Bone mineral densitometry in patients on hemodialysis: difference between genders and what to measure

Orlić, Lidija; Crnčević, Željka; Pavlović, Draško; Zaputović, Luka

Source / Izvornik: **Renal Failure, 2010, 32, 300 - 308**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.3109/08860221003611661

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:453829

Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: http://www.tandfonline.com/loi/irnf20

Bone mineral densitometry in patients on hemodialysis: difference between genders and what to measure

Lidija Orlic, Zeljka Crncevic, Drasko Pavlovic & Luka Zaputovic

To cite this article: Lidija Orlic, Zeljka Crncevic, Drasko Pavlovic & Luka Zaputovic (2010) Bone mineral densitometry in patients on hemodialysis: difference between genders and what to measure, Renal Failure, 32:3, 300-308, DOI: 10.3109/08860221003611661

To link to this article: http://dx.doi.org/10.3109/08860221003611661

Renal Failure, 32, 300–308, 2010

ISSN: 0886-022X print / 1525-6049 online
DOI: 10.3109/08860221003611661

informa
healthcare

CLINICAL STUDY

Bone mineral densitometry in patients on hemodialysis: difference between genders and what to measure

Lidija Orlic[1], Zeljka Crncevic[2], Drasko Pavlovic[3] and Luka Zaputovic[4]

[1] *Department of Nephrology, University Hospital Rijeka, Rijeka, Croatia*

[2] *Department of Endocrinology, University Hospital Rijeka, Rijeka, Croatia*

[3] *Department of Nephrology, Sestre Milosrdnice University Hospital, Zagreb, Croatia*

[4] *Department of Cardiology, University Hospital Rijeka, Rijeka, Croatia*

ABSTRACT

Introduction: Chronic kidney disease (CKD) and osteoporosis are important health problems. There is an interrelationship between osteoporosis and CKD. Bone densitometry is the "gold" standard in the diagnosis of osteoporosis. Unfortunately, there are some problems with the interpretation of bone densitometry in CKD patients. The goal of this study was to determine bone mineral density (BMD) in CKD patients, to assess the difference between genders and different sites of bone densitometry correlation between BMD and laboratory parameters, and to assess the most optimal measuring site. Methods: We studied 134 hemodialysis (HD) patients (62 females, 72 males). The mean age was 56.4 ± 12.4 years and the mean duration of HD was 54.4 ± 60 months. BMD of the lumbar spine (posterior–anterior projection and lateral projection), hip (femoral neck, trochanter, intertrochanter, total femur, the Ward's Triangle), and forearm (ultradistal (UD), middistal (MID), distal third portion, and total forearm) was measured using dual X-ray absorptiometry (DXA) (Hologic Delphi apparatus). Values were expressed as BMD, *T*-score, and *Z*-score. Results: Females had lower values of BMD in all measurement points. There were no significant differences in *T*- and *Z*-scores of forearm between males and females. Age was in a positive correlation with lumbar spine BMD in males and females. There was a negative correlation with neck and forearm BMD in both groups. Serum parathyroid hormone (PTH) was also in negative correlation with hip and forearm BMD in both groups. The best correlation of BMD in different sites was between forearm and neck. Conclusion: BMD data in CKD patients should be interpreted with caution and appendicular skeletal sites should be included in the evaluation.

Keywords: bone mineral density; dual X-ray absorptiometry; chronic kidney disease; hemodialysis; osteoporosis

Received 16 July 2009; revised 25 October 2009; accepted 10 January 2010
Correspondence: Lidija Orlic, Department of Nephrology, Rijeka University Hospital, T. Strizica 3, 51000 Rijeka, Croatia; fax: +38551407156; E-mail: lidija.orlic@ri.t-com.hr

INTRODUCTION

Chronic kidney disease (CKD) and osteoporosis are among the most significant health problems in the developed world.[1,2] Osteoporosis, generally defined as a bone disorder characterized by an increased risk of fracture, is the most commonly diagnosed bone disease.[3]

The diagnosis of osteoporosis is based on bone mineral density (BMD) criteria, established 15 years ago by the World Health Organization (WHO). It is most often assessed by dual X-ray absorptiometry (DXA). Indeed, the WHO criteria for the diagnosis of osteoporosis are only for DXA. Results are expressed as BMD (g/cm^2) or *T*- and *Z*-scores. The *T*-score is the number of SDs from the mean of a healthy young adult population. The *Z*-score is the number of SD from the mean of a healthy age and gender-matched population.[3,4] The *T*-score is the "gold" standard in defining osteoporosis. WHO criteria for the diagnosis of osteoporosis are only the *T*-score, while the *Z*-score could provide useful information in patients with secondary, that is, not age-related osteoporosis. The most common skeletal sites measured by DXA are the lumbar spine and the proximal femur. Peripheral sites, that is, the forearm, may also be measured. In the general population, the risk of fracture increases as the *T*-score goes down, approximately 2.5 times with each 1 SD decrease in bone mass.[3,5]

Bone disease, that is, renal bone disease, is one of the most significant complications of CKD. There is higher risk of developing fractures among CKD

patients compared to the general population.[6,7] Bone turnover is extremely varied in CKD patients, from high to low turnover, depending on the parathyroid hormone (PTH) level.[8] The differing effects of PTH on cortical and trabecular bone are well known, that is, excess PTH has catabolic effects on cortical and anabolic effects on trabecular bone.[9] Therefore, caution is required in CKD patients when assessing a reduction in bone mass by any of the densitometric methods. Indeed, because of the different changes in bone reduction rate and the different pathogenesis of bone loss, it is difficult to apply WHO criteria in renal bone disease.[10] At this moment, we do not have a standard method to evaluate bone loss in CKD patients and we have not yet decided upon the optimal measurement site (axial or appendicular).[8,10] Furthermore, there are differences in expressing DXA results (BMD, *T*-, or *Z*-score) when evaluating bone loss in renal bone disease.[4,10]

The goal of this study is to determine BMD at specified measurement points using the DXA method to ascertain the difference between genders, to determine a correlation in measurement points on the skeleton, and to try to locate the most optimal site for measuring BMD in dialysis patients. The aim of this study is also to investigate the prevalence of osteopenia and osteoporosis by using different criteria.

SUBJECTS AND METHODS

Patients

Overall, 134 patients, 62 females and 72 males, on maintenance hemodialysis (HD) were included in a cross-sectional study after obtaining their informed consent. All patients were from a single dialysis center. The mean age was 56.4 ± 12.4 years and the mean duration of HD treatment was 54.0 ± 60.9 months. All of the patients were on bicarbonate dialysis with a calcium concentration of 1.5 mmol/L for 12–15 hours per week for the last 5 years with hollow-fiber dialyzers with a polysulfone membrane. Blood flow was 300–500 mL/min, and the flow of the dialysate was 500 mL/min. The water for dialysis was prepared by the reverse osmosis method. Its conductivity was below 10 μs/cm^3. All of the patients in therapy had been treated with phosphate binders (calcium carbonate, sevelamer hydrochloride). Aluminum hydroxide has not been used as a phosphate binder in our patients for more than 20 years. We also used an active form of vitamin D3 (calcitriol) in a daily dose between 0.25 and 0.5 μg, according to the clinical recommendations for patients being treated by HD [Kidney Disease Outcomes Quality Initiative (K/DOQI)]. Patients were not treated with estrogens, calcitonin, bisphosphonates, teriparatide, or androgens. Patients on dialysis for less than 6 months and patients who had taken corticosteroids or who had a parathyroidectomy were excluded from the study. All females were postmenopausal or permanently amenorrheic. Two patients had a hip fracture and one had a fracture of a metatarsal bone in their medical histories. The prevalence of vertebral fractures was not studied.

The etiology of renal failure was glomerulonephritis in 48 patients (36%), hypertensive nephropathy in 13%, pyelonephritis in 9%, tubulointerstitial nephritis in 8%, diabetic nephropathy in only 8%, polycystic kidney in 7%, other renal disease in 16%, and unknown in 3%.

Bone mineral density

BMD was assessed by DXA using a Hologic apparatus model Delphi W (S/N 70616). It was performed by trained technicians. Daily calibration was used to maintain the manufacturer's precision standards. We measured BMD at the following sites: the lumbar spine, the hip, and the forearm. The lumbar spine was measured in posterior–anterior (PA at L1–L4) projection and lateral–lateral (LL at L2–L3) projection. The hip was measured in the area of the neck, the trochanter (Troch), the intertrochanter (Inter), the total hip, and the Ward's Triangle (Ward's). The forearm, that is, radius of the nondominant side, was measured in its ultradistal (UD) part, the middistal (MID) forearm, one-third, that is, 33% forearm (1/3), and the total forearm. The results are expressed as BMD (g/cm^2) and as a *T*-score and a *Z*-score. The *T*-score and the *Z*-score in the area of the lumbar spine in the lateral direction were not counted for men. According to the WHO, osteoporosis is defined as a *T*-score < –2.5 and low bone mass, or osteopenia, as it was previously known, as a *T*-score from –1 to –2.5. The International Society for Clinical Densitometry (ISCD) recommends BMD measurement of the posteroanterior lumbar spine (L1–L4) and hip (total and neck). The lateral spine should not be used for diagnosing osteoporosis, but it may have a role in monitoring. In certain circumstances, the 33% radius (one-third radius) of the nondominant forearm may be used for diagnosis. *Z*-score patients were grouped as below the expected range for age (*Z*-score < –2, proposed by the ISCD) or low bone mass (*Z*-score < –1, as proposed by the Osteoporosis Work Group).[4,10]

Biochemistry

The concentrations of calcium, phosphate, and alkaline phosphatase (ALP) were measured by standard biochemical methods and the product of calcium and phosphate was calculated. Plasma PTH was measured by a commercial chemiluminescence method for intact

PTH (chemiluminescence method: Diagnostic Products Corp., Los Angeles, California, USA), and the range of normal value was between 1.1 and 7.3 pmol/L.

Statistical analyses

Continuous data are expressed as a mean ± SD. Comparisons between the two groups were made by the *T*-test. Correlation was determined by Pearson's correlation coefficient. Statistical significance was defined as $p < 0.05$.

RESULTS

Demographic and biochemical data

There was no difference in age between females and males. Female patients were on HD for a longer time, but the difference was not statistically significant. PTH levels were significantly lower in male patients (PTH 57.3 vs. 79.8 pmol/L, $p = 0.02$) as were ALP levels (83.4 vs. 116.9 U/L, $p = 0.02$). There was no statistically significant difference in the other laboratory parameters (Table 1).

TABLE 1. Demographics, clinical, and laboratory parameters of the study group.

Variable	Mean ± SD	Range
Male ($N = 72$)		
Age (years)	56.2 ± 12.6	33–83
Dialysis duration (months)	49.7 ± 61	6–300
BMI (kg/m^2)	25.4 ± 3.3	21–34
iPTH (pmol/L)	57.3 ± 59.6*	5–263
Calcium (mmol/L)	2.3 ± 0.2	2.0–2.5
Phosphate (mmol/L)	1.8 ± 0.4	1.0–2.8
Calcium phosphate product (mmol^2/L^2)	4.1 ± 1.0	3.0–6.7
ALP (U/L)	83.4 ± 40.7†	50–325
Female ($N = 62$)		
Age (years)	56.7 ± 11.8	32–83
Dialysis duration (months)	59.5 ± 60.1	6–250
BMI (kg/m^2)	25.0 ± 4.8	17–35
iPTH (pmol/L)	79.8 ± 67.9*	3–260
Calcium (mmol/L)	2.3 ± 0.2	2.0–2.6
Phosphate (mmol/L)	1.8 ± 0.4	1.1–2.8
Calcium phosphate product (mmol^2/L^2)	4.5 ± 2.1	3.0–6.7
ALP (U/L)	116.9 ± 108†	52–850

Notes: BMI, body mass index; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase.
*$p = 0.02$; †$p = 0.02$.

Bone densitometric data

The results show that female patients had lower BMD in all measured sites, as expected. In both groups, the highest value of BMD was in the area of the intertrochanter and the lumbar spine (PA) (Table 2).

The lowest values for the *T*-scores in females were at the lumbar spine LL (–3.1 ± 1.3) and at MID forearm (–2.3 ± 1.9), and for males at UD forearm (–1.6 ± 1.4). In both the groups, the lowest values for the *Z*-scores were at the UD forearm, for females –1.0 ± 1.5 and for males –0.9 ± 1.5 (Table 2).

The mean *T*-score at the hip was significantly lower in female patients; however, there was no significant difference of the *T*-score at the appendicular part of skeleton, that is, forearm, other than significant differences at MID forearm (–2.3 ± 1.9 vs. –1.4 ± 1.7, $p = 0.01$). At the hip there was also a significant difference in *Z*-scores, whereas there was no difference in *Z*-score at the forearm (Table 2).

Correlation between BMD and laboratory and clinical parameters

In male patients, BMD was correlated positively with age in the area of the lumbar spine (PA). There was a negative correlation with age in the neck of the hip and the Ward's. BMD correlated negatively with the duration of HD only in the measurement sites in the forearm. BMI and BMD were in a positive correlation in the area of the forearm and the hip (intertrochanter and total hip). There was no correlation between PTH and BMD at the site of the lumbar spine, but there was a negative correlation in the area of the hip (trochanter, intertrochanter, and total hip) and at all sites of the forearm. There was no statistically significant correlation of BMD with calcium, phosphorus, and the product of calcium and phosphorus. Serum ALP was negatively correlated with BMD at all sites, except in the area of the neck and the Ward's (Table 3).

In females there was positive correlation between BMD and age in the area of the lumbar spine (LL). There was a negative correlation with age in the area of the hip (neck and the Ward's) and in all measurement sites of the forearm. The duration of dialysis was in a negative correlation at all sites except in the area of the lumbar spine (LL). There was positive correlation between BMD and BMI in the areas of the lumbar spine (AP and LL) and the hip (neck, trochanter, intertrochanter, total, and the Ward's); however, there was no correlation of BMI and forearm BMD. Serum PTH was negatively correlated with BMD at all sites, except at the Ward's triangle and the lumbar spine LL. There was no significant correlation with calcium and the product of calcium and phosphorus. ALP was negatively correlated to BMD in all measurement points (Table 4).

TABLE 2. Mean BMD, *T*-score, and *Z*-score in female and male patients.

	Female ($N = 62$)	Male ($N = 72$)	p
Lumbar spine			
PA (total)			
BMD (g/cm^2)	0.866 ± 0.158	1.011 ± 0.182	
T-score	−1.6 ± 1.4	−0.7 ± 1.7	0.001
Z-score	−0.4 ± 1.5	−0.2 ± 1.7	NS
LL (total)			
BMD(g/cm^2)	0.587 ± 0.116	0.799 ± 0.195	
T-score	−3.1 ± 1.3	–	
Z-score	−0.6 ± 1.3	–	
Hip			
Neck			
BMD(g/cm^2)	0.679 ± 0.130	0.808 ± 0.125	
T-score	−1.5 ± 1.2	−0.9 ± 1.0	0.001
Z-score	−0.4 ± 1.1	−0.1 ± 0.9	0.00007
Troch			
BMD (g/cm^2)	0.547 ± 0.106	0.692 ± 0.116	
T-score	−1.5 ± 1.0	−0.6 ± 0.9	<0.00001
Z-score	−0.7 ± 1.0	−0.3 ± 0.9	<0.00001
Inter			
BMD (g/cm^2)	0.893 ± 0.167	1.088 ± 0.163	
T-score	−1.3 ± 1.09	−0.6 ± 0.9	<0.00001
Z-score	−0.7 ± 1.2	−0.2 ± 0.9	<0.00001
Total			
BMD (g/cm^2)	0.757 ± 0.136	0.941 ± 0.138	
T-score	−1.4 ± 1.2	−0.6 ± 0.9	<0.00001
Z-score	−0.6 ± 1.1	−0.3 ± 0.9	<0.00001
Ward's			
BMD (g/cm^2)	0.490 ± 0.154	0.597 ± 0.174	
T-score	−2.1 ± 1.3	−1.3 ± 1.2	0.04
Z-score	−0.3 ± 1.3	−0.1 ± 1.2	0.002
Forearm			
UD			
BMD (g/cm^2)	0.311 ± 0.081	0.425 ± 0.097	
T-score	−2.0 ± 1.6	−1.6 ± 1.4	NS
Z-score	−1.0 ± 1.5	−0.9 ± 1.5	NS
MID			
BMD(g/cm^2)	0.466 ± 0.100	0.613 ± 0.092	
T-score	−2.3 ± 1.9	−1.4 ± 1.7	0.01
Z-score	−0.9 ± 1.7	−0.8 ± 1.7	NS
One-third			
BMD(g/cm^2)	0.571 ± 0.113	0.745 ± 0.091	
T-score	−1.9 ± 1.9	−1.3 ± 1.5	NS
Z-score	−0.6 ± 1.8	−0.5 ± 1.6	NS
Total			
BMD(g/cm^2)	0.451 ± 0.096	0.600 ± 0.086	
T-score	−2.0 ± 2.1	−1.5 ± 1.6	NS
Z-score	−0.9 ± 1.7	−0.7 ± 1.6	NS

Notes: BMD, bone mineral density; PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third; NS, not significant.

TABLE 3. Correlation between BMD of measurement sites laboratory and clinical parameters, expressed as a coefficient of correlation (r) in male patients.

	Lumbar spine		Hip					Forearm			
	PA total	LL total	Neck	Troch	Inter	Total	Ward's	UD	MID	1/3	Total
Age	0.300*	NS	−0.293†	NS	NS	NS	−0.314*	NS	NS	NS	NS
HD	NS	NS	NS	NS	NS	NS	NS	−0.295†	−0.390‡	−0.351*	−0.388‡
BMI	NS	NS	NS	NS	0.322*	0.294†	NS	0.279†	0.284†	NS	0.271†
iPTH	NS	NS	NS	−0.277†	−0.263†	−0.280†	NS	−0.286†	−0.340*	−0.306*	−0.346*
Ca	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Ca × P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
ALP	−0.254†	−0.281†	NS	−0.261†	−0.248†	−0.256†	NS	−0.232†	−0.385‡	−0.377‡	−0.378‡

Notes: BMD, bone mineral density; PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third; BMI, body mass index; iPTH, intact parathyroid hormone; Ca, calcium; P, phosphorus; ALP, alkaline phosphatase; NS, not significant.
$^{\star}p < 0.01$; $^{\dagger}p < 0.05$; $^{\ddagger}p < 0.001$; ($r = 0.302$, $p < 0.01$), ($r = 0.232$, $p < 0.05$), ($r = 0.372$, $p < 0.001$).

TABLE 4. Correlation between PTH and BMD in measurement sites expressed as a coefficient of correlation (r) in female patients.

	Lumbar spine		Hip					Forearm			
	PA total	LL total	Neck	Troch	Inter	Total	Ward's	UD	MID	1/3	Total
Age	NS	0.273*	−0.277*	NS	NS	NS	−0.366†	−0.326†	−0.381†	−0.384†	−0.380†
HD	−0.453‡	NS	−0.436‡	−0.315*	−0.356†	−0.384†	−0.280*	−0.394†	−0.426‡	−0.422‡	−0.425‡
BMI	0.328†	0.328†	0.406‡	0.356†	0.383†	0.421‡	0.310*	NS	NS	NS	NS
iPTH	−0.384†	NS	−0.369†	−0.359†	−0.390†	−0.400‡	NS	−0.342†	−0.414‡	−0.371†	−0.398‡
Ca	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
P	0.272*	NS	NS	0.300	NS	NS	NS	NS	NS	NS	NS
Ca × P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
ALP	−0.360†	−0.274*	−0.463‡	−0.480‡	−0.508‡	−0.527‡	−0.385†	−0.349†	−0.349†	−0.375†	−0.331†

Notes: PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third; BMI, body mass index; iPTH, intact parathyroid hormone; Ca, calcium; P, phosphorus; ALP, alkaline phosphatase; NS, not significant.
$^{\star}p < 0.05$; $^{\dagger}p < 0.01$; $^{\ddagger}p < 0.001$; ($r = 0.250$, $p < 0.05$), ($r = 0.325$, $p < 0.01$), ($r = 0.395$, $p < 0.001$).

Correlations of BMD among different sites are given in Tables 5 and 6. Correlation ranged from 0.100 to 0.991 among different sites in males and from 0.319 to 0.993 in females. The best correlation for males and females was between MID forearm and the total hip and the intertrochanter ($r = 0.769$ and 0.761 in females; $r = 0.534$ and 0.537 in males). We found better correlation between axial and appendicular skeletal sites in females than in males.

Osteoporosis

The prevalence of osteoporosis in males, according to ISCD recommendations (T-score < −2.5), was 10% in lumbar spine AP projection and 3% in hip neck. At other sites, the prevalence of a T-score < −2.5 was between 0 and 29%. In the same group, the prevalence of low bone mass (T-score between −1.0 and −2.5) was between 33 and 49% (Table 7).

In female patients, the prevalence of osteoporosis based on the same criteria was 31% in lumbar spine AP projection, 18% in hip neck, and 18% in total hip. At other sites, the T-score < −2.5 was between 16% and up to 68% in LL lumbar spine. The prevalence of low bone mass was between 26% and up to 55% in the hip neck (Table 7).

According to the Z-score, the prevalence of low bone density (Z-score<−1) in male patients was between 15 and 50% and the Z-score below the

TABLE 5. Correlation between BMD of individual measurement sites expressed as a coefficient of correlation (*r*) in female patients.

	PA total	LL total	Neck	Troch	Inter	Total	Ward's	UD	MID	1/3	Total
PA	1	0.571	0.687	0.709	0.722	0.752	0.620	0.643	0.581	0.568	0.610
LL	0.571	1	0.458	0.513	0.413	0.466	0.413	0.392	0.374	0.319	0.373
Neck	0.687	0.458	1	0.737	0.871	0.911	0.842	0.716	0.740	0.717	0.750
Troch	0.709	0.513	0.737	1	0.799	0.872	0.698	0.700	0.635	0.584	0.653
Inter	0.722	0.413	0.871	0. 799	1	0.980	0.794	0.749	0.769	0.739	0.778
Total	0.752	0.466	0.911	0.872	0.980	1	0.805	0.763	0.761	0.727	0.773
Ward's	0.620	0.413	0.842	0.698	0.794	0.805	1	0.618	0.598	0.581	0.616
UD	0.643	0.392	0.716	0.700	0.749	0.763	0.618	1	0.865	0.792	0.905
MID	0.581	0.374	0.740	0.635	0.769	0.761	0.598	0.865	1	0.792	0.993
1/3	0.568	0.319	0.717	0.584	0.739	0.727	0.581	0.792	0.792	1	0.963
Total	0.610	0.373	0.750	0.653	0.778	0.773	0.616	0.905	0.993	0.963	1

Notes: BMD, bone mineral density; PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third.

TABLE 6. Correlation between BMD of individual measurement sites expressed as a coefficient of correlation (*r*) in male patients.

	PA	LL	Neck	Troch	Inter	Total	Ward's	UD	MID	1/3	Total
PA	1	0.659	0.298	0.559	0. 449	0.480	0.211	0.371	0.311	0.289	0.358
LL	0.659	1	0.416	0.529	0.470	0.513	0.361	0.435	0.353	0.261	0.394
Neck	0.298	0.416	1	0.633	0.727	0.795	0.821	0.286	0.281	0.194	0.287
Troch	0.559	0.529	0.633	1	0.800	0.873	0.460	0.478	0.443	0.331	0.466
Inter	0.449	0.470	0.727	0.800	1	0.976	0.555	0.512	0.534	0.345	0.540
Total	0.480	0.513	0.795	0.873	0.976	1	0.621	0.527	0.537	0.365	0.548
Ward's	0.211	0.361	0.821	0.460	0.555	0.621	1	0.184	0.152	0.100	0.153
UD	0.371	0.435	0.286	0.478	0.512	0.527	0.184	1	0.758	0.394	0.802
MID	0.311	0.353	0.281	0.443	0.534	0.537	0.152	0.758	1	0.842	0.991
1/3	0.289	0.261	0.194	0.331	0.345	0.365	0.100	0.394	0.842	1	0.838
Total	0.358	0.394	0.287	0.466	0.540	0.548	0.153	0.802	0.991	0.839	1

Notes: BMD, bone mineral density; PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third.

expected range for age (*Z*-score < –2.0) was between 5 and 22% (Table 8). In female patients, the prevalence of low bone mass density according to the *Z*-score was 23% at the Ward's, up to 56% at UD forearm, and the prevalence of *Z*-score below the expected range for age was between 5 and 26% (Table 8).

DISCUSSION

In our study, a significant percentage of patients on HD had significantly decreased BMD as assessed by *T*- or *Z*-score. The reduced *T*- or *Z*-score was not the same on all measured skeletal sites and there was also a difference between genders. The prevalence of osteoporosis, defined as a *T*-score < 2.5 at peripheral skeletal sites (forearm), was up to 35% in females and 29% in males. At the central part of skeleton, the prevalence was 20% in males at the Ward's Triangle and more than 68% in LL lumbar spine in females. Reduced bone mass, that is, a *T*-score between –1 and –2.5, was detected in more patients, but the difference in prevalence between skeletal sites was less pronounced.

There are suggestions that the *Z*-score should be used in evaluating bone density in CKD patients. The ISCD has recommended that the *Z*-score should be expressed as *Z*-score of –2.0 or lower and defined as

TABLE 7. Osteoporosis and reduced bone mass compared to *T*-score.

	Normal *N* (%)	Reduced bone mass *N* (%)	Osteoporosis *N* (%)
Lumbar spine			
PA			
Male	38 (53)	24 (33)	10 (14)
Female	22 (35)	21 (34)	19 (31)
LL			
Male	–	–	–
Female	4 (6)	16 (26)	42 (68)
Hip			
Neck			
Male	36 (50)	34 (47)	2 (3)
Female	17 (27)	34 (55)	11 (18)
Troch			
Male	43 (60)	29 (40)	0 (0)
Female	16 (26)	34 (55)	12 (19)
Inter			
Male	43 (60)	28 (39)	1 (1)
Female	24 (39)	28 (45)	10 (16)
Total			
Male	43 (60)	29 (40)	0 (0)
Female	20 (32)	31 (50)	11 (18)
Ward's			
Male	22 (30)	35 (49)	15 (21)
Female	9 (14)	29 (47)	24 (39)
Forearm			
UD			
Male	22 (30)	30 (42)	20 (28)
Female	16 (26)	25 (40)	21 (34)
MID			
Male	26 (36)	25 (35)	21 (29)
Female	13 (21)	27 (44)	22 (35)
1/3			
Male	30 (42)	27 (37)	15 (21)
Female	18 (29)	25 (40)	19 (31)
Total			
Male	26 (36)	27 (37)	19 (26)
Female	16 (26)	24 (39)	22 (35)

Notes: PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third.

TABLE 8. *Z*-score in female and male patients.

	$Z < -1$ *N* (%)	$Z < -2$ *N* (%)
Lumbar spine		
PA		
Male	28 (39)	8 (11)
Female	18 (29)	5 (8)
LL		
Male	–	–
Female	26 (42)	6 (10)
Hip		
Neck		
Male	12 (17)	3 (5)
Female	20 (32)	3 (5)
Troch		
Male	24 (33)	4 (6)
Female	27 (43)	6 (10)
Inter		
Male	16 (22)	3 (5)
Female	21 (34)	6 (10)
Total		
Male	13 (18)	3 (5)
Female	19 (31)	6 (10)
Ward's		
Male	11 (15)	3 (5)
Female	14 (23)	4 (6)
Forearm		
UD		
Male	35 (49)	15 (21)
Female	35 (56)	16 (26)
MID		
Male	36 (50)	16 (22)
Female	28 (45)	14 (23)
1/3		
Male	28 (39)	13 (18)
Female	25 (40)	12 (19)
Total		
Male	35 (49)	13 (18)
Female	27 (43)	14 (23)

Notes: PA, posterior–anterior; LL, lateral–lateral; Troch, trochanter; Inter, intertrochanter; Ward's, Ward's Triangle; UD, ultradistal; MID, middistal; 1/3, one-third.
$Z < -1$, low bone density, $Z < -2$ bellow the expected range for age.

"below the expected range for age" and a *Z*-score above –2.0 is "within the expected range for age."[4] On the contrary, nephrologists in the Osteoporosis Work Group suggested that in CKD patients low bone density could be defined as a *Z*-score of –1.0 or less.[10] Therefore, we used both criteria. Low bone density, that is, a *Z*-score < –1, depending on the skeletal site, was detected in up to 50% of male patients and 56%

of female patients. Interestingly, the prevalence was higher at peripheral skeletal sites. The prevalence of a *Z*-score < −2.0, below the expected range for age, was less than 11% in all central skeletal sites in females and males and much higher at the peripheral skeletal sites. In both groups, the prevalence of a *Z*-score below the expected for age range at the peripheral skeletal sites was between 18 and 26%. This is indisputable because the criteria that we are using and the sites that we are measuring significantly influence osteoporosis or low bone mass.

It is well known that there is a correlation between BMD measurements made in the same patient at different skeletal sites. It varies between $r = 0.4$ and $r = 0.9$.[5,11] In our patients the correlation between BMD at different skeletal sites varied between $r = 0.1$ and $r = 0.99$. There was a difference in correlation between different skeletal sites in females and males. Generally, a better correlation between different skeletal sites was observed in female patients.

Age, gender, hormonal factors, BMI, and PTH level are risk factors for osteoporosis, that is, reduced bone mass.[12] There are some other risk factors in dialysis patients, for example, the length of time on dialysis. In our patients there was a negative correlation between the length of time on HD treatment and bone density at the forearm in males and females but at the central part of skeleton only in females. In males there was no correlation between age and forearm bone mass, and in female patients there was a negative correlation between age and forearm bone mass.

As expected, a negative correlation was observed between PTH level and BMD. In female patients, the correlation at peripheral and central skeletal sites was better than in males. In addition, PTH and most probably other hormonal deficiencies, that is, the deficiency of estrogen, have an added effect on the loss of bone mass at the lumbar spine in females.

Renal bone disease, as one CKD–mineral bone disorder (MBD), is caused by a combination of several metabolic disorders resulting from chronic kidney insufficiency.[6,9] The most important ones are phosphate reduction, serum calcium disorder, deficiency of vitamin D, and increased PTH level.[13] In some CKD patients, particularly diabetics and older patients, low levels of PTH could be found. Low bone turnover is a histological picture of low PTH level in CKD patients. In patients with a high PTH level, the characteristic histological picture of bone is high turnover.[6,8] In both types of bone changes in CKD patients that is, high or low bone turnover normal bone density could be found.[8,10,12,14] There is one more important point in CKD–MBD – the high incidence of pathological calcifications, particularly vascular calcification. The incidence of calcification is similar in patients with low and high turnover bone disease.[8,9]

The prevalence of low bone mass and bone fractures is high among CKD patients. In some studies, the prevalence of low bone mass, that is, osteoporosis was up to 80% at the mid-radius, 47% at the hip neck, a bit less at lumbar spine, and less than 30% and around 50% at the total body.[12,15–17] In many studies, a different prevalence was observed and even a difference between HD and peritoneal dialysis was observed.[16–19] There is also much data showing that the fracture risk in CKD patients is very high, more than 4 times higher than in the general population.[4,20] The goal of our study was not to investigate the prevalence of bone fractures. However, we did observe only three patients with fractures. Most probably we would have found a greater number of pathological fractures if we had used another method, such as X-ray of the spine. However, bone densitometry is a good method in evaluating bone density in the general population and the results, that is, BMD or *T*-score, are strong predictors of fracture risk. Unfortunately, this is not so with CKD patients. There are many reasons for this. First, bone quality in CKD is severely affected not only by aging (as is most often the case in the general population), but also by a severe disarrangement of mineral metabolism.[1,6,12] Bone density (assessed by one of the densitometric methods) is only one part of bone quality in CKD patients. Bone turnover is the second important part, although the "gold standard" in assessing bone turnover is an invasive method, that is, bone biopsy.[10]

DXA is the "gold" standard in the diagnosis of bone loss in the general population.[1,3] Central skeletal sites are the most important. BMD, expressed as a *T*-score, should be used in evaluating osteoporosis.[4] From our study and others, it is clear that DXA results should not be interpreted so simply in CKD patients. There are many reasons for this. In patients with high turnover bone disease resulting from secondary hyperparathyroidism, changes on peripheral skeletal sites which mean more cortical bone, for example, up to 95 at the distal third of radius, are more pronounced.[8] DXA of central skeletal sites, that is, the lumbar spine, has some technical limitations in CKD patients.[11,21] A high incidence of aortic calcifications and the endplate osteosclerosis of vertebral bodies could have an impact on DXA results. The forearm thus seems to be a promising site. The ISCD has suggested that DXA scans should be performed in the distal third of the radius in patients with hyperparathyroidism. The problem is that this is valuable for patients with primary hyperparathyroidism, whereas bone changes in secondary hyperparathyroidism are a bit different.[4] Unfortunately, it is not possible to distinguish trabecular and cortical bone with DXA.

Therefore, at present DXA scans at more sites should be recommended for patients with CKD–MBD, including appendicular, for example, distal forearm, but also at the central part of the skeleton. Finally, the question is whether to use the *T*-score or the *Z*-score. The *T*-score is useful only in Caucasian females. At present, we do not know what *Z*-score value should be used in distinguishing CKD patients with low bone mass.

In our study, we tried to determine the optimal site of bone mass measurement in CKD patients. There are some limitations in this study. Most important, it is a cross-sectional study with a relatively small number of patients and the use of only one method (DXA). Regardless of these limitations, we have shown that there is reduced bone mass in HD patients, that there is a different reduction between skeletal sites and between genders, and also that there is a difference if the results are expressed as a *T*-score or a *Z*-score. Undoubtedly, more long-term studies with DXA and other methods, for example, peripheral quantitative computed tomography (pQCT), are required.[21]

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

REFERENCES

[1] Stehman-Breen C. Osteoporosis and chronic kidney disease. *Semin Nephrol.* 2004;24:78–81

[2] Gal-Moscovici A, Sprague SM. Osteoporosis and chronic kidney disease. *Semin Dial.* 2007;20:423–430.

[3] Levis S, Altman R. Bone densitometry: Clinical consideration. *Arthritis Rheum.* 1998;41:577–578.

[4] Baim S, Binkley N, Bilezikian JP, et al. Official positions of the international society for clinical densitometry end executive summary of the 2007 ISCD position development conference. *J Clin Densitom.* 2008;11:75–91.

[5] Adams J, Bishop N. DXA in adults and children. In: Rosen JE, ed. *Primer on the Metabolic Bone Disease and Disorders of Mineral Metabolism*. Washington, DC: American Society for Bone and Mineral Research; 2008:152–158.

[6] Elder G. Pathophysiology and recent advances in the management of renal osteodystrophy. *J Bone Miner Res.* 2002;17:2094–2105.

[7] KDOQI, National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* 2003;42(3):1–201.

[8] Martin KJ, Olgaard K, Coburn JW, et al. Diagnosis, assessment and treatment of bone turnover abnormalities in renal osteodystrophy. *Am J Kidney Dis.* 2004;43:558–565.

[9] Hruska KA, Mathew S. Chronic kidney disease mineral bone disorder (CKD-MBD). In: Rosen JE, ed. *Primer on the Metabolic Bone Disease and Disorders of Mineral Metabolism*. Washington, DC: American Society for Bone and Mineral Research; 2008:343–349.

[10] Cunningham J, Sprague SM, Cannata-Andia J, et al. Osteoporosis in chronic kidney disease. *Am J Kidney Dis.* 2004;43:566–571.

[11] Grampp S, Genant HK, Mathur A, et al. Comparison of noninvasive bone mineral measurements in assessing age-related loss, fracture discrimination, and diagnostic classification. *J Bone Miner Res.* 1997;12:697–711.

[12] Ersoy FF. Osteoporosis in the elderly with chronic kidney disease. *Int Urol Nephrol.* 2007;39:321–331.

[13] Pavlović D, Tomić Brzac H. Prevention and treatment of secondary hyperparathyroidism: Still a challenge for the nephrologist? *Nephrol Dial Transplant.* 2003;18(5):45–46.

[14] Lindberg JS, Moe MS. Osteoporosis in end-stage renal disease. *Semin Nephrol.* 1999;19:115–122.

[15] Kanenko TM, Foley RN, Gilbertson DT, Collins AJ. Clinical epidemiology of long-bone fractures in patients receiving hemodialysis. *Clin Orthop Relat Res.* 2007;457:188–193.

[16] Negri AL, Barone R, Quiroga MA, et al. Bone mineral density: Serum markers of bone turnover and their relationships in peritoneal dialysis. *Perit Dial Int.* 2004;24:163–168.

[17] Ersoy FF, Passadakis SP, Tam P, et al. Bone mineral density and its correlation with clinical and laboratory factors in chronic peritoneal dialysis. *J Bone Miner Metab.* 2006;24:79–86.

[18] Urena P, Bernard-Poenaru O, Ostertag A, et al. Bone mineral density, biochemical markers and skeletal fractures in hemodialysis patients. *Nephrol Dial Transplant.* 2003;18:2325–2331.

[19] Leinau L, Perazella MA. Hip fractures in end-stage renal disease patients: Incidence, risk factors and prevention. *Semin Dial.* 2006;19:75–79.

[20] Doumouchtsis KK, Kostakis AI, Doumouchtsis SK, et al. Associations between osteoprotegerin and femoral neck BMD in hemodialysis patients. *J Bone Miner Metab.* 2008;26:66–72.

[21] Bacchetta J, Boutroy S, Jillrad L, et al. Bone imaging and chronic kidney disease: Will high-resolution peripheral tomography improve bone evaluation and therapeutic management? *J Ren Nutr.* 2009;19:44–49.