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ORIGINAL ARTICLE

Evaluation of the Relation Between Vascular and Cardiac Calcification and Osteoporosis, and Detection of Risk Factors in Patients Undergoing Hemodialysis

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Abstract

Introduction: Our aim in this study was to detect the presence and the grade of mitral and aortic calcification, and aortic stiffness, and the relationship between bone mineral density (BMD) and vascular calcification in patients undergoing hemodialysis.

Methods: Patients participating in the hemodialysis program were included in the study. Echocardiography was performed to determine the presence of mitral and aortic calcification, as well as aortic stiffness. The BMD was measured using dual energy x-ray absorptiometry (DEXA) from the radial region of the arm without an arteriovenous fistula, and from the lumbar and femoral regions. The BMD values were classified as T and Z scores.

Results: Sixteen female and 36 male patients were included in the study. Mitral valve calcification was detected in 22 (42.3%) and aortic valve calcification in 25 (48.1%) patients. Aortic valve calcification and aortic stiffness were correlated with age and parathormone. Aortic stiffness was correlated with the calcium–phosphorus product. There was a correlation between the radial region Z score and aortic stiffness. The radial region T score was consistent with osteoporosis in both genders. The results of the radial region BMD were associated with gender and duration of dialysis.

Discussion and Conclusion: Age was associated with both aortic valve calcification and aortic stiffness, whereas aortic and mitral valve calcification and aortic stiffness were not correlated with the femoral, lumbar, and radial region bone mineral densitometry results. The DEXA results for the radial region may provide more accurate information about bone density in patients undergoing hemodialysis.

Keywords: Bone density; chronic renal failure; DEXA; echocardiography; vascular calcification.

End-stage renal failure results in the development of cardiovascular alterations. The risk of vascular calcification increases parallel with a reduced renal function. Cardiovascular calcification is associated with cardiovascular events and clinical outcomes that increase mortality. In most of the cases with vascular calcification, the central mechanism is an abnormal bone metabolism. Osteoporosis is generally detected due to low bone mineral densitometry findings.

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Both idiopathic osteoporosis and renal osteodystrophy cause an increased bone fragility and fractures. However, these disorders have different pathophysiological features.

A total of 52 patients in a routine hemodialysis program were evaluated prospectively to assess the relationship between vascular and cardiac calcification and osteoporosis in patients undergoing hemodialysis and to determine risk factors.

Materials and Methods

A total of 52 patients in the routine hemodialysis program in our hospital were included in the study. Patients with known cardiovascular diseases were excluded.

Signed informed consent forms were obtained from all patients who agreed to participate in the study. An ethics committee approval was obtained.

Demographic characteristics of the patients were recorded. A detailed clinical history was obtained from all patients. Known cardiovascular risk factors, hypertension and lipid disorders, diabetes mellitus (DM), smoking history, a family history of cardiovascular disease, and drugs that were used continuously were recorded.

The time since the onset of hemodialysis treatment was expressed in months.

Laboratory parameters including urea, creatinine, calcium, phosphorus, alkaline phosphatase, albumin, hemoglobin, C-reactive protein (CRP), ferritin, low-density lipoprotein, cholesterol, triglyceride, high-density lipoprotein, bicarbonate, and parathormone (PTH) levels were measured. Calcium measurements were recorded according to adjusted albumin values. These measurements were made using an ARCHITECT C-8000 (ABBOTT) device. PTH was measured with a COBAS e 411 (ROCHE) device. Hemoglobin was measured using a Cell Dyn-3700 (ABBOTT) device.

Body mass index (BMI) was calculated according to the following formula: weight (kg)/height (cm)^2. Patients' BMI was calculated based on the measurements taken between the days of dialysis sessions.

For transthoracic two-dimensional (2-D), M-mode and color flow, Doppler measurements, an ACUSON Sequoia C512–branded echocardiography device (Siemens, Mountain View, Atlanta, USA) with a 4 MHz transducer was used. Echocardiographic evaluation was performed by the same cardiologist who was blinded to clinical data on the day when patients did not undergo dialysis.

The aortic stiffness index (AS) was calculated using the following formula: AS=log(SBP/DBP)/(Aomax–Aomin)/Aomin.

The following parameters were determined by transverse parasternal projection: the aortic valve area (AVA-cm^2) and the mitral valve area (MVA-cm^2).

In addition, aortic semilunar and mitral valve calcifications were evaluated (19), and patients were divided into those whose heart valves were with and without calcification.

Patients' bone mineral densitometry measurements were performed by dual energy X-ray absorptiometry (DEXA) from the lumbar vertebrae, forearm, and femoral regions (Hologic QDR 4500, Hologic, Inc., Wallham, Mass, USA). With this technique, bone density per bone unit area was expressed in grams/cm^2. Absolute BMD values and Z and T scores of femoral and lumbar vertebrae and distal radius were recorded.

Distal-radius bone density was measured from the arm without an arteriovenous fistula. The femoral, vertebral, trabecular bone, radius, and cortical bone densities were evaluated. Measurements were evaluated according to standard deviation related to a young-age population of the same gender relative to the T score; According to the criteria by the World Health Organization, these scores were interpreted as follows: normal (0.1 to −1.0), osteopenia (−1.0 to −2.5), and osteoporosis (<−2.5). The Z score was measured relative to the age- and gender-matched population. A statistical analysis was performed using the SPSS 17.0 program. Descriptive analysis, chi-square test, the Kruskal–Wallis test, and T test were used. Correlation coefficient was calculated by Pearson's correlation analysis. A p-value less than 0.05 was considered to be statistically significant.

Results

The study population included 52 patients (16 females [30.8%] and 36 males [69.2%]). The mean age was 56.69±13.96 years. The mean age of female and male patients was 56.38±11.78 and 56.83±14.98 years, respectively. Thirteen patients (25%) were diagnosed with DM.

Patients were in the routine hemodialysis program 3 days a week for 4 hours. They were receiving calcitriol and phosphorus-binding agents, according to their calcium, phosphorus, and PTH values (Table 1).

The mean overall aortic stiffness in patients was 1.58±0.32. This value was 1.65±0.31 for women and 1.55±0.33 for men without any statistically significant difference between the genders (p=0.32) (Table 2).

Aortic stiffness correlated weakly with age (p=0.02, r=0.3). On the other hand, calcium–phosphorus product and aortic stiffness were significantly correlated (p=0.007, r=–0.38).

There was a weak negative correlation between aortic valve calcification and PTH levels (p=0.02 and r=–0.31, respectively). A weakly significant correlation was detected between the age and pathology levels in patients with and without aortic valve calcification (p=0.02, r=0.305) (Fig. 1).

Bone densitometry: The mean femoral score of our patients was –1.57±1.13 (–4.2–0.80), and their mean femoral Z score was –0.61±1.22 (–3.1–2.5). The mean femoral score was –2.11±1.34 (–4.20–0.70) in female and –1.33±0.95 (–3.10–0.80) in male patients, with a statistically significant difference between both genders (p=0.021). The mean lumbar T score of our patients was –1.73±1.75 (–5.2–2.5), and lumbar Z score was –0.75±1.98 (–5.10–5.2). Mean lumbar T score was –2.68±1.45 (–5.10–0.50) in females and –1.31±1.72 (–5.20–2.5) in males with a statistically significant difference between both genders (p=0.008) (Table 3).

A weak correlation was detected between the radial Z score and aortic stiffness (r=0.28).

A significant correlation was detected between the radial Z score and alkaline phosphatase levels (p=0.008).

Radial BMD results were significantly correlated with patient gender and duration of dialysis (p=0.000 and p=0.043, respectively).

When the femoral, lumbar, and radial bone densitometry values were evaluated, a significant difference was not found between the normal, osteopenic, and osteoporotic groups as for aortic stiffness (p=0.36, 0.31, and 0.15, respectively).

No significant correlation was found between the femoral bone densitometry measurements and mitral valve calcification (p=0.76) (Fig. 2).

No significant correlation was detected between the

Table 1. Biochemical parameters (mean+SD)

	Mean±SD
BUN (mg/dl)	68.51±16.30
Creatinine (mg/dl)	9.00±2.71
Calcium (mg/dl)	9.17±0.60
Phosphorus (mg/dl)	4.98±1.34
PTH (pg/ml)	290.97±258.05
CaxP (mg/dl)	46.23±12.07
Albumin (g/dl)	3.64±0.35
Hemoglobin (g/dl)	11.30±1.46
CRP (mg/L)	7.83±7.39
Ferritin (ng/ml)	700.57±402.98
LDL (mg/dl)	85.67±27.94
Cholesterol (mg/dl)	164.69±52.50
Triglyceride (mg/dl)	240.42±194.06
HDL (mg/dl)	32.57±7.11
Bicarbonate (mmol/L)	22.12±1.75
ALP (U/L)	121.39±78.92
kt/v	1.42±0.26
VKİ	24.45±4.51
Duration of dialysis (mo)	91.90±77.18

Table 2. Echocardiographic findings (mean+SD) (*p-value was estimated using t test)

	Female	Male	Mean±SD	P*
Aortic stiffness	1.65±0.31	1.55±0.33	1.58±0.32	0.32
Aortic valve area (cm^2)	2.51±0.46	2.70±1.04	2.64±0.90	0.38
Mitral valve area (cm^2)	3.86±1.03	3.41±0.87	3.55±0.94	0.12

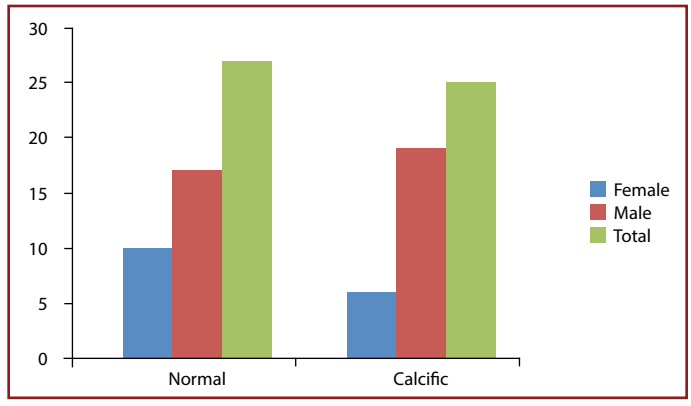

Figure 1. Distribution of aortic valve calcifications between male and female patients.

Table 3. DEXA measurements (mean+SD) (*p-value was estimated using t test)

	Female	Male	Mean	P*
Femoral				
BMD	0.75±0.24	0.89±0.15	0.85±0.19	0.015
T score	–2.11±1.34	–1.33±0.95	–1.57±1.13	0.021
Z score	1.10±1.29	–0.41±1.14	–0.61±1.22	0.06
Lumbar				
BMD	0.74±0.16	0.93±0.18	0.87±0.19	0.001
T score	–2.68±1.45	–1.31±1.72	–1.73±1.75	0.008
Z score	–1.43±1.37	–0.46±2.13	–0.75±1.98	0.11
Radial				
BMD	0.35±0.09	0.46±0.06	0.42±0.09	<0.001
T score	–4.10±1.80	–3.35±2.27	–3.58±2.15	0.24
Z score	–2.90±1.64	–2.89±2.05	–2.89±1.92	0.98

femoral bone densitometry results and aortic valve calcification (p=0.72) (Fig. 3).

No significant correlation was detected between the lumbar bone densitometry results and mitral valve calcification (p=0.22) (Fig. 4).

No correlation was detected between the lumbar bone densitometry results and aortic valve calcification (p=0.86) (Fig. 5).

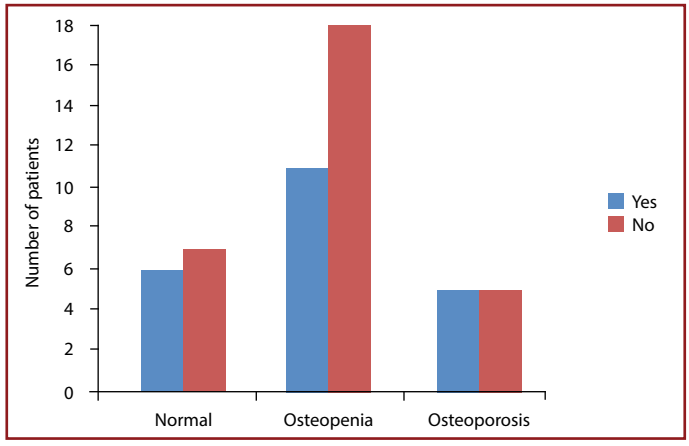

Figure 2. Correlations with mitral valve calcification based on femoral bone densitometry results.

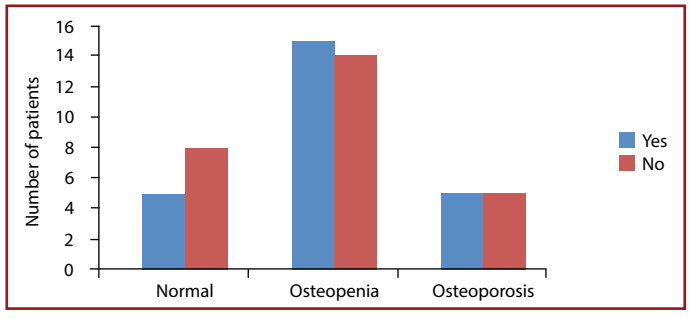

Figure 3. Correlations with aortic valve calcification based on femoral bone densitometry results.

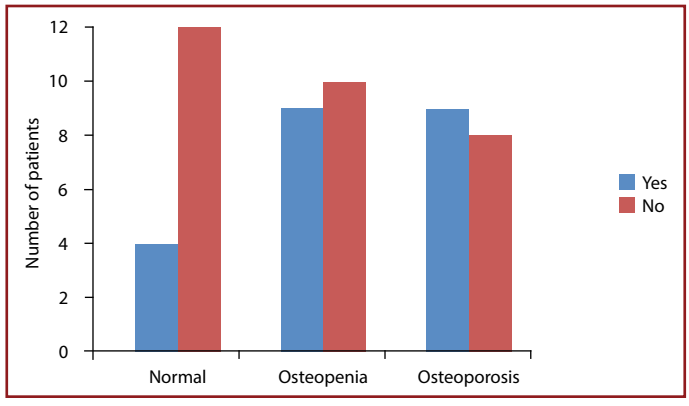

Figure 4. Correlations with mitral valve calcification based on lumbar spine bone densitometry results.

No significant correlation was detected between the radial bone densitometry measurements and mitral valve calcification (p=0.59) (Fig. 6).

No significant correlation was detected between the radial bone densitometry measurements and aortic valve calcification (p=0.79) (Fig. 7).

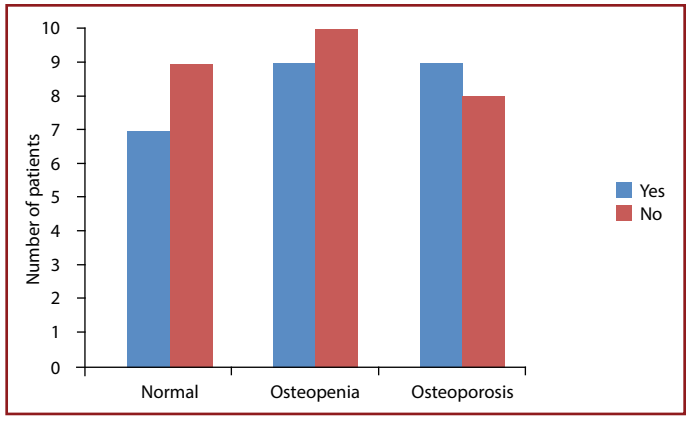

Figure 5. Correlations with aortic valve calcification based on lumbar spine bone densitometry results.

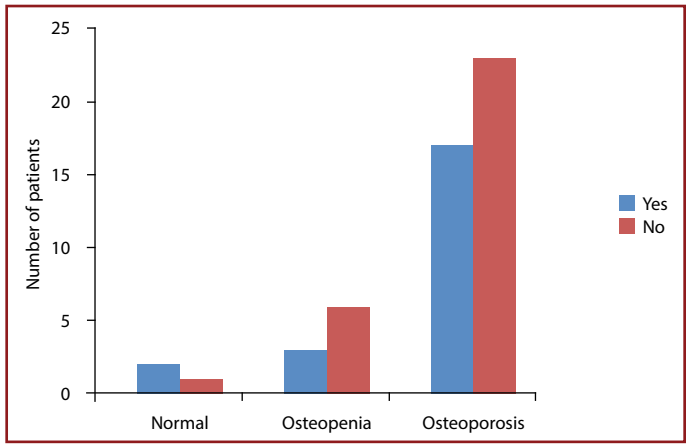

Figure 6. Correlations with mitral valve calcification based on radial bone densitometry measurements.

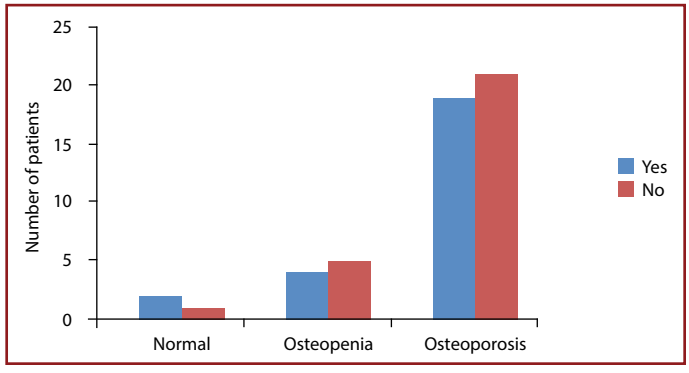

Figure 7. Correlations with aortic valve calcification based on radial bone densitometry measurements.

Discussion

In our study, aortic stiffness and aortic mitral valve calcification were determined, and the relationship between them and the bone densitometry measurements of the patients were investigated. In addition, biochemical parameters and other features associated with aortic stiffness and aortic and mitral calcification were studied. The findings of our study were compared with those from the other studies.

In a study by Aoki et al. [1], the relationship between vascular calcification, arterial stiffness, and bone mineral densitometry measurements was investigated in 83 chronic hemodialysis patients. The aortic calcification index was found to be positively correlated with age, duration of dialysis, pulse pressure, and CRP, while a significant correlation was not detected between the aortic calcification index and serum markers of BMD.

Age, the pulse pressure, albumin, and CRP values were significantly correlated with the aortic calcification index. Aortic calcification index had been found to be inversely correlated with the bone mineral densitometry measurements.

A close relationship between vascular calcification and arterial stiffness was indicated in patients undergoing hemodialysis. Measurement of the hand bone mineral densitometry was labeled as a useful tool in the evaluation of renal diseases related to bone metabolism disorders.

In our study, aortic stiffness was positively correlated with age and calcium–phosphorus product, while aortic stiffness was not correlated with the serum markers of BMD, duration of dialysis, CRP value, serum markers of albumin, and mineral metabolism.

A significant correlation was not detected between mitral valve calcification, age, and CRP values. However, a correlation was noted between aortic valve calcification and age. In our study, there was no correlation between the lumbar, femoral, and radial bone densitometry results detected in patients with and without aortic and mitral valve calcification.

A relationship was found between the radial region Z score and aortic stiffness. In our study, PTH levels were significantly lower in patients with aortic calcification when compared to those without it, whereas no relationship between the radial region T score and the PTH level was detected. In addition, the results of the radial region bone densitometry were compatible with osteoporosis in male and female patients, and a significant correlation was found between the radial region BMD results, age, and duration of dialysis.

In the study by Toussaint et al. [2], the relationship between the bone mineral densitometry results, arterial stiffness, and vascular calcification was studied in 45 patients undergoing hemodialysis (male, 64%; diabetics 38%) with a median age of 58 years. Aortic vascular calcification was found to be positively correlated with the onset time of hemodialysis and DM.

An increase in arterial stiffness was positively correlated with age, DM, and vascular calcification whereas the age at onset of hemodialysis and DM were correlated with aortic calcification, age and DM were associated with arterial stiffness. Lumbar and femoral neck T scores were determined as 0.14 and −1.66, respectively.

Fifty-two patients undergoing hemodialysis were included in our study, and 25% of them were diabetic. In our study, aortic stiffness was consistent with age, whereas no relationship between the duration of dialysis, DM, and the femoral–lumbar–radial group bone densitometry measurements was detected.

Aortic vascular calcification was consistent with age in our study, while the duration of dialysis was not compatible with DM. PTH levels were significantly lower in the aortic calcification group. However, the mean T score of the lumbar region tended to be lower in our study, and a statistically significant difference was detected between male and female patients. The reason for this is that female patients participating in the study may have a tendency to osteoporosis due to their higher mean age.

In the study conducted by Orlic et al. [3], the lumbar, femoral, and forearm bone mineral densitometry measurements in 134 patients undergoing hemodialysis was performed. All DEXA measurements were found to be lower in female patients, while T and Z scores of the forearm were not different. Age was found to be positively correlated with lumbar DEXA results in males and females. In both groups, a negative correlation between femoral and forearm DEXA results was detected. A negative correlation was also found between the PTH values and femoral and forearm DEXA results.

In our study, the femoral and lumbar region T and Z scores were statistically significant in females and males, whereas the radial region T and Z scores were not statistically significant. However, in both male and female patients, the mean radial T score was consistent with osteoporosis, and a statistically significant relationship was found between the radial region BMD values, gender, and duration of dialysis.

In a study, Joki et al. [4] demonstrated that lower BMD and elevated serum phosphorus values were associated with high arterial stiffness in patients undergoing dialysis. In our study, no correlation was found between arterial stiffness and low BMD values and hyperphosphatemia. However,

a significant correlation was found between the calcium–phosphorus product and aortic stiffness.

In a study that included 79 patients undergoing hemodialysis, Torun et al. [5] investigated the association between inflammation and calcification of the cardiac valve, and they observed cardiac vascular calcification in 46% of the cases, including mitral valve calcification in 6%, aortic valve calcification in 14%, and calcification of both valves in 20% of these patients. Patients with valvular calcification were found to be significantly older than those without. When compared with the patients without valvular calcification, significantly higher phosphate and CRP values were detected in the valvular calcification group, which were also significantly proportional to the age of patients undergoing hemodialysis.

In our study, mitral and aortic valve calcifications were detected in 42.3% and 48.1% of patients, respectively, while calcifications of both valves were found in 36.5% of the cases. There was no correlation between patients with and without mitral and aortic valve calcification with respect to CRP, phosphorus level, and duration of dialysis. However, a correlation was detected between age and aortic calcification.

Nign et al. [6] investigated the relationship between bone disease secondary to hyperparathyroidism and bone mineral densitometry results in 185 patients, and they detected a decrease in bone mineral densitometry measurements proportional with the increase in patients' age at dialysis. In our study, a significant relationship was found between the results of forearm BMD and the patient's age at dialysis. In addition, the radial region densitometry results were consistent with osteoporosis in both female and male patients. In dialysis patients, densitometry measurements of other regions can be used to detect osteoporosis.

Leskinen et al. [7] investigated the correlation between vascular calcification and arteriosclerosis in 36 dialysis patients with chronic kidney disease. They had detected mitral and aortic valve calcification in 50% and only mitral valve calcification in 31% of their patients. They had determined risk factors for valvular calcification as the duration of the dialysis treatment and age of the patients. Mitral valve calcification was found to be five-fold higher in diabetic patients, and diabetes was found to be a significant risk factor for mitral valve calcification in patients with chronic renal failure.

In our study including 52 patients, mitral valve and aortic valve calcifications were found in 42.3, and 48.1% of the patients, respectively. Any correlation was not found between the presence or absence of diabetes and aortic and mitral calcification. A significant correlation was detected between aortic calcification and age, while any significant relationship could not be found between gender, duration of dialysis, and aortic and mitral calcification.

In a study conducted by Porazko et al. [8] including 77 patients undergoing hemodialysis, age was related to arterial stiffness such patients. In our study, a correlation was found between aortic stiffness and age.

In the study by Volkov et al. [9] on heart valve calcification in 132 patients undergoing hemodialysis, with chronic renal failure, heart valve calcification was detected in 38.9% of the patients, and age and duration of dialysis were correlated with heart valve calcification. In our study, 52 patients were included, and heart valve calcification was found in 36.5% of the patients. However, duration of hemodialysis was not associated with heart valve calcification. This finding may be due to the low number of cases in our study.

In the study by Guey et al. with 63 hemodialysis patients on factors related to low bone mass, lower bone mass density (osteopenia–osteoporosis) was detected in 81% of the patients. Lower bone mass densities were found in the lumbar spinal and femoral neck regions in 46% and 73% of the patients, respectively. Lumbar and femoral osteoporosis was detected in 8% and 10% of these cases, respectively.

In our study, femoral and lumbar osteoporosis was detected in 19.2% and 32.6% of the cases, respectively. Serum albumin levels were positively correlated with body weight and femoral and lumbar BMD, whereas a negative correlation existed between age, alkaline phosphatase, and PTH (levels 10). In our study, there was a significant difference between the lumbar and femoral region T scores in terms of gender, and the reason for this difference could be the tendency for osteoporosis due to the high average age of female patients.

In the study by Nakai et al. [11], bone mineral densitometry measurements were performed in hemodialysis patients using DEXA, and radial scores were associated with BMD and duration of hemodialysis in male hemodialysis patients, while in female hemodialysis patients, a correlation between BMD, age, and duration of hemodialysis could not be detected. In our study, radial T scores were compatible with osteoporosis in both women and men.

Conclusions

In our study, mitral calcification and aortic calcification were found in 42.3% and 48.1% of the patients, respectively. At the same time, aortic calcification was also observed with an increasing age. The rate of aortic calcification was found to be increased in the group with low PTH levels. Aortic

stiffness deteriorates with aging and a high calcium–phosphorus product.

In our study, when the results of the radial, femoral, and lumbar region bone densitometry measurements were evaluated, no relation was found between the aortic stiffness and aortic/mitral valve calcification groups and the normal, osteopenic, and osteoporotic groups. The lack of such a relationship may be due to a small number of our cases. However, a weak relationship was found between radial Z scores and aortic stiffness. When the results of the densitometry measurements of the lumbar and femoral regions were compared, a statistically significant difference was found between both genders. This result may be related to the high age average of female patients. Radial region T scores were compatible with osteoporosis in both genders, and the DEXA results of this region may provide accurate information about the bone density in patients undergoing hemodialysis. A statistically significant difference was found between the duration of dialysis and the decrease in the radial cortical BMD.

Ethics Committee Approval: The approval of the local Ethics Committee was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.P., F.N.Ö.A.; Design: E.P., F.N.Ö.A.; Data Collection or Processing: E.P.; Analysis or Interpretation: E.P.; Literature Search: E.P.; Writing: E.P.

Conflict of Interest: None declared.

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