Necessity of Monitoring Non-HLA Antibodies in Ventricular Assist Device Recipients.

Sandy von Salisch, Duska Dragun, Hartmuth B. Bittner, Jens Garbade, Maja-Theresa Dieterlen, Stefan Dhein, Friedrich W. Mohr, Markus J. Barten. Department of Cardiac Surgery, Heart Center Leipzig, Leipzig, Germany; Clinic for Nephrology and Intensive Care Medicine, Charité-Universitätsmedizin Berlin, Berlin, Germany

Objective: It is known that patients bridged to heart transplantation with ventricular assist device (VAD) have a higher incidence to develop antibodies directed against human leukocyte antigen (HLA). Both HLA antibodies and non-HLA antibodies like major histocompatibility complex class I-related chain A (MICA) and functional autoantibodies against angiotensin type 1 receptor (AT1R) and endothelin receptor A (ETAR) are implicated in the pathogenesis of acute rejection (AR) and cardiac allograft vasculopathy (CAV). Hence, in this study we monitored HLA and non-HLA antibodies in VAD recipients (VADR) during the first year after VAD-implantation.
Methods: Sera of 29 VADR were analyzed by Luminex for HLA and MICA (cut-off 3) and by ELISA for AT1R and ETAR antibodies (cut-off 17 Units). Blood transfusions, VAD-type, gender and age were reviewed.
Results: The average age of the group was 53.6±13.4 years (26 men). The majority of VADR were positive for AT1R (65.5%) and ETAR (68.9%) antibodies. Of note, most of the VADR showed extremely high antibody titres up to 1000 U (27.6% each) or up to >2000 U (AT1R: 24.1%; ETAR: 34.5%). Almost half of the VADR, 48.2%, developed moderate titres of HLA and/or MICA antibodies within the first year. Out of these VADR 27.5% were antibody positive for HLA-class I, 24.1% positive for HLA-class II antibodies and 17.2% positive for MICA antibodies, respectively. In particular, an accumulation of antibodies with specificities was observed against: (1) HLA class I: HLA-A68, -A80, -B67, -B73, -B76; (2) HLA class II: HLA-DR-1, -DR4 or -DR9, and (3) MICA: MICA07, -19, and -27.
No significant difference in the number of received blood products were observed between antibody-negative or -positive VADR, but AT1R/ETAR positive VADR received a higher amount of blood transfusions (55.5±77.6 vs. 16.1±9.5).
Conclusion: This study revealed for the first time the incidence of non-HLA antibodies in VADR. As both HLA and non-HLA antibodies like AT1R/ETAR and MICA are involved in the pathogenesis of AR and CAV, monitoring for both HLA and non-HLA antibodies should be included in clinical routine. Especially, high-titres of AT1R/ETAR antibodies may identify potential heart transplant recipients with a high immunological riskt, who warrant particular attention.
Keywords: Alloantibodies; Heart transplant patients; Graft survival; Heart failure