■ ♣Sat-301 ■

Clinical significance of C3d fixing DSA on ABMR and Graft outcome in kidney transplant recipients

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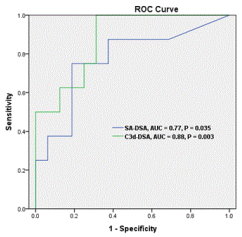
Background/Aims: Donor specific anti-HLA antibodies (DSA) are a major cause of antibody mediated rejection (ABMR) and allograft loss. Although the presence of DSA is considered as a reliable biomarker for ABMR, it is unclear it would be clinically relevant, so it need to validate whether C3d fixing DSA could predict ABMR and/or graft outcome. Our study was to evaluate clinical significance of C3d fixing DSA and SA (single antigen) DSA on ABMR and graft outcome. **Methods:** We examined 220 stable KTRs for development of de novo DSAs from July 2013 to July 2016. We biopsied 24 recipients who had de novo DSA identified by Luminex PRA and tested SA Luminex assays. Clinical data was analyzed for graft function and survival and ABMR was diagnosed, with Banff 2013 criteria. **Results:** 24 of 220 (10.9%) stable KTRs had PRA-DSAs, A median timing of DSA occurring was 9.6 (0.2-24) year of post-transplantation. 18 of 220 (8.2%) recipients had SA-DSAs (Peak MFI, 5162±1203). 13 of 220 (5.9%) recipients had C3d-DSAs (Peak MFI, 4567.7±1820). The Incidence of ABMR was 3.6% (8 of 220). Three recipients had graft failure at 2.6 (0.5- 3) year after ABMR. The incidence of ABMR was significantly higher in C3d-DSA (+) than those in SA-DSA (+) (7 of 11, 63.3% vs. 7 of 18, 38.9%, P=0.03)(Table 1). Most of C3d-DSAs were anti-HLA class2 antibodies (11 of 13, 84.6%), especially anti-DQ antibody was dominant (9 of 11, 81.8%). Peak MFI of C3d-DSA is highly correlated with peak MFI of SA- DSA (r=0.71, P<0.001). ROC curve showed C3d-class2 is a more accurate test to diagnose ABMR than class2-DSA (P<0.001)(Figure 1). Significant predictors of graft failure on multivariate analysis were high serum creatinine at the time of biopsy, ABMR, Chronic ABMR and Class2, C3d-DSA (+). **Conclusions:** We demonstrated that class2-DSA, especially class2, C3d-DSA of anti-DQ is associated with high risk for development of ABMR and graft failure. Class 2, C3d-DSA(+) may be a better marker to predict ABMR and lower graft survival rate, than class2, C3d-DSA(+). We suggested immune surveillance with C3d-DSA and subsequent allograft biopsy may be useful method to recognize development of ABMR and to prevent graft failure.

C3d-DSA is more accurate test to detect ABMR than SA-DSA



Comparisons of histopathology, immunology, and clinical outcomes by C3d-DSA

variable	C3d positive (n=11)	C3d negative (n=13)	P value
Histopathology, Banff 2013			
ABMR	7 (63.3%)	1 (7.7%)	<0.01
CABMR	4 (36.4%)	2 (15.4%)	0.66
Microvascular inflammation (G+PTC ≥2)	7 (63.3%)	1 (7.7%)	<0.01
C4d-positive	3(27.3%)	3 (23.1%)	0.59
Class I –DSA	3 (23.1%)	3 (27.3%)	0.19
Class II –DSA	9 (81.8%)	5 (38.5%)	0.047
Class I, C3d-DSA	1 (9.1%)	1 (7.7%)	0.71
Class II, C3d-DSA	9 (81.8%) /	0 /	<0.01
Peak MFI, median (range)	4107 (1507-27947)	0 (0-966)	
Anti- DQ	8/9 (88.9%)		-
Delta eGFR(ml/min/1.73m2)	-7.5±6.6	-5.8±5.8	0.49
Delta Cr.(mg/dl)	0.5±0.3	0.1±0.1	0.21
Graft loss	3 (27.3%)	0	0.08

All continuous variables are displayed as median ± SD,
Fisher's exact test. Mann-Whitney test ,G; glomerulitis, PTC; peritubular capillitis

■ ♣Sat-302 ■

Non-alcoholic fatty liver disease and its fibrosis are related to the risk of chronic kidney disease

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Background/Aims: Although non-alcoholic fatty liver disease (NAFLD) is known to be associated with increased prevalence of chronic kidney disease (CKD), there are few studies evaluating the longitudinal effect of NAFLD and its fibrotic severity on CKD development. Moreover, the issue whether this prognostic impact is independent of metabolic syndrome has not been fully explored. Therefore, this study investigated the independent association of NAFLD and advanced liver fibrosis with incident CKD using a large-scale, community-based, prospective cohort. **Methods:** Among 10,030 participants from the Korean Genome Epidemiology Study, 6,757 non-CKD participants were included. NAFLD was defined as a NAFLD liver fat score of ≥-0.640. Severity of liver fibrosis was assessed by NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4), and Forns index. Study outcome was incident CKD, defined as estimated glomerular filtration rate <60 mL/min/1.73m2 and/or proteinuria of more than 1+ on dipstick. **Results:** During a mean follow-up of 113.7±42.4 months, CKD developed in 1,437 patients (21.3%; 22.4/1,000 person-years). Multivariable Cox analysis indicated that NAFLD patients had a significantly higher risk of developing CKD compared to the non-NAFLD group (hazard ratio [HR]=1.208, 95% confidence interval [CI]=1.051-1.390). Furthermore, NAFLD patients with advanced degree of liver fibrosis had a greater risk of incident CKD (quartile 4 of NFS, HR=1.404, 95% CI=1.048-1.881; quartile 4 of FIB-4, HR=1.508, 95% CI-1.103-2.062; quartile 1 as reference). Of note, the prognostic impact of both NAFLD and liver fibrotic severity on CKD development was independent of metabolic syndrome. **Conclusions:** NAFLD and advanced liver fibrosis were independently associated with higher risk of incident CKD, suggesting that assessing NAFLD and its fibrotic burden can help to stratify the risk of adverse kidney outcomes in these populations

Table 2. Uni- and multivariable Cox regression analyses of NAFLD for the CKD development

	NAFLD (vs. no)	
	HR (95% CI)	P
Crude	1.656 (1.487-1.845)	<0.001
Model 1	1.484 (1.331-1.654)	<0.001
Model 2	1.423 (1.275-1.588)	<0.001
Model 3	1.208 (1.051-1.390)	0.01

Table 4. Uni- and multivariable Cox regression analyses of fibrosis degree for CKD development in patients with NAFLD

	Crude		Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
NFS						
Quartile 1	1 (reference)		1 (reference)		1 (reference)	
Quartile 2	1.535 (1.150-2.050)	0.004	1.215 (0.904-1.634)	0.20	1.239 (0.922-1.665)	016
Quartile 3	2.206 (1.674-2.907)	<0.001	1.505 (1.126-2.010)	0.01	1.526 (0.142-2.039(	0.004
Quartile 4	2.538 (1.953-3.329)	<0.001	1.368 (1.022-1.832)	0.04	1.404 (1.048-1.881)	0.02
FIB-4						
Quartile 1	1 (reference)		1 (reference)		1 (reference)	
Quartile 2	1.568 (1.155-2.129)	0.004	1.088 (0.798-1.485)	0.59	1.107 (0.811-1.511)	0.52
Quartile 3	2.543 (1.915-3.376)	<0.001	1.274 (0.940-1.727)	0.12	1.316 (0.97-1.785)	0.08
Quartile 4	3.201 (2.426-4.224)	<0.001	1.424 (1.044-1.943)	0.03	1.508 (1.103-2.062)	0.01