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OPEN PEER REVIEW

Comparison of CT Scan and Bone Mineral Densitometry for Diagnosing Osteoporosis and Osteopenia in Patients with Chronic Kidney Disease

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

3 comments · 4 May 2025 – 8 May 2025

Referee 1 Reviewer

MAJOR REVISION 4 May 2025

Dear AE
I had the privilege of reviewing the study titled "Comparison of CT scan and Bone Mineral Densitometry for Diagnosing Osteoporosis and Osteopenia in Patients with Chronic Kidney Disease".
However, there are a few areas for further improvement which the authors should consider:
-There is an inconsistency in sample size: at one point, it says 322 patients were included, but later it refers to "data from 958 men and women." This discrepancy must be clarified.

-Several grammatical errors and awkward phrasings should be corrected (e.g., “estimsated” → “estimated,” “increasing growing” → choose one).

-The study uses DXA as a reference, but does not validate HU measurements against bone histomorphometry or QCT (quantitative CT).

-HU values were taken at the L1 vertebral body, but other studies often use L3 or average multiple levels:

Single vertebral HU may not represent overall vertebral bone status.
L1 may be more prone to degenerative changes or anatomical variation.
No justification is given for why L1 was chosen over L2–L4.

-Add a brief paragraph discussing limitations, such as:

Retrospective design.
Limited number of patients with advanced kidney failure.
Single-center study.

Associate Editor

MAJOR REVISION 4 May 2025

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript is a valuable piece of research. But some revisions are needed. The authors should revise it based on the comments. Also, a minor change should be made in the abstract:
-The study design should be mentioned in the first line of the method section of the ABSTRACT.

Editor-in-Chief

MAJOR REVISION 8 May 2025

It requires a major revision.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Prof.Einollahi

Hello

- **Journal:** Nephro-Urology Monthly
- **Manuscript ID:** 161015
- **Manuscript Title:** Comparison of CT scan and Bone Mineral Densitometry for Diagnosing Osteoporosis and Osteopenia in Patients with Chronic Kidney Disease

We sincerely appreciate the reviewer's constructive feedback. Below are our point-by-point responses and the corresponding revisions made in the manuscript:

Yours sincerely

Response to reviewers

Reviewer 1

-There is inconsistency in sample size: at one point, it says 322 patients were included, but later it refers to "data from 958 men and women." This discrepancy must be clarified.

Response: Thank you.

We apologize for the confusion. The initial screening involved 958 patients; however, after applying exclusion criteria (e.g., incomplete records, more than 6 months between CT and DXA, absence of CKD), 322 eligible patients remained. We clarified this in the Methods section as follows:

> Of 958 patients initially screened for eligibility, 322 met the inclusion criteria after exclusions for: (1) incomplete medical records, (2) time interval >6 months between CT and DXA, and (3) absence of CKD (as per exclusion criteria). Based on the given formula, with α=5%, a sensitivity of 0.9, an estimation error of 5%, and a prevalence rate of osteopenia and osteoporosis of 0.6 among patients with kidney failure in this study, ultimately, 322 individuals were included in the analysis.

$$n \geq \frac{z^2_{1-\alpha/2}\, sens(1-sens)}{d^2\, prev}$$

-Several grammatical errors and awkward phrasings should be corrected (e.g., "estimsated" → "estimated," "increasing growing" → choose one).

- The manuscript has been thoroughly edited, and all grammatical issues have been corrected.

-The study uses DXA as a reference, but does not validate HU measurements against bone histomorphometry or QCT (quantitative CT).

- Limitation regarding the use of DXA:

We acknowledge this limitation. While DXA is the clinical gold standard for diagnosing osteoporosis (as mentioned in our Background), we agree that QCT/histomorphometry could provide deeper validation. However, these were not retrospectively available.

We added this limitation to the Discussion section:

Limitation

While our study utilized DXA as the reference standard—consistent with current clinical guidelines for osteoporosis diagnosis in CKD [12]—the lack of comparison with QCT or histomorphometry may limit the mechanistic interpretation of HU values. QCT, in particular, could provide 3D volumetric bone density data and differentiate trabecular vs. cortical bone loss [14]. However, given the retrospective nature of our study and the routine clinical use of DXA, this limitation does not invalidate our primary finding that L1 HU measurements correlate significantly with DXA-based diagnoses. We encourage future studies to explore multi-modal imaging approaches in CKD patients. The retrospective design may affect data completeness (e.g., inconsistent follow-up CTs).

- Only 2.8% of our cohort (9/322) had Stage 4-5 CKD, consistent with sampling challenges in other CKD studies [10].

- Single-center data may limit generalizability, though our hospital's national referral role mitigates this concern. These factors should be considered when interpreting our results.

-HU values were taken at the L1 vertebral body, but other studies often use L3 or average multiple levels:

Single vertebral HU may not represent overall vertebral bone status.
L1 may be more prone to degenerative changes or anatomical variation.
No justification given for why L1 was chosen over L2–L4.

- Justification for selecting L1 vertebra:

Response: We selected L1 because:

1. Clinical feasibility: L1 is consistently included in routine chest/abdominal CT scans (unlike L3/L4, which may be missed in limited scans).

2. Supporting evidence: Prior studies (e.g., Pickhardt et al., 2013) validated L1 HU for opportunistic screening.

3. Technical reasons: L1 is less prone to degenerative changes compared to lower lumbar vertebrae (Zou et al., 2019).

We added this explanation to the Procedure subsection in the Methods:

> "HU measurement for each vertebra was obtained by selecting the largest possible ROI in the central portion of the vertebral body, excluding cortical margins. We focused on L1 for the following reasons: (1) its consistent inclusion in routine chest/abdominal CT scans (unlike lower lumbar vertebrae, which may be excluded in limited protocols); (2) lower sensitivity to degenerative changes compared to L2–L4, as supported by previous studies [Pickhardt et al., 2013; Zou et al., 2019]; and (3) clinical feasibility for opportunistic screening. The software calculated the mean HU value in the ROI. Typically, one to three measurements were obtained from this region."

-Add a brief paragraph discussing limitations, such as:

Retrospective design.
Limited number of patients with advanced kidney failure.
Single-center study.

- Thank you for your helpful suggestion. As recommended, a paragraph on the study's limitations has been added to the end of the Discussion section. It acknowledges the retrospective design, limited number of patients with advanced kidney failure, and the single-center nature of the study.

2. *Reviewer 2:*
In the paragraphs about incidence rates or fracture rates, it would be more valuable if you could add exact percentages or relative risk (RR) or hazard ratio (HR).

- Thank you for your valuable insight. We revised the Background and Discussion sections and added a specific hazard ratio for fracture risk in CKD stage 5 based on a recent meta-analysis. The following sentence and citation were included:

> “Furthermore, a recent meta-analysis reported that patients with CKD stage 5 had a significantly higher fracture risk, with a pooled hazard ratio (HR) of 2.63 (95% CI: 1.74–3.98), compared to individuals without CKD.”

> “Furthermore, consistent with our findings, Hall et al. (2018) reported in a prospective cohort study that veterans with stage 3 CKD had an adjusted subdistribution hazard ratio (sdHR) of 1.07 (95% CI: 1.02–1.11) for fractures compared to those without CKD.”

Line 56 has a small typo:
"sensitive tofactors"
It should be corrected to: "sensitive to factors"
Typo (linguistic error):
"estimsated" in line 91 → correct: estimated.
"Hospital" is used several times without the full name (Baqiyatallah Hospital) (lines 95, 98, 119). In English articles, it is better to give the full name of the hospital for clarity.

- Thank you for your valuable insight. The manuscript has been thoroughly edited, and all grammatical issues have been corrected.

Need to mention the ethics code number:
It is better to also include the ethics approval code number (IR code or Institutional Review Board code). Most reputable journals consider this mandatory.
Ambiguity in the forearm comparison:

.Thank you for your comment -
Ethics approval and consent to participate
The ethical approval for this study was obtained from the Baqiyatallah University of Medical Sciences (Ethical NO:F2R12P75). All the experiments of this study were conducted in accordance to the relevant guidelines and regulations or in accordance to the Declaration of Helsinki. Written informed consent was obtained from the patients

The comparison of L1 density with forearm was very weak (sensitivity 8.13%,

NPV only 5.69%).

However, the text is consistent in tone and explanation as in the other sections. It would be better to state that "the diagnostic performance of CT-derived L1 bone density in predicting forearm osteoporosis was poor."
(i.e., you should report the negative result clearly and directly.)

- Clarification regarding L1:

Thank you for your insightful comment. As advised, we revised the relevant section in the Discussion to clearly reflect the poor diagnostic performance of CT-derived L1 bone density in predicting forearm osteoporosis. The updated sentence reads:

> "Unlike the spine and femur, the diagnostic performance of L1 bone density obtained by CT scan in predicting osteoporosis in the forearm was poor, with a sensitivity of only 8.13% and a negative predictive value of 5.69%. These findings suggest that L1 bone density by CT scan is not a reliable tool for assessing osteoporosis in the forearm.

No suggestions for future research: It would have been better to add a sentence or two at the end about the need for further studies (e.g., in larger populations or examining other confounding factors such as medications).

- Thank you for your helpful comment. As suggested, we added a sentence to the Conclusion emphasizing the need for further studies in larger and more diverse populations, and the importance of accounting for potential confounding variables such as medications.

> "Future studies with larger sample sizes and more diverse populations are recommended to validate these findings. Moreover, evaluating the effects of medications, nutritional status, and other potential confounding factors on CT-derived bone density measurements would provide deeper insight into the utility of this screening approach."

Measurement of overall accuracy: The conclusion only mentions sensitivity and specificity; it would be better to also mention the overall accuracy of the test that you calculated (e.g., 94.4%).

- Thank you for your suggestion. We added the overall diagnostic accuracy (validity) of CT-derived L1 bone density compared to spinal DXA (94.4%) to the Conclusion section:

> "This method demonstrated a high diagnostic accuracy, with an overall test validity of 94.4% in comparison to spine bone."

Associate Editor's Comments:

Associate Editor 1:
Dear EIC,
Thanks to the authors and appreciation to the researchers. The manuscript is a valuable research. But some revisions are needed. Authors should revise it based on comments. Also minor change should be done in abstract:
-Study design should be mentioned in first line of method section of ABSTRACT

Response to the Editor:

> "Thank you for your kind remarks and constructive feedback. As requested, we have revised the abstract by adding the study design in the first sentence of the Methods section. The revised sentence now reads:

> 'A descriptive-analytical cross-sectional study was conducted on 322 kidney failure patients admitted to Baqiyatallah Hospital in 2021.'

> We appreciate your guidance and attention to detail."

2 Revision 1

4 comments · 31 Aug 2025 – 4 Sep 2025

Referee 2 Reviewer

ACCEPT 31 Aug 2025

Given the amendments made to the article, this article is approved by me. Best wishes to the esteemed authors.

Referee 1 Reviewer

ACCEPT 1 Sep 2025

Dear AE,
I reviewed the manuscript ID 163318 after revision. The authors have adequately addressed all the comments and concerns raised during the initial review. The revisions have substantially improved the quality, clarity, and scientific rigor of the manuscript. I have no further reservations, and in my opinion, the article is now suitable for publication.

Associate Editor

ACCEPT 1 Sep 2025

Dear EIC.
Previous errors have been corrected, and there are no further recommendations.

Editor-in-Chief

ACCEPT 4 Sep 2025

Accept