THE ROLE OF TCF7L2 RS7903146 IN CORONARY ARTERY DISEASE IN NON-DIABETIC KIDNEY TRANSPLANT RECIPIENTS

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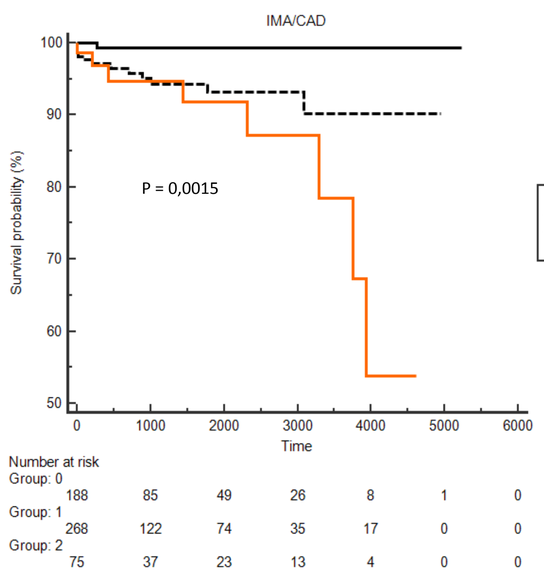
OBJECTIVES

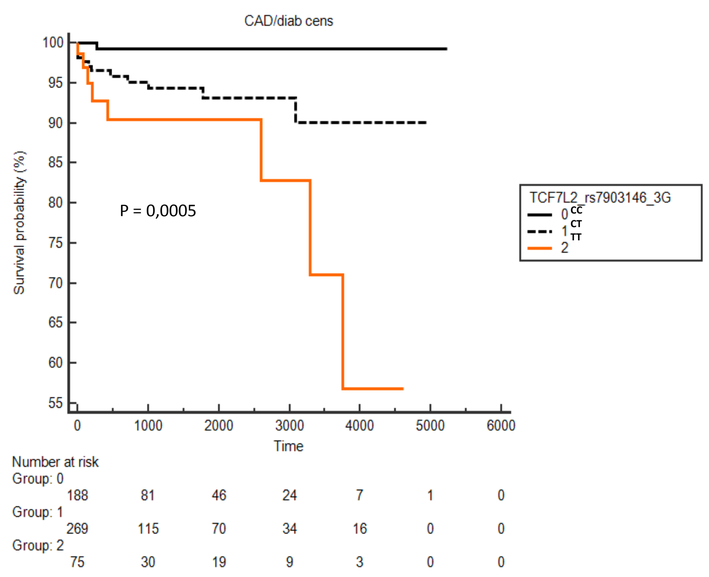
The effects of the *TCF7L2* rs7903146 C>T polymorphism on cardiovascular disease have been studied in the general population with conflicting results (1-2-3). Kidney transplant recipients (KTR) are prone to impaired glucose homeostasis and inflammation, which are both modulated by this genetic variant (3). On this basis, we performed a pilot study investigating the association of *TCF7L2* rs7903146 with ischemic cardiac events (ICE) in a large mainly Caucasian population of KTR followed-up at our Center

METHODS

We proposed this study to all KTRs who have been transplanted at our Kidney Transplant Centre over the past 15 years. Patients with pre-transplant diabetes were excluded and patients who developed post-transplant diabetes were censored at the time of diagnosis. ICE included symptomatic ischemic heart disease and acute myocardial infarction (AMI). Genomic DNA was extracted from peripheral blood by using the QiaAmp DNA Mini Kit (Qiagen Milan, Italy). Comparisons between *TCF7L2* rs7903146 genotype groups were performed by one-way analysis of variance (ANOVA) for continuous variables and chi-square analysis for categorical variables. Event-free survival analysis was performed with an actuarial Kaplan-Meyer method.

Parameter	CC (n=178)	CT (n=255)	TT (n=73)	P
Age (years)	52.1 ± 13.3	52.6 ± 11.6	52.5 ± 11.8	0.908
Male	62.4%	65.1%	67.1%	0.736
Total HLA mismatches	2.96 ± 1.06	2.83 ± 1.04	2.82 ± 1.00	0.429
BMI (Kg/m^2)	24.0 ± 3.3	24.2 ± 3.5	23.6 ± 3.8	0.389
Ever smoker	55.4%	56.5%	57.4%	0.966
Hypertensive	86.3%	80.5%	89.1%	0.113
Any previous cardiovascular event	18.5%	17.3%	15.7%	0.802
Previous ischemic heart event	11.2%	6.7%	8.2%	0.243
Previous stroke	1.1%	2.4%	0%	0.303
Delayed Graft Function	21.9%	20.4%	24.7%	0.729
Serum Creatinine at discharge (mg/dL)	2.04 ± 0.94	2.08 ± 0.84	2.09 ± 1.20	0.885
eGFR at discharge (mL/min/1.73m^2)	35.4 ± 20.4	32.4 ± 15.6	32.5 ± 14.0	0.170
PTDM	8.4%	14.1%	27.4%	<0.001





RESULTS

We included 506 patients, who received a KTx from a deceased donor (95.3%) and were on tacrolimus (90.9%), mycophenolate mofetil (MMF) or mycophenolic acid (MPA) (94.5%) and steroid therapy (82.6%). Incidence of ICE was 3.1% and 5.3% at 1 and 5 years, respectively. No differences in baseline characteristics could be noted between TCF7L2 rs7903146 CC (178/506=35.2%), CT (255/506=50.4%) and TT (73/506=14.4%) patients. As for TCF7L2 rs7903146 genotype, the 5-year risk of cardiac ischemic events was 0.8% in CC patients, 7.2% in CT patients and 9.7% in TT patients (p for trend <0.001). Previous cardiac ischemic events (HR: 8.69, 95%CI: 3.57-21.16, p<0.001), TCF7L2 rs7903146 (for each T allele, HR: 2.99, 95%CI: 1.62-5.52, p<0.001), DGF (HR: 2.42, 95%CI: 0.98-5.95, p=0.056) and HLA-mismatches (for each mismatch: HR: 1.55, 95%CI: 1.00-2.43, p=0.053) were independent predictors of post-transplant ICE in a multivariate Cox regression model. The area under the ROC curve of the sum of beta-coefficients of this model was 0.790 (95%CI 0.701-0.879), greater than the model built on only clinical variables (p=0.003).

CONCLUSIONS

In conclusion our data suggest, for the first time, that *TCF7L2* rs7903146 T allele is strongly associated with clinical events related to post-transplant symptomatic ICE in non-diabetic KTRs. As risk models for post-transplant cardiovascular diseases have shown suboptimal accuracy so far, the introduction of this polymorphism might a useful tool to improve predictive models of ICE after KTx.

References

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