

had been identified. In those 19 HUVECs that were homozygous for the risk alleles of SNP #1, #2 and #3, we found a tendency towards higher mRNA-expression for p14^{ARF}, p15^{INK4b} and MTPA.

Our results support data from large cohort studies in normal populations suggesting a higher risk for cardiovascular events in individuals carrying certain SNPs in senescence associated genes. Notably, this holds true in a population at high risk for cardiovascular events. The preliminary data points towards a role of the investigated SNPs for the expression profile in endothelial cells.

Table 1. Percentage of patients who are either homozygote or heterozygote for the risk or non-risk allele, respectively. Exact Fisher's test is used.

P051 RECIPIENT AND DONOR BODY MASS INDEX AS IMPORTANT RISK FACTORS FOR DELAYED KIDNEY GRAFT FUNCTION

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Introduction: Recipient obesity is associated with worse outcome after kidney transplantation, whilst the number of overweight patients on the waiting list is increasing. We investigated whether donor and/or recipient BMI correlate with the occurrence of delayed graft function (DGF) after kidney transplantation.

Methods: Retrospective analysis of 1132 consecutive cadaveric kidney transplants between 01/2000 and 12/2009. Recipients/donors were divided into four groups according to their BMI (< 20, 20–25, > 25–30, > 30). DGF was defined as the requirement for more than one dialysis within the first post-transplant week. Impact of recipient-, donor- and transplant-characteristics were analyzed using uni- and multivariate analyses.

Results: Overall DGF rate was 32.4%, mean BMI was 23.75 (SD ± 3.8) for all recipients and 24.68 (SD ± 3.6) for all donors (median age 44.0; 40.3% female). In univariate analyses DGF rate was 25.2%, 29.8%, 40.9% and 52.6% in recipients with a BMI < 20, 20–25, > 25–30 and > 30 respectively ($P < 0.0001$). Donor BMI < 20, 20–25, > 25–30 and > 30 resulted in a DGF rate of 22.5%, 31.0%, 37.3% and 51.2% ($P < 0.0001$) in univariate analyses. Acute rejection (AR) rate in the DGF-group was 24.9% vs. 9.7% ($P < 0.0001$). BMI in AR-rejection was 24.72 versus 22.4 ($P = 0.0001$). Multivariate analyses revealed overweight in the recipient as an independent risk factor for DGF.

Conclusion: Not only recipient but donor BMI as well closely correlates with the incidence of DGF after cadaveric kidney transplantation. Awareness thereof should have an impact on peri- and post transplant measures in order to avoid DGF and complications thereof in cadaveric renal transplant recipients.

P052 INCIDENCE AND CHARACTERISTICS OF CYTOPENIA IN RENAL ALLOGRAFT RECIPIENTS EXPOSED TO 200 VS. 100 DAYS OF VALGANCICLOVIR PROPHYLAXIS – A SUBANALYSIS OF THE IMPACT STUDY

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Background: Extending valganciclovir (VGCV) prophylaxis in kidney transplant recipients from 100 to 200 days significantly decreases the incidence of CMV disease and viremia. This subanalysis of the IMPACT study assesses clinically relevant cytopenic events.

Methods: In this international, randomized, prospective, double-blind study in 318 CMV D+/R- patients received VGCV prophylaxis of 900 mg/d to 200 days post transplant (200d), in comparison to 100 days followed by placebo to day 200 (100d). Adverse events (AE) and serious adverse events (SAE) for leukopenia/neutropenia were assessed according to clinical severity and temporal occurrence in association to VGCV exposure. Furthermore, a toxicity grading was applied to assess captured central laboratory values.

Results: In total, 97 (30.3%) and 46 recipients (14.4%) experienced leukopenia and neutropenia as an AE at least once during the defined assessment period, respectively (Table). Leukopenia was graded mild/moderate in 76.9% (30/39) and in 91.4% (53/58) cases in the 100- and 200-day treatment group, respectively. Neutropenia – affecting less than 15% of patients – was graded as SAE in 37.5% (9/24) and 45.5% (10/22) cases in the 100- and 200-day treatment groups, respectively.

The proportion of patients with treatment emergent grade 4 white blood cell count abnormalities was similar during the first (0.6% vs. 1.3%) and the second 100 days (0.7% vs. 1.4%) in the 100- and 200-day groups, respectively. For neutropenia, the proportion were 5.5% vs. 6.4% (first 100 days) and 4.0% vs. 2.1% (second 100 days) in the 100- and 200-day groups, respectively.

Conclusion: The overall occurrence of AE for leukopenia and neutropenia in the study was low, with a marked decrease in incidences during the second 100 days of VGCV treatment. Leukopenia and neutropenia continued to occur even after cessation of VGCV exposure in the 100-day treatment group, although at a lower rate.

P053 PROTECTIVE ROLE OF APOLIPOPROTEIN E IN AN EXPERIMENTAL MODEL OF ACUTE RENAL ALLOGRAFT REJECTION

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Objective: Apolipoprotein E (Apo E) is a multifunctional protein, originally described in the context of lipoprotein metabolism and cardiovascular disease. More recently, anti-inflammatory functions of ApoE have been documented. ApoE was studied in the context of several inflammatory disorders, but its role in the pathogenesis of acute organ rejection is unknown. In this study, we test the hypothesis that ApoE attenuates acute renal allograft rejection.

Methods: The Dark Agouti or Brown Norway to Lewis rat strain combination was used to investigate fatal acute rejection. In addition, Fischer 344 kidneys were transplanted to Lewis rats to study reversible acute rejection. Isograft recipients and untreated Lewis rats were used as controls. ApoE mRNA expression was tested in intravascular leukocytes accumulating in the blood vessels of renal grafts and in graft tissue. Apo E protein levels were assessed in graft tissue and in plasma.

Results: Intravascular graft leukocytes and renal tissue obtained from animals undergoing reversible acute rejection expressed increased levels of ApoE mRNA, whereas during fatal rejection, ApoE expression remained unchanged. On the protein level, no changes in ApoE were seen in graft tissue and in plasma. However, we do not know if local leukocytic ApoE expression results in increased ApoE concentrations inside graft blood vessels. To test the protective potential of ApoE, recipients of Brown Norway kidneys were treated with ApoE-mimetic peptide. Preliminary data suggest that this treatment can reverse fatal acute rejection.

Conclusions: ApoE may play a protective role in acute organ rejection and may have a therapeutic potential.

P055 ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION USING ANTIGEN-UNSPECIFIC IMMUNOADSORPTION

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Purpose: ABO-incompatible kidney transplantation accomplished by desensitization with antigen-specific immunoabsorption (IA) results in good outcomes. However, a unique adsorption device is needed creating high cost.

Methods: From August 2005 to August 2010, 19 patients were desensitized for ABO-incompatible living donor kidney transplantation. Six patients treated with antigen-specific IA and 12 patients treated with antigen-unspecific IA were analyzed. A protocol was established with several differences to the original Stockholm protocol: (1) a starting isoagglutinin titer of > 1:128 was accepted, (2) use of antigen-unspecific IA, (3) number of preoperative IA dependent on starting antibody titer, (4) target isoagglutinin titer at transplantation < 1:16, (5) no postoperative IA, (6) no intravenous immunoglobulins, and (7) basiliximab induction on days 0 and 4.

Results: Median starting isoagglutinin titer before desensitization in Coombs technique was 1:32 and 1:64 in patients with antigen-specific IA and antigen-unspecific IA, respectively. Six patients that received antigen-specific IA had a median of 5 IA treatments, 12 patients with antigen-unspecific IA had a median of 6 IA treatments. Median average titer drop in Coombs technique was 1.2 and 1.7 in antigen-specific IA and antigen-unspecific IA, respectively. In two patients (33%) and four patients (33%) with antigen-specific IA and antigen-unspecific IA, IA was not sufficient for recipient desensitization and a median of 8 and 2 additional plasmapheresis treatments were performed, respectively. One patient with a starting isoagglutinin titer of 1:1,024 (Coombs) had 6 treatments with antigen-specific IA and 12 plasmapheresis treatments but could not have been transplanted. The 18-month graft survival rate for the 17 ABO-incompatible living donor kidney transplants was 100%. One male recipient who was desensitized according to the Stockholm protocol died 44 months after ABO-incompatible living donor kidney transplantation from sudden cardiac death with a serum creatinine of 1.2 mg/dl. All other patients were alive with a functioning allograft at last visit. At last follow-up, median serum creatinine for 16 patients was 1.5 mg/dl, median MDRD-GFR 54 ml/minutes/1.73 m², and median urinary protein to creatinine ratio 0.1.

Conclusion: We present a simplified protocol for the desensitization for ABO-incompatible kidney transplantation that is also used for the desensitization of crossmatch-positive patients with only minor modifications.

P056 EXPRESSION OF TUBULAR WATER AND SODIUM CHANNELS IN HIGHLY SENSITIZED KIDNEY TRANSPLANT PATIENTS WITH ALLOGRAFT DYSFUNCTION

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Purpose: Kidney allograft dysfunction is often accompanied by disturbances of salt and water homeostasis. The aim of this study was to further clarify the role of the water channels, aquaporins (AQPs) and the epithelial sodium channel (ENaC) after kidney transplantation.