Abstract# 721

Angiotensin II Type I Receptor Antibodies and Kidney Graft Outcome.

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Purpose: In kidney transplantation, antibodies specific for non-HLA antigens has been associated with augmented risk for antibody mediated rejection (AMR) because of their ability to determine vascular lesions and consequently allograft injury. Some studies associated antibodies specific for Angiotensin II Type-1 Receptor (AT1R) with antibody-mediated kidney allograft rejection. To analyzed the role of HLA and non-HLA antibodies on graft survival, we studied de novo development of AT1R-antibodies in kidney transplanted patients showing or not donor-specific anti-HLA antibody (DSA) production and correlated the results of antibody analysis with kidney graft outcome.

Methods: Sera from 52 kidney transplanted patients were analyzed for AT1Rantibodies using a new ELISA assay. Thirty-two of the 52 patients had had developed post-transplant DSA; in 27 of these we also tested the ability of DSA to fi x C1q. As for graft outcome, 31 patients suffered graft failure/dysfunction for AMR defined by clinical data and/or histopathologic findings according to the Banff classification. Data on C4d staining of biopsies were available in 22 patients only.

Results: Sixteen (31%) of the 52 kidney transplanted patients resulted DSA negative/ AT1R-antibody negative and did not show AMR: 3 of these suffered graft dysfunction for chronic allograft nephropathy, and 6 had hypertension. Twenty (38%) patients were DSA positive/AT1R-antibody negative: 16 suffered graft failure/dysfunction for AMR, and 4 had hypertension. Thirteen of the 15 DSA positive/AT1R-antibody negative patients were tested for C1q antibodies and showed positivity for C1q fixing DSA. Twelve (23%) patients resulted DSA positive/AT1R-antibody positive: all showed graft failure/dysfunction for AMR, and 11 were C1q-DSA positive also. The remaining 4 (8%) patients showed DSA negative/AT1R-antibody positive results: 3 suffered graft dysfunction for AMR. The production of DSA only or DSA plus AT1R-antibodies showed significant associations with kidney graft failure/ dysfunction ($P=0.0006$ and $P<0.0001$ respectively).

Conclusion. Our study confirms the crucial role of HLA-DSA production in kidney transplantation and underlines the synergic effects of AT1R-antibody development. Monitoring for anti-AT1R should help in patients risk assessment and represents a non-invasive tool for identifying patients who need specific therapies to prolong graft survival.