Cardio-ankle vascular index is predicted by fibroblast growth factor 23 and intima-media thickness in non-dialysis chronic kidney disease

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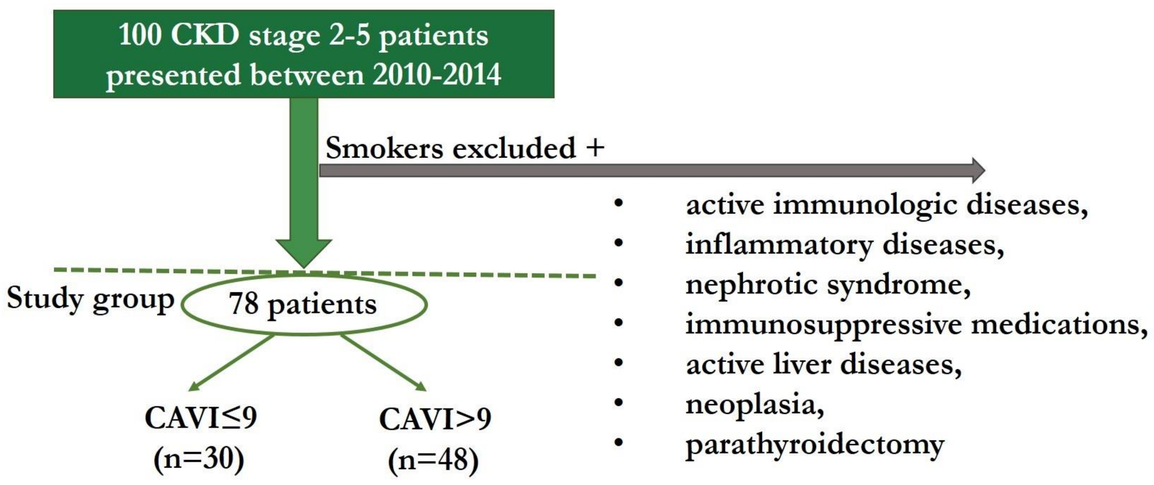
Introduction

Data on the main determinants of arterial stiffness in chronic kidney disease (CKD) are still a matter of debate. In this regard, we aimed to assess the predictors of arterial stiffness evaluated by cardio-vascular index (CAVI) in a non-dialysis CKD cohort.

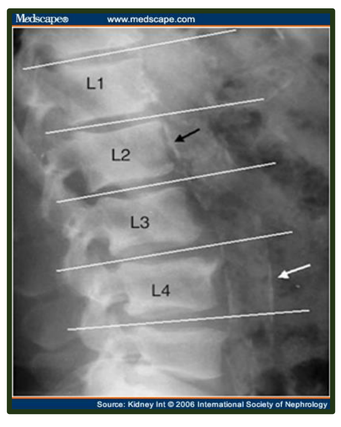
Methods

Study design: unicenter, cross-sectional study (Fig. 1):



Study parameters:

- Past medical history, clinical and laboratory parameters (regarding inflammatory status, kidney function and mineral metabolism) were obtained.
- Plasma c-terminal FGF23 was measured by ELISA.



- Arterial calcifications were assessed by the lumbar aortic calcification score (according to Kauppila) (**Fig. 2**).

Fig. 2. Kauppila score

- CAVI was measured by automatic waveform analyzer -VaSera VS-1000. The maximum value of left and right measurements was recorded and used in the analysis.

Statistical analysis:

Spearman rank correlation and multiple regression were used.

Subjects

- Median age 63 (52;74) years, 56% male;
- Median eGFR 31 (16;45)mL/min, 72% in stages 3 and 4 CKD;
- High prevalence of arterial hypertension (81%);
- Low prevalence of diabetes mellitus (30%).

Results

Abdominal aortic calcifications (Kauppila score ≥1) were found in 48% of subjects, over 50% of them having clinically evident atherosclerosis.

Arterial stiffness (defined by CAVI >9) was observed in 62% of cases. Higher serum phosphate and higher intima-media thickness (IMT) were noticed in patients with arterial stiffness (**Table 1**). Meanwhile, left ventricular hypertrophy was present in similar proportions irrespective of CAVI (46.6% vs. 52.1%, p=0.64).

Table 1. Main study parameters by arterial stiffness

	CAVI ≤9 (38%)	CAVI>9 (62%)	*p*
Age	68 (61;72)	57.5 (45.5;74)	0.1
eGFR (ml/min/m²)	40 (20;57)	25 (15;37)	0.2
CRP (mg/L)	3 (2;5.2)	3.5 (2;7)	0.9
Alkaline phosphatase (UI/L)	87 (65;103)	70 (56;105)	0.2
Calcidiol (ng/mL)	15.5 (10;20)	13.3 (9;19)	0.4
Ionized calcium (mg/dL)	4 (3.8;4)	4.1 (3.9;4.3)	0.6
Serum phosphate (mg/dL)	3.3 (2.9;3.8)	3.7 (3.3;4.2)	***0.04***
iPTH (pg/mL)	91 (64;178)	114 (64;246)	0.8
c-terminal FGF23 (pmol/L)	0.23 (0.12;0.64)	0.62 (0.22;1.8)	0.1
Interventricular septum (mm)	10 (9;12)	11 (9;13)	0.6
Hypertension (%)	86.7	77.1	0.9
Ankle-Brachial Index max (ABI)	1.11 (1;1.2)	1.14 (1;1.2)	0.8
IMT (mm)	0.06 (0.05;0.08)	0.09 (0.06;0.1)	***0.001***

In bivariate analysis, CAVI was positively correlated with IMT (rs= 0.53, p<0.001), cFGF23 (rs= 0.27, p=0.01), and PO4 (rs= 0.24, p=0.04), while inversely with eGFR (rs= –0.22, p=0.04).

However, in a multiple regression model which explained 29% of CAVI variation, only log(cFGF23) (B=1.10; 95%CI 0.37 to 1.83, p=0.004) and log(IMT) (B=0.76; 95%CI 0.44 to 1.06, p<0.001) were retained as independent predictors (**Table 2**).

Table 2. Independent predictors of CAVI

Variable	B	SE	Beta	95% CI for Exp(B)	p
logIMT	0.75	0.15	0.47	0.44 to 1.06	0.001
logFGF23	1.1	0.36	0.29	0.37 to 1.83	0.004

Adjusted R^2=0.29, p<0.004
Dependent variable: LogCAVI
Adjusted for eGFR, age and gender.

Conclusions

Arterial stiffness seems to be associated with increased levels of fibroblast growth factor-23 and IMT in a cohort of relatively young, non-smoker, stage 2 to 5 non-dialysis CKD patients, suggesting FGF23 involvement in the CKD-MB related vascular disease.

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