ANALYSIS OF SIGNIFICANCE OF VASCULAR REJECTION IN KIDNEY TRANSPLANT BIOPSY SAMPLES

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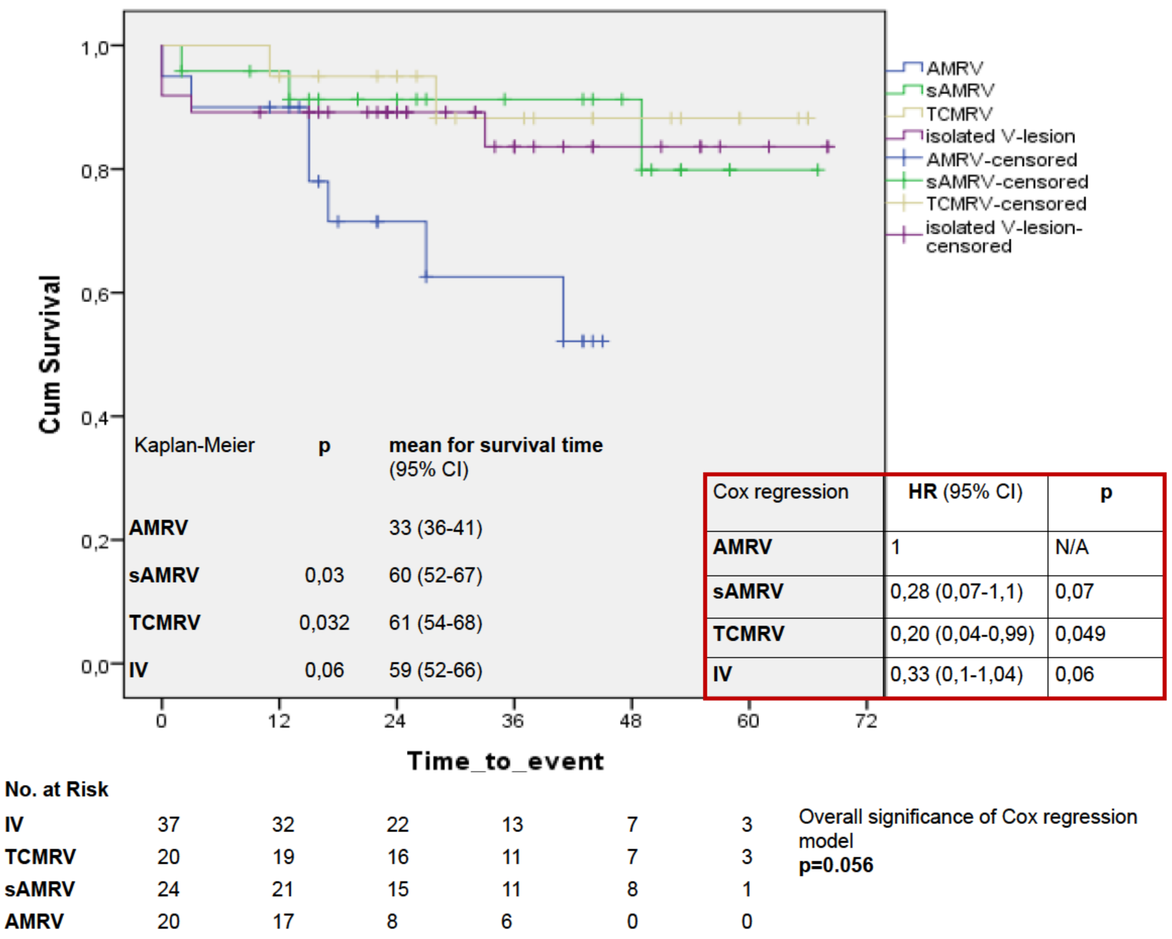
OBJECTIVES

Acute vascular rejection (AVR) is a severe clinical condition with detrimental impact on kidney allograft survival. Although it has been thought to be T-cell mediated process, recent clinical findings showed its association with donor specific antibodies (DSA) and resistance to conventional treatment. Therefore, correct assessment of AVR phenotype would be beneficial for improving long-term prognosis of kidney allograft.

Fig. 1: Kaplan-Meier curves of death censored graft survival in 4 groups of AVR



Kaplan-Meier	p	mean for survival time (95% CI)
AMRV		33 (36-41)
sAMRV	0,03	60 (52-67)
TCMRV	0,032	61 (54-68)
IV	0,06	59 (52-66)

Cox regression	HR (95% CI)	p
AMRV	1	N/A
sAMRV	0,28 (0,07-1,1)	0,07
TCMRV	0,20 (0,04-0,99)	0,049
IV	0,33 (0,1-1,04)	0,06

No. at Risk						
IV	37	32	22	13	7	3
TCMRV	20	19	16	11	7	3
sAMRV	24	21	15	11	8	1
AMRV	20	17	8	6	0	0

Overall significance of Cox regression model
p=0.056

Tab. 2: Baseline characteristics of patients with vascular rejection

	IV (n= 37)	TCMRV (n= 20)	AMRV (n= 20)	sAMRV (n= 24)	p
Age (yr)	52,6 ± 12,2	49,3 ± 13,1	48,7 ± 12,9	49,8 ± 14,9	0,658
Men, n (%)	36 (70)	15 (75)	10 (50)	19 (79)	0,18
ReTx, n (%)	4 (11)	1 (5)	10 (50)	4 (17)	**0,01**
HLA MM total	3 (3- 3,4)	4 (2,5-5)	4 (3-5)	3,5 (3-5)	0,12
Dialysis duration (mm)	27 (11-40)	16 (4,5-38,1)	43,5 (22,5-94,5)	18,5 (9-27)	**0,022**
PRA at Tx	2 (0-8)	1 (0-13)	5 (0-24,5)	18,5 (9-27)	0,484
PRA peak	6 (2-14)	8 (2-20)	24 (2,5-54)	2 (0-16)	0,13
Induction, n (%)					
none	6 (16)	5 (25)	3 (15)	8 (33)	**0,01**
basiliximab	14 (51)	12 (60)	5 (25)	11 (46)	
rATG	10 (27)	2 (10)	5 (25)	1 (4)	
rATG+ PP+ (IVIG)+ (RTX)	2 (5)	1 (5)	7 (35)	4 (17)	
Bx for cause, n (%)	23 (62)	15 (75)	19 (95)	22 (92)	**0,009**
Deceased donor, n (%)	29 (78)	14 (70)	14 (70)	17 (71)	0,85
ECD, n (%)	19 (61)	9 (60)	5 (33)	5 (29)	0,08
DGF, n (%)	14 (39)	7 (35)	7 (35)	10 (42)	0,96
Follow-up (mm)	29 (21-41)	37,5 (25-56)	20 (14,5-41)	31 (15,5-49,5)	0,07
V-lesion grade, n (%)					
1	32 (87)	13 (65)	13 (65)	12 (50)	**0,048**
2	3 (8)	6 (30)	7 (35)	11 (46)	
3	2 (5)	1 (5)	0 (0)	1 (4)	

METHODS

We reviewed 1015 patients who underwent kidney transplantation between 2010 and 2014 in order to identify those who suffered from AVR. Retrospectively, the phenotype of vascular rejection was assessed according to histopathologic finding and presence of DSA (Tab. 1).T-cell mediated vascular rejection (TCMRV) included severe tubulointerstitial inflammation. Antibody mediated vascular rejection (AMRV) included features of microvascular inflammation, C4d positivity and DSA positivity. As suspected antibody mediated rejection (sAMRV) were marked cases fulfilling 2 out of 3 features of antibody mediated rejection. Isolated v-lesion (IV) was assessed as unique group of AVR regardless of DSA presence.

Phenotype	g+ ptc	i	t	v	C4d	DSA	n
IV	0	<2	<2	1-3	neg	neg/ pos	37
TCMRV	0	0-3	0-3	1-3	neg	neg	20
AMRV	0-3	0-3	0-3	1-3	neg/ pos	pos	20
sAMRV	0-3	0-3	0-3	1-3	neg/ pos	neg/pos	24

Tab. 1: Phenotype characteristics of each patients group

RESULTS

We identified 101/1015 (10%) patients with an episode of AVR. Phenotype of acute vascular rejections was assessed as IV in 37 (37%), TCMRV in 20 (20%), AMRV in 20 (20%) and sAMRV in 24 (24%) patients. AVR was mostly diagnosed from indication biopsies as accompanied by kidney allograft dysfunction (Tab. 2). Worst graft survival was observed in AMRV group (mean for time survival 33 months) compared to 60 months in sAMRV, 61 months in TCMRV and 59 months in IV group (Fig. 1). Chronic rejection developed mostly in AMRV (45%) and sAMRV (37,5%), less often in TCMRV (15%) and IV (19%) group. HLA antibodies were evaluated in 57% of all AVRs and found to be positive in 27 % patients. Patients with histological features of antibody mediated rejection (AMRV, sAMRV) showed positive donor specific antibodies in 48%. Steroids was the most common used therapeutic modality in IV group (78 %) and TCMRV group (80%) while observed steroid resistance was quite low (3% and 25% patients, respectively) compared to sAMRV (50%) and AMRV (66%).

CONCLUSIONS

Acute vascular rejection is a significant histological finding and represents 41% of all acute rejection episodes in patients after kidney transplantation. Humoral phenotype of acute vascular rejection was associated with highest incidence of chronic rejection and worst graft survival. High incidence of chronic rejection but better graft survival was observed in sAMRV. Better graft prognosis was confirmed for cellular phenotype of acute vascular rejection.

Abbreviations: AMRV – antibody mediated vascular rejection, AVR – acute vascular rejection, Bx – biopsy, DGF – delayed graft function, ECD – extended criteria donor, IV – izolated v-lesion, mm – months, MM – mismatch, neg – negative, PP – plasmapheresis, pos – positive, ReTx – repeated transplantation, RTX – rituximab, TCMRV – T-cell mediated vascular rejection, sAMRV – suspected antibody mediated vascular rejection, Tx – transplantation, yr - years

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