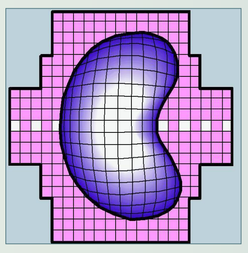
Fibroblast growth factor 23 is dominantly predicted by the decline in renal function in non-dialysis chronic kidney disease



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Introduction

Fibroblast growth factor 23 (FGF23) has a major role in the chronic kidney disease related mineral and bone disorder (MBD-CKD). Yet, its determinants are still disputed.

Accordingly, we aimed to assess the correlations of serum c-terminal FGF23 with other mineral metabolism parameters and the main determinants of its elevation in non-dialysis CKD patients.

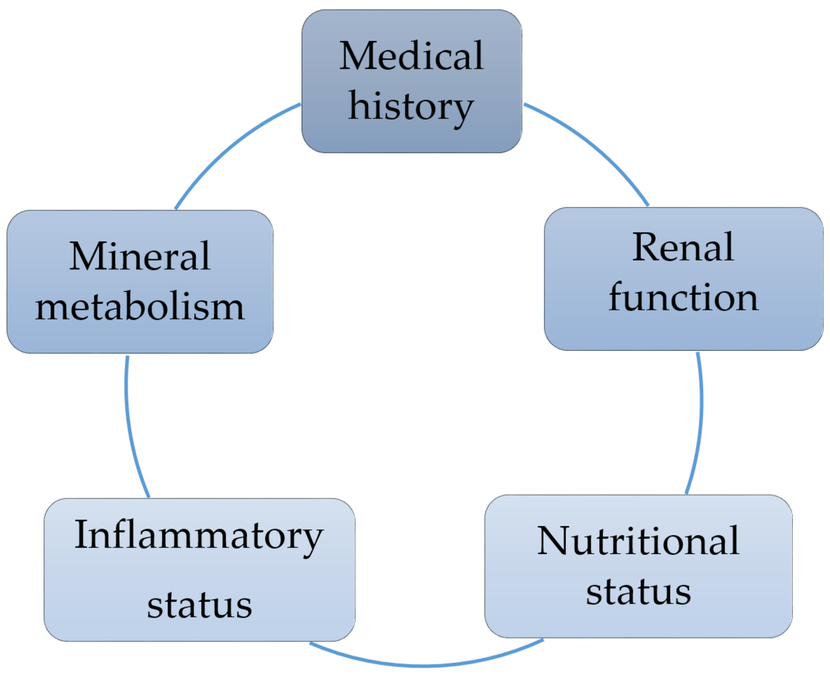
Materials and methods

Study design: Single-center, cross-sectional study.

Subjects: Ninety-one adult Caucasian patients [60% male, 61 (50;71) years old] with non-dialysis CKD [11% stage 2, 41% stage 3, 32% stage 4 and 16% stage 5] were enrolled.

Exclusion criteria were: nephrotic syndrome, active immunologic diseases, immunosuppression therapy, and parathyroidectomy.

Figure 1. Recorded data:



Plasma c-terminal FGF23 was measured by ELISA.

Statistical analysis:

Spearman rank correlation was used to measure the association between two variables and binary logistic regression to evaluate the independent predictors for the cFGF23 levels.

Results

The entire cohort had a high prevalence of arterial hypertension (84%) and nutritional vitamin D deficiency defined as serum calcidiol <30ng/mL (90%), but a relative low prevalence of diabetes mellitus (25%) and active smoking (16%).

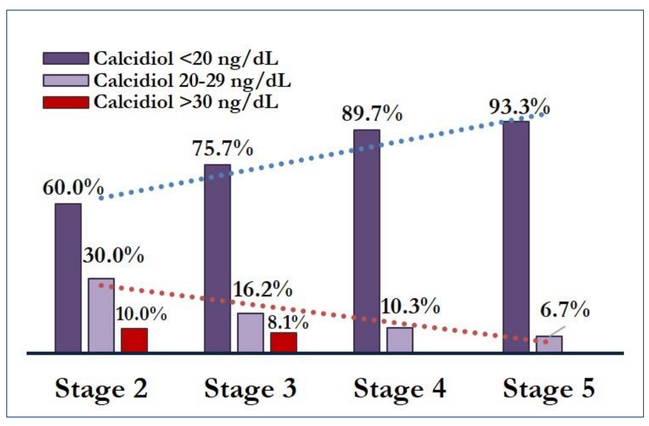
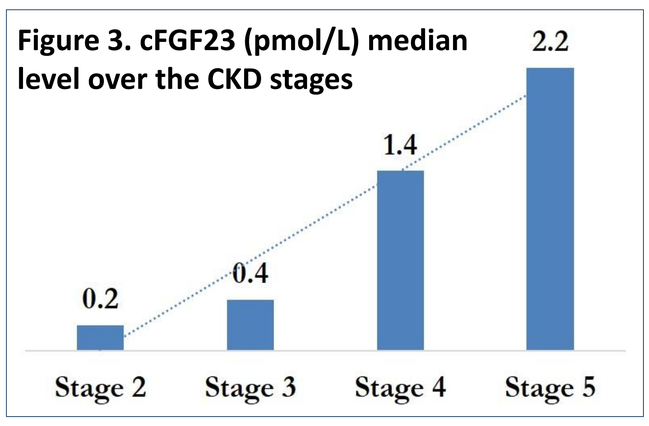


Figure 2. Calcidiol level over the CKD stages



Higher levels of c-terminal FGF23 than the upper laboratory reference limit (1.06 pmol/L) were found in 35% of subjects, 81% of whom were in advanced CKD (stages 4 and 5). Those with elevated cFGF23 had also increased levels of serum parathyroid hormone (iPTH), phosphate (PO4), and urinary albumin-to-creatinine ratio, but lower glomerular filtration rate (eGFR).

	c-terminal FGF23 ≤1.06 (64.8%)	c-terminal FGF23 >1.06 (35.2%)	*p*
Age	64(57;75)	54.5 (36;70)	0.2
eGFR (ml/min/m²)	36 (25;50)	16 (14;24)	***0.001***
UACR (mg/g)	67 (16;435)	539 (47;1387)	***0.01***
Ionized calcium (mg/dL)	4 (3.8;4.2)	4 (4;4.3)	0.9
Serum phosphate (mg/dL)	3.4 (3;4)	4 (3.6;4.7)	***0.002***
iPTH (pg/mL)	83.5 (62;123)	200 (114;363)	***0.001***
c-terminal FGF23 (pmol/L)	0.24 (0.1;0.5)	2.3 (1.7;4.1)	***0.001***
Calcidiol (ng/mL)	13.4 (10;20)	13.8 (9;18.5)	0.9
Calcidiol ≤ 20 ng/ml (%)	80	81	0.8
Alkaline phosphatase (UI/L)	70 (60;102)	93 (60;124)	0.2
Calcium salts use (%)	17	53	***0.001***

In bivariate analysis, serum c-terminal FGF23 positively correlated with iPTH (*rs*= 0.37, *p*<0.001), PO4 (*rs*= 0.36, *p*<0.001), urinary albumin-to-creatinine ratio (*rs*= 0.36, *p*=0.001) and negatively with eGFR (*rs*= –0.47, *p*<0.001).

Nonetheless, in a model of logistic regression, after adjusting for age and gender, only lower eGFR (OR= 0.18; 95%CI 0.06 to 0.51, *p*=0.001), and treatment with calcium salts (OR= 4.7; 95%CI 1.54 to 14.2, *p*=0.006) were the independent predictors of cFGF23:

Variable	*B*	*SE*	*Exp(B)*	*95% CI for Exp(B)*	*p*
Log(eGFR)	–1.73	0.54	0.18	0.06 to 0.51	0.001
Calcium salts use	1.55	3.5	4.7	1.54 to 14.2	0.006
Adjusted R^2 = 0.42, *p*<0.001					
Dependent variable: cFGF23 level < or > than 1.06 pmol/L (binary)					
Variables entered in step 1: Log(Age), Gender, Log(eGFR), Log(uACR), Log(iPTH), Treatment with calcium salts.					

Conclusions

In a relatively young cohort of stage 2-5 CKD patients, where the prevalence of sub-optimal calcidiol levels was high, increased cFGF23 levels were generally lower than reported, but canonically increased along CKD stages.

A higher cFGF23 was related mainly to the decline in kidney function, as its main determinants were the decrease in eGFR and therapy with calcium salts (a surrogate measure of hyperphosphatemia, also related to renal function).

References

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