DOES VKORC1 POLYMORPHISM INFLUENCE CORONARY ARTERY CALCIFICATIONS IN CHRONIC KIDNEY DISEASE PATIENTS?

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Background/ Aim

Vitamin K epoxide reductase complex subunit 1 (VKORC1) haplotype combinations were found to be associated with the risk of developing vascular diseases. The C-allele of polymorphism rs2359612 (VKORC1: c.283+837C>T) (see **Fig. 1**) in the VKORC1 gene has been reported to represent a major risk factor for coronary heart disease, stroke, and aortic dissection in Chinese non uremic patients. Chronic kidney disease (CKD) patients develop two to five times more wide spread vascular calcifications than healthy age-matched subjects. However, to date no study reported any effect of VKORC1 genetic polymorphism on arterial calcifications in this population.
Purpose of this study was therefore to evaluate the risk of arterial calcifications associated with this polymorphism in CKD patients.

Methods

One hundred and ninety non dialyzed CKD patients (111M/79F, median age: 71 [27-95]) at various stages of kidney disease were tested for VKORC1 genotyping and underwent chest multi-detector computed tomography for coronary calcification scoring. In addition, a standard carotid doppler ultrasound was used to identify occlusive carotid atheromatous plaques. A detailed medical history including history of atherosclerotic CV disease (defined by the presence of at least: coronary heart disease, cerebrovascular disease or peripheral vascular disease) was also recorded.

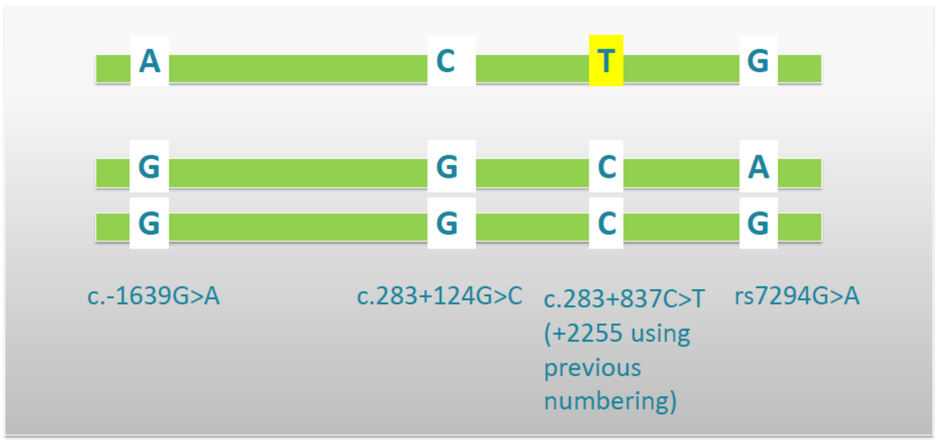

Figure 1: VKORC1 most common haplotypes

Results

1. Clinical and biological characteristics for the 190 CKD patients are summarized in **Table 1**.

Parameter	Value
BMI *kg/m²*	26.6 [14.3-47.7]
Smoking habits (current and past)	91 (47.9%)
Diabetes	60 (31.6%)
Hypertension	175 (92.1%)
Anti-vitamin K treatment	7 (3.7%)
Coronary heart disease	40 (21.1%)
Cerebrovascular disease	14 (7.4%)
Peripheral vascular disease	30 (15.8%)
Presence of atheromatous plaque	102 (53.7%)
eGFR (MDRD) *mL/min/1.73m²*	33.3 [6.5-91.9]
>60 mL/min/1.73m²	19 (10.0%)
60-30 mL/min/1.73m²	90 (47.4%)
<30 mL/min/1.73m²	81 (42.6%)
Total cholesterol *mmol/L*	5.2 [2.3-9.2]
LDL-cholesterol *mmol/L*	2.9 [1.1-6.5]
HDL-cholesterol *mmol/L*	1.5 [0.6-3.4]
Hs-CRP *mg/L*	2.1 [0.1-56.1]
Calcium *mmol/L*	2.4 [1.7-2.7]
Phosphate *mmol/L*	1.07 [0.58-2.34]
PTH *pg/mL*	47.0 [4.0-493.0]
Coronary calcium scoring	188 [0-3942]

Table 1. Characteristics of the chronic kidney disease patients.

2. Patients with the presence of at least 1 copy of the VKORC1 rs2359612 T allele (haplotype A) presented a tendancy to higher atheromatous plaque after adjustment for confounder factors (p=0.098).

By contrast, no association between VKORC1 polymorphism and both calcium scoring (p=0.28) and CV history (p=0.24) was observed.

Genotype analysis	VKORC1c.283+837C>T allele Cases (%)	VKORC1 c.283+837C>T allele Cases (%)	*P*-value
	CC	CT and TT	
Calcium scoring >100	32 (28.6%)	80 (71.4%)	0.28
Calcium scoring <100	30 (39.0%)	47 (61.0%)	
CV History	17 (27.0%)	46 (73.0%)	0.24
No CV History	46 (36.0%)	82 (64.0%)	
Atheromatous plaque (-)	25 (42.4%)	34 (57.6%)	0.098
Atheromatous plaque (+)	28 (27.2%)	75 (72.8%)	

Table 2. Association of TF polymorphism with CAC, atheromatous plaque and CV history.

Conclusion

Our results showed that in CKD patients, contrary to chinese non uremic subjects, the VKORC1 polymorphism is not associated with a higher risk of coronary calcifications. These data have to be further confirmed by larger sample size studies.