

## **DEPOSITION OF C4D IN FAILED CARDIAC ALLOGRAFTS IN ASSOCIATION WITH NON-HLA IGM ANTIBODIES**

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**Objectives:** The presence of pre-existing IgG antibodies to donor HLA antigens results in rapid rejection of transplanted organs, and this situation is usually avoided. However, non-HLA antibodies, especially of the IgM class, also called autoreactive antibodies, are not thought to affect graft survival. We performed a retrospective study of 616 adult cardiac transplant recipients to investigate the role of pre-formed IgM non-HLA antibodies on cardiac allograft survival and whether they are associated with C4d deposition.

**Methods:** The survival of 616 adult cardiac transplant recipients has been investigated. Antibodies were defined using cytotoxicity (CDC) assays, and HLA specificities were defined using Luminex and ELISA-based systems. Hearts specimens (either post-mortem or last biopsy before death) from 34 patients who died in the first year were available for immunocytochemical analysis for C4d deposition.

**Results:** HLA-specific antibodies were present in 31/616 heart recipients; in 7 of these patients, the antibodies were donor-specific. Non-HLA IgM antibodies were detected in 59/616 recipients who did not have HLA-specific antibodies; these patients had a 1yr, 2, 5 and 10 year survival of 55.9, 54.2, 48.0, and 41.7% compared to 75.5, 73.6, 66.6 and 55.5% for those without antibodies ( $p=0.0037$  logrank). Positive capillary staining for C4d was found in post mortem material from 19/34 patients; 2/6 with donor specific IgG; 13/17 with non-HLA IgM; and 4/11 from patients negative for IgG antibodies.

**Conclusions:** The presence of C4d positive capillaries in a high proportion of post-mortem samples from patients with pre-transplant non-HLA IgM antibodies suggests humoral rejection in this group of patients.