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Impact of early rejection and ABO-incompatible kidney transplantation on chronic antibody-mediated rejection and graft outcome.

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Objectives: ABO-incompatible (ABOi) kidney transplantation (KT) has a higher rate of early antibody-mediated rejection (ABMR). Early rejection has been reported to be associated with chronic ABMR and poor long-term allograft outcomes. However, it is controversial for association of ABOi KT with chronic ABMR.

Methods: We analyzed living-donor KT patients from Severance Hospital and Seoul National University Hospital between January 2010 and December 2019. Cox regression analysis was performed to investigate impact of ABOi KT and early rejection on chronic ABMR and composite kidney outcome (eGFR decline ≥ 50% or graft failure).

Results: Among 1,790 patients, there were 1,251 ABO-compatible (ABOc) KT, 323 ABOi KT, and 216 HLA-incompatible (HLAi) KT patients. During a median follow-up of 5.9 years, there were more ABMR within 1 year in the ABOi KT vs. ABOc KT (13.2% vs. 4.8%) with similar acute T-cell mediated rejection (TCMR) (24.9% vs. 29.5%). Both early ABMR and TCMR increased risk for chronic ABMR after 1 year and composite kidney outcome independently of ABOi KT. ABOi KT had a higher risk for *de novo* DSA production; however, a lower risk for chronic ABMR (aHR 0.55, 95% CI 0.34-0.89) without significant impact on composite kidney outcome after adjustment for early rejection. HLAi KT was not associated with lower risk for chronic ABMR.

Conclusions: Although higher incidence of early ABMR could contribute to poor graft outcome in ABOi KT, lower incidence of chronic ABMR might mitigate the bad impact of early ABMR on long-term graft outcome in ABOi KT.

Table 1. Incidence of rejection according to donor incompatibility

	Donor incompatibility			*P* value
	ABO compatible	ABO incompatible	HLA incompatible	
No. of patients	1251	323	216	
Early active antibody-mediated rejection				
Events, n (%)	44 (4.8)	35 (13.2)	42 (23.1)	<0.001
Early acute T cell-mediated rejection				
Events, n (%)	283 (29.5)	67 (24.9)	30 (13.8)	<0.01
Late chronic antibody-mediated rejection				
Events, n (%)	43 (4.9)	4 (1.6)	13 (7.6)	0.015

Table 2. Association of ABO-incompatibility and early rejection with de novo DSA, late chronic antibody-mediated rejection, and composite kidney outcome

	De novo DSA		Chronic antibody-mediated rejection		Composite kidney outcome	
	HRs (95% CI)	*P*	HRs (95% CI)	*P*	HRs (95% CI)	*P*
Early active antibody-mediated rejection	2.10 (1.13-3.91)	0.020	2.22 (1.24-4.00)	0.010	2.29 (1.52-3.34)	0.001
Early acute T-cell mediated rejection	1.67 (0.98-2.86)	0.060	4.21 (2.78-6.40)	0.000	1.40 (1.03-1.91)	0.030
ABO-incompatibility	1.79 (1.15-2.92)	0.020	0.54 (0.29-0.99)	0.048	1.36 (0.96-.1.91)	0.080
HLA-incompatibility	1.66(0.90-3.08)	0.100	1.42(0.75-2.70)	0.275	1.14 (0.72-1.82)	0.550