ABSTRACT

Background. Better biomarkers of CKD reflecting responses to decreased glomerular filtration rate (GFR) are needed. We determined the value of estimated GFR (eGFR) as a threshold for the increase of plasma cFGF23 (C-terminal) and intact fibroblast growth factor-23 (iFGF23) concentrations in the course of chronic kidney disease (CKD) and compared this eGFR value with values related to increased serum intact parathyroid hormone (iPTH) or phosphorus concentrations in an elderly population.

Methods. We measured plasma iFGF23, cFGF23, serum phosphorus, calcium, albumin, creatinine, urea, cystatin C, iPTH and vitamin 25-OH-D3 in 3780 population-based study participants aged ≥65 years.

Results. Serum phosphorus concentrations hardly increased until mean eGFR reached 47.3 ± 4.7 mL/min/1.73 m² but then increased exponentially. Similarly, both iPTH and iFGF23 increased slightly in early CKD but then increased exponentially when eGFR reached 55.0 ± 4.2 mL/min/1.73 m² for iPTH and 51.6 ± 5.7 mL/min/1.73 m² for iFGF23. The departure point for exponential increases in cFGF23 preceded those for iPTH and iFGF23 and occurred at a mean eGFR of 57.7 ± 7.8 mL/min/1.73 m². The prevalence of increased iFGF23 occurred at a remarkably higher eGFR value than that of cFGF23 across the CKD stages.

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Fibroblast growth factor 23 (FGF23) and early chronic kidney disease in the elderly

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**Conclusions.** The increase in cFGF23 preceded both the increase in iPTH and iFGF23 as eGFR declined. Increased plasma iFGF23 level did not precede the rise in serum iPTH concentrations and did not occur before stage-3 CKD in elderly persons. However, cFGF23 was not an early marker of CKD in the elderly subjects.

**Keywords:** chronic kidney disease, elderly population, fibroblast growth factor 23

**INTRODUCTION**

Fibroblast growth factor-23 (FGF23) is a circulating hormone mainly produced by osteoblasts and osteocytes [1]. FGF23 plays an important role in phosphorus homeostasis [2] enhancing its renal excretion [3] and decreasing its absorption in the gastrointestinal tract [4]. FGF23 synthesis and secretion is stimulated by the intake of foods with a high phosphorus content, parathyroid hormone (directly or indirectly by enhancing calcitriol synthesis) and calcitriol [5], whereas the increase of serum phosphate caused by other factors than phosphorus consumption seems to be a weaker FGF23 stimulus [6]. The assessment of FGF23 concentration comprises both the intact fibroblast growth factor-23 (iFGF23) and C-terminal (cFGF23) forms, measured in the circulation. iFGF23 is the full-length, biologically active and most abundant form in the circulation, whereas cFGF23 are inactive fragments [7]. In the early stages of chronic kidney disease (CKD), perhaps even before circulating parathyroid hormone (PTH) level increases, elevated plasma FGF23 concentration prevents phosphorus retention in the circulation [8]. Additionally, FGF23 inhibits the activity of 1α-hydroxylase (CYP27B1) resulting in decreased synthesis of the hormonally active form of vitamin D [9]. In early CKD stages, increased FGF23 secretion precedes the enhancement of PTH release [10]. However, recently Filler et al. showed that the early increase in plasma FGF23 concentration was mainly related to the decrease of glomerular filtration rate (GFR) estimated on the basis of cystatin C measurements [11]. We determined the threshold of GFR at which plasma cFGF23 and iFGF23 concentrations begin to rise and compared this value with estimated glomerular filtration rate (eGFR) with those related to increase in serum intact parathyroid hormone (iPTH) or phosphorus concentrations in the elderly subjects.

**MATERIALS AND METHODS**

**Setting**

The PolSenior study was a large, multicentre, interdisciplin ary, publicly funded research project focussed on elderly subjects conducted in Poland in the years 2007–11, described in detail in a previous study [12]. The research sample consisted of 3780 respondents (1798 women and 1982 men) composed of six similar-sized age cohorts (65–69, 70–74, 75–79, 80–84, 85–89, 90 years and older) representative of the entire Polish elderly population not receiving vitamin D substitution/therapy (due to a potential interference with FGF23 secretion). The participants were recruited using a three-stage stratified, proportional draw. The response rate was 43%. During three visits performed in places of residence by trained nurses, a questionnaire survey, comprehensive geriatric assessment and blood and urine sampling were done. The presented sub-study of the PolSenior project was based on measurements in plasma samples stored at −70°C.

**Measurements**

Serum phosphorus, calcium, uric acid, albumin (also in urine), creatinine and urea concentrations were previously assessed by automated system (Modular PPE, Roche Diagnostics GmbH, Mannheim, Germany) in a single certified laboratory with inter-assay coefficients of variability of <1.4, 1.5, 1.7, 1.7, 2.3, 1.7%, respectively. Serum iPTH level was assessed by electrochemiluminescence method (ECLIA) using commercially available kits on Cobas E411 analyser (Roche Diagnostics GmbH) with inter-assay coefficients of variability of <6.5%. We measured serum cystatin C by ELISA (R&D Systems, Minneapolis, MN, USA), with inter-assay coefficients of variability of <5.9% and vitamin 25-OH-D$_3$ by radioimmunoassay method (DIAsource ImmunoAssays, Nivelles, Belgium), with inter-assay coefficients of variability of <5.3%. We measured plasma iFGF23 and cFGF23 concentrations by ELISA (Immunotopics, San Clemente, CA, USA), with mean intra- and inter-assay coefficients of 4.4 and 6.1% for iFGF23 and 2.4 and 4.7% for cFGF23, respectively.

**Data analysis and statistics**

We estimated GFR according to four formulas: short and full equation from the Modification of Diet in Renal Disease (MDRD) study [13, 14], Cockcroft-Gault [15] and Hoeck [16], and diagnosed subjects with CKD when eGFR was <60 mL/min/1.73 m$^2$ (full MDRD formula) or albumin/creatinine ratio was ≥30 mg/g. G1–G4 CKD stages were scored according to Levy et al. [17]. We identified obesity according to the WHO criteria [18], and hypertensives on the basis of home measurements during two visits, when the average systolic blood pressure was at least 140 mm Hg and/or average diastolic blood pressure was at least 90 mm Hg, or the subject reported receiving antihypertensive medications. We established diagnosis of coronary artery disease (CAD) and diabetes based on medical history, medication and fasting serum glucose of ≥126 mg/dL. Subjects with amino-terminal pro-B-type natriuretic peptide (NT-proBNP) values of >2000 pg/mL were classified as having heart failure, whereas the values between 400 and 2000 pg/mL were classified as uncertain and values of <400 pg/mL excluded the heart failure diagnosis in patients without CKD. We established the normal ranges of iFGF23 and cFGF23 as values of 5–95% among 135 well-nourished [12] or more points in the short version of the mini nutritional assessment (MNA) scale from 2009 [19] and body mass index (BMI) ≥18.5 kg/m$^2$ elderly (age range 65–91 years) study subjects with eGFR$_{MDRD}$ of ≥90 mL/min/1.73 m$^2$ and without heart failure and cancers—reference group.

We relied on STATISTICA 10.0 PL (StatSoft, Poland, Cracow), StataSE 12.0 (StataCorp LP, TX, USA) and R.
software (http://www.r-project.org/). Statistical significance was set at a p-value of <0.05. All tests were two-tailed. Imputations were not done for missing data. Nominal and ordinal data were expressed as per cent whereas interval data were expressed as mean value ± SD in the case of normal distribution or as median (interquartile range) in the case of data with skewed distribution. For comparison of data between man and woman, the Student’s t-test for independent data was used in the case of a normal distribution or after appropriate variable transformations for highly skewed variables. For non-Gaussian continuous variables, the U Mann–Whitney test was used. Categorical variables were compared using χ² tests. Distribution of variables was evaluated by the Shapiro–Wilks test, and homogeneity of variances was assessed by the Levene test. The Mantel–Haenszel linear-by-linear association χ² test was used to check whether the frequency of increased levels of phosphate (≥4.6 mg/dL), intact PTH (≥65 pg/mL), iFGF23 (>18.7 ng/mL) and cFGF23 (>82 RU/mL) occurs more often in subsequent CKD stages. The associations between eGFR values (for each formula) and plasma iFGF23 or cFGF23 levels were done with a three-step procedure. In the first step, in order to model the interaction between plasma iFGF23 or cFGF23 levels and eGFR values, adjusted to serum phosphorus, 25-(OH)-D₃, iPTH, albumin concentrations and BMI, multivariate adaptive regression splines (MARS) procedure was used. MARS is a nonparametric regression procedure that makes no assumption about the underlying functional relationship between the dependent and independent variables. In the second step for each of the eGFR centile group, the mean eGFR values and plasma iFGF23 or cFGF23 levels were calculated using quartile regression. Finally in the third step, the distance-weighted least-squares method was used to illustrate a systematic relation between eGFR values and plasma iFGF23 or cFGF23 levels. The relationship between eGFR values and serum calcium, phosphorus, 25-(OH)-D₃ and iPTH concentrations was used with the same procedure presented earlier, excluding the MARS step. In order to find the departure (cut-off) points in which the iFGF23, cFGF23, phosphorus and iPTH levels raised from the baseline level, we used the Time Domain Constrained Fuzzy c-Regression Models (TDCFCRM), which was presented previously [20] with details. Based on the well-known Fuzzy c-Regression Models clustering algorithm with additional modification, assume that clustered objects (here points of regression models) represent the consecutive in time domain samples of data. Ordinary least-square method was used to assess regression model coefficient. Goodness of fit of obtained regression models was assessed with the determination coefficient R². To obtain meta-regression model coefficient, based on four eGFR models, we used the weighted least univariate squares approach [21].

RESULTS

Study population

We studied 3780 subjects, 1982 men and 1798 women. (Table 1). Almost half (46%) had CKD that was slightly more prominent in women than men. Hyperphosphataemia (phosphate concentration ≥4.6 mg/dL) was diagnosed in only 1.1% of the study population, and secondary hyperparathyroidism met the criteria serum iPTH level of ≥65 pg/mL in 15.2%. Serum vitamin 25-OH-D₃ levels of <30 ng/mL were observed in 39.3% of the study population. Low serum vitamin 25-OH-D₃ levels also characterized 61.8% of subjects with secondary hyperparathyroidism. All creatinine-based eGFR formulas showed significantly higher mean values in men than in women. In contrast, the Hoek formula revealed higher eGFR values in women (Table 1). Additionally, the MDRD full formula showed the lowest eGFR values, whereas the Hoek equation gave the highest values.

Parameters according to CKD stages

The normal range for iFGF23 and cFGF23 among 135 well-nourished (MNA-SF ≥12 points) elderly subjects with eGFRMDRDfull of ≥90 mL/min/1.73 m² was 3.8–18.7 ng/mL and 21–82 RU/mL, respectively. The prevalence of increased iFGF23 was remarkably lower than cFGF23 in CKD patients across CKD stages. Moreover, the frequency of increased cFGF23 was greater than that of secondary hyperparathyroidism (Figure 1). Parameters of calcium–phosphate homeostasis were plotted against all eGFR estimates. Figure 2 shows the relationship between kidney function and circulating phosphorus, calcium, 25-(OH)-D₃ and iPTH levels. Figure 3 demonstrates the relationship between kidney function and plasma iFGF23 and cFGF23 levels respectively, adjusted to calcium–phosphate parameters. Serum calcium levels remained unchanged across all CKD stages, whereas 25-OH-D₃ vitamin values declined linearly with progressively diminishing eGFR. The decline was estimated at 1.44 (1.16–1.72) ng/dL for every 10 mL/min/1.73 m². Serum phosphorus concentrations increased very slightly up to a mean eGFR of 47.3 ± 4.7 mL/min/1.73 m² and then increased exponentially (Figure 2, Table 2). In a similar fashion, serum iPTH levels were modestly increased with declining eGFR in the early CKD stages. The departure point from the baseline was at a mean eGFR of 55.0 ± 4.2 mL/min/1.73 m², at a higher by 7.7 mL/min/1.73 m² of eGFR values than for serum phosphorus concentration. Similarly, changes in both plasma iFGF23 and cFGF23 levels were small across CKD stage 2 (Figure 3). The departure point from the baseline for exponential increase occurred at a mean eGFR of 51.6 ± 5.7 mL/min/1.73 m² for iFGF23 and at 57.7 ± 7.8 mL/min/1.73 m² for cFGF23 (Table 2) The eGFR value for the exponential increase in cFGF23 in relation to iFGF23 and iPTH was greater by ∼3–6 mL/min/1.73 m².

DISCUSSION

We described the sequence of compensatory mechanism to maintain phosphorus levels in a general elderly population with 45.6% prevalence of CKD. Secondary hyperparathyroidism develops in patients with eGFR of <60 mL/min/1.73 m² [22]. Our results support the previous findings. We observed a significant increase in the prevalence of secondary
hyperparathyroidism across all CKD stages. The increase of serum phosphorus levels identified early CKD patients with a cut-off value of eGFR of 46.9 mL/min/1.73 m², starting at quite low circulating phosphate concentration (3.35 ± 0.03 mg/dL). It should be noted that, the percentage of subjects with elevated phosphorus level (1.1%) was relatively low. This quite low circulating phosphate concentration (3.35 ± 0.03 mg/dL). It should be noted that, the percentage of subjects with elevated phosphorus level (1.1%) was relatively low. This might be related to a low phosphorous intake (low consumption of beverages and meat) in our elderly population. However, the prevalence of secondary hyperparathyroidism was substantially greater (13.1%) which partially corresponded to our 25-OH-D₃-deficiency rate (61.8%).

We hypothesized that increased FGF23 secretion precedes PTH elevation in the course of CKD [8, 23, 24]. Few studies have tried to elucidate the associations between eGFR values and both circulating PTH and FGF23 levels across the early stages of CKD, with inconclusive results. The pioneer study performed among 80 patients with CKD stages from 1 to 5 showed an exponential increase of cFGF23 across CKD stages [8]. The low number of patients and the heterogeneity of the study group precluded the determination of eGFR cut-off point for the exponential increase in plasma FGF23 concentration. A later multicentre study performed among 3879 patients in all CKD stages revealed the threshold of eGFR at which the slopes of both cFGF23 and iPTH increase using cubic spline function. These investigators showed that the exponential increase in cFGF23 took place in eGFR values of 57.8 mL/min/1.73 m² and preceded the increase of iPTH by 10.9 mL/min/1.73 m² [25]. In line with these earlier studies, we showed that the increase of circulating cFGF23 precedes PTH elevation in the course of CKD by ~4 mL/min/1.73 m². These authors showed that elevated circulating cFGF23 level (≥100 RU/mL) is frequently observed even in patients with iPTH within the normal range. Thus, Isakova et al. suggested that FGF23 is an earlier than iPTH marker of phosphate homeostasis disturbances in patients with CKD [25], whereas, the Heart and Soul Study including 792 subjects with stable cardiovascular disease diagnosed with stages from 1 to 3 found that the slope of cFGF23 becomes steeper in the second stage of CKD, independent from age, race, sex, blood pressure, diabetes and nutritional status. No precise threshold value was provided [10]. Additionally, according to Pavik et al. who studied 87 patients at different (1–5) CKD stages, the cFGF23 curve established by fitting a two-segment, non-linear model, departed from baseline eGFR at 47 mL/min/1.73 m², with iPTH at 34 mL/min/1.73 m² [26]. We observe that this study was underpowered for such an analysis.

In contrast, we found that the increase of iFGF23 secretion did not occur earlier than iPTH in the course of CKD. Our data suggest that both compensatory mechanisms are simultaneously activated in the third stage of CKD, at least in elderly patients. Prior to increase of circulating cFGF23 than iFGF23 in the course of CKD suggests the accumulation of inactive FGF23 fragments secondary to the decreased biodegradation by damaged kidneys. Therefore, iFGF23 level

Table 1. Study group characteristics, mean ± SD or median (interquartile range)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>78.9 ± 8.6</td>
<td>79.1 ± 8.5</td>
<td>78.7 ± 8.8</td>
<td>0.13</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.2 ± 5.0</td>
<td>27.4 ± 4.4</td>
<td>29.1 ± 5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>145.0 ± 21.9</td>
<td>146.6 ± 22.1</td>
<td>145.5 ± 21.8</td>
<td>0.20</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>82.9 ± 11.3</td>
<td>81.2 ± 11.4</td>
<td>84.7 ± 10.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>3.33 ± 0.51</td>
<td>3.14 ± 0.47</td>
<td>3.54 ± 0.47</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.40 ± 0.60</td>
<td>9.35 ± 0.60</td>
<td>9.44 ± 0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>3.33 ± 0.51</td>
<td>3.14 ± 0.47</td>
<td>3.54 ± 0.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25- (OH) D₃ (ng/mL)</td>
<td>39.11 ± 22.47</td>
<td>41.90 ± 23.55</td>
<td>36.02 ± 20.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>iFGF23 (pg/mL)</td>
<td>8.08 (5.52)</td>
<td>7.86 (5.43)</td>
<td>8.29 (5.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cFGF23 (RU/mL)</td>
<td>51.15 (36.51)</td>
<td>49.65 (35.50)</td>
<td>52.61 (38.49)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CKD—eGFR[MDRD]< 60 mL/min/1.73 m² and/or ACR ≥ 30 mg/g.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; 25- (OH) D₃, vitamin D₃; iPTH, intact parathormone; iFGF23, intact fibroblast growth factor; cFGF23, c-terminal fibroblast growth factor; CKD, chronic kidney disease; ACER, albumin/creatinine ratio; eGFR-MDRD full and short, estimated glomerular filtration rate Modification of Diet in Renal Disease Study full and short formulas; eGFR–CG, estimated glomerular filtration rate Cockcroft–Gault formula; eGFR–Hoek, estimated glomerular filtration rate Hoek’s formula.
measurements do not add too much to the methods using assessment of compensatory mechanisms against phosphorus retention in the early stages of CKD in an elderly population.

The variability of obtained cut-off values related to the different methods used for eGFR calculation was remarkable. We underscore the fact that no method of eGFR estimation has been validated in the elderly. Some authors suggested that...

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**FIGURE 1:** Prevalence of hyperphosphataemia, secondary hyperparathyroidism and elevated iFGF23 and cFGF23 according to G CKD stages (G1—≥ 90 mL/min/1.73 m², G2a—89–75 mL/min/1.73 m², G2b—eGFR 74–60 mL/min/1.73 m², G3a—59–45 mL/min/1.73 m², G3b—44–30 mL/min/1.73 m²).

**FIGURE 2:** A second-order polynomial regression with the distance-weighted least-squares method showing the relationship between kidney function and calcium (upper left) phosphorus (lower left), 25-(OH)-D₃ (upper right) and iPTH (lower right). Dashed vertical line shown following stages of chronic kidney disease G CKD stages (G1—≥ 90 mL/min/1.73 m², G2—89–60 mL/min/1.73 m², G3a—59–45 mL/min/1.73 m², G3b—44–30 mL/min/1.73 m² and G4—eGFR 29–15 mL/min/1.73 m²).
the use of serum cystatin C or alternative eGFR estimations are better markers than creatinine itself and derived eGFR estimates of kidney function in this population [27]. We did not use the recently developed CKD-EPI formula to estimate GFR since that technique was not calibrated to an isotope dilution mass spectrometry method. According to our data, the departure points of eGFR estimated on the basis of four different formulas for iFGF23 are 45.7–59.2 mL/min/1.73 m² and do not proceed to the point for iPTH, whereas the departure points of eGFR for cFGF23 are 49.3–68.1 mL/min/1.73 m² and proceed to the point for iPTH excluding GFR estimation using the Cockcroft–Gault formula. The previously published large studies [10, 25] assessed cFGF23 levels only, which explains the inconsistencies compared with our data. Moreover, an additional confounder involved the results of different eGFR formulas, heterogeneity of the studied population, nutritional habits and alternative statistical methods.

Similarly to the results obtained by Isacova et al. [25], we observed that cFGF23 levels increased prior to iPTH values as eGFR declined. The upper limit of normal cFGF23 values was lower (82 versus 100 RU/mL) in our subjects. However, even lower reference cFGF23 values were reported (31.6–40.9 RU/mL) earlier [10]. The observed discrepancies might be related to different prevalence of hyperphosphataemia between study groups, probably related to a low phosphorus intake by our elderly subjects. Thus far, the normal range of iFGF23 in the elderly has not been defined for certain. Our study revealed that the prevalence of increased cFGF23 values across CKD stages was greater than that of iFGF23. This observation further supports the hypothesis that decreased FGF23 kidney biodegradation is an important mechanism of cFGF23 concentration increase in the circulation. Additionally, the results obtained in the Heart and Soul Study showed that cFGF23 may be a marker of early stages of CKD [9]; however, our results do not confirm this observation at least in the elderly population. We found neither significantly increased in iFGF23 nor increased cFGF23 before 3a stage CKD occurred (eGFR 45–59 mL/min/1.73 m²).

Our study has limitations. We have no information on the dietary behaviours of our subjects. The assays we employed are commercially available but have not been universally standardized. We ignored circulating Klotho, an additional phosphate regulator, in our subjects. We are aware of limited information concerning eGFR estimates in the elderly. Nevertheless, our study is the first performed in the largest elderly-based population. We assessed both plasma iFGF23 and cFGF23 levels and established the normal ranges of these parameters in elderly persons with and without impaired eGFR (≥90 mL/min/1.73 m²).

**FIGURE 3:** A second-order polynomial regression with the distance-weighted least-squares method showing the relationship between kidney function and iFGF23 (upper panel) or cFGF23 (lower panel), adjusted to mineral metabolism parameters (MARS). Dashed vertical line shown following stages of chronic kidney disease G CKD stages (G1—≥90 mL/min/1.73 m², G2—89–60 mL/min/1.73 m², G3a—59–45 mL/min/1.73 m², G3b—44–30 mL/min/1.73 m² and G4—eGFR 29–15 mL/min/1.73 m²).

Table 2. Estimation of eGFR departure points (according to different formulas) for the exponential increase of iFGF23, cFGF23, iPTH and phosphorus

<table>
<thead>
<tr>
<th>eGFR</th>
<th>iFGF23 (pg/mL)</th>
<th>cFGF23 (RU/mL)</th>
<th>iPTH (pg/mL)</th>
<th>Phosphorus (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>eGFR cut-off</td>
<td>cut-off point</td>
<td>eGFR cut-off</td>
<td>cut-off point</td>
</tr>
<tr>
<td>MDRDshort</td>
<td>59.2</td>
<td>12.6</td>
<td>68.1</td>
<td>68.5</td>
</tr>
<tr>
<td>MDRDfull</td>
<td>52.0</td>
<td>12.4</td>
<td>57.2</td>
<td>68.3</td>
</tr>
<tr>
<td>CG</td>
<td>45.7</td>
<td>12.6</td>
<td>49.3</td>
<td>75.1</td>
</tr>
<tr>
<td>Hoek</td>
<td>49.6</td>
<td>14.1</td>
<td>56.2</td>
<td>81.5</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>51.6 ± 5.7</td>
<td>12.9 ± 0.8</td>
<td>57.7 ± 7.8</td>
<td>73.3 ± 6.3</td>
</tr>
<tr>
<td>± 95% CI</td>
<td>42.6–60.7</td>
<td>11.7–14.2</td>
<td>45.3–70.1</td>
<td>63.3–83.4</td>
</tr>
</tbody>
</table>

Cut-off points were estimated with TDCFCRM algorithm.
iPTH, intact parathormone; iFGF23, intact fibroblast growth factor; cFGF23, c-terminal fibroblast growth factor; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease Study full and short formulas; CG, Cockcroft–Gault formula; Hoek, Hoek's formula.
We conclude that the increase in cFGF23 precedes both the rise in iPTH and iFGF23, but is not an early marker of CKD in the elderly. The increase in plasma iFGF23 level does not precede the rise in serum iPTH concentration and does not occur before CKD stage 3 in elderly persons.

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CONFLICT OF INTEREST STATEMENT

None declared.

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