04 and 0.009, respectively). Moreover, the genotype of FCGR3A correlated with serotype-specific opsonophagocytic function, reaching statistical significance ($p < 0.05$) at month 1 for 9/13 serotypes and at month 12 for 6/13 serotypes. Heterozygotes for FCGR3A had the lowest antibody response after pneumococcal vaccination. On the contrary, heterozygotes tended to have more antibodies against HLA class I and impaired kidney function.

CONCLUSION

Taken together, our current data indicate that heterozygosity for FCGR3A may be unfavorable in kidney transplant recipients.

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P08-03 Core signature of rejection-specific cytokines and chemokines in heart biopsies after transplantation

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INTRODUCTION

Allograft rejection remains one of the limiting factors for survival after HTX. The aim of this project was to characterize the cytokine/chemokine network in heart biopsies and peripheral blood plasma after HTx. The quantified cytokine/chemokine concentrations could reflect the ischemia/reperfusion response as well as rejection status of the allograft. Therefore, we hypothesize that in heart biopsies with histopathological proven acute rejection the microenvironment is significantly altered and potentially specific cytokine/chemokine patterns could predict allograft rejection.

METHODS

Heart biopsies (N=181 biopsies; 52 patients) and peripheral blood samples (N=147 samples; N=52 patients) were obtained between 6 days and 5 years after HTX. Using Luminex-based multiplex assays 50 immune mediators in tissue lysates and peripheral blood plasma were quantified. Concentrations of samples with histopathologic confirmed acute rejection and without signs of acute rejection were compared in lysates and plasma. Moreover correlation of tissue and plasma was performed.

RESULTS

With regard to the rejection status we identified significant differences in lysate concentrations. Especially CXCL9/MIG, CXCL4/MIP-1β and CXCL10/

IP-10 showed significantly elevated concentrations in biopsies with proven rejection ($p<0.001$). In addition, we identified individual long-term changes of single patients after transplantation and significant differences comparing tissue lysates with plasma concentrations. Interestingly, we found no strong correlation between plasma and lysate concentrations.

CONCLUSION

We could detect a core signature for biopsies with pathologically secured rejection consisting of increased concentrations of the chemokines CXCL9/MIG, CXCL10/IP-10, CXCL3/ MIP-1α and CXCL4/MIP-1β. This signature is clearly distinguished from the pattern we found in matched plasma samples and importantly there was no correlation between the measured protein concentrations in plasma and tissue lysates. Therefore, we hypothesize that biopsies remain indispensable for the diagnosis of heart rejection.

P08-04 Donor T and NK cells with a special tissue-resident memory phenotype migrate into the periphery of lung transplant recipients – a potential feature for tolerance development

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INTRODUCTION

Subsequent to lung transplantation (LuTx), the migration of lymphocytes from the transplanted lung into the periphery induces a transient chimerism of donor passenger cells in recipient blood. We characterized the phenotype of donor T/NK cells to investigate whether they might represent tissue-resident memory (TRM) cells.

METHODS

Lymphocyte dynamics in recipient blood were determined in n=97 LuTx patients directly (T0), 24 hours (T24) and 3 (wks) weeks after LuTx using flow cytometry. Donor cells were analyzed by HLA class I allele-specific mAb in n=44 LuTx-recipients. The same markers were used to determine the phenotype of lymphocytes present in organ storage solution (perfusate, n=111),

recipient explanted lung parenchyma (n=28) and donor trachea (n=17). Single cell mRNA sequencing of explant lung parenchyma was conducted (n=16).

RESULTS

In peripheral blood of all recipients, donor-derived T/NK cells were detected at T0, T24 and 3wks after LuTx, had higher CD69 expression compared to recipient cells, and were mostly $CCR7^-$ memory cells. This phenotype was similar to T/NK cells in corresponding perfusates. In recipient parenchyma and donor trachea, most $CD69^+$ T/NK cells showed co-expression of other tissue residency markers (i.e. CD103, CD49a, PD-1). These markers were not found in circulating donor lymphocytes and perfusates, indicating they represent distinct memory T/NK subsets. Sc-mRNA sequencing confirmed distinct TRM T cell subsets in lung parenchyma. Patients with high frequencies of donor T cells showed a trend towards chronic lung allograft dysfunction- (CLAD-) free survival 2 years post-LuTx.

CONCLUSION

Our results demonstrate that donor T/NK cells found in the periphery of lung transplant recipients are a distinct subset from circulating lymphocytes and TRM cells present in lung tissue, since they express CD69 but lack expression of other classical TRM markers. Donor T cells might be clinically relevant for tolerance induction and long-term survival after transplantation due to their unique features.

P08-05 Longitudinal dynamics of soluble and cellular immune mediators in pediatric liver transplantation (pLTx) identified cytokine/ chemokine signatures potentially associated with recovery

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INTRODUCTION

In the European multicentre "ChilSFree" study, we aimed to characterize longitudinal dynamics of soluble and cellular immune mediators during the first year after pLTx in order to identify potential biomarker candidates associated with outcome.

METHODS

Using Luminex-based multiplex technique, we measured 50 cytokines/ chemokines, growth and adhesion factors in recipient plasma at eight visits: before (V0), day 7/14/21/28 (D7/14/21/28), 3/6/12 months (3/6/12Mo) after pLTx (n=244). Absolute cell counts and relative proportions of immune populations in patient blood (n=180) were quantified by flow cytometry.

RESULTS

The longitudinal dynamics of soluble immune mediators after pLTx revealed major changes in plasma secretome from V0-D21. While timing was dominant first, at later visits, the patterns identified patients with specific recovery patterns. One pattern was characterized by the absence of pro-inflammatory markers CXCL8/9/10/12, CCL7, reduced liver enzymes (ALT, AST, GGT), rejection score and, hence, might be predictive for improved outcome after pLTx. Of note, this special pattern was observed few weeks after pLTx and could, therefore, predict superior outcome and allow to adjust immunosuppression.

The longitudinal dynamics of immune cells revealed that absolute cell counts and proportions of myeloid cells peaked at D7, followed by gradual decrease at later visits. Simultaneously, $CD4^+$ and $CD8^+$ T and $CD56^+$ NK cell counts were reduced at D7 but recovered at D21 with a further increase at 12Mo. Independently of visits, also some cellular immune patterns were linked to reduced inflammation and improved liver enzyme functions. The dynamic of T and NK cells but not B cells, granulocytes and monocytes after pLTx was affected substantially by the age of patients.

CONCLUSION

Cellular and soluble blood secretome signatures may act as biomarker candidate for improved outcome after pLTx, hence, paving the way to early adjustment of IS regimes and improved therapeutic options.

P08-07 CXCR4 blockade reduces the severity of murine heart allograft rejection by plasmacytoid dendritic cell-mediated immune regulation

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INTRODUCTION

Allograft-specific regulatory T cells (T_{reg} cells) are crucial for long-term graft acceptance after transplantation. Although adoptive T_{reg} cell transfer has been proposed, major challenges include graft-specificity and stability. Thus, there is an unmet need for the direct induction of graft-specific T_{reg} cells. We hypothesized a synergism of the immunotolerogenic effects of rapamycin (mTOR inhibition) and plerixafor (CXCR4 antagonist) for T_{reg} cell induction.

METHODS

BALB/c (allogeneic) or C57BL/6J (syngeneic) mice served as heart donors and C57BL/6J as transplant recipients. Animal experiments adhered to EU directive 2010/63/EU and were approved (#G1071/09). Heterotopic intra-abdominal heart transplantation (HTX) was performed as previously described (1). Allograft function was evaluated daily by palpation. C57BL/6J recipients received injections with plerixafor (1 or 5 mg/kg s.c.) and/or rapamycin (0.4 mg/kg i.p.) two days before, immediately after HTX and every other day for 14 days. The subclinical dosage of rapamycin allowed to early distinguish differences in allograft survival.

RESULTS

The combined treatment consisting of Plerixafor and Rapamycin lead to a longer prolongation of allograft survival compared to rapamycin-only ($p<0.001$).

Median allograft survival time in recipients from the non-treatment, plerixafor (P1 and P5 mg/kg), rapamycin and combined treatment group P1R or P5R were 8, 10, 10, 44, 49 and 78 days, respectively. Hearts of the respective syngeneic controls survived the whole observation period of 100 days.

Moreover, fibrosis and myocyte lesions were significantly reduced in the combined treatment group when compared to sole Rapamycin-treatment. Although less $CD3^+$ T cell infiltrated, higher T_{reg} cell numbers were observed. These findings were accompanied by a plerixafor-dependent plasmacytoid dendritic cell-mobilization as in vivo pDC-depletion abrogated the plerixafor-mediated increase in T_{reg} cell numbers and led to a reduced allograft survival.

CONCLUSION

Our pharmacological approach allowed to increase T_{reg} cell numbers due to pDC-mediated immune regulation. Therefore pDCs can be an attractive immunotherapeutic target in addition to plerixafor treatment.

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P08-09 Fast tacrolimus metabolism does not promote new onset of diabetes after kidney transplantation (NODAT)

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INTRODUCTION

New-onset of diabetes mellitus (NODAT) after kidney transplantation (KTx) induced by tacrolimus is an important issue [1]. Fast tacrolimus metabolism, which can be estimated by concentration/dose (C/D) ratio, is associated with increased nephrotoxicity and unfavourable outcomes after KTx [2]. Herein, we elucidate, whether fast tacrolimus metabolism increases also the risk for NODAT.

METHODS

Data from 596 nondiabetic patients treated with tacrolimus-based immediate-release immunosuppression at the time of KTx between 2007 and 2015 were retrospectively analyzed. The median follow-up time after KTx was 4.7 years (IQR 4.2 years). Our analysis was complemented by experimental modeling of fast and slow tacrolimus metabolism kinetics in cultured insulin-producing pancreatic cells (INS-1 cells), which were stressed by exposure to glucose and palmitate.

RESULTS

During the follow-up period, 117 (17.2%) patients developed NODAT. Of all patients, 210 (35.2%) were classified as fast metabolizers (CD ratio <1.05). Fast tacrolimus metabolizers did not have a higher incidence of NODAT than slow tacrolimus metabolizers ($p=0.496$). Consistent with this, insulin secretion and viability of tacrolimus-treated INS-1 cells exposed to 12h of tacrolimus concentrations analogous to serum profiles of fast or slow tacrolimus metabolizers or to continuous exposure did not differ ($p=0.286$).

CONCLUSION

In conclusion, fast tacrolimus metabolism is not associated with increased incidence of NODAT after KTx. Short time incubation of INS-1 cells with tacrolimus using different concentration profiles led to comparable effects on cell viability and insulin secretion *in vitro*.

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P08-10 The effect of tacrolimus formulation (prolonged-release vs. immediate-release) on its susceptibility to drug-drug interactions with St. John´s Wort

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INTRODUCTION

Tacrolimus, an often-used immunosuppressant, is metabolized by cytochrome P450 3A (CYP3A) and is susceptible to interaction with the CYP3A4 and P-glycoprotein inducer St. John's Wort (SJW) [1]. CYP3A enzymes are predominantly expressed in the small intestine and liver. Prolonged-release tacrolimus (PR-Tac) formulations are absorbed in more distal intestinal sections [2], thereby potentially bypassing intestinal first-pass metabolism. Envarsus®, a tacrolimus formulation that is absorbed largely in the colon, is considerably less susceptible to CYP3A inhibition by voriconazole [3].

We aimed to analyze the effect of SJW on tacrolimus pharmacokinetics after immediate release (IR-Tac; Prograf®) and PR-Tac (Envarsus®) formulations and to evaluate whether CYP3A4 activity (estimated with a midazolam microdose) and CYP3A5 genotype correlate with these changes.

METHODS

We included 18 healthy volunteers (including 7 CYP3A5 expressors) in this randomized, cross-over, phase I clinical trial who received a single oral tacrolimus dose (IR-Tac or PR-Tac, 5 mg each) alone or during SJW (300 mg TID starting 10 days before tacrolimus and continued for 3 more days). Concentrations were quantified using UPLC-MS/MS methods and pharmacokinetics were analyzed by non-compartmental methods.

RESULTS

SJW decreased IR-Tac exposure (AUC) 0.73-fold (90% CI 0.60–0.88) and maximum concentration (C_{max}) 0.61-fold (0.52-0.73). With PR-Tac, the decrease in AUC was 0.67-fold (0.55–0.81) and C_{max} 0.69-fold (0.58-0.82), with no statistical difference between the two formulations (p = 0.60). The extent of interaction appeared to be less pronounced in volunteers with higher baseline CYP3A4 activity and in CYP3A5 expressors.

CONCLUSION

In contrast to CYP3A inhibition, CYP3A induction by SJW showed a similar extent of interaction with both tacrolimus formulations. A higher metabolic capacity and presence of a functional CYP3A5*1 allele appeared to attenuate the extent of induction by SJW, possibly due to presystemic SJW metabolism or limited inducibility in individuals with already high CYP3A activity.

ACKNOWLEDGEMENT

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P08-11 Long-term compromised immune regulation after rituximab induction in blood group incompatible living-donor renal transplantation – 5 year results of a prospective pilot study

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INTRODUCTION

An increased frequency of severe infectious diseases and BK viremia has been described after ABOi renal transplantation. As rituximab induction may alter immunoregulation in these patients, we analyzed clinically relevant immune parameters in a prospective renal transplant study up to 5 years posttransplant.

METHODS

Mononuclear cell subsets (peripheral blood; lymph nodes), intracellular cytokine responses, CD4 helper function and in-vitro B cell responses were assessed pretransplant and up to 5 years posttransplant in 85 renal transplant recipients (living donation: n=25 ABO incompatible (ABOi), n=30 ABO compatible (ABOc); deceased donation (DD): n=30, all ABO compatible).

RESULTS

Severe infectious diseases occurred more often in ABOi than ABOc recipients within 2 years posttransplant (P=0.042) but not beyond. The incidence of BK viremia was significantly enhanced in rituximab versus non-rituximab

treated patients (1 year, P=0.009; 5 years, P=0.029). After rituximab induction in ABOi recipients, counts of peripheral blood B cell subsets were profoundly downregulated even 3 years posttransplant and reached the level of non-ABOi recipients after 4 years (memory B cells after 5 years). T-dependent and T-independent B cell responses were significantly impaired in ABOi patients up to 2 years posttransplant (P=0.010 and P=0.053), whereas CD4 helper activity was not compromised. CD4+ T cell counts were significantly lower in ABOi compared to ABOc recipients at 3 and 6 months (P=0.025 and P=0.046), but showed no differences in the percentage of Tregs. In regional lymph nodes of ABOi patients, we found a significant downregulation of CD20+ cells (P<0.0005), naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation.

CONCLUSION

An increased frequency of severe infectious diseases and BK viremia in rituximab treated ABOi renal transplant recipients may be explained by significantly downregulated CD4+ T cell counts up to 6 months and a profoundly delayed B cell repopulation, together with compromised B cell responses up to 2 years posttransplant. IL-10, as a key player in chronic BK virus infection, was not upregulated in rituximab-treated ABOi transplant recipients.

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P08-12 The use of prolonged-release tacrolimus twice a day (BID) might be beneficial for selected kidney transplant recipients

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INTRODUCTION

Tacrolimus either as prolonged- or immediate-release is part of the standard immunosuppressive therapy in kidney transplant recipients. Its highly variable metabolism rate and narrow therapeutic window requires close drug monitoring and individual dosing. Fast tacrolimus metabolism is associated with reduced kidney transplant survival.

METHODS

We describe a case of a 47 y old female transplant recipient who presented with declining kidney transplant function over time as well as a high immunological risk constellation. Tacrolimus trough levels were in the lower target range despite high doses administered. The graft biopsy revealed typical signs of calcineurin inhibitor toxicity in the absence of acute or chronic rejection, especially without any evidence of transplant glomerulopathy. Exceedingly high serum levels of immediate-release tacrolimus were confirmed in the area under the concentration time curve (AUC). Switching to a belatacept- or mTOR inhibitor-based regimen was not considered an option. Therefore, we administered prolonged-release tacrolimus twice daily in adjusted dosage in order to reduce progress of CNI toxicity as well as to secure an optimal therapeutic drug level.

RESULTS

After the change in medication, the AUC for oral tacrolimus and the transplant function improved despite higher tacrolimus trough levels and lower total dose administered.

CONCLUSION

The administration of prolonged-release tacrolimus twice daily might be beneficial for selected patients, and especially for patients with fast tacrolimus metabolism. However, the transplant community should critically discuss the off-label use. The performance of the AUC for oral tacrolimus is necessary to identify high serum levels that cause renal toxicity. It furthermore ensures optimal adjustment of the medication dosage, especially in the use of prolonged-release tacrolimus twice daily.

P08-13 Tailored immunosuppression with LCPT extended release tacrolimus based on NFAT-regulated gene expression

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INTRODUCTION

There is a narrow therapeutic window for immunosuppression (IS) with calcineurin (CNI) inhibitors. The immunosuppressive effect of CNIs differs between individuals. Therefore, the drugs` trough levels do not reflect IS and should be replaced by pharmacodynamic monitoring. Since nuclear factor of activated T-cells (NFAT)-depending gene expression correlates with cyclosporine induced IS, this study was designed to evaluate the effect of LCPT extended release Tac on NFAT regulated residual gene expression (RGE).

METHODS

Gene expressions of interleukin-2, interferon-γ and granulocyte-macrophage colony-stimulating factor and three reference genes were measured with droplet digital polymerase chain reaction (ddPCR) in whole blood samples at day 2, 7, 14, month 1 and 6 until 1 year after LT in 23 patients transplanted between February 2019 and June 2020. The RGE after Tac intake was calculated as $c_{peak}/c_0 x100$, where c_0 is the adjusted number of transcripts at the Tac predose level and c_{peak} is the number of transcripts at peak level. IS consisted of LCPT extended-release Tac introduced directly after LT, mycophenolic acid, and a corticosteroid-taper for 3 months.

All reported p-values are two-sided. $P \leq 0.05$ are considered statistically significant. To quantify the relationship between Tac peak levels and NFAT-RGE the bivariate nonparametric correlation coefficient by Spearman was calculated.

To describe time to infection a Kaplan Meier method was used. All statistical analysis was performed using SAS 9.4.

RESULTS

Tac peak levels and NFAT-RGE showed a strong inverse correlation (r=-0,8). Our descriptive analysis shows that although patients show a Tac trough level within the targeted therapeutic window, RGE might be too low, resulting in a higher risk for infection. Infection free survival was significantly different between RGE groups <30 and ≥30 (p<0.0001), while Tac trough values were comparable between the groups. Estimated glomerular filtration rate (eGFR) and creatinine were not different between the groups.

CONCLUSION

Tailored IS monitored with NFAT-RGE is promising to decrease infectious complications by optimization of the IS level in LT recipients on LCPT extended release Tac.

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Poster Session 09: Liver and visceral transplantations, Political/ economic/ legal aspects; challenges of "young" transplant recipients; Ethics in transplantation medicine

P09-02 Use of high-risk liver allografts in the era of normothermia

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INTRODUCTION

Liver transplantation (LT) is limited by organ shortage. Accordingly, LT is increasingly dependent on the use of marginal or extended criteria donors (ECD). ECD liver grafts are more susceptible to static-cold storage-related ischemia-reperfusion injury, which is associated with a higher risk of postoperative complications such as primary-non function (PNF) or early allograft dysfunction (EAD). Hence, quality assessment and prediction of liver function are pivotal prerequisites to ensure recipient safety. Normothermic machine perfusion (NMP) is increasingly utilized in LT for its potential of liver graft viability assessment prior to transplantation.

METHODS

This is an observational retrospective single center study of recipients undergoing LT following liver graft NMP between 10/19 and 05/22 at Muenster University Hospital. Liver grafts were stratified by ECD criteria. Centre definition of ECD criteria under consideration of NMP included: donor age >80 years, rescue allocation, donor risk index (DRI) > 2.0, >30% macro- or >60% micro steatosis, cold ischemia time (CIT) >8 hours, resuscitation, liver weight >2 kilogram. Primary endpoints were patient and graft survival.

RESULTS

A total of 94 NMPs were included, resulting in 90 LTs. 71 of 90 livers (79%) were ECD organs (noECD: n=19, 1ECD: n=18, 2ECD: n= 31, 3+ECD: n=22). Local protocol requires a minimum of 6 hours NMP before LT. Decision on transplantability of allografts was primarily based on perfusate lactate clearance. Perfusate lactate < 2 mmol/l at 6 hours of NMP was determined as eligible for transplant. Donor age, DRI, CIT and NMP time were comparable between groups. Mean recipients Model for End Stage Liver Disease (MELD) score was 31 for noECD, 23 for 1ECD, 24 for 2ECD, and 16 for 3+ECD. 90-day patient and death- censored graft survival for noECD, 1ECD, 2ECD and 3+ECD were 74%, 100%, 90%, 95% and 95%,100%, 93% and 95%, respectively.

CONCLUSION

Using NMP perfusate lactate is sufficient for evaluation of allograft viability of marginal donation after brain death liver grafts. 90-day patient and graft survival were comparable between subgroups. Thus, patient outcome is mainly driven by recipient MELD score.

P09-03 A multinational survey to define textbook outcome in liver transplantation

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INTRODUCTION

Textbook Outcome (TO) is a standardized composite quality measure based on multiple postoperative outcomes that represents the ideal "textbook" hospital stay. To date, only a few studies have assessed TO in the context of liver transplantation (LT), varying in the composition of the underlying composite endpoints. However, to make results valid and comparable, it is necessary to agree on the composition of TO endpoints. In this study we conducted a multinational survey within the Eurotransplant (ET) region to compile TO for LT and applied a 3- and 5-item version of this endpoint to our own patient cohort.

METHODS

Representatives of all ET liver transplant programs were invited to participate in a web-based survey designed to assess possible components of a TO in LT. Based on the responses and the ranking obtained, the 5 most important items were identified. Subsequently, an assessment of TO in our patient population of all liver transplant recipients at our center from January 2017 to December 2021 was performed.

RESULTS

28 representatives of 38 active liver transplant programs in the ET region responded to our survey. Composite textbook outcome endpoint was formed based on the 5 highest ranked responses: 1. no mortality within 90 days, 2. Freedom of retransplantation or relisting within 90 days, 3. normal liver function at discharge, 4. no prolonged length of hospital stay (>75th percentile of

all liver transplant patients), 5. no surgical complication ≥ grade 3 (Clavien-Dindo classification (CDC)). Depending on which items were included in the composite endpoint, the following TO was achieved in our cohort: top 3 = 68%, top 5 = 34%. The most important feature resulting in failure of achieving TO was surgical complication ≥ grade 3 CDC.

CONCLUSION

Base on this mutlinational survey, we show that the most universal accepted components of TO in LT are »no mortality within 90 days«, »freedom from retransplantation or relisting within the first 90 days« and »normal liver function at discharge«. This definition of a textbook outcome could serve as an easily measured composite endpoint for early postoperative outcomes after LT.

P09-05 Risk factors for steatosis after liver transplantation

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INTRODUCTION

Nonalcoholic steatohepatitis (NASH) is one of the leading causes for liver transplantation (LT). Recurrence or de novo development of steatosis after LT is observed frequently. Aim of this study is to describe potential risk factors.

METHODS

In this retrospective study, we analyzed biopsies at the time of LT (Baseline, BL) and after 1-3 years (control biopsy, C) as well as clinical and laboratory parameters of patients, who received a LT between 2005 and 2020 at the University Hospital Münster. Biopsies were blindedly evaluated by a single pathologist according to the NAFLD activity score (NAS) and graded into steatosis grade 0 (<5% affected hepatocytes), grade 1 (>5-33%), grade 2 (>33-66%) and grade 3 (>66%).

RESULTS

In total, 164 patients were included. Median age at LT was 53 years (IQR 44-61). 67.7% were male. The most common indications for LT were alcoholic liver disease (N=51, 30.5%), HCC (N=35, 21%) and NASH (N=19, 11.4%). There was no significant change in BMI (kg/m^2) between BL and C (BL: median 25.2 (IQR 22-29.1) vs. C: median 24.9 (IQR 22-28))(p=0.101). The grade of steatosis did not significantly differ between BL and C (p=0.122). At BL, 60% of the subjects had grade 0 steatosis vs. 65% at C. Grade 1 was found in 25.5% at BL

vs. 22.2% at C; grade 2 in 7.1% at BL vs. 5.6% at C and grade 3 in 11.5% at BL vs. 6.9% at C. The grade of steatosis remained the same in 47.1% of subjects, an increase ≥ 1 grade was observed in 20.7% and a decrease in 32.1%. A significant increase in steatosis was observed in subjects with the following characteristics: obesity (p=0.027) and men with low HDL levels (<50mg/dl, p=0.021) at the time of BL, obesity (p=0.002), elevated triglycerides (>150mg/dl), p=0.007) and metabolic syndrome (p=0.002) at the time of C. Men had a significantly greater decrease in steatosis (p=0.004).

CONCLUSION

We identified obesity, low HDL levels (<50mg/dl) in men, elevated triglycerides (>150mg/dl) and metabolic syndrome as risk factors for steatosis after LT.

P09-06 Pleural effusions following liver transplantation – time for a strategic change?

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INTRODUCTION

Pleural effusion (PE) following liver transplantation (LT) is a common pulmonary complication and has been associated with worse outcomes. In this retrospective study we assessed the incidence, prognosis and risk factors in patients with posttransplant PE.

METHODS

241 patients who received liver transplantation at our center between January 2017 and December 2021 were included in this retrospective study. Demographics, pulmonary and cardiac function testing, laboratory studies, intraoperative transfusion/infusion volumes, postoperative management, and outcomes were analyzed.

RESULTS

In the immediate postoperative period 183 (75,9%) patients developed PE following LT, of which 59 % were right-sided. Of those who developed pleural effusion, 64 % required pleural drainage and the need for intensified respiratory treatment. Outcomes for patients with and without PE were compared using univariate and multivariate analysis. Hypalbuminemia, large volume shifts and transfusions following intraoperative blood loss were identified as associated factors. Liver transplant recipients who developed PE had a longer hospital stay compared to those without (49.6 $\pm$ 6.59 days vs 26.1 $\pm$ 7.25 days).

CONCLUSION

In sum, we found that post-LT PE was associated with higher morbidity and healthcare utilization. Future prospective studies are needed to further clarify risk factors for developing PE following LT and to identify preemptive therapeutic strategies, if necessary.

P09-07 Biological abdominal wall expansion in pediatric liver recipients after transplantation with large-for-size organs

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INTRODUCTION

After pediatric split liver transplantation intraabdominal loss of domain due to a large-for-size left lateral graft is a frequent problem for fascial closure and potentially leads to reduced liver perfusion and abdominal compartment syndrome [1]. Therefore, delayed fascial closure with use of temporary silastic meshes and reoperation [2] or alternative fascial bridging procedures [3,4] are necessary.

METHODS

Between March 2019 and October 2021 biological meshes were used for abdominal wall expansion in 6 cases of pediatric split liver transplantation. These cases were analyzed retrospectively.

RESULTS

1 male and 5 female children with median age of 6 months (range: 0-57 months) and weight of 6 kg (range: 3.5-22 kg) received a large-for-size left lateral graft. Graft-to-recipient weight ratio (GRWR) was 4.8% (range: 1.5-8.5%) in median. Biologic mesh implantation for abdominal wall expansion was done in median 5 days (range: 3-11 days) after transplantation when signs of abdominal compartment syndrome with portal vein thrombosis in 3 and of the liver artery in 1 case occurred. In 2 cases bovine acellular collagen matrix and 4 cases ovine reinforced tissue matrix was used. Median follow up was 12.5 months (range: 4-28 months) and showed good liver perfusion

by duplex sonography and normal corporal development without signs of ventral hernia. One patient died because of a fulminant graft rejection and emergency re-transplantation 11 months after initial transplantation.

CONCLUSION

Biologic meshes can be used as safe method for abdominal wall expansion to achieve fascial closure in large-for-size children liver transplant recipients. Usage for primary fascial closure can be considered in selected patients.

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P09-08 Analysis of humoral and cellular response after the third and fourth SARS-CoV-2 vaccination in liver transplant recipients

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INTRODUCTION

Liver transplant recipients (LTR) show a decreased immune response after two SARS-CoV-2 vaccinations compared to healthy controls (HC) (1). This study aimed to assess the vaccine-induced humoral and cellular response after a third and fourth vaccination.

METHODS

In this prospective study, the humoral (anti-S RBD assay, Roche) and cellular (IGRA, EUROIMMUN) immune responses were determined after homologous mRNA-based SARS-CoV-2 vaccination of 106 LTR after a first booster and in 36 LTR after a second booster dose. Also a sensitive assay measuring cytokine production following the *in vitro* expansion of spike-specific T cells was done.

RESULTS

After the first booster vaccination, anti-S 1-RBD SARS-CoV-2 antibodies were detectable in 92% (97/106) of patients. The median anti-S RBD level increased 104-fold, but stayed significantly lower than in HC (1891.0 vs. 21857.0 AU/mL, $p<0.001$). In patients who were tested after the second vaccination and were found seronegative (<0.8 AU/mL), a third dose induced seroconversion

in 76% (19/25). Using an Interferon-gamma release assay (IGRA), a spike-specific T-cell response was detected in 72% (28/39) after the third vaccination compared to 32% (11/34) after the second vaccination. Altogether, only 7% (3/45) of LTR had neither a detectable antibody nor IGRA response after the third as compared to 19% (5/27) after the second vaccination. In a multivariate regression analysis, first vaccination within the first year after LT (OR: 8.00, p=0.023), eGFR <45 mL/min (OR: 4.72, p=0.006), and low lymphocyte counts (OR: 5.02, p=0.008) were risk factors for a low antibody response (anti-S RBD <100 AU/mL). A second booster dose induced seroconversion in 60% (3/5), and a 9-fold increase of the median antibody titer (134.6 vs. 1196.0 AU/mL).

CONCLUSION

After booster vaccinations, LTR achieved high seroconversion rates, rising anti-S antibody titers, and an increasing spike-specific T-cell response. However, the immune response remained significantly lower than in HC. Therefore, a second booster vaccination should be considered in LTR, in particular in patients with low antibody titers.

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P09-10 Extrahepatic adipose tissue could induce a preferable liver regeneration after liver resection in healthy living liverdonors

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INTRODUCTION

Extrahepatic body fat could be a relevant factor affecting liver regeneration after partial hepatectomy. The aim of this study was to evaluate the potential role of body fatty tissue in liver regeneration capacity after liver resection in a cohort of living donors.

METHODS

We observed liver regeneration in 120 patients: 70 living donors who underwent right hepatectomy and 50 recipients who got a right graft transplantation. Liver volumetry and body fat analysis were performed based on the computed tomography images with volumetry software. The gain of liver volume was calculated between three points in time considering the absolute and percentage values: before surgery and early (median 10 days, range 4-21) and late (median 27 weeks, range 18-40) after surgery. Pearson´s correlation was used to examine the potential correlation between adipose tissue and liver regeneration.

RESULTS

Pearson´s correlation showed a significant correlation between the subcutaneous fat mass index (sFMI) and early ($r = 0.173$, $P = 0.030$), as well late ($r = 0.395$, $P = 0.0004$) percental liver volume gain in the whole collective. The early percental volume gain was strongly influenced through the discrepancy of regeneration period ($r = 0.403$, $P = 0.000002$), as well the age ($r = -0.158$, $P = 0.042$). A multiple regression involving age and regeneration period as further independent variables beside sFMI showed a significant effect of

sFMI on the early (ß = 0.206, T = 2.464, P = 0.015), as well late (ß = 0.368, T = 3.594, P = 0.0006) percental liver volume gain. Under stratification in donor´s and recipient´s collectives, the effect of extrahepatic adipose tissue appears just in the donor´s collective: early (ß = 0.219, T = 2.137, P = 0.036) and late (ß = 0.390, T = 2.552, P = 0.015) percental volume gain.

CONCLUSION

Subcutaneous adipose tissue is a positive predictive factor to estimate the goodness of liver regeneration after partial hepatectomy in normostenic donors.

Posters

P10-03 Procalcitonin elevation of unexpected cause in a heart-transplanted patient with end-stage renal disease

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INTRODUCTION

The massive increase in mortality of patients with end-stage kidney disease (ESRD) is mainly due to cardiovascular reasons. However, cardiac events often present atypically and non-invasive diagnostic workup is not validated in patients with chronic kidney disease (CKD).

METHODS

Case report.

RESULTS

A 50-year-old male with ESRD who had undergone heart-transplantation 9 years ago was evaluated for potential kidney transplantation. Routinely performed examinations such as myocardial scintigraphy, chest x-ray, pulmonary function test, urology and gastrointestinal assessment showed no pathologies. In a routine blood test, elevated infection parameters including procalcitonin (PCT), C-reactive protein and leucocytes were detected. Vital parameters and physical examination were normal, and the patient denied symptoms such as coughing, shortness of breath or chest pain. A CT scan revealed no sign of infection but showed impaired contrast enhancement of the myocardium. ECG recording confirmed ST-elevation myocardial infarction and the patient was treated with anti-platelet medication and anticoagulation. TTE demonstrated decreased EF of 20%. Invasive heart catheterization detected no acute stenosis but dissolved in-stent thrombosis. The patient

required dialysis treatment due to progression of renal failure as a result of impaired cardiac output. Blood and urine cultures remained negative.

CONCLUSION

CKD is a major cardiovascular risk factor. Invasive vs. non-invasive cardiac diagnostic prior to kidney transplantation are discussed controversially. KDIGO guideline 2020 recommends non-invasive coronary artery disease (CAD) screening for asymptomatic patients at high risk for CAD. However, there is no specific guideline for previously heart-transplanted candidates for kidney transplant. A risk stratification for cardiac complications and pre-kidney transplant assessment should be implemented in clinical practice.

Elevation of infection parameters including PCT can be a sign of myocardial infarction in the absence of infection. Especially in heart-transplanted patients myocardial ischemia may be asymptomatic. This calls for an increased awareness for atypical signs such as abnormal laboratory findings.

P10-05 Mate kidney transplant analysis; single-center retrospective experience

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INTRODUCTION

There is an ongoing need for developing accurate prediction scores of post-transplant outcomes following kidney transplantation (KTx). Paired-kidney studies have been used to evaluate the impact of recipient and transplant factors on transplant outcomes by attenuating the donor confounders[1,2]. Furthermore, the preimplantation biopsy provides a histological evaluation of the graft quality, although its prediction ability in the posttransplant outcomes remains unclear[3].

METHODS

In this retrospective, observational, monocentric study, we analyzed a cohort of 200 mate kidney transplant recipients, within a mean observational time of 85 months. The aim of the study was to determine which recipient, donor, or transplant factors as well as which histological findings of the preimplantation biopsy correlate with the graft survival. Variables included age, -BMI, -sex, dialysis exposure prior to transplantation, mismatches for A-B-DR loci between donor and recipient, cardiovascular risk factors, cold ischemia time, acute tubular injury in the preimplantation biopsy, and at least one episode of rejection after KTx. The primary outcomes were graft loss or death with a functioning graft.

Generalized linear mixed model analysis for testing outcomes was performed. Given the fact that each donor donated each recipient a kidney, graft survival was examined in a relevant data structure where recipients' variables were stratified as donor-dependent variables. Gamma Akaike corrected and Bayesian information criteria were utilized to verify data model goodness of fit. Gamma regression distribution was utilized for data modeling.

Sequential Bonferroni was utilized for contrasting estimated means difference calculation. Statistical significance was set at $p<0.05$.

RESULTS

We found that the absence of severe tubular injury in the preimplantation biopsy correlates with better graft long-term survival after KTx ($p < 0,001$).

CONCLUSION

Our findings support the role of the preimplantation biopsy in the surveillance and long-term outcomes after KTx. Prospective studies implicating tubular biomarkers are needed for improving the accuracy of the current prediction tools and the current post-transplantation management.

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P10-07 Textbook outcome in liver transplantation – an international definition

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INTRODUCTION

Traditional quality assessment for liver transplantation has mainly relied on assessing individual outcome parameters, such as morbidity, mortality, rejection rates, length of hospital stay and readmission rates. We hereby aimed to define a textbook outcome, the most desirable outcome, of liver transplant patients (TO) as an composite measures.

METHODS

An online survey was conducted (surveymonkey.com) inviting all members of the International Liver Transplantation Society (ILTS) to participate. The survey invitation occurred via the online newsletter in September and October in 2021. Statements about TB were predefined and agreement of greater the 70% was considered as consensus. The thereby defined TO was thereafter applyied on a single center cohort (Charité - Universitätsmedizin Berlin) from 1/2010 to 12/2017, excluding children <18.

RESULTS

In total 25 persons finished the online survey to define textbook outcome in liver transplantation. Most of all participants were surgeons (n=18) followed by hepatologists (n=4). Following parameter met the consensus criteria define for individual TB: Absence of in-hospital mortality (74% agreement), 90-day mortality (74%), graft loss within 90 days (71%), early allograft dysfunction

defined by the EAD –score (76%), grade 3 intraoperative incidents (76%), complications according to clavien-dindo III or higher (75%) and unplanned readmission within 30 days (80%). The experts also agreed that ICU stay and total hospital stay should not exceed 7 and 20 days. Presence of rejection was not considered for TB.

Applying this TB definition on our cohort we found that 9,3% (53 / 567) fulfilled all criteria.

CONCLUSION

Textbook outcome in liver transplantation is a composite measure that captures the most desirable surgical outcomes as a single indicator. This is the first international definition for such a parameter, which could be incorporated as primary endpoint in future RCTs.

P10-11 Kidney transplantation during COVID-19 pandemic

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INTRODUCTION

Due to the COVID-19 pandemic the number of kidney transplants has shown a significant reduction. Estimating the risk of transmission of the coronavirus is of great importance. Strategies need to be developed to eliminate the risk of infection during the transplantation process.

METHODS

We present the case of a 41-year-old male who developed a SARS-CoV-2 infection after receiving a kidney transplant from a deceased donor who sufferend from COVID-19 with no evidence of a lung infection. The recipient had been on hemodialysis for more than three years. The immunosuppressive therapy was started with basiliximab, prednisolone, tacrolimus, and mycophenolate mofetil. Anti-thymocyte globulin (ATG) was not used.

RESULTS

The liquid preserving the kidney transplant tested negative for SARS-CoV-2 RNA. A prophylactic treatment for COVID-19 was initiated with SARS-CoV-2 neutralizing antibody Sotrovimab. It was ascertained at a later point that a high level of SARS-CoV-2 antibodies was present in the recipient before transplantation (> 2080 BAU/ml) and before the antibody treatment. After surgery the patient was taken into isolation. Within a week the recipient tested positive for SARS-CoV-2 with a CT value of 31 without showing symptoms. All the following tests had a negative result. Due to a COVID 19-outbreak on the ward, the initial positive test could be seen as an infection spread from the staff. Thus it cannot be assumed the kidney transplant was the source of the patient's infection. A nosokomial infection appears more likely.

The recipient remained stable throughout his stay in hospital and was discharged two weeks after surgery with a serum creatinine level of 0,93 mg/dl.

CONCLUSION

At the moment there is no proof that a kidney recipient will be infected with the coronavirus by a SARS-CoV-2 positive donor. There is no evidence to suggest that a donor kidney from a deceased person with an acceptable level of serum creatinine would have COVID-19-related damage.

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