International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Atia NA et al. Int J Reprod Contracept Obstet Gynecol. 2022 Dec;11(12):3305-3310
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20223121

Original Research Article

The diagnostic value of endometrial thickness and volume measurements by transvaginal three-dimensional ultrasound in patients with perimenopausal bleeding

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Received: 05 October 2022
Accepted: 01 November 2022

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ABSTRACT

Background: Endometrial hyperplasia (EH) represents a spectrum of irregular morphological alterations, whereby abnormal proliferation of the endometrial gland results in increased thickness of endometrial tissue with alterations of glandular architecture (shape and size) and in an increase in gland-to-stroma ratio when compared to endometrium from the proliferative phase pf the cycle. The aim of this study was to detect the role of measurement of endometrial thickness and volume by transvaginal three-dimensional ultrasound as predictors of abnormal endometrial pathology in women with peri menopausal abnormal uterine bleeding.
Methods: This study was conducted at the department of obstetrics and gynecology of Tanta University Hospital. The cases were selected from admitted patient suffering from perimenopausal uterine bleeding. The study started after protocol approval from 2020 to 2022. The calculated sample size was 50 cases. The studied cases were subjected to 3D-TVS measuring endometrial volume and endometrial thickness, study uterine size, shape, endometrial curettage and histopathological examination.
Results: Regarding provisional diagnosis by ultrasound in the examined patients, the most frequent diagnosis was benign endometrial pathology: 46% (n=23) of all cases then endometrial hyperplasia 44% (n=22) then endometrial carcinoma 10% (n=5), there was statistically significant difference between the three endometrial pathologies regarding endometrial thickness ($p<0.001$), and endometrial volume ($p<0.001$).There was statistically significant difference between the benign endometrial pathology and endometrial carcinoma regarding endometrial thickness ($p<0.001$), and endometrial volume ($p<0.001$).There was statistically significant difference between the endometrial hyperplasia and endometrial carcinoma regarding endometrial thickness ($p<0.001$), and endometrial volume ($p<0.001$).
Conclusions: From our study we conclude that histopathological examination of the endometrium is the gold standard for diagnosis or exclusion of endometrial pathology. 3D ultrasound is a reasonably accurate, helpful, and non-invasive tool for assessing the endometrium.

Keywords: Endometrial thickness, Perimenopausal bleeding, Transvaginal

INTRODUCTION

Endometrial hyperplasia (EH) represents a spectrum of irregular Morphological alterations, whereby abnormal proliferation of the endometrial gland results in increased thickness of endometrial tissue with alterations of glandular architecture (shape and size) and in an increase in gland-to-stroma ratio when compared to endometrium from the proliferative phase pf the cycle.[1,2] The proliferating glands in EH can vary greatly in size and shape, and cytologically atypia may be present. Historically, several different terms have been employed to describe this abnormal proliferation of the endometrium, including adenomatous hyperplasia, atypical hyperplasia, carcinoma, and polyps.[3] In asymptomatic premenopausal and postmenopausal

women, the thickness of endometrium is not determined, while endometrial stripe abnormalities such as heterogeneity or cystic changes to the endometrium may be crucial for the diagnosis of EH.[4] Abnormal uterine bleeding is probably the most common symptom in gynecologic practice up to 33% of women referred to the gynecological outpatient clinics have abnormal uterine bleeding and this proportion rises to 69% in the premenopausal group.[5] Endometrial sampling is the gold standard for diagnosing abnormalities in the endometrial tissues with sensitivity ranging from 85-95%.[6]

The aim of this study was to detect the role of measurement of endometrial thickness and volume by transvaginal three-dimensional ultrasound as predictors of abnormal endometrial pathology in women with peri menopausal abnormal uterine bleeding.

METHODS

The study design was cross sectional trial. This study was conducted at the department of obstetrics and gynecology of Tanta University Hospital. The cases were selected from admitted patient suffering from perimenopausal uterine bleeding. The study started after protocol approval from 2020 to 2022. The calculated sample size was 50 cases

Inclusion criteria

Age range 45 to 55 years, patient complaining from abnormal uterine bleeding and BMI (≥18.5-≤29.9) kg/m^2.

Exclusion criteria

Patient taking anticoagulant- blood disease and coagulopathy, hypertension, thyroid disorders, drug intake that cause bleeding, recent hormonal contraception, any hormonal therapy in the last 3 months and recent endometrial curettage.

All patients in this study were subjected to the followings: i) history taking, ii) clinical examination: general examination, vital signs measuring (blood pressure, pulse, temperature), comprehensive general and systemic examination, local pelvic gynecological examination including bimanual PV examination and Cusco speculum examination

The studied cases were subjected to: 3D-TVS measuring endometrial volume and endometrial thickness using virtual organ computer aided analysis (vocal), ultrasound sonar was done to study uterine size, shape, and exclusion of any uterine pathology the endometrial volume is measured in plane Aby delineating the endometrial margin at the endometrial-myometrial interface from the fundus to the internal cervical canal in a number of parallel slices which are1-2mm apart the actual volume was calculated by the built-in computer program using VOCAL (Samsung Medison Co-Ltd Seoul, Korea), Endometrial curettage and histopathological examination, comparison of endometrial volume and thickness obtained by vocal, and results of histopathological examination were done.

Statistical analysis

SPSS statistics for windows (Statistical Package for the Social Sciences) version 26 (IBM, Armonk, NY, USA) was used for statistical analysis of the collected data. Shapiro-Wilk test was used to check the normality of the data distribution. All tests were conducted with 95% confidence interval. P (probability) value <0.05 was considered statistically significant. Charts were generated using SPSS' chart builder and Microsoft Excel for windows 2019. Quantitative variables were expressed as mean and standard deviation, median, inter-quartile range, minimum and maximum as appropriate while categorical variables were expressed as frequency and percentage. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated using the receiver operating characteristic (ROC) curve and the cross tabs function. Cohen's kappa (κ) was run to measure reliability and agreement between.

RESULTS

Demographic data showed that the mean±SD participant's age was (46.60±3.780) years ranging from 45 to 55 years. More than half 29 (58%) of the study participants live in urban areas, while only 21 (42%) live in rural areas (Table 1).

Endometrial volume and thickness demonstrated that the mean±SD endometrial thickness was 12.79±4.628 mm ranging from 7.20 to 29.30 mm. The mean±SD endometrial volume was 17.58±7.897 ml ranging from 9.80 to 43.20 ml (Table 2).

Table 1: Demographic characteristics and medical history of the studied sample.

All patients (n=50)		Mean±SD	Median	Range	IQR
Age (years)		46.60±3.780	47.00	45.00, 55.00	43.75, 49.00
Residence	Urban	58.0% (29)			
	Rural	42.0% (21)			

Data is expressed as mean and standard deviation, median, range and interquartile range or as percentage and frequency.

Table 2: Endometrial thickness (mm) and endometrial volume (ml) in the studied patients.

All patients (n=50)	Mean±SD	Median	Range	IQR
Endometrial thickness (mm)	12.79±4.628	11.60	7.20, 29.30	9.98, 13.93
Endometrial volume (ml)	17.58±7.897	14.35	9.80, 43.20	12.10, 20.50

Data is expressed as mean and standard deviation, median, range and interquartile range.

Table 3: Final diagnosis by pathological examination in the studied patients.

All patients (n=50)	Frequency	Percentage
Proliferative endometrium	17	34.0
Endometrial hyperplasia without atypia	15	30.0
Endometrial hyperplasia with atypia	6	12.0
Endometrial carcinoma	6	12.0
Atrophic endometritis	4	8.0
Irregular endometrial shedding	2	4.0

Data is expressed as percentage and frequency.

Table 4: Comparison of endometrial thickness and endometrial volume according to presence of malignancy by pathological examination in the studied patients.

	No malignancy (n=44)	Malignancy (n=6)	95% CI	P value
Endometrial thickness (mm)	10.65±2.048	18.95±8.965	-11.34, -5.25	<0.001
Endometrial volume (ml)	14.46±3.406	30.42±10.299	-20.05, -5.16	<0.001

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when <0.05.

Table 5: Comparison of endometrial thickness and endometrial volume according to endometrial pathology by pathological examination in the studied patients.

	Benign endometrial pathology (n=23)	Endometrial hyperplasia (n=21)	Endometrial carcinoma (n=6)	P	P1	P2	P3
Endometrial thickness (mm)	9.94±1.944	11.43±1.909	18.95±8.965	<0.001	0.159	<0.001	<0.001
Endometrial volume (ml)	13.32±2.544	15.60±3.566	30.42±10.299	<0.001	0.095	<0.001	<0.001

Data is expressed as mean and standard deviation. P is significant when <0.05. P1: benign endometrial pathology versus endometrial hyperplasia. P2: benign endometrial pathology versus endometrial carcinoma. P3: endometrial hyperplasia versus endometrial carcinoma.

Regarding the final diagnosis by pathological examination, it was found that the most common final diagnosis was proliferative endometrium in 17 (34%) of patients, then and endometrial hyperplasia without atypia as both of them was found in 15 (30%) of patients, then endometrial hyperplasia with atypia in 6 (12%) of patients, then endometrial carcinoma in 6 (12%) of patients then atrophic endometritis in 4 (8%) of patients, irregular endometrial shedding was the least common final diagnosis in only 2 (4%) of patients (Table 3).

Regarding to endometrial thickness and endometrial volume according to presence of malignancy by pathological examination in the studied patients, endometrial thickness was found to be statistically significant higher in malignancy 18.95±8.965 mm than it was in no malignancy 10.65±2.048 mm, (p<0.001). Also, endometrial volume was found to be statistically significant higher in malignancy 30.42 ± 10.299 ml than it was in no malignancy 14.46±3.406 ml, (p<0.001) (Table 4). There was statistically significant difference between the benign endometrial pathology and endometrial carcinoma regarding endometrial thickness (p<0.001), and endometrial volume (p<0.001). There was statistically significant difference between the endometrial hyperplasia and endometrial carcinoma regarding endometrial thickness (p<0.001), and endometrial volume (p<0.001) (Table 5).

Regarding to diagnostic profile of endometrial thickness and endometrial volume in diagnosis of benign endometrial pathology, the endometrial thickness was acceptable in diagnosis of benign endometrial pathology with significant area under curve of 0.780. At endometrial thickness 12.85 mm, maximum sensitivity was 66.7% and specificity was 68.4%, PPV was 40.0%, NPV was 95.0%,

with accuracy 84.0%. The endometrial volume was acceptable in diagnosis of benign endometrial pathology with significant area under curve of 0.947. At endometrial volume 21.75 ml, maximum sensitivity was 83.3% and specificity was 95.5%, PPV was 71.4%, NPV was 97.7%, with accuracy 94.0% (Table 6).

Table 6: Diagnostic profile of endometrial thickness and endometrial volume in diagnosis of benign endometrial pathology.

	Endometrial thickness (mm)	Endometrial volume (ml)
AUC	0.780	0.947
95% CI of AUC	0.550, 1	0.860, 1
P value	0.027	< 0.001
Cutoff point	12.85	21.75
Youden's J index	0.531	0.788
Sensitivity	66.7%	83.3%
Specificity	86.4%	95.5%
PPV	40.0%	71.4%
NPV	95.0%	97.7%
Accuracy	84.0%	94.0%

P is significant when <0.05.

DISCUSSION

Perimenopause is a period of transition due to a decline in ovarian function. There are systemic hormonal changes, which are evidenced by an early and late stage. The early stage is mostly marked by irregular cycles followed by a second stage of increasing longer periods of amenorrhea of 60 days or more.[7]

The diagnosis of endometrial lesions is usually made through diagnostic curettage and a hysteroscopic biopsy, but this clinical application is limited due to its originality, high risk, high price, and difficulty in expanding the uterus after menopause. The ultrasound measurement of ET and EV is a sensitive method of the noninvasive differential diagnosis of endometrial diseases.[8]

Transvaginal sonography (TVS) has permitted the use of higher frequency ultrasound waves at greater proximity of the uterus. It is relatively cheap, needing no anesthesia, is non-invasive and can be the first diagnostic step in the evaluation of AUB.[9]

Our study results have revealed that the mean parity was 1.80±1.498.

Odeh et al reported the mean parity was 3.55±2.21 and in the study by Shokouh et al, the mean parity was 3.12±1.6.[10,11] Azim et al and Khan et al reported a higher incidence of AUB with increase in parity.[12,13]

El Kady et al study revealed that, atrophic endometrium was the most common finding (26/90=28.9%), hyperplasia without atypia in (36/90=40.0%), hyperplasia with atypia (18/90=20.0%) and endometrial carcinoma was found in (10/90=11.11%).[14]

Ebrashy et al examined 65 cases by both TVS 2D and 3D ultrasound and the results were by 2D ultrasound: 20% were normal, 10.67% showing endometrial polyps, 44.61% having myomas either single or multiple, 18.46% had thickened endometrium while by 3D ultrasound: 13.84% were normal.[15]

Odeh et al evaluated the accuracy of endometrial volume measurement in the diagnosis of endometrial carcinoma and endometrial hyperplasia and found that 17.9% of patients had an endometrial polyp, 12.5% had hyperplasia and 7.6% had endometrial carcinoma.[10]

In our study, provisional diagnosis by ultrasound in the examined patients, the most frequent diagnosis was Benign endometrial pathology: 46% (n=23) of all cases followed by endometrial hyperplasia 44% (n=22) followed by endometrial carcinoma 10% (n=5).

Similar to Liao et al study, among the 250 patients, 202 patients (80.8%) had endometrial benign lesions and 48 patients (19.2%) had endometrial carcinoma.[16]

In our study, the endometrial thickness was found to be statistically significant higher in malignancy in no malignancy.

Similarly, Liao et al study results have revealed that the difference in endometrial thickness between malignant and benign endometrial lesions was significant (15.64±7.26 versus 9.24±5.06 mm).[16]

Also, similar to Liu et al and Hanafi et al, and studies, in which endometrial thickness, and volume of malignant patients were all significantly higher than those of benign patients.[17,18]

However, some studies have reported that 38% of patients with type II endometrial carcinoma have an endometrial thickness of <4 mm.[19]

Bruchim et al showed that the mean endometrial thickness for all patients without cancer was (6.3±4.3) and it was significantly lower than that of patients with endometrial carcinoma ($p<0.01$), whose endometrial thickness was more than 10 mm, and no cases of endometrial carcinoma was found in any patients with endometrial thickness of less than 5 mm.[20] On the contrary, Phillip et al suggested that the correlation between imaging and pathology was not reliable.[21] Half of their cases with endometrial cancer had an endometrial thickness between 3 mm and 4 mm. Seventy percent of the women with endometrial thickness greater than 5 mm had a benign pathology. Moodley and Roberts chose endometrial thickness to be at least 4 mm in postmenopausal women as a limit value to exclude malignancy unless there are another risk factors.[21,22]

Transvaginal ultrasound uses the natural passage of the human body to avoid interference from the abdominal wall and intestinal gas. The probe directly reaches the vaginal canal, and the lesion is closely observed, showing the uterine cavity more clearly. Under normal circumstances, early EC can be characterized by abnormal thickening of the endometrium, which can be seen in the uneven middle and high echo, the intimal shape is irregular.[23]

In our study, the endometrial thickness was acceptable in diagnosis of malignant endometrial pathology with significant area under curve of 0.780. At endometrial thickness 12.85 mm, maximum sensitivity was 66.7% and specificity was 68.4%, PPV was 40.0%, NPV was 95.0%, with accuracy 84.0%. While it had no role in diagnosis of endometrial hyperplasia.

In another study comprising of 51 premenopausal patients with complaints of irregular bleeding, Smith et al observed sensitivity of 67%, specificity 75%, positive predictive value of 14%, and negative predictive value of 97% assuming >8 mm endometrial thickness as cut off value.[24]

In the third study in 177 women with peri- and postmenopausal bleeding who underwent vaginosonographic examination followed by HPE of the endometrium, Tongsong et al found an ET of 7 mm and less to reliably predict normal endometrium (100% sensitivity and 46% specificity) and hence advocated to offer the option of diagnostic curettage to women with thick endometrium (≥7 mm).[25]

In contrast our results aren't consistent with the study of Saha et al who found that vaginal ultrasonographic evaluation of ET is not valuable to predict malignancy in females of AUB and the study of Tabor et al who found that ET cut-off <4 mm alone to exclude malignancy isn't a reliable parameter as 4% of malignancy would still be missed, with false-positive rate as high as 50%.[26,27]

CONCLUSION

From our study we conclude that histopathological examination of the endometrium is the gold standard for diagnosis or exclusion of endometrial pathology. 3D ultrasound is a reasonably accurate, helpful, and non-invasive tool for assessing the endometrium.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of Faculty of Medicine, Tanta University

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Cite this article as: Atia NA, El Namoury MM, Farhat MA, Hamouda MS. The diagnostic value of endometrial thickness and volume measurements by transvaginal three-dimensional ultrasound in patients with perimenopausal bleeding. Int J Reprod Contracept Obstet Gynecol 2022;11:3305-10.