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Original Research Article

EVALUATION OF ASSOCIATION BETWEEN BONE MINERAL DENSITY AND VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE PATIENTS

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Abstract: *A one-year prospective study was conducted in the Nephrology Department of Nishtar Hospital, Multan, to analyze the association between bone mineral density and vascular calcification in patients with chronic kidney disease. The study included 80 patients at various stages of chronic kidney disease. Vascular calcification was calculated using echocardiography, the Kauppila score, and the ankle-brachial index. Bone mineral density was computed by using total body densitometry. The study results showed that 41.25% of the patients (33 patients) had a Kauppila score more significant than one. Peripheral vascular calcification was observed in 22.5% of the patients (18), whereas 40% (36) had valvular calcification. Moreover, ABI and heart lesions were found to be positively correlated. The study also revealed that bone mineral density was an independent determinant, and valvular calcification was significantly associated with the total BMD and BMD of the femoral neck and femur. Therefore, the study concluded that there is a significant correlation between vascular calcification and bone mineral density in patients with chronic kidney disease.*

Keywords: Chronic Kidney Disease, Ankle-Brachial Index, Abdominal Aortic Calcification, Bone Mineral Density

Introduction

Chronic kidney disease is a common disease occurring in 10% of individuals globally (Ketteler et al., 2018). Alongside, the incidence of mineral bone disorder associated with chronic kidney disease has also increased, which leads to premature arteriosclerosis and generalized vascular calcification (VC) (Iseri et al., 2020). Moreover, CKD-MBD impairs bone health due to osteoporosis and renal osteodystrophy. Renal osteodystrophy is a bone disorder in which the quality of bone tissue is impaired, and bone mineral density (BMD) is reduced because of an abnormal bone turnover rate. CKD-MBD increases the risk of fractures and is associated with increased vascular senescence, stiffening, and VC. Bone and mineral disorders increase morbidity and mortality in patients with end-stage kidney disease (ESKD) and CKD (Kakani et al., 2019; Marchais et al., 2008; Zhang et al., 2019). In the general population, dual-energy X-ray absorptiometry (DEXA) is used to estimate the bone mineral density of lumber and femoral. Still, it is not very accurate in CKD patients due to vertebral articular calcification and abdominal aorta (Camacho et al., 2020). Thus, total body DEXA is preferable for measuring BMD in CKD patients. However, from a clinical and diagnostic point of view, total body DEXA is informative rather than a diagnostic tool. Studies have shown that in CKD patients, BMD in cortex-rich bones is affected more than trabecular bone; these sites are more useful clinical predictors (Kanis et al., 2019). The use of DEXA in CKD patients remains debatable. Moreover, there is limited data on the epidemiology, pathophysiology, and diagnosis of patients with VC or low BMD. Only a few studies have been conducted on the association between bone disorders and VC (Aleksova et al., 2018; Salam et al., 2021). In this study, we will evaluate the association between bone mineral density and vascular calcification in patients with CKD.

Methodology

A prospective study was conducted in the Nephrology Department of Nishtar Medical Hospital from January 2022 to January 2023. A total of 80 patients younger than 18 years old and diagnosed with CKD were included in the study. All patients provided their consent. The Hospital Ethical Board approved the study design.
The clinical data of the participants was recorded. Central VCs were detected through radiography of the abdominal aorta. A semi-quantitative scoring system was used for assessing the progression of vascular calcification. Calcific deposits were graded as 0- no deposits, 1 small deposit filling 1/3rd of the aortic valve, 2 deposits filling 1/3rd to 2/3rd of the aortic wall, and 3- deposits in 2/3rd of the aortic segments. Kauppila's calcification score was then calculated by adding the grading of 8 aortic segments (Uhlinova et al., 2022). Scoring ranged from 0 to 24. Abdominal aorta calcification (ACC) score was considered normal (0), moderate (1-6), and severe calcification (7-24).
The ankle-brachial index (ABI) was used to assess peripheral VC. ABI was measured after asking the patient to rest for 15 minutes. ABI value was classified as > .9 on either foot, ≥ .9 - < 1.3 on both feet and ≥ 1.3 on either foot. Heart valve lesions were assessed through echocardiography. DEXA (dual x-ray absorptiometry) scans were used to assess bone mineral density (BMD).

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Laboratory investigations were assessed, including serum hemoglobin, serum triglyceride, serum total cholesterol, serum C-reactive protein, serum uric acid, serum phosphate, serum urea, serum creatinine, and serum albumin. Serum total alkaline phosphatase was measured through kinetic colorimetric assay. Roche was used to assess Serum 25(OH)D and intact parathyroid hormone (iPTH). ELISA assessed intact fibroblast growth factor 23.

All data was evaluated and analyzed using SPSS version 24. Mean ± SD was used to calculate continuous data, and categorical data was presented using percentages. Wilcoxon rank test was performed for pair-wise comparison. Multivariate analysis was conducted to analyze the association between Kauppila score, ABI, and study variables. The correlation between study elements and DEXA was evaluated by Factorial regression analysis. P value <0.05 was considered significant.

Results

There were 32 (40%) males and 48(60%) females. The mean age of the patients was 54±10 years. The most common causes of CKD were diabetes mellitus (28.7%) and hypertension (27.5%). 33(41.25%) patients had Kauppila score > 1. 18 (22.5%) patients had evidence of peripheral vascular calcification. 36 (40%) patients had valvular calcification. Mean eGFR and creatinine were 35.3 ml/min and 261.8 µmol/L respectively.

There was a significant association between age and BMD of the femoral neck (P<.05). The top level was inversely correlated with total BMD and BMD of the pelvis, ribs, L1-L4, total spine, and femur. There was an inverse correlation between iPTH and BMD of ribs, total spine, spine L1-L4, neck, and femoral. Hb level was positively correlated with BMD of the pelvis, ribs, neck, femoral, and femur. Similarly, eGFR was positively correlated with BMD of the pelvis (p = .04) and ribs (p = .003). BMD was associated with hemoglobin, iPTH, and tALP levels.

According to multivariate analysis, the BMD of the femoral neck was significantly correlated with ABI and AAC. The BMD of the total spine was significantly associated with AAC, the BMD of the ribs, and L1-L4 with ABI (Table I).

According to factorial regression analysis, valvular calcification was significantly correlated with total BMD and BMD of the femur and femoral neck. Type and age were inversely associated BMD of the femoral neck and femur (Table II)

Table I Multivariate analysis of the correlation between Kauppila score and BMD (keeping ABI as the independent variable)

	Coefficient	95% CI	P-value
Kauppila score			
BMD total spine	-25.2	-40.2 — -10.1	.001
BMD femoral neck	-34.6	-48.3 — -16.8	.001
ABI			
BMD spine L1-L4	-.76	-1.35 — -.22	.01
BMD femoral neck	-2.22	-3.08 — -1.34	.001
BMD ribs	-1.68	-2.75 — -0.64	.002

ACC was positively correlated with age (P=.001), cholesterol (P=.01), and total calcium (P = .004). Heart valve lesions (P=.002), tALP (p = .001), and diabetes mellitus (p = .002) were associated with elevated ABI.

Table II factorial regression analysis

	Coefficient	95% CI	P-value
BMD total femur			
Age	.03	-.05 — -.01	.02
Heart valve calcinosis	-2.49	-4.51 — -.46	.01
S-tALP	-.02	-.04 — -.01	.01
BMD femoral neck			
Age	-.03	-.06 — -.01	.001
Heart valve calcinosis	-2.61	-4.29 — -.92	.003
S-tALP	-.02	-.02 — -.01	.001
BMD total			
Age	-.02	-0.05 — .01	.08
Heart valve calcinosis	-.89	-3.68 — -.06	.04
S-tALP	-.01	-0.02 — .01	.1

Discussion

We evaluated the association between BMD and VC in CKD patients using noninvasive techniques for assessing vascular calcifications and DEXA for measuring bone mass density in various sites. The results showed that the Kauppila score was associated with total spine and femoral neck bone mineral density. In contrast, ABI was significantly associated with bone density of ribs, spine vertebrae 1-4, and femoral neck. Calcinosis of the heart valve was correlated to BMD of the total body and femoral neck and femur. Previous studies have evaluated the association between BMD and VC use, but the findings of these studies are controversial. For instance, there is an inverse association between the VC of superficial femoral arteries and femoral BMD (Leow et al., 2021). Few studies found no correlation between BMD and VC parameters (Aleksova et al., 2018; Salam et al., 2021). However, our results align with previous studies, which found that the progression of vascular calcification causes increased bone loss (Lewis et al., 2019). A study showed that aorta calcification in older women increases the risk of fractures (Dalla Via et al., 2023).

There are various noninvasive methods for assessing bone quality in CKD-MBD. Among these techniques are high-resolution quantitative computed tomography, magnetic resonance imaging, and conventional quantitative computed tomography. DEXA is the most easily accessible and low-dose modality for measuring BMD (Evenepoel et al., 2017). A study showed that BMD measured by DEXA was significantly associated with bone histomorphometry information given by bone biopsy, indicating the accuracy of DEXA in patients with CKD (Carvalho et al., 2017). The optimal choice for the type of DEXA depends upon its purpose in clinical practice. In the current study, total body DEXA was used. Moreover, proportions of trabecular and cortical bones vary at different skeletal sites; for instance, vertebrae have higher trabecular bone, while long bones are

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cortical-rich sites. This site-specific assessment is essential for the analysis of CKD MBD. CKD patients have more severe loss of cortical bone compared to trabecular bone. Studies show that cortex-rich sites are most helpful in predicting outcomes in these patients (Cohen-Solal et al., 2020).

The current study found a significant association between heat valve lesions and high ABI. This finding suggests that ABI is a simple yet effective tool for evaluating VC. Studies have shown that pathologically low or high ABI, heart valve fibrosis, and calcinosis increase cardiovascular and all-cause mortality in CKD patients (Leow et al., 2021; Ureña-Torres et al., 2020). Therefore, detecting any extraosseous calcification marker is an effective tool for routine practice. In this study, hemoglobin, iPTH, and tALP were found to be associated with BMD. Moreover, tALP was positively correlated with ABI. Our study also found a positive correlation between parathyroid and phosphorus levels and VC in CKD patients, consistent with previous studies (Bover et al., 2021). There was no association between VC or BMD and the level of plasma iFGF-23 and new bone biomarkers, similar to the results of previous studies, despite the seemingly strong association between ACC and iFGF-23 (Krishnasamy et al., 2017). This study has some limitations. First is the small sample size. Second, DEXA was used for BMD measurement; this method does not provide proportion-wise analysis of long bones for better site-specific BMD measurement.

Conclusion

The findings of this study suggest essential correlation between BMD and VC in CKD patients. Moreover, heart lesions are associated with total BMD and BMD of femoral neck and femur. There also is a significant association between lesions of heart valves and high ABI. Various noninvasive methods can be used to evaluate bone disease and vascular calcification in CKD patients.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned.
Consent for publication
Approved
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Conflict of interest

The authors declared absence of conflict of interest.

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