

The impact of surgical menopause on metabolic syndrome, bone mineral density, and vasomotor symptoms

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Summary

Purpose: The aim of this study is to compare the effects of surgical and natural menopause on vasomotor symptoms, osteoporosis, and metabolic syndrome. **Materials and Methods:** Seventy menopausal women fulfilling the inclusion criteria were divided into two groups according to surgical and natural menopause. Metabolic syndrome (MS) was defined according to the International Diabetes Federation. Vasomotor symptoms were scored according to the presence of hot flashes and night sweats. The participants had a bone mineral density (BMD) evaluation of the total lumbar spine and total hip bone. **Results:** The rates of vasomotor symptoms were similar among groups ($p > 0.05$). MS was significantly higher in surgical menopause group than in natural menopause group ($p < 0.05$). Women with surgical menopause were found to be more osteopenic at level L1-L4 ($p < 0.05$). Furthermore there were no differences between the femoral neck, femora total T scores, and BMDs of two groups. **Conclusion:** Compared with natural menopause, surgical menopause was found to be associated with higher rates of MS and osteoporosis but not with vasomotor symptoms.

Key words: Surgical and natural menopause; Vasomotor symptoms; Bone mineral density; Metabolic syndrome.

Introduction

Menopause is characterized by the loss of hormones produced by the ovaries. In surgical menopause ovarian function decreases abruptly [1], but in natural menopause, levels of estrogen, progesterone, and androgen decrease slowly over years [2]. Metabolic syndrome (MS) increases in prevalence after menopause and consists of insulin resistance, abdominal obesity, dyslipidemia, elevated blood pressure, and proinflammatory and prothrombotic states [3]. Furthermore menopausal symptoms such as hot flashes, poor memory, vaginal dryness, and changes in sexual desire often appear during the menopausal transition. Postmenopausal osteoporosis is directly linked to declining serum levels of estrogen [4] which has an important role on bone formation in women by acting on osteoblasts and osteoclasts. The aim of the present study is to compare whether the prevalence rates of climacteric symptoms, bone mineral density (BMD) and MS were different among women in surgical menopause or in natural menopause.

Materials and Methods

Thirty-five surgical menopausal and 35 natural menopausal women fulfilling the inclusion criteria were analyzed in this study. The subjects were recruited from the outpatient menopause clinic of the Department of Gynecology and Obstetrics, at Marmara University, after obtaining written informed consent from all participants. The study protocol was approved by the Ethics Com-

mittee of the university. A detailed history was taken and the physical, pelvic examinations and pelvic ultrasound of patients were made by the same physician.

Natural menopause was defined as amenorrhea for more than one year in women older than 40 years and whose FSH level > 40 IU/L. Women who underwent bilateral oophorectomy for benign reasons after the age of 40 years and FSH level > 40 IU/L were considered to be in surgical menopause. The subjects had not taken any medications (hormone replacement therapy and/or osteoporosis treatment), that could affect the biochemical profile and BMD. The exclusion criteria included malignancy and systemic diseases (diabetes mellitus, thyroid dysfunction, renal dysfunction, and hepatic dysfunction). Furthermore, women who reached natural menopause before bilateral oophorectomy and/or women who had been in menopause for more than five years were excluded.

Menopausal symptoms were scored according to the presence of hot flashes and night sweats. Diagnosis of MS was made according to the International Diabetes Federation definition as central obesity plus any two of the four additional factors: systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg (or treatment of previously diagnosed hypertension), fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L) (or previously diagnosed type 2 diabetes), triglycerides ≥ 150 mg/dL (1.7 mmol/L) (or specific treatment for this lipid abnormality); HDL cholesterol < 50 mg/dL (1.29 mmol/L) (or specific treatment for this lipid abnormality) [5].

Body mass index (BMI) was calculated as weight(kg)/height square (m²). Waist and hip circumferences were measured. Blood pressure was measured twice at ten minutes apart with the participants in sitting position from brachial artery.

For biochemical analyses, venous blood samples were collected between 8:00 a.m. and 10:00 a.m., after an overnight fasting and

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Table 1. — Clinical, hormonal, metabolic characteristics, and bone mineral density of groups.

Variable	Surgical menopause (n=35)	Natural menopause (n=35)	<i>p</i>
Age (years)	50.05±2.74	50.62±3.78	0.472
Gravidity	2.9±2.06	3.11±2.09	0.689
Parity	2.57±1.44	2.57±1.61	1.00
Abortions	0.34±1.16	0.54±1.01	0.445
BMI (kg/m ²)	31.24±4.87	30.00±5.2	0.309
BUN (mg/dl)	14.05±3.09	12.79±2.91	0.083
Cr (mg/dl)	0.68±0.11	0.67±0.09	0.741
AST(U/L)	23.91±10.24	21.54±4.56	0.215
ALT(U/L)	23.28±6.86	20.82±6.97	0.142
Menopause duration (months)	30.28±12.53	34.14±15.25	0.252
Vasomotor symptom	22(%62,85)	20(%57,14)	0.626
Metabolic syndrome	14(%40)	6(%17,14)	0.034*
HOMA-IR	3.19±2.73	2.64±0.18	0.359
Systolic blood pressure (mmHg)	133.28±15.00	121.14±13.57	0.001**
Diastolic blood pressure (mmHg)	80.62±9.80	70.08±10.26	<0.001**
HDL cholesterol (mg/dl)	54.00±10.04	61.54±13.79	0.011*
LDL cholesterol (mg/dl)	134.86±31.72	143.28±28.95	0.251
Total cholesterol (mg/dl)	213.85±37.28	229.77±38.33	0.083
Triglycerides (mg/dl)	125.57±2.19	124.14±58.25	0.914
L1-L4 T score	-1.01±1.35	-0.43±1.04	0.048*
L1-L4 BMD (gr/cm ²)	1.025±0.16	1.09±0.12	0.045*
Femoral neck T score	-0.40±1.02	-0.11±0.80	0.185
Femoral neck BMD (gr/cm ²)	0.90±0.11	0.93±0.09	0.186
Femora total T score	0.17±1.04	0.17±0.93	0.510
Femoral total BMD (gr/cm ²)	0.97±0.12	0.99±0.11	0.451

Values are expressed as mean ± SD. HOMA-IR: homeostasis model assessment-insulin resistance, BMI: body mass index, BUN: blood urea nitrogen, AST: aspartate aminotransferase, ALT: alanine aminotransferase, BMD: bone mineral density.

* $p < 0.05$ ** $p < 0.01$

the levels of hemoglobin, fasting blood glucose, blood urea nitrogen (BUN), creatinine, AST, ALT, LDL cholesterol, HDL cholesterol, triglycerides, total cholesterol, and fasting insulin values were measured spectrophotometrically. Insulin resistance, defined by the homeostasis model assessment of insulin resistance (HOMA-IR), was calculated using the following equation: $HOMA-IR = \text{fasting insulin } (\mu\text{U/L}) \times \text{fasting glucose } (\text{mmol/L}) / 22.5$ [6].

The participants had a BMD evaluation of the total lumbar spine (supine evaluation of vertebrae L1-L4) and the total hip bone using dual-energy X-ray absorptiometry (DEXA). T-scores were defined as numbers of standard deviations below the mean BMD for young controls matches for sex [7].

All data were analyzed using Statistical Package for the Social Sciences 22.0. The distribution of data was measured by Kolmogorov-Smirnov test. Data are presented as mean ± standard deviation, number and percentage. Student's *t*-test or Mann-Whitney *U* test was used for comparisons of the quantitative data and Chi-square test was used for comparisons of the qualitative data. The results were considered significant if *p* values were < 0.05 and highly significant if *p* < 0.01.

Results

Table 1 shows the clinical, hormonal, and metabolic characteristics and bone mineral density of the two groups (surgical menopause and natural menopause). Seventy subjects between the age 47 and 54 years were enrolled in the study, 35 of which had surgical menopausal and 35 of which had

natural menopausal. There were no statistically significant differences between the groups according to demographic and biochemical values. BMI was similar between the two groups. Women with surgical menopause were found to be more osteopenic at level L1-L4 ($p < 0.05$). Furthermore there were no differences between the femoral neck, femoral total t scores, and BMDs of two groups. There was no difference between groups in terms of presence of vasomotor symptoms. Surgical menopausal group had a higher rate of MS than natural menopausal group ($p < 0.05$). Surgical menopausal group had a higher systolic and diastolic blood pressure ($p < 0.01$), but their HDL cholesterol levels were lower than the natural menopausal group ($p < 0.05$). LDL cholesterol, total cholesterol, and triglyceride levels, as well as the HOMA-IR levels were not significantly different between the two groups.

Discussion

Oophorectomy has been shown to increase cardiovascular disease risk and MS is one of the major risk factors for cardiovascular disease [8]. The MS rate has been found to be 28.2% among women in natural menopause and 29.2% among women in surgical menopause [9]. Additionally in a study by Hidalgo *et al.*, MS incidence was found to be 35% and 25% for surgical and natural menopause patients, respectively [10]. In the present study, the overall MS rates

were 40% among women in surgical menopause and 17.14% among women in natural menopause.

The cause of hypertension in postmenopausal women is controversial because of menopause and aging simultaneously [11]. In a study by Dorum *et al.*, higher blood pressures in surgical menopause patients were detected [12]. Similarly, the present authors found statistically significant elevated blood pressures in the surgical menopause group. There are conflicting results about lipid metabolism in postmenopausal women. An increase in serum levels of total cholesterol, LDL cholesterol and triglycerides [13, 14] and a decrease in HDL cholesterol level have been reported in women in natural menopause [15, 16]. In the present study neither total cholesterol levels nor triglyceride and LDL cholesterol levels were different in the surgical and natural menopause groups. However HDL cholesterol levels were statistically significantly lower in the surgical menopause group. The present authors believe that low HDL cholesterol levels and increased blood pressures in the surgical menopause group cause cardiovascular risk in oophorectomized patients. Fasting blood glucose is another component of metabolic syndrome. Postmenopausal women with less than five years duration of menopause had an increased risk of abdominal obesity and higher fasting glucose levels [17]. HOMA-IR which is calculated by using fasting blood glucose and fasting insulin levels is the most commonly used method for determining insulin resistance. In the present study, HOMA-IR values were not statistically different in each patient group but HOMA-IR values were higher in the surgical menopause group. The present authors believe that high insulin resistance in surgical menopause group will reach statistical significance in studies with larger patient population.

A study of BMD measured by DEXA found that, compared with natural menopausal ones, women who underwent oophorectomy had almost twice the rate of bone loss six years after surgery [18]. In another study, where quantitative CT was used to measure spine density, lower bone loss percentages were reported in women with natural menopause, although their differences did not reach statistical significance [19]. In the present study among the patient groups with similar menopause durations, the L1-L4 vertebra t scores and BMDs were significantly lower in the surgical menopause group but there were no difference in femoral bone density.

Studies have reported high rates of hot flushes and sweating among postmenopausal women [20, 21]. A study reported prevalence rates of 53.3% for hot flushes and 49.2% for sweating in its population of menopausal women [10]. In the present study, there was no difference between groups in terms of presence of vasomotor symptoms.

In conclusion, MS is more common in the oophorectomized patient group. Oophorectomy in premenopausal women may cause the sudden onset of climacteric symptoms and induce bone loss. Therefore ovarian conservation

at the time of hysterectomy for benign disease should be considered.

Conclusion

Compared with natural menopause, surgical menopause was found to be associated with higher rates of metabolic syndrome and osteoporosis but not vasomotor symptoms.

Conflict of interest

The authors declare no conflict of interest.

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