TACROLIMUS TROUGH SERUM LEVELS ARE ASSOCIATED WITH SUBCLINICAL INFLAMMATION IN THREE MONTH SURVEILLANCE BIOPSIES PERFORMED IN STABLE RENAL TRANSPLANTS

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Introduction:

Subclinical inflammation in stable renal transplants has been associated with progression of interstittial fibrosis/tubular atrophy and a lower graft survival in stable grafts. Patients receiving a tacrolimus-based immunosuppression have a lower prevalence of subclinical rejection. The aim is to evaluate subclinical inflammation and the immunophenotype of graft infiltrating cells in 3-month surveillance biopsies performed in stable grafts and its relationship with clinical variables.

Patientes and Methods:

Three-month surveillance biopsies are done in renal transplants fulfilling the following criteria: a) glomerular filtration rate (MDRD) > 40 mL/min, b) proteinuria < 0.8 g/dday, and c) informed consent. At the time of biopsy a blood sample to evaluate HLA antibodies by Luminex technology was obtained. Renal biopsies were evaluated according to the last up date of the Banff criteria and the number of graft infiltrating cells (CD45, CD3, CD20, CD68, CD56) was evaluated by immunohistochemestry.

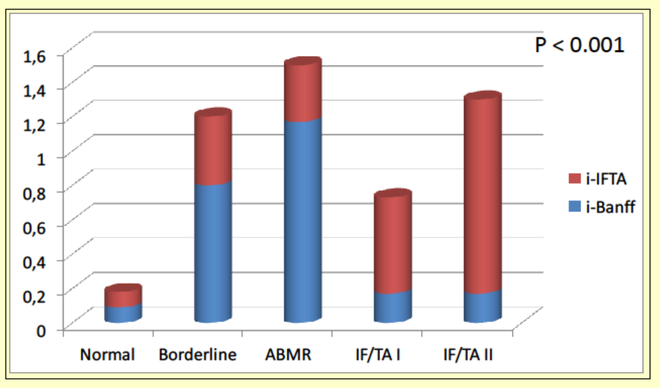
Clinical and demographic variables by histologic diagnoses

Variable	Normal	Borderline	ABMR	IF/TA I	IF/TA II	P-value
Donor age	47 ± 15	56 ± 19	46 ± 11	59 ± 14	63 ± 10	0.0023
Living/deceased	9/31	1/8	2/2	6/34	0/11	ns
Patient age	49 ± 13	54± 18	491± 9	58 ± 12	63 ± 10	0.0033
Gender (M/F)	29/11	5/4	2/2	30/10	10/1	ns
1st Tx/Re-Tx	38/2	8/1	1/3	33/7	11/0	<0.001
Time of bx	4.6 ± 1.5	3.5 ± 0.8	3.3 ± 1.7	4.2 ± 1.4	4.6 ± 1.6	ns
eGFR at bx	64 ± 18	61 ± 33	61 ± 36	56 ± 14	53 ± 15	ns
Proteinuria	0.3 ± 0.2	0.3 ± 0.1	0.3 ± 0.2	0.2 ± 0.1	0.3 ± 0.2	ns

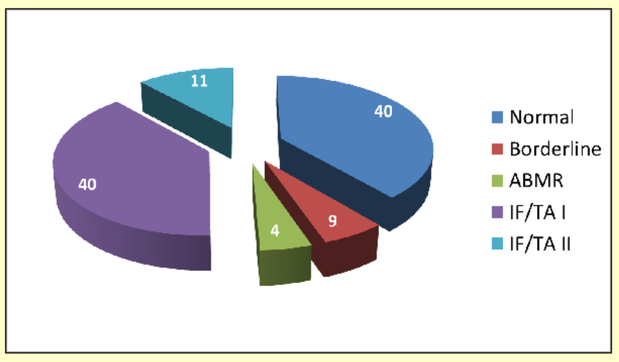
Histologic s variables by tacrolimus levels.

Variable	TAC low	TAC high	P-value
N	58	41	
TAC levels	7.3 ± 1.3	11.8± 2.2	<0.001
Proteinuria	0.2 ±0.1	0.3 ± 0.1	ns
g-score	0.2 ± 0.6	0.2 ± 0.5	ns
i-score	0.5 ± 0.7	0.2 ± 0.4	0.0065
t-score	0.2 ± 0.4	0.1 ± 0.4	ns
v-score	-	-	-
ah-score	0.3 ± 0.5	0.5 ± 0.7	ns
cg-score	-	-	-
ci-score	0.7 ± 0.7	0.8 ± 0.7	ns
ct-score	0.7 ± 0.5	0.8 ± 0.6	ns
cv-score	0.5 ± 0.7	0.6 ± 0.7	ns

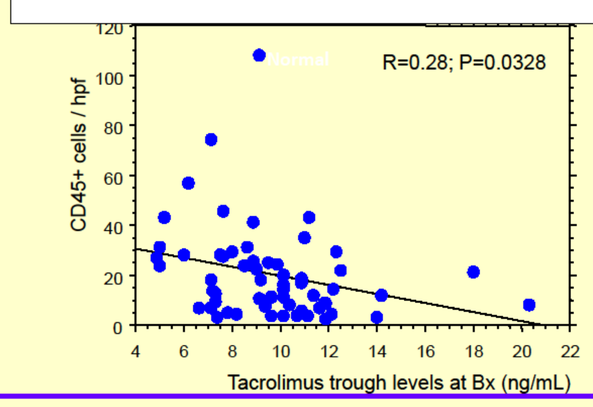
INTERSTITIAL INFILTRATING CELLS AT 3 MONTHS and at 1 year
(i-total = i-Banff + i-IF/TA)

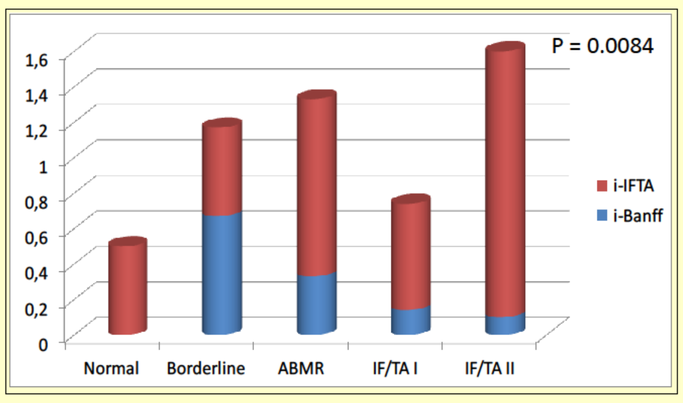


3-MONTHS SURVEILLANCE BIOPSIES
eGFR > 30 mL/min & proteinuria < 0.8 g/day
02/2012 to 05/2014
N=85



TACROLIMUS TROUGH LEVELS AND
INTERSTITIAL INFILTRATING CELLS
(adjusted for DSA at the time of Bx)





Results:

Between February 2012 and May 2014 we performed 85 biopsies. In 82 out of 85 patients immunosuppression consisted in tacrolimus, mycophenolate and steroids. Histological diagnoses were as follows: a) normal (n=33), b) borderline changes (n=5), c) antibody-mediated rejection (n=4) that was only observed in patients with donor-specific antibodies at the time of transplant and d) interstitial fibrosis/tubular atrophy (n=43). De novo donor-specific antibodies were not observed in any patient. There was an association between tacrolimus trough levels at the time of biopsy and the degree of graft inflammation evaluated by means of Banff criteria and immunohistochemestry (table 1).

Conclusions:

The prevalence of subclinical rejection in non-sensitized patients treated with tacrolimus, mycophenolate and steroids is rather low (6.2%). A higher tacrolimus exposure is associated with a lower degree of graft inflammation.

References:

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