Bone Loss in Oophorectomized Thai Women†

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Abstract

This prospective analysis was done in 95 postmenopausal women to observe bone loss rate between 59 natural and 36 surgical menopausal women with or without hormonal replacement therapy (HRT). Bone mass measurement was performed at lumbar spines (L_1-L_4) and hip by dual energy X-ray absorptiometer at 0, 6 and 12 months. The results revealed that in the non-HRT group there was significant faster bone loss rate of lumbar spines (LS) and hip (H) of the surgical group at 12 months (Natural group : LS = -1.11%, H = +2.38% ; Surgical group : LS = -4.51%, H = -0.66%, $P<0.05$). However, there was no significant difference in bone changes of lumbar spines and hip between natural and surgical group with HRT at 12 months (Natural : LS = +2.0%, H = +4.06% ; Surgical : LS = +0.62%, H = +2.28%, $P>0.05$). This observation showed that without HRT oophorectomized women had greater magnitude of bone loss than women who entered menopause naturally.

Loss of bone mineral in the spine and femur is an important result of estrogen deficiency related to menopause[1-3]. In Thailand, it is fairly common for the gynecologist to perform bilateral oophorectomy in premenopausal patients aged above 40 who undergo hysterectomy. The major reason for doing bilateral oophorectomy is prevention of ovarian cancer. In retrospect, this was actually an illogical reason, because most women have a low risk of ovarian cancer[4]. However, because it is widely believed that the only function of the ovaries after childbearing is to produce estrogen and progesterone and that these hormones could be adequately replaced, the ovaries are considered expendable. Little thought was given to the major effects of oophorectomy, particularly, acceleration of osteoporosis[4].

In postmenopausal women, estrogen replacement therapy has been shown to effectively protect and augment existing bone mass[5-7] and to reduce the incidence of fractures of the distal radius and hip[8-10].

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Hence, we conducted this prospective analysis to assess the bone loss rate of different groups of women who entered menopause naturally or surgically, with or without hormonal replacement therapy (HRT).

MATERIAL AND METHOD

This prospective study was done in 120 postmenopausal women visiting the menopause clinic, Chulalongkorn University. All women were healthy and at least 6 months but less than 10 years since entering menopause, either naturally or surgically (undergone bilateral oophorectomy). Postmenopausal status was confirmed by measurement of serum gonadotropin and estradiol levels. These women had no clinical bone diseases, had not received any hormone regimen within the previous 1 year. None were taking drugs known to affect bone changes. Women were also excluded from the study if they had evidence of chronic disease or laboratory abnormalities that could interfere with interpretation of the results of treatment. Women with an initial evaluation of bone density revealing osteoporosis (Bone mineral density (BMD) below -2.5 SD) were excluded from the study. All participants were informed of all the details before entering the study. All patients were randomly allocated to receive hormonal replacement therapy (HRT) or no treatment as shown in Table 1.

This 12 month study was conducted in a prospective open trial method. Bone mineral density (BMD) was measured using Dual Energy X-ray Absorptiometer (DEXA), Hologic 2000, osteometer. Long term precision was 1.5 per cent. A standard region of measurement, including L_1-L_4 was scanned. Patients with severe osteoarthritic changes or compression of vertebrae were excluded from the study. Bone mineral density of hip was measured at the nondominant side. Results were expressed in grams of ashed bone per unit area of bone scanned (gram per square centimeter, g/cm^2). The bone measurement was performed at first visit before commencing the study and then repeated every 6 months until completing the 12 month period.

Per cent changes from baseline in bone mineral density of the lumbar spines and hip were determined after 6 and 12 months since beginning the study by using unpaired *t*-test and analysis of variance.

RESULTS

Of all the women, 95 completed the 12 month study and were recruited for the analysis. Forty-four women were in the non-HRT group in which 27 and 17 women had natural and surgical menopause, respectively. Of the 51 women in the HRT group, 32 and 19 were in the natural and surgical group, respectively. The population characteristics of each group are shown in Table 2 and 3. Per cent changes of bone mineral density of lumbar spines and hip of each group were compared as in Fig. 1-4.

Table 1. Regimen of hormonal replacement therapy.

Group	Type of menopause	Regimen used*
HRT	1. Natural	1. Cyclic : EV (2 mg) + Norgestrel (0.5 mg)
		2. Cyclic : CEE (0.625 mg) + Medrogestone (5 mg)
		3. Combine continue regimen : CEE (0.625 mg) + MPA (2.5 mg)
	2. Surgical	1. Cyclic : CEE (0.625 mg)
		2. Cyclic : 17 Beta-estradiol 1.5 mg
Non-HRT		Calcium 1,000 mg/d ±
		Parasympatholytics as needed

* All regimens were by oral route except 17 Beta-estradiol which was by percutaneous route
HRT = Hormonal replacement therapy
Cyclic = Estrogen on days 1-21 ± progestin on day 12-21
EV = Estradiol valerate, CEE = Conjugated equine estrogen
MPA = Medroxy progesterone acetate
Combine Continue regimen = Estrogen and progestin daily

Table 2. Population characteristics of the natural (N=27) and surgical (N=17) menopausal women in the non-HRT group.

Character	Natural (Mean ± SD)	Surgical (Mean ± SD)	P <value (P<0.05)
1. Age (yr)	49.48±3.53	46.18±4.57	P = 0.017
2. BW (kg)	59.90±12.90	62.84±11.11	NS
3. Height (cm)	155.31±5.50	154.85±2.93	NS
4. T-men (yr)	2.70±1.98	3.47±3.09	NS
5. Mean baseline BMD (g/cm^2)			
- Lumbar spines (L_1 - L_4)	0.98±0.13	0.97±0.11	NS
- Hip	0.85±0.12	0.85±0.09	NS

HRT = Hormonal replacement therapy
SD = standard deviation, yr = year, kg = kilogram, cm = centimetre,
T-men = Time since menopause, BMD = Bone mineral density
g/cm^2 = Gram per square centimetre

Table 3. Population characteristics of the natural (N=32) and surgical (N=19) menopausal women in the HRT group.

Character	Natural (Mean ± SD)	Surgical (Mean ± SD)	P <value (P<0.05)
1. Age (yr)	50.31±4.08	45.89±5.86	P = 0.007
2. BW (kg)	54.36±5.33	55.83±9.65	NS
3. Height (cm)	154.24±4.53	152.84±4.03	NS
4. T-men (yr)	3.59±2.88	4.68±4.62	NS
5. Mean baseline BMD (g/cm^2)			
- Lumbar spines (L_1 - L_4)	0.86±0.14	0.84±0.13	NS
- Hip	0.79±0.12	0.79±0.13	NS

HRT = Hormonal replacement therapy
SD = standard deviation , yr = year, kg = kilogram, cm = centimetre
T-men = Time since menopause , BMD = Bone mineral density
g/cm^2 = Gram per square centimetre

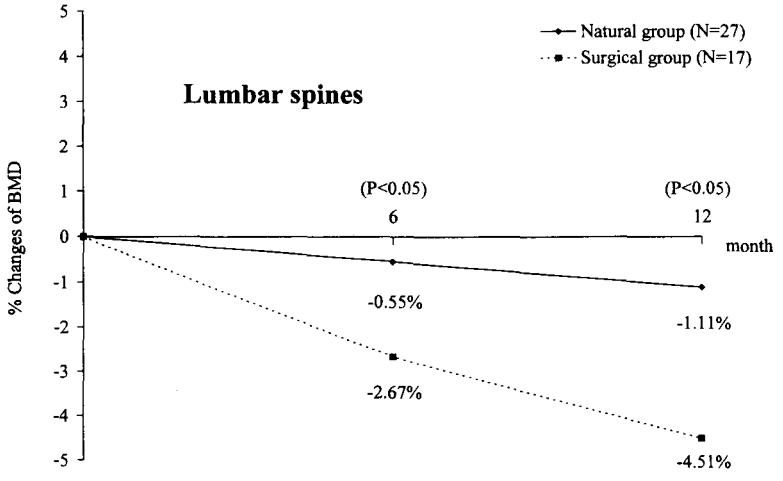

Fig. 1. Per cent changes of bone mineral density (BMD) in natural and surgical menopausal women without hormone replacement (Lumbar spines : L_1-L_4).

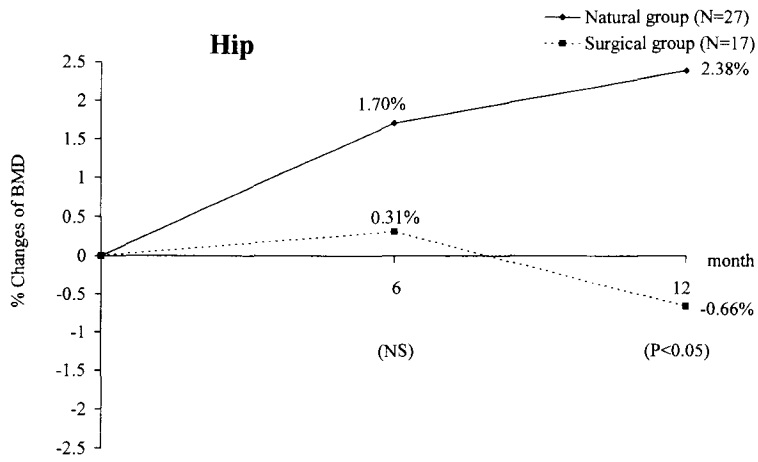

Fig. 2. Per cent changes of bone mineral density (BMD) in natural and surgical menopausal women without hormone replacement (Hip).

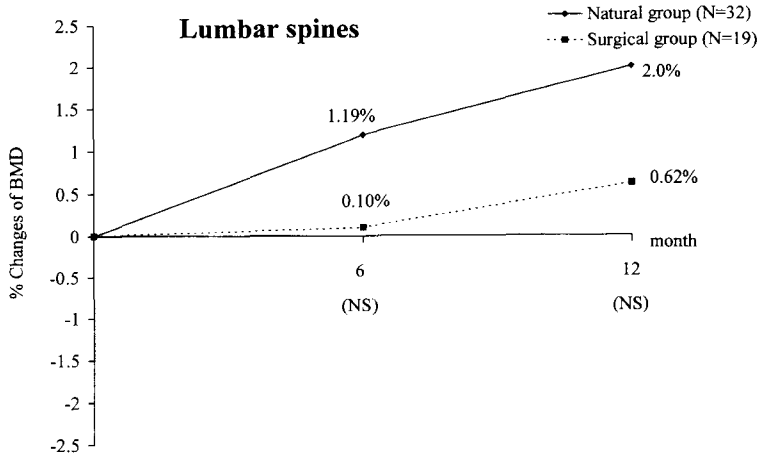

Fig. 3. Per cent changes of bone mineral density (BMD) in natural and surgical menopausal women with hormone replacement (Lumbar spines : L_1-L_4).

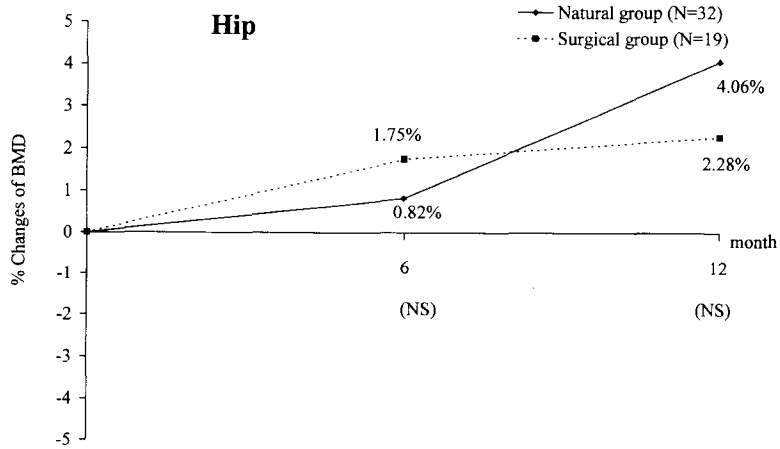

Fig. 4. Per cent changes of bone mineral density (BMD) in natural and surgical menopausal women with hormone replacement (Hip).

DISCUSSION

The results in this study revealed that, without HRT, BMD of lumbar spines decreased significantly faster in the surgical than in the natural menopausal women, at 6 and 12 months. However, the difference of per cent changes of BMD of hip between the two groups was significant only at 12 months. This is probably because the main composition of bone in the spine is trabecular type which has a faster bone turnover rate than the hip bone composition which contains more cortical bone which has a slower turnover rate[11]. Hence, significant change in BMD of the spine could be seen sooner than the hip.

The incidence of osteoporosis is higher in young women who have undergone bilateral oophorectomy than in older women with natural menopause[12]. As in this study, the mean age of the surgical group was significantly lower than the natural group, this is probably because the former mostly underwent bilateral oophorectomy premenopausally, and the result revealed faster bone loss in the surgical group.

The ovary produces not only estrogen and progesterone, in fact it also secretes testosterone and androstenedione which in turn, undergoes peripheral conversion to estrone[13]. In women entering menopause naturally, the circulating level of androstenedione is about one half that seen prior to menopause[14]. Testosterone levels do not fall appreciable, and in most women secretes more testosterone than the premenopausal ovary[13]. After surgical oophorectomy, there is a significant decrease in androgen production which accompanies estrogen loss[15]. Hughes et al,[16] revealed that in patients undergoing surgical castration after spontaneous menopause, testosterone and androstenedione levels fell by half, whereas, estradiol levels were unaffected. The magnitude of bone loss in the surgical group was more obvious in this study. This is probably due to the abrupt decrease of ovarian hormone levels, compared to natural menopause when the ovary gradually decreases in secreting hormones. However, with HRT, bone loss can be prevented as shown is Fig. 3 and 4 and the magnitude of difference in per cent changes of BMD was not statistically significant. The problem of androgen loss in oophorectomized women has led some to question the need for androgen-estrogen replacement therapy. Watts et al,[17] compared the effect of oral estrogens and estrogens plus androgen on BMD, and found that both treatment regimens prevented bone loss at the spine and hip, but the latter was associated with a significant increase in spinal bone mineral density.

In conclusion, this study revealed rapid bone loss in women undergoing surgical oophorectomy. Estrogen can prevent bone loss to a certain level. Whether addition of androgen will have a more beneficial effect, is a matter for research that will add more information in the future.

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การสูญเสียกระดูกอย่างรวดเร็วในสตรีไทยที่ได้รับการตัดรังไข่ทั้งสองข้าง

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ได้ศึกษาวิเคราะห์อัตราการสูญเสียกระดูกในสตรีวัยหมดระดู 95 ราย โดยเปรียบเทียบสตรีที่หมดระดูตามธรรมชาติ 59 ราย และสตรีที่หมดระดูจากการตัดรังไข่ทั้งสองข้าง 36 ราย ทั้งในกลุ่มที่ได้รับและไม่ได้รับฮอร์โมนทดแทน โดยตรวจวัดความหนาแน่นของกระดูกบริเวณกระดูกสันหลังระดับ L_1-$_4$ (LS) และกระดูกสะโพก (H) ด้วยเครื่อง Dual energy X-ray absorptiometer ก่อนเริ่มต้นการศึกษาและหลังการศึกษาที่ 6 และ 12 เดือน ผลการศึกษาพบว่าในกลุ่มที่ไม่ได้รับฮอร์โมนทดแทน สตรีที่หมดระดูจากการตัดรังไข่ทั้งสองข้าง จะมีการสูญเสียกระดูกทั้งในส่วนกระดูกสันหลังและกระดูกสะโพกเร็วกว่าสตรีที่หมดระดูตามธรรมชาติที่ 12 เดือน อย่างมีนัยสำคัญทางสถิติ (เปอร์เซนต์การเปลี่ยนแปลงของกระดูกในสตรีที่หมดระดูตามธรรมชาติ : LS = -1.11%, H = +2.38%; สตรีที่หมดระดูจากการผ่าตัด : LS = -4.51%, H = -0.66%, P<0.05) อย่างไรก็ตาม ไม่พบความแตกต่างอย่างมีนัยสำคัญของการเปลี่ยนแปลงของเนื้อกระดูกระหว่างสตรีที่หมดระดูตามธรรมชาติ และสตรีที่หมดระดูจากการผ่าตัดที่ได้รับฮอร์โมนทดแทนเมื่อครบ 12 เดือน (เปอร์เซนต์การเปลี่ยนแปลงของเนื้อกระดูกในสตรีที่หมดระดูตามธรรมชาติ : LS = +2.0%, H = +4.06%; สตรีที่หมดระดูจากการผ่าตัด : LS = +0.62%, H = +2.28%, P>0.05) ผลจากการศึกษานี้แสดงให้เห็นว่า ในสตรีที่หมดระดูจากการผ่าตัดและไม่ได้รับฮอร์โมนทดแทน จะมีการสูญเสียเนื้อกระดูกอย่างรวดเร็วกว่าเมื่อเทียบกับสตรีที่หมดระดูตามธรรมชาติ

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