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Pretransplant Anti-Lamin A/C Antibodies as a Non-HLA Biomarker for Antibody-Mediated Rejection in Kidney Transplantation

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Objectives : Antibody-mediated rejection (AMR) is a primary cause of allograft failure. While HLA donor-specific antibodies (DSA) are major drivers, AMR often occurs in their absence, highlighting the role of non-HLA antibodies. This study aimed to identify clinically significant pretransplant non-HLA antibodies associated with AMR risk.

Methods : We conducted a multicenter study of 1,015 ABO-compatible kidney transplant recipients, divided into discovery (n=558) and validation (n=457) cohorts. Pretransplant sera were screened for 39 non-HLA antibodies using a multiplex bead assay. The primary outcome was biopsy-proven AMR. Cox proportional hazards models were adjusted for age, sex, BMI, desensitization, HLA mismatch, preformed DSA, and donor type.

Results : Among 39 antibodies, only anti-Lamin A/C (LMNA) was consistently associated with AMR in both cohorts. A 1-standard deviation increase in anti-LMNA levels was associated with a higher risk of AMR in the discovery (aHR=1.36, P<0.05) and validation (aHR=1.37, P<0.001) cohorts. Subgroup analyses revealed strong associations among living-donor recipients and in DSA-positive AMR cases. In exploratory analysis, pretransplant anti-LMNA levels >80th percentile were significantly associated with DSA-positive AMR (aHR=23.57, P=0.03) after full adjustment. No associations were found with T-cell mediated rejection or death-censored graft failure.

Conclusions : Pretransplant anti-LMNA antibodies are independent risk factors for AMR, particularly in living-donor and DSA-positive recipients. Anti-LMNA testing may improve immunologic risk stratification beyond conventional HLA-DSA screening.