Bone Mineral Density among Patients Undergoing Continuous Ambulatory Peritoneal Dialysis (CAPD)

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Apart from the conventional risks, low bone mineral density (BMD) is one of the risk factors for bone fracture. Interestingly, the incidence of bone fracture is highest among patients with chronic renal failure, but there is little data comparing the BMD of patients undergoing continuous ambulatory peritoneal dialysis (CAPD) with normal persons. The authors, therefore, compared the BMD between sex-, age- and bodyweight-matched CAPD patients and normal persons. The femoral neck, lumbar spine and total BMD were measured by dual energy X-ray absorptiometry in 62 CAPD patients and normal persons. In unadjusted analysis, femoral neck and total BMD in CAPD patients was significantly lower than normal controls in both men and women, while there was no significant difference at lumbar spine BMD between the two groups. The results were unchanged after adjusting for age, body weight and height (0.13 and 0.29 g/cm^2, $p < 0.001$*, for femoral and total BMD, respectively and 0.001 g/cm^2,* $p = 0.96$ *for lumbar spine BMD). In conclusion, low BMD is already a major risk factor for hip fracture, and this risk is exacerbated by CAPD. BMD measurement should be incorporated into the routine care of CAPD patients in order to identify incipient osteoporosis, so that it may be treated to prevent fractures.*

Keywords: *Bone mineral density, Chronic renal failure, Dialysis, Osteoporosis*

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Renal osteodystrophy, a common problem in chronic renal failure patients, is associated with an increased risk of fracture[1-5]. The spectrum of renal osteodystrophy varies[2-6], but bone histomorphometry (invasive, painful and costly) is the gold standard for evaluating and classifying it. Measurement of bone mineral density (BMD) is a non-invasive approach for identifying patients at high risk of bone loss[7,8]; cuing the need for fracture prophylaxis among patients with a low BMD. Previous studies reported a high prevalence of low BMD and high incidence of fracture in patients undergoing pre-dialysis, hemodialysis, and continuous ambulatory peritoneal dialysis (CAPD)[4,9,10]; however, most studies compared BMD with only age- and sex-matched normal persons[11-16], thus these studies lacked a comparison with a body-weight-matched control. In fact, age and bodyweight collectively accounted for 40 to 60 per cent of the variance in BMD in the population[17]. Decreased body weight was one of the independent predictors of low BMD and, the related body mass index (BMI) was low among general osteoporotic patients.

Chronic renal failure, especially among dialyzed patients, results in a high prevalence of malnourishment and low lean body mass[18]. The present study was designed to test the hypothesis that low BMD in CAPD patients is not influenced by low body mass. The authors, therefore, aimed to measure and compare BMD in sex-, age- and body weight-matched CAPD patients and normal persons.

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Material and Method

Setting and Subjects

The authors performed a cross-sectional investigation of 62 chronic renal failure patients (30 men; 32 women) from the Srinagarind Hospital Dialysis Unit, who had been on CAPD treatment for more than 6 months (range, 15-147 months; interquatile range (IQR): 33 to 99). Just over half (53.1 per cent) of the

women were post-menopausal. The authors excluded persons with: 1) a history of metabolic bone disorders (other than postmenopausal bone loss); 2) cancer with known metastasis to the bone; 3) menopause before the age of 40; 4) at least one ovary removed; 5) a history of taking medications affecting calcium and bone metabolism (*i.e.* steroids, thyroid hormone, bisphosphonates, fluoride or calcitonin, but not calcium and vitamin D supplementation); 6) a history of hospitalization in the previous 3 months; and, 7) a history of parathyroidectomy.

The etiology of chronic renal failure was diabetic kidney disease (42.9 per cent), glomerular disease (2.4 per cent), tubulointerstitial disease (14.3 per cent) and unknown etiology (40.5 per cent). Patients were dialyzed using 1.5 to 2.0 L bag exchanges 4 times per day. The calcium in the peritoneal dialysate was 3.5 mEq/L. Serum phosphate was controlled by calcium-containing phosphate-binding agents. Only 4.52 per cent of the patients were taking aluminum hydroxide. None of the patients was taking vitamin D analogs or had an experience of fractures since the dialysis began.

Normal controls were selected from the authors previous data set[19]. The normal subjects averaged 50.0 ± 16.4 years of age (range, 20 to 84) and weighed an average 56.8 ± 9.9 kg (range, 31.4 to 97.1).

The study was approved by the Khon Kaen University Ethics Committee and informed consent was obtained from each of the subjects. The study was conducted in accordance with the 1975 Helsinski Declaration (as revised in 1983).

Bone Mineral Density Measurements

The femoral neck, total lumbar spine and total BMD (g/cm^2) were measured by dual-energy X-ray absorptiometry (DXA) using a Lunar DXP-IQ densitometer (GE Lunar Radiation Corp, Madison, WI, USA). The coefficient of variation for BMD in normal subjects at the authors' institution was 1.5 per cent for the lumbar spine and 1.3 per cent for the femoral neck. T-scores were calculated using the local population peak, young, mean values (in men vs. women viz. 1.04 ± 0.13 vs. 0.94 ± 0.14 g/cm^2 for the femoral neck, 1.16 ± 0.13 vs. 1.15 ± 0.11 g/cm^2 for the lumbar spine, and 1.20 ± 0.12 vs. 1.17 ± 0.10 g/cm^2 for the total body, respectively).

Statistical analysis

Descriptive statistics were computed for each sex and group (CAPD and normal control) separately and presented as the mean and standard deviation (SD). In order to address the research question, a nested case-control analysis was performed, in which two sex-, age- (± 1 year) and body weight (± 2 kg) matched individuals, one from the CAPD sample and the other from the normal control, were randomly selected from the data set.

Sixty-two (30 men; 32 women) pairs of individuals satisfied these criteria. The difference in the ratio between CAPD patients and the normal controls was then tested using the paired *t*-test. In order to test for any difference between CAPD patients and normal controls, an analysis of covariance was performed in which the BMD was treated as the outcome variable, while age, weight, and height were the covariates, and CAPD or non-CAPD was the risk factor. Estimates of the model parameters were based on the least square method via the SPSS 9.0 (SPSS, Inc, Chicago). Statistical significance was set at $p < 0.05$.

Results

Demographic Characteristics

Data from 124 subjects (62 CAPD patients and 62 normal controls) were analyzed. There was no significant difference between the CAPD patients and the normal subjects with respect to age or sex distribution. Age averaged 56 for both men and women and mean body weight averaged 55 and 63 kg in men and women, respectively. However, CAPD men were shorter than normal men ($p < 0.001$), whereas CAPD women were taller ($p < 0.001$) than normal women (Table 1). The prevalence of osteoporosis in CAPD patients vs normal controls at the femoral neck, lumbar spine and total body was 16.1, 9.7 and 59.1 vs 4.8, 12.9 and 1.6 per cent, respectively.

In CAPD patients, a higher weight was associated with higher BMD in men ($r = 0.45$, $p = 0.02$ for the femoral neck, $r = 0.37$, $p = 0.061$ for the lumbar spine and $r = 0.27$, $p = 0.18$ for total BMD), and in women ($r = 0.42$, $p = 0.03$ for femoral neck, $r = 0.23$, $p = 0.023$ for lumbar spine and $r = 0.28$, $p = 0.15$ for total BMD).

Advancing age was associated with a significantly reduced femoral neck and lumbar spine BMD in CAPD men ($r = -0.43$, $p = 0.03$ for the femoral neck, $r = -0.40$, $p = 0.04$ for the lumbar spine) while the association was not significant for total BMD ($r = -0.23$, $p = 0.26$). In CAPD women, advancing age was associated with a significantly reduced femoral neck BMD ($r = -0.41$, $p = 0.04$) while the association was not significant for the lumbar spine and total BMD ($r = -0.06$, $p = 0.74$ and $r = -0.35$, $p = 0.06$, respectively).

Table 1. Characteristics of CAPD patients and normal subjects

	CAPD	Normal	Mean Difference	95% CI	p value
Men	(n=30)	(n=30)			
Age (yr)	56.70±11.86	56.33±12.25	0.37	-0.09, 0.82	0.933
Body weight (kg)	54.93±10.22	55.38±8.87	-0.44	-1.43, 0.55	0.776
Height (cm)	154.63±5.18	160.18±5.85	-5.55	-7.68, -3.42	<0.001
BMI (kg/m^2)	22.96±4.16	21.55±3.03	1.42	0.66, 2.17	0.001
BMD (g/cm^2)					
Femoral neck	0.74±0.12	0.90±0.16	-0.16	-0.23, -0.09	<0.001
Lumbar spine	1.01±0.18	1.12±0.27	-0.11	-0.20, -0.01	0.029
Total	0.81±0.12	1.16±0.13	-0.35	-0.41, -0.30	<0.001
Women	(n=32)	(n=32)			
Age (yr)	56.19±9.34	56.00±9.35	0.19	-4.32, 4.69	0.933
Body weight (kg)	63.25±9.30	63.93±9.44	-0.68	-5.53, 4.17	0.776
Height (cm)	164.94±4.83	154.33±5.57	10.61	7.88, 13.34	<0.001
BMI (kg/m^2)	23.23±3.09	26.82±3.51	-3.59	-5.34, -1.83	<0.001
BMD (g/cm^2)					
Femoral neck	0.83±0.15	0.92±0.16	-0.10	-0.19, 0.00	0.048
Lumbar spine	1.09±0.18	1.02±0.19	0.08	-0.03, 0.18	0.153
Total	0.91±0.20	1.15±0.11	-0.24	-0.32, -0.16	<0.001

BMI; body mass index, BMD; bone mineral density

Difference in BMD between CAPD patients and controls after sex, age and weight adjustment

After matching for sex, age and body weight, 30 and 32 pairs of men and women, respectively, were analyzed. In the univariate regression analysis, sex did not affect the BMD at any site; therefore, a regression analysis was performed with the data for the men and women combined. In both sexes, after adjusting for age, weight and height, the femoral neck and total BMD in the CAPD patients was significantly lower than in the normal controls. For instance, the femoral neck and total BMD in the CAPD patients was 0.13 and 0.29 g/cm^2, respectively, which was significantly lower ($p < 0.001$) than in the normal controls and yet there was no difference for the lumbar spine BMD (0.001 g/cm^2, $p = 0.96$) (Table 2).

Table 2. Effects of age, body weight, height and CAPD status on BMD: estimates of the parameters of the analysis of covariance stratified by sex and BMD site

Effects	Coefficients	SE	p-value
Femoral neck BMD			
Age (+5 yr)	-0.025	0.006	<0.001
Weight (+5 kg)	0.027	0.006	<0.001
Height (+5cm)	0.002	0.009	0.794
Status (CAPD)	-0.125	0.024	<0.001
Lumbar spine BMD			
Age (+5 yr)	-0.019	0.008	0.012
Weight (+5 kg)	0.022	0.008	0.010
Height (+5cm)	0.012	0.013	0.343
Status (CAPD)	0.001	0.033	0.965
Total BMD			
Age (+5 yr)	-0.017	0.006	0.004
Weight (+5 kg)	0.023	0.006	<0.001
Height (+5cm)	0.004	0.010	0.694
Status (CAPD)	-0.285	0.025	<0.001

SE; standard error

Discussion

This was the first study to compare the BMD of CAPD patients with sex-, age- and body weight matched normal persons. After adjusting for age and body weight, CAPD treatment was an independent risk factor for low BMD. The present findings demonstrated that BMD was decreased at the femoral neck and the total body compared with the control group. Based on the WHO criteria, the prevalence of osteoporosis was high, particularly at the total body.

Most studies of CAPD patients have compared BMD with age- and sex-matched persons then reported the results in terms of osteopenia and osteoporosis according to the WHO criteria[2,20,21]. The prevalence of osteoporosis in those reports varied between 13.8 and 48.6 per cent. The body weight and body mass index, the factors accounting for bone mass, were not considered in previous studies. Low body weight, resulting from malnutrition, was commonly seen in dialyzed patients, especially CAPD[18]; however, the

present study demonstrated that CAPD treatment was an independent risk factor for low BMD after adjusting for body weight.

Low BMD is one of the risk factors for fracture in the general population. Hip fracture is an important worldwide public health problem, which causes considerable disability (with significant personal and economic costs), morbidity and mortality[22-25]. The incidence increases exponentially with advancing age[26]. But recent studies also reported a high incidence of hip fracture in persons with chronic renal failure including those undergoing pre-dialysis, hemodialysis, CAPD, and transplants[3,4,27]. The factors specific to renal failure, such as metabolic bone disease, β2 microglobulin-related amyloidosis, hypogonadism, avascular necrosis, and chronic acidosis, may, in a multifactorial cascade, increase bone loss among renal failure patients.

The present findings must be interpreted in the context of a number of potential strengths and weaknesses. The limitations of the present study were lack of information on PTH, osteocalcin, vitamin D level, and other bone markers. Hyperparathyroidism was the unique finding in chronic kidney disease patients. The correlation between the level of PTH and the degree of osteopenia is not well demonstrated, and the authors do not have the data to test a correlation. Negri *et al*[28] found that iPTH was correlated with BMD in CAPD patients while Pasadakis reported a negative correlation between the level of PTH and BMD[29]. Another limitation was the lack of bone histomorphometry to accurately diagnose the type of renal osteodystrophy and to detect the presence of osteoporosis.

The present study demonstrated low BMD in CAPD patients compared with normal persons. Intervention that increases BMD such as treatment of osteodystrophy through exercise and fracture prevention should be incorporated in the treatment plan for CAPD patients. It is recommended that BMD be measured, as it is a simple, non-invasive tool for identifying incipient osteoporosis, which should precipitate treatment and therefore reduce the risk of fracture.

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การศึกษาเปรียบเทียบความหนาแน่นของกระดูกระหว่างผู้ป่วยไตวายเรื้อรังที่ได้รับการรักษาด้วยการล้างไตทางช่องท้องกับคนปกติ

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ได้ทำการศึกษาเปรียบเทียบความหนาแน่นของกระดูกในผู้ป่วยไตวายเรื้อรังที่ได้รับการรักษาด้วยการล้างไตทางช่องท้องกับคนปกติที่มีเพศเดียวกัน อายุเท่ากันและน้ำหนักตัวใกล้เคียงกัน โดยได้ทำการวัดความหนาแน่นของกระดูกที่ตำแหน่งกระดูกสะโพก กระดูกสันหลังระดับเอว และกระดูกทั้งตัวด้วยเครื่องวัดความหนาแน่นของกระดูก (Lunar DPX-IQ) จำนวนกลุ่มละ 62 ราย ผลการศึกษาพบว่าในผู้ป่วยไตวายเรื้อรังที่ได้รับการล้างไตทางช่องท้องทั้งเพศชายและเพศหญิงมีความหนาแน่นของกระดูกต่ำกว่าคนปกติที่ตำแหน่งกระดูกสะโพกและกระดูกทั้งร่างกายอย่างมีนัยสำคัญทางสถิติ ในขณะที่ไม่พบความแตกต่างระหว่างสองกลุ่มที่ตำแหน่งกระดูกสันหลังระดับเอว และเมื่อทำการวิเคราะห์ข้อมูลโดยพิจารณาถึงผลของอายุ น้ำหนักตัวและส่วนสูง พบว่าผลการศึกษาไม่เปลี่ยนแปลง โดยพบว่าผู้ป่วยไตวายเรื้อรังที่ได้รับการล้างไตทางช่องท้องมีความหนาแน่นของกระดูกสะโพกและกระดูกสันหลังระดับเอวต่ำกว่าคนปกติเท่ากับ 0.13 และ 0.29 กรัมต่อตารางเซนติเมตรตามลำดับ ในขณะที่ตำแหน่งกระดูกสันหลังระดับเอวพบความแตกต่าง 0.001 กรัมต่อตารางเซนติเมตรซึ่งไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ โดยสรุปการศึกษานี้แสดงให้เห็นว่าผู้ป่วยไตวายเรื้อรังที่ได้รับการรักษาด้วยการล้างไตทางช่องท้องมีความหนาแน่นของกระดูกต่ำกว่าปกติซึ่งอาจเพิ่มความเสี่ยงในการเกิดกระดูกหักได้ ดังนั้นในผู้ป่วยไตวายเรื้อรังที่ได้รับการล้างไตทางช่องท้องทุกรายจึงควรได้รับการตรวจวัดความหนาแน่นของกระดูกเพื่อหาโรคกระดูกพรุนและควรได้รับการรักษาที่เหมาะสมเพื่อป้องกันการเกิดกระดูกหักต่อไป