Diagnosis of Early Delayed Graft Function (DGF) Using TIMP-2*IGFPB-7 Product in Transplant Recipients: Preliminary Results

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Results: At time of transplantation, ADV-CD4Tvis were detectable in 30/31 patients (immunosuppression group), CMV-CD4Tvis and BK-CD4Tvis only in 12/31. No significant ADV- or HSV-DNAemia was found; only two patients showed transient CMV-DNAemia based on CMV-reactivation. Five primary CMV-infections with seroconversion and boost of CMV-CD4Tvis were observed without significant CMV-DNAemia. The mean level of ADV-CD4Tvis was 2.63 (SD 3.23), 2.03 (SD 1.8) and 1.97 (SD 3.34) 1,6,12 and 24 months after KTxs. In case of CD4Tvis <2 cells/µl 125 dose reductions of immunosuppressants (96% based on ADV-CD4Tvis) were performed in 28/31 children with a median of 4 Tvis-based dose reductions (range 0-10) per patient. 48% of these were carried out in the first six months. After ADV-CD4Tvis levels were observed with subsequent increase after dose reduction of the immunosuppression, ADV-CD4Tvis are most suitable for immune monitoring, especially of BKV-nephropathy (even in children) and stable combined with ADV or HSV-DNAemia. Random monitoring of ADV-CD4Tvis is recommendable especially in the first post-KTx year to prematurely identify overimmunosuppression.

Conclusions: Under the intensified immunosuppression during the initial post-KTx period low ADV-CD4Tvis levels were observed with subsequent increase after dose reduction of the immunosuppression. ADV-CD4Tvis are most suitable for immune monitoring, cause of BKV-nephropathy (even in children) and stable combined with ADV or HSV-DNAemia. Routine monitoring of ADV-CD4Tvis is recommendable especially in the first post-KTx year to prematurely identify overimmunosuppression.

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PO2190
Regulatory T Cells, BK Virus Infection, and Long-Term Outcomes in Kidney Transplant Recipients


Background: Regulatory T cells (Tregs) may inhibit pathogen-specific immunity in infectious disorders. We monitored Treg levels during BK virus (BKV) viremia/viruria, examined pattern of Tregs that might contribute BKV infection, and assessed their prognostic value for the KTx outcomes.

Methods: We evaluated 20 KTxs recipients (male:13, mean age:41±12 years, living donor 15) in whom BKV viremia/viruria was detected at a median 12.6 (IQR, 4.6-31.2) months after KTxs. Serum and urine BKV DNA were measured by real-time PCR at baseline, 1 and 3 months after detection of BKV viremia/viruria. Lymphocyte profile and CD4(+)CD25highCD127low/− FoxP3+ Tregs were measured by flow cytometry concurrently at these time points. Graft outcomes over 8 years were examined in relation to BK viremia, viruria levels, and lymphocyte profiles.

Results: At the time of diagnosis of BKV viremia/viruria, 17 (85%) patients were on calcineurin inhibitor (CNI)-based triple immunosuppression. CNI was discontinued in 9 patients, sirolimus was started in 3 of them. Mycophenolic acid was switched to azathioprine or the dose was decreased in all patients. Reduction in overall immunosuppression was associated with improvement of BKV viremia/viruria. Tregs and CD4(+)CD25highCD127low/− FoxP3+ Tregs were measured by flow cytometry concurrently at these time points. Graft outcomes over 8 years were examined in relation to BK viremia, viruria levels, and lymphocyte profiles.

Conclusions: Tregs may play a role in BKV infection, reduction in the overall amount of immunosuppression is associated with improvement of BKV viremia/viruria accompanied by a decrease in Treg levels. Future work is needed to discriminate predictors of allograft failure in patients with BK nephropathy.

PO2191
Expansion and Characterization of Regulatory T Cell Populations from Korean Kidney Transplant Recipients

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Background: The development of immunosuppressants has enabled remarkable progress in kidney transplantation (KT). However, current immunosuppressants cannot achieve induction of immune tolerance and their nonspecific immunosuppressive effects result in many adverse effects. Regulatory T cells (Tregs) play crucial roles in controlling allospecific immune responses. This study evaluated the distribution of Tregs and their effects on kidney allograft function in Korean KT recipients.

Methods: We enrolled 144 KT recipients with stable graft function between 1989 and 2018. Differentiation and expansion of Tregs were studied by flow cytometry to compare the Tregs subpopulations. Tregs were defined as CD4(+)CD25highCD127low/−FoxP3+ cells.

Results: Among the 144 patients, 75 patients (65.8%) were males and mean follow-up period was 144.3±111.5 months. All patients received calcineurin inhibitors as maintenance immunosuppressants. Patients with follow-up period more than 144.3 months tended to have more gaging Tregs numbers than that in shorter follow-up period (92.3±142.4 vs. 50.1±76.4, p=0.061, respectively). There were no significant differences in Tregs subpopulations between patients with patients with creatinine more than 1.5 mg/dl and patients with serum creatinine less than 1.5 mg/dl. In terms of the number of Tregs, when the trough level of tacrolimus was at an appropriate level, the number of Tregs tended to be higher than that of Tregs when the trough level of tacrolimus was low or high, and the organ function of the transplant was also stable.

Conclusions: Tregs counts may be associated with transplant outcomes considering that there is a relationship between these cells and kidney graft function.

Regulatory T cell subpopulation according to the patient’s characteristics.

PO2192
Diagnosis of Early Delayed Graft Function (DGf) Using TIMP-2*IGFBP-7 Product in Transplant Recipients: Preliminary Results

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Background: DGF is acute kidney injury (AKI) defined as need for dialysis within one week of renal transplant. AKI is defined by a change in serum creatinine (SCR), however early recognition is limited by delay in creatinine rise. Accurate early biomarkers may lead to prevention or treatment of established AKI. The product of two novel biomarkers of cell cycle arrest, tissue Inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein (IGFBP-7) have shown promise in predicting AKI. In prior studies, TIMP-2*IGFBP-7 ≤0.3 had high negative predictive value and ≥2 high positive predictive value for AKI.

Aims - 1) Investigate the early diagnostic value of TIMP-2*IGFBP-7 for DGf; 2) Correlate TIMP-2*IGFBP-7 with long term graft function.

Methods: This is a prospective, double-blinded single center observational study with post-enrollment of 150 transplant recipients. Urine TIMP-2*IGFBP-7 was measured in (ng/mL)1/1000 with a commercial kit, Nephrocheck (Astute Medical, San Diego, CA) at 4-12 hours, 48-72 hours and 72-96 hours post-transplant. SCR was measured just prior to transplant, 1 week post-transplant, and at 1, 3, 6, 9 and 12 months post-transplant.
Results: Thus far, 64 patient samples have been collected, 11 with DGF. Mean TIMP-2*IGFBP-7 means were higher than prior reports, suggesting mild renal injury in the peritransplant period in those patients without DGF. The current sample size is too nonsignificant.

Methods: (i) RNA-sequencing of native kidney from 6 HCT recipients with kidney injury was performed. We compared the transcriptome profile to that of allograft kidney. (ii) Urine samples from 9 HCT recipients were collected. We calculated the CTOT-04 signature score for each recipient. We compared the score to that of kidney allograft recipients.

Results: Of the 4188 genes (26% of 16375) that were different (FDR-P<0.05), shared genes revealed enrichment of innate and adaptive immune system pathways. Urinary cell CTOT-04 signature score was higher in AKI/inflammation/injury in HCT recipients is immune mediated, (ii) urinary mRNA profile may be used as a noninvasive biomarker.

Conclusions: These preliminary results confirm the use of TIMP-2*IGFBP product measured by Nephrocheck in the diagnosis and prediction of DGF in the post-kidney transplant period as early as 4-12 hours, and peaking at 24-48 hours. The non-DGF TIMP-2*IGFBP-7 means were higher than prior reports, suggesting mild renal injury in the peritransplant period in those patients without DGF. The current sample size is too small and underpowered as of yet to draw conclusions on prediction of long-term renal dysfunction.

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