Bone microarchitecture is more severely affected in patients on hemodialysis than in those receiving peritoneal dialysis

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We used high-resolution quantitative computed tomography to study the microarchitecture of bone in patients with chronic kidney disease on dialysis. We compared bone characteristics in 56 maintenance hemodialysis (21 women, 14 post-menopausal) and 23 peritoneal dialysis patients (9 women, 6 post-menopausal) to 79 healthy men and women from two cohorts matched for age, body mass index, gender, and menopausal status. All underwent dual-energy X-ray absorptiometry of the spine and hip to measure areal bone mineral density, and high-resolution peripheral quantitative computed tomography of the radius and tibia to measure volumetric bone mineral density and microarchitecture. When compared to their matched healthy controls, patients receiving hemodialysis and peritoneal dialysis had a significantly lower areal bone mineral density in the hip. Hemodialysis patients had significantly lower total, cortical, and trabecular volumetric bone mineral density at both sites. Hemodialysis patients had significantly lower trabecular volumetric bone mineral density and microarchitecture at the tibia than the peritoneal dialysis patients. Overall, peritoneal dialysis patients were less affected, their cortical thickness at the distal tibia being the only significant difference versus controls. Thus, we found more severe trabecular damage at the weight-bearing tibia in hemodialysis compared to peritoneal dialysis patients, but this latter finding needs confirmation in larger cohorts.

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The physiological mechanisms regulating blood levels of calcium, phosphate, vitamin D, and parathyroid hormone (PTH) are often impaired in chronic kidney disease (CKD), inducing both an increased incidence of vascular or soft tissue calcifications and bone structural impairment. Skeletal changes may occur years before the main clinical manifestations of bone disorders in CKD (i.e., pain and fractures).[1] The risk of fracture exceeds that of the normal population in both patients with pre-dialysis CKD and dialysis patients. Indeed, a twofold increase in hip fracture risk in patients with moderate-to-severe kidney disease and a fourfold increase in dialysis men and women have been observed in the United States.[2,3] Moreover, young dialysis patients (age <45 years) have a 80-fold higher relative risk of hip fracture than age- and sex-matched controls subjects.[3] Studies have identified risk factors for fracture in dialysis patients that included traditional risk factors (i.e., aging, female gender, lower body weight, Caucasian race, impaired physical functioning, tobacco exposure, and use of psychoactive drugs) and specific comorbidities often associated to CKD such as peripheral vascular disease, history of kidney transplant, and either low or high PTH levels.[4–7]

The majority of studies of bone loss in CKD have been performed with dual-energy X-ray absorptiometry (DXA) to measure the areal bone mineral density (aBMD) at the spine and proximal femur. However, even though this quantitative technique is commonly used to screen individuals at risk of fragility fracture in the general population, its value among CKD patients is debated because of several technical limitations, such as the overestimation of spine aBMD and *T*-score because of aortic calcifications and the inability to distinguish cortical (Ct) and trabecular (Tb) bone.[8–10] Therefore, newer imaging modalities with improved spatial resolution, such as peripheral quantitative computed tomography (pQCT)[11] and more recently high-resolution pQCT (HR-pQCT) or magnetic resonance imaging, have been developed, to allow a three-dimensional assessment of microarchitecture, thus providing a more accurate estimation

of bone quality and strength. HR-pQCT has been previously described and has already been used to assess bone microstructure in predialysis patients,[12–15] but was rarely used to investigate bone health in dialysis patients.

The aims of this single-center cross-sectional study were: (1) to compare aBMD measured by DXA, volumetric BMD (vBMD), and bone macro and microarchitecture parameters assessed by HR-pQCT in maintenance hemodialysis (HD) patients and peritoneal dialysis (PD) patients with healthy controls, (2) to compare those results between the two different types of dialysis groups, and (3) to examine associations between bone data, and clinical and biochemical variables in both dialysis groups.

RESULTS

Characteristics of study patients

HR-pQCT data at the tibia were not analyzed only in one man, due to movement artefacts.

As shown in Table 1, HD patients were younger and less likely to be Caucasian than PD patients.

As shown in Table 2, HD patients had a higher degree of acidosis and greater concentrations of 25OH vitamin D than PD patients.

The proportion of patients receiving a native vitamin D, active vitamin D and calcium supplementation, a non-calcium phosphate binder (sevelamer or lanthanum carbonate), and cinacalcet–HCl treatment was not different between dialysis groups (Table 2). About 20% of patients in both groups had history of corticosteroid exposure and only two HD patients and one PD patient were currently receiving corticosteroids. No patient had history of bisphosphonates, gonadal steroids, or aromatase inhibitors exposure.

DXA results in HD and PD patients

Total hip *T*-score was lower in HD and PD patients in comparison with their matched controls, whereas there was no difference at the lumbar spine (Table 3). No difference was observed in PD vs. HD patients at both sites.

Macroarchitecture in HD and PD patients

At both sites, HD men and women had significant lower Ct cross-sectional area, compared with their matched controls (Tables 3 and 4). PD patients had significant lower Ct cross-sectional area versus controls.

Microarchitecture in HD and PD patients

Figure 1 illustrates a distal tibial analysis (two-dimensional slice) by HR-pQCT in a male control aged 34 years (Figure 1a) and a male patient (Figure 1b) aged 26 years who has been treated with hemodialysis for 13 months. He suffered from hypertensive nephrosclerosis. His cortex is thinand he had qualitative impairment of trabecular bone. HD patients had both Tb and Ct bone impairment compared with their matched controls. At the tibia, HD patients had lower total, Ct and Tb vBMD, lower Ct.Th and Tb.Th, as well as a lower Tb.N, compared with their matched controls (Table 3). Moreover, they had higher Tb.Sp and Tb.SpSD than controls. At the radius, HD patients had also lower total, Ct and Tb vBMD, lower Ct.Th and Tb.Th than controls, and the same trend than at the tibia was observed for Tb.N, Tb.Sp, and Tb.SpSD, but it did not reach statistical significance (Table 3). Bone parameters were analyzed

Table 1 | Characteristics of the dialysis patients

	HD patients (*n*=56)	PD patients (*n*=23)
Age (years)	51 ± 16*	60 ± 16
Gender (M/F)	35/21	14/9
Caucasian race (%)	70*	96
Menopausal status for women (%)	67	67
Diabetes mellitus (%)	25	13
Weight (kg)	71 ± 16	77 ± 13
Height (cm)	168 ± 10	167 ± 8
Body mass index (kg/m^2)	25.3 ± 5.1	27.5 ± 3.8
Main cause of kidney disease (n)		
Chronic glomerulonephritis	12	6
Tubular and interstitial disease	5	1
Vascular disease	10	5
Diabetes	11	2
Polycystic kidney disease	6	7
Hereditary nephropathy	3	0
Others	9	2
Dialysis duration (months; median (IQR))	20 (6–41)	14 (5–28)
Parathyroidectomy (%)	9	0
History of transplantation (%)	14	4
History of fragility fractures (%)	4	0
History of tobacco exposure (%)	57	52
Current smokers (%)	16	13

Abbreviations: F, female; HD, hemodialysis; IQR, interquartile range; M, male; PD, peritoneal dialysis. *$P<0.05$ when comparing HD versus PD patients.

Table 2 | HD and PD patients' serum values and medication use

	HD patients (*n*=56)	PD patients (*n*=23)
Calcium (mg/dl)	9.00 ± 0.68	9.00 ± 0.70
Phosphate (mg/dl, median (IQR))	4.8 (4.9–6.4)	4.9 (4.2–6.3)
Bicarbonate (mol/l/l)	22.2 ± 2.2*	24.2 ± 3.5
CRP (mg/l, median (IQR))	3.8 (1.6–10.8)	2.6 (1.8–4.4)
25(OH) vitamin D (ng/ml)	28 ± 14*	19 ± 11
1,25$(OH)_2$ vitamin D (pmol/l)	50 ± 27	38 ± 19
BSAP (μg/l)	21.8 ± 18.3	17.7 ± 11.3
iPTH (pg/ml, median (IQR))	299 (99–472)	320 (172–511)
iPTH < 130 pg/ml (%)	29	13
iPTH (130–585) pg/ml (%)	52	70
iPTH > 585 pg/ml (%)	20	17
History of corticosteroid treatment > 3 months (%)	20	22
Native vitamin D supplement (%)	30	22
Active vitamin D supplement (%)	43	50
Calcium supplement (%)	57	44
Phosphate binder (%)	55	61
Cinacalcet–HCl (%)	23	17

Abbreviations: BSAP, bone-specific alkaline phosphatase; CRP, C-reactive protein; HD, hemodialysis; iPTH, second-generation intact parathyroid hormone; IQR, interquartile range; PD, peritoneal dialysis.
*$P<0.05$ when comparing HD versus PD patients.