

# Occurrence of Non-HLA Antibodies Against MICA, AT1R and ETAR after Heart Transplantation Is Associated with Cardiac Allograft Vasculopathy



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**Objective:** Cardiac allograft vasculopathy (CAV) after heart transplantation (HTx) is a major therapeutic challenge, occurring in over 50% of HTx recipients in the first years after transplantation. Antibodies against human leukocyte antigens (HLA) or non-HLA antigens like major histocompatibility complex class I-related chain A (MICA), angiotensin type 1 receptor (AT1R) or endothelin receptor A (ETAR) gain in importance as modulators of allograft function and survival.

**Methods:** Sera of 116 HTx recipients were screened post-transplantation for MICA, HLA class I and class II antibodies by Luminex-technology and for AT1R and ETAR antibodies by ELISA. Coronary angiography was performed to diagnose CAV according to ISHLT recommended guidelines. For statistical analysis gender, age, status of CAV, PRA level before HTx and the number of blood transfusions was documented.

**Results:** 38% of the HTx recipients (n=44) developed CAV whereas coronary angiographic diagnosis of CAV level identified 35 patients with CAV1, seven patients with CAV2 and two patients with CAV3. HTx recipients developed antibodies against HLA (12.9%) to a lower extend than against non-HLA antigens, especially against AT1R (35.3%) and ETAR (47.4%). CAV appeared in 27.1% of recipients with non-HLA antibodies, whereas 5.8% of the recipients with HLA antibodies developed CAV. Significant more recipients with CAV were positive for AT1R (30.2%) and ETAR (37.2%) antibodies compared to CAV-positive recipients that were positive for HLA class I (2.3%), HLA class II (9.3%) and MICA (13.9%) antibodies ( $p < 0.05$ ). Furthermore, recipients with non-HLA antibodies developed CAV earlier (69.1mo) than recipients without these antibodies (80.1mo).

**Conclusions:** HTx recipients with diagnosed CAV possess a higher frequency for positive detection of non-HLA antibodies, especially against AT1R and ETAR. Additionally, non-HLA antibodies are linked to earlier incidence of CAV after HTx. The screening of HLA and especially of non-HLA antibodies after HTx is recommended to identify patients with an increased risk for CAV.

## Assigned speakers:

MD, PhD Markus Barten, University Leipzig, Heart Center , Leipzig , Germany