Effect of Body Mass Index on Endometrial Thickness in Asymptomatic Postmenopausal Women

Asemptomatik Postmenopozal Kadınlarda Vücut Kitle İndeksinin Endometrium Kalınlığına Etkisi

Vücut Kitle İndeksi-Menopozda Endometrial Patoloji / Body Mass Index-Endometrial Pathology in Menopause

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Özet

Amaç: Asemptomatik postmenopozal kadınlarda vücut kitle indeksi ile endometrial kalınlık arasındaki ilişkiyi saptamak. Gereç ve Yöntem: Bakırköy Kadın ve Çocuk Hastalıkları Eğitim Araştırma Hastanesi menopoz polikliniğine başvuran asemptomatik 114 kadın prospektif çalışmaya dahil edildi. Transvaginal ultrasonografi ile yapılan ölçümde endometrial kalınlığı ≥ 5mm olan 30 kadın çalışma grubu, <5 mm olan 84 kadın kontrol grubu olarak alınıp vücut kitle indeksinin endometrial kalınlığa etkisi araştırıldı. Çalışma grubundan Pipelle ile endometrial biopsi alındı. İstatistiksel analizde Student-t test ve Pearson korelasyon analizi kullanıldı. Bulgular: Çalışma grubunda vücut kitle indeksi ve östrojen seviyesi kontrol grubuna göre istatistiksel olarak anlamlı olarak yüksekti (p<0.05, p<0.05). Çalışma grubunda ortalama endometrium kalınlığı 6.76±1.14 mm iken kontrol grubunda 2.83±0.99 mm olarak bulundu (p<0.05). Vücut kitle indeksi ile endometrial kalınlık arasında pozitif korelasyon saptandı (p< 0.001). Her iki grup arasında yaş, menopoz süresi ve progesteron düzeyleri arasında istatistiksel olarak anlamlı fark bulunamadı (p>0.05). Tartışma: Asemptomatik obez postmenopozal kadınlar endometrial patolojiler açısından risk taşımaktadırlar. Postmenopozal dönemde endometrial patolojiler için genel tarama önerilmese de özellikle obez postmenopozal kadınların ultrasonografi ile endometrial kalınlığının takibi önemlidir.

Anahtar Kelimeler

Postmenopozal Dönem; Vücut Kitle İndeksi; Endometrial Kalınlık; Endometrial Patoloji

Abstract

Aim: To investigate the correlation between body mass index and endometrial thickness in asymptomatic postmenopausal women. Material and Method: This prospective cohort study was conducted on 114 postmenopausal women who followed at Bakirkoy Woman and Child Disease Research and Educational Hospital. The study group composed of 30 postmenopausal women endometrial thickness ≥ 5mm and control group composed of 84 postmenopausal women with endometrial thickness < 5mm. The groups were analyzed according to body mass index. The endometrial biopsy was performed from the study group by Pipelle endometrial sampler. The results were compared by using Student-t test and Pearson correlation analysis. Results: In the study group body mass index and estrodiol levels were significantly higher than the control group (p<0.05, p<0.05). The mean thickness of the endometrium was 6.76 ± 1.14 mm in the study group and 2.83±0.99 mm in the control group (p<0.05). There was a positive correlation between body mass index and endometrial thickness (p<0.001). There was no significant difference between two groups as to age, menopause time, estrodiol and progesteron levels. Discussion: Asymptomatic obese postmenopausal women have a high risk of developing endometrial pathologies. Although screening for endometrial pathology is not recommended for the general population, for high-risk populations like obese postmenopausal women, it may be important.

Keywords

Postmenopausal Period; Body Mass Index; Endometrial Thickness; Endometrial Pathology

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Introduction

Clinically, menopause is defined as the absence of menstrual period for at least 12 months [1]. In this period especially some complications observed more frequently than normal: osteoporosis, cardiovascular disease, endometrial hyperplasia (EH) and endometrial cancer (EC). The prevention of all these complications may provide a high quality of life.

Obesity is an increasing problem in the world. In Turkey nearly half of the women (44.2%) are determined as obese. It was informed that the prevalence in women older than 50 years were significantly increased (50.2%) [2]. In postmenopausal women, adipose tissue is the dominant source of estrogen; increased adipose tissue in obese postmenopausal women leads to increased estrogen [3]. It is clear that progesteron levels decrease in menopausal status. Decrease in progesteron is caused high levels of unopposed estrogen which is a risk factor for EH and EC [4].

Obesity is a risk factor for EH. The main problem about EH is progression risk of EC. The risk of progression depends on the histological diagnosis of EH. The risk is lower for women with complex EH (3%) compared with cytological atypia (8–29%) [5]. There is currently no routine screening test for EH or EC. Transvaginal sonography (TVUS) is routinely performed in postmenopausal women. Thickness of the endometrium that is measured by TVUS in postmenopausal woman may be an indicator of pathology. But in postmenopausal women without vaginal bleeding, the threshold separating normal from abnormally thickened endometrium is not known [6]. Currently in the United Kingdom (UK) an endometrial thickness (ET) over 5 mm requires further investigation by hysteroscopy and endometrial biopsy due to the risk of EC. It is thought that by using a cut-off of 5 mm, the majority of cases of both EH and EC can be further diagnosed and investigated [7].

In this study we aimed to investigate the correlation between BMI and ET and definition of the cut-off value of ET in asymptomatic postmenapousal women.

Material and Method

This prospective cohort study was conducted on 114 women who followed at Bakirkoy Woman and Child Disease Research and Educational Hospital between 1stMarch- 31st November 2001. The women subject to this study were asymptomatic, had no menstruel bleeding at least for one year and had no pathology on cervical smear. The exclusion criteria were having any malignancy or endometriosis, using hormone replacement therapy, having chemotherapy or radiotherapy before.

The demographic and clinical data were noted: gravidity, parity, weight, height, hypertension, diabetes mellitus, time of menopause, smoking and alcohol use, family history of cancer. Estrodiol (E2), progesteron, follicle stimulating hormone (FSH) and luteinizing hormone (LH) were evaluated from the venous blood sample at 8-10 a.m. by radioimmunassay technique. Body mass index (BMI) was calculated using the weight (in kg) divided by the square of the height (in meters) (BMI = weight (kg) / height^2 (m^2)). The World Health Organization (WHO) classification was used for BMI. WHO defines normal body weight as a BMI of 18 to 25, overweight as a BMI of 25 to 30, obesity as a BMI of ≥ 30, and morbid obesity as a BMI of ≥ 40 [8].

Ultrasonographic examination of all women were evaluated by the same doctor. TVUS was performed for the evaluation of ET. The ET was measured on the longitudinal axis of uterus. The measurement was performed between the echogenic part of endometrial-myometrial conjuction.

The women were divided in two groups according to ET: study group that ET was ≥ 5mm (number = 30) and control group that ET was < 5mm (number=84). The endometrial biopsy was performed on the study group by Pipelle endometrial sampler.

According to the objectives of the study, the collected data was analyzed by using appropriate statistical tests. Continuous variables with normal distribution were presented as mean ± SD. Student-t test was performed for the comparison of groups for ET and $p<0.05$ was performed for statistically significance. For all cases Pearson correlation analysis was performed.

Results

There were 114 asymptomatic postmenopausal women in our study. No patients departed from the study and there was no vaginal bleeding or malignancy during the study.

Table 1 shows the characteristics of women in our study. There was no significant difference between the groups with regard to age, parity, menapouse time. We performed Pipelle biopsy from all the patients in group 1. The results of histopathology are shown on Table 2. There was no malignancy on the histopathologic reports.

Table 1. Characteristics of women in study group (n=30) and control group (n=84)

	Study group (N=30)	Control group (N=84)	
	Mean±Std. Dev.	Mean±Std. Dev.	p value
Age (year)	51± 3.7	51± 4.7	>0.05
Menopause time (year)	3.43± 2.66	3.93± 3.36	>0.05
BMI [1] (kg/m2)	33.84±5.12	30.65±5.35	<0.05
Parity	3.53± 1.81	3.06±1.83	>0.05
Endometrial thickness (mm)	6.76± 1.14	2.83±0.99	<0.05
Estrodiol (pg/ml)	61.89±96.01	27.06±54.76	<0.05
Progesteron(ng/ml)	0.34± 0.22	0.31±0.21	>0.05
FSH [2] (U/L)	50.46±19.06	63.91±26.44	<0.05
LH [3] (U/L)	22.75±5.8	29.94±11.41	<0.05

[1]Body Mass Index; [2] Follicle stimulating hormone; [3] Luteinizing hormone

Table 2. Endometrial thickness and biopsy results

Histopathology	Number (%)	Mean endometrial thickness (mm)	Mean BMI (kg/m2)
Insufficient material	2 (6.7)	5.6	26.47
Proliferative endometrium	8 (26.7)	6.3	36.58
Secretuar endometrium	6 (20)	7.03	31,56
Simple cystic hyperplasia	6 (20)	7.3	35.01
Polypoid formation	3 (10)	7.8	35.68
Mucinous material	3 (10)	6.1	30.47
Atypic glandular hyperplasia	2 (6.7)	7.4	33.22

In study group, BMI and E2 levels were significantly higher than control group ($p<0.001$, $p<0.05$) (Table 3). There was no dif-

ference between two groups according to progesteron levels. FSH and LH levels were significantly higher in control group (p<0.05, p<0.05) but there was no correlation between these hormons and ET (p = 0.15 for study group and p = 0.22 for control group). The mean thickness of the endometrium was 6.76±1.14 mm in the study group and 2.83±0.99 mm in the control group (p<0.05). There was a positive correlation between BMI and ET (p<0.001) (Table 4).

Table 3. Body mass index in groups

BMI [1] (kg/m2)	≥ 30 (N / %)	<30 (N / %)	p value
Group 1	24 (80)	6 (20)	<0.001
Group 2	47 (55.95)	37 (44.05)	
[1]Body Mass Index			

Table 4. Endometrial histopathology and BMI in study group

Number of patients (%)	11(36.7)	19 (63.3)	p value
BMI [1] (kg/m2)	35.12	29.5	<0.001
Endometrial histopathology	Positive	Negative	
[1]Body Mass Index			

Discussion

The rate of obesity is increasing worldwide. Obesity causes not only cardiovascular problems but also multiple problems in every part of the body. Furthermore it is a major risk factor for EH. The overall peak incidence of EH in women between 50-54 years has been estimated at 386/100.000. Cumulative 20-year progression risk among women who remain at risk for at least one year is less than 5% for nonatypical EH but is 28% for atypical EH [9].

Although the relationship between obesity and EH is robust, underlying mechanisms are not well defined. Obesity adversely affects insulin homeostasis [10]. Hyperinsulinemia has several different adverse effects: It is associated with EH, it might be a key factor that triggers and promotes endometrial hyperplastic lesions. Insulin also induces androgen synthesis by ovaries and adrenals, providing substrate for adipose tissue conversion to estrogen. Especially aromatase activity in increased adipose tissue will cause the secretion of excess estrone which is not opposed by progesteron [11]. Arikan et al. reported a decrease in sex hormone binding globulin (SHBG) as the BMI increases [12]. Insulin and decrease in SHBG associated with obesity cause to increase bioavailability of systemic steroid hormones [13].

Adipose tissue is responsible for the synthesis and secretion of several polypeptide growth factors and cytokines, known as adipokines. Two of these adipokines, leptin and adiponectin, are taken roles in energy homeostasis, and are implicated as mediators of the effects of obesity on cancer development. Leptin levels are positively correlated with white adipose tissue mass and are therefore increased in obesity. Leptin plays role in hormone-dependent neoplasms by activating aromatase [14]. Leptin appears to participate in proliferative processes of the endometrium [15]. Balbi et al. reported that increased leptin levels participated the proliferative processes of the endometrium depending on BMI. In this study they showed that mean leptin concentration in serum was higher in patients who had EH than in controls (p<0.005) and the leptin levels depended on BMI [16]. Adiponectin levels are negatively correlated with body fat and BMI. Adiponectin functions as an insulin sensitizer, and low serum adiponectin reversely correlates with insulin resistance [17]. Moreover, adiponectin can inhibit cell proliferation, invasiveness and angiogenesis in vitro by suppression of estrogen receptor α and vascular endothelium growth factor [18].

Linkov et al. demonstrated decreased EH and decreased B-cell infiltration with surgically induced weight loss [19]. These data showed the relationship between obesity and EH, and implicated tissue inflammation in obesity-related EH. Furthermore, these data suggest that surgically induced weight loss reverses EH.

There are several studies about the relationship betwen obesity and ET in the literature. Epplein et al. compared nonobese women to obese women (BMI > 30 kg/m²) and showed nearly quadruple increase in the incidence of EH with atypia. They also showed women with BMI >40 kg/m² were at 13 times more risk of EH with atypia and 23 times more risk of EH without atypia [20]. Although age, weight and BMI showed a significant positive correlation with ET. Barboza et al. and Warming et al. showed a positive and significant correlation between increase in ET and BMI, demonstrating the influence of obesity on ET [21, 22]. On the other hand, Nakamura et al. concluded that BMI was not a risk factor for endometrial thickning in Japanese women. In this study ET in obese (BMI >25 kg/m²) and nonobese women (BMI <25 kg/m²) were 2.2 mm and 1.5 mm, respectively and there was no significant difference (p=0.27) [23]. Our results showed that BMI was significantly higher than control group (p<0.05) and there was a positive correlation between BMI and ET (p<0.001). After the histopathological evaluation two atypic glanduler hyperplasia were reported in our study. The mean ET of these women were 7.4 mm and their BMI were significantly higher than in control group (p<0.05). Total abdominal hysterectomy and bilateral oophorectomy with frozen section were performed for these patients. There was no malignancy on the final pathology. The other endometrial pathologies assosiated with obesity and ET in our study group were polypoid formation, simple cystic hyperplasia and atypic glandular hyperplasia including 11 (36.7%) women.

In our study we found that asymptomatic, obese postmenopausal women had a higher risk of developing endometrial pathology including hyperplasia, polipoid formation. In this current study also the pathology of proliferative endometrium was found 26.7%. In asymptomatic postmenopausal women the cut-off values of ET for EH are unclear [6, 24]. According to our results we suggest screening for endometrial pathologies in obese postmenopausal women that ET is measured ≥ 5 mm. One of the strong characteristics of this study is its prospective design, which allowed standardization of the type of measurement or evaluation. Furthermore design of study according to ET and the analysis of BMI effects on ET were makes the study stronger. The number of the patients and the absence of endometrial biopsy from control group were the limitation of our study. But the cut-off value of ET ≥ 5mm was our strict criteria for endometrial biopsy. If we would compose the groups according to intra-uterine pathologies at the first phase of the study, perhaps, the affects of BMI would be much more reliable.

Competing interests

The authors declare that they have no competing interests.

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