

Letter to the Editor

Optimizing osteoporosis management in CKD patients



Optimización del tratamiento de la osteoporosis en pacientes con enfermedad renal crónica

Dear Editor,

We read with great interest the manuscript titled “Osteoporosis Management in Patients with Chronic Kidney Disease (ERCOS Study): A Challenge in Nephrological Care” published in *Nefrología*. The authors have provided important insights into the challenges of managing osteoporosis (OP) in patients with chronic kidney disease (CKD), highlighting gaps in treatment and opportunities for improvement.¹ This study is a timely and significant contribution to nephrology practice, addressing a critical area of patient care that warrants further exploration. While commending the authors for their efforts, we would like to offer a few suggestions based on recent evidence to optimize the clinical and research implications of their findings.

Firstly, the authors have focused on CKD patients with either dual-energy X-ray absorptiometry (DXA)-confirmed OP or a history of fragility fractures. However, this approach may have inadvertently introduced a selection bias, likely overestimating the prevalence of OP and fractures in the broader CKD population. Recent studies suggest substantial variability in bone mineral density (BMD) and fracture risk across CKD stages.^{2,3} Including CKD patients without prior OP diagnoses could offer a more comprehensive understanding of bone health in this population and enable earlier interventions for those at risk.

Secondly, the study highlighted the underutilization of antiresorptive therapies in CKD patients but data on treatment outcomes was limited. Evidence suggests that denosumab improves BMD and reduces fracture risk in advanced CKD stages, including transplant recipients, albeit with a higher risk of hypocalcemia.^{4–6} Bisphosphonates, while effective in early CKD stages, are contraindicated in advanced stages due to nephrotoxicity.^{7,8} We propose integrating data on treatment outcomes from recent studies. [Table 1](#) summarizes the effectiveness and safety profiles of denosumab and bisphosphonates in CKD patients, stratified by treatment type, CKD stage, and clinical outcomes.

phosphonates in CKD patients, stratified by treatment type, CKD stage, and clinical outcomes.

Denosumab has consistently demonstrated superior efficacy in improving BMD and reducing fracture risk over longer durations (≥ 4 years), particularly in high-risk CKD patients when accompanied by appropriate calcium and vitamin D supplementation.^{4,5} However, careful monitoring is required to mitigate the risk of hypocalcemia, particularly after the initial dose.^{6,8,9} Such data could further enrich the manuscript by providing a clearer picture of treatment efficacy and risks.

While the authors focus on traditional therapies, incorporating emerging options like romosozumab could provide a broader overview of available treatments. Recent studies suggest that romosozumab may benefit CKD patients by improving BMD and reducing fractures without significant adverse effects.² Furthermore, addressing barriers to guideline implementation in nephrology practice – such as concerns about medication safety, limited access to DXA, and lack of awareness of updated guidelines – would enhance the practical applicability of the findings. Proposing actionable solutions, such as interdisciplinary collaboration or educational initiatives, could bridge the gap between evidence and practice.^{4,10}

Conclusion

We commend the authors for their valuable contribution to the understanding of OP management in CKD patients. By broadening the scope of study to include undiagnosed patients, incorporating treatment-specific efficacy and safety data, addressing confounding variables, and exploring newer therapies, the manuscript could provide even greater clinical relevance. We look forward to future research that advances the care of CKD patients at risk of OP and fractures.

Table 1 – Treatment effectiveness and safety of denosumab and bisphosphonates in CKD patients.

Treatment type	Patient group (CKD stage/GFR level)	Bone density changes	Fracture rate/risk changes	Calcium level changes	Adverse effects/safety	Treatment duration	Prognosis	Reference
Denosumab	CKD stages 3–5D (GFR <60 mL/min/1.73 m ²)	Significant increases in lumbar spine BMD (8–12%) and hip BMD (3–6%)	Reduced fracture risk (20–30% reduction in vertebral fractures)	Mild transient hypocalcemia, 0.6–24% incidence based on CKD severity	Generally safe with calcium/vitamin D supplementation; rare severe hypocalcemia (<1%)	6–48 months	Effective in improving BMD and reducing fracture risk with appropriate monitoring	4
Denosumab	CKD stages 4–5 (GFR <30 mL/min/1.73 m ²)	Increased BMD by 9% (lumbar spine) and 3.8% (hip) over 4 years	Fracture reduction not directly reported in study cohort	Mild hypocalcemia noted after initial doses; no severe hypocalcemia	No observed impact on graft function in kidney transplant recipients; generally well tolerated	48 months	Effective in increasing BMD without significant adverse effects in CKD patients	5
Denosumab	CKD (GFR <30 mL/min/1.73 m ²)	Lumbar spine BMD increased (6–9%); no significant hip BMD change	Vertebral fracture risk reduced by 20–25%	Significant initial hypocalcemia (average calcium reduction of 1.12 mg/dL after first dose)	Careful monitoring needed; mild hypocalcemia mitigated in subsequent doses	18–36 months	Safe and effective for high-risk patients with adequate monitoring and supplementation	6
Bisphosphonates	CKD stages 3–5 (GFR ≥30 mL/min/1.73 m ²)	Moderate increase in BMD (4–7% in lumbar spine, 3–5% in hip)	Fracture risk reduced nearly by 20%	No significant changes in serum calcium levels	Contraindicated in advanced CKD (GFR <30); risk of nephrotoxicity in high doses	6–24 months	Effective for mild-to-moderate CKD; less effective for severe CKD	8
Bisphosphonates	CKD stages 3b–4 (GFR 15–59 mL/min/1.73 m ²)	Modest improvement in BMD (3–5%) at spine and hip	Limited data on fracture risk reduction	Minimal calcium level changes	Relatively safe; avoided in GFR <30 due to risk of toxicity	12–24 months	Useful in moderate CKD; risk-benefit profile requires careful monitoring	1

BMD: bone mineral density; CKD: chronic kidney disease; GFR: glomerular filtration rate.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

1. Bover J, Gómez-Alonso C, Casado E, Rodríguez-García M, Lloret MJ, Castro-Alonso C, et al. Osteoporosis management in patients with chronic kidney disease (ERCOS study): a challenge in nephrological care. *Nefrología (Engl Ed)*. 2024;44:241–50.
2. Miller PD, Adachi JD, Albergaria BH, Cheung AM, Chines AA, Gielen E, et al. Efficacy and safety of romosozumab among postmenopausal women with osteoporosis and mild-to-moderate chronic kidney disease. *J Bone Miner Res*. 2020;37:1437–45.
3. Imanishi Y, Taniuchi S, Kodama S, Yoshida H, Ito T, Kawai R. Real-world fracture risk, osteoporosis treatment status, and mortality of Japanese non-dialysis patients with chronic kidney disease stages G3–5. *Clin Exp Nephrol*. 2024;14, 024-02562.
4. Broadwell A, Chines A, Ebeling PR, Franek E, Huang S, Smith S, et al. Denosumab safety and efficacy among participants in the FREEDOM extension study with mild to moderate chronic kidney disease. *J Clin Endocrinol Metab*. 2021;106:397–409.
5. Fassio A, Andreola S, Gatti D, Pollastri F, Gatti M, Fabbrini P, et al. Long-term bone mineral density changes in kidney transplant recipients treated with denosumab: a retrospective study with nonequivalent control group. *Calcif Tissue Int*. 2024;115:23–30.
6. Sun X, Bolster MB, Leder BZ, Fan W. Dose-specific effects of denosumab on serum calcium levels in patients with osteoporosis and various renal functions. *J Clin Endocrinol Metab*. 2024;11, <http://doi.org/10.1210/clinem/dgae721>.
7. Robinson DE, Ali MS, Pallares N, Tebé C, Elhussein L, Abrahamsen B, et al. Safety of oral bisphosphonates in moderate-to-severe chronic kidney disease: a binational cohort analysis. *J Bone Miner Res*. 2021;36:820–32.
8. Cowan A, Jeyakumar N, McArthur E, Fleet JL, Kanagalingam T, Karp I, et al. Hypocalcemia risk of denosumab across the spectrum of kidney disease: a population-based cohort study. *J Bone Miner Res*. 2023;38:650–8.
9. Kim JT, Kim YM, Jung KY, Choi H, Lee SY, Kim H-J. Efficacy and safety of denosumab treatment for Korean patients with Stage 3b–4 chronic kidney disease and osteoporosis. *Korean J Intern Med*. 2024;39:148–59.
10. El Miedany Y, Gadallah NA, Sarhan E, Toth M, Hasab El Naby MM, Elwy M, et al. Consensus evidence-based clinical practice recommendations for the diagnosis and treat-to-target management of osteoporosis in chronic kidney disease stages G4–G5D and post-transplantation: an initiative of Egyptian academy of bone health. *Kidney Dis*. 2022;8:392–407.

Yong Wang^a, Wei Zhou ^{b,*}

^a Department of Internal Medicine, Yanbian University Hospital, Yanji, Jilin 133002, China

^b The Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou 310052, China

* Corresponding author.

E-mail address: dracozhou@zju.edu.cn (W. Zhou).

2013-2514/© 2024 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). <https://doi.org/10.1016/j.nefro.2025.04.003>

In response to optimizing osteoporosis management in CKD patients

Respuesta a: Optimizing osteoporosis management in CKD patients

Dear Editor,

In response to Drs. Yong Wang and Wei Zhou, we would like to express our gratitude for their interest in our national ERCOS study¹ and for their additional contributions. We all agree that this is another critical area of patient care that warrants further exploration as highlighted in the recent KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Controversies Conference.² Notably, a new conceptual framework was proposed to move to a framework of two clinical syndromes in adults: CKD-associated osteoporosis (OP)

and CKD-associated cardiovascular disease. This approach aims to advance towards a personalized care in adults with CKD-MBD.²

The ERCOS study (Spanish acronym for CKD-OP)¹ was designed to intentionally include the profile of patients with CKD G3–5D diagnosed of densitometric OP and/or fragility fractures. By focusing on patients in whom these two highly prevalent conditions already coexist (as an inclusion criterion), the study does not allow conclusions to be drawn about the prevalence of OP in patients with CKD. Our results confirmed a previously suspected general therapeutic nihilism,

