

IMPACT OF KIDNEY DYSFUNCTION WITH CLASS II DONOR SPECIFIC ANTIBODY (DSA) ON GRAFT SURVIVAL

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Background

Despite improved early graft survival (currently over 90% at 1-year) long-term graft loss rate has not been reduced. Both HLA antibodies and HLA donor specific antibodies (DSA) have been shown to contribute to acute and chronic allograft nephropathy (CAN), particularly the former. In a longitudinal study, HLA antibodies were linked to graft failure. Recently, Class II DSA have been shown to correlate with graft failure in renal transplant recipients with grafts surviving at least one year.

Materials and Methods

Longitudinal studies were conducted during Sep 2004-Aug 2007 for HLA antibodies in 351 kidney transplant recipients using the Luminex laboratory screening assay system. Among them, 72 recipients with transplant dysfunction after the first year post-transplant were followed for at least 6 months after HLA antibody testing. All patients had at least one year of graft functioning and lowest serum creatinine (SCr) ≤ 2.0 mg/dl. The Luminex solid phase bead assay was used to test for DSA.

Results

Two-thirds of the recipients with transplant dysfunction had HLA antibodies and 60% had DSA. Only one out of 20 patients without antibodies rejected a graft compared with 12 out of 43 patients with post-transplant DSA ($P=0.04$) and 2 out of 9 patients with non-donor specific antibodies (NDSA) ($P=0.16$). Fractions of graft failures among patients with class II antibodies (Class II only, I & II, DR, and DQ) were statistically significantly higher than those of patients without post-transplant HLA antibodies (Table).

In Figure 1, grafts of Class II DSA groups (Class II only or Class I & II group) continued to fail beyond 1 year after transplantation when compared with the other 3 groups (No Ab, Non DSA, or Class I only group), however, the differences in graft survival between Class II and other groups were not statistically significant ($P=0.05$) due to insufficient numbers of patients. Grafts of Class II DSA groups (Class II only or Class I & II group) continued to fail within 1 year after HLA antibody detection (Figure 2).

Table 1. Outcomes of recipients with transplant dysfunction according to HLA antibody groups

HLA Ab Category	N	Graft Failure N (%)	P value	Current SCr ≥ 4.0 or Graft Failures	P value
No Ab (ref)	20	1 (5.0)	(ref)	7 (35.0%)	(ref)
Non DSA	9	2 (22.2)	0.16	3 (33.3%)	0.93
DSA	43	12 (27.9)	0.04	24 (55.8)	0.12
Class I only	13	2 (15.4)	0.31	6 (46.2%)	0.52
Class II only	23	7 (30.4)	0.03	16 (56.5%)	0.06
Class I & II	7	3 (42.9)	0.02	5 (71.4%)	0.10
Class II	30	10 (33.3)	0.02	22 (60.0%)	0.08
DR	24	9 (37.5)	0.01	14 (58.3%)	0.12
DQ	13	5 (38.5)	0.02	8 (61.5%)	0.14

Figure 1. Overall graft survival of *de novo* HLA antibody groups (No Ab, Class I Only, Class II Only, Class I+II, and Non DSA groups).

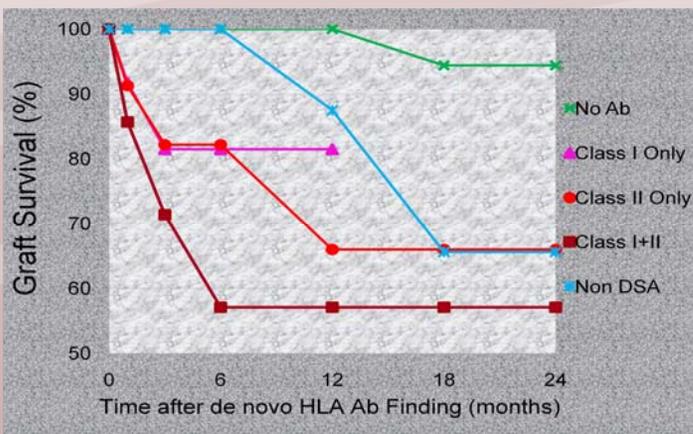
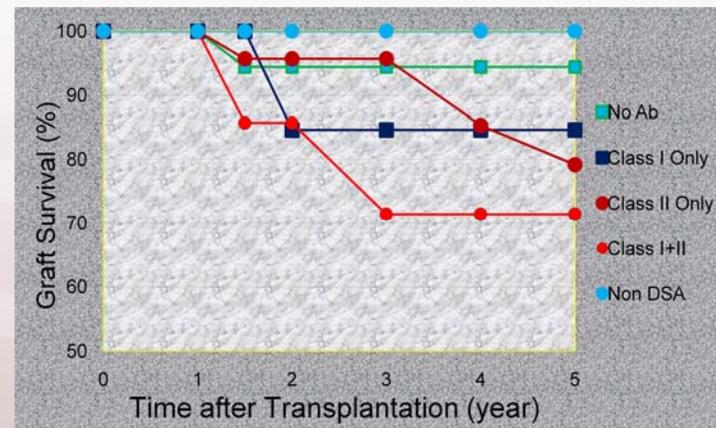


Figure 2. Graft survival since *de novo* HLA antibody detection according to HLA antibody group (No Ab, Class I Only, Class II Only, Class I+II, and Non DSA groups).



Discussion

The differences in graft survival rates between Class II and other groups did not reach a statistical significance due to insufficient number of patients. Larger prospective studies are needed to understand the impact of *de novo* HLA antibody on not only CAN but also graft survival beyond 1 year after transplantation.

Conclusion

Significant association between post-transplant HLA Class II antibodies and graft failure strongly suggests the importance of post-transplant monitoring of HLA antibodies. We postulate that amelioration of CAN graft loss will depend on DSA identification and successful immunosuppressive treatment to reduce DSA titres.