



# The significance of sonographically thickened endometrium in asymptomatic postmenopausal women

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## Objective

To investigate the correlation between sonographic, hysteroscopic, and pathological findings in postmenopausal asymptomatic patients with sonographically thickened endometrium.

## Methods

The records of postmenopausal patients who attended the Menopause Outpatient Clinic of a tertiary women's hospital in Ankara, Turkey between January 1, 2012 and December 15, 2013 were retrieved. A total of 266 postmenopausal women without vaginal bleeding underwent hysteroscopic evaluation and endometrial sampling. Patients whose pathological records indicated an endometrial thickness equal to or greater than 6 mm (double layer) on transvaginal ultrasonography without any symptoms were included in the study.

## Results

The most frequently detected focal intrauterine lesions in asymptomatic women were endometrial polyps, which were diagnosed in 168 (63.1%) cases. Twenty-four (9%) patients were diagnosed as having simple hyperplasia, 4 (1%) atypical hyperplasia, and 8 (3%) endometrial adenocarcinoma. Two of the patients with adenocarcinoma were diagnosed based on endometrial polyps, and 6 cases showed endometrial hyperplasia on hysteroscopy, while histological examination showed endometrial carcinoma.

## Conclusion

We suggest 10.5 mm as the cutoff value for endometrial thickness and recommend hysteroscopy following dilatation and curettage to increase diagnostic efficacy and provide definitive treatment in asymptomatic postmenopausal women with thickened endometrium.

**Keywords:** Postmenopause; Endometrium; Endometrium cancer; Hysteroscopy

## Introduction

Endometrial cancer is the most common malignancy of the female reproductive system, and its incidence has been rapidly increasing in recent years [1]. It has become the 5th most common cancer among women in Turkey. While postmenopausal bleeding is the most common symptom of endometrial cancer and is encountered in 90% of cases, up to 20% of women may have no symptoms at the time of diagnosis depending on the sensitivity and specificity of the screening tools.

With the liberal use of transvaginal ultrasonography (TVUSG) in gynecology practice, endometrial lesions are incidentally detected in increasing numbers of asymptomatic

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postmenopausal women. In clinical practice, this routine use increases the detection rate of possible pathologic findings and may lead to a large number of endometrial biopsies. Although TVUSG seems to increase the chances of early endometrial cancer diagnosis, it is not a reliable screening method [2]. From this point of view, while a considerable amount of literature has been published on the significance of TVUSG in postmenopausal women with bleeding [3,4], discussion regarding the importance of a thickened endometrial echo in asymptomatic postmenopausal women has remained scarce and controversial [5,6].

Previous studies have agreed that an endometrial thickness threshold cutoff value of 5 mm constitutes an abnormal test result in postmenopausal women with vaginal bleeding [7], because the risk of malignancy decreases to 1 in 1,000 below the 5-mm cutoff value. However, a standardized cutoff value for postmenopausal women without vaginal bleeding that accurately differentiates normal endometria from pathologically thickened endometria has not been established.

Although different diagnostic modalities have been used for many years, dilatation and curettage (D&C) is considered the gold standard diagnostic method for endometrial pathological findings, and the majority of previous studies have compared D&C with transvaginal sonography [6,8].

However, it is well known that when D&C is performed blindly without hysteroscopy, it has limited power in defining intracavitary pathologies. In the literature, only a few studies have evaluated the correlation between pathological and hysteroscopy findings [6,8].

The aim of this paper was to investigate the necessity of histological evaluation in postmenopausal asymptomatic patients with a sonographically thickened endometrium and to evaluate the correlation between sonographic, hysteroscopic, and pathological findings.

## Materials and methods

A retrospective study was performed between January 1, 2012 and December 15, 2013 at the Menopause Outpatient Clinic of a tertiary training and research hospital. Approval from the Institutional Local Ethics Committee and Institutional Education and Planning Committee was obtained. The medical and pathological records of postmenopausal patients who attended the outpatient clinic during this period and

who had an endometrial thickness equal to or greater than 6 mm (double layer) without any symptoms were included in the study. Patients were defined as postmenopausal if they had experienced 12 consecutive months of amenorrhea. Premenopausal and perimenopausal women, patients on hormone replacement therapy, and patients with a history of endometrial hyperplasia, endometrial cancer, or tamoxifen use were excluded. A team of 4 physicians treated all of the patients.

Patients' age, body mass index (BMI), age at menopause, years passed since menopause, endometrial stripe thickness on TVUSG, histopathological results of endometrial sampling, hysteroscopy findings, and comorbid medical illnesses associated with endometrial cancer such as diabetes mellitus and hypertension were collected from medical records.

TVUSG was performed using a 5 MHz vaginal transducer (General Electric LOGIQ A5, Waukesha, WI, USA), followed by fractional D&C and diagnostic hysteroscopy performed under general anesthesia using a 4.5-mm device (exterior shaft) with 30° optics (Karl Storz, Tuttlingen, Germany). Operative hysteroscopy was performed in patients with endometrial lesions. When intracavitary pathologies were detected, the cervix was dilated to 10 mm. Then, all identified lesions were completely removed using a 26 French (9-mm diameter) resectoscope and a 30° lens (Karl Storz) with a monopolar electrode utilizing (1.5%) glycine irrigant solution via an electronic fluid-management system (Endomat; Karl Storz), with 80 watts of low-voltage waveform delivered by an electrosurgical unit (Covidien, Mansfield, MA, USA).

All statistical analyses were performed using Statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA). Variables are presented with descriptive statistics (mean±standard deviation for continuous variables and number and percentage for categorical variables).

## Results

Data from 266 patients with no complaint of vaginal bleeding and an endometrial thickness measurement of 6 mm or more on TVUSG were included in the present study. The mean age of the participants was 58.8±15.1 years. The mean age at menopause, duration of menopause, BMI, and endometrial stripe thickness was 48.8±7.1 years, 12.4±7.2 years, 27.4±6.5 kg/m<sup>2</sup>, and 11.02±2.8 mm, respectively. The

baseline characteristics of the study cohorts are detailed in Table 1.

A total of 152 (57.1%) cases presented with an endometrial thickness of 6–10 mm. Seventy patients (26.3%) had an endometrial thickness of 11–15 mm, 14 (10.5%) had a thickness of 16–20 mm, and 8 (6.1%) had a thickness greater than 20 mm.

Our results showed that 90.3% of the asymptomatic postmenopausal women had intracavitary lesions according to the accepted cutoff value for endometrial thickness of 5 mm. Intracavitary pathologies were detected at a rate of 49.6% in patients with an endometrial thickness of 6–10 mm.

On hysteroscopic analysis, no pathology was detected in 34 patients, while 136 patients were diagnosed with polyps, 80 with hyperplasia, 8 with submucous myoma, and 8 with atrophic endometrium (Table 2). When the histopathological reports of 168 patients (63.1%) with asymptomatic thickened endometrium were analyzed, the presence of endome-

trial polyps was confirmed via histopathological examination in 118 cases. Twenty-four patients (9%) were diagnosed with simple hyperplasia, while 4 (1%) had atypical hyperplasia, and 8 (3%) were found to have endometrial adenocarcinoma on histopathological analyses of the specimen. Two of the patients with adenocarcinoma were diagnosed based on an endometrial polyp.

The mean endometrial thickness was 13.1±7.1 mm in patients diagnosed with endometrial polyps and 12.0±2.1 mm in endometrial cancer cases. Patients who were diagnosed with endometrial polyps (n=8) or endometrial hyperplasia (n=6) during the hysteroscopy procedure were found to have adenomyosis on histopathological examination.

The hysteroscopic findings were then compared with the histopathological diagnoses. Among the 136 patients who were diagnosed with polyps on hysteroscopy, histological examination confirmed the presence of an endometrial polyp in 118 patients, while histopathological examination revealed adenomyosis in 8 cases, myoma in 8 cases, and adenocarcinoma in 2 cases. On the other hand, in 40 patients diagnosed with endometrial hyperplasia on hysteroscopy, histopathological examination showed endometrial polyps, and 4 patients with presumed myoma were also found to have polyps (Table 2).

The histological findings were compared with the endometrial thickness (double layer) measured by transvaginal sonography (Table 3). With consideration of atypical hyperplasia and endometrial cancer (area under the receiver operating characteristic curve [AUC]=0.676; *P*=0.040), the optimal cutoff value for atypical hyperplasia and malignant lesions was found to be 13.5 mm, with 58% sensitivity and 75% specificity. When we added subjects without atypical hyperplasia to this group, the optimal cutoff value for premalignant and

**Table 1.** Demographics and patient characteristics

Characteristics	Values
Age (yr)	58.8±15.1 (42–78)
Age at menopause (yr)	48.8±7.1 (40–58)
Duration of menopause (yr)	12.4±7.2 (2–20)
BMI (kg/m <sup>2</sup> )	27.4±6.5 (20–43)
Endometrial stripe thickness (mm)	11.02±2.8 (6–28)
Comorbid medical illnesses	
Hypertension	90 (33.8)
Diabetes mellitus	20 (7.5)

Data are expressed as mean±standard deviation with (range) or number (%).

BMI, body mass index.

**Table 2.** Comparison of hysteroscopic and histopathological findings

Hysteroscopy findings	Histopathologic diagnosis							
	PE (n=26)	Polyp (n=168)	Simple hyperplasia (n=24)	Atypical hyperplasia (n=4)	Adenomyosis (n=14)	Atrophy (n=10)	Myoma (n=12)	Ca (n=8)
Normal (n=34)	26	6	-	-	-	2	-	-
Atrophy (n=8)	-	-	-	-	-	8	-	-
Carcinoma	-	-	-	-	-	-	-	-
Myoma (n=8)	-	4	-	-	-	-	4	-
Hyperplasia (n=80)	-	40	24	4	6	-	-	6
Polyp (n=136)	-	118	-	-	8	-	8	2

PE, proliferative endometrium; Ca, adenocarcinoma.

**Table 3.** Comparison of histological findings and endometrial thickness (double layer) measured by transvaginal sonography

Histological findings	Patient No.	Endometrial thickness	Distribution of findings according to endometrial thickness (mm)			
			6–10	11–15	16–20	>20
Proliferative endometrium	26 (9.8)	9.5±3.5	20 (13.2)	6 (8.6)	-	-
Polyp	168 (63.2)	13.1±7.1	94 (61.8)	46 (65.7)	18 (64.3)	10 (62.5)
Simple hyperplasia	24 (9.0)	11.0±4.0	4 (2.6)	12 (17.1)	8 (28.6)	-
Atypical hyperplasia	4 (1.5)	18.3±1.9	-	-	2 (7.1)	2 (12.5)
Adenomyosis	14 (5.3)	7.8±2.0	14 (9.2)	-	-	-
Atrophy	10 (3.8)	8.3±2.1	10 (6.6)	-	-	-
Myoma	12 (4.5)	14.1±7.3	6 (3.9)	4 (5.7)	-	2 (12.5)
Carcinoma	8 (3.0)	12.0±2.1	4 (2.6)	2 (2.9)	-	2 (12.5)
Total	266 (100.0)	11.0±2.8	152 (57.1)	70 (26.3)	28 (10.5)	16 (6.0)

Data are expressed as mean±standard deviation or number (%).

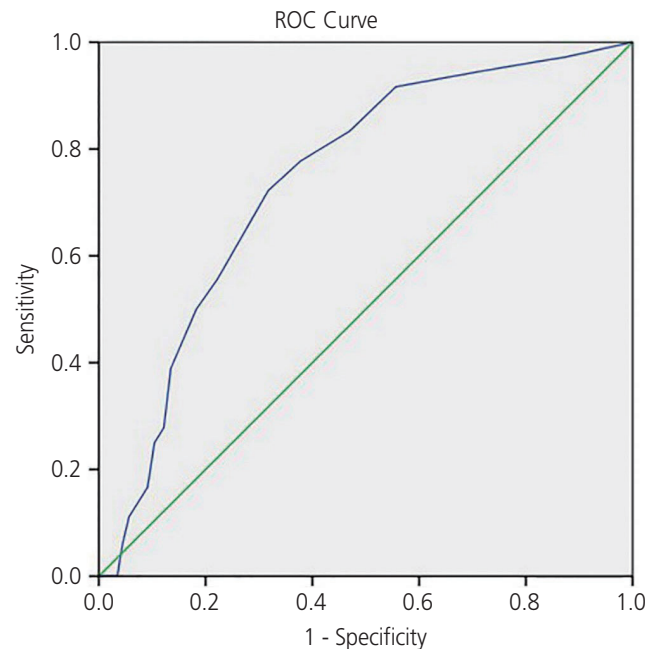
malignant lesions was found to be 10.5 mm, with 77% sensitivity and 62% specificity (AUC=0.740;  $P=0.01$ ; 95% confidence interval [CI], 0.66–0.81) (Fig. 1). A significant cut-off value for polyps could not be established, and they were evaluated independently from the endometrial thickness (AUC=0.456;  $P=0.45$ ; 95% CI, 0.45–0.59).

## Discussion

The current study aimed to investigate the clinical significance of histological and hysteroscopic evaluations of increased endometrial stripe thickness detected by TVUSG in postmenopausal women without any symptoms of vaginal bleeding.

After menopause, atrophic changes occur in the endometrium due to estrogen deficiency. Therefore, for cases of increased endometrial thickness detected on TVUSG in the postmenopausal period, several endometrial thickness cutoff values have been considered to indicate the need for further evaluation [9]. Although the significance of TVUSG and hysteroscopy in postmenopausal women with bleeding has been evaluated in several studies [3,4], data on asymptomatic postmenopausal women with thickened endometrium are limited.

In our study, 168 patients (63.1%) had endometrial polyps. Similarly, Kim et al. [10] reported that endometrial polyps were the most frequently detected focal intrauterine lesions in asymptomatic postmenopausal women. Interestingly, while 57.1% of the patients in our study had an endometrial



**Fig. 1.** Receiver operating characteristic (ROC) curves analysing the optimal cut-off value for premalignant and malignant lesions. Endometrial thickness in premalignant and malignant lesion prediction (area under the receiver operating characteristic curve=0.740;  $P=0.01$ ; 95% confidence interval, 0.66–0.81).

thickness of 6–10 mm, only 26.3% showed a thickness of 11–15 mm.

While Schmidt et al. [11] and Lev-Sagie et al. [12] reported that no malignancy was detected concomitant to endometrial polyps, an evaluation of 560 asymptomatic women with an endometrial thickness >5 mm on transvaginal ultrasonography showed a cancer development incidence of 0.1%

based on the presence of a polyp [13], and this ratio was as high as 2.7% in symptomatic women. In a recent study, 438 women were evaluated, and the incidence of polypoid carcinoma in symptomatic women was found to be 10%, whereas it was as low as 0.9% in asymptomatic women [14].

In Antunes et al.'s study [15], 78.5% of the 475 cases presented with endometrial polyps, while 2.7% were found to be carcinomatous polyps. In our study, we reported only 1 case (1.1% of adenocarcinoma that was identified based on an endometrial polyp within an endometrial stripe thickness of 11–15 mm.

Although Schmidt et al. [11] reported that the prevalence of premalignant and malignant lesions was low in endometrial polyps, a 5.3 times increased prevalence was demonstrated in women aged over 60 years in their study. As a result, we recommend that polyps detected in postmenopausal women should be removed and examined histologically. However, it may be technically difficult to completely remove polypoid structures using D&C, in which case hysteroscopy should be performed.

In our study, intrauterine pathologies were detected in 132 (49.6%) patients with an endometrial thickness of 6–10 mm. Osmers et al. [9] proposed an endometrial thickness of 8 mm as a cutoff value for the diagnosis of pathological endometrial changes, with a sensitivity of 81% and specificity of 89% for the diagnosis of endometrial pathologies. Endometrial cancer was found in 3.5% of patients in the symptom-free group.

In contrast, a large cohort of postmenopausal women was evaluated in the United Kingdom Collaborative Trial of Ovarian Cancer Screening study (UKCTOCS). When an endometrial thickness cutoff value of 5 mm was used for the diagnosis of endometrial cancer or atypical hyperplasia, it showed a sensitivity of 80.5% and a specificity of 85.7% [16]. Meanwhile, no endometrial cancer was reported in postmenopausal women without vaginal bleeding with an endometrial thickness of 5 mm or above in a study by Worley et al. [17]. In our study, the optimal cutoff value for premalignant and malignant lesions was found to be 10.5 mm, with 77% sensitivity and 62% specificity (Fig.1).

In a study by Schmidt et al. [11], intrauterine pathologies were detected in 127 (41.7%) patients who had endometrial thickness measurements of 6–10 mm, while endometrial cancer was identified in 4% of the patients and 4 of the 5 carcinoma cases occurred in patients with an endometrial

thickness less than 10 mm.

In the study by Saatli et al. [18] of 530 asymptomatic cases, 5 adenocarcinoma cases (0.9%) were detected using a cutoff value of 5 mm, and it was concluded that 1 case of cancer was identified for every 106 cases examined.

In Breijer et al.'s meta-analysis [19], the prevalence of endometrial carcinoma and atypical endometrial hyperplasia in asymptomatic women who were not receiving hormone replacement therapy was found to be 0.62% and 0.59%, respectively, and they proposed the use of endometrial thickness as a predictor for premalignant and malignant lesions in women with vaginal bleeding. In a study by Gambacciani et al. [20], only 1 case (0.7%) of endometrial cancer was detected among 148 asymptomatic postmenopausal women who underwent hysteroscopy based on the endometrial thickness measured via ultrasonography.

In our study, a total of 266 cases were examined, and endometrial adenocarcinoma was detected in 8 (3%) cases; in 4 of the 8 detected endometrial cancer cases (1.5%), the endometrial thickness was between 6 and 10 mm. There were 4 cases of endometrial hyperplasia with atypia that showed endometrial thickness greater than 16 mm, and endometrial hyperplasia was found in 1.5% (n=4) of cases.

Conversely, Yasa et al. [21] found that 11 patients with an endometrial thickness of 11 mm or less had endometrial hyperplasia and endometrial cancer on histological examination.

In a study by Smith-Bindman et al. [22], a theoretical model was developed, according to which the risk of endometrial cancer was found to be 6.7% in asymptomatic postmenopausal women when the endometrial thickness was greater than 11 mm, with a very low incidence of 0.002% among women with endometrial thickness less than 11 mm. Therefore, using a cutoff below 10 or 11 mm would lead to biopsies in approximately 1% of normal postmenopausal women.

In the present study, our results are in agreement with those discussed above in that the endometrial thicknesses observed in the endometrial cancer cases were reported to be 6–10 mm (n=4), 11–15 mm (n=2), and >20 mm (n=2). These data highlight the clinical importance of the possibility of detecting a cancer case originating from a thinner endometrium.

In the present study, hysteroscopy was limited in the diagnosis of endometrial polyps in some cases. In 40 patients, areas identified as endometrial hyperplasia during hysteroscopy



were histopathologically diagnosed as endometrial polyps. In addition, although their hysteroscopic appearance was suggestive of endometrial polyps in 4 cases, histologic examination diagnosed them as submucous myomas, which did not match the final pathology (Table 2). In line with our study, Widrich et al. [23] also showed that not every structure with a polypoid appearance met the pathologic criteria for a polyp on hysteroscopy. In our study, while 6 cases were hysteroscopically described as endometrial hyperplasia, histological examination diagnosed them as endometrial carcinoma. Therefore, it is very important to combine hysteroscopy and histopathology to obtain a final diagnosis [24].

One of the limitations of our study is its retrospective design, which limited our ability to analyze the causes and effects of endometrial hyperplasia. Therefore, larger prospective trials are warranted, and an individualized assessment based on patient characteristics and risk factors for endometrial pathologies should be conducted in asymptomatic postmenopausal women.

In conclusion, although we determined an optimal cutoff value for premalignant and malignant lesions of 10.5 mm, our current study also revealed that 8 endometrial cancer cases were detected, 2 on a polypoid basis, in patients with an endometrial thickness of 10 mm or less. Therefore, every patient whose endometrial thickness falls below this cutoff value should still be thoroughly evaluated according to their particular conditions. D&C and hysteroscopy are endometrial sampling techniques used to diagnose endometrial abnormalities. Although D&C is considered the gold standard for endometrial sampling, hysteroscopy has the advantages of achieving a panoramic view of the uterine cavity and hysteroscopy-guided biopsy.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

## Ethical approval

Approval from the Institutional Local Ethics Committee and Institutional Education and Planning Committee was obtained (27.12.2013/170).

## Patient consent

The patients provided written informed consent for the publication and the use of their images.

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