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Can vaginal ultrasound replace diagnostic curettage in the detection of endometrial pathology in post-menopausal bleeding?

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Abstract

Background and objective: Post-menopausal bleeding due to endometrial abnormalities is a common diagnostic challenge facing the ultrasonogists and referring gynecologists. This study aimed to detect the validity of transvaginal ultrasound to detect endometrial pathologies and its sensitivity and specificity for determining endometrial carcinoma in women with postmenopausal bleeding.

Methods: A diagnostic accuracy study of transvaginal ultrasound and diagnostic curettage was conducted for evaluation of endometrial pathology in the College of Medicine, Hawler Medical University from October2016to January 2018. The sample size included 55 women with post-menopausal vaginal bleeding. The ultrasound findings were compared with histopathological results of endometrial biopsy.

Results: Out of 55 women, 49.09% had endometrial atrophy, 29.09% had endometrial hyperplasia, 16.36% had endometrial polyp, 3.64% had endometrial carcinoma, and 1.82% had hyperplasia with atypia according to histopathological findings. The sensitivity of ultrasound in detecting cancer was 66.7%, the specificity was 100%, the positive predictive value (PV) was 100%, and the negative predictive value was 98.1%. The total agreement rate was 98.2%.

Conclusion: Transvaginal ultrasound is an excellent diagnostic tool to determine whether further investigation with histopathological examination of endometrial biopsy is necessary for postmenopausal vaginal bleeding.

Keywords: Transvaginal ultrasound; Postmenopausal bleeding; Endometrial pathology.

Introduction

Postmenopausal bleeding refers to vaginal bleeding that occurs after twelve months of amenorrhea in a woman of the age where the menopause can be expected.[1] It can also be defined as the time in a woman's life when the woman stops having a menstrual period permanently and is no longer fertile.[2] However, it can be applied to younger women following premature ovarian failure or premature menopause.[3] Vaginal bleeding is a common post menopausal complaint representing 5% of all gynecology outpatient consultations.[4] The incidence of postmenopausal bleeding is 10% in the general population immediately after menopause.[5] The causes of postmenopausal bleeding include endometrial atrophy (approximately 75% of cases),[3] endometrial polyps, submucosal fibroids, endometrial hyperplasia (simple, complex and atypical), endometrial carcinoma (approximately 10%), and estrogen withdrawal.[6] Non-gynecological causes include trauma, systemic diseases like hypertension, hypothyroidism, and bleeding disorders.[3] Endometrial abnormalities are common diagnostic challenges facing the radiologist and referring specialist gynecologist. Ultrasound is the primary imaging modality in this workup; findings if further investigations done like sonohysterography, hysterosalpingography, magnetic resonance imaging, and computed tomography are often correlated

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with ultrasound findings. In the last decades, transvaginal ultrasound has become widely used in the evaluation of women with postmenopausal bleeding. transvaginal ultrasound was introduced in the early 1990s, a strategy with transvaginal ultrasound as the initial investigation, the possibility of endometrial abnormalities strongly reduced, and further evaluation with diagnostic curettage is according to the ultrasound results.[7] The normal postmenopausal endometrium is thin, echogenic, regular and homogeneous. There is controversy regarding post-menopausal endometrial thickness, some authors have found that endometrial thickness decreases with increasing age,[6] in general, a double-layer thickness of less than 5mm without focal thickening excludes significant disease and is consistent with endometrial atrophy.[6,8] The mean post-menopausal endometrial thickness is thinner than in premenopausal women. Thickening of the endometrium may indicate the presence of pathology. In general, the thicker the endometrium, the higher the likelihood of important pathology, i.e., endometrial cancer being present. The threshold in the UK is 5 mm; a thickness of >5 mm gives 7.3% likelihood of endometrial cancer.[9] In a woman with postmenopausal bleeding, if the endometrial thickness is less than 5 mm uniformly, the probability of carcinoma is less than 1%.[10,11] transvaginal ultrasound demonstrates the type of abnormality seen within the endometrial cavity.[10] For example, endometrial hyperplasia, polyps, or carcinoma. Classically, endometrial hyperplasia affects the entire endometrium and results in thickening of the endometrium.[10] All types of endometrial hyperplasia (cystic, adenomatous, atypical) can cause diffuse smooth or, less commonly, focal hyperechoic endometrial thickening. Endometrial hyperplasia is considered whenever the endometrium appears to exceed 5mm in thickness.[6] Endometrial polyps manifest as focal areas of endometrial thickening, on vaginal sonography they appear as a hyperechoic lesion with a regular outline. The polyp may be broad-based and sessile or pedunculated, and the stalk of the polyp may be seen if sufficient fluid is present in the endometrial cavity.[12] The finding of a single feeding vessel or single vascular stalk to a suspected polyp has been demonstrated to confirm the presence of a polyp with a specificity and negative predictive value of 95% and 94% respectively.[13] Endometrial carcinoma may occur in the form of a polyp, within endometrial hyperplasia, or as a heterogeneous endometrial mass with a widened irregular cavity, other ultrasound features of endometrial carcinoma include heterogeneity and irregular endometrial thickening. These signs are nonspecific and can be seen in endometrial hyperplasia as well as polyps. However, polypoid tumors cause more diffuse and irregular thickening than a polyp and more heterogeneity than endometrial hyperplasia. A more specific ultrasound sign is irregularity of the endometrium-myometrium border, a finding that indicates invasive disease and usually cancer are highly vascular with many supplying vessels.[6,10] Pathological confirmation of the histology is needed in all cases. Endometrial biopsy is performed if the endometrial cavity is irregular, the endometrium has diffuse or focal widening greater than 5 mm, or if the whole endometrium has not been adequately assessed.[1,10] Although endometrial cancer accounts for 6% of all female cancers, it causes only about 3% of all cancer-related deaths. This study aimed to see whether transvaginal ultrasound can replace diagnostic curettage in the detection of endometrial pathologies in post- menopausal bleeding and to find the sensitivity and specificity of transvaginal ultrasound in the detection of endometrial carcinoma in postmenopausal women with bleeding.

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Methods

This was a prospective diagnostic accuracy study done in the College of Medicine, Hawler Medical University from October 2016 to January 2018. The study included 55 women with post-menopausal vaginal bleeding. The transvaginal ultrasound findings of the endometrium were compared with histopathological results of endometrial biopsy using dilatation and curettage (D&C). The exclusion criteria were women on hormone-replacement therapy, diabetic and hypertensive patients, those with blood disorders and patients with vaginal pathologies or pelvic masses whether ovarian or uterine. The study was approved by the Research Ethics Committee of the College of Medicine, Hawler Medical University. A written informed consent was obtained from each participant in the study. Vaginal ultrasound and D&C procedures were explained to the patients. The ultrasound examinations were made by an experienced radiologist in a private clinic using General Electric (GE), Voluson 6, endo-vaginal transducer E 8-MHZ. It was performed after asking the woman to empty her bladder, and she was asked to undress from the waist down, lie in a dorsal position on the examination couch, a sheet was provided to cover her. She was asked to bend her legs.The probe was cleaned and covered with a plastic or latex sheath after the gel has been placed on the transducer tip. Then, the transducer was inserted into the vagina. The sound beam was directed by rotating and angling the probe from anterior to posterior and sliding it in and out and transverse and longitudinal sections of the endometrium were obtained. The endometrium was analyzed for morphology, outline, thickness, vascularity, endometrial-myometrial junction, focal abnormality, texture, and the presence of fluid or masses in the cavity. The thickest part of the endometrium was obtained, and maximum endometrial thickness in the sagittal plane was measured from echogenic to the echogenic border. The adjacent hypoechoic myometrium and fluid in the cavity were not included. In the presence of endometrial fluid, the measurement of the two separate layers of the endometrium, excluding the fluid, were added to determine the endometrial thickness, endometrial abnormalities reported were they found, endometrial atrophy was diagnosed when a double-layer thickness of equal or less than 5 mm without focal thickening.[9] Endometrial hyperplasia was diagnosed when there was regular generalized diffuse thickening of entire endometrial cavity exceeding 5 mm. Endometrial polyp was diagnosed or suggested when there wasa focal hyperechoic thickening of endometrial cavity and having a single vascular stalk or feeding vessel using color Doppler ultrasound. During assessing the endometrial cavity, endometrial carcinoma was suggested when there was irregular and heterogeneous thickening of endometrial cavity. More specific sign was abnormal high vascularity of irregularly thickened area, but only color Doppler was used. After each scanning, the transducer was withdrawn gently toward fornix to avoid discomfort to the patient, and the probe was cleaned. Patients were referred to Erbil Maternity Hospital for dilation and curettage, which was conducted in the theater by specialist gynecologist under general anesthesia according to the hospital regulations. Specimens were sent for histopathological examination and interpreted by specialist pathologists.

Statistical analysis

Data were analyzed using the statistical package for the social sciences (version 22). Frequencies and percentages were calculated. McNemar test was used (in the 2X2 tables) when the results of ultra-sound were compared with the histopathological findings (of the same patients); as in the following table:

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Ultrasound findings	Histo-pathological findings		P value (By McNemar)
	Positive	Negative	
Positive	TP	FP	
Negative	FN	TN	
Total	TP+FN	FP+TN	

TP=True positive; TN=True negative;
FP=False positive; FN=False negative.
Sensitivity = TP / (TP+FN)*100.
Specificity = TN / (FP+TN)*100.
P value ≤ 0.05 was considered statistically significant.

Results

The mean age of the participants ±SD was 58.42 ± 4.4 years, ranging from 50 to 70 years, and the median age was 58 years. Table 1 shows that the highest proportion of the patients (47.3%) were in the age range of 55-59 years. Only 12.7% aged 65 years or more. Results of transvaginal ultrasound showed that 49.1% of the women had normal thin endometrium, 20% had thick regular endometrium, 16.4% had polyp, and 14.5% had thick irregular endometrium. Endometrial carcinoma was suspected in two out of eight patients with thick irregular endometrium depending on vascularity, and disturbance of endometrial-myometrial junction. Details are shown in Table 2, Figures 1 and 2.

Table 1: Age distribution of the studied sample.

Age (years)	No.	%
50-54	9	16.4
55-59	26	47.3
60-64	13	23.6
≥ 65	7	12.7
Total	55	100.0

Table 2: Distribution of the studied sample by transvaginal ultrasound findings.

Ultrasound findings	No.	%
Normal thin endometrium (atrophic endometrium)	27	49.1
Polyp	9	16.4
Thick regular (suggestive of hyperplasia)	11	20.0
Thick irregular*(complex hyperplasia)	8	14.5
Total	55	100.0

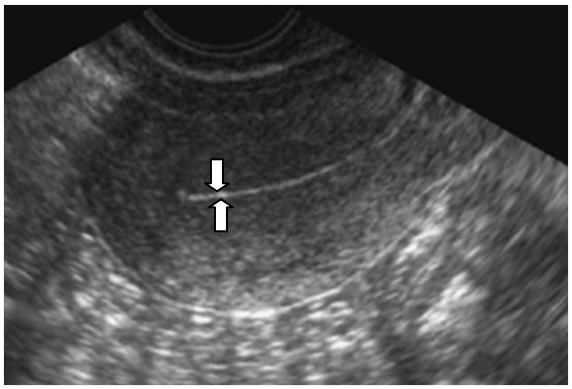

Figure 1: 51 year-old woman with post-menopausal bleeding transvaginal sagittal ultrasound shows atrophic endometrium that measures 2mm (arrowheads).

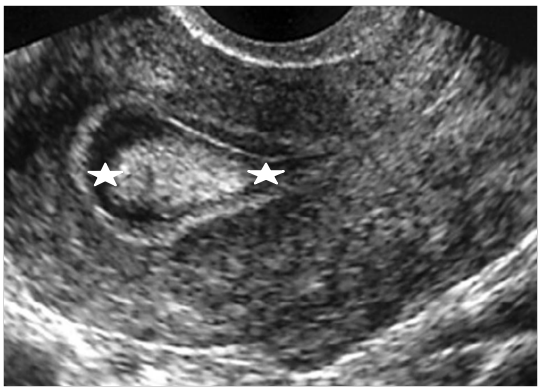

Figure 2: Transvaginal ultrasound showing a thick endometrial cavity with hyperechoic mass inside suggestive of a polyp.

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The histopathological examination showed that 49.1% of the women had atrophic endometrium. Others diagnosed as having simple endometrial hyperplasia (16.4%), polyp (16.4%), and complex hyperplasia (10.9%), as shown in Table 3. Table 4 shows complete agreement between transvaginal ultrasound and histopathological findings regarding the detection (diagnosis) of normal endometrium (27 cases), polyp (9 cases), and cancer (2 cases). Seventeen cases were diagnosed as hyperplasia by ultrasound; 52.9% of them found to have simple endometrial hyperplasia according to the histopathological results, and 35.3% had complex hyperplasia.

Table 3: Distribution of the studied sample by histopathological diagnosis.

Histopathology results	No.	%
Atrophic endometrium	27	49.1
Hyperplasia with atypia	1	1.8
Simple endometrial hyperplasia	9	16.4
Polyp	9	16.4
Endometrial carcinoma	2	3.6
Complex endometrial hyperplasia	6	10.9
Chronic endometritis	1	1.8
Total	55	100.0

Table 4: Comparison between transvaginal ultrasound and histopathological findings.

	Histo-pathological findings							
	Atrophic endometrium	Hyperplasia with atypia	Endometrial hyperplasia	Polyp	Endometrial carcinoma	Complex hyperplasia or cystic glandularhyperplasia	Chronic endometritis	Total
Transvaginal ultrasound findings	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Normal thin endo-metrium	27 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	27 (100.0)
Polyp	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)
Hyperplasia	0 (0.0)	1 (5.9)	9 (52.9)	0 (0.0)	0 (0.0)	6 (35.3)	1 (5.9)	17 (100.0)
Cancer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)
Total	27 (49.1)	1 (1.8)	9 (16.4)	9 (16.4)	2 (3.6)	6 (10.9)	1 (1.8)	55 (100.0)

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Table 5a presents results of transvaginal ultrasound and histopathology of the same patients. The sensitivity of ultrasound in detecting endometrial carcinoma was 66.7%, the specificity was 100%, the predictive value (PV) positive was 100%, and the PV negative was 98.1%. The total agreement rate was 98.2% as presented in Table 5b.

Discussion

Post-menopausal bleeding is a significant symptom that requires special concern because it may be the only clinical manifestation of endometrial carcinoma, which is regarded as the most common gynecological malignancies. It is the fourth most common cancer in western countries, and it is the commonest malignancy of the female genital tract in developed countries. Unlike other malignancies, endometrial cancer because of early presentation with vaginal bleeding when diagnosed in early stage, there is a possibility of curative treatment by hysterectomy. In contrast, with increased staging, the survival decreases.[14] Gynecologists have long approached postmenopausal bleeding as "endometrial cancer until proved otherwise. Endometrial pathologies whether benign or malignant are common causes of postmenopausal bleeding; 90% of women with endometrial cancer present with postmenopausal bleeding.[3] Vaginal sonography is the first line of investigation or approach in postmenopausal bleeding, and it is preferred over biopsy because it is a painless, inexpensive, less invasive procedure to visualize endometrial cavity with no complications, high negative predictive values and it may be more sensitive for detecting endometrial carcinoma than a blind biopsy. Timmermans et al. found that transvaginal ultrasonography is the first line test in the assessment of postmenopausal bleeding.[15] The present study revealed that the mean age of patients was 58.42 years; the majority of patients presented with postmenopausal bleeding were in the age group 55-59 years, while El-Mowali et al. observed the mean age in Egypt women having postmenopausal bleeding was 52.6 years, range 48-56 years.[16] The current study revealed that the commonest cause of uterine bleeding is endometrial atrophy. The majority of patients with postmenopausal vaginal bleeding experience bleeding secondary to atrophic changes of the vagina or endometrium.[17] The American College of Obstetricians and Gynecologists has opined that in

Table 5 a: Accuracy of transvaginal ultrasound in detecting endometrial carcinoma compared with histopathology.

Transvaginal ultrasound findings	Histopathology (D&C)		Total	*P* value
	CA	No CA		
Cancer	2	0	2	1*
No cancer	1	52	53	
Total	3	52	55	

*By McNemar test

Table 5b: Indicators for accuracy of ultrasound in detecting cancer compared with histopathology.

Sensitivity	Specificity	PV positive	PV negative	Agreement
66.7%	100%	100%	98.1%	98.2%

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postmenopausal women with bleeding when presented with a thin distinct endometrial echo on transvaginal ultrasonography of 4mm or less has a risk of malignancy of 1 in 917. Therefore, an endometrial biopsy is not required, and the most likely diagnosis in such cases is an atrophic endometrium.[17] In this study, the second most common cause of postmenopausal bleeding was endometrial hyperplasia, whether simple or complex endometrial hyperplasia (27.3%). Two cases were missed to be diagnosed correctly by ultrasound; first was a case of endometrial hyperplasia with atypia, and the second was a case of chronic endometritis. In the last case, the woman presented with one episode of vaginal bleeding. On vaginal sonography, the endometrium was irregular a vascular on color Doppler, and its thickness was 6.7mm. Our study revealed endometrial polyps in nine cases (16.36%),and all polyps were pedunculated and fortunately single vascular stalk or feeding vessels easily recognized by vaginal ultrasound using color Doppler. The current study revealed two cases of endometrial carcinoma(3.6%) in which the endometrial thicknesses were 13 mm and 11.6mm. In both cases, the endometrium was irregularly thickened, hypervascular, and in one case the endometrial-myometrial junction was not clear. On this basis, the endometrial carcinoma was suggested. These findings are in agreement with other studies like El-Mowafi et al. where out of 42 postmenopausal patients, 19 cases showed atrophic endometrium (45.2%),19% endometrial hyperplasia, 26.2% endometrial polyp,endometritis (4.8%), endometrial carcinoma (4.8%).[17] Another study done by Sonali showed that out of 174 postmenopausal women suffering from uterine bleeding, 48.85% were endometrial atrophy, 9.77% polyp, 13.80% hyperplasia, 10.34% endometrial carcinoma and 5.75% hyperplasia with atepia.[18] Another study done by Tsikouras et al. observed on 123 postmenopausal women with suspicious endometrium >5mm, endometrial polyp was 7.13%, one cervical polyp with extension in the cavity, endometrial atrophy was 73.1%, atrophic endometritis was 8.13%, hyperplasia was 1.62% and hyperplasia with atepia was 0.18%.[19] Another study done in Turkey on women with uterine bleeding including pre and postmenopausal age group out of 244 women, 10.9% were polyp, endometritis 6.8%,3.1% atrophic endometrium,1.1% endometrial carcinoma.[20] Another study done by Memon et al. on 112 postmenopausal women with uterine bleeding showed postmenopausal atrophic endometrium in 64 (57.14%) patients, endometrial polyp in 5 (4.16%) patients, endometrial hyperplasia in 27 (24.10%) patients, endometrial carcinoma in 8 (7.14%) patients, pyometra in four (3.57%) patients and fibroid uterus in four (3.57%) patients.[21] While in the study done by Moradan et al.,[22] the reported results on transvaginal sonography were atrophy in 30 (50%), hyperplasia in 13 (21.66%), endometrial polyp in 16 (26.66%) and carcinoma in one (1.6%). Another study conducted by Sadoon et al.[24]on 142 patients reported that the incidence of endometrial pathology was found to be of 23.9% and only 5% for endometrial carcinoma, also they found that benign endometrial pathologies are the most common cause of postmenopausal bleeding, this in agreement with our study. The current study revealed that the sensitivity of vaginal ultrasound for detection of endometrial carcinoma was 66.7%, the specificity was 100%, the predictive value (PV) positive was 100%, and the PV negative was 98.1%. The total agreement rate was 98.2%. This is in comparison to a study done by Gull et al. that showed a sensitivity of 100%, specificity of 60%, positive predictive value of 25% and negative predictive value of 100%.[24] However, Moradan et al. in their study in Iran on 60 women with postmenopausal bleeding revealed the sensitivity, specificity, positive and negative

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predictive values of transvaginal ultrasound in the diagnosis of uterine pathologies were 83.3%, 86.7%, 86.2 and 83.9%, respectively.[22] Another study done in our locality in Erbil showed sensitivity and specificity of vaginal ultrasound in the detection of endometrial pathologies were 100% and 94.7%.[25] Another study done by Showkat et al. showed a sensitivity of transvaginal ultrasound in the detection of endometrial carcinoma of 67%, specificity 100%, accuracy 98%, positive predictive value 100% and negative predictive value 97%.[26]

Conclusion

Transvaginal sonographic scanning is gold slandered investigation for postmenopausal women with vaginal bleeding. It provides important information regarding uterine and endometrial pathologies. It also has an outstanding role in the detection of endometrial carcinoma to start necessary treatment depending on endometrial thickness. No women with endometrial thickness ≤5mm were diagnosed as having endometrial cancer or endometrial pathology. A woman who has endometrial thickening and other positive findings on ultrasound, such as increased vascularity with color Doppler, in homogeneity of endometrium, particulate fluid, or thickened endometrium, should be further evaluated by endometrial biopsy. Also, we conclude that with the use of vaginal ultrasound we can reduce the number of patients requiring the endometrial biopsy depending on the ultrasound results whether further investigation is necessary with diagnostic curettage or other forms of endometrial biopsy.

Competing interests

The authors declare that they have no competing interests.

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