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Original article

Importance of transvaginal ultrasonography before endometrial sampling in asymptomatic postmenopausal patients



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ABSTRACT

Endometrial cancer is the most common gynecologic cancer. Transvaginal ultrasonography (TV USG) is considered to be the first-line diagnostic method for the evaluation of endometrial cancer.

213 asymptomatic postmenopausal patients (192 benign, 21 patients malignant endometrial findings after endometrial sampling) who underwent evaluation with gray-scale TV USG at maximum 48 h before endometrial sampling were included.

Except for hypertension ($P = 0.004$) and endometrial thickness ($P = 0.003$), there was no significant difference in the demographic data, endometrial fluid and endometrial cystic areas detected on TV USG between the groups. A cut-off value of 8.35 mm for endometrial thickness yielded 98.05% positive predictive value with 95% CI.

If the endometrial thickness is ≥ 8.35 mm at TV USG performing endometrial curettage will be reasonable not to wait until 11 mm and endometrial sampling is not required if TV USG shows fluid and cystic areas in the endometrial cavity.

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1. Introduction

Endometrial cancer is the most common gynecologic cancer, and its incidence has increased worldwide over the last two decades [1]. The incidence of endometrial cancer in the US is 25.1/100 000 and approximately 8.4/100 000 annually in Turkey [2,3].

Endometrial cancer has been reported to be more common in women aged >60 years or during postmenopausal period [4]. The most common reason for hospital admittance is vaginal bleeding [4].

Transvaginal ultrasonography (TV USG) is considered to be the first-line diagnostic method for the evaluation of endometrial cancer because it provides detailed images and offers favorable sensitivity and cost effectiveness profile.

In patients with postmenopausal vaginal bleeding, biopsy is recommended when the endometrial thickness, detected using TV USG, is >4 or 5 mm [4–8]. In a retrospective analysis of asymptomatic postmenopausal patients conducted in 2004, endometrial cancer risk was 6.7% in the patient group with an

endometrial thickness of ≥ 11 mm and 0.002% in the group with an endometrial thickness of <11 mm [5]. However, no consensus has yet been established regarding the necessity of performing endometrial sampling based on the endometrial thickness measured using TV USG in the asymptomatic patient group.

During the evaluation of the endometrium using USG, fluid can be incidentally detected in the endometrial cavity at a rate of 4–14% [9,10]. Previous studies have suggested that the detection of endometrial fluid can be used to predict endometrial cancer, but some studies have also advocated that endometrial fluid could be secondary to cervical stenosis and might be of no importance [4–9]. Although published studies have linked the observation of multiple cystic spaces in the endometrial cavity during TV USG with endometrial hyperplasia, only few studies have demonstrated its relationship with endometrial malignancy [11].

In our study, we aimed to investigate the role of endometrial thickness, endometrial fluid, and endometrial cystic area detected using TV USG in predicting endometrial cancer in asymptomatic patients.

2. Methods

In our study, postmenopausal patients without active bleeding complaints who were admitted to the Obstetrics and Gynecology

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Clinic at the Tepecik Education and Research Hospital and underwent endometrial sampling between December 2014 and December 2016 were retrospectively reviewed. Ethics committee approval was obtained from the Tepecik Training and Research Hospital Local Ethics Committee. Patients aged ≥ 50 years, those who were amenorrheic for at least 1 year, those who underwent evaluation with gray-scale TV USG at maximum 48 h before endometrial sampling, those who underwent abdominal and pelvic examinations, and those with properly recorded USG and examination results on the hospital information system were included.

Patients who previously underwent endometrial curettage for postmenopausal vaginal bleeding, those with a history of gynecologic or other cancers, those on tamoxifen therapy, those who have received oral or transdermal hormone replacement therapy during the menopausal period, those with suboptimal endometrial thickness measurement on TV USG, and those with missing data on the hospital information system were excluded.

Our hospital is a high-volume tertiary center for Turkey's western region. As patients were referred to our hospital from all around western region our patients might be riskier than normal patient population. Therefore, a complete gynecological examination including TV USG is performed routinely all postmenopausal patients in our clinic who have chronic pelvic pain, asymptomatic pelvic mass on exam or family history of breast and ovarian cancer and if required performing endometrial sampling with Pipelle device at our outpatient clinic. If the Pipelle endometrial sampling fails, we make probe curettage under anesthesia as required by examination findings if there is no medical contraindication. Hence TV USG before endometrial sampling was performed to all patients included in our study and TV USG is performed in our clinic by experienced gynecologists and obstetricians and radiologists specializing in gynecological diseases and obstetrics. Endometrial sampling can also be performed on patients who do not have postmenopausal vaginal bleeding but who have endometrial cystic area, endometrial fluid, and endometrial solid lesions incidentally detected using TV USG.

Endometrial double wall thickness is measured in our clinic using transvaginal or abdominal USG in the sagittal plane along the long axis of the uterus by measuring the thickest point between two basal endometrial surfaces.

The detection of an anechoic area in the uterine cavity regardless of its size is defined as the presence of endometrial fluid, whereas the detection of anechoic areas in millimeters in the endometrial cavity is defined as endometrial cystic area.

Demographic data and TV USG results of patients were retrieved from the hospital information system records. Systemic diseases other than hypertension and diabetes mellitus were listed

under the heading of "other systemic diseases" (such as hypothyroidism, hyperthyroidism, systemic lupus erythematosus, asthma, chronic obstructive pulmonary disease, and atherosclerotic heart disease).

The pathological diagnosis of patients in whom malignancy was detected with endometrial sampling was confirmed via the final pathological examination performed after hysterectomy.

2.1. Statistical analysis

SPSS 22.0 program was used for statistical analysis. The variables were first checked using appropriate tests of normality. The independent *t*-test was used for continuous parametric variables, Mann-Whitney *U*-test was used for non-parametric variables, and chi square test was used for categorical variables. $P < 0.05$ was considered significant. ROC curve was used to demonstrate the predictive power of endometrial thickness measured using TV USG for endometrial pathologies. Sensitivity, specificity, and positive and negative predictive values for endometrial thickness, endometrial fluid, and endometrial cystic area were calculated within 95% CI.

3. Results

Five hundred and forty-eight patients who underwent endometrial sampling between December 2014 and December 2016 were retrospectively reviewed. Two hundred and forty-six patients were excluded because they were premenopausal or perimenopausal. Of 302 postmenopausal patients, 90 were excluded because of postmenopausal vaginal bleeding and 9 were excluded because their records were inaccessible. Two hundred and twenty three postmenopausal patients without menopausal vaginal bleeding who underwent endometrial sampling and met the inclusion criteria were retrospectively reviewed. Patients were divided into two groups: 192 (90.15%) patients who had benign findings after endometrial sampling and 21 (9.85%) who had malignant findings after endometrial sampling.

Except for hypertension ($P = 0.004$), there was no significant difference in the demographic data such as age, menopause duration, parity, body mass index (BMI), diabetes mellitus, and other systemic diseases between the groups (Table 1). Among the patients with malignant findings after endometrial sampling, endometrial thickness measured using USG was 4–8 mm in six (28.5%), 8–12 mm in six (28.5%), 12–16 mm in five (21.5%), and 16–24 mm in four (21.5%) patients.

The findings of TV USG performed before endometrial sampling are summarized in Table 2. Endometrial thickness measured on the sagittal plane along the long axis of the uterus using TV USG was

Table 1
Demographic data of asymptomatic postmenopausal patients undergoing endometrial sampling according to pathology results.

Demographic data	Endometrial curettage showing benign findings (n, 192)	Endometrial curettage showing malignant findings (n, 21)	P value
Age, median (min–max)	63 (53–88)	61.5 (54–74)	0.951
Menopause duration (min–max)	12.7 (12–39)	10.8 (13–24)	0.324
Parity, median (min–max)	3.1 (0–10)	2.5 (1–4)	0.860
BMI (min–max)			
Hypertension			0.004 ^a
Yes n (%)	133 (69.5%)	6 (28.6%)	
No n (%)	59 (30.5%)	15 (71.4%)	
Diabetes mellitus			0.161
Yes n (%)	153 (79.7%)	14 (66.6%)	
No n (%)	39 (20.3%)	7 (33.3%)	
Other systemic diseases			0.981
Yes n (%)	110 (57.5%)	12 (57.4%)	
No n (%)	82 (42.5%)	9 (42.9%)	

^a Ki square test.

Table 2

Transvaginal ultrasonography results of asymptomatic postmenopausal patients undergoing endometrial sampling according to the pathological examination results.

Transvaginal ultrasound results	Endometrial curettage showing benign findings (n, 192)	Endometrial curettage showing malignant findings (n, 21)	P value
Endometrial thickness, mm median (min–max)	6.85 (1–35)	12.15 (4–27)	0.003
Endometrial fluid			0.381 ^a
Yes	29 (14.8%)	2 (9.5%)	
No	162 (85.2%)	19 (91.5%)	
Endometrial cystic area			0.164 ^a
Yes	18 (9.4%)	4 (19%)	
No	173 (90.6%)	17 (81%)	

^a Fisher's exact test.**Table 3**

The success of endometrial thickness detected by transvaginal ultrasonography in predicting the results of endometrial sampling.

Cut-off value for endometrial thickness	Sensitivity % (95% CI min–max)	Specificity % (95% CI min–max)	Positive predictive value % (95% CI min–max)	Negative predictive value % (95% CI min–max)	P value
8.35 mm	67.97% (59.15%–75.94%)	71.43% (41.9%–91.61%)	95.60% (90.40%–98.05%)	19.61% (13.85%–27.00%)	0.005
11 mm	83.59% (76.02%–89.55%)	57.14% (28.86%–82.34%)	94.69% (90.65%–97.04%)	27.59% (17.31%–40.95%)	0.002

significantly thicker in patients with malignant findings after endometrial sampling results than in those with benign findings after endometrial sampling (12.15 mm vs. 6.85 mm, respectively; $P = 0.003$). There was no significant difference between endometrial fluid and endometrial cystic areas detected on TV USG and endometrial sampling results (Table 2). Sub-analyses were performed to demonstrate the relationship between endometrial sampling results and endometrial thickness measured using TV USG. In the ROC curve analysis, the area under the curve was 0.743 ± 0.06 (95% CI, 0.614–0.872) ($P = 0.003$) (Fig. 1). According to the ROC curve analysis, an endometrial thickness of 8.35 mm was determined as the cut-off value for the prediction of endometrial sampling results. A cut-off value of 8.35 mm yielded 75.94% sensitivity and 98.05% positive predictive value with 95% CI, whereas the commonly accepted cut-off value of 11 mm yields

89.55% sensitivity and 97.04% positive predictive value within 95% CI (Table 3).

4. Discussion

For endometrial sampling in patients with postmenopausal vaginal bleeding, a cut-off value of 5 mm for endometrial thickness proposed by ACOG in 2009 or of 4 mm proposed by the Society of Radiologists in Ultrasound in 2001 are commonly accepted for endometrial sampling [4–8]. However, there are no similar committee decisions for asymptomatic patients without postmenopausal vaginal bleeding. In a meta-analysis of 32 studies involving 11 100 patients conducted in 2012, it was determined that an increase in the endometrial thickness could not be an indication for screening for endometrial malignancy [12].

However, Smith-Bindman et al., who aimed to demonstrate the relationship between the results of endometrial sampling and endometrial thickness in asymptomatic postmenopausal patients, found a significant relationship between malignancy and an endometrial thickness of ≥ 11 mm [5,6]. In our study, we determined that endometrial thickness measured through the transvaginal route could predict endometrial malignancy in asymptomatic postmenopausal patients. Our results are consistent with those of several previous studies [13–16]. Although no consensus has been reached in the literature, an endometrial thickness of ≥ 11 mm is accepted by several institutions as a cut-off value for sampling in asymptomatic postmenopausal patients.

Four (28.5%) patients diagnosed with malignancy on pathological examination in the present study had an endometrial thickness of ≤ 8 mm. According to our ROC curve analysis, taking a cut-off value of 8.35 mm instead of the widely used 11 mm resulted in a higher specificity and positive predictive values but a lower sensitivity. Several previous studies have recommended different endometrial cut-off values between 5 and 15 mm for endometrial sampling [5,13–17].

In asymptomatic postmenopausal patients, endometrial fluid can be the result of cervical stenosis due to atrophic changes [18]. In a community-based study of asymptomatic postmenopausal patients in 2016, Jokubkiene et al. [19] found that the probability of incidentally detecting endometrial fluid was approximately 12%, and out of out of 63 patients who were incidentally detected with endometrial fluid, 62 had an endometrial thickness of < 5 mm. As in

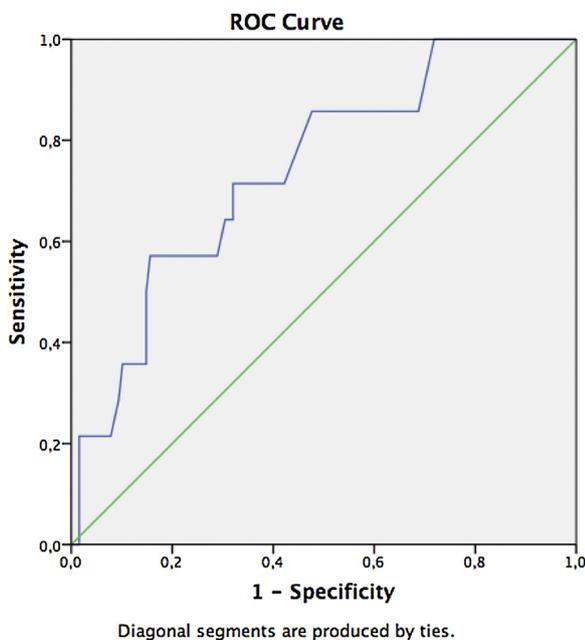


Fig. 1. Effect of endometrial thickness detected using transvaginal ultrasonography in predicting the results of endometrial sampling.

our study, several previous studies have indicated that the incidental detection of endometrial fluid in asymptomatic patients is not particularly significant in terms of predicting malignancy [20–22]. The presence of cystic areas within the endometrial cavity is often associated with endometrial hyperplasia [11]. Studies have also associated the detection of cystic areas during endometrial examination with the focal activation of the foci of adenomyosis and use of antineoplastic agents such as tamoxifen and anastrozole [23]. However, only few studies have evaluated the relationship between endometrial malignancy and endometrial cystic areas. In our study, no significant relationship was found between endometrial cystic areas and endometrial malignancy.

This study contains the results of our clinic on a topic where there is still no consensus in the literature. This is one of the few studies in the literature aiming to determine the relationship between endometrial cystic appearance and malignancy.

The strength of this study was that we used strict patient selection criteria, and the limitation was its retrospective design. However, we tried to overcome this limitation by using strict selection criteria during our retrospective review of patient results on the hospital information system.

In conclusion, endometrial sampling is not required in asymptomatic postmenopausal patients if TV USG shows fluid and cystic areas in the endometrial cavity. TV USG may be a useful technique for early detection of endometrial pathologies for postmenopausal patients with asymptomatic pelvic mass, family history of breast and ovarian cancer. But also performing TV USG for all patients like a screening method is not cost effective due to low sensitivity of TV USG. Hence TV USG might be performed for only chosen patients and if endometrial thickness was detected as above 8.3 mm at transvaginal ultrasound endometrial sampling should be performed for detecting endometrial malignant lesions earlier.

Performing endometrial sampling in this patient group is deemed appropriate because of its low morbidity and potential to lead early diagnosis but may lead to increased costs. Because of the increasing incidence of endometrial cancer and changes in medicolegal and ethical issues, it would be appropriate to conduct randomize-control prospective studies and define standardized committee approaches for asymptomatic postmenopausal patients similar to those defined for patients with postmenopausal vaginal bleeding.

Conflicts of interest

The authors have no conflicts of interest relevant to this article to disclose.

Contributors' statements

Dr. Kanmaz designed the study, drafted the initial manuscript, made statistical analysis and approved the final manuscript as submitted.

Dr. İnan carried out the initial analyses, critically reviewed the manuscript and approved the final manuscript as submitted.

Dr. Beyan and Dr. Budak designed the data collection instruments and coordinated data collection at hospital information system, critically reviewed the manuscript, and approved the final manuscript as submitted.

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