Abstract# 681

Angiotensin Type 1 Receptor Antibodies and Cardiac Allograft Vasculopathy Late After Heart Transplantation: A New Pathway for Coronary Endothelial Injury?

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Cardiac Allograft Vasculopathy (CAV) is the main cause of late graft failure after heart transplant (HT), with chronic immune-mediated endothelial injury as a major pathogenetic mechanism for its development. Recent studies suggest an increasing role for immune responses against non-HLA antigens in the pathogenesis of allograft rejection. In this context, angiotensin type 1 receptors (AT1R) represent a non-HLA target associated with antibodies (ab) development, related to several manifestations of vascular injury, including malignant hypertension and autoimmune vascular diseases. Following initial findings linking AT1R ab to microvasculopathy early after HT, herein we tested the hypothesis that, late after HT, AT1R ab could be related to angiographically detected CAV. Between 2008 and 2013 we enrolled consecutive HT recipients with CAV, as assessed by coronary angiography, and for whom a serum sample for off-line assay was available. Among all the remaining HT recipients followed by our center, we chose a control group matched for age and gender, with availability of serum drawn within 3 months from a CAV-negative angiography. AT1R ab were assessed by a commercial ELISA assay and concentrations expressed as median (25th–75th percentile). 72 patients fulfilled inclusion criteria: 79% males, 40% with pre-HT ischemic etiology, 57±13y old at a median (range) of 6 (1-25)y after HT, and 53% affected by CAV. Median AT1R ab concentration was 5.97 (2.37-10.46) U/ml. While age, gender, and time from transplant were not associated with AT1R levels, patients with CAV tended to have higher AT1R ab levels than those without (7.74(2.85-11.19) vs. 5.16(1.61-8.05) U/ml; P=0.09). ROC analysis identified a level of AT1R ab of 8 U/ml as the most accurate threshold associating with CAV (P=0.03). Multivariate logistic analysis showed that patients with AT1R ab ≥ 8U/ml retained 3-fold odds for CAV, after adjusting for possible confounders, including time from HT, pre-HT ischemic etiology, and renal function (P=0.03). This cross-sectional study provides first suggestive evidence that AT1R ab may be involved in CAV development late after HT. Further longitudinal analyses including non-immune mediated CAV risk factors are needed to confirm these preliminary findings.