

# The Comparison of Diagnostic Modalities in Patients with Postmenopausal Uterine Bleeding

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**OBJECTIVE:** To investigate the diagnostic values of dilatation and curettage, transvaginal sonography, sonohysterography and hysteroscopy in diagnosing the intracavitary pathologies in women with postmenopausal bleeding.

**STUDY DESIGN:** 30 women diagnosed as postmenopausal bleeding were included into the study. All patients underwent transvaginal sonography and sonohysterography as primary evaluation; hysteroscopy and dilatation and curettage were performed immediately in seven days after primary evaluation.

**RESULTS:** No woman with an endometrial thickness of  $\leq 5$ mm was diagnosed as having endometrial cancer. In women with an endometrial thickness of  $\leq 5$ mm, transvaginal sonography showed a sensitivity 100%, specificity 48%, positive predictive value (PPV) 18% and negative predictive value (NPV) 100% in detecting neoplastic changes. The sensitivity, specificity, PPV, NPV and accuracy of sonohysterography for detecting all endometrial pathologies were 100%, 73%, 54%, 100% and 80% respectively. These findings for hysteroscopy were 100%, 78%, 58%, 100% and 83% respectively.

**CONCLUSION:** Transvaginal sonography as the primary tool in diagnosing postmenopausal lesions should be supported with sonohysterography. Patients with focal intracavitary lesion diagnosed on sonohysterography should undergo hysteroscopic evaluation enabling direct visualization and sampling of the endometrial cavity as the gold standard.

**Key Words:** Postmenopausal bleeding, Ultrasonography, Sonohysterography, Hysteroscopy

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## Introduction

Postmenopausal bleeding (PMB) carries a risk for malignant endometrial pathologies and several strategies and/or cut off values are proposed for detecting these abnormal findings.<sup>1</sup> Transvaginal sonography (TVS), is a widely used diagnostic tool as a primary step in women with PMB. Recently, sonohysterography (SHG) has become a crucial imaging test in the triage of PMB and most of the focal lesions in this patient population require tissue diagnosis, even when the imaging features suggest benign lesions.<sup>2</sup> Either dilatation and curettage (D&C) or hysteroscopy (HS) are advocated as the gold standard for tissue diagnosis but both procedures carry some risk for morbidity especially in the cohort of women with PMB.

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The aim of this study was to investigate the diagnostic efficacy of TVS, SHG, D&C and HS in patients with PMB.

## Material and Method

38 consecutive patients with postmenopausal vaginal bleeding who referred to gynecology clinic of our hospital were enrolled into this prospective study. The diagnosis of postmenopausal bleeding was made when the menopausal status of women with vaginal bleeding was confirmed on the basis of amenorrhea for a year as well as a serum FSH level of  $>40$  mIU/mL and E2 level of  $<20$  pg/mL. Three patients with cervical stenosis precluding the interventions and five women on hormone replacement therapies were excluded from the study.

Initially all women underwent TVS (5 MHz linear probe, Acuson, Mountain View, CA, USA). After confirming the continuity of endomyometrial junction, endometrial thickness was measured from its outer margins at its thickest portion on sagittal plane without taking the hypoechoic inner myometrium into account. Fluid collections in endometrial cavity were not included into the measurements. Increased focal

endometrial thicknesses were interpreted as polyps and in submucosal masses continuing with myometrium having the same echogenicity, submucous myomas were suspected. After recording the findings in TVS, SHG was performed in same session. The distention of endometrial cavity was achieved by introducing 10 to 20 ml of saline solution under ultrasonographic guidance. Endometrial thickness was measured separately on both sides. Hyperechogenic masses of various dimensions and shapes not intervening into the endomyometrial distance were classified as polyps and solid masses with round shapes and mixed echogenicities disturbing the inner myometrial line and protruding into the endometrial cavity as submucous myomas. Diffuse or focal increases in endometrial thicknesses with significant changes along the uterine cavity were interpreted as hyperplasia and irregular thickening with different echogenicities as endometrial cancer.

All patients underwent diagnostic HS under general anesthesia in maximum 7 days. A thin, pale and smooth surfaced cavity with petechial spots was diagnosed as atrophic endometrium. Endometrial polyps were smooth surfaced pediculated or unpediculated structures covered with endometrium and submucous myomas were usually sessile lesions with shiny, vascularised surfaces not covered with endometrium. Smooth or polypoid thickening of endometrial surface with forming of 'endometrial sulcus' when pressure applied with the hysteroscope were diagnosed as hyperplasia. If these thickenings were accompanied with significant irregularities, necrotic areas, glandular and vascular disarrangements, carcinoma was the suspicion.

D&C was performed in same session with HS. Histopathologic diagnoses were inactive endometrium, proliferative or secretory endometrium, hyperplasia and carcinoma.

Written consent was obtained from all participants. The diagnostic values of these modalities were assessed separately and in combination. Mann-Whitney-U test and Fisher exact test were used for statistical evaluation. Sensitivity was defined as the proportion of actual positives which are correctly identified and specificity as the proportion of negatives which are correctly identified. The positive predictive value described the proportion of patients with positive test results who are correctly diagnosed and the negative predictive value is the proportion of patients with negative test results who are correctly diagnosed.  $p < 0.05$  was accepted for statistical significance.

## Results

Demographic variables of the patients are shown on table 1. 3(10%) had diabetes mellitus and 16 (53.3%) hypertension. 3 women were diagnosed as endometrial carcinoma. No women had a history of infertility.

Table 1: Demographic variables of the patients

<b>Age</b>	
mean $\pm$ sd	57.0 $\pm$ 7.94
(min-max)	(42 -74)
<b>Age at the onset of the menopause</b>	
mean $\pm$ sd	47.3 $\pm$ 4.68
(min-max)	(37-55)
<b>Duration of the menopause</b>	
mean $\pm$ sd	10.1 $\pm$ 7.9
(min-max)	(2-28)

### TVS Results

Mean endometrial thickness was 8.13 $\pm$ 7.11 (1-27) mm. In 43.3% of patient's endometrial thickness was measured as  $\leq$  5mm. The lowest endometrial thickness in cancer and polyp patients was 10 and 5 mm, respectively. The sensitivity, specificity, PPV, NPV of TVS for detecting malignant endometrial pathologies were 100%, 48%, 18% and 100% respectively.

### SHG Results

In 56.7% the cavity was diagnosed as normal. 20% had endometrial polyp, 10% irregular endometrium and 6.7% submucous myoma. In 2 (6.7%) of patients, a diagnosis could not be established because of the insufficient intracavitary distension. Insufficient intracavitary distension was regarded as a pathological condition and one of these patients revealed as endometrial cancer in histopathological investigation and other as atrophic endometrium which later revealed as submucous myoma in hysteroscopy. No endometrial pathology was diagnosed in D&C in apparently normal cavities with SHG. The sensitivity, specificity, PPV, NPV and accuracy of SHG for detecting endometrial pathologies were 100%, 73%, 54%, 100% and 80% respectively. All patients with submucous myoma, endometrial polyp and carcinoma were diagnosed with SHG, depicting its sensitivity in these pathologies as 100 %.

### Hysteroscopic Results

Hysteroscopic diagnoses are summarized on table 2. Endometrial atrophy was regarded as normal because of the postmenopausal status of the women. Comparison of hysteroscopic diagnoses with D&C results are shown on table 3. The sensitivity, specificity, PPV, NPV and accuracy of HS for detecting endometrial pathologies were 100%, 78%, 58%, 100% and 83% respectively.

Table 2: Hysteroscopic Diagnoses

	n	%
Normal cavity	18	60
Endometrial polyp	6	20
Submucous myoma	3	10
Endometrial carcinoma	3	10
Total	30	100

Table 3. Comparison of Hysteroscopic Diagnoses with D&amp;C Results

		D&C Results				Total
		Normal	Atrophy	Endometrial polyp	Endometrial Carcinoma	
Hysteroscopic Diagnoses	Normal cavity	5	13	0	0	18
	Endometrial polyp	0	3	0	0	3
	Submucous myoma	2	0	4	0	6
	Endometrial carcinoma	0	0	0	3	3
	Total	7	16	4	3	30

In our series, if a cut off value of endometrial thickness is set on 5 mm; all endometrial carcinomas were identified whereas 2 endometrial polyps were undiagnosed. All patients with endometrial carcinoma were detected with D&C but this modality missed all of 3 patients with submucous myoma and 2 of 6 women with polyps.

## Discussion

PMB is pathological condition which affects 0.5-1% of postmenopausal women every year. Astrup et al. reported the incidence of PMB as 10.7%.<sup>3</sup> It responsible for 5 % of admissions to gynecology clinics and is one of the early signs of endometrial cancer.<sup>4</sup> Because early diagnosis of endometrial cancer is essential for a good prognosis, ruling malignant pathologies out is the main goal of management of PMB. The diagnosis of endometrial carcinoma is made histopathologically. Specimens can be collected via simple endometrial sampling, HS or D&C Assuming that only 30% of women with PMB have endometrial pathologies, 70% of them may undergo unnecessary interventions increasing the diagnostic costs.

There is an association of endometrial thickness and endometrial pathologies in PMB. The PPV of TVS is proportional with the thickness measured.<sup>5,6</sup> Therefore TVS is preferred as the primary step in diagnosing PMB. Karlsson et al reported in their series of 1138 women with PMB, setting an endometrial thickness of 5 mm, TVS revealed sensitivity, specificity, PPV and NPV for detecting in endometrial cancer 94%, 78%, 69% and 96% respectively. A cut off value of 5 mm missed 2 of 114 cancer patients but no patient was failed to detect if the cut off value was lowered to 4 mm.<sup>1</sup> In our series no patient with cancer was undiagnosed with a cut of value of 5 mm. The sensitivity of TVS in detecting focal intracavitary lesions like polyp and myomas is lower and reported to be 67-78 % in the literature.<sup>7-9</sup>

SHG is an effective, simple and well tolerated method in visualizing the endometrial cavity. Because of it's higher sensitivity in detecting focal lesions, it has been recommended by some authors as the primary diagnostic step.<sup>7</sup> Hysterectomy or

hysteroscopic findings were used as the gold standard, SHG has a sensitivity of 93-100 % and a NPV of 6-15% in diagnosing intracavitary focal lesions.<sup>10-12</sup> But it is somewhat unsatisfactory in differentiating malignant and benign lesions. Ludwin et al reported the sensitivity and specificity of SHG in detecting all endometrial pathologies, polyps and hyperplasias 97% and 90%, 100% and 83% and 84% and 95%, respectively.<sup>13</sup> Wolman reported the sensitivity and specificity of SHG in detecting intracavitary lesions in a double blinded prospective study with 47 women with PMB as 86% and 100 %.<sup>14</sup> Ozturk et al reported the sensitivities of TVS, SHG and HS in diagnosing all endometrial pathologies as 100 % whereas specificity and PPV were similar for both TVS and SHG (76%, 89%, respectively) and higher for hysteroscopy (100%).<sup>15</sup> In our series, we found that the sensitivity, specificity, PPV, NPV and accuracy of SHG for detecting endometrial pathologies were 100%, 73%, 54%, 100%, and 80% respectively. One of the 2 women with insufficient intracavitary distension was revealed as endometrial cancer and the other as submucous myoma. In 71 % of advanced and 12 % of early endometrial cancer insufficient intracavitary distension may occur and this condition should be regarded as a pathological condition suggesting malignancy.<sup>16</sup>

Hysteroscopic biopsy is considered as the gold standard in diagnosing endometrial pathologies. Blind biopsies can sample less than the half of the endometrial tissue creating a high false negativity rate.<sup>17,18</sup> This rate is 2-6% in D&C and 3% in diagnostic HS.<sup>19,20</sup> Angioni et al. reported the sensitivity and specificity of blind biopsy in detecting endometrial polyps and submucous myomas as 11 % and 93 % and 13% and 100%, respectively in patients with PMB. The sensitivity and specificity of HS in endometrial polyps were 100%, 97% and 100%, 98% in submucous myomas, respectively.<sup>21</sup>

In our series, the sensitivity and the specificity of HS for detecting endometrial polyps were 100% and 90%. D&C failed to detect all of 3 patients with submucous myoma and 2 of 6 women with polyps diagnosed by HS. The sensitivity and the specificity, of HS for detecting endometrial cancer were 100% and 100%. All patients with endometrial carcinoma

were detected with D&C. The sensitivity and the specificity of D&C for detecting all endometrial pathologies were 58% and 100% whereas sensitivity for local lesions was 44 %. Sendag et al. reported the sensitivity, specificity, PPV, and NPV of HS for detecting all endometrial pathologies were 95.9%, 82%, 75.8% and 97.2%, respectively.<sup>22</sup>

Polyps are risk factors for developing endometrial cancer and 24% may show precancerous and 1.5% malignant changes. They have recurrence rate three times higher with D&C compared to hysteroscopic resection. This reveals the importance of HS in women with PMB.<sup>23</sup> D&C has relatively low sensitivity and accuracy rates in detecting benign focal lesions but it's accordance with HS is relatively high (94%) if the focal lesions are excluded.<sup>23</sup>

Litta et al. compared the value of TVS and hysteroscopic biopsy in diagnosing endometrial cancer in 220 women with PMB. They reported sensitivity, specificity, PPV and NPV of TVS 55.6%, 49.7%, 83.3%, and 98.1%, respectively if a cut off level of 4 mm is set. They also reported the sensitivity, specificity, PPV, and NPV of HS as 100%, 49.6%, 81.3%, and 100%, respectively and concluded that hysteroscopic biopsy should preferred in all women with PMB.<sup>24</sup>

Because of the association of endometrial thickness and endometrial pathologies in women with PMB, TVS should be the primary diagnostic step due to its simplicity and non-invasiveness. SHG is superior to TVS in diagnosing of all endometrial pathologies. Otherwise SHG is at least as effective as HS in diagnosing focal intracavitary lesions. But, it has its limitations in differentiating malignant and benign lesions. HS allows inspecting the whole endometrial cavity with sampling from suspicious areas under direct visualization and diminishes the false negative rate of D&C in women with PMB.

In conclusion, as the primary diagnostic step in PMB TVS, should be combined with SHG in diagnosis. HS seems to be the gold standard in intracavitary focal pathologies or in circumstances where the cavity is not properly assessed by SHG, because of its ability of collecting samples under direct vision.

## Postmenopozal Uterin Kanamalı Hastalarda Tanı Yöntemlerinin Karşılaştırılması

**AMAÇ:** Postmenopozal vajinal kanamalı kadınlarda intrakaviter patolojilerin tanısında transvajinal sonografi, sonohisterografi, histeroskopi, dilatasyon ve küretajın tanılma değerlerinin araştırılmasıdır.

**GEREÇ VE YÖNTEM:** Postmenopozal kanaması olan 30 hastaya ilk değerlendirmede transvajinal sonografi ve sonohisterografi uygulandı. Bunu takiben 7 gün içinde tüm hastalara tanılma histeroskopi ve ardından dilatasyon ve küretaj yapıldı.

**BULGULAR:** TVS ile  $\leq 5$ mm endometrial kalınlığı olan hiçbir hastada endometrium kanserine rastlanmadı. Endometrial ka-

lınlık eşik değeri 5mm alındığında transvajinal sonografinin neoplastik değişiklikleri saptamadaki duyarlılığı %100, spesifitesi %48, pozitif prediktif değeri (PPD) %18, negatif prediktif değeri (NPD) %100 bulundu. Sonohisterografinin tüm endometrial patolojileri saptamadaki duyarlılığı %100, spesifitesi %73, PPD %54, NPD %100 ve doğruluğu %80 bulundu. Bu değerler histeroskopi için sırasıyla %100, %78, %58, %100 ve doğruluk %83 olarak hesaplandı.

**SONUÇ:** Postmenopozal kanamalı olgularda tanıda ilk basamak olan transvajinal sonografi, sonohisterografi ile desteklenmelidir. Sonohisterografide fokal intrakaviter lezyon saptanan olgularda, tanıda kavitenin direkt gözlemlenmesine ve aynı anda biyopsi alınmasına imkan sağlayan histeroskopik değerlendirilmenin altın standart olduğunu düşünmekteyiz.

**Anahtar Kelimeler:** Postmenopozal kanama, Ultrasonografi, Sonohisterografi, Histeroskopi

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