

# Renal Osteodystrophy in Ramathibodi Hospital : Histomorphometry and Clinical Correlation

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## Abstract

The spectrum and clinical relevance of renal osteodystrophy in Thai dialysis patients are unknown. A study was conducted on the prevalence and clinico-pathological correlation of renal osteodystrophy in chronic dialysis patients who attended Ramathibodi Renal Transplant Clinic between September 1996 and March 1998. All possible volunteers were enrolled irrespective of musculoskeletal symptoms. Fifty six dialysis patients, including 17 (30.4%) CAPD and 39 (69.6%) hemodialysis patients, participated in this study. Serum calcium, phosphate, iPTH, and bone specific alkaline phosphatase were determined. Transiliac crest bone specimens were measured with an average of 30 fields/specimen by a specific computer program for bone histomorphometry (Osteomeasure), and were also studied for dynamic by double tetracycline label. Bone mineral density (BMD) was also determined by DEXA scan. The type of bone pathology was based on Fournier's criteria for renal osteodystrophy. The mean $\pm$ SEM for age was  $45.52\pm 1.74$  years, dialysis duration  $42.26\pm 5.54$  (range 1-156) months, calcium phosphate product  $52.31\pm 2.77$ , and iPTH  $307.73\pm 62.04$  pg/ml. The following types of renal osteodystrophy were found: adynamic bone 23 (41.1%), hyperparathyroid 16 (28.6%), mixed type 11 (19.6%), mild lesion 3 (5.4%), osteomalacia 2 (3.6%), and osteosclerosis 1 (1.8%) cases. Two cases of aluminum related bone disease were found. The distribution of different bone diseases was not affected by mode of dialysis or vitamin D supplement, but it was affected by dialysis duration. High turnover bone diseases were associated with longer dialysis duration ( $63.19\pm 8.9$  vs  $23\pm 4.73$  months), higher iPTH ( $541.53\pm 109.32$  vs  $87.77\pm 15.76$  pg/ml), and higher bone specific alkaline phosphatase ( $25.43\pm 5.04$  vs  $9.62\pm 1.34$  mg/ml) when compared to low turnover bone diseases,  $p < 0.05$ . Intact PTH of greater than 200 pg/ml was a good predictor for high turnover bone diseases (74% sensitivity and 96% specificity). BMD at torch and wards areas varied inversely with

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dialysis duration ( $r = -0.3$  and  $r = -0.4$ , respectively;  $p < 0.05$ ). Chronic dialysis patients had a greater tendency of bone loss compared to the general Thai population. There was no difference in BMD between CAPD and hemodialysis patients or different types of bone lesions.

**Conclusion:** Significant bone diseases are common among Thai chronic dialysis patients. Adynamic bone disease is the most common bone lesion followed by hyperparathyroid and mixed type. The spectrum of bone diseases is affected mainly by dialysis duration. Intact PTH is a good predictor of high turnover bone disease. Greater bone loss than in the general population is common in our patients and is also accentuated by longer dialysis duration.

**Key word :** Renal Osteodystrophy, High Turnover Disease, Low Turnover Bone Disease, Dialysis, Intact PTH, Bone-specific Alkaline Phosphatase

**CHANGSIRIKULCHAI S, DOMRONGKITCHAIPORN S, SIRIKULCHAYANONTA V, et al**  
**J Med Assoc Thai 2000; 83: 1223-1232**

Abnormalities of hormonal and mineral metabolism in patients with chronic renal failure lead to complex bone disorders, defined as renal osteodystrophy (ROD). Although a few patients are symptomatic, renal bone disease occurs early in the course of renal failure<sup>(1-9)</sup>. Because of improvement in patient survival, renal osteodystrophy has become a common long term severe complication in dialysis and renal transplant patients<sup>(10-12)</sup>. Patients with severe renal osteodystrophy can suffer from bone pain or fracture, proximal myopathy, hypercalcemic syndrome with nausea, vomiting, confusion or psychiatric disturbance, and extensive soft tissue calcifications with hyperphosphatemia. The histopathological spectrums of this entity have been classified as mild lesion, adynamic bone disease, osteomalacia, hyperparathyroid, and mixed type. In the past, osteitis fibrosa was the predominant bone lesion found among patients with renal osteodystrophy. The clinical relevance of this diagnosis is obvious when the patient is symptomatic. The therapeutic approach clearly depends on a precise diagnosis of the underlying bone pathology. Therapeutic options may be diametrically opposed because the syndrome of fracturing osteopathy, metastatic calcifications, and hypercalcemia with hyperphosphatemia may be caused either by severe hyperparathyroidism or by aluminum bone diseases<sup>(13)</sup>. In the case of severe osteitis fibrosa surgical

parathyroidectomy should be performed, whereas, in the case of aluminum bone disease, parathyroidectomy would worsen the clinical picture and is contraindicated. Therefore, it appears essential to assess the type of renal osteodystrophy, and in particular the rate of bone turnover, before undertaking any therapeutic or prophylactic measure. Our understanding of the factors involved in the pathogenesis and progression of different types of renal osteodystrophy has progressed recently and led to a refinement of its treatment and prevention<sup>(14)</sup>. The spectrum of renal osteodystrophy, however, has been evolving<sup>(15)</sup>, increasing in frequency of adynamic bone disease in parallel with a progressive decline in the incidence of osteitis fibrosa.

Dialysis in Thailand has been done for more than 15 years with a progressive improvement in patient survival and quality of life. There were more than 1500 dialysis patients and 600 new cases during 1997 (reported in the 1997 annual meeting of the Thai Royal College of Physicians by the Thailand Renal Replacement Therapy Registry). Unfortunately, knowledge of renal osteodystrophy and its clinical significance in Thai patients is not available. With the limitation in bone histomorphometry and histology technique, accurate diagnosis for different types of renal osteodystrophy has been done with difficulty.

With recent advances in bone histomorphometry technique, the study on the spectrum of renal osteodystrophy has become possible for the first time in Thailand. We, therefore, report the prevalence and clinical relevance of various bone lesions in Thai chronic dialysis patients and assess the influence of risk factors for renal osteodystrophy. We also determine the effects of renal osteodystrophy and dialysis modality on bone mineral density in our dialysis population.

## METHOD

### Subjects

There were approximately 350 patients with end stage renal disease on the Ramathibodi kidney transplantation waiting list between September 1996 and March 1998. Most patients were referred from various dialysis centers in Thailand for kidney transplantation. All those adult pretransplant patients, irrespective of their musculoskeletal symptoms, were invited to participate in this study. Patients who had received bone-affecting treatment, such as corticosteroids, calcitonin, and bisphosphonate within one year before this study were excluded. Fifty-six patients (31 men and 25 women), 69.6 per cent on hemodialysis and 30.4 per cent on CAPD, participated in this study. Their mean  $\pm$  SEM age was  $45.52 \pm 1.74$  years. Mean duration of dialysis was  $42.26 \pm 5.54$  months. There were 3.6 per cent diabetic patients. Primary kidney diseases were unknown in most patients. Most hemodialysis patients were dialysed with 3.5 meq/l dialysate calcium, bicarbonate hemodialysis with 4 to 5 hours per session, 2 times per week. Most CAPD patients used 2.5 meq/l calcium dialysate solution with 8 liters exchange per day. At the time of this study, most patients had variable dosages of calcium carbonate as phosphate binder. For patients who had vitamin D supplement, most of them received 0.25 ug/day of 1-alpha-hydroxy vitamin D orally.

### Biochemistry

Predialysis blood sampling and blood samples drawn from CAPD patients were taken after overnight fast at the time of bone biopsy. Plasma calcium and phosphate were determined by using a Technicon Auto Analyzer. Serum calcium was corrected ( $Ca_C$ ) for serum albumin according to the formula  $Ca_C$  (mg/dl) = serum calcium, mg/dl + [0.8x (4-albumin, g/dl)]. Plasma iPTH was determined by using a commercial immunoradiometric assay for

intact human PTH 1-84 (ELSA- PTH, CIS bio international, France). The range of normal iPTH values was 10-60 pg/ml. Plasma total alkaline phosphatase was measured by an automated method (normal value, 20-90 U/L). Bone specific alkaline phosphatase was measured by using a immunoradiometric assay (Alkphase-B, Metra Biosystem, Inc, USA). The range of normal values was 4.81-20.53 mg/ml for men and 5.31-14.87 mg/ml for females aged < 50 years, and 5.67-23.71 mg/ml for females aged > 50 years.

### Radiology

Each patient underwent: (1) skeletal survey comprising plain radiographs of both hands, antero-posterior and lateral thoraco-lumbar spine, (2) measurements of vertebral (L<sub>2</sub>-L<sub>4</sub>), femoral neck, torch, and wards, triangle bone mineral density were performed at the time of bone biopsy by dual energy X-ray absorptiometry (Lunar Expert XL, Lunar Corp., USA). Precision of the DEXA measurement in a general population within the department had previously been measured at L<sub>2</sub>-L<sub>4</sub>, and neck of femur was 1.2 and 0.6 per cent, respectively. The bone density data are presented as Z scored in order to relate them to age-and sex-matched normal value for an Asian population.

### Bone biopsy and bone histomorphometry

Bone samples were taken from the anterior iliac crest with an electric drill (Straumann AG, Waldenburg, Switzerland). The bone biopsy was performed 2-4 days after tetracycline double labeling (3 days on, 14 days off, and 3 days on with 1 g of tetracycline/day). All patients were biopsied under local anesthesia with 2 per cent xylocaine. Most of them tolerated to the procedure well. No serious complication occurred. The bone specimens, 6 mm diameter and 20-30 mm length, were fixed for 24 hours in methanol, dehydrated, and embedded in methylmethacrylate. Undecalcified sections of 6 micron thickness were made by using a heavy-duty microtome (Polycut). Sections were stained with modified Masson-Goldner trichrome stain(16) for histomorphometric measurement. The aurin tricarboxylic acid stain (Aluminon)(17) was used to measure the extent of aluminum deposit at the bone-osteoid interface. If specimens had positive stain for aluminon, a further stain with Perls stain was done to exclude cross reaction with iron deposit. Other sections were stained with Von-Kossa and hemato-

xylin-eosin stain for routine histological examination. Unstained sections, 15 micron thickness, were prepared for fluorescent light microscopy. The sections were analyzed quantitatively for static and dynamic parameters of bone formation and bone resorption. Histomorphometric measures were carried out with a semiautomatic image analyzer (Osteomeasure, Osteometric Inc, Atlanta, USA). Approximately 30 different fields were analyzed for the same bone biopsy specimen. Histomorphometric parameters were expressed according to Parfitt's standardized nomenclature as follows<sup>(18)</sup>:

#### Static

Bone volume	BV/TV	%
(Absolute) Osteoid volume	OV/TV	%
Osteoid surface	OS/BS	%
Osteoid thickness	O.th	μm
Osteoblastic surface	Ob.S/BS	%
Osteoclastic surface	Oc.S/BS	%
Osteoclast number	N.Oc/T.Ar	/mm <sup>2</sup>
Eroded surface	ES/BS	%
Medullary fibrosis	Fb.Ar	%

#### Dynamic

Mineral apposition rate	MAR	μm/day
Double labelled surface	dL.S/BS	%
Single labelled surface	sL.S/BS	%
Bone formation rate tissue level BFR/BS		μm <sup>3</sup> /μm <sup>2</sup> /day

$$BFR/BS = [(MS/BS) \times MAR] / 100$$

MS/BS (Mineralizing surface%) : extent of tetracycline labeled surface as a % of total trabecular bone surface (dL.S + 1/2 sLS).

On the basis of histomorphometry, the patients were classified into the following groups based on Fournier's criteria: 1) osteitis fibrosa, 2) mixed osteopathy, 3) mild lesion, 4) adynamic bone disease, and 5) osteomalacia<sup>(19)</sup>. Normal histomorphometric parameters were obtained from 15 normal Thai adults without bone disease, 7 men and 8 women, mean age  $35.08 \pm 2.79$  (range 19-58) years.

In order to study intra-observation variance included in the histomorphometry, five measurements of the same section from five patients with different bone pathology were performed at intervals without being informed to the observer. The coefficient of variation (CV) for the intra-observation variation was less than 5 per cent for bone volume, osteoid surface, osteoid thickness, osteoblastic surface, osteoclast number, eroded surface, and fibrotic area, but more than 10 per cent for osteoclast surface. The intersection variation was determined by measuring 5 sections from one patient. The CV for the intersection variation was less than 5 per cent in osteoid thickness and eroded surface, but more than 10 per cent for osteoblastic, and osteoclastic surface. However, the rather high CV for osteoblastic and osteoclastic surfaces did not affect the classification of different types of bone lesion.

#### Statistical Analysis

Results are reported as mean  $\pm$  SEM. The distribution of all variables was examined. Chi square and Kruskall-Wallis test were used for non-normally distributed variables and for several independent samples. Pearson's correlation and multiple logistic regression analysis were used to determine bivariate correlation and multifactorial analysis, respectively. There is significant difference if *p* value is less than 0.05.

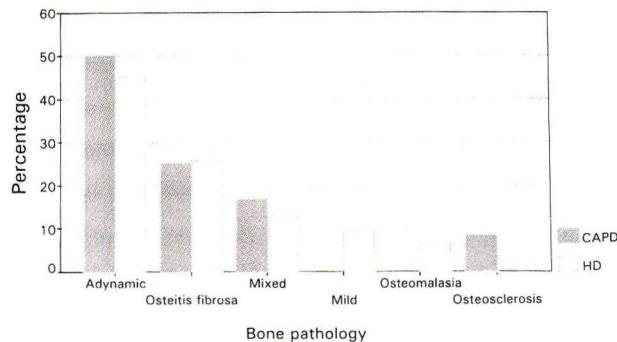
## RESULTS

#### Bone histology

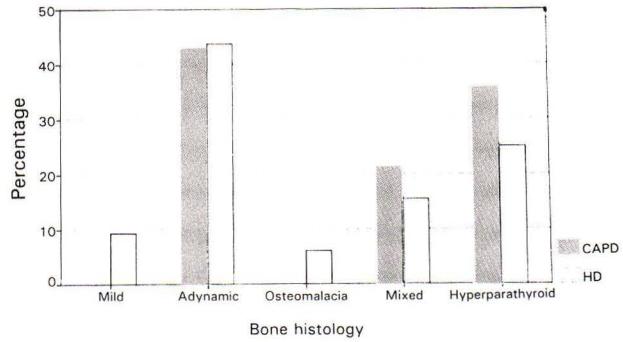
The distribution of bone pathology and quantitative histomorphometric determinations, including values from normal controls, are shown in Table 1. Adynamic bone disease was the most

Table 1. Bone histomorphometric values in normal and different bone diseases.

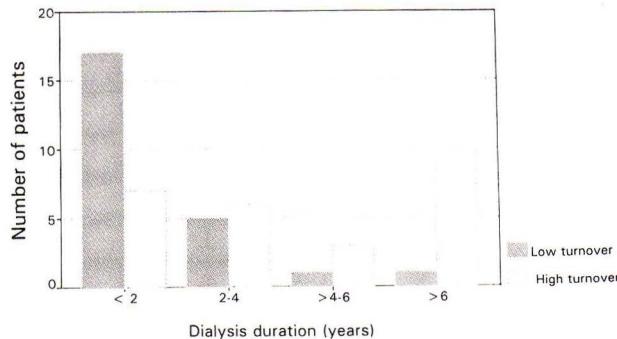
Parameters	Normal	Adynamic bone	Hyperparathyroid	Mixed	Osteomalacia	Mild
N	15	23 (41.1%)	16 (28.6%)	11 (19.6%)	2 (3.6%)	3 (5.4%)
BV/TV	$25.89 \pm 1.89$	$17.9 \pm 0.92$	$24.10 \pm 2.07$	$23.46 \pm 2.30$	$17.75 \pm 7.00$	$19.35 \pm 1.93$
OV/TV	$0.92 \pm 0.28$	$0.80 \pm 0.16$	$3.54 \pm 0.66$	$2.83 \pm 0.47$	$5.71 \pm 1.64$	$1.94 \pm 0.68$
OS/BS	$5.79 \pm 1.07$	$11.15 \pm 1.68$	$27.61 \pm 2.82$	$23.11 \pm 3.14$	$39.68 \pm 4.25$	$23.90 \pm 6.09$
O.Th	$9.39 \pm 0.81$	$7.08 \pm 0.25$	$9.30 \pm 0.59$	$8.30 \pm 0.63$	$15.43 \pm 0.16$	$8.03 \pm 0.52$
Ob.S/BS	$0.19 \pm 0.11$	$0.03 \pm 0.02$	$4.19 \pm 1.41$	$0.86 \pm 0.26$	$0.00 \pm 0.00$	$0.00 \pm 0.00$
Oc.S/BS	$0.09 \pm 0.05$	$0.02 \pm 0.01$	$1.70 \pm 0.63$	$0.19 \pm 0.05$	$0.10 \pm 0.10$	$0.02 \pm 0.02$
N.Oc/T.Ar	$0.16 \pm 0.07$	$0.06 \pm 0.03$	$5.38 \pm 1.92$	$0.72 \pm 0.25$	$0.26 \pm 0.26$	$0.14 \pm 0.07$
ES/BS	$5.23 \pm 0.62$	$5.13 \pm 0.47$	$9.94 \pm 0.82$	$8.32 \pm 0.65$	$3.92 \pm 0.36$	$1.27 \pm 0.00$
Fb.Ar	$0.00 \pm 0.00$	$0.00 \pm 0.00$	$0.39 \pm 0.16$	$0.06 \pm 0.03$	$0.20 \pm 0.20$	$0.00 \pm 0.00$
BFR/BS	$0.065 \pm 0.01$	$0.02 \pm 0.00$	$0.29 \pm 0.06$	$0.20 \pm 0.08$	$0.01 \pm 0.01$	$0.05 \pm 0.00$



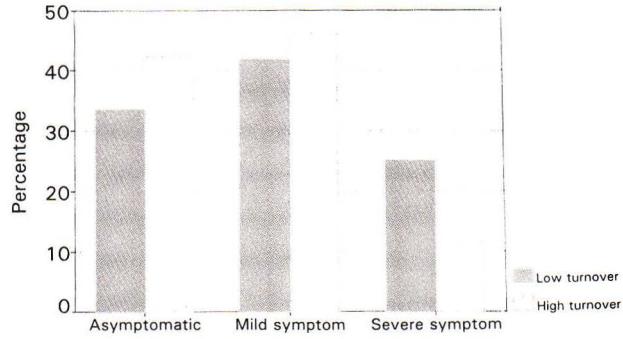
**Fig. 1.** The distribution of different types of bone disease in renal osteodystrophy.



**Fig. 2.** The distribution of different types of bone disease classified by mode of dialysis.



**Fig. 3.** The distribution of high and low turnover bone diseases classified by dialysis duration.



**Fig. 4.** Severity of musculoskeletal symptoms classified by bone turnover.

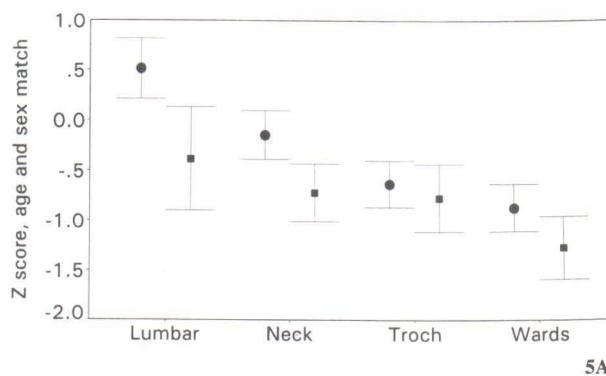
common histological diagnosis, followed by osteitis fibrosa and mixed lesion, respectively, (Fig. 1). There were only two cases of osteomalacia and one case of osteosclerosis. Only two cases of aluminum related bone disease were found, one being classified as mixed type and the other as osteomalacia. There were minor differences in the distribution of the different bone lesions between CAPD and hemodialysis patients, (Fig. 2). The most common bone pathology was osteitis fibrosa in CAPD patients, but it was adynamic bone disease in hemodialysis patients. Among CAPD patients, high turnover bone lesions were the predominant bone pathology, whereas, high turnover and low turnover bone lesions accounted for almost the same proportion in hemodialysis patients. However, the difference in the distribution of the different bone lesions between

CAPD and hemodialysis patients was not significant ( $p > 0.05$ ). There was no relationship between vitamin D supplement and bone lesions. The ratios of high turnover to low turnover bone lesions were 16:14 and 10:11, virtually almost 1:1, in patients with and without vitamin D supplement, respectively ( $p > 0.05$ ). Fig. 3 depicts the relationship of dialysis duration and bone lesions. High turnover bone lesions became clearly more predominant when dialysis duration was longer, accounting for 90.9 per cent among patients with dialysis duration greater than 6 years. In order to find factors that affected the types of bone lesion, multiple logistic analysis was used. Factors included in the analysis were sex, age at the start of dialysis, presence or absence of vitamin D supplement, dialysis duration, mode of dialysis, serum calcium and phosphate levels at the

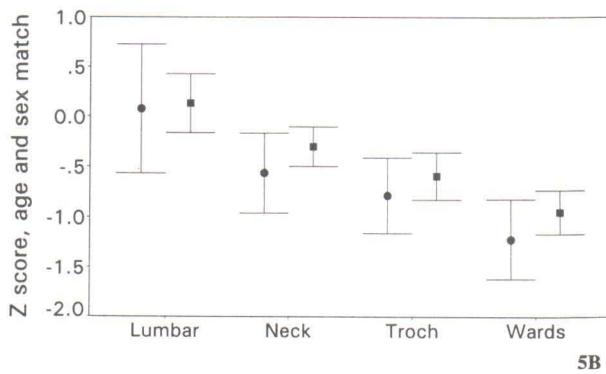
time of bone biopsy. Dialysis duration was found to be the only single independent factor that affected the types of bone lesion, ( $p = 0.014$ ). There was no association between the severity of musculoskeletal symptoms and the types of bone lesion, (Fig. 4).

**Table 2. Bone mineral density at various sites in chronic dialysis patients.**

Bone mineral density parameter	Z-adjusted age, sex match (95% CI)
Femur : wards	-1.03 ± 0.19 (-1.52, -0.78)
Femur : neck	-0.37 ± 0.18 (-0.89, -0.13)
Femur : troch	-0.65 ± 0.20 (-1.13, -0.37)
Lumbar (L2 - L4)	0.12 ± 0.28 (-0.58, 0.55)



5A

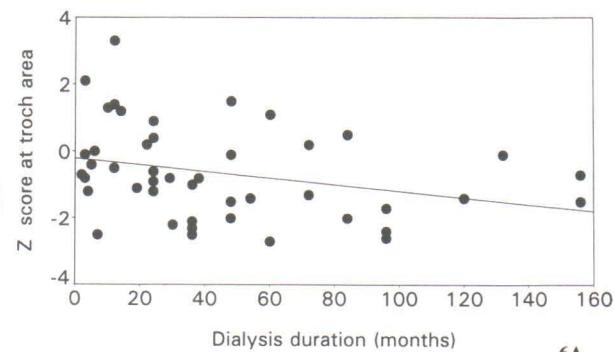


5B

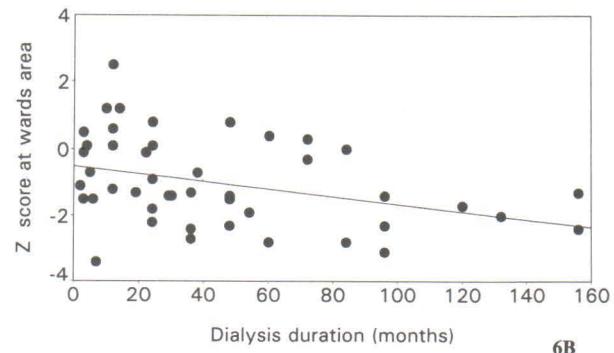
**Fig. 5.** Bone mineral density classified by A) rates of bone turnover : ● low turnover bone diseases, ■ high turnover bone diseases B) modes of dialysis ; ● CAPD, ■ hemodialysis.

### Radiology

The mean values of bone mineral density at various sites lay within  $\pm 2SD$  of the mean age-and sex-matched normal values for an Asian population, (Table 2). However, there were 14.9, 12, 21.3 and 25.5 per cent of patients who had a bone mineral density of less than -2 SD below normal values at lumbar, neck, torch, and wards of femur, respectively. Patients with high turnover bone lesions tended to have lower bone mineral density at all measured areas when compared to patients with low turnover bone lesions, (Fig. 5A). However, the differences were not significant ( $p > 0.05$ ). CAPD patients had lower bone mineral density when compared to hemodialysis patients, but the differences were also not significant ( $p > 0.05$ ), (Fig. 5B). Bone mineral density at wards and torch areas varied inversely with dialysis duration ( $r = -0.4$  and  $-0.3$ , respectively;  $p < 0.05$ ), (Fig. 6A and B). However, no correlation was found between dialysis duration and femoral neck or lumbar area ( $p > 0.05$ ).



6A



6B

**Fig. 6.** Correlation between dialysis duration and BMD A) at troch, B) at wards

Table 3. Biochemical values classified by bone lesions and modes of dialysis.

Biochemical parameter	Bone lesion		Mode of dialysis	
	Low turnover (95%CI)	High turnover (95%CI)	CAPD (95%CI)	HD (95%CI)
serum calcium	9.76±0.26 (9.28, 10.37)	9.82±0.20 (9.38, 10.27)	9.62±0.22 (9.13, 10.12)	9.86±0.20 (9.48, 10.32)
serum phosphate	5.24±0.40 (4.37, 6.09)	5.61±0.36 (4.81, 6.39)	5.51±0.47 (4.54, 6.66)	5.24±0.31 (4.53, 5.83)
total alkaline phosphatase	87.13±12.01 (63.36, 114.72)	139.25±29.73 (77.76, 200.74)	120.60±34.66 (46.26, 194.94)	103.59±16.41 (71.21, 139.35)
bone specific alkaline phosphatase	9.62±1.34 (6.89, 12.65)	25.43±5.04 (15.15, 38.33)	19.98±5.43 (6.89, 33.31)	15.93±3.19 (9.67, 23.25)
serum iPTH	87.77±15.76 (55.50, 123.38)	541.53±109.32 (313.36, 818.49)	372.81±108.50 (109.11, 636.42)	278.62±76.02 (122.10, 447.08)

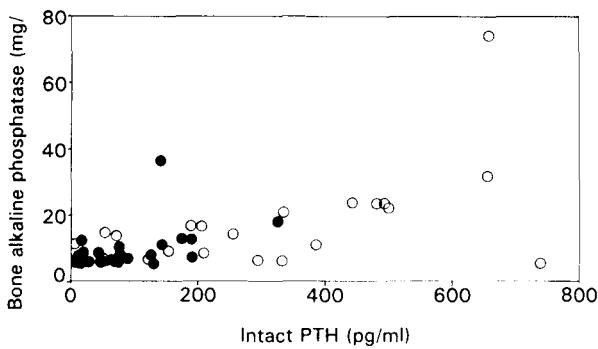


Fig. 7. The relationship between iPTH and bone specific alkaline phosphatase in patients with high (○) and low (●) turnover bone diseases.

The majority of patients, 60.9 per cent, had normal X-ray findings. Only 13.15.2 and 10.9 per cent of patients had X-ray findings typical for hyperparathyroid bone disease, non-specific soft tissue calcification, and degenerative changes, respectively. Therefore, the X-ray findings had little diagnostic value for the spectrums of bone disease.

#### Biochemistry and clinical findings

Serum calcium, serum phosphate, total alkaline phosphatase, bone-specific alkaline phosphatase, and intact parathyroid hormone classified by bone lesions and mode of dialysis are shown in Table 3. Significant differences were found only in

bone-specific alkaline phosphatase and intact PTH between high turnover and low turnover bone lesions. There was significant correlation between iPTH and bone-specific alkaline phosphatase, (Fig. 7). Intact PTH of greater than 200 pg/ml was a good predictor for high turnover bone disease (74% sensitivity and 96% specificity). Bone-specific alkaline phosphatase of greater than 20 mg/ml was associated with 48 per cent sensitivity and 96 per cent specificity for the prediction of high turnover bone disease. The combination of both parameters did not result in a greater diagnostic value than the individual parameter.

#### DISCUSSION

In our study, the most common bone lesion found among chronic dialysis patients was adynamic bone disease followed by osteitis fibrosa and mixed lesion. When classified by rate of bone turnover, low and high turnover accounted for almost the same proportion, almost 1:1. This finding is consistent with several recent reports in which the frequency of adynamic bone disease increased, even in the absence of an aluminum overload, in parallel with the progressive decrease in the prevalence of osteitis fibrosa or secondary hyperparathyroid bone lesion(15,20-22). We also found only two cases of aluminum intoxication. The very low prevalence of aluminum intoxication in this study may be attributed to the rapid declining use of aluminum containing phosphate binders in our population and improvement in the water treatment systems in most dialysis units in Thailand. Desferoxamine (DFO) chelation test and total bone aluminum content were not done in this study due to the high false nega-

tive DFO test among dialysis patients who have abstained from aluminum containing phosphate binder for some time(23) and the lower sensitivity of total bone aluminum than stainable aluminum in the detection of significant aluminum intoxication(24). However, one could argue that a more sensitive method(25) might detect aluminum even in our patients. If this is the case, we should find higher prevalence of osteomalacia. Therefore, we conclude that the high incidence of adynamic bone disease in our population resulted for non-aluminum related factors. Diabetes mellitus, aging, aluminum intoxication, and CAPD have been identified as risk factors of low bone turnover(22). It is unlikely to be the case in our study as there were only two diabetic patients and we were unable to demonstrate an association between the patients' age and types of bone lesion. We also failed to demonstrate the relationship between the modes of dialysis and bone lesions. The distributions of different bone lesions in both CAPD and hemodialysis patients in our study were not different. In the Sherrard *et al* study (15), the prevalence of adynamic or low turnover bone disease in CAPD patients was much higher than osteitis fibrosa, whereas, high turnover bone disease was the predominant bone lesion among our CAPD patients. The difference may result from the higher dialysis fluid calcium concentration (3.5 mEq/L) used by most CAPD patients in the Sherrard *et al* study when compared to the dialysis fluid calcium concentration (2.5 mEq/L) used in our CAPD patients. The supraphysiological calcium concentrations in the peritoneal dialysis fluid is probably an important factor causing oversuppression of parathyroid gland function. We also failed to demonstrate the effect of vitamin D supplement on the distribution of different bone lesions. Among those who had vitamin D supplement, most patients received 0.25 ug/day of 1-alpha-hydroxy vitamin D orally, a dose that may not have significant effect on parathyroid-bone axis in this population. Therefore, no difference in the distribution of different bone lesions was observed. However, we did find significantly higher iPTH levels in patients with high bone turnover than those in patients with low bone turnover. This reflects a higher parathyroid suppression in patients with low bone turnover. The causes of increased high prevalence of low turnover bone disease in our population are still uncertain. Most of our patients had vitamin D supplement for a certain duration in the predialytic period. This

might result from over suppression of parathyroid function in the predialytic period and the effect still persists after the initiation of dialysis.

Although we found no differences in serum calcium, serum phosphate, and calcium-phosphate product between high and low turnover bone diseases, the single serum calcium and phosphate levels determined at the time of bone biopsy could by no means reflect calcium and phosphate metabolism in the past. Further prospective studies should be done to address this question. The only factor found to affect bone pathology is the dialysis duration. Patients with a longer dialysis duration tend to have high turnover bone diseases. This may result from persistent secondary hyperparathyroidism resulting from long standing phosphate retention(26). If it is the case, bone lesions in most patients with low turnover bone will turn into high turnover bone lesions in the future. In fact, the natural history of adynamic bone disease is still unknown. It needs further follow-up to study the clinical picture of the disease.

Regarding the bone mineral density, we found a tendency to have lower bone mineral density in our studied population as shown by the increased number of patients with bone mineral density of less than 2 SD for age- and sex-match normal value. The severity tends to be accentuated with increasing time on dialysis. The modes of dialysis and types of bone lesion have little effect on bone mineral density at the studied areas. As the life expectancy is increasing among dialysis patients and this group of patients are subjected to steroid-induced bone loss after renal transplantation(27-29), more attention to prevent bone loss should be paid to decrease fracture risks in patients with long term dialysis.

Our findings are similar to those reported by Gabay *et al*(30) where significant bone loss in lumbar spine, femoral shaft and femoral neck were found. They also found an inverse correlation between BMD and dialysis duration. Variable findings, however, have been reported from different studies on bone mineral density in end stage renal disease patients. For example, in the Eeckhout *et al* study(31) no bone loss at lumbar spine was observed in dialysis patients. The conflicting results might be caused by the different groups of population, dialysis duration, dialysis techniques and medications in various populations. However, most studies, including our study, have demonstrated significant bone loss in chronic dialysis patients.

In conclusion, relevant bone diseases are also common among Thai chronic dialysis patients. Adynamic bone disease is the most common bone pathology followed by osteitis fibrosa and mixed type. Intact parathyroid hormone above 200 pg/ml is a good predictor of high turnover bone disease. Bone pathology and bone mineral density are

affected by dialysis duration. Significant bone losses in various sites are common among chronic dialysis patients.

#### ACKNOWLEDGMENT

The authors wish to thank Patcharee Karnsombud for the preparation of the bone specimens.

(Received for publication on November 18, 1998)

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## ภาวะกระดูกผิดปกติในผู้ป่วยไตวายเรื้อรังก่อนทำการเปลี่ยนไตในโรงพยาบาลรามาธิบดี

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Renal osteodystrophy คือภาวะกระดูกผิดปกติที่พบในผู้ป่วยไตวายเรื้อรังมีได้หลายชนิด ซึ่งไม่เคยมีการศึกษาในไทยมาก่อน จึงทำการศึกษาอุบัติการณ์ ความสัมพันธ์ทางคลินิกและพยาธิสภาพของ renal osteodystrophy ในผู้ป่วยลังได้ถาวร 56 คน ผู้ป่วยได้รับการรักษาด้วย CAPD และ hemodialysis จำนวน 17 และ 39 รายตามลำดับ ผู้ป่วยมีอายุ  $45.52 \pm 1.74$  ปี ระยะเวลาของการบันดัดทดแทนภาวะไตวาย  $42.26 \pm 5.54$  เดือน ผลคุณแคลลิเซียม-ฟอลัฟต์  $52.31 \pm 2.77$ , iPTH  $307.73 \pm 62.04$  pg/ml renal osteodystrophy ที่พบเป็น adynamic bone 41.1%, hyperparathyroid 28.6%, mixed bone 19.6%, mild lesion 5.4%, osteomalacia 3.6%, และ osteosclerosis 1.8% aluminum toxicity 2 ราย ปัจจัยที่มีผลต่อชนิด renal osteodystrophy คือระยะเวลาของการรักษาโดยในกลุ่ม high turnover จะมีระยะเวลาการรักษา, ค่า iPTH และ bone specific alkaline phosphatase สูงกว่าที่พบในกลุ่ม low turnover bone ( $p < 0.05$ ) ค่า iPTH  $> 200$  pg/ml จะสัมพันธ์กับ high turnover bone (74% sensitivity, 96% specificity) Bone mineral density จะลดลงเมื่อระยะเวลาการรักษานานขึ้น ( $r = -0.4$  ใน wards และ  $-0.3$  ใน troch,  $p < 0.05$ )

สรุป ภาวะกระดูกผิดปกติมีความล้าคุณในผู้ป่วยที่ได้รับการบันดัดทดแทนภาวะไตวายเรื้อรังโดยเป็นชนิด adynamic bone มากที่สุด ระยะเวลาการรักษาจะมีผลต่อชนิด renal osteodystrophy และ bone mineral density ค่า iPTH ที่สูงจะสัมพันธ์กับ renal osteodystrophy ชนิด high turnover

**คำสำคัญ :** Renal Osteodystrophy, High Turnover Bone Disease, Low Turnover Bone Disease, Dialysis, Intact PTH, Bone-specific Alkaline Phosphatase

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