Influence of pretransplant class I and II non-donor-specific anti-HLA immunization on immunologic outcome and graft survival in kidney transplant recipients.

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Background: Sensitization against Human Leukocyte Antigens (HLA) measured as Panel Reactive Antibodies (PRA) is associated with an impaired patient and graft survival. The detailed influence of pretransplant anti-HLA sensitization (pPRA) on immunologic outcome and the individual effects of anti-HLA class I and class II antibodies remain undetermined.

Methods: We investigated the effect of anti-HLA sensitization on immunologic outcome parameters and graft survival in a retrospective long-term study. We included 1150 adult kidney transplant recipients (KTR) who had no pretransplant donor-specific antibodies (DSA) and were transplanted 1995-2014. Demographics, clinical data and long-term outcomes over a period of maximal 20 years were assessed. Pretransplant peak PRA (pPRA) was determined using solid-phase essays Elisa and Luminex. Anti-HLA immunization was defined as pPRA >0%.

Results: KTR with pretransplant anti-HLA immunization showed a significantly higher proportion of females, previous transplantations and longer time on dialysis (Table 1).

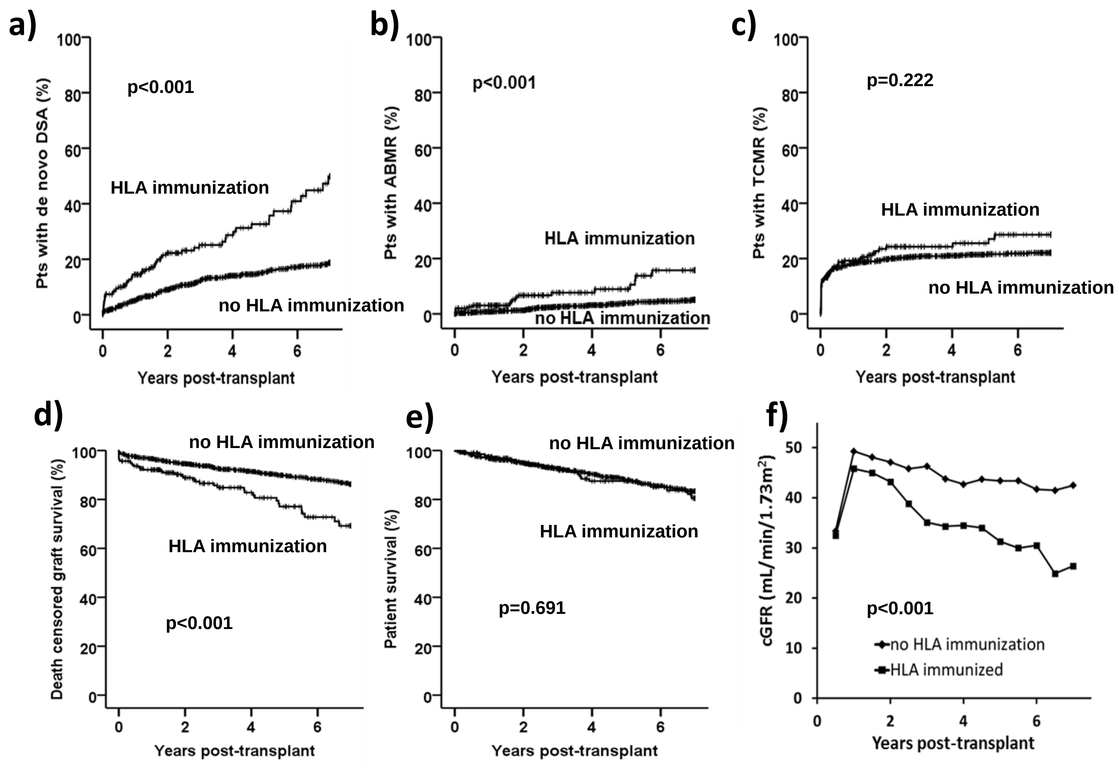
Table 1

	no pre-transplant immunization n=942	pre-transplant immunization n=208	p
Median follow up, years (IQR)	5.9 (2.8-9.4)	3.6 (1.5-6.9)	<0.001
Mean recipient age, years (SD)	50 (15)	50 (16)	0.909
Mean donor age, years (SD)	53 (15)	53 (14)	0.697
Female sex, n	319 (34%)	121 (58%)	<0.001
Median time on dialysis, years (IQR)	3.6 (1.4-6.3)	3.9 (2.9-7.3)	0.010
Prior kidney transplantation , n	7 (1%)	25 (12%)	0.001
Living donor, n	323 (34%)	57 (27%)	0.061
Median HLA-mismatches, n (IQR)	2.8 (1.7)	2.8 (1.6)	1.000
Mean cold ischemia time, hours (SD)	8.5 (6.1)	9.3 (6.0)	0.102
Delayed graft function (DGF)	282 (30%)	70 (94%)	0.319
Best Creatinine, mg/dL	1.1 (0.9-1.4)	2.2 (0.9-1.4)	0.954

SD, standard deviation; IQR, interquartile range.

They were at a significantly higher risk for developing de novo DSA, antibody mediated rejections (ABMR), had a poorer death censored graft survival (DCGS) and a lower cGFR. There was no significant difference in the incidence of T-cell mediated rejections (TCMR) or patient survival (Figure 1 a-f).

Figure 1



Cox proportional hazards models showed a significant association of both class I and class II pretransplant anti-HLA immunization with development of de novo DSA (class I HR 2.57, p<0.001, class II HR 2.49, p<0.001), ABMR (class I HR 3.74, p<0.001, class II HR 2.36, p=0.025) and death censored graft loss (class I HR 2.49, p<0.001, class II HR 1.93, p=0.005). A multivariate model adjusted for all relevant factors (recipient age, donor age, gender, time on dialysis, prior kidney transplantation, HLA-mismatches and cold ischemia time) revealed only class I but not class II pretransplant HLA immunization as a significant independent risk factor for de novo DSA, ABMR and death censored graft loss (HR 2.76, p<0.001, HR 4.16, p<0.001 and HR 2.07, p<0.001, respectively).

Conclusion: Mainly non-donor-specific pre-transplant HLA class I immunization is an independent risk factor for the development of de novo DSA, ABMR and graft loss.

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