

Transplantation. 2013 Oct 24. [Epub ahead of print]

Increased Negative Impact of Donor HLA-Specific Together With Non-HLA-Specific Antibodies on Graft Outcome.

Reinsmoen NL, Lai CH, Mirocha J, Cao K, Ong G, Naim M, Wang Q, Haas M, Rafiei M, Czer L, Patel J, Kobashigawa J.

Source

1 HLA Laboratory, Cedars-Sinai Medical Center, Los Angeles, CA. 2 Biostatistics Core, Research Institute and General Clinical Research Center and Cardiothoracic Surgery, Cedars-Sinai Medical Center, Los Angeles, CA. 3 MD Anderson Medical Center, Houston, TX. 4 Pathology, Cedars-Sinai Medical Center, Los Angeles, CA. 5 Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA. 6 Address correspondence to: Nancy L. Reinsmoen, Ph.D., D(ABHI) HLA Laboratory, Cedars-Sinai Medical Center, 8723 Alden Dr, SSB # 197, Los Angeles, CA 90048.

Abstract

BACKGROUND:

De novo donor HLA-specific (dnDSA) and non-HLA antibodies including antiangiotensin type 1 receptor antibodies (AT1R-abs) have been associated with antibody-mediated rejection (AMR) and decreased graft survival as well as cellular-mediated rejection (CMR) and early onset of microvasculopathy in heart transplantation. The aim of our study was to determine the impact of anti-AT1R-ab and anti-donor HLA-specific antibody (DSA) on clinical outcomes.

METHODS:

Pretransplant and posttransplant sera from 200 recipients transplanted between May 2007 and August 2011 were tested for DSA (Luminex-based single antigen bead assay) and AT1R-ab (enzyme-linked immunosorbent assay). Two cutoff levels (≥ 17 and ≥ 12 units) were used to define high and intermediate binding of AT1R-ab. Clinical parameters examined were 5-year AMR/CMR (\geq grade 2), coronary artery vasculopathy, and survival.

RESULTS:

At 2 years after transplant, freedom from AMR and/or CMR was 95.4% for those with no DSA ($n=175$), 66.9% for those with dnDSA ($n=19$), and 25% for those with DSA at transplant ($n=6$) ($P<0.0001$). Neither ≥ 17 nor ≥ 12 units of pretransplant levels indicated a significant difference in freedom from AMR and/or CMR. When both dnDSA and AT1R-ab ≥ 17 or ≥ 12 units were considered, freedom from AMR and/or CMR decreased to 50% and 45% ($P<0.0001$), respectively. Coronary artery vasculopathy and survival were not significantly impacted.

CONCLUSIONS:

These results show the increased negative impact of dnDSA and AT1R-ab on freedom from AMR and/or CMR and an increased hazard ratio when both parameters are considered. Both HLA- and non-HLA-specific antibodies seem to impact graft outcome in heart transplantation.