นิพนธ์ต้นฉบับ

BMD fracture threshold for hip fractures in Thai elderly women

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Objective: *To study the threshold of fracture of the proximal femur in Thai elderly women.*

Design: *Prospective randomized study.*

Setting: *In patient, Department of Orthopaedic and Rehabilitation Medicine, Faculty of Medicine, Chulalongkorn University.*

Subjects: *Sixty-seven post-menopausal women with age range of 60-90 years, thirty - one of them had hip fractures were studied.*

Results: *Thai women with hip fractures showed a significant decrease in total BMD of the femoral neck compared with age-matched control. BMD in total subjects decreased with advancing age. The fracture threshold of hip fracture, defined as the mean BMD of the femoral neck in the patients with hip fracture plus 2SD (M + 2SD), was 0.769 gm/cm^2. We also analysed the predictive value of total BMD for hip fracture using a receiver-operating characteristic (ROC) curve. The cut-off point at 0.65 gm/cm^2 (90 % sensitivity and 50 % specificity) can be used to predict the likelihood of hip fracture.*

Conclusion: *Theoretically, to prevent hip fracture in elderly women,the BMD is to be kept above the fracture threshold. With limited knowledge about the incidence and natural history of hip fracture in Thailand, we need more studies to determine routine measurements of BMD and hormonal replacement in postmenopausal women.*

Key words: *Fracture threshold for hip fracture, BMD.*

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ระหว่างปี พ.ศ.2535-2537 คณะผู้วิจัยได้ทำการวัดความหนาแน่นกระดูกข้อสะโพกในผู้หญิง 67 ราย ที่มีอายุระหว่าง 60-92 ปี ในจำนวนนี้มีผู้ป่วยข้อสะโพกหัก 31 ราย และผู้ที่ได้รับการศึกษาเปรียบเทียบอีก 36 ราย ความหนาแน่นกระดูกวัดโดยวิธี Dual Energy X-ray Absorptiometry (DXA) ผลของการวัดพบว่าความหนาแน่นรวมของกระดูกข้อสะโพกในผู้ป่วยที่มีข้อสะโพกหักต่ำกว่าความหนาแน่นกระดูกของผู้ป่วยปกติอย่างมีนัยสำคัญ นอกจากนี้ยังพบว่าความหนาแน่นกระดูกข้อสะโพกลดลงเมื่ออายุมากขึ้นอย่างมีนัยสำคัญ ดัชนีชี้วัดภาวะกระดูกข้อสะโพกหัก (Fracture threshold) เป็นค่าที่คำนวนได้จากค่าความหนาแน่นเฉลี่ยในกลุ่มที่มีข้อสะโพกหักบวกกับ 2 เท่าของความเบี่ยงเบนมาตรฐาน (Mean + 2 SD) ซึ่งคำนวนได้เท่ากับ 0.769 กรัม/ซม^2 นอกจากนี้ผู้วิจัยยังได้คำนวนค่าความเสี่ยงต่อการหักของกระดูกข้อสะโพกโดยใช้ ROC curve พบว่า ที่ความหนาแน่นกระดูกข้อสะโพกเท่ากับ 0.65 กรัม/ซม^2 มีโอกาสเสี่ยงต่อกระดูกข้อสะโพกหักมาก (ที่ระดับความไว 90% และความจำเพาะ 50%) ซึ่งค่านี้ก็สามารถใช้เป็นดัชนีบ่งชี้ภาวะเสี่ยงต่อกระดูกข้อสะโพกหักได้เช่นกัน ค่าดัชนีภาวะกระดูกข้อสะโพกหักนี้มีประโยชน์ ในการช่วยการตัดสินใจในการให้การรักษาภาวะกระดูกโปร่งบางในสตรีวัยหมดประจำเดือน ในทางทฤษฎีแพทย์ต้องให้การรักษาผู้ป่วยที่มีภาวะกระดูกโปร่งบางเพื่อให้มีระดับความหนาแน่นกระดูกสูงกว่าค่าดัชนีชี้วัดภาวะกระดูกข้อสะโพกหัก การรักษาส่วนใหญ่มุ่งเน้นการให้ฮอร์โมน ซึ่งมีโอกาสเสี่ยงต่อผลข้างเคียง อย่างไรก็ตาม ในประเทศไทยยังขาดข้อมูลของความหนาแน่นกระดูกในสตรีวัยหมดประจำเดือน และขาดการศึกษาระบาดวิทยาของภาวะกระดูกข้อสะโพกหัก ซึ่งจะนำมาตัดสินใจวางแผนการรักษาเพื่อป้องกันภาวะกระดูกหักจากภาวะโปร่งบางของกระดูกต่อไป

Osteoporosis, the commonest metabolic bone disorder, is characterized by reduction in bone mass that compromises the biomechanical integrity of the skeleton and leads to an increase risk for fracture. In the United States of America, annual incidence of hip fracture is 98-99 in each 100,000 population which resulted in about 210,000 to 213,000 cases per year.[1] Hip fracture constitutes a major public health problem with an increasing incidence in industrialized countries. An exponential increase in hip fracture rates after age 50 has been documented; 32 % of women and 17% of men are affected by age 90.[2] A 12 % increase in mortality during the first 4 months due to the fracture and its complications has also been documented.[2] At the Mayo Clinic, Rochester, Minnesota, USA, the median cost of direct medical care for a fracture of the proximal femur related to osteoporosis was $ 5,644 which caused the annual cost for hip fracture in the United States to be in excess of one billion dollars.[3]

In Thailand there has been no known national epidemiologic study of the overall incidence of hip fracture among the elderly. But it has been estimated that there are about 14 hip fractures in each 100,000 population.[4] The Thai incidence is thus much lower than in the United States. In Chulalongkorn Hospital during 1985-1990, there were 466 hip fractures in patients aged over 50 years. The female to male ratio was 1.89 to 1. The patients stayed in the hospital from 1 to 8 weeks, with an average of 23 days.[4] There were some patients who had severe medical complications. We belive that hip fracture in the elderly will be a significant problem as our population lives longer.

Retrospective studies that measured the bone mass in proximal femurs had generally found lower bone mass in women who experienced hip fractures compared to age-matched controls.[5] The patients had osteoporosis in which the structure of the bone was changed. In cancellous bone, the integrity of the trabecular network was reduced. Increased endosteal and intracortical resorption caused thinning of the cortical bone. These mechanisms led to a reduction in bone strength. Bone strength itself depends on several factors such as bone mineral density (BMD), bone structure and size, material properties of the bone matrix and the ability to heal microfractures. However, BMD is the most important determinant of bone fragility.[6-8]

For early diagnosis of osteoporosis, there are various methods to quantify bone mass but BMD is currently used. Bone that predominatly consists of trabecular structure might may be the preferred measuring site for assessment of mineral density because bones in these areas, such as the hip, proximal humerus and distal radius, were fractured more frequently than the thick cortical bone sites. Nowadays,dual x-ray absorptiometry (DXA) is the preferred method in measuring bone mineral density compared to single proton absorptiometry (SPA) and dual photon absorptiometry (DPA). The use of DXA has resulted in shorter scan times,and greater accuracy and precision.[7] The usual location for the DXA measurements are the lumbar spines and proximal femur. The correlation between DPA and DXA were found to be excellent in the spine and hip.

To prevent hip of fracture, we need a test that predicts the chance of fracture in an individual

patient so that intervention can be initiated before irreversible bone loss has occurred. A BMD fracture threshold has been definded as the 90th percentile of the BMD for the of patients with fractures,[9] or a value of 2 S.D. below mean BMD in normal, young persons.[10] However,there is no sharp dividing line for bone density separating persons at high risk for fracture from others. Thus, we need a fracture threshold to be a threshold for treatment decision.[11] In Thailand, there has not previously been a study of hip fracture threshold, and our study was limited to Chulalongkorn Hospital. The aim of our this study was to determine the fracture threshold in our patients as we need a parameter to start prevention of hip fracture in our hospital.

Materials and Methods

We collected data during the period January 1992 to December 1994. The inclusion criteria for our studied cases were female patients aged 60 years or more who had hip fracture caused by simple falling and already admitted in our department. Patients who had secondary osteoporosis or pathologic fracture or who were bed-ridden for more than one month were excluded from this study. The control subjects were female patients aged 60 years or older who attended our department for ailments other than hip fracture.

All of the studied patients were tested for blood chemistry, and radiologic studies were performed to determine secondary osteoporosis. All patients experienced bone mineral density measurement by DXA scan (Hologic QDR 2000). The measurements were at the unaffected hip following operations to treat the fractured hips. The control subjects were measured in either hip. For every case, we measured the bone density at 4 regions; the neck region, the troch region,the intertroch region and at Ward's triangle. Measurements were read out in grams per square centimeter.

Result

During the 2 year period we examined a total of 31 cases and 36 controls. The cases were diagnosed to be 16 intertrochanteric fractures and 15 femoral neck fractures. The mean age of the cases was 75.94 years while the mean age of the controls was 70.33 years (Table 1). All of the patients experienced their fractures by simple falling. Most of them were admitted within the first week after the accident. The result of the BMD measurements in both cases and controls are shown in Table 2.

Table 1. Age unmatched group in cases and controls.

	Case (years)		Control (years)		P
	mean	S.D.	mean	S.D.	t-test
Age	75.94	8.60	70.33	7.05	0.005

Table 2. Result of BMD in aged unmatch group.

BMD site	Case (years)		Control (years)		P
	mean	S.D.	mean	S.D.	t-test
Neck	0.465	0.102	0.558	0.103	0.000
Troch	0.368	0.115	0.441	0.102	0.007
Inter	0.591	0.172	0.692	0.216	0.041
Total	0.505	0.132	0.639	0.128	0.000
Ward	0.270	0.117	0.345	0.101	0.006

* Total BMD is a mean value in group of neck BMD, troch BMD and intertroch BMD.

Analysis

In an aged-unmatched t-test, as shown in Table 1, there was a significant difference between the age of cases and control groups ($P<0.05$). The bone mineral density in various sites of the hip in both groups are also shown to be significantly different.

In an age-matched t-test (Table 3) 19 cases and 19 controls in the same age were matched so that the ages of both groups were not significantly different. THE BMD in these groups are shown in Table 4. Total BMD measurements were shown to be significantly different ($P < 0.05$) while the individual BMD values of the neck, troch, intertroch, and Ward's triangle of both groups were not significantly different.

Table 3. Age in matched group in cases and controls.

	Case (N=19)		Control (N=19)		P
	mean	S.D.	mean	S.D.	t-test
Age	72.368	9.069	72.473	8.746	0.971

Table 4. BMD (Age matched)

	Case (N=19)		Control (N=19)		P
	mean	S.D.	mean	S.D.	t-test
Neck	0.485	0.109	0.549	0.119	0.144
Troch	0.370	0.108	0.434	0.108	0.076
Inter	0.589	0.166	0.645	0.256	0.435
Total	0.508	0.125	0.626	0.148	0.011
Ward	0.282	0.118	0.341	0.113	0.126

The relationship between the BMD at each site and the age the among the 31 cases and 36 controls were determined by using multiple regression analysis and analysis of covarience (Tables 5 and 6). The analysis revealed that there was a very significant correlation between total BMD and age and that the bone mass had a negative correlation with advancing age. In the analysis of covarience the total BMD showed the best correlation with age.

Table 5. Muliple Regression in total samples (N=67) : to determine BMD by age.

	R2	Signif F
Age / Neck	0.258	0.000
Age / Troch	0.150	0.001
Age / Inter	0.070	0.031
Age / Total	0.197	0.000
Age / Ward	0.205	0.000

Table 6. Analysis of Covarience (covariate : age).

	F	Signif F
Neck	6.549	0.013
Froch	3.343	0.072
Inter	2.065	0.156
Total	10.155	0.002
Ward	2.918	0.092

To determine the threshold for likely hip fracture in our study, the receiver operating characteristic curve (ROC curve) was plotted using the data from all subjects.The ROC curve of total

BMD and ward's triangle BMD were shown to be good the diagnostic tools to determine the point which the hip joint bones were likely to fracture (Table 7 and Figure 1). In this study, we used the total BMD for determining the fracture threshold. The cut-off point of 0.65 gm/cm^2 yielded 90 % sensitivity and 50% specificity which would be the determining point.

Table 7. Sensitivity and Specificity for prediction of hip fracture by using total BMD.

Cut off point	Sensitivity (a/a+c)	Specificity (d/b+d)	False positive rate (1-specificity)
gm/cm2	%	%	%
< or = 0.40	16	97	3
< or = 0.45	23	97	3
< or = 0.50	36	83	17
< or = 0.55	58	75	25
< or = 0.60	77	58	42
< or = 0.65	90	50	50
< or = 0.70	100	39	61
< or = 0.75	100	17	83

a = cases which BMD below cut off point

b = controls which BMD below cut off point

c = cases which BMD above cut off point

d = controls which BMD above cut off point

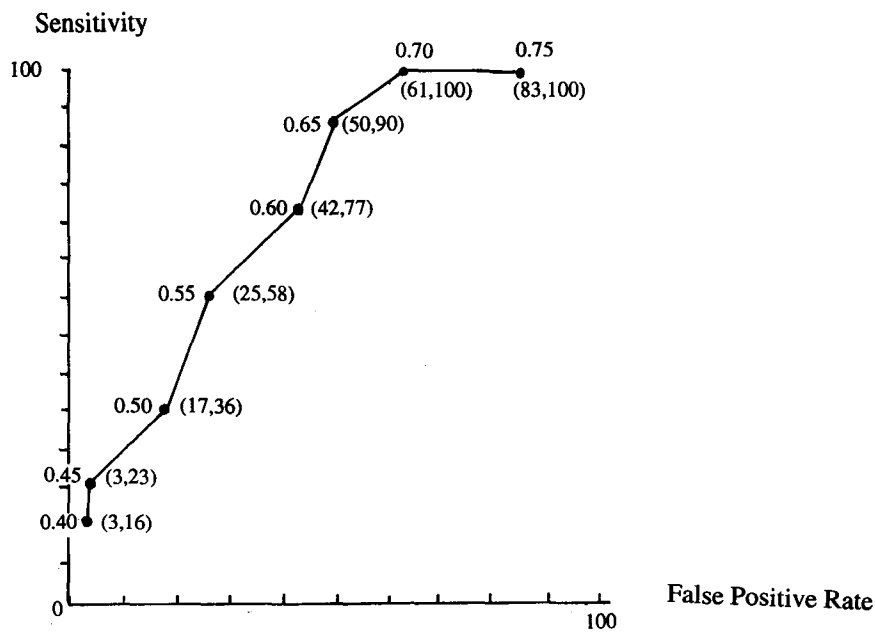

Figure 1. ROC curve for prediction of hip fracture using total BMD.

Theoretically, the BMD fracture threshold could be determined by a point at 2 standard deviations above the mean BMD in the group of fracture patients[10] (mean + 2 S.D.). In this study, the fracture threshold determined by that method was 0.769 gm/cm^2 (0.505 + 2 (0.132) gm/cm^2).

Discussion

This study revealed that the hip bone mass in our patients decreased with advancing age whether or not they had fractures of the hip. The bone mass in the group with hip fractures was significantly lower than in the group without fractures (aged matched total BMD data). So the lower bone mass may change the structure of the bone and predispose them to fracture more easily. Cumming, et al[8], stated that low hip bone density was a stronger predictor of hip fracture than bone density at other sites, and that each standard deviation decrease in femoral neck bone density increased the risk of hip fracture by 2.6 times. Johnston, et al,[7] reviewed articles and found that a decrease of 1 standard deviation in bone mass at other sites was associated with an increase of 50-100 percent in the incidence of fracture. But hip fracture is a multifactorial issue.[12] There are other factors that predispose hip fracture, such as falling, weight of the subject etc.

The fracture threshold for hip fracture is the cut-off point of bone density to determine the bone strength that could prevent hip fracture. At present, there is no agreement in Thailand on the threshold level of BMD so as to identify which patients should be treated, or to determine the length of treatment. Riggs, et at,[13] proposed to use the 90th percentile of BMD for the group with fractures to be the fracture threshold. With this method, Ryan,et al,[9] estimated the fracture threshold to be 0.656 gm/cm^2. In some other studies [10,14,15] the fracture threshold was determined to be 0.63 gm/cm^2 by using mean plus 2 S.D. (sensitivity 90 %, specificity 28 %). By using the R.O.C. curve, the BMD fracture threshold in our study was calculated to be 0.65 gm/cm^2 (sensitivity 90 %, specificity 50 %). This fracture threshold was close to the mean BMD level in the control group.

Theoretically,to prevent hip fracture the bone density must be maintained above the fracture threshold throughout the subjects life [16] Hormonal therapy has been suggested[11,17] early after the menopause period to prevent osteoporotic fractures but long term hormonal therapy may cause complications.[9] The Royal Collage of Physicians recommended that "women aged above 50 years of age should have their bone density measured and estrogen offered to those below a specific threshold"[18] If we follow this recommendation, we would have to start measurement of bone mass in perimenopausal women and this measurement would affect the decision to start prevention of osteoporotic fractures by various medications such as estrogen, dietary calcium, vitamin suppliments and sodium fluoride. Some other measures, such as dietary changes, safety precautions for falling, etc, would also be considered.[19]

In Thailand we need more studies about the risk of hip fracture and a national epidemiologic study to determinc the scope of osteoporotic fractures. However, the measurement of BMD is an expensive method and should not be recommended as a nationalwide procedure, similar

to some other preventive medications such as hormonal therapy. We also need concensus to assist with this problem.

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