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Inverse association between bone microarchitecture assessed by HR-pQCT and coronary artery calcification in patients with end-stage renal disease

Daniel Cejka [a,b], Michael Weber [b,c], Danielle Diarra [a,b], Thomas Reiter [a,b], Franz Kainberger [b,d], Martin Haas [a,b,*]

[a] Division of Nephrology and Dialysis, Department of Medicine III, Medical University Vienna, Vienna, Austria
[b] Medical University Vienna, Vienna, Austria
[c] Department of Radiology, Medical University Vienna, Vienna, Austria
[d] Division of Neuroradiology and Musculoskeletal Radiology, Department of Radiology, Medical University Vienna, Vienna, Austria

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ABSTRACT

It is a matter of debate whether vascular calcification and bone loss are simultaneously occurring but largely independent processes or whether poor bone health predisposes to vascular calcification, especially in patients with kidney disease. Here we investigated the association between the changes of microarchitecture in weight bearing bone and the extent of coronary artery calcification in patients with chronic renal failure.

The bone microarchitecture of the tibia using high-resolution peripheral quantitative computed tomography (HR-pQCT), bone mineral density using dual X-ray absorptiometry (DXA) of the lumbar spine, femoral neck and distal radius as well as coronary artery calcification using multi-slice CT and reported as Agatston score were measured in 66 patients with end-stage renal disease on chronic hemodialysis. Markers of bone turnover, vitamin D status and intact parathyroid hormone (iPTH) were assessed.

CAC score was found to be <100 in 39% and ≥ 100 in 61% of patients. The median [95% CI] total CAC score was 282 [315–2587]. By univariate analysis, significant correlations between CAC and age ($R = 0.52$, $p < 0.001$), weight ($R = 0.3$, $p < 0.01$) and serum cross laps (CTX, $R = -0.39$, $p < 0.01$) were found, and parameters of bone microarchitecture were numerically but not significantly lower in patients with CAC scores ≥ 100. In multivariate analysis stratifying for gender and correcting for age, tibial density (D_{tot}) and bone volume/total volume (BV/TV) were significantly lower in patients with CAC scores ≥ 100 ($p < 0.05$ for both).

Low trabecular bone volume and decreased cortical bone density are associated with coronary artery calcification in dialysis patients.

Introduction

Chronic kidney disease is a major cardiovascular risk factor [1]. Mortality is approximately 5-fold increased in patients with end-stage renal disease requiring dialysis treatment compared to the general population, with cardiovascular disease being the most common cause of death [2,3]. Vascular calcification occurs early and progresses rapidly in patients on dialysis [4,5], and coronary artery calcification (CAC) is an independent risk factor for mortality in end-stage renal disease patients [6,7]. Although the excessively high incidence and prevalence of vascular calcification are well known, the pathophysiologic mechanisms leading to accelerated vascular calcification are still incompletely understood. The so-called "non-traditional" vascular risk factors seem to become more important for the development of cardiovascular disease as renal function declines. Disorders in mineral and bone metabolism are thought to contribute significantly to cardiovascular morbidity in renal patients [8]. Currently, data on the relationship between bone health and vascular calcification are controversial. An association between bone mineral density and vascular calcification has been reported in the general population [9–11] as well as in patients with end-stage renal disease [12,13]. Additionally, correlations between bone turnover or bone volume and vascular calcification have been reported for iliac bone biopsies taken from dialysis patients [14,15]. However, other studies did not find a relationship between bone parameters and vascular calcification in the general population [16–18] or renal patients [19,20].

So far, studies investigating the relationship between bone and vascular calcification had to rely on rather insensitive methods such as conventional bone mineral density measurements using dual X-ray

* Corresponding author at: Division of Nephrology and Dialysis, Department of Internal Medicine III, Medical University Vienna, Waehringer Guertel 18-20, Vienna 1090, Austria. Fax: +43 431 40400 4392.
E-mail addresses: daniel.cejka@meduniwien.ac.at (D. Cejka), michael.weber@meduniwien.ac.at (M. Weber), danielle.diarra@meduniwien.ac.at (D. Diarra), thomas.reiter@meduniwien.ac.at (T. Reiter), franz.kainberger@meduniwien.ac.at (F. Kainberger), martin.haas@meduniwien.ac.at (M. Haas).

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absorptiometry (DXA) or involved invasive bone biopsies to obtain sufficient information on bone microarchitecture [9–11,14,15]. With high-resolution peripheral quantitative computed tomography (HR-pQCT), detailed information on bone microarchitecture can be obtained non-invasively [21]. Due to its high resolution (approx. 82 μm), HR-pQCT allows for visualization of trabecular and cortical structures. Other methods used so far, such as quantitative computed tomography (qCT), lack the ability to study the trabecular compartment of bone in detail. Similar to histomorphometric analysis of bone biopsy samples, static bone parameters such as bone volume or trabecular number can be obtained with HR-pQCT. Recently, HR-pQCT measurements were reported to be useful in identifying renal patients with a history of low trauma fracture, which underscores the utility of HR-pQCT in this population [22,23].

The aim of this study was to investigate the association between bone microarchitecture measured by HR-pQCT and coronary artery calcification assessed by computed tomography in end-stage renal disease patients.

Materials and methods

Patients

All subjects were recruited from the hemodialysis center of the Medical University Vienna. A chart review was performed for demographic data, dialysis duration, calcium and vitamin D intake, phosphate binder or calcimimetic therapy, previous renal transplantations, intake of oral anticoagulants and other aspects of the patients' medical history. Patients with a history of bisphosphonate use within 5 years prior to study entry were excluded from participation. Dialysis duration was defined as the time from the first day of dialysis to the measurement of HR-pQCT. In patients who had undergone renal transplantation between different periods of dialysis, the intermittent time of a functioning graft was excluded. The study protocol was reviewed and approved by the ethics committee of the Medical University Vienna. The study was conducted in accordance with the Declaration of Helsinki, and all participants gave their written informed consent to participate.

Serologic parameters

Each parameter was determined by calculating the mean of all measurements performed during 12 months prior to the HR-pQCT and DXA investigations. Alkaline phosphatase (AP) was measured by enzyme kinetic analysis (Metra Biosystems, Behring Diagnostic, Germany). Osteocalcin (OC), intact parathyroid hormone (iPTH), c-telopeptide pyridinoline cross-links of type I collagen (CTX, cross laps) and 25-hydroxy-cholecalciferol (25-(OH)-D_3) were determined by electrochemiluminescence (Modular and Elecsys Systems, Roche, Switzerland). Calcitriol (1,25-$(OH)_2$-D_3) was analyzed after chromatographic separation by a radioimmunoassay (DiaSorin, U.S.A). Calcium and phosphate were quantified by routine clinical chemistry analyzers (Olympus, Japan). All measurements were performed according to the standards of Good Laboratory Practice (GLP).

High-resolution peripheral quantitative computed tomography (HR-pQCT)

Trabecular and cortical microarchitecture was determined by performing HR-pQCT at the tibia, as reported previously (23). In short, 110 CT slices were obtained at each site, and a 9-mm-long 3D volume was reconstructed from these. A threshold-based algorithm was used to distinguish trabecular bone from cortical bone. The data were converted into the following histomorphometric parameters: total density (D_{tot} [mg HA/cm^3]), cortical density (D_{cort} [mg HA/cm^3]), trabecular density (D_{trab} [mg HA/cm^3]), cortical thickness (Ct.Th [mm]), trabecular thickness (TbTh [mm]), trabecular number (TbN [mm^1]), bone volume (BV/TV [%]) and trabecular separation (Tb1/NSD [mm]). Tb1/NSD is a measure of the heterogeneity of the trabecular structure. Greater heterogeneity results in a higher Tb1/NSD.

Bone mineral density by dual-energy X-ray absorptiometry

Areal bone mineral density measurements (aBMD) were performed with dual-energy X-ray absorptiometry on a QDR-4500 scanner (Hologic, Waltham, MA), using the manufacturer's recommended standard procedures for the postero-anterior lumbar spine at L_1–L_4, the distal radius (total) and the proximal femur at the femoral neck, trochanter, intertrochanteric region, total region and Ward's triangle. Patients underwent conventional lateral x-ray imaging of the lumbar spine to exclude falsely elevated aBMD readings due to vertebral compression. Vertebrae showing compression (Genant criteria [24]) or other deformations were excluded from analysis. The aBMD is given in g/cm^2, and the individual patients' results are expressed as *t*-scores.

Cardiac calcium scoring

The ECG-gated cardiac computed tomographies (CT) to measure coronary calcifications were performed on a 16-slice scanner (Siemens Somatom 16, Siemens, Forchheim, Germany). All scans were performed in cranio-caudal direction with patients placed in supine position. ECG electrodes were placed outside the field of view of the planed examination. All scans were performed during inspiratory breath hold with prospective electrocardiogram (ECG)-triggering set at 75% of the RR interval. No contrast material was injected. All coronary artery calcification (CAC) data sets were analyzed by a single technician with more than 5 years of experience in cardiac CT imaging using a commercially available software package ("Syngo CaScore"; Siemens Healthcare, Forchheim, Germany). Coronary artery calcium scores were separately obtained for each of the main epicardial coronary arteries [left main artery (LMA), left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA)] and summed to obtain total CAC. For every patient, CAC values were calculated using the Agatston score as described previously [25,26]. Following commonly used classifications of coronary artery calcification severity [27,28], a cutoff CAC score of 100 was chosen to discriminate between patients with absent-to-mild and patients with moderate-to-severe coronary artery calcification.

Statistical analysis

Results are described as mean values with 95% confidence intervals [95% CI] unless specified otherwise.

Continuous data were compared by the Mann–Whitney *U* test and nominal data by the Pearson's χ^2 test. Bivariate associations between the total coronary calcification score and all other parameters were analyzed by Spearman correlation coefficient. All significant variables of the bivariate analysis were included in a linear regression analysis. Analyses of covariance (ANCOVA) were used to compare the age- and gender-corrected HR-pQCT and DXA measurements between patients with and without coronary calcification. Data were analyzed with SPSS (version 17.0; SPSS, Chicago, IL). *p*-values less than 0.05 were considered statistically significant.

Results

Patient characteristics

Of 66 patients studied, 62 were Caucasian, 3 were Indian and 1 was African. Causes of renal failure were glomerulonephritis (17%), diabetic nephropathy (15%), hypertensive/vascular disease (11%), polycystic kidney disease (5%), pyelonephritis/vesico-ureteral reflux (5%) and other known (24%) or unknown (23%) diseases. Twenty patients had undergone previous kidney transplantation. Twelve patients had

received one kidney transplant, 5 patients had received 2 transplants and 3 patients had received 3 transplants. Body weight was higher in men compared to women (84 [76–97] kg vs 62 [457–72] kg, $p < 0.001$). Body mass index (men: 25.5 [24–31], women: 26 [22–29], $p = 0.7$), distribution of age (men: 60 [50–66] years; women 55 [46–72] years, $p = 0.3$) and time on dialysis (men: 21 [14–74] months; women: 50 [30–75] months, $p = 0.5$) were similar for men and women.

The median total CAC of the entire study cohort was 282 [315–2587]. Among 26 patients with a CAC score below 100, 17 patients had no detectable calcifications. No statistically significant differences were found for age, dialysis duration, preexisting cardiovascular disease and medication such as phosphate binders, statins, vitamin D supplements or history of steroid intake between patients with Agatston scores below and above 100. As for serologic markers of bone turnover, c-telopeptide cross laps (CTX) were significantly lower in patients with CAC above 100. Among cholesterol fractions, HDL was found to be significantly higher in patients with CAC above 100. Demographic data of the entire study cohort and according to CAC status are shown in Table 1.

Coronary artery calcification and bone parameters

Men were more likely to have CAC ≥100 (72% vs 44%, $p < 0.02$) and had significantly higher CAC scores than women (Table 2). With the exception of cortical density (D_{cort}) and trabecular thickness (TbTh), all parameters of bone microarchitecture measured by HR-pQCT differed significantly between men and women (Table 2). The areal bone mineral density of the radius measured with DXA was significantly lower in women. Neither lumbar spine nor femoral neck BMD differed significantly between men and women (Table 2).

Table 2
Coronary artery calcification (CAC), bone microarchitecture (HR-pQCT) and bone mineral density (DXA) in male and female patients (mean; 95% CI).

	Men	Women	*p*
CAC score (Agatston)			
Total score	1535 [*789–2281*]	514 [*117–911*]	0.01
Left main artery	46 [*6–86*]	6 [*0–15*]	0.035
Left anterior descending	630 [*333–927*]	208 [*68–349*]	0.018
Circumflex artery	193 [*2–384*]	57 [*0–123*]	0.24
Right coronary artery	667 [*298–1035*]	242 [*0–519*]	0.017
HR-pQCT Tibia			
D_{tot} (mg HA/cm^3)	255 [*234–276*]	209 [*182–236*]	0.012
D_{cort} (mg HA/cm^3)	803 [*781–826*]	795 [*762–828*]	0.74
Ct.Th (mm)	1.04 [*0.93–1.14*]	0.80 [*0.68–0.91*]	0.004
D_{trab} (mg HA/cm^3)	150 [*136–164*]	116 [*98–134*]	0.003
BV/TV (%)	12.5 [*11.3–13.7*]	9.9 [*8.4–11.3*]	0.004
TbN (mm^{-1})	1.81 [*1.66–1.95*]	1.40 [*1.24–1.56*]	<0.001
TbTh(mm)	0.07 [*0.06–0.07*]	0.07 [*0.06–0.08*]	0.76
Tb1/NSD (mm)	0.25 [*0.21–0.28*]	0.48 [*0.32–0.64*]	<0.001
DXA			
Lumbar spine g/cm^2	0.98 [*0.92–1.04*]	0.88 [*0.82–0.95*]	0.072
Lumbar spine *t*-score	−0.9 [*−1.5* to *−0.4*]	−1.5 [*−2.1* to *−0.9*]	0.31
Femoral neck g/cm^2	0.70 [*0.65–0.75*]	0.63 [*0.58–0.68*]	0.054
Femoral neck *t*-score	−1.8 [*−2.2* to *−1.4*]	−1.9 [*−2.4* to *−1.5*]	0.49
Radius (total) g/cm^2	0.53 [*0.49−0.57*]	0.42 [*0.39−0.45*]	<0.001
Radius (total) *t*-score	−2.8 [*−3.6* to *−2.1*]	−2.8 [*−3.5* to *−2.2*]	0.85

Associations between bone microarchitecture and coronary artery calcifications

In the univariate analysis, significant correlations between CAC and age ($R = 0.52$, $p < 0.001$), weight ($R = 0.3$, $p < 0.01$) and serum cross laps (CTX, $R = -0.39$, $p < 0.01$) were found, while an inverse

Table 1
Baseline characteristics (mean [95% CI] or percentage) of patients with a coronary artery calcification (Agatston) score < or >100. p-values are given for differences between patients with low and high Agatston scores.

	All patients	CAC score <100	CAC score ≥100	p
n/men/women	66/39/27	26/11/15	40/28/12	0.04
Age (years)	59 [55–62]	50 [45–55]	64 [60–67]	<0.001
Body mass index (kg/m^2)	25 [24–26]	24 [23–26]	25 [24–27]	0.48
Body weight (kg)	72 [68–76]	67 [60–74]	74 [70–79]	0.043
Dialysis vintage (months)	59 [39–79]	71 [26–116]	51 [33–68]	0.85
History of low trauma fracture (%)	25	23	27	0.7
Smokers (%)	25	36	17	0.12
Diabetes mellitus (%)	32	36	30	0.78
Previous transplantations (%)	32	31	33	1
Peripheral vascular disease (%)	20	12	25	0.33
History of stroke (%)	14	8	18	0.46
History of myocardial infarction (%)	14	4	20	0.13
Calcium carbonate (%)	35	38	33	0.79
Aluminum hydroxide (%)	65	68	63	0.79
Lanthanum carbonate (%)	13	16	10	0.7
Sevelamer hydrochloride (%)	51	52	50	1
Cinacalcet (%)	15	12	18	0.72
Vitamin D supplement (%)	52	52	53	1
Statins (%)	18	20	18	1
History of corticosteroid use (%)	24	31	20	0.38
Total cholesterol (mg/dL)	181 [168–194]	170 [144–196]	188 [174–203]	0.09
LDL cholesterol (mg/dL)	99 [90–108]	93 [76–110]	103 [93–114]	0.19
HDL cholesterol (mg/dL)	47 [43–50]	41 [36–47]	50 [45–55]	0.016
Calcium (mg/dL)	8.9 [8.7–9.0]	8.8 [8.5–9.0]	9.0 [8.8–9.2]	0.2
Phosphate (mg/dL)	5.9 [5.6–6.2]	6,0 [5.4–6,5]	5.8 [5.4–6.2]	0.57
Alkaline Phosphatase (U/L)	105 [81–128]	123 [68–177]	93 [74–112]	0.35
Osteocalcin (pg/mL)	204 [138–269]	273 [111–434]	163 [114–211]	0.063
C-telopeptide (ng/mL)	2.1 [1.8–2.5]	2.7 [2.1–3.3]	1.7 [1.4–2.0]	0.003
Intact PTH (pg/mL)	288 [210–366]	316 [182–450]	269 [170–368]	0.46
25 (OH) D3 (nmol/l)	42 [37–46]	44 [36–51]	41 [35–46]	0.59
1,25 (OH)2 D3 (pg/mL)	13 [11–15]	13 [9–16]	13 [11–15]	0.54

Note: Conversion factors for units: calcium in mg/dL to mmol/L, ×0.25; phosphate in mg/dL to mmol/L, ×0.32; 25(OH)D3 in ng/mL to nmol/L, ×2.5; 1,25(OH)2 D3 in pg/mL to pmol/L, ×2.6.

Table 3
Coronary artery calcification (CAC), bone microarchitecture (HR-pQCT) and bone mineral density (DXA) stratified for CAC status (mean; 95% CI). p-values are given for differences between patients with CAC scores below and above 100.

	All patients	Agatston score <100	Agatston score ≥100	p
Coronary artery calcification				
Total score	1118 [641–1594]	17 [6–29]	1833 [1123–2543]	<0.001
Left main artery	30 [6–54]	3 [0–9]	47 [7–86]	0.034
Left anterior descending	458 [270–645]	11 [2–20]	748 [470–1025]	<0.001
Circumflex artery	137 [23–252]	3 [0–7]	225 [38–412]	<0.001
Right coronary artery	493 [248–738]	0.1 [0–0.4]	814 [436–1191]	<0.001
HR-pQCT Tibia				
D_{tot} (mg HA/cm^3)	236 [219–253]	246 [214–277]	230 [210–250]	0.26
D_{cort} (mg HA/cm^3)	800 [782–818]	824 [801–846]	785 [758–811]	0.053
Ct.Th (mm)	0.94 [0.86–1.02]	1.01 [0.88–1.14]	0.90 [0.79–1.00]	0.18
D_{trab} (mg HA/cm^3)	136 [125–148]	137 [116–157]	136 [121–150]	0.67
BV/TV (%)	11.4 [10.5–12.4]	11.7 [10.1–13.2]	11.3 [10.1–12.5]	0.56
TbN (mm^{-1})	1.64 [1.53–1.76]	1.61 [1.40–1.83]	1.66 [1.53–1.80]	0.46
TbTh (mm)	0.07 [0.07–0.07]	0.07 [0.07–0.08]	0.07 [0.06–0.07]	0.068
Tb1/NSD (mm)	0.34 [0.27–0.41]	0.39 [0.23–0.55]	0.31 [0.24–0.37]	0.57
DXA				
Lumbar spine g/cm^2	0.94 [0.90–0.99]	0.94 [0.87–1.01]	0.94 [0.88–1.01]	0.94
Lumbar spine t-score	−1.2 [−1.6 to −0.8]	−1.2 [−1.8 to −0.5]	−1.2 [−1.7 to −0.6]	0.87
Femoral neck g/cm^2	0.67 [0.64–0.71]	0.66 [0.61–0.72]	0.68 [0.63–0.73]	0.91
Femoral neck t-score	−1.8 [−2.1 to −1.6]	−1.9 [−2.4 to −1.4]	−1.8 [−2.2 to −1.5]	0.73
Radius g/cm^2	0.48 [0.45–0.51]	0.49 [0.44–0.54]	0.48 [0.44–0.52]	0.82
Radius t-score	−2.8 [−3.3 to −2.4]	−2.5 [−3.1 to −1.8]	−3.1 [−3.8 to −2.4]	0.23

correlation between CAC and tibial density (D_{tot}) was only of borderline significance ($R = -0.24$, $p = 0.053$). All bone parameters were numerically lower (trabecular heterogeneity higher) in patients with CAC scores ≥100, but differences did not reach statistical significance (Table 3). Differences in cortical density of the tibia approached borderline significance ($p = 0.053$).

In multivariate analysis stratifying for gender and correcting for age (Table 4), tibial density (D_{tot}) and bone volume/total volume (BV/TV) were significantly lower in patients with CAC scores ≥100 ($p < 0.05$ for both).

Discussion

To our knowledge, this is the first study investigating the association between bone microarchitecture measured by HR-pQCT and coronary artery calcification in patients with end stage renal disease. The key finding of this study is that patients with CAC scores ≥100 have a lower trabecular bone volume and total density of the tibia compared to patients with lower CAC scores, independent of sex and age.

It is currently a matter of debate whether increased vascular calcification in chronic kidney disease is driven by bone loss, or whether the simultaneous vascular and osseous changes are simply linked by age and duration of dialysis. While some studies have reported a significant association between bone parameters and vascular calcification [9–13,15], others reported that such associations were lost after multivariate analysis, especially when correcting for age [16–20,29].

In this study the significant association between bone microarchitecture and the prevalence of coronary artery calcification is suggestive of a pathophysiological link between bone and vasculature in dialysis patients. A possible explanation could be that low bone volume (and hence lower bone surface) leads to a decreased short-term buffering capacity of dietary calcium loads, which may be further aggravated by a decreased calcium buffering capacity due to altered chemical composition of bone matrix found in chronic kidney disease patients (reviewed in [30]).

So far, only one population-based study with 693 subjects investigated the association between bone microarchitecture assessed by HRpQCT and vascular calcification [31]. Chow et al. found that in randomly selected subjects, trabecular number and separation were inversely associated with aortic calcification in men over 50 years, but not in women. All other significant univariate associations between parameters of bone microarchitecture and vascular calcification were lost after correction for age. In our study with dialysis patients, we found similar changes in both men and women, independent of age. The findings

Table 4
Age-corrected HR-pQCT parameters of the tibia in men and women with a total coronary artery calcification CAC score below or above 100 (mean; 95% CI).

	D_{tot} (mg HA/cm^3)	D_{cort} (mg HA/cm^3)	Ct.Th (mm)	D_{trab} (mg HA/cm^3)	BV/TV (%)	TbN (mm^{-1})	TbTh (mm)	Tb1/NSD (mm)
Men								
CAC score <100 (n = 11)	289	815	1.19	168	14	1.99	0.07	0.22
95% CI	[248–332]	[771–860]	[0.99–1.39]	[141–196]	[12–17]	[1.72–2.26]	[0.06–0.09]	[0.05–0.40]
CAC score ≥100 (n = 28)	241	804	0.98	142	12	1.73	0.07	0.26
95% CI	[216.07–266.55]	[777–831]	[0.87–1.1]	[126–159]	[11–13]	[1.58–1.9]	[0.06–0.08]	[0.15–0.36]
Women								
CAC score <100 (n = 15)	228	811	0.87	126.8	11	1.44	0.08	0.52
95% CI	[192–265]	[773–850]	[0.69–1.04]	[102–151]	[9–13]	[1.21–1.68]	[0.07–0.09]	[0.36–0.67]
CAC score ≥100 (n = 12)	189	768	0.71	105	9	1.38	0.07	0.44
95% CI	[149–228]	[726–810]	[0.53–0.9]	[79–131]	[7–11]	[1.12–1.63]	[0.06–0.08]	[0.28–0.60]
p	0.03	0.20	0.06	0.08	0.03	0.21	0.14	0.78

Abbreviations: D_{tot}, total density; D_{cort}, cortical density; Ct.Th, cortical thickness; D_{trab}, trabecular density; BV/TV, bone volume; TbN, trabecular number; TbTh, trabecular thickness; Tb1/NSD, heterogeneity of trabecular separation.

were statistically significant despite a considerably smaller study population, which underscores the severity of bone and mineral metabolism disorders found in dialysis patients. Obviously, the pathophysiologic influence of chronic kidney failure on bone is stronger than classical determinants of bone health such as age and gender.

In the present study, almost all parameters of bone microarchitecture tended to be lower in patients with higher CAC scores. Besides significant differences in total density (D_{tot}) and bone volume (BV/TV), differences in cortical thickness (Ct.Th) and trabecular density (D_{trab}) were close to statistical significance. Thus, both the cortical as well as the trabecular compartment seem to be associated to some extent with vascular calcification in dialysis patients.

Patients with CAC scores ≥100 were significantly heavier compared to patients with lower CAC scores. This might be explained by the fact that the majority of patients with higher CAC scores were men. Despite male overrepresentation in the CAC >100 group, all bone parameters except trabecular heterogeneity were numerically lower in this group. As male dialysis patients generally have higher DXA and HR-pQCT parameters than women (Table 2, [23]), this finding is again supporting the concept of a bone-vasculature cross-talk in dialysis patients. Among parameters of bone turnover, CTX was significantly lower in patients with CAC scores ≥100, while alkaline phosphatase tended to be lower in this group. This may suggest an association between low bone turnover and CAC.

This study has several limitations, with the lack of information on bone turnover derived from bone biopsy studies probably being the most relevant. Since the predictive values of serological markers of bone turnover are very low in dialysis patients [32] and HR-pQCT cannot detect unmineralized osteoid, actual bone turnover can only be estimated in the patient population studied here. Uncontrolled secondary hyperparathyroidism might be a confounding factor, although iPTH levels did not differ significantly between patients with low and high CAC scores. Uncontrolled hyperparathyroidism may lead to loss of appendicular bone [33] and predispose to vascular calcification [34]. However, iPTH levels in the current study population were reasonably well controlled, with only 5 patients showing iPTH levels above 9 times the upper limit of normal, which is the recommended upper level of iPTH by current treatment guidelines for dialysis patients [32]. From previous bone biopsy studies, it can be estimated that a considerable number of the patients in this study were likely to have a dynamic bone disease rather than high bone turnover [35]. Another limitation is that no information regarding calcification of other parts of the vascular tree such as the abdominal aorta is available in this study. The arterial system of dialysis patients shows several predilection sites for vascular calcification, which may be due to different sites of origin of vascular smooth muscle cells during embryogenesis [36]. Thus, the association between bone microarchitecture and vascular calcification reported here apply only to the distal tibia and the coronary arteries. Furthermore, association does not prove causality. Other limitations include the mono-centric and cross-sectional nature of the study design, which included a heterogeneous patient population such as post-renal transplant patients, diabetics and patients of both genders. The relatively small sample size in this study has to be acknowledged, limiting extensive multivariate correction for possible confounders. Nevertheless, statistically significant findings presented here despite small sample size underscore the biological relevance of the findings.

In conclusion, our study suggests that loss of trabecular bone volume and bone density in dialysis patients is linked with calcification of the coronary vessels. However, it will need prospective and interventional studies to certify the association between bone structure and density with changes of vascular calcification.

Disclosure statement

The authors have nothing to disclose.

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