Mineral bone disorder and osteoporosis in hemodialysis patients

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Abstract

Background: Bone disease is common in patients undergoing hemodialysis. It is the result of bone turnover abnormalities and the decrease of bone mineral density (BMD). We aimed to determine the usefulness of serum bone turnover markers and BMD measurement by dual-energy x-ray absorptiometry (DXA) in hemodialysis patients.

Methods: We conducted a cross-sectional study including 90 hemodialysis for more than 12 months. Bone mineral density was assessed by DXA. Peripheral blood samples were obtained from each patient before dialysis in a fasting state within a week of the DXA. Biochemical variables of calcium and phosphate were measured. One bone formation marker (bone-specific alkaline phosphatase (bAP), one bone resorption marker (carboxy-terminal telopeptides of type 1 collagen (CTX)) were measured. Total alkaline phosphatase (TAP), intact parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23) which is a bone-derived hormone were also measured.

Results: CTX values were 6.25 times higher than the normal limit of the assay. Bone alkaline phosphatase levels were less than 10 ng/mL in 28.8% of cases. 23% of patients have osteoporosis and 45% have osteopenia. Femoral BMD had negative correlations with age and PTH levels. FGF23 levels were significantly increased in patients with osteoporosis affecting the lumbar. The levels of bAP and CTX showed a positive correlation. Both circulating bAP and CTX levels showed also positive correlations with PTH levels. Fractures, observed in 12.2% of cases, were associated with low PTH values and the existence of osteoporosis.

Conclusions: Our study showed that osteoporosis and fracture are common in dialysis patients. The reduced BMD was associated with advanced age and elevated levels of PTH. Markers of bone turnover and FGF23 may play a role in the diagnosis of bone disease in hemodialysis patients. DXA measurement is necessary for the monitoring for bone loss.

Keywords: Osteoporosis, Hemodialysis, Fracture, Bone mineral density, Fibroblast growth factor 23, Bone specific alkaline phosphatase, Carboxy-terminal telopeptide of type 1 collagen

Background

Bone disease is highly prevalent in patients with chronic kidney disease on dialysis (CKD-5D) [1]. It can induce serious bone health problems, especially fragility fractures. Bone disease in patients with CKD-5D is the result of bone turnover abnormalities and the decrease of bone mineral density (BMD). Bone biopsy remains the gold standard for the diagnosis of bone turnover abnormalities. However, it is an invasive method and repetitive assessment of bone status cannot be possible. Measurements of

serum bone turnover markers are not common practice in the management of CKD-5D patients [1]. Fibroblast growth factor-23 (FGF23) is a circulating factor produced by osteocytes. This hormone inhibits phosphate reabsorption and renal production of 1,25(OH) vitamin D. FGF23 regulates phosphate and vitamin D. This hormone plays an important role in bone metabolism of patients with chronic kidney disease [2]. Moreover, the assessment of bone mass in patients under dialysis is not yet codified. Both bone resorption and bone formation markers in patients with CKD-5D may be up- or down-regulated by systemic hormones such as parathormone. The measurement of BMD by dual-energy x-ray absorptiometry (DXA) is recommended only in patients with a history of

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fractures. Multiple factors are associated with reduced BMD and may affect bone health [3].

This study aimed to determine the usefulness of serum bone turnover markers by measuring one bone formation marker (bone-specific alkaline phosphatase) and one bone resorption marker (carboxy-terminal telopeptides of type 1 collagen) and the usefulness of the BMD by DXA in patients with CKD-5D. We aimed also to assess the frequency and risk factors of osteoporosis and osteoporotic fracture in hemodialysis patients.

Methods

Patients

We conducted a cross-sectional study including patients in maintenance hemodialysis three times weekly for more than 12 months.

Exclusion criteria included patients younger than 20 years, premature menopause (occurring before the age of 40), prolonged immobilization and patients receiving treatments related to mineral metabolism (long-term steroids, hormone replacement therapy, and bisphosphonate). Patients with a history of gastrectomy, parathyroidectomy, neoplasia or hysterectomy were excluded from this study. Patients with disease that may affect bone such as chronic inflammatory bowel disease, cirrhosis, and endocrinopathies except diabetes were also excluded.

Demographic and clinical data, including age, gender, anthropometric measurements, body mass index (weight/height^2), comorbidities, menopausal status, etiology of kidney disease, and duration of dialysis were collected. We inquired also about low trauma fractures since starting dialysis.

Measurements of biochemical variables

Peripheral blood samples were obtained from each patient before dialysis in a fasting state within a week of the DXA. Biochemical variables of calcium and phosphate were measured using an in vitro photometric assay for automated clinical chemistry analyzers.

Plasma intact PTH (PTH) levels were measured using chemiluminescent microparticle immunoassay. Normal values range from 15-65 pg/mL.

Serum concentrations of 25(OH) vitamin D (25(OH)D) were measured using chemiluminescent immunoassay. Vitamin D deficiency was defined as 25(OH)D values lower than 10 ng/mL, vitamin D insufficiency was defined as 25(OH)D values between 10 and 30 ng/mL [4]. Recommended rates of vitamin D ranged between 30 and 70 ng/mL.

Bone alkaline phosphatase (bAP), a marker of osteoblastic activity, was measured using an immunosorbent enzyme-linked assay.

C-terminal telopeptide of type I collagen (CTX), a marker of osteoclastic activity, was measured by chemiluminescent immunoassay.

Fibroblast growth factor 23 (FGF23) was measured with the ELISA technique. Normal values range from 30 to 176 pg/mL.

Measurements of BMD

Dual-energy X-ray absorptiometry (DXA) was performed to assess bone mineral density (BMD). Instrument quality control was performed regularly. Bone mass density, expressed in gm/cm^2, was measured at the lumbar spine, total hip, femoral neck, and total body.

In the lack of diagnostic criteria for defining osteoporosis in men and premenopausal women, we used WHO criteria as a cutoff point. Osteopenia corresponded to T-score more than – 2.5 SD but less than – 1 SD. Osteoporosis was defined as T-score less than or equal to – 2.5 SD in at least one of these sites: lumbar spine, femoral neck or total hip [5].

Fragility fractures

Fragility fractures were defined as fractures resulting from low-trauma (fall from standing-height or lower).

Lateral dorsal and lumbar spine X-rays were performed to assess vertebral fracture.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 19.0 was used to perform statistical analysis. Means and standard errors were calculated. Comparisons were performed using Student's *t*-test and analysis of variance (ANOVA) for normally distributed variables. The chi-square test was used to analyze categorical data. The multiple linear regression was performed to identify predictors of low bone mass. The significance level was set at < 0.05. Correlations were reported as either the Pearson correlation coefficient.

Results

Patients' characteristics

A total of 90 patients were included in the study. All of them were Caucasian. There were 58 men (64%) with a sex ratio of 1.8. The mean age was 53.01 years [20; 89]. Sixty-eight percent of patients were under the age of 50 years. There were 8 post-menopausal women. The duration of hemodialysis was less than 5 years in 61% of patients whereas it was more than 10 years in only two cases. The calcium intake was noted in 97% of cases with a mean dose of 1.89 g daily [0.5; 3]. Only 30% of patients were orally supplemented with 0.5 microg of alfacalcidol daily.

Hyperphosphatemia was noted in 62.22% and hypocalcemia was found also in 62.22%. Fifty-six percent of

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patients have PTH values between 2 and 9 times the upper normal limit of the assay. However, 19% of patients have PTH values less than 2 times the upper normal limit of the assay. Insufficiency and deficiency of vitamin D were found respectively in 41.11 and 44.44% of cases. CTX values were 6.25 times higher than the normal limit of the assay.

Only 6 patients had CTX levels within the normal range. Bone alkaline phosphatase levels were less than 10 ng/mL in 26 cases and higher than 25 ng/mL in 31 cases. Table 1 summarized the clinical and biological characteristics of patients.

Prevalence of osteoporotic fracture
Osteoporotic fractures were noted in 12.22% of cases ($n = 11$) and had occurred after the age of 50 years in 9 cases. Vertebral fractures are the most common type of osteoporotic fractures, found in 6 patients, followed by hip fractures noted in 3 cases. For the two other cases, there were wrist fracture and tibial fracture.

Table 1 Clinical and biological characteristics of patients

Age, mean ± SD yesars		53.01 ± 14.66
Height, mean ± SD cm		162.78 ± 9.77
Weight, mean ± SD Kg		68.33 ± 13.48
Body mass index, mean ± SD kg/m^2		25.79 ± 4.67
Smoking (n (%))		50 (55.5)
Adequate exposure to sunlight (n (%))		55 (61)
Comorbidities	Diabetes (n (%))	38 (42)
	Hypertension (n (%))	60 (66)
	Dyslipidemia	12 (13)
Duration of dialysis, mean ± SD years		3.94 ± 1.99
Causes of CKD	Diabetic nephropathy (n (%))	30 (33.3)
	Vascular nephropathy (n (%))	6 (6.6)
	Glomerulonephritis (n (%))	40 (44.5)
	Amyloidosis (n (%))	1 (1.2)
	Polycystic kidney disease (n (%))	4 (4.4)
	Tubulointerstitial nephropathy (n (%))	9 (10)
Calcium (2–2.25 mmo/L)		2.08 ± 0.32
Phosphate (2–2.25 mmo/L)		1.84 ± 0.57
Albumin (30-45 mmom/L)		35.45 ± 5.64
Total alkaline phosphatase (60–220 U/L)		88.35 ± 72.56
PTH (12-65 pgmL)		425.7 ± 380.8
25 OH-vitamin D (ng/L)		15.76 ± 11.58
bAP (ng/mL)		26.84 ± 26.99
CTX (ng/mL)		2.49 ± 1.51
FGF 23 (pg/mL)		221.87 ± 248.96

Data are presented as mean ± standard deviation, *CKD* Chronic kidney disease, *PTH* Parathyroid hormone, *bAP* bone alkaline phosphatase, *CTX* C-terminal telopeptide of type I collagen, *FGF 23* Fibroblast growth factor 23

Prevalence of osteoporosis
As shown in Table 2, osteoporosis was common among patients undergoing hemodialysis. 23% of patients have osteoporosis and 45% have osteopenia. Osteoporosis affected the hip more than the spine.

Correlation between biological parameters
There was a positive correlation between bAP and CTX. Moreover, both bone markers showed positive correlations with serum PTH levels. Table 3 demonstrated correlations between biological parameters.

Associated factors of BMD
As illustrated in Table 4, patients with osteoporosis were older than patients without osteoporosis. Men had higher DXA BMD than women at only the total body (1.160 ± 0.141 vs 1.053 ± 0.105 g/cm^2, $p < 10^{-3}$).

The mean BMD was significantly lower among patients with a history of diabetes at the total hip femoral (0.894 ± 0.162 in patients with diabetes vs. 0.894 ± 0.162 in patients without diabetes, p: 0.003). Diabetic nephropathy was the most common etiology associated with decreased BMD at the femoral site whereas patients with polycystic kidney disease tended to have higher BMD than the other patients (0.789 ± 0.118 g/cm^2 in patient with diabetic nephropathy vs. 0.980 ± 0.249 in patient with polycystic kidney disease, p: 0.031).

Parathyroid hormone levels were significantly increased in patients with osteoporosis affecting the total hip. Fibroblast growth factor 23 levels were significantly increased in patients with osteoporosis affecting the lumbar. However, vitamin D levels did not differ significantly between patients with and without osteoporosis.

The Pearson's correlations between clinical, anthropometric, biological and BMD were presented in Table 5.

As shown in Table 6, age and PTH levels significantly predicted the total hip BMD.

Associated factors of fractures
As demonstrated in Table 7, PTH levels were significantly lower in patients with fractures. Besides, patients with osteoporosis had more osteoporotic fractures than patients without osteoporosis.

Discussion
Patients with chronic kidney disease on dialysis (CKD-5D) are at increased risk of osteoporosis and fractures than the general population [6]. In this bone DXA densitometry-based study, we detected that osteoporosis was common in dialysis patients, observed in 23% of cases. Indeed, literature data showed that the prevalence of osteoporosis varied from 4 to 47% at the lumbar spine and from 10 to 64% at the femoral site [7–15]. Moreover, Avramovski et al. [16] demonstrated that the

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Table 2 Results of bone mass in hemodialysis patients

	BMD (g/cm^2)	T-score (SD)	Osteopenia		Osteoporosis	
			N	%	N	%
Lumbar spine	1.156 ± 0.218	− 0.465 ± 1.748	30	33	8	9
Total hip	0.854 ± 0.152	−1.44 ± 1.14	40	44	18	20
Femoral Neck	0.877 ± 0.150	−1.3 ± 1.15	45	50	12	13.33
Overall	–	–	42	45	18	23

BMD Bone mineral density, *SD* Standard deviation, *N* Number, %: percentage

progression of bone mass loss was significantly greater in chronic hemodialysis patients than in general population patients. Using DXA assessment, Sit D et al. [13] showed that the lumbar spine was the region with the highest prevalence of osteoporosis. However, other studies are consistent with our study showing that osteoporosis affected the total hip (20%) more than the lumbar spine (9%). DXA technology can overestimate the BMD measured in the lumbar because of the existence of osteophytes and aortic calcification, frequently observed in hemodialysis patients [17].

Bone mass loss is considered as the consequence of several factors in hemodialysis patients. Several studies are consistent with our study showing that BMD decreased as age increased [14, 17, 18]. The effect of gender on bone mass in hemodialysis is controversial [19, 20]. We found that BMD was significantly lower in women at the total body. The impact of diabetes on BMD is not yet clear. According to the study of Elder et al., we found that BMD at total hip was lower among dialysis patients with diabetes [21].

Chronic kidney disease is associated with hyperphosphatemia and hypocalcemia, observed in 62.22% in our patients, and induce secondary hyperparathyroidism. Fifty-six percent of patients have PTH values between 2 and 9 times the upper normal limit of the assay as recommended by KDIGO [1]. Observational studies demonstrated that PTH values at the extremes (lower than 2 times and more than 9 times) are associated with an increased relative risk of death in dialysis patients.

Table 3 Pearson's correlation between biological parameters

	TAP	Vitamin D	PTH	bAP	CTX
TAP	–	−0.234*	0.430***	0.850***	0.558***
Vitamin D	−0.234*	–	−0.121	− 0.212	−0.089
PTH	0.430***	−0.121	–	0.559***	0.578***
bAP	0.850***	−0.212	0.559***	–	0.701***
CTX	0.558***	−0.089	0.578***	0.701***	–
FGF 23	0.062	0.247*	−0.169	−0.642	− 0.058

Date are presented as the r value in Pearson's correlation test * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. *TAP* Total alkaline phosphatase, *PTH* Parathyroid hormone, *bAP* bone alkaline phosphatase, *CTX* C-terminal telopeptide of type I collagen, *FGF 23* Fibroblast growth factor 23

Table 4 Comparison of clinical and biological characteristics between patients with and without osteoporosis

	Normal	Osteopenia	Osteoporosis	p
Age (years)				
Lumbar	52.03 ± 14.18	52.55 ± 14.26	65.87 ± 10.07	**0.034**
Total hip	49.58 ± 15.02	51.71 ± 12.86	63.94 ± 11.39	**0.001**
All	50.06 ± 15.09	50.42 ± 13.50	63.94 ± 11.39	**0.001**
Age of onset of HD (years)				
Lumbar	49.33 ± 14.42	49.03 ± 14.57	63.37 ± 10.02	**0.031**
Total hip	50.06 ± 15.09	48.84 ± 13.58	60.5 ± 11.64	**0.001**
All	46.87 ± 14.71	48.21 ± 14.16	63.85 ± 14.82	**< 10^{-3}**
PTH (pg/mL)				
Lumbar	410.67 ± 402.97	496.15 ± 385.55	430.16 ± 383.98	0.425
Total hip	265.87 ± 237.20	518.56 ± 420.46	512.46 ± 426.62	**0.013**
All	249.01 ± 217.38	516.89 ± 414.78	512.46 ± 426.62	**0.006**
Vitamin D (ng/mL)				
Lumbar	14.29 ± 10.50	19.00 ± 13.44	15.76 ± 11.68	0.185
Total hip	16.61 ± 10.71	16.28 ± 11.38	13.25 ± 14.03	0.59
All	16.80 ± 10.74	16.11 ± 11.13	13.25 ± 14.03	0.576
CTX (ng/mL)				
Lumbar	2.50 ± 1.58	2.60 ± 1.46	1.85 ± 1.06	0.45
Total hip	2.41 ± 1.51	2.57 ± 1.55	2.38 ± 1.46	0.84
All	2.25 ± 1.36	2.71 ± 1.64	2.38 ± 1.46	0.43
bAP (ng/mL)				
Lumbar	25.23 ± 27.27	30.99 ± 30.22	20.77 ± 9.41	0.54
Total hip	22.80 ± 25.93	29.18 ± 30.26	27.51 ± 22.18	0.67
All	19.48 ± 19.73	31.33 ± 32.08	27.51 ± 22.18	0.21
FGF 23 (pg/mL)				
Lumbar	192.90 ± 242.32	194.50 ± 229.21	428.13 ± 275.64	**0.039**
Total hip	203.32 ± 203.32	278.28 ± 278.28	250.28 ± 250.28	0.731
All	185.37 ± 203.32	229.46 ± 278.28	240.43 ± 250.28	0.731

HD Hemodialysis, *PTH* Parathyroid hormone, *bAP* bone alkaline phosphatase, *CTX* C-terminal telopeptide of type I collagen, *FGF 23* Fibroblast growth factor 23

Significant at $p < 0.05$ set in boldface

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Table 5 Pearson's correlation between clinical, anthropometric, biological and BMD

	BMD L	BMD TH	BMD FN	BMD FA	BMD TB
Age	−0.134	−0.289**	− 0212*	− 0.290**	− 0.190
Duration of dialysis	0.072	− 0.021	− 0.060	0.016	− 0.121
BMI	0.073	−0.082	− 0.020	− 0.095	0.014
Albumin	0.057	−0.05	−0.111	− 0.131	−0.027
TAP	−0.083	−0.144	− 0.109	−0.294**	− 0.277**
PTH	−0.140	− 0.275**	−0.232*	− 0.326**	− 0.343***
Vitamin D	−0.004	0.239*	0.216*	0.142	0.091
bAP	−0.122	−0.176	0.182	−0.299**	− 0.353***
CTX	0.022	−0.055	−0.071	− 0.260*	−0.206
FGF 23	−0.670	−0.149	− 0.780	− 0.054	− 0.08

Date are presented as the r value in Pearson's correlation test * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. *BMD* Body mass density, *L* Lumbar spine, *TH* Total hip, *FN* Femoral Neck, *FA* Forearms, *TB* Total Body, *PTH* Parathyroid hormone, *bAP* bone alkaline phosphatase, *CTX* C-terminal telopeptide of type I collagen, *FGF 23* Fibroblast growth factor 23

Nevertheless, until now, there is no reference range of PTH values corresponding with normal bone turnover [22]. As in our study, Taal et al. [7] showed that the total hip BMD had a negative correlation with PTH. Besides, TAP correlated negatively with BMD in the total body. We didn't find an association between the serum albumin level and BMD. Even if Huang et al. [23] found a positive correlation between serum albumin levels and femoral neck BMD in dialysis patients. Lai et al. [24] showed that there was no relationship between these parameters.

Even if CTX is cleared by the kidney, our study showed that circulating bAP and CTX levels are correlated with serum PTH levels. Serum CTX levels have been found to predict bone loss in patients under dialysis [25, 26]. Several studies have also demonstrated that

Table 6 Predicting models of total hip BMD and total body BMD

Model	Standardized coefficients β	P	Total R²	P
TH BMD				
Age	−0.337	0.001		
Vitamin D	0.079	0.00	0.238	< 10⁻³
PTH	−0.307	0.002		
FA BMD				
Age	−0.426	0.000	0.268	< 10⁻³
TAP	− 0.248	0.213		
bAP	0.89	0.375		
PTH	−0.118	−0.916		
CTX	−0.271	0.093		

BMD Body mass density, *TH* Total hip, *FA* Forearms, *PTH* Parathyroid hormone, *TAP* Total bone alkaline phosphatase, *bAP* bone alkaline phosphatase, *CTX* C-terminal telopeptide of type I collagen

Table 7 Comparison between patients with and without osteoporotic fractures

	Fracture		
	No	Yes	P
Age (ans)	51.94 ± 14.53	60.63 ± 13.33	0.06
BMI (kg/m²)	25.76 ± 4.43	26.05 ± 6.40	0.84
Ca (mmol/L)	2.06 ± 0.4	2.10 ± 0.31	0.757
P (mmol/L)	1.86 ± 0.59	1.65 ± 0.44	0.262
TAP (U/L)	90.32 ± 76.42	74.45 ± 33.44	0.500
Vit D (ng /mL)	15.59 ± 11.52	16.96 ± 12.47	0.716
PTH (pg/mL)	444.38 ± 401.56	293.24 ± 110.65	**0.010**
CRP (mg/L)	8.03 ± 12.35	9.09 ± 11.06	0.75
Albumin (g/L)	33.99 ± 8.60	36.32 ± 6.72	0.391
CTX (ng/mL)	2.53 ± 1.53	2.20 ± 1.43	0.504
bAP (ng/mL)	27.06 ± 27.19	25.43 ± 26.79	0.854
FGF23 (pg/mL)	221.14 ± 260.32	226.95 ± 156.43	0.992
BMD lumbar	1.150 ± 0.22	1.130 ± 0.20	0.740
BMD total hip	0.859 ± 0.149	0.814 ± 0.176	0.356
Overall			
Normal (n (%))	26 (32.9)	4 (36.4)	**0.043**
Osteopenia (n (%))	40 (50.6)	2 (18.2)	
Osteoporosis (n (%))	13 (16.9)	5 (45.5)	

BMI Body mass index, *Ca* Calcium level, *P* Phosphorus level, *TAP* Total alkaline phosphatase, *vitD* 25(OH) vitamin D, *PTH* Parathyroid hormone, *BMD* Body mass density Significant at $p < 0.05$ set in boldface

CTX concentrations are raised in patients with CKD-5D and correlate well with BMD measurements [27]. Moreover, Maeno et al. [26] reported that CTX levels significantly correlate with annual bone loss with sensitivity and specificity at respectively 41 and 83%.

Nevertheless, in another study, serum CTX levels were not different between patients with and without loss of BMD at the distal radius [28].

FGF23 plays an important role in regulating bone mineralization. In our study, FGF23 levels were significantly increased in patients with osteoporosis affecting the lumbar. High FGF23 levels were associated with reduced osteoid thickness in children undergoing dialysis [29]. However, in other studies, BMD was not correlated with serum FGF23 levels [30].

Insufficiency on vitamin D, observed in 41.11% in our study, is common among dialysis patients [31–35]. There has been much debate about the relationship between vitamin D and BMD. Several studies have demonstrated that low vitamin D level induced a decrease of cortical BMD in the presumed healthy adult [36]. Our study revealed a positive correlation between vitamin D levels and femoral BMD.

Fracture rates, observed in 12.1% in our study, are greatly increased in dialysis patients compared to the

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general population [37]. From our study, it is evident that lower PTH value was associated with an increased risk of osteoporotic fracture. It has been demonstrated that both high and low PTH levels can be associated with a high fracture rate [38, 39].

Another finding of interest in our study is that osteoporotic fractures were associated with the existence of osteoporosis. In a meta-analysis, Jamal et al. suggested that BMD is lower in patients with stage 5 CKD who have fractures [40]. The relationship between BMD measured by DXA and fracture in dialysis patients remains unclear.

There are numerous limitations to our study. First, it is a cross-sectional study. Besides, some other factors which might be associated with osteoporosis such as dosage of heparin and hypogonadism were not studied.

Conclusion

Our study showed that osteoporosis and fracture are common in patients under dialysis. We highlighted that bone mass loss is the consequence of several factors including age, diabetes and elevated levels of PTH. Osteoporotic fracture risk was associated with the existence of osteoporosis suggesting that DXA measurement is mandatory for the monitoring of bone loss. Our study showed also that both circulating bAP and CTX levels correlated positively with PTH levels. We suggest that bone metabolic markers including BAP and CTX may accurately reflect bone turnover. FGF23 levels were significantly increased in patients with lumbar osteoporosis. Certainly, FGF23 plays a role in the pathogenesis of bone disease in patients with CKD-5D. Other larger longitudinal studies are necessary to codify the assessment of bone disease.

Abbreviations
25(OH)D: 25(OH) vitamin D; bAP: bone-specific alkaline phosphatase; BMD: Bone mineral density; CKD-5D: Chronic kidney disease on dialysis; CTX: Carboxy-terminal telopeptides of type 1 collagen; DXA: Dual-energy x-ray absorptiometry; FGF23: Fibroblast growth factor 23; PTH: Intact parathyroid hormone; TAP: Total alkaline phosphatase

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