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The outcome and risk factor of refractory T cell mediated rejection (TCMR) on renal allograft transplantation based on the Korean organ Transplantation registry (KOTRY)

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Objectives : Refractory TCMR (rTCMR) is a rare but critical complication affecting allograft survival. We analyzed the outcome and risk factors of rTCMR after kidney transplantation in a Nationwide prospective cohort study.

Methods : The primary outcome was death-censored graft failure. We divided recipients within the first year of transplantation into three groups based on TCMR. We categorized the groups as follows: Group 1 as the "No TCMR", Group 2 as "Resolved TCMR" (one TCMR episode and no treatment failure), and Group 3 as "rTCMR" (either two TCMR instances or treatment failure) within the first year of transplantation.

Results : A total of 10,391 kidney transplant donor-recipient pairs were analyzed. Within the first-year post-transplant, 15.7% (n=1,641) experienced a rejection event, including clinical rejection. Among them, rTCMR occurred in 6.58 % (n=108), and resolved TCMR occurred in 30.59 % (n=502). The hazard ratios (HR) for death-censored graft failure in resolved TCMR and rTCMR, compared to no TCMR, were 2.69 (95% C.I 1.953-3.705) and 10.31 (95% C.I 7.200-14.756), respectively. Multivariate Cox regression analysis revealed a strong association between graft failure and desensitization, recipient sex (female), and delayed graft function (DGF) in Group 2 and Group 3. DGF was identified as a predictor for rTCMR with a HR of 2.0 (95% C.I 1.091-3.664). The development of mixed rejection involving both TCMR and antibody-mediated rejection (ABMR) was notably pronounced in the rTCMR group compared to the resolved group (McNemar's test, $p < 0.09$, $p < 0.033$, respectively).

Conclusions : The rTCMR is fatal risk factor to allograft survival. In rTCMR, the occurrence rate concurrently with ABMR was high. Sex, desensitization, and DGF were identified as significant risk factors for graft failure in rTCMR compared to resolved TCMR.

paired biopsy_KSN.png

	None		Resolved			Refractory				
	1st biopsy (n = 1,219)	2nd biopsy (n = 1,219)	1st biopsy (n = 84)	2nd biopsy (n = 84)	McNemar	1st biopsy (n = 85)	2nd biopsy (n = 85)	McNemar		
No rejection	1,106 (90.7)	873 (71.6)	No rejection	0	38 (45.2)	No rejection	0	0		
Borderline	78 (6.4)	285 (23.4)	Borderline	0	37 (44.0)	Borderline	0	0		
TCMR	0	0	TCMR	84 (100)	0	TCMR	85 (100)	85 (100)		
			stage IA	28(33.3)		stage IA	25 (29.41)	31 (36.47)		
			stage IB	8 (9.5)		stage IB	14 (16.47)	22 (25.88)		
			stage IIA	28 (33.3)		stage IIA	25 (29.41)	18 (21.18)		
			stage IIB	7 (8.3)		stage IIB	4 (4.71)	3 (3.53)		
			stage III	1 (1.2)		stage III	1 (1.18)	1 (1.18)		
			unspecified	12 (14.3)		unspecified	15 (17.65)	10 (11.76)		
ABMR	35 (2.9)	61 (5.0)	ABMR	4 (4.8)	9 (10.7)	0.09	ABMR	2 (2.35)	8 (9.41)	0.033
stage I	1	6	stage I	1	2		stage I	1 (1.18)	1 (1.18)	
stage II	4	6	stage II	1	1		stage II	0 (0.00)	2 (2.35)	
stage III	1	3	stage III	0	0		stage III	1 (1.18)	2 (2.35)	
unspecified	29	46	unspecified	4	6		unspecified	0 (0.00)	3 (3.53)	
IFTA	96 (7.9)	147 (12.1)	IFTA	18 (21.4)	25 (29.8)	0.06	IFTA	7 (8.24)	15 (17.65)	0.045