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**O R I G I N A L A R T I C L E**

**Specificity, strength, and evolution of pretransplant donor-specific HLA antibodies determine outcome after kidney transplantation**

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| In this cohort study (N = 924), we investigated the evolution and clinical significance of pretransplant donor‐specific HLA antibodies (preDSA), detected in the single‐ antigen beads assay but complement‐dependent cytotoxicity crossmatch‐negative. Donor specificity of the preDSA (N = 107) was determined by high‐resolution genotyping of donor‐recipient pairs. We found that in 52% of the patients with preDSA, preDSA spontaneously resolved within the first 3 months posttransplant. PreDSA that persisted posttransplant had higher pretransplant median fluorescence intensity values and more specificity against DQ. Patients with both resolved and persistent DSA had a high incidence of histological picture of antibody‐mediated rejection (ABMRh; 54% and 59% respectively). Patients with preDSA that persisted posttransplant had worse 10‐year graft survival compared to resolved DSA and preDSA‐negative patients. Compared to cases without preDSA, Cox modeling revealed an increased risk of graft failure only in the patients with persistent DSA, in the presence (hazard ratio [HR] = 8.3) but also in the absence (HR = 4.3) of ABMRh. In contrast, no increased risk of graft failure was seen in patients with resolved DSA. We conclude that persistence of preDSA posttransplant has a negative impact on graft survival, beyond ABMRh. Even in the absence of antibody‐targeting therapy, low median fluorescence intensity DSA and non‐DQ preDSA often disappear early posttransplantation and are not deleterious for graft outcome. |