JEIMP
The Journal of European Internal Medicine Professionals

Original Article

Investigation of Factors Affecting the Formation of Secondary Non-Traumatic Fractures Due to Mineral Bone Disorder in Hemodialysis Patients: A Single-Center Experience

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J Eur Int Prof. Year; 2025, Volume: 3, Issue: 3
Submitted at: 17.05.2025 Accepted at: 04.07.2025 Published at: 06.08.2025
doi 10.5281/zenodo.16733918

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Abstract

Background: In our study, we aimed to determine whether demographic data and biochemical parameters of patients undergoing hemodialysis influence the prediction of secondary non-traumatic fractures due to mineral bone disorder caused by chronic kidney disease.

Methods: This cross-sectional study was conducted by retrospectively scanning the records of patients aged 18 years and older who had undergone hemodialysis for at least six months at our hospital's hemodialysis unit between 2017 and 2022. A total of 272 patients meeting the inclusion criteria were examined through hospital records.

Results: Of the 272 patients included in the study, 57.7% were males, and the median age was 65 years. Non-traumatic fractures were detected in 32 (11.8%) patients. Non-traumatic fractures were significantly more common in female patients compared to males (18.3% vs. 7%; p=0.008). Eight patients had undergone parathyroidectomy, and among them, non-traumatic fractures were significantly more frequent compared to those who had not undergone the procedure (50% vs. 10.6%; p=0.008). Patients using steroids had significantly more non-traumatic fractures compared to non-users (26.9% vs. 10.2%; p=0.021). The duration of dialysis was significantly longer in patients with non-traumatic fractures compared to those without (60.5 months [7 - 324] vs. 39.5 months [7 - 330]; p=0.017). The risk of non-traumatic fractures was found to be 3.66 times higher in women, 4.17 times higher in steroid users, and increased by 0.7% with each additional month of dialysis.

Conclusion: This study investigated factors influencing non-traumatic fractures associated with mineral bone disorder in hemodialysis patients. Female gender, steroid use, parathyroidectomy, and dialysis duration were found to increase the risk of fractures. No significant association was found between fractures and other laboratory parameters or medications used by patients to regulate bone mineral metabolism.

Keywords: Hemodialysis Units, Hospital, Chronic Kidney Disease-Mineral and Bone Disorders, Non-Traumatic Fracture

INTRODUCTION

According to the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI), chronic kidney disease (CKD) is defined as either a glomerular filtration rate (GFR) less than 60 mL/min/1.73 m² persisting for at least three months or structural and/or functional abnormalities of the kidney, regardless of GFR decline (1). Renal replacement therapy (RRT) should be considered for patients reaching end-stage kidney disease. RRT options include dialysis and kidney transplantation. Dialysis is further subdivided into two modalities: hemodialysis and peritoneal dialysis, with hemodialysis being the most widely used method worldwide (2).

As GFR declines, abnormalities emerge within the bone-mineral axis. Alterations in plasma calcium, phosphorus, parathyroid hormone (PTH), and vitamin D disrupt

normal bone-mineral homeostasis, adversely affecting bone volume and strength. Consequently, mineral and bone disorders associated with CKD develop (3). PTH influences bone by stimulating osteoblasts and osteoclasts, thereby increasing calcium and phosphorus release from bone. PTH, alongside abnormalities in calcium, phosphorus, fibroblast growth factor-23 (FGF-23), and vitamin D metabolism, contributes to altered bone turnover, impaired mineralization, and extraskeletal calcifications. Kidney Disease Improving Global Outcomes (KDIGO) recommends using the term "chronic kidney disease-mineral and bone disorder (CKD-MBD)" to define this multisystemic condition (4). KDIGO classifies CKD-related bone pathology into four categories: osteitis fibrosa (high-turnover renal osteodystrophy secondary to hyperparathyroidism), osteomalacia (mineralization defect accompanied by low osteoclast and osteoblast activity), adynamic bone disease (low-turnover), and mixed osteodystrophy (mineralization defect with either high or low bone turnover) (5,6).

With progression of renal injury and decreasing GFR, the kidney's ability to excrete phosphorus diminishes, resulting in elevated plasma phosphorus. Increased phosphorus levels stimulate PTH secretion from the parathyroid glands, simultaneously binding calcium and leading to reduced plasma calcium concentrations. Furthermore, declining activity of the renal enzyme 1-alpha hydroxylase, synthesized in proximal tubules, reduces production of calcitriol, the active form of vitamin D, thus decreasing intestinal calcium absorption. Elevated phosphorus levels also enhance FGF-23 secretion, further diminishing calcitriol levels. Reduced plasma calcium concentrations trigger calcium-sensitive receptors (CaSR) within the parathyroid glands, promoting additional PTH secretion. Additionally, ongoing kidney damage weakens the negative feedback provided by vitamin D receptors (VDR) in the parathyroid glands due to decreased calcitriol, further exacerbating PTH secretion. These mechanisms collectively result in secondary hyperparathyroidism (7,8). Bone-mineral abnormalities begin as early as CKD stage 2 and affect nearly all patients by stage 5 (9). Factors contributing to sustained increases in PTH secretion include elevated phosphorus, decreased calcium, reduced calcitriol, elevated FGF-23, reduced vitamin D receptor expression in parathyroid glands, diminished calcium-sensing receptor expression, and decreased fibroblast growth factor receptor and klotho expression (10).

Mineral and bone disorders are closely linked to increased cardiovascular mortality and fracture risk. Bone biopsy remains the gold standard for diagnosing and differentiating mineral-bone disorders. However, due to its invasiveness and potential complications, biopsy is not commonly employed in routine practice. Instead, several laboratory parameters have emerged as practical diagnostic and monitoring tools, including plasma calcium, phosphorus, intact PTH (iPTH), and alkaline phosphatase (bone-specific or total) (11,12).

Radiological assessment is also valuable for diagnosis and differentiation of these disorders. In high-turnover bone disease, subperiosteal resorption and brown tumors may occur, particularly affecting ribs, pelvic bones, and long bones. Osteomalacia may present radiologically with pseudo-fractures. Low-turnover bone diseases may demonstrate osteopenia or appear normal on imaging studies (13).

Bone mineral density (BMD) measurements cannot differentiate between specific bone disorders but are recommended for assessing fracture risk in patients prone to mineral-bone disorders or osteoporosis (14). Extraskeletal calcification can affect vascular structures and soft tissues. Some guidelines advocate abdominal radiography to visualize vascular calcifications, whereas echocardiography assists in detecting cardiac valve calcifications (3).

The aim of this study was to investigate demographic and biochemical parameters that influence the prediction of secondary non-traumatic fractures related to CKD-associated mineral and bone disorders in patients undergoing hemodialysis.

METHODS

Study Design

This study was conducted by retrospectively reviewing hospital records of patients aged 18 years or older who had undergone hemodialysis for at least six months in our dialysis unit between 2017 and 2022. Patients meeting the inclusion criteria—aged at least 18 years and receiving hemodialysis treatment for a minimum of six months—were enrolled. Patients were excluded if they had a history of malignancy, pregnancy, kidney transplantation, peritoneal dialysis, fractures due to high-energy trauma (e.g., traffic accidents, falls from heights), or incomplete clinical data. Fractures were confirmed clinically and documented radiologically.

Demographic data, medications, comorbid diseases, and laboratory parameters of all included patients were recorded. Additionally, hospital records were reviewed to determine whether patients had been hospitalized due to non-traumatic fractures or had undergone parathyroidectomy within the five-year study period.

STATISTICAL ANALYSIS

Descriptive statistics included mean, standard deviation (SD), median, minimum (min), maximum (max), frequency (n), and percentage (%) values. Normality of quantitative variables was assessed using the Kolmogorov–Smirnov test (if $n > 50$) and the Shapiro–

Wilk test (if n ≤ 50). Comparisons between groups were performed using Student's t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical data were compared using the chi-square test. Binary logistic regression analysis was conducted to identify variables associated with non-traumatic fractures and to calculate estimated relative risks. A p-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 23.0.

RESULTS

A total of 272 patients were included in the study. Among these, 157 were males and 115 were females. Patient ages ranged from 23 to 97 years, with a median age of 65 years. Non-traumatic fractures were significantly more common in females compared to males (18.3% vs. 7%; p=0.008).

Among the 272 patients, 8 had undergone parathyroidectomy. Non-traumatic fractures were significantly more frequent in patients who had undergone parathyroidectomy compared to those who had not (50% vs. 10.6%; p=0.008). Similarly, non-traumatic fractures were significantly more common among patients using steroids compared to non-users (26.9% vs. 10.2%; p=0.021).

No significant differences were observed between patients with and without non-traumatic fractures in terms of hypertension, diabetes mellitus, coronary artery disease, cerebrovascular events, or medication use, including selective serotonin reuptake inhibitors (SSRIs), angiotensin-converting enzyme inhibitors (ACE-Is)/ angiotensin receptor blockers (ARBs), anticoagulants/ antiplatelets, insulin, oral antidiabetics, active vitamin D, sevelamer, cinacalcet, calcium carbonate, calcium acetate, or lanthanum carbonate. These findings are presented in **Table 1.**

Dialysis duration was significantly longer among patients with non-traumatic fractures compared to those without fractures (60.5 months vs. 39.5 months; p=0.017). However, no significant differences were detected regarding age, BMI, hemoglobin, albumin, corrected calcium, phosphorus, PTH, alkaline phosphatase (ALP), bicarbonate (HCO_3), LDL-cholesterol, Kt/V, or dialysate

Table 1. Comparison of the frequencies of categorical data according to patients' nontraumatic fracture status

Variable		Non-traumatic Fracture		p value
		Present (n=32)	Absent (n=240)	
Parathyroidectomy	**Present** **Absent**	4 (% 50) 28 (% 10.6)	4 (% 50) 236 (% 89.4)	0.008
Hypertension	**Present** **Absent**	31 (% 11.9) 1 (% 9.1)	230 (% 88.1) 10 (% 90.9)	1.000
Diabetes Mellitus	**Present** **Absent**	12 (% 10.4) 20 (% 12.7)	103 (% 89.6) 137 (% 87.3)	0.695
Coronary artery disease	**Present** **Absent**	10 (% 8.8) 22 (% 13.8)	103 (% 91.2) 137 (% 86.2)	0.286
Cerebrovascular event	**Present** **Absent**	4 (% 6.7) 28 (% 13.2)	56 (% 93.3) 184 (% 86.8)	0.245
Steroid	**Present** **Absent**	7 (% 26.9) 25 (% 10.2)	19 (% 73.1) 221 (% 89.8)	0.021
SSRI	**Present** **Absent**	11 (% 10,4) 21 (% 12,7)	95 (% 89.6) 145 (% 87.3)	0.708
ACE-İ/ARB	**Present** **Absent**	7 (% 17.5) 25 (% 10.8)	33 (% 82.5) 207 (% 89.2)	0.284
Anticoagulant/ Antiplatellet	**Present** **Absent**	15 (% 9.7) 17 (% 14.4)	139 (% 90.3) 101 (% 85.6)	0.320
Insulin	**Present** **Absent**	11 (% 10.7) 21 (% 12.4)	92 (% 89.3) 148 (% 87.6)	0.811
Oral Antidiabetic	**Present** **Absent**	4 (% 13.8) 28 (% 11.5)	25 (% 86.2) 215 (% 88.5)	0.759
Active vitamin D	**Present** **Absent**	26 (% 12.3) 6 (% 9.8)	185 (% 87.7) 55 (% 90.2)	0,760
Sevelamer	**Present** **Absent**	13 (% 15.9) 19 (% 10)	69 (% 84.1) 171 (% 90)	0.242
Cinacalcet	**Present** **Absent**	8 (% 15.7) 24 (% 10.9)	43 (% 84.3) 197 (% 89.1)	0.470
Calcium Carbonatte	**Present** **Absent**	12 (% 12.8) 20 (% 11.2)	82 (% 87.2) 158 (% 88.8)	0.861
Calcium Acetate	Present Absent	16 (% 10.8) 16 (% 12.9)	132 (% 89.2) 108 (% 87.1)	0.730
Lanthanum Carbonate	Present Absent	0 (% 0) 32 (% 12.3)	11 (% 100) 229 (% 87.7)	0.372

Table 1. Comparison of patients' non-traumatic fracture conditions in terms of quantitative data

Variable	Non traumatic Fracture		p value
	Present	Absent	
Age	64 (26 - 92)	65 (23 - 97)	0.910
BMI (kg/m²)	22.6 (15 – 32.8)	24.1 (15.6 – 41.4)	0.225
Hemoglobin (g/dL)	10.77 ± 2.07	11.05 ± 1.77	0.415
Albumin (g/dL)	3.74 (2.6 – 4.7)	3.8 (1.4 – 4.9)	0.592
Corrected Calcium (mg/dL)	8.59 ± 0.8	8.53 ± 0.76	0.644
Fosfor (mg/dL)	4 (1.1 – 6.3)	4.3 (0.9 – 9.6)	0.329
PTH (pg/mL)	309 (27 - 3258)	304 (1.96 - 2016)	0.979
ALP (IU/l)	140 (57 - 371)	114 (36 - 779)	0.094
HCO3 (mEq/L)	19.55 (14.4 – 25.2)	20.05 (8.2 – 26.8)	0.799
LDL (mg/dL)	76.5 (37 - 133)	76 (20 - 229)	0.539
Kt/V	1.47 (1.33 – 1.77)	1.45 (0.99 – 1.75)	0.261
Dialysate Calcium (mmol/L)	1.5 (1.25 – 1.75)	1.5 (1.25 – 1.75)	0.607
Dialysate Duration (month)	60.5 (7 - 324)	39.5 (7 - 330)	0.017

BMI, Body Mass Index; **PTH**, Parathyroid Hormone; **ALP**, Alkaline Phosphatase; **HCO_3**, Bicarbonate; **LDL**, Low-Density Lipoprotein; **Kt/V**, Dialysis Adequacy Index.

calcium levels between the two groups. These findings are presented in **Table 2.**

The risk of non-traumatic fractures was found to be 3.66 times higher in female patients, 4.17 times higher in steroid users, and increased by 0.7% with each additional month of dialysis. These findings are presented in **Table 3.**

In the ciclopirox group, itch scores improved from a mean of 15.89 (95% CI: 14.76-17.02) to a median of 5, representing a reduction of 10.89 points (paired Cohen's d = 3.70, p<0.001). In the mometasone group, scores improved from a mean of 16.97 (95% CI: 15.37-18.57) to a median of 5, representing a reduction of 11.97 points (paired Cohen's d = 2.84, p<0.001). For pre-treatment scores, there was no significant difference between the ciclopirox group (mean: 15.89, SD: 2.94) and mometasone group (mean: 16.97, SD: 4.21), with a between-group difference of 1.08 points (Cohen's d = 0.30, p=0.26). Similarly, post-treatment scores showed no significant difference between groups (p=0.22), with both groups achieving similar median scores of 5.

DISCUSSION

In the advanced stages of chronic kidney disease and among patients undergoing hemodialysis, bone mineral disorders commonly develop. These conditions are closely linked to elevated cardiovascular mortality and an increased fracture risk. To mitigate complications from bone mineral disorders, target laboratory values have been established, and therapeutic approaches are continuously being developed.

Studies investigating fractures in end-stage kidney disease have examined gender influences. Jadoul et al. reported that female hemodialysis patients had a 1.41-fold increased risk for hip fractures and a 1.59-fold increased risk for any non-traumatic fracture compared to males (15). Similarly, Patricia et al. found a 1.81-fold higher risk of non-traumatic fractures among women (16). Stehman-Breen et al. further corroborated these findings, reporting a 2.26-fold greater risk of hip fractures in females (17).

Consistent with prior studies, our study demonstrated significantly higher non-traumatic fracture rates in females compared to males (18.3% vs. 7%; p=0.008). Our adjusted analysis indicated that female gender and steroid use were associated with increased fracture likelihood, although the magnitude of the odds ratios may be inflated due to the limited number of fracture

Table 3. Risk factors for non-traumatic fractures and estimated relative risk ratios

		OR	% 95 CI	p value
Risk Factors for Non-Traumatic Fracture	**Age**	1.012	0.985 – 1.040	0.396
	Female Gender	3.660	1.589 – 8.430	0.002
	BMI	0.926	0.837 – 1.024	0.135
	Dialysis Duration	1.007	1.001 – 1.013	0.025
	Steroid Use	4.170	1.476 – 11.782	0.007

events. Specifically, the adjusted odds ratio for fracture occurrence in female patients was 3.66 (95% CI: 1.59–8.43).

Previous literature has also examined the relationship between parathyroidectomy and fracture risk in patients with end-stage renal disease. Jadoul et al. identified a significant association between parathyroidectomy and previous hip fractures (15). Elevated PTH levels lead to bone marrow fibrosis, increased osteoblast-osteoclast activity, and osteitis fibrosa cystica (18). Parathyroidectomy, by improving these conditions, can potentially enhance bone quality and reduce the risk of long-term fractures.

In a study by Rudser et al., the risk of hip fractures in hemodialysis patients without prior fractures was 0.68 times lower in those who underwent parathyroidectomy compared to those who did not (19). Similarly, a Sweden-based study by Isaksson et al. found a significant reduction in hip fracture risk among female hemodialysis patients who underwent parathyroidectomy (20). However, in a study by Ishani et al., which examined 4.435 hemodialysis patients, no significant reduction was found in the fracture rate one year before vs. one year after parathyroidectomy (21).

Contrary to some previous findings, our study identified significantly higher non-traumatic fracture rates among patients who underwent parathyroidectomy compared to those who did not. This discrepancy may arise from our smaller sample size and lack of adjustment for fracture timing relative to surgery. Therefore, this association should be interpreted cautiously.

Steroid usage increases fracture risk, even at low doses (prednisolone equivalent 2.5–7.5 mg daily) (22). However, studies evaluating steroid use and fracture risk in hemodialysis patients remain limited. Jadoul et al. reported a 1.4-fold increase in fracture risk among steroid users (15). Our study similarly identified significantly higher fracture rates in steroid users (26.9% vs. 10.2%), with a notably elevated fracture risk (odds ratio: 4.17).

Several studies have linked fracture risk to dialysis duration. Wakasugi et al. observed increased hip fracture risk starting one year post-hemodialysis initiation (23). Alem et al. and Jadoul et al. similarly reported increased fracture risks correlated with longer dialysis duration (15,24). Matias et al. found a significant relationship between dialysis duration and fracture prevalence (median duration 93 months) (16). Our study reinforced these findings, noting significantly longer dialysis durations among patients with fractures (60.5 vs. 39.5 months) and a 0.7% incremental fracture risk per additional dialysis month.

Literature on PTH levels and fracture risk has yielded inconsistent results. Jadoul et al. identified elevated PTH (>900 pg/mL) as an independent fracture risk factor, while Stehman-Breen et al. found no significant association (17). Our study also found no significant difference in median PTH levels between fracture and non-fracture patients (309 vs. 304 pg/mL).

Studies in the literature have reported varying results regarding cinacalcet use and fracture risk. In a study by Geoffrey et al., cinacalcet was shown to lower parathyroid hormone levels more effectively than placebo in hemodialysis patients (26). In the EVOLVE study by Moe et al., which examined the effects of cinacalcet on fractures in hemodialysis patients, cinacalcet was compared to placebo. When factors such as female gender, previous fractures, and advanced age—which increase fracture risk—were excluded, cinacalcet reduced fracture rates by 16-29%. However, when these factors were included in the analysis, no significant relationship between cinacalcet and reduced fracture risk was found (27). Similarly, in our study, no significant relationship was found between cinacalcet use and fractures (p=0.470), consistent with some prior studies. Our findings were calculated without excluding fracture risk factors; thus, a larger sample size and adjusted calculations may yield different results.

Important biochemical parameters indicating renal osteodystrophy include calcium, phosphorus, albumin, and alkaline phosphatase. In our study, we also examined the relationship between these values and fractures. A multicenter study conducted by Jadoul et al., involving 12 countries, found that calcium and phosphorus levels were not significant in predicting newly occurring fractures. However, patients with phosphorus levels above 5.5 mg/dL and calcium levels above 10.2 mg/dL had a higher likelihood of previous fractures (15). Consistent with these findings, our study did not detect a relationship between non-traumatic fractures and calcium or phosphorus levels.

Sevelamer, calcium acetate, calcium carbonate, and lanthanum are phosphate-binding agents. Our study examined the relationship between these medications and fractures. Studies investigating this relationship are limited. Ferreira et al. compared calcium-based phosphate binders with sevelamer and found no significant difference between the two groups in bone turnover and mineralization after one year. Sevelamer was shown to increase bone formation, but the study did not specify whether this was associated with a lower fracture risk (28).

Another study by Ruospo et al. found that sevelamer reduced mortality compared to calcium-based binders, but reported no significant relationship between sevelamer and fracture risk (29). Similarly, our study found no significant association between fractures and the use of sevelamer, calcium acetate, calcium carbonate,

or lanthanum.predict response to empirical antifungal treatment. Currently, it is not known whether steroid or antifungal treatment is superior to each other in these occult fungal infections, and these findings indicate that this should be investigated with randomized clinical trials.

Our investigation offers a contribution to the literature by demonstrating that a new empirical treatment approach may be beneficial for a symptom that commonly seen in daily practice. It also provides new research topics related to better defining populations that may benefit from empirical antifungal therapy.

Limitations of the Study

The retrospective and observational design limits the ability to establish causal relationships. Second, the relatively small sample size, particularly the limited number of fracture events, may have inflated the magnitude of the reported odds ratios and reduced statistical power. Additionally, we did not adjust for the timing of fractures relative to procedures like parathyroidectomy, potentially introducing temporal bias. The lack of data on bone mineral density, nutritional status, physical activity, and lifestyle factors, which may influence fracture risk could have resulted in residual confounding. Lastly, our findings are from a single-center study, limiting the generalizability to broader hemodialysis populations. Future studies with larger samples, prospective designs, and comprehensive covariate adjustments are required to validate our findings.

CONCLUSION

This study demonstrated that female gender, steroid use, history of parathyroidectomy, and longer dialysis duration were significantly associated with an increased risk of non-traumatic fractures in hemodialysis patients. Conversely, no significant relationships were identified between fracture risk and biochemical parameters (such as calcium, phosphorus, and PTH levels) or medications used for managing bone-mineral disorders. Given the study's limitations, larger prospective studies are necessary to validate these findings and guide clinical practices aimed at reducing fracture risks among patients undergoing hemodialysis.

DECLARATIONS

Ethics Approval: This study was approved by Giresun University Clinical Research Ethics Committee (IRB no:12-13.02.2025). The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki and its subsequent amendments, ensuring full adherence to ethical guidelines for research involving human participants.

Financial Disclosure: The authors declare that no financial support was received for the research, authorship, and/or publication of this work. The author(s) have no financial relationships relevant to this work to disclose.

Conflict of Interest Declaration: The authors declare that they have no conflicts of interest to declare.

Informed Consent:

Availability of Data and Material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AI: Artificial intelligence tools were used to assist in language editing and improving the clarity of the manuscript. However, all scientific content, data analysis, and interpretations were carried out by the author, who bear full responsibility for the content and conclusions of this work.

REFERENCES

1. Scott IA, Scuffham P, Gupta D, Harch TM, Borchi J, Richards B. Going digital: a narrative overview of the effects, quality and utility of mobile apps in chronic disease self-management. *Aust Health Rev.* 2020;44(1):62-82. doi:10.1071/AH18064
2. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. *JAMA.* 2019;322(13):1294-1304. doi:10.1001/jama.2019.14745
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl.* 2009;(113):S1-S130. doi:10.1038/ki.2009.188
4. Moe S, Drüeke T, Cunningham J, et al. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* 2006;69(11):1945-1953. doi:10.1038/sj.ki.5000414
5. Seck SM, Dahaba M, Ka EF, Cisse MM, Gueye S, Tal AO. Mineral and bone disease in black african hemodialysis patients: a report from senegal. *Nephrourol Mon.* 2012;4(4):613-616. doi:10.5812/numonthly.4225
6. Martin KJ, Olgaard K, Coburn JW, et al. Diagnosis, assessment, and treatment of bone turnover abnormalities in renal osteodystrophy. *Am J Kidney Dis*. 2004;43(3):558-565. doi:10.1053/j.ajkd.2003.12.003
7. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis.* 2003;41(1):1-12. doi:10.1053/ajkd.2003.50007
8. Atkins RC. The epidemiology of chronic kidney disease. *Kidney Int Suppl*. 2005;(94):S14-S18. doi:10.1111/j.1523-1755.2005.09403.x
9. Thomson P, Stirling C, Traynor J, Morris S, Mactier R. A prospective observational study of catheter-related bacteraemia and thrombosis in a haemodialysis cohort: univariate and multivariate analyses of risk association. *Nephrol Dial Transplant.* 2010;25(5):1596-1604. doi:10.1093/ndt/gfp667
10. Cunningham J, Locatelli F, Rodriguez M. Secondary hyperparathyroidism: pathogenesis, disease progression, and therapeutic options. *Clin J Am Soc Nephrol.* 2011;6(4):913-921. doi:10.2215/CJN.06040710
11. Bervoets AR, Spasovski GB, Behets GJ, et al. Useful biochemical markers for diagnosing renal osteodystrophy in predialysis end-stage renal failure patients. *Am J Kidney Dis.* 2003;41(5):997-1007. doi:10.1016/s0272-6386(03)00197-5
12. Cavalier E, Delanaye P, Moranne O. Variability of new bone mineral metabolism markers in patients treated with maintenance hemodialysis: implications for clinical decision making. *Am J Kidney Dis.* 2013;61(5):847-848. doi:10.1053/j.ajkd.2012.12.013
13. Alexander AJ, Jahangir D, Lazarus M, Sprague SM. Imaging in Chronic Kidney Disease-Metabolic Bone Disease. *Semin Dial.* 2017;30(4):361-368. doi:10.1111/sdi.12598
14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl (2011).* 2017;7(1):1-59. doi:10.1016/j.kisu.2017.04.001
15. Jadoul M, Albert JM, Akiba T, et al. Incidence and risk factors for hip or other bone fractures among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study. *Kidney Int.* 2006;70(7):1358-1366. doi:10.1038/sj.ki.5001754
16. Matias PJ, Laranjinha I, Azevedo A, et al. Bone fracture risk factors in

prevalent hemodialysis patients. *J Bone Miner Metab.* 2020;38(2):205-212. doi:10.1007/s00774-019-01041-9
17. Stehman-Breen CO, Sherrard DJ, Alem AM, et al. Risk factors for hip fracture among patients with end-stage renal disease. *Kidney Int.* 2000;58(5):2200-2205. doi:10.1111/j.1523-1755.2000.00394.x
18. Hruska KA, Teitelbaum SL. Renal osteodystrophy. *N Engl J Med.* 1995;333(3):166-174. doi:10.1056/NEJM199507203330307
19. Rudser KD, de Boer IH, Dooley A, Young B, Kestenbaum B. Fracture risk after parathyroidectomy among chronic hemodialysis patients. *J Am Soc Nephrol.* 2007;18(8):2401-2407. doi:10.1681/ASN.2007010022
20. Isaksson E, Ivarsson K, Akaberi S, et al. The Effect of Parathyroidectomy on Risk of Hip Fracture in Secondary Hyperparathyroidism. *World J Surg.* 2017;41(9):2304-2311. doi:10.1007/s00268-017-4000-0
21. Ishani A, Liu J, Wetmore JB, et al. Clinical outcomes after parathyroidectomy in a nationwide cohort of patients on hemodialysis. *Clin J Am Soc Nephrol.* 2015;10(1):90-97. doi:10.2215/CJN.03520414
22. Tanaka I. Glucocorticoid and bone. Efficacy and safety of bisphosphonate in treatment of glucocorticoid induced osteoporosis [Article in Japanese]. Clin Calcium. 2014 Sep;24(9):1371 1378.
23. Wakasugi M, Kazama JJ, Kikuchi K, et al. Hemodialysis Product and Hip Fracture in Hemodialysis Patients: A Nationwide Cohort Study in Japan. *Ther Apher Dial.* 2019;23(6):507-517. doi:10.1111/1744-9987.12807
24. Alem AM, Sherrard DJ, Gillen DL, et al. Increased risk of hip fracture among patients with end-stage renal disease. *Kidney Int.* 2000;58(1):396-399. doi:10.1046/j.1523-1755.2000.00178.x
25. Lindberg JS, Culleton B, Wong G, et al. Cinacalcet HCl, an oral calcimimetic agent for the treatment of secondary hyperparathyroidism in hemodialysis and peritoneal dialysis: a randomized, double-blind, multicenter study. *J Am Soc Nephrol.* 2005;16(3):800-807. doi:10.1681/ASN.2004060512
26. Block GA, Martin KJ, de Francisco AL, et al. Cinacalcet for secondary hyperparathyroidism in patients receiving hemodialysis. *N Engl J Med.* 2004;350(15):1516-1525. doi:10.1056/NEJMoa031633
27. Moe SM, Abdalla S, Chertow GM, et al. Effects of Cinacalcet on Fracture Events in Patients Receiving Hemodialysis: The EVOLVE Trial. *J Am Soc Nephrol.* 2015;26(6):1466-1475. doi:10.1681/ASN.2014040414
28. Ferreira A, Frazão JM, Monier-Faugere MC, et al. Effects of sevelamer hydrochloride and calcium carbonate on renal osteodystrophy in hemodialysis patients. *J Am Soc Nephrol.* 2008;19(2):405-412. doi:10.1681/ASN.2006101089
29. Ruospo M, Palmer SC, Natale P, et al. Phosphate binders for preventing and treating chronic kidney disease-mineral and bone disorder (CKD-MBD). *Cochrane Database Syst Rev.* 2018;8(8):CD006023. Published 2018 Aug 22. doi:10.1002/14651858.CD006023.pub3