Pattern of Bone Loss in Surgical Menopause : A Preliminary Report

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Abstract

The objective of our study was to assess bone mineral density between surgical menopausal women without hormonal replacement and perimenopausal women. This randomized study group included fifty surgical menopausal women and fifty perimenopausal women. Both groups were assessed in body height, body weight and body mass index. The bone mineral density of the distal radius, midradius, femoral neck, lumbar spine and total body in both groups was determined by dual energy X-ray absorptiometry (DEXA). Data analysis was used ANOVA test and rate of bone loss equation. Both groups were similar with respect to body height, body weight and body mass index. As compared with the values in perimenopausal group, bone mineral density of the surgical menopausal group was significantly lower at distal radius, midradius, femoral neck, lumbar spine, and total body (0.267 *vs* 0.312 g/cm^2, 0.609 *vs* 0.692 g/cm^2, 0.762 *vs* 0.930 g/cm^2, 0.980 *vs* 1.153 g/cm^2, and 1.029 *vs* 1.141 g/cm^2). In the postmenopausal period less than 9 years, the estimated rate of bone loss at the lumbar spine and the distal radius were higher than the other sites (3.05, 2.70 per cent/year). While the postmenopausal period more than 9 years, the estimated rate of bone loss at the femoral neck was higher than the other sites (2.70 per cent/year). Pattern of bone loss in the surgical menopause is responsible for type I osteoporosis in the first 9 years postmenopause and type II osteoporosis in the after 9 years postmenopause. Prevention of bone loss in the surgical menopausal women should be instituted immediately after surgery.

It is well known that a rapid loss of bone mass occurs in women following menopause[1,2]. Estrogen deficiency has been implicated in its pathogenesis. This causal role for estrogen deficiency is supported by the more frequent occurrence of vertebral fractures in women than men[3]. The loss of bone mass occurred in an accelerated pattern during the first 3 to 5 years after the natural menopause and followed by a slower age-related type of loss[4,5]. Therefore, type I postmeno-

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pausal osteoporosis was usually found within 15 to 20 years of the menopause[4]. Because the bone loss affects mainly trabecular bones, the three most common fractures seen after the menopause are of the vertebrae, ultradistal radius, and neck of the femur[4,6]. For the women who had undergone oophorectomy during young adulthood, there was also significantly lower bone mineral density at midradius, femoral neck and lumbar spine than the perimenopausal women[7]. Hormonal replacement therapy is one of the preventive methods which slow bone mineral loss in natural postmenopausal women[8-10]. The purposes of this study are :- 1) to assess cross sectional bone mineral density of Thai women who had undergone bilateral oophorectomy and did not receive hormonal replacement therapy using bone mineral density of normal perimenopausal Thai women as the baseline values. 2) to study the pattern of bone mineral density loss in these surgical menopausal women.

PATIENTS AND METHOD

Patients selection

From July 1, 1993 to June 30, 1994, there were patients who underwent total hysterectomy and bilateral oophorectomy at Ramathibodi Hospital. The indications for the surgery included benign tumor, endometriosis and pelvic abscess. Fifty patients were randomized from these cases. All 50 patients did not receive any hormonal replacement therapy since surgery and also did not have any malignant nor metabolic diseases. Because actual baseline bone mineral density of these surgical menopausal women were not obtained, the baseline bone mineral density in these groups were estimated from the bone mineral density of fifty perimenopausal women who had irregular menstruation or amenorrhea less than 12 months without any risk factors for osteoporosis, such as smoking and family history of bone disease by randomization. Both groups of women were matched for body height, weight and body mass index. The mean ages (± SD) of the surgical menopausal group and perimenopausal group were 50.16 ± 6.74 (range 33-74) and 48.98 ± 2.76 (range 41-53) years, respectively, and the mean intervals after menopause of the surgical menopausal group was 8.75 ± 3.89 years.

Method for measuring bone mineral density

The bone mineral density (BMD) of both groups were assessed at distal radius, midradius, femoral neck, anteroposterior lumbar spine and total body by dual energy X-ray absorptiometry (DEXA) (Lunar model DPX, Lunar Co. Madison, WI). The method for analysis of the BMD of the forearm was carefully selected to measure the only ultradistal part of both ulnar and radius. The area of interest was localized by manually setting a first cross-sectional line touching the upper part of ulnar and across the radius. Then the computer will automatically set a second line one centimeter parallele to the first line. The BMD were analysed using the areas between the two lines which were called ultradistal ulnar and ultradistal radius. The lunar DPX system had a built-in software and a phantom for daily quality control of the soft tissue and bone attenuation. The standard dual energy of the X-ray beam was used for correction of the soft tissue attenuation in the measurement of BMD especially in the axial skeleton and hip region. The precision error *in vitro* was less than 1 per cent coefficient variation.

The surgical menopausal women were divided into five subgroups according to duration of menopause for each 3 years interval. The rate of bone mineral density change of each surgical menopausal subgroups were evaluated by using bone mineral density of the perimenopausal group as the baseline values.

Analysis of the data was performed with ANOVA test. The presence of statistic significance was accepted at P value < 0.05. As compared with the values in the perimenopausal group, the bone mineral density in the surgical menopausal group in the apparent amount and rate of bone loss attributable to estrogen deficiency were calculated from the following equation[7]:

$$\text{Amount of bone loss (\%)} = \frac{\text{BMD in the perimenopausal group} - \text{BMD in the surgical menopausal group}}{\text{BMD in the perimenopausal group}} \times 100$$

where BMD denotes bone mineral density, and:

$$\text{Rate of bone loss (\%)} = \frac{\text{\% bone loss}}{\text{year after oophorectomy}}$$

Table 1. Characteristics of the surgical menopausal group and the perimenopausal group.

Characteristic	Surgical menopausal group	Perimenopausal group	P-value
No of subjects	50	50	
Age (years)	50.16±6.74	48.98±2.76	NS
Body weight (kg)	56.30±8.72	58.33±7.82	NS
Height (cm)	154.70±5.15	155.59±5.07	NS
Body mass index	23.83±0.33	24.09±0.30	NS

NS - non-significant

Table 2 Bone mineral density (mean ± SD) at various scanning sites in the surgical menopausal group and the perimenopausal group.

Measurement site	Bone mineral density (g/cm^2)		Average rate of bone loss (per cent/year)	P-value
	Surgical menopausal group (n=50)	Perimenopausal group (n=50)		
Distal radius	0.267±0.045	0.312±0.046	1.60	< 0.01
Midradius	0.609±0.093	0.692±0.075	1.33	< 0.01
Femoral neck	0.762±0.129	0.930±0.150	2.01	< 0.01
Lumbar spine	0.980±0.158	1.153±0.149	1.67	< 0.01
Total body	1.029±0.089	1.141±0.073	1.09	< 0.01

RESULTS

The characteristics of the patient groups are shown in Table 1. There were no differences in body height, body weight and body mass index between both groups ($p > 0.05$). Compared with values in the perimenopausal group, the bone mineral density was significantly lower in the surgical menopausal group at distal radius, midradius, femoral neck, lumbar spine and total body ($p < 0.01$) (Table 2). The average rate of bone loss of the surgical menopausal women was most striking at the femoral neck followed by lumbar spine, distal radius, midradius and least apparent at the total body (Table 2). However, with more detailed analysis of bone mineral density among the five subgroups with different duration of surgical menopause, there was no difference of the BMD at all regions between perimenopausal women and group of less than 3 years surgical menopausal women (Table 3). But the other subgroups which are the women with surgical menopause of more than 3 years showed significantly decreased BMD at all regions except the midradius which was mostly cortical bone (Table 3). The average rate of bone loss at all regions in the surgical menopausal group which was divided into five subgroups, according to duration of menopause for each 3 years interval, are shown in Table 4. The average rate of bone loss at the distal radius was higher than the other sites in the first 9 years of the menopausal period. Meanwhile the average rate of bone loss at femoral neck was highest in the group of more than 9 years after menopause (Table 4). The pattern of bone loss at various scanning sites in the surgical menopausal group is shown in Fig. 1.

DISCUSSION

Cessation of ovarian function characteristic of the menopause is associated with accelerated bone loss[5]. Both estrogen deficiency and aging have been implicated in the pathogenesis of osteoporosis in postmenopausal women. Estrogen deficiency may be the predominant cause of bone loss during the first two decades after a natural menopause[7]. This was confirmed by the presence of estrogen receptors in the bone[11]. The deprivation of estrogen accelerated osteoporosis, regardless of age, resulting in weakening of bone and subsequent

Table 3. Bone mineral density (mean ± SD) at various scanning sites in the surgical menopausal group with divided interval after menopause and the perimenopausal group

Measurement sites	Bone mineral density (g/cm^2) Interval after menopause in surgical menopausal group (year)					Perimenopausal group. (n=50)
	≤3 (n=9)	4-6 (n=7)	7-9 (n=14)	10-12 (n=12)	>12 (n=8)	
Distal radius	0.317±0.036#	0.273±0.039@	0.254±0.189@	0.244±0.023*	0.236±0.032*	0.312±0.046
Midradius	0.689±0.041#	0.636±0.083#	0.635±0.084#	0.567±0.074#	0.514±0.096#	0.692±0.075
Femoral neck	0.889±0.060#	0.832±0.072*	0.806±0.129*	0.660±0.084*	0.697±0.129*	0.930±0.150
Lumbar spine	1.155±0.094#	0.991±0.096*	1.016±0.134*	0.888±0.163*	0.893±0.123*	1.153±0.149
Total body	1.100±0.082#	1.024±0.064*	1.047±0.087*	0.984±0.078*	0.987±0.079*	1.141±0.073

\# - not significance as compared with the perimenopausal group.
@ - P< 0.05 as compared with the perimenopausal group.
* - P< 0.01 as compared with the perimenopausal group.

Table 4. Average rate of bone loss at various scanning sites in the surgical menopausal group divided interval after menopause.

Measurement sites	Average rate of bone loss (per cent/year) Interval after menopause (year)				
	≤3	4-6	7-9	10-12	>12
Distal radius	-	2.70	2.30	2.03	1.47
Midradius	0.22	1.76	1.02	1.68	1.56
Femoral neck	2.20	2.29	1.65	2.70	1.52
Lumbar spine	-	3.05	1.47	2.14	1.37
Total body	1.80	2.23	1.02	1.27	0.81

fractures, initially of the wrist, later of the vertebrae, finally of the femoral neck[4,12]. The women who had undergone oophorectomy during young adulthood will develop early menopausal condition. Castration unnecessarily deprives a woman of an ovarian source of estrogen synthesis[13]. This study shows that compared with values in the perimenopausal women, bone mineral density of all regions was significantly lower in the surgical menopausal women. This could imply that surgical menopause significantly ($P < 0.01$) reduced bone mineral density at multiple sites of bones (Table 2). Thus, the risk of bone fractures in the surgical menopausal women would also increase at these skeletal sites.

Peak bone mass is determined by a combination of four major factors : genetic make up, nutrition, exercise and hormone milieu[14]. Bone loss from midlife (age 35 to 40 years) onward is inevitable, but the rate of loss is subtle. From age 40 to menopause, women loose approximately 0.3 per cent to 0.5 per cent of the cortical bone per year; this accelerates to 2 per cent to 3 per cent per year immediately after menopause with reduced rate after 8 to 10 years[15]. The estimated rate of bone loss at different sites in this study ranged from 1.09 to 2.01 per cent per year in the surgical menopausal group, in particular the femoral neck the rate of bone loss was highest in the late postmenopausal period (of more than 9 years). In the postmenopausal period of 4-6 years, the estimated rate of bone loss at the lumbar spine was higher than the other sites. But in the postmenopausal period of 7 to 9 years group, the estimated rate of

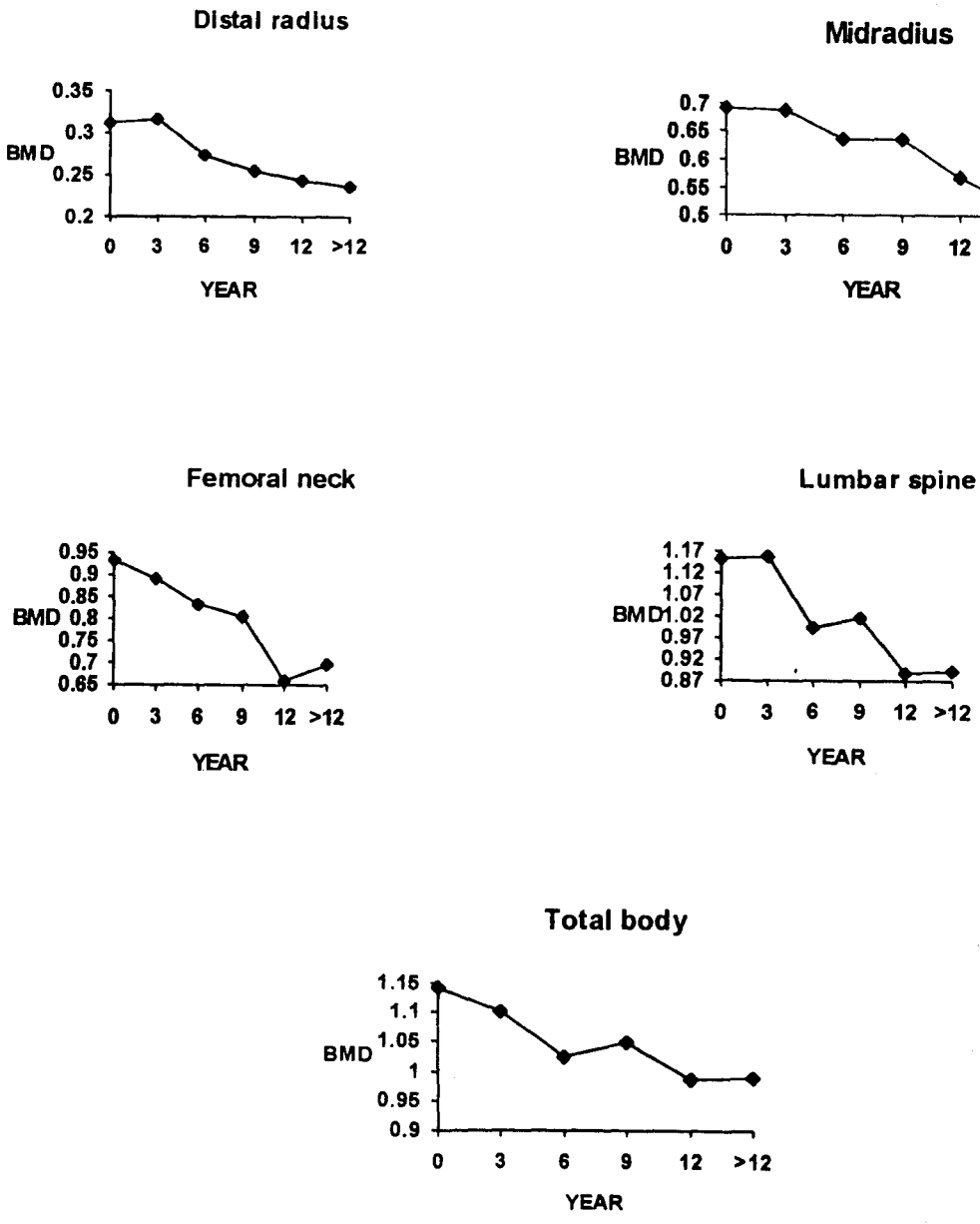

Fig. 1. Pattern of bone loss at various scanning sites in the surgical menopausal group with divided interval after menopause.

bone loss at distal radius was highest. The pattern of bone loss in this study correlates with the accelerated postmenopausal bone loss[16]. The postmenopausal bone loss during the first 4 to 8 years after menopause usually occurs at the sites rich in cancellous bone[16]. The vertebral body and the ultradistal radius contain large amounts of cancellous bone. This postmenopausal bone loss is responsible for type I osteoporosis[17,18]. But after 9 year postmenopausal period, the bone loss was high at the femoral neck that contains substantial proportions of both cortical and cancellous bone. It is mainly responsible for type II osteoporosis [17,18]. This study showed that bone mineral den-

sity in the surgical menopausal women with the interval after surgery of more than three years was significantly lower than that of the perimenopausal women at the distal radius, femoral neck, lumbar spine and total body. From the clinical point of view, prevention of bone loss in the surgical menopausal women is the most important. Hormonal replacement should be instituted immediately after surgery. This would reduce the risk of osteoporotic fracture. Other protection of bone loss should also be provided regarding diet, exercise, avoidance of smoking and alcohol abuse, and calcium supplementation[19]. There are significant morbidity and mortality attributable to osteoporosis related fractures, thus new therapeutic and preventive modalities must be continually evaluated and appropriately applied in high risk population.

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รายงานเบื้องต้นของรูปแบบการสูญเสียความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ออกทั้งสองข้าง

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การศึกษาตรวจหาการเปลี่ยนแปลงความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ออกทั้งสองข้างที่ไม่ได้รับฮอร์โมนทดแทนโดยเปรียบเทียบกับความหนาแน่นของกระดูกในสตรีวัยใกล้หมดระดูเป็นเกณฑ์มาตรฐาน โดยสุ่มตัวอย่างสตรีวัยหมดระดูจากการผ่าตัดรังไข่ออกทั้งสองข้างจำนวน 50 คน และสตรีวัยใกล้หมดระดูจำนวน 50 คน ทำการตรวจบันทึกน้ำหนักตัว ส่วนสูง และดัชนีความหนาของร่างกายของกลุ่มตัวอย่างทั้งสอง และทำการวัดความหนาแน่นของกระดูกที่ตำแหน่งส่วนปลายของกระดูกเรเดียส ส่วนกลางของกระดูกเรเดียส ส่วนคอของกระดูกต้นขา กระดูกสันหลังระดับเอว และกระดูกทั่วตัว โดยวิธี dual energy X-ray absorptiometry (DEXA) ข้อมูลวิเคราะห์โดยใช้วิธี ANOVA และใช้สมการอัตราการสูญเสียความหนาแน่นของกระดูก ทั้งสองกลุ่มมีน้ำหนักตัวเฉลี่ย ส่วนสูงเฉลี่ย และดัชนีความหนาของร่างกายเฉลี่ย ไม่แตกต่างกัน ความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ทั้งสองข้าง เมื่อเปรียบเทียบกับความหนาแน่นของกระดูกในสตรีวัยใกล้หมดระดูพบว่าความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ทั้งสองข้างต่ำกว่าอย่างมีนัยสำคัญ ที่ตำแหน่งส่วนปลายของกระดูกเรเดียส ส่วนกลางของกระดูกเรเดียส ส่วนคอของกระดูกต้นขา กระดูกสันหลังระดับเอว และกระดูกทั่วตัว (0.267 ต่อ 0.312 กรัม/ต.ร.ซ.ม. 0.609 ต่อ 0.692 กรัม/ต.ร.ซ.ม. 0.762 ต่อ 0.930 กรัม/ต.ร.ซ.ม. 0.980 ต่อ 1.153 กรัม/ต.ร.ซ.ม. และ 1.029 ต่อ 1.141 กรัม/ต.ร.ซ.ม. ตามลำดับ) ในสตรีที่ผ่าตัดรังไข่ออกทั้งสองข้างในเวลาน้อยกว่า 9 ปี อัตราการสูญเสียความหนาแน่นของกระดูกที่ตำแหน่งกระดูกสันหลังระดับเอว และส่วนปลายของกระดูกเรเดียสจะสูงกว่าที่ตำแหน่งอื่น (3.05 และ 2.70 เปอร์เซ็นต์ต่อปี) ขณะที่สตรีที่ผ่าตัดรังไข่ออกทั้งสองข้างในเวลาที่นานกว่า 9 ปี จะพบว่า อัตราการสูญเสียความหนาแน่นของกระดูกที่ตำแหน่งคอของกระดูกต้นขาสูงกว่าที่ตำแหน่งอื่น (2.70 เปอร์เซ็นต์ต่อปี) รูปแบบการสูญเสียความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ออกทั้งสองข้างจะเข้าได้กับโรคกระดูกพรุน แบบที่ 1 ในช่วงระยะเวลาหลังผ่าตัด 9 ปีแรกและเข้าได้กับโรคกระดูกพรุนแบบที่ 2 ในช่วงระยะเวลาหลังผ่าตัดนานเกินกว่า 9 ปี

ดังนั้นการป้องกันการสูญเสียความหนาแน่นของกระดูกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ออกทั้งสองข้างควรกระทำทันทีหลังการผ่าตัด

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