CARD8 POLYMORPHISM PREDICT UTI INFECTION ONSET AFTER RENAL TRANSPLANTATION

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INTRODUCTION and OBJECTIVES

NLRP3 inflammasome is composed of the NLRP3 scaffold protein, CARD containing adaptor protein, and caspase-1. Activation of inflammasome leads to assembly of the multiprotein complex that cleaves and activates caspase-1, resulting in cleavage of pro-interleukin-1β (pro-IL-1β) and release of IL-1β that triggers downstream inflammatory response. NLRP3 inflammasome activation contributes to host defense against numerous bacterial infections including E. Coli infections.

Aim of our study was to investigate the association between the risk of urinary tract infection (UTI) and CARD8 polymorphism rs2043211, which leads to a severely truncated protein (p.C10X) in a cohort of renal transplant patients (KTRs).

METHODS

We retrospectively analyzed the CARD8 polymorphism of 188 KTR. 129 (68.6%) had "homozygous TT" while 59 (31.4%) were "allele A" carriers. For all participating patients immunosuppressive maintenance therapy included steroids, mycophenolate mofetil and calcineurin inhibitors.

RESULTS

The mean age of recipients at the time of transplant was 45.5±13.23 years and a majority of them were males 114 (60.6%). 57of 188 patients (31%) were treated with CyA, 126 (68.5%) with FK. Majority of our KTR (76.9%) presented 3 or 4 HLA mismatches. There were no significant differences between the TT and A carriers KTRs about transplant age, donor age, dialysis time, DGF, cold ischemia time or rate of acute rejection.

UTI infection was detected in 56 (29.8%) KTR of which 28 (21%) in TT patients and 28 (47.5%) in A carriers (chi-square p=0.0006; **Figure 1**). The main bacterium detected was E. Coli (80%). To determine the impact of CARD8 polymorphism on UTI onset in the first year post transplantation we performed univariate and multivariate logistic regression analysis. At multivariate analysis, independently from recipient age, DGF, acute rejection, CNI and CIT the A carriers KTRs showed a higher risk for UTI infection respect to TT KTRs (OR 3.47, 95%CI 1.67-7.22, p=0.0008, **Table 1**).

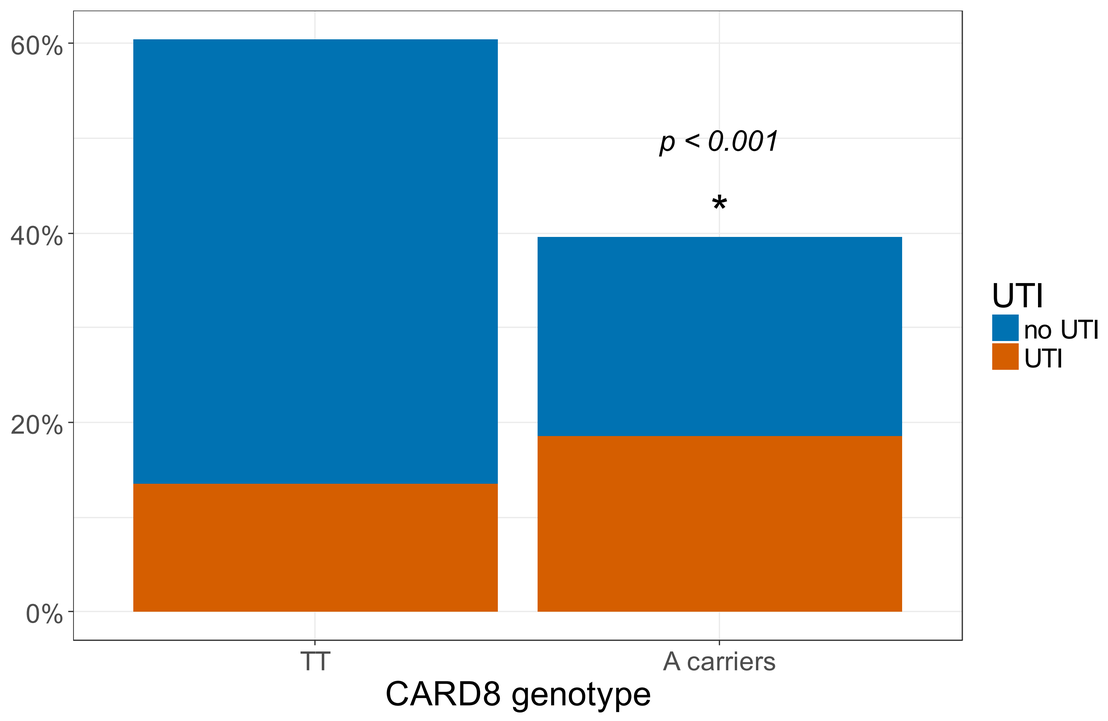

Figure 1. Frequency of UTI in the first year after transplantation by CARD8 polymorphism

	Crude OR (95%CI)	Adjusted OR (95%CI)	p
Recipient Age (years)	1.04 (1-1.08)	1.06 (1.01-1.11)	0.01
CARD8 *allele A carriers* (vs *TT*)	2.97 (1.13-7.81)	3.47 (1.67-7.22)	0.001
CIT (hours)	1 (0.98-1.01)	0.99 (0.97-1)	0.08
FK (vs CsA)	1.4 (0.53-3.7)	1.55 (0.53-4.5)	0.418
RA (vs no RA)	1.02 (0.98-1.06)	1.03 (0.95-1.05)	0.943
DGF (vs no DGF)	3.14 (1.31-11.03)	3.1 (1.41-16.93)	0.031

Table1. Uni- and Multivariable Logistic Regression for UTI onset in the first year post transplantation

CONCLUSIONS

IN CONCLUSION, OUR FINDINGS SUGGEST THAT CARD8 POLYMORPHISM MAY CONTRIBUTE TO UTI INFECTION ONSET IN THE FIRST YEAR AFTER RENAL TRANSPLANTATION LIMITING NLRP3 INFLAMMASOME ACTIVITY FOR HOST DEFENSE AGAINST BACTERIAL URINARY INFECTION.

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