# The Relation between Vascular Calcification in Hemodialysis Patients and Osteoporosis

**Original Article**

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## ABSTRACT

**Background:** Cases with end-stage renal disease who get regular hemodialysis were at a higher risk of death due to the high frequency of cardiovascular disease. The objective of the work was to assess the prevalence of osteoporosis and vascular calcification (VC) in hemodialysis individuals utilizing dual-energy X-ray absorptiometry (DEXA) scans and the aortic calcification index (ACI) and to investigate the relationship between these conditions.

**Methods:** This cross-sectional work had been conducted on 84 patients aged >18 years old, both sexes, on regular hemodialysis using an arteriovenous fistula for more than 6 months. All patients were subjected to computed tomography abdomen and DEXA.

**Results:** ACI was significantly greater in individuals with osteoporosis than those with normal bone density ($P$=0.007). Total leucocyte count and parathyroid hormone (PTH) were significantly higher in the ACI ≤ 0.25 group than ACI > 0.25 group ($P$=0.002). A strong negative correlation existed between ACI and both femur neck T-scores and lumbar vertebrae T-scores, which was significant ($P$<0.001). A strong positive correlation existed between age and ACI ($P$=0.012). For T-scores, a moderate negative correlation existed between femur T-scores, age ($P$<0.001), and PTH ($P$=0.001), but weak and non-significant correlations with dialysis duration, phosphorus, and calcium ($P$> 0.07).

**Conclusion:** Osteoporosis, and VC present issues for hemodialysis cases, with osteoporotic individuals having higher body mass index, and PTH levels, in addition to a strong negative connection between ACI and bone mineral density.

**Key Words:** Aortic calcification index, hemodialysis, osteoporosis, vascular calcification.

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## BACKGROUND

Cases with end-stage renal disease (ESRD) who get regular hemodialysis were at an elevated risk of death leading to a high frequency of cardiovascular disease (CVD). Up to forty- fifty percent of individuals with ESRD die from CVD, indicating a rapidly developing atherosclerotic burden, and extensive arterial calcification. This case group has an elevated risk of developing vascular calcification (VC). Bone damage was quite common in persons with chronic kidney disease on hemodialysis (CKD-5D)[1].

Cases with ESRD, particularly those using regular hemodialysis, frequently have low bone density. ESRD cases typically experience accelerated bone loss led to aberrant bone turnover, which results in an elevated prevalence of bone health issues ex osteopenia, osteoporosis[2].

Osteoporosis is a skeletal bone illness defined by reduced bone strength, which leads to bone fragility, and increases the risk of bone fractures. World Health Organization (WHO) defines osteoporosis based on bone mineral density (BMD) measures taken at the lumbar spine or femoral neck[3].

Currently, dual-energy X-ray absorptiometry (DEXA) is the preferred technique for assessing BMD owing to its exceptional precision, accuracy, brief scan duration, and little radiation exposure. Absolute BMD values, Z-scores (number of standard deviations beneath the average for the same age group), and T-scores (number of standard deviations beneath the BMD of a younger reference cohort) for the lumbar spine and right femoral neck were documented as BMD (g/cm²), T-score, and Z-score for the femoral neck, total, and L1 to L4 regions. The WHO established the following classifications depending on the density of bones in Caucasian females: normal bone,

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T-score above -1; osteopenia, T-score ranging from -1 to -2.5; osteoporosis, T-score below -2.5[4].

The incidence of this metabolic bone disease is significantly elevated in the population, and fractures attributable to osteoporosis are more common occurrences. VC was formerly characterized as a passive process, commonly seen as a degenerative outcome of age[5].

The aim of the work was to assess the prevalence of osteoporosis and VC in hemodialysis patients utilizing DEXA scans and the aortic calcification index (ACI) and to investigate the relationship between these conditions.

## PATIENTS AND METHODS

This cross-sectional work had been conducted on 84 participants aged >18 years old, both sexes, on regular hemodialysis using an arteriovenous fistula for more than 6 months. The study was done from November 2022 to September 2023 after approval from the Ethics Committee (IRB:143). The work had been performed by the Declaration of Helsinki. Each subject provided an informed written consent.

Criteria for exclusion were patients with osteoporosis secondary to gastrointestinal causes (such as liver diseases, inflammatory bowel disease (IBD), malabsorption, irritable bowel syndrome (IBS), hematological or oncological causes, immunological causes (such as multiple sclerosis, inflammatory arthritis) and drug-induced causes (such as steroids, proton pump inhibitors (PPIs), anticoagulants, anti-epileptic drugs).

Each participant had been exposed to complete taking of history , physical examinations, laboratory tests [full blood picture (CBC), haemoglobin (Hb), red blood cells (RBCs), white blood cells (WBCs), platelet count, calcium (Ca), phosphorus (PO4), parathyroid hormone (PTH), and alkaline phosphatase (ALP)] and radiological investigations [computed tomography (CT) abdomen and DEXA]

Aortic calcification had been characterized as an area of ≥one mm² with a density of ≥130 Hounsfield units. ACI had been measured by dividing the total score for calcification on all slices by twelve, multiplying by the inverse of the number of slices, and then by 100%. The CT abdomen parameters included a slice thickness of 1-2.5 mm, a slice interval of 1-2 mm, a helical (spiral) scan mode, a tube voltage (kVp) of 120, and a tube current (mA) set based on the patient's size and the specific scanner. The scan field of view (FOV) covered the entire abdominal aorta and surrounding structures, with a gantry rotation time of 0.5 seconds or less.

Bone density testing was performed using DEXA scans. Cases were positioned supine or prone on the DEXA table, with proper alignment to ensure the region of interest (usually the lumbar spine, hip, or forearm) was centered. A dedicated DEXA scanner with low-dose X-rays was used, and common sites for bone density assessment included lumbar spine (L1-L4), and total hip. DEXA scan parameters included high-energy (140 kVp) and low-energy (70 kVp) X-rays, a scanning speed that determined the movement of the X-ray source and detector, and a pixel size that defined the spatial resolution. The T-score from the DEXA scan indicated bone density compared to a healthy 30-year-old, with categories defined by WHO as normal bone density (T-score of -1.0 or above), osteopenia (T-score between -1.0, -2.5), osteoporosis (T-score of -2.5 or lower).

### *Statistical analysis*

The study used SPSS to analyze pre-coded data, summarizing quantitative and qualitative variables using mean, SD, median, and IQR. Comparisons were made using chi-square tests, independent tests, one-way ANOVA tests, and nonparametric Kruskal Wallis and Mann- Whitney tests. Other statistical tests were used as needed, with a *P value* less than 0.05 indicating statistical significance.

## RESULTS

More than half the included patients (52.8%, 47 females) were females, while males represented 41.57% (37 patients). The mean age was 56.98 ± 14.66. Regarding CVD risk, 27.38% (23 patients) had IHD, while 71.4% had no reported CVD risk. Most patients (76.19%, 64 patients) had a normal BMI, 17.85% were overweight (BMI twenty-five–29.9), and only 5.95% (5 patients) were obese. Neurological diseases were reported in 8.33% (7 patients) with a history of stroke, while 90.48% had no adverse neurological history. All patients underwent regular hemodialysis for a mean duration of 7 ± 0.48, with vascular access maintained for a mean of 4.88 ± 1.27. Regarding etiologies behind their ESKD, HTN was the most common cause of ESKD. It was prevalent among 30.95% of included patients (26 patients). This was followed by Diabetes mellitus, which was prevalent among 15.48% of included patients. Polycystic kidney disease was the third most common cause of ESKD among included patients (Table 1).

**Table 1:** Demographic data and etiology of ESKD of the studied patients

| | | N=84 |
|---|---|---|
| Age (years) | | 56.98±14.66 |
| Sex | Female | 47(55.95%) |
| | Male | 37(44.04%) |
| BMI (kg/m$^2$) | 18.5: 24.9 | 64(76.19%) |
| | 25: 29.9 | 15(17.85%) |
| | 30: 34.9 | 5(5.95%) |
| Duration of hemodialysis (years) | | 7±0.48 |
| Time of vascular access (years) | | 4.88±1.27 |
| CVD | IHD | 23(27.38%) |
| | Post CABG | 1(1.19%) |
| | Negative | 60 (71.4%) |
| CNS | Stroke | 7(8.33%) |
| | Intracranial hemorrhage | 1(1.19%) |
| | Negative | 76(90.48%) |
| Etiology of ESRD | | |
| Both atrophic kidneys, HTN | | 1(1.19%) |
| Cardiorenal post covid | | 1(1.19%) |
| Cardiorenal syndrome | | 1(1.19%) |
| CIN | | 1(1.19%) |
| Congenital atrophic kidneys | | 1(1.19%) |
| DM | | 13(15.48%) |
| FSGS | | 3(3.57%) |
| GN | | 1(1.19%) |
| HTN | | 26(30.95%) |
| MPGN | | 1(1.19%) |
| Multiple myeloma | | 1(1.19%) |
| Neurogenic bladder | | 1(1.19%) |
| NSAIDs | | 7(8.3%) |
| Polycystic kidney disease | | 11(13.09%) |
| Post streptococcal GN | | 1(1.19%) |
| Reflux nephropathy | | 1(1.19%) |
| Sarcoidosis | | 1(1.19%) |
| SLE | | 3(3.57%) |
| Unknown | | 9(10.7%) |

Data are presented as mean ± SD or frequency (%). ESKD: end-stage renal disease, BMI: body mass index, CVD: cardiovascular disease, IHD: ischemic heart disease, CABG: coronary artery bypass graft, CNS: central nervous system, ESRD: end-stage renal disease, HTN: hypertension, CIN: cervical intraepithelial neoplasia, DM: diabetes mellitus, FSGS: focal segmental glomerulosclerosis, MPGN: membranoproliferative glomerulonephritis, GN: glomerulonephritis, NSAIDs: non-steroidal anti-inflammatory drugs, SLE: systemic lupus erythematosus.

Regarding laboratory investigations, the mean Hb level was 10.1 ± 1.62. The mean TLC was 6.38 ±2.97. The mean PLT count was 220.96 ± 103.34. Mean Ca level was 9.43 ±0.79. The mean PO4 level was 4.78 ± 1.35. The mean PTH level was 471.87 ± 650.69. The mean ALP level was 371.66 ± 253.15. Regarding radiological investigations, the mean neck of femur T-score was -1.91 ± 0.98. In addition, the mean Lumbar Vertebra T-score was -0.88 ± 1.75. The mean ACI was 0.18 ± 0.16 (Table 2).

**Table 2:** Laboratory and radiological investigations of the studied patients

| | | N=84 |
|---|---|---|
| Laboratory investigations | Hb | 10.1±1.62 |
| | TLC | 6.38±2.97 |
| | PLT | 220.96±103.34 |
| | Ca | 9.43±0.79 |
| | $PO_4$ | 4.78±1.35 |
| | PTH | 471.87±650.69 |
| | ALP | 371.66±253.15 |
| Radiological investigations | Neck of femur T-score | -1.91±0.98 |
| | Lumbar vertebra T-score | -0.88±1.75 |
| | ACI | 0.18±0.16 |

Data are presented as mean ± SD. Hb: hemoglobin, TLC: total leucocyte count, PLT: platelets count, Ca: calcium, $PO_4$: phosphate, PTH: parathyroid hormone, ALP: alkaline phosphatase, ACI: aortic calcification index.

Demographic data and laboratory investigations were insignificantly different between both groups. ACI was significantly greater in patients with osteoporosis than those with normal bone density ($p$=0.007), but not significantly different between osteoporosis, and osteopenia. ACI < 0.25 was significantly greater in patients with normal bone density than those with osteopenia and osteoporosis ($p$=0.031). ACI > 0.25 was significantly greater in patients with osteoporosis than those with osteopenia and normal bone density ($p$=0.031) (Table 3).

**Table 3:** Difference between study groups concerning their demographic data, laboratory investigations, and ACI

| | | Osteoporosis (n=20) | Osteopenia (n=52) | Normal bone density (n=12) | *P* |
|---|---|---|---|---|---|
| Age | | 63.3±11.28 | 57.48±13.8 | 47.58±18.5 | 0.169 |
| Sex | Female | 15(75.0%) | 27(51.9%) | 5(41.66%) | 0.11 |
| | Male | 5(25.0%) | 25(48.0%) | 7(58.33%) | |
| Laboratory investigations | Hb | 9.65±1.7 | 10.17±1.56 | 10.48±1.83 | 0.75 |
| | TLC | 5.83±3.66 | 6.36±2.61 | 7.6±3.31 | 0.16 |
| | PLT | 235.9±84.88 | 227.06±114.79 | 190.67±91.33 | 0.26 |
| | Ca | 9.76±0.81 | 9.26±0.76 | 9.61±0.61 | 0.98 |
| | $PO_4$ | 4.82±1.13 | 4.62±1.29 | 5.03±1.37 | 0.78 |
| ACI | | 0.23±0.16 | 0.19±0.17 | 0.06±0.07 | 0.009* |
| | | P1= 0.798, P2= 0.002*, P3= 0.007* | | | |
| ACI < 0.25 | | 8(40.0%) | 22(42.31%) | 11(91.67%) | 0.031* |
| ACI > 0.25 | | 12(60.0%) | 30(57.69%) | 1(8.33%) | |

Data are presented as mean ± SD or frequency (%). * Significant P value<0.05. P1: osteoporosis vs osteopenia, P2: osteopenia vs normal bone density, P3: normal bone density vs osteoporosis. Hb: hemoglobin, TLC: total leucocyte count, PLT: platelets count, Ca: calcium, $PO_4$: phosphate, ACI: aortic calcification index.

Age was significantly greater in the ACI > 0.25 group than in the ACI ≤ 0.25 group ($p$<0.05). TLC and PTH were significantly greater in the ACI ≤ 0.25 group than ACI > 0.25 group ($P$=0.002). Sex, Hb, PLT, Ca, PO4 and ALP were insignificantly different between both groups (Table 4).

**Table 4:** Comparison between two groups concerning their demographic data and laboratory investigations

| | | ACI ≤ 0.25 (n=41) | ACI > 0.25 (n=43) | *P* |
|---|---|---|---|---|
| Age (years) | | 55.8±18.5 | 61.83±12.07 | 0.029* |
| Sex | Female | 31(50.8%) | 16(69.6%) | 0.12 |
| | Male | 30(49.2%) | 7(30.4%) | |
| Laboratory investigations | Hb | 10.25±1.61 | 9.65±1.56 | 0.87 |
| | TLC | 6.71±3.98 | 5.61±2.15 | 0.002* |
| | PLT | 222.64±79.18 | 227.48±85.15 | 0.6 |
| | Ca | 9.45±0.97 | 9.35±0.63 | 0.7 |
| | $PO_4$ | 4.8±1.04 | 4.52±1.23 | 0.67 |
| | PTH | 486.94±1069.13 | 468.38±676.74 | 0.019* |
| | ALP | 376.11±184.29 | 387.04±231.25 | 0.169 |

Data are presented as mean ± SD.* Significant *P value*<0.05. Hb: hemoglobin, TLC: total leucocyte count, PLT: platelets count, Ca: calcium, $PO_4$: phosphate, PTH: parathyroid hormone, ALP: alkaline phosphatase.

A strong negative correlation existed between ACI and both femur neck T-scores (-0.495) and lumbar vertebrae T-scores (-0.498), that was statistically significant ($p$<0.001) (Table 5).

**Table 5:** Correlation between ACI and T scores of the studied patients

| | | ACI |
|---|---|---|
| Neck of femur T- score | r | -0.495** |
| | *P* | <0.0001* |
| Lumbar vertebra T- score | r | -0.498** |
| | *P* | <0.0001* |

r: correlation coefficient. * Significant *P value*<0.05. ACI: aortic calcification index

There was a strong positive correlation between age, and ACI ($p$=0.012), but weak, non-significant negative correlations between ACI, Ca, PO4, and ALP ($p$> 0.117). For T-scores, there was a moderate negative correlation between femur T-scores, age ($p$<0.001), and PTH ($p$=0.001), but weak and non-significant correlations with dialysis duration, PO4, and Ca ($p$ > 0.07). No significant related were found between lumbar vertebrae T-scores, demographic data, or laboratory investigations (Table 6).

**Table 6:** Correlation between ACI, T score of femur, and Y score of lumbar vertebrae and demographic data and laboratory investigations of the studied patients

| | | ACI | T score femur | T score vertebrae |
|---|---|---|---|---|
| Age | r | 0.274 | -0.301 | -0.092 |
| | *P* | 0.012* | <0.001 | 0.394 |
| Duration of hemodialysis | r | 0.143 | 0.193 | -0.089 |
| | *P* | 0.194 | 0.07 | 0.405 |
| PTH | r | 0.009 | -0.361 | -0.022 |
| | *P* | 0.933 | 0.001 | 0.837 |
| ALP | r | -0.090 | 0.037 | 0.056 |
| | *P* | 0.415 | 0.728 | 0.604 |
| $PO_4$ | r | -0.173 | 0.073 | -0.073 |
| | *P* | 0.117 | 0.494 | 0.499 |
| Ca | r | -0.077 | -0.048 | -0.163 |
| | *P* | 0.486 | 0.657 | 0.128 |

r: correlation coefficient. * Significant *P value*<0.05. ACI: aortic calcification index, PTH: parathyroid hormone, ALP: alkaline phosphatase, $PO_4$: phosphate, Ca: calcium.

## DISCUSSION

The PTH-associated bone disease affects BMD in hemodialysis cases, along with other key risk variables like advanced age, age of menarche, woman gender, and a history of previous fractures. Protective variables for

bone mass loss in this population include BW, Hb, weekly heparin dosage, and a history of parathyroidectomy[6].

Our study showed that, regarding age, our results showed that the mean age was 56.98 ± 14.66 years. Our results are in the same context as Slouma et al.[7] who aimed to evaluate the mineral bone disorders and osteoporosis in haemodialysis individuals, they reported that the mean age of patients was 53.01 ± 14.66 years

Our study showed that, regarding sex distribution, in our study, we found that more than half of the included patients (52.8%, 47) were females. While males represented (41.5%, 37) of included patients. Females represented 75% of patients with osteoporosis in comparison to 51.9% of patients with osteopenia. Our results were in the same context as Khan et al.[8] reported that forty-two men and seventy-eight women cases were enrolled in this study.

Regarding BMI, we found that most included cases (76.19 %, sixty-four cases) had normal body mass index. 17.85 % of included cases were overweight (BMI between twenty-five, and 29.9 kg/m$^2$). Obesity was present among Only 5.95 % of included cases (five cases).

Our results showed Mean duration of hemodialysis was 7 ± 7.48 which was in the same context as Urena et al.[9] reported that the mean duration of hemodialysis was 6.4± 6.8 years, our results agreed with Sakata et al.[10] reported that in ESRD cases mean Duration of hemodialysis was 8.42± 6.00 years.

In our studies, regarding comorbidities, 23 patients had IHD. 1 patient had CABG. 60 patients had free cardiac disease 7 patients had previous strokes. 1 patient had previous intracranial he. 76 patients had no history of CNS problems.

In our study, regarding the etiology behind their ESKD, we found that hypertension was the most common cause of ESKD. It was prevalent among 30.95% of included patients (26 patients). This was followed by Diabetes mellitus, which was prevalent among 15.48% of included patients. Polycystic kidney disease was the third most common cause of ESKD among included patients of ESKD. Our results are in the same context as Avramovski et al.[11] reported that in the HD group among eighty cases, there were 37 (46.2%) had HTN and 16 (20%) had DM.

In our study, regarding laboratory findings, our current study showed that the mean Hb level was 10.1 ± 1.62 (anemia). The mean TLC was 6.38 ± 2.97. The mean PLT count was 220.96 ± 103.34. The mean Ca level was 9.43 ± 0.79. The mean PO4 level was 4.78 ± 1.35. The mean PTH level was (higher than normal) 471.87 ± 650.69. The mean ALP level was 371.66 ± 253.15 (higher than normal). Our study is in the same context as Sakata et al.[10] reported that in ESRD patients mean HB level was 8.80± 1.53 and the mean PO4 level was 5.40± 2.98.

In our study, calcium levels showed a significant negative association with ACI and osteopenia, but a positive correlation with osteoporosis. A negative association existed between femur T-scores, PTH levels (r=-0.361, *P*=0.001), PTH levels were significantly greater in osteoporotic cases compared to those with osteopenia, and normal bone density (*P*<0.001). Our result agreed with Slouma et al.[7] stated that a statistically significant difference existed among studied BMD groups regarding PTH (*P*= 0.006).

It also tested the association between the VC ACI and mean PTH serum levels. We found that mean PTH serum levels were significantly increased among those with low ACI when compared to those with higher ACI (*P*=0.019). Our studies are in the same context as what was reported by Hu et al.[12] reported that a good negative correlation existed between median PTH serum levels and abdominal ACI.

Our studies showed that there were 20 patients with Osteoporosis, 52 cases with Osteopenia, and twelve with Normal bone density, The mean Neck of femur T- score was -1.91 ± 0.98 (osteopenia). The mean Lumbar vertebra T-score was -0.88± 1.75 (normal bone density). This was in the same context as what was reported by Tariq et al.[13] conducted a systematic review recently to identify the prevalence of bone mineral abnormalities among cases with CKD.

It compared ACI across groups and found that ACI was significantly greater in osteoporotic cases contrasted to those with normal bone density (*P*=0.007), but not significantly different between osteoporosis, and osteopenia (*P*=0.798). Sixty percent of osteoporotic cases and 57.69 % of osteogenic cases had ACI > 0.25. cases were divided into low (ACI ≤ 0.25, n=41), high (ACI > 0.25, n=43) VC groups. There was a significant negative association between ACI, both femur neck T-scores (-0.495), and lumbar vertebrae T-scores (-0.498), with *P*<0.001. Also, Taniwaki et al.[14] evaluated aortic calcification in hemodialysis cases with diabetes mellitus, they reported that in non-diabetic cases age was a significant, independent factor related to increased ACI *P*<0.001.

Limitations of the work involved that the sample size was relatively small. The work had been in a single centre. The follow-up of participants was limited to a relatively short period. So, we recommended that high-risk ESRD patients should undergo DXA scans for osteoporosis screening and ACI assessment for VC.

## CONCLUSION

Osteoporosis and VC present significant challenges for hemodialysis patients. Our study revealed that most patients had osteopenia in the femur neck. Patients with osteoporosis exhibited significantly higher BMI and PTH levels compared to those with osteopenia or normal bone density. Approximately 51% (43/84) of patients showed

evidence of VC (high ACI), with most cases occurring in the osteoporosis (12/43) and osteopenia (30/43) groups. ACI was significantly correlated with age. A significant negative correlation existed between VC (measured by ACI) and BMD (T-scores of the lumbar vertebrae and femur neck) across all patients. These findings highlight a strong association between BMD and VC in hemodialysis patients. Further prospective studies are needed to deepen our understanding of this critical relationship.

## ABBREVIATIONS

**VC:** Vascular calcification, **DEXA:** Dual-energy X-ray absorptiometry, **ACI:** Aortic calcification index, **PTH:** Parathyroid hormone, **ESRD:** End-stage renal disease, **WHO:** World health organization, **BMD:** Bone mineral density, **SDs:** Standard deviations, IBD: Inflammatory bowel disease, **CVD:** Cardiovascular disease, **IBS:** Irritable bowel syndrome, **CBC:** Complete blood picture, **Hb:** Hemoglobin, **WBCs:** White blood cells, **RBCs:** Red blood cells, **Ca:** Calcium, **PO4:** Phosphorus, **ALP:** Alkaline phosphatase, **CT:** Computed tomography, **FOV:** Field of view.

## ETHICS APPROVAL

The research was carried out in the Department of Nephrology, Armed Forces College of Medicine, Cairo, Egypt, November 2022 to September 2023, (IRB:143).

## CONSENT TO PARTICIPATE

Informed written consent was obtained from the patients.

## AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## AUTHORS' CONTRIBUTION

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Eman Ebraheim Sarhan], [Hany Hafez Lotfy] and [Mostafa Fouad Mohamed Elseknedy]. The first draft of the manuscript was written by [Ahmed Abdelmonem Emara] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## CONFLICT OF INTERESTS

There are no conflicts of interest.

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