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Prognostic use of c1q-fixing antibodies after kidney transplantation

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Introduction. Antibody-mediated rejection (ABMR) is the major cause of allograft failure. We studied the evolution and prognostic effect of pre-formed and de novo anti-HLA antibodies after renal transplantation (RT) using with percentage of virtual reactive antibodies.

Material and Methods. We studied 591 patients who underwent RT between January 2008 and December 2012, followed to June 2014 (median 40 months, interquartile range 26-58). The percentage of virtual reactive antibodies was calculated with the Eurotransplant program periodically before RT, at the time of RT, at months 1, 3 and 6 post-RT, and thereafter annually.

Results.

Of the 51 patients (8.6%) who formed de novo donor specific antibodies (DSA) (70.6% class II) 21 experienced AMR, and 7 lost the graft. In the remaining 14, the DSA became negative after treatment in 7, in 3 the mean fluorescence intensity (MFI) increased and in 4 the MFI remained unchanged.

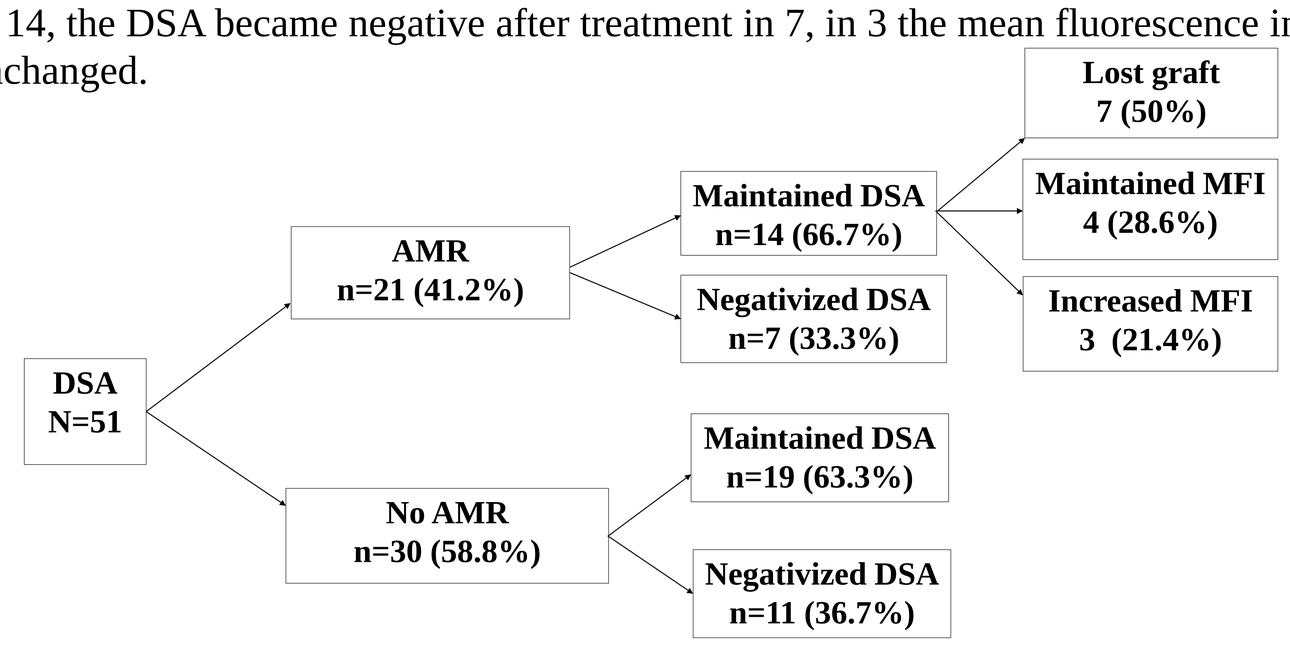


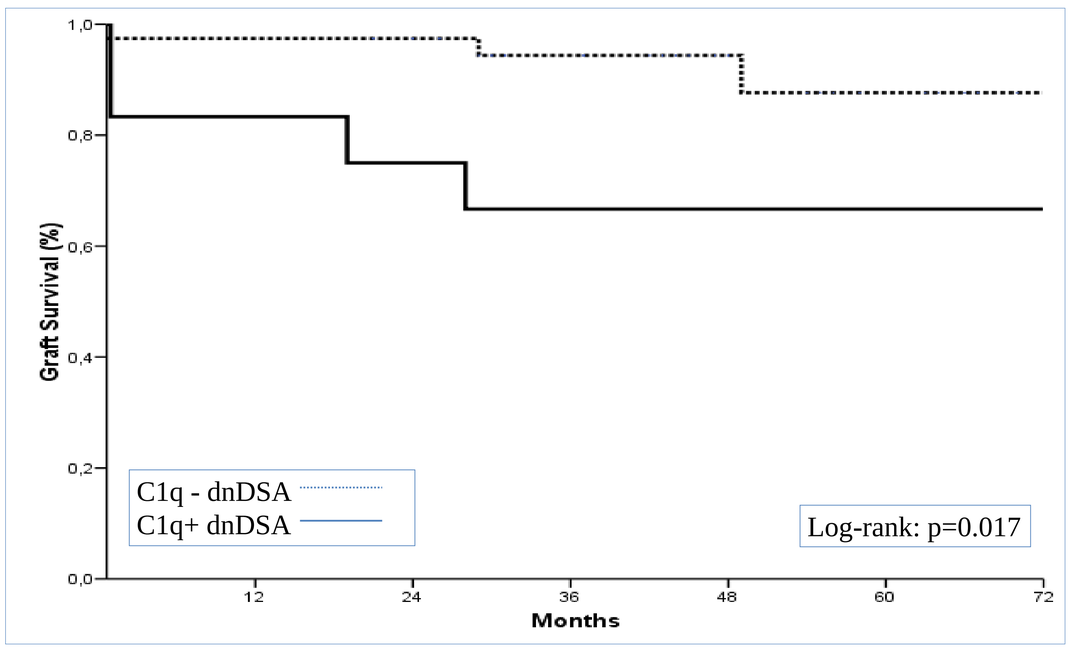
Figure 1. Evolution of the de novo donor specific anti-HLA antibodies (DSA), the mean fluorescense intensity (MFI) and the incidence of antibody-mediated rejection (AMR).

Table 1. By general linear modeling, repeated measurement showed a progressive increase of anti-HLA antibodies (percent virtual reactive antibodies) in all patients and in those with preformed antibodies.

	All patients (n=307)	Preformed antibodies (n=31)
Pre KT	3.5±13.3	34.7±26.1
3 months	3.7±13.1	-
6 months	4.0±13.7	36.4±26.3
12 months	4.4±15.2	35.1±26.4
24 months	6.0±19.2	53.6±28.3
36 months	8.4±23.9	66.7±31.2
p	**<0,001**	**<0,001**

C1q-fixing by de novo DSA was associated with a 6-fold risk of graft loss (OR 6.00, 95% CI 1.12-32.25; p=0.03), with a graft survival at six years of just 66.7% vs. 87.6% (p=0.001).

Figure 2. Graft Survival in patients with de novo donor specific antibodies according to whether they did or dit not fix C1q.



Multivariate logistic regression analysis showed that risk factors for novo DSA were cellular rejection, pre-RT antibodies and delayed graft function.

Table 2. Risk factors for novo donor specific antibody formation.

	Univariate analysis		Multiavariate analysis	
Clinical predictors (n=591)	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Donor age (per year)	0.99 (0.98-1.01)	0.465	-	
Recipient age (per year)	0.98 (0.96-1.00)	0.074	-	
Donor gender (male)	1.02 (0.57-1.82)	0.941	-	
Recipient gender (male)	0.62 (0.38-1.12)	0.105	-	
Retrasplantation (yes vs. no)	8.15 (4.41-15.05)	<0.001		
CIT (hours)	1.01(0.95-1.07)	0.747	-	
DGF (yes vs. no)	2.50 (1.38-4.55)	0.003	2.05 (1.01-4.15)	0.046
IT (yes vs. no)	2.25 (0.87-5.79)	0.095		
Time since dialysis (months)	1.02 (1.01-1.02)	<0.001	-	
Cellular AR (%) (yes vs. no)	5.78 (3.19-10.47)	<0.001	5.80 (2.82-11.90)	<0.001
Cellular AR (%) (except borderline) (yes vs. no)	4.28 (2.11-8.68)	<0.001	-	
Pretransplant antibodies (yes vs. no)	16.64 (8.58-32.27)	<0.001	12.34 (5.34-28.50)	<0.001
Creatinine at 12 months (mgs/dL)	1.71 (1.04-2.83)	0.035	-	

OR: Odds ratio; CI: confidence interval; CIT: cold ischemia time; DGF: delayed graft function; IT: Induction treatment; AR: acute rejection.

Conclusion. **Following RT there is expansion of formation of anti-HLA antibodies, with C1q-fixing de novo DSA having a worse prognosis.**

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