CD45 and Vimentin as novel markers of graft outcome in a cohort of Kidney transplanted patients

Alfieri C [1], Regalia A.[1], Simonini P. [1], Ikehata M. [2], Rastaldi M.P. [2],Moroni G [1], Messa P.[1]

[1]Unit of Nephrology, Dialysis and kidney transplantation, Fondazione Istituto di Ricerca e Cura a Carattere Scientifico Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.

[2]Research Laboratory of Nephrology, Fondazione Istituto di Ricerca e Cura a Carattere Scientifico Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.

Background

Kidney transplantation (KTx) is the best therapy in presence of chronic kidney disease. Renal biopsy gives several clinical information about the graft and its prognosis. The aim of our study was to evaluate the prevalence of generic anomalies and the prognostic role of CD45 and Vimentin, respectively markers of inflammation and epithelial-mesenchimal transition.

Material and Methods

One hundred forty nine biopsy performed for clinical reasons in KTx patients (between 2009 and 2013) were processed for general histology. A minimum of 3 pictures were taken and a mean of 15±4 glomeruli were evaluated for each patient. Tubular atrophy (TA), interstitial infiltration (I-Inf) and fibrosis (IF) were defined as absent, Mild, moderate, and severe, whereas glomerulosclerosis (GS) as % of glomeruli affected. In addiction, specific stainings for CD45, vimentin (Vim) were performed and quantified as % of positive area using Imagej software. Clinical and biochemical data were collected at the time (T0), 6 and 12 mts before and after the KBx, whereas FGF-23, osteoprotegerin, fetuin and 25-OH-VITD (VIT D) levels only at T0 (Table I). A follow up time of 12 months was considered.

Results

GS was present in 25±22% glomeruli/biopsy. TA,I-Inf and IF were respectively mild in 21%,18% and 26%, moderate in 22%,30% and 26% and severe in 30%,18% and 28% of patients (Table II). CD45 and VIM were both directly correlated each other and with creatinine and inversely with eGFR and VITD (Figure 2A-D). VIM was directly related to GS degree. During the follow-up, 32 patients restarted dialysis (HD+). DD+ had lower eGFR at the time of biopsy, and significantly higher positivity for CD45 and VIM than the others. In logistic regression, differently from VIM, CD45 was independent to eGFR in predicting HD+. Moreover, by means of ROC CURVE, CD45 and VIM resulted good markers in sensitivity and specificity in predicting HD+: (AUC: CD45=0,678;VIM=0,673 – Figure 2D-E).

Parameter	All pts n=149	HD- n=117	HD+ n=32	All pts n=149
Number of patients	149	177	32	-
Age at Bx (years)	44±14	50 ±13	49 ±12	0.71
Age at Tx (years)	50 ±12	44 ±14	41 ±11	0.29
Sex (M/F)	83/66	65/52	18/14	0.94
Kind of transplant (deceased donor/living donor)	123/23	97/20	29/3	0.27
Time from Tx (years)	6 ±10	5 ±6	7 ±6	0.12
CMV IgG pos N (%)	107 (72)	82 (70)	25 (78)	0.92
HCV pos N (%)	9 (6)	4 (3)	5 (15)	0.01
HbsAg pos N (%)	4 (3)	3 (2)	1 (3)	0.88
Indication to Bx N (%) :				
-Proteinuria	22 (15)	20 (17)	2 (8)	0.05
-Reduced RF	89 (60)	71 (61)	18 (56)	
-Both	21 (14)	12 (10)	9 (28)	
-Others	17 (11)	15 (12)	2 (8)	

Parameter	All pts n=149	HD- n=117	HD+ n=32	p
SBP (mmHg)	133 ±20	113 ±16	136 ±18	0.47
DBP (mmHg)	81 ±11	81 ±11	83 ±10	0.52
Creatinine 12 mo. before Bx (mg/dL)	1.65 ±0.46	1.55 ±0.39	1.92 ±0.52	0.0004
eGFR 12 mo before Bx (ml/min)	51 ±18	55 ±18	43 ±14	0.005
Creatinine at Bx (mg/dL)	2.61 ±1.6	2.4 ±1.5	3.5 ±1.6	0.0004
eGFR at Bx (ml/min)	37 ±19	41 ±20	23 ±8.7	<0.0001
eGFR 12 mo. after Bx (ml/min)	41 ±15	43 ±15	26 ±8	0.003
Blood glucose (mg/dL)	87 ±23	89 ±22	84 ±26	0.32
Mean UProt/24h 12 mo. before Bx (g)	0.58 ±0.69	0.50 ±0.65	0.80 ±0.78	0.12
UProt/24ht at Bx (g)	1.17 ±1.9	0.9 ±1.08	2.29 ±3.62	0.0006
Mean UProt/24h 12 mo. after Bx(g)	0.79 ±1.07	0.6 ±0.67	2.5 ±2.34	<0.0001
Number of antihypertensive drugs	2.1 ± 1.1	2 ± 1.1	2.4 ± 1.2	0.687
PTH (pg/mL)	139 ±133	128 ±112	201 ±203	0.02
Ca (mg/dL)	9.29 ±0.9	9.33 ±0.97	9.17 ±0.85	0.40
P (mg/dL)	3.71 ±1.23	3.61 ±1.3	4.08 ±0.91	0.06
ALP (U/dL)	80 ±38	79 ±39	88 ±38	0.24
25(OH)D(ng/mL)	16.7 ±11.3	17 ±11	13 ±8	0.22

Table I: Clinical and biochemical characteristics of our cohort. CMV: Citomegalovirus - HCV: Haepatitis virus C - HbsAg: Hepatitis B surface antigen - RF: Renal Function; SBP: Systolic Blood Pressure - DBP: Diastolic Blood Pressure - eGFR: Glomerular Filtration Rate estimated with MDRD formula - uProt: urinary Protein excretion, HD+:Patients that restarded dialysis during the follow-up time.

Histological lesion	All pts n=149	HD- n=117	HD+ n=32	p
Sclerotic glomeruli (% ± DS)	25 ±22	22 ±20	37 ±25	0.0009
Tubular Atrophy N(%)				
-No	40 (27)	34 (29)	6 (19)	<0.0001
-Mild	32 (21)	30 (26)	2 (6)	
-Moderate	33 (22)	29 (25)	4 (12)	
-Severe	44 (30)	24 (20)	20 (63)	
Interstitial Fibrosis N(%)				
-No	32 (21)	28 (24)	4 (12)	0.0004
-Mild	37 (25)	34 (30)	3 (10)	
-Moderate	39 (26)	32 (25)	7 (22)	
-Severe	41 (28)	23 (19)	18 (56)	
Interstitial Infiltrate N(%)				
-No	52 (34)	41 (38)	10 (31)	0.06
-Mild	27 (18)	25 (22)	2 (7)	
-Moderate	44 (30)	34 (30)	10 (31)	
-Severe	27 (18)	10 (10)	31 (31)	

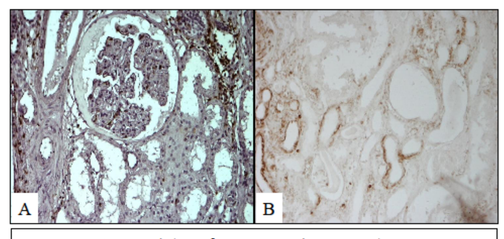
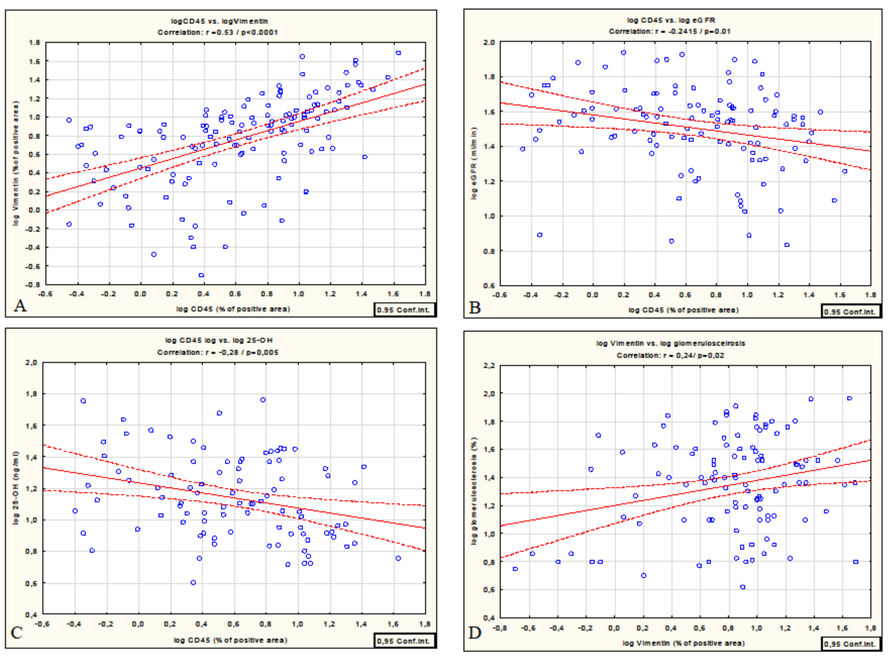


Figure 1: CD45 (A) and Vimentin (positivity) in KTx biopsies

Histological marker	All pts n=149	HD- n=117	HD+ n=32	p
CD45	6.9± 7.3	6.3 ± 5.8	12.1 ± 10.6	0.0002
Vimentin	8.7 ± 9.1	5.5 ± 7.4	14.4 ± 12.7	0.001

Table II: Histologic finding in KTx biopsies. CD 45 and vimentin positivity was calculated as positive % of total area



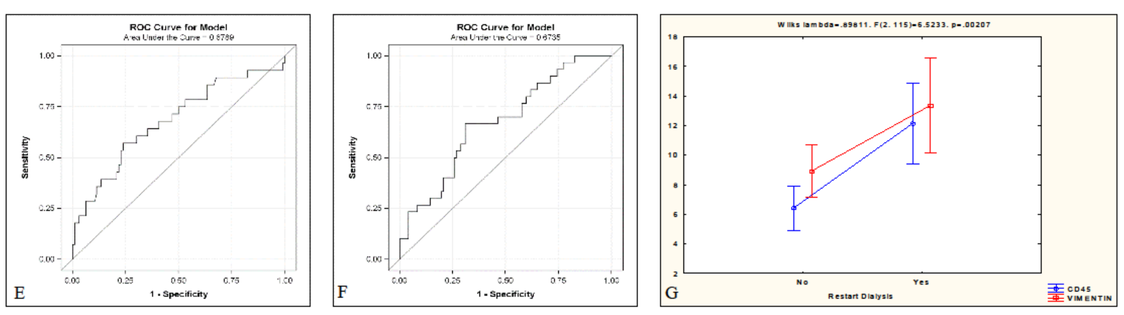


Figure 2: Univatriate regression between CD45-Vimentin (A), CD45-eGFR T0 (B), CD45-25OHvitD (C), VIM-Glomerulosclerosis (D). ROC Curve (prediction of restart dialysis during the year of follow-up): CD45 (E), Vimentin (F). ANOVA test: Group:Restart dialysis; Independent variables CD45/Vimentin (G).

Conclusions

CD45 and VIM, obtained in kidney transplant biopsies for clinical indications, were correlated each other and seem to predict graft outcome. Despite its correlation with renal function at T0, the prognostic role of CD45 is independent from creatinine and eGFR. Vitamin D levels seem to possibly influence inflammation and fibrotic processes in renal grafts.

Email address of the author:

carlo.alfieri1@gmail.com

51ERA-EDTA

376--MP

N) Renal Transplantation. N2) Clinical epidemiology of renal transplantation.

Carlo Maria Alfieri

DOI: 10.3252/pso.eu.51era.2014

Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM THE NETHERLANDS MAY 31 JUNE 3 2014

PosterSessionOnline.com