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Association between Vascular Calcification and Bone Mineral Density in Chronic Hemodialysis Patients: A Single Moroccan Center Experience

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Abstract

Introduction: Chronic kidney disease-mineral and bone disorders (CKD-MBD) are characterized by generalized vascular calcification (VC) and impaired bone health. We aimed to investigate the relationship between VC and bone mineral density (BMD) in chronic hemodialysis patients. **Methods:** A cross-sectional study included 40 chronic hemodialysis patients for at least 6 months. For the assessment of VC, abdominal aorta lateral lumbar X-rays were used, and for the analysis of bone mineral density, dual-energy X-ray absorptiometry (DXA) at the lumbar spine (LS) and femoral neck (FN) was provided. **Results:** Forty patients were included; the average age was 59 ± 16 years, 47% were women, and the median of hemodialysis duration was 54 months. The prevalence of AAC was 57.5%; and the median AAC score was 3 [0.10]. The prevalence of osteoporosis at the lumbar spine was 27.5%, while at the femoral neck, it was 32.5%. The mean BMD at the lumbar spine was 0.999 ± 0.213; and at the femoral neck, it was 0.814 ± 0.239. In the correlation analysis, there was a significant association between AAC and BMD; ACC was inversely correlated with BMD of the spine ($r = -0.368$, $p = 0.019$) and femoral neck ($r = -0.578$, $p < 0.001$). In linear regression analysis, with AAC as the dependent variable, there was a statistically significant negative relationship with BMD of the spine ($p = 0.024$), and BMD of the femoral neck ($p = 0.002$). **Conclusion:** Our study demonstrated that the presence of CV reduces BMD in hemodialysis patients; this implies the need for early diagnosis and optimal management of CKD-MBD. We believe that the results of our study will help in the planning of future research, as they also confirm the existence of the vascular-bone axis.

Subject Areas

Nephrology

Keywords

Bone Mineral Density, Hemodialysis, Vascular Calcification

1. Introduction

Cardiovascular disease is the major cause of death in patients with chronic kidney disease (CKD) [1] [2].

Chronic kidney disease-mineral and bone disorders (CKD-MBD) cause detrimental disturbances in the mineral balance, bone turnover, and the development of severe vascular calcification (VC).

VC in the coronary arteries and the aorta has been recognized as an important risk factor for cardiovascular disease in hemodialysis (HD) patients [3]. Furthermore, there is an association between cardiovascular mortality and osteoporosis [4] [5].

A relationship exists between increased VC and loss of bone mineral density (BMD), with recent experimental studies showing the mechanisms that link these two processes [6].

This association has also been linked to clinical outcomes, as the severity of osteoporosis and VC is correlated to a higher risk of cardiovascular mortality [7] [8].

Even though many factors in the uremic condition stimulate the development and progression of VC, dysregulated mineral and bone metabolism have a fundamental role in the pathogenesis of VC in CKD [9].

However, there is little information available regarding the relationship between vascular calcification and BMD in end stage renal disease (ESRD) patients.

Therefore, we conducted the present study to evaluate the relationship between aortic calcification and BMD in chronic HD patients.

2. Methods

2.1. Study Design

This is a transverse monocentric descriptive and analytical screening study, conducted over a period of 30 days, from March 2024 to June 2024, at the Department of Nephrology Dialysis and Kidney Transplantation at Mohammed V Military Teaching Hospital. The study included 40 chronic HD patients in the HD unit, who underwent a bone mineral density assay with dual-energy X-ray absorptiometry (DXA) and benefited from a screening for calcifications of the abdominal aorta by profile abdominal radiography.

Inclusion criteria were age ≥ 18 years and duration of dialysis ≥ 6 months.

Exclusion criteria included taking corticosteroids, fractures of the lumbar spine or femur, inability to perform the radiological examination, and patient refusal.

Clinical, biological, and therapeutic data were collected based on the review of medical records and dialysis data, as well as the patient's history, to complete a digitized information sheet.

2.2. Clinical and Biological Data

The clinical data collected were: age, gender, primary cause of ESRD, duration of dialysis; physical activity and cardiovascular risk factors: diabetes, hypertension, smoking.

Additionally, a balance sheet including the determination of calcemia, phosphoremia, alkaline phosphatases (APL), intact parathormone 1 - 84 (PTH), albumin and 25OH vitamin D.

Biochemistry data were collected in the same month as the BMD measurement and the abdominal profile radiography.

2.3. Therapeutic Modalities

Our patients were dialyzed three times a week at a rate of 4 hours per session. The dialysate bath contained 3 mmol/l potassium and 1.50 mmol/l calcium.

All the patients were treated with the post dilution hemodiafiltration using the Nikkiso DBB EXA and a high permeability membrane.

Regarding oral treatment, the phosphate binders calcium carbonate and vitamin D and calcimimetics were administered to the patients to maintain phosphocalcic balance.

2.4. Radiological Data

Profile abdominal X-ray: Assessment of abdominal aorta calcification.

The existence of vascular calcifications was assessed by the abdominal profile radiography, as recommended by the KDIGO working group [10], carried out in a standing position using equipment allowing to obtain a digital imagery. The X-ray was interpretable when it included:

The last two thoracic vertebrae and the first two sacral vertebrae.

The portion of the abdominal aorta between L1 and L4 was analyzed.

Aortic calcifications were sought on the anterior and posterior slopes of each segment and scored according to the score validated by Kauppila and Schousboe.

A rating of 0 to 3 was assigned to these calcifications according based on their length:

0: no calcific deposits in front of the vertebra.

1: <1/3 of the segment.

2: 1/3 - 2/3 of the segment.

3: 2/3 or more of the segment.

The aortic calcium score is obtained by summing of the 8 points (2 points for each vertebra) and varies between 0 and 24.

The interpretation of the radiological results was carried out by radiologists who were not informed of the clinical and biological data of the patients.

Bone mineral density assay with dual-energy X-ray: Assessment of bone mineral density.

BMD was assessed by DXA at the LS and FN.

All scans were performed by certified operators and analyzed by experienced rheumatologists.

BMD was measured as the ratio of grams per centimeter squared (g/cm^2).

Reference data was used to calculate T-scores relative to young healthy adults.

Based on the World Health Organization definition, osteoporosis is determined by on the BMD T-score to define osteoporotic (t score ≤ −2.5) and non-osteoporotic (t score > −2.5) [11].

2.5. Statistical Analysis

First, we conducted a descriptive analysis using means and medians for quantitative variables and frequencies for qualitative variables. In the second step, the analytical study was carried out by correlation test: Spearman rank order correlation method.

To predict AAC from BMD, a linear regression model was performed to determine significant associations between BMD and the Kauppila score.

Statistical significance is defined as $P < 0.05$.

All analyses were performed with SPSS version 21 software.

3. Results

This study consisted of 40 chronic hemodialysis patients. Their mean age was 59 ± 16 years and 52% were female. The median duration of hemodialysis was 54 months [31, 108]. Diabetic nephropathy predominated among the etiologies of end-stage renal disease (35%).

65% of our patients were hypertensive, 15% were smokers. The average BMI was 25 ± 5 (see **Table 1**).

Regarding the treatment influencing the phosphocalcic metabolism, 82% of the patients were taking elemental calcium carbonate at an average dose of 1.3 g, either as a phosphorus complexing agent, or for the treatment of hypocalcemia, and 65% were on vitamin D derivatives.

The prevalence of AAC was 57.5%, and the median AAC score was 3 [0.10].

The prevalence of osteoporosis at the lumbar spine was 27.5%, and at the femoral neck, it was 32.5%. The mean BMD at the lumbar spine was 0.999 ± 0.213; and at the femoral neck, it was 0.814 ± 0.239.

In the correlation analysis, there was a significant association between ACC and BMD, AAC was inversely correlated with BMD of the spine ($r = -0.368$, $p = 0.019$) and femoral neck ($r = -0.578$, $p < 0.001$) (see **Table 2**).

In linear regression analysis, with AAC as the dependent variable, a statistically significant negative relationship with BMD of the spine ($p = 0.024$), and BMD of the femoral neck ($p = 0.002$) was revealed (see **Table 3**).

4. Discussion

Normal bone homeostasis seems to be essential for maintaining a healthy cardiovascular system [12].

Table 1. Characteristics of the study population.

Data	Results
Gender*	
Women	21 (52)
Men	19 (48)
Age (years)**	59 ± 16
Duration of dialysis (months)***	54 (31 - 108)
Initial nephropathy*	
Diabetic nephropathy	14 (35)
Chronic interstitial tubulo nephropathy	8 (20
Vascular nephropathy	6 (15)
Glomerular nephropathy	6 (15)
Indeterminate nephropathy	6 (15)
Hypertension	35 (65)
BMI*	25 ± 5
Smoking*	6 (15)
APL (UI/l)***	120 (89 - 167)
Ca (mg/l)**	87 ± 11
Ph (mg/l)**	43 ± 16
PTH (pg/ml)	500 (50 - 1100)
Vit D (µg/l)**	31 ± 14
KT/V**	1.6 ± 0.15
Ca element(g)***	1.3 (1 - 1.5)
Vitamin D derivatives*	35 (65)
ScoreAAC***	3 (0 - 10)
AAC*	23 (57)
BMD LS**(g/cm^2)	0.814 ± 0.239
BMD FN**(g/cm^2)	0.999 ± 0.213
Tscore LS***	−1.31 (−3.70 - 2.50)
Tscore FN***	−1.61 (−6.60 - 2.70)
Osteoporosis LS*	11 (27.5)
Osteoporosis FN*	14 (32.5)

*Expressed in staff (%); **Expressed as average ± standard deviation; ***Expressed in median (quartiles).

Table 2. Correlation between AAC and BMD in study population.

	coefficient r	P-value
ACC		
BMD spine	−0.368	0.019
BMD femoral neck	−0.578	<0.001

Table 3. Linear regression analysis with AAC, as dependent variable and BMD, as independent variable; in the study population.

	B	95% IC	P
BMD spine	−12.08	(−22.46, −1.69)	0.024
BMD femoral neck	−14.21	(−22.46, −5.47)	0.002

The presence of VC, disturbed bone metabolism, and decreased BMD coincide in many different medical conditions, the so-called calcification paradox [13] [14].

Several observational studies report an association between low BMD and the presence of VC. This association is found in aging, diabetes, chronic kidney disease, osteoporosis, and some rare bone diseases [12] [15].

Therefore, the question was raised regarding the extent to which the development and presence of VC also affect bone tissue, thereby linking the dysfunction of the two tissues in a pathological cross-talk.

The bone remodeling cycle is a complex process of bone resorption, formation, and mineralization of newly formed osteoid. Although key functions of the osteoblast, osteoclast, and osteocyte in bone turnover have been identified, the plausible mechanistic link between them is not well understood [16].

The presence of disturbed bone turnover and development of soft tissue calcification is especially observed in CKD patients [15] [17]. As kidney function declines, these patients develop severe disturbances in their mineral balance, namely phosphate retention, low calcium, and altered levels of klotho, fibroblast growth factor23 (FGF23), PTH, and calcitriol. Consequently, kidney disease causes fragile bone and impairs of the bone's ability to buffer calcium and phosphate [18] [19].

Although many factors in the uremic condition stimulate the development and progression of VC, it is believed that the dysregulated mineral and bone metabolism plays a fundamental role in the pathogenesis of VC in CKD [9].

Our study was designed to evaluate associations between VC and BMD in hemodialysis patients using non-invasive methods, the Kauppila score for assessment VC and DEXA for measurement of BMD in different skeletal sites.

Our work highlighted clinically important relationships between VC and BMD of the femoral neck and spine in hemodialysis patients. In some previous studies, potential associations between VC and BMD were sought using different methods for the evaluation of VC and BMD, but the results of these studies are somewhat controversial. For example, Toussaint *et al.* showed an inverse association between VC and femoral BMD measured by DEXA [20]. A similar interplay between the two pathological processes of VC and bone disorders was also described in some experimental studies [7] [21] [22].

However, some other researchers were unable to find any correlation between VC and BMD parameters [23] [24].

Bone biopsy is the gold standard for the evaluation of bone tissue quality: turnover, mineralization and volume; however, despite of being recommended by KDIGO guidelines, the utility of this invasive method in routine clinical practice is limited [25].

There is a quite large number of non-invasive approaches to assess bone quality in kidney-related bone disease.

The most accessible low-dose radiation imaging modality used in routine practice for measuring bone mass and density is DEXA. Additionally, new KDIGO guidelines have changed the paradigm for using DEXA BMD as a predictive tool for fractures. In CKD patients, [10] [25] [26] suggest that a lateral view of lumbar spine radiographs can be utilized to detect the presence of aortic calcifications as reasonable alternatives to computed tomography; this method is effective and simple for evaluating VC [11]. Moreover, a combined approach may provide very good prognostic information.

5. Conclusions

Our work highlighted inverse relationships between AAC and BMD in chronic hemodialysis patients. This implies the need for early diagnosis and optimal management of CKD-MBD.

We believe that the results of our study will help in the planning of future research, as they also confirm the existence of the vascular-bone axis.

Strengths and Limitations

This study must be interpreted with some limitations.

There is a relatively small number of participants. Another source of potential bias is the cross-sectional design of this study. In spite of this fact, it provides a good basis for future research on the vascular-bone axis, for the detection and assessment of the relationship between bone and vasculature.

Conflicts of Interest

The authors declare no conflicts of interest.

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