

Endometrial Thickness Measurement for Detecting Endometrial Cancer in Women with Postmenopausal Bleeding

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ABSTRACT

Background: Postmenopause is defined as the permanent cessation of menstruation for one year due to failure of the ovarian follicular activity.

Objective: This work aimed to study the role of endometrial thickness measured by transvaginal sonography in the detection of endometrial carcinoma in women with postmenopausal bleeding. **Patients and Methods:** A cross-sectional study was conducted on 120 women with postmenopausal bleeding admitted to the Obstetrics & Gynecology Department at Zagazig University hospitals through the period from September 2018 to September 2019. All cases were subjected to full history, full clinical examination, transvaginal sonography, and diagnostic endometrial biopsy which was taken for histopathological examination. We exclude premenopausal women and postmenopausal patients in HRT.

Results: This study showed TVS evaluation of ET of the studied cases ranged from 1 to 20 mm with a mean of 9.65 mm. Also, 48.3% of the cases had endometrial thickness more than 10 mm, 34.2% had less than 5 mm, and 17.5% had from 5 to 10mm. that 34.2% of the studied cases had atrophic endometritis, 26.7% had an endometrial polyp, 17.5% had simple hyperplasia, 7.5% had atypical hyperplasia and 14.2% had endometrial adenocarcinoma.

Conclusions: Transvaginal sonography evaluation of endometrial thickness is not sensitive enough to detect cancer of the endometrium and therefore couldn't replace histological evaluation of the endometrial tissue in women with postmenopausal bleeding.

Keywords: Endometrial thickness, Endometrial cancer (EC), Abnormal uterine bleeding

INTRODUCTION

Endometrial cancer (EC) is the most common gynecological cancer and has an increasing incidence in postmenopausal women⁽¹⁾. Endometrial cancer represents 3.6% of all new cancer cases in the United States with a mortality rate reaches 1.9% of all cancer death⁽²⁾.

Postmenopausal bleeding (PMB) is highly suspicious of being assigned to the presence of endometrial cancer or premalignant lesions. Nearly every endometrial cancer patients report PMB at some point and around 5-12% of PMB results from endometrial cancer⁽³⁾. Postmenopausal bleeding is an early symptom of endometrial cancer leads to its detection in earlier stages with subsequently better outcomes⁽⁴⁾.

Endometrial thickness (ET) is measured by transvaginal ultrasonography as the maximum anterior-posterior thickness of the endometrial echo on along axis transvaginal view of the uterus⁽⁵⁾. Women with postmenopausal bleeding and endometrial thickness <5mm measured with TVS have a low risk of endometrial cancer⁽⁶⁾. While sonographic endometrial thickness >5mm is associated with a high risk of endometrial cancer in women with postmenopausal bleeding⁽⁷⁾. This study aimed to evaluate the role of TVS in the diagnosis of endometrial cancer in women with postmenopausal bleeding.

PATIENTS AND METHODS

This cross-sectional study included 120 women with postmenopausal bleeding admitted to the Obstetrics & Gynecology Department at Zagazig University hospitals through the period from September 2018 to September 2019.

Inclusion criteria: Female patients with postmenopausal bleeding (permanent cessation of menstruation for 1 year).

Exclusion criteria: Asymptomatic postmenopausal women. Postmenopausal ladies on hormone replacement therapy. Patients with already known malignancies. Patients with thyroid disorders. Patients with a systemic blood disease.

Ethical Consideration:

Written informed consent was obtained from all participants and the study was accepted by the Research Ethics Committee of the Faculty of Medicine, Zagazig University.

The study was carried out on experiments involving human subjects in compliance with the Code of Ethics of the World Medical Association (Declaration Helsinki).

All cases were subjected to full history, full clinical examination; general, abdominal, and pelvic



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examination to assess the general condition of the patient and possible detection of the local cause of vaginal bleeding as well as to examine the size of the uterus, affection of adnexa, and parametrium. Laboratory Investigations included CBC, coagulation profile, LFT, KFT, RBS, urine analysis were also done.

All patients received transvaginal ultrasound using (Voluson 730 proV unit, GE medical systems, Zipg, Austria) ultrasound machine with 20 endovaginal probe with a frequency of 7 MHz to measure the endometrial thickness and evaluate endometrial morphology.

TVS for evaluation of size and contour of the uterus, and endometrial thickness in mm. Measurement of endometrium was obtained in exact midsagittal plane excluding sub endometrial sonolucent area. Parameters to be recorded as thickness, texture, abnormal focal lesions.

Patients were divided according to endometrial thickness into 3 categories:

- Category A: patients with Et less than 5 mm.
- Category B: Patients with ET from 5 mm to 10 mm.
- Category C: Patients with ET more than 10 mm.

Operative Design:

Diagnostic curettage or hysteroscopic guided biopsy was done for histopathological examination. All data were subjected to statistical analysis.

Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations, and outcome measures coded, entered, and analyzed using Microsoft Excel software.

Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis.

RESULTS

Table (1): Demographic data of the studied cases

Variable		(n=120)	
Age: (year)	Mean ± SD	57.73 ± 6.67	
	Range	48 - 74	
BMI: (kg/m²)	Mean ± SD	32.73 ± 3.11	
	Range	24 - 39	
Variable		N	%
Parity:	0	2	1.7
	2 - 4	92	76.6
	5 - 7	26	21.7

Sd: Standard deviation

This study showed that the age of the studied cases ranged from 48 to 74 years with a mean of 57.73 years. Regarding BMI it ranged from 24 to 39 kg/m² with a mean of 32.73 kg/m². Finally, 76.6% had parity between 2 to 4 times.

Table (2): History of the studied cases

Variable		(n=120)
Duration of menopause: (Years)	Mean ± SD	7.21 ± 5.40
	Median	5.5
	Duration of bleeding: (days)	
Mean ± SD	29.76 ± 24.97	
Median	21	

Sd: Standard deviation

This study showed that the duration of menopause among the studied cases ranged from 1 to 22 years with a mean of 7.21 years. Regarding the duration of bleeding, it ranged from 2 to 90 days with a mean of 29.76 days.

Table (3): Endometrial thickness among the studied cases

Variable	(n=120)	
ET: (mm)		
Mean ± SD	9.65 ± 5.88	
Median	10	
Variable	N	%
Classification:		
<5 mm	41	34.2
5-10 mm	21	17.5
>10 mm	58	48.3

Sd: Standard deviation

This study showed that the ET of the studied cases ranged from 1 to 20 mm with a mean of 9.65 mm. Also, 48.3% of the cases had endometrial thickness more than 10 mm, 34.2% had less than 5 mm, and 17.5% had from 5 to 10 mm.

Table (4): Histopathological diagnosis among the studied cases

Variable	(n=120)	
	N	%
Diagnosis:		
Benign		
Atrophic endometritis	41	34.2
Endometrial polyp	32	26.7
Simple hyperplasia	21	17.5
Atypical hyperplasia	9	7.5
Malignant		
Endometrial adenocarcinoma	17	14.2

This study showed that 34.2% of the studied cases had atrophic endometritis, 26.7% had an endometrial polyp, 17.5% had simple hyperplasia, 7.5% had atypical hyperplasia and finally, 14.2% had endometrial adenocarcinoma.

Table (5): Comparison between benign and malignant cases in endometrial thickness among the studied cases

Variable	Benign (n=103)		Malignant (n=17)		MW	P-value
ET: (mm)						
Mean ± SD	8.63 ± 5.59		15.82 ± 3.32		4.49	<0.001**
Median	9		17			
Variable	N	%	N	%	χ ²	P-value
Classification:						
<5 mm	41	39.8	0	0	16.88	<0.001**
5-10 mm	20	19.4	1	5.9		
>10 mm	42	40.8	16	94.1		

SD: standard deviation

MW: Mann Whitney test

χ²: chi-square test

** : Highly significant (P<0.01)

There was a highly statistically significant increase in the mean endometrial thickness among malignant cases compared to benign ones. Also, there was a highly statistically significant increase in the frequency of cases that had ET more than 10 mm in malignant cases compared to benign ones.

Table (6): Relation between the histopathological diagnosis and endometrial thickness among the studied cases

Variable	Atrophic endometritis (n=41)		Endometrial polyp (n=32)		Simple hyperplasia (n=21)		Atypical hyperplasia (n=9)		Endometrial adenocarcinoma (n=17)		F	P-value
ET: (mm)	a		b		b		b		c		122.7	<0.001**
Mean ± SD	2.49 ± 0.68		12.38 ± 3.14		12.76±2.90		13.61±3.76		15.82 ± 3.32			
Variable	N	%	N	%	N	%	N	%	N	%	χ ²	P
Classification:											129.1	<0.001**
<5 mm	41	100	0	0	0	0	0	0	0	0		
5-10 mm	0	0	12	37.5	5	23.8	3	33.3	1	5.9		
>10 mm	0	0	20	62.5	16	76.2	6	66.7	16	94.1		

SD: standard deviation

F: ANOVA test

χ²: chi-square test

** : Highly significant (P<0.01)

There was a highly statistically significant increase in the mean endometrial thickness among endometrial adenocarcinoma cases compared to other cases and a highly statistically significant decrease in the mean endometrial thickness among atrophic endometritis cases compared to other ones. Also, there was a highly statistically significant increase in the frequency of cases had ET more than 10 mm in endometrial adenocarcinoma compared to other cases and an increase in the frequency of cases had ET less than 5 mm among atrophic endometritis compared to other cases.

Table (7): Correlation between the endometrial thickness and demographic and history of the studied cases

Variable	ET (n=120)	
	r	P
Age (years)	0.01	0.99 NS
BMI (Kg/m²)	0.15	0.11 NS
Parity	-0.03	0.78 NS
Duration of menopause	-0.07	0.48 NS
Duration of bleeding	-0.11	0.24 NS

r: Spearman's correlation coefficient

NS: Non-significant (P>0.05)

There was no correlation between the endometrial thickness and any of the studied parameters among the cases.

DISCUSSION

Across sectional study where 120 female patients with postmenopausal bleeding were assigned to TVS measurement of endometrial thickness, endometrial sampling and histopathological examination. It was found that mean age (μ) = 57.7 ± 6.67, the mean BMI (μ) = 32.7 ± 3.11, the mean parity (μ) = 3.7 ± 1.2 and the mean ET (μ) = 9.65 ± 5.88.

Endometrial biopsy was received from all cases (n=120) which 17 of them had endometrial cancer with a mean endometrial thickness of 15.82mm. Forty-one of them had atrophic endometrial with a mean endometrial thickness of 2.49 mm.

Thirty-two cases of them had endometrial polyp with a mean thickness of 15.38mm and 30 cases of them were diagnosed as endometrial hyperplasia with a mean thickness of 12.76mm.

This is in a line with the study of **Kim et al.** (7) in which the predominant endometrial growth was high in patients who had endometrial thickness > 9.5mm.

Several studies, however, have been done to detect the value of vaginal ultrasonography to evaluate endometrial thickness as a parameter for excluding endometrial abnormalities. Concerning endometrial abnormality, if a 5mm cut-off limit was used for endometrial thickness, a positive predictive value of 87.3% and a specificity of 96%, and a sensitivity of 100% for identifying endometrial abnormality were obtained. One of the earliest was the study done by **Osmer et al.** (8) who studied 155 normal postmenopausal women using 4mm endometrial thickness cut-off limit by vaginal ultrasound and reported a sensitivity of 81%.

Moreover, in a study conducted by **Granberg et al.** (9) to determine the value of endovaginal ultrasonography in women presenting with postmenopausal bleeding by comparing it to classical diagnostic curettage, 205 patients were considered. Patients were scanned endovaginally the day before operation by a transducer of 7MHz frequency. Then, curettage was performed by an experienced

gynecologist. No endometrial abnormality was found in the endometrium was less than 5mm thickness.

Goldstein et al.⁽¹⁰⁾ suggested 6mm as a cut-off point, **Granberg et al.**⁽⁹⁾ found it reasonable to have a cut-off limit for normal postmenopausal endometrium at 5mm including both layers. **Tongsong et al.**⁽¹¹⁾ found that an endometrial thickness of greater than 7mm in the anteroposterior dimension, usually indicated hyperplasia or carcinoma in the postmenopausal patient **Guner et al.**⁽¹²⁾ suggested taking a 4mm cut-off point for excluding endometrial abnormality in postmenopausal women, and a cut-off point of 8mm in premenopausal women.

Malinova and Pehlivanov⁽¹³⁾ studied that women with postmenopausal bleeding by transvaginal sonography. They compared these results together with the results of 30 control women concerning the histopathological results of endometrial biopsy. They found no cases of endometrial cancer when the endometrial thickness is <6mm. They conducted that a cut-off value of 6mm has a sensitivity of 100% and that there is no need to perform curettage if the endometrium <6mm.

As regard studying endometrial thickness for benign lesions in this study is 1-18mm, and the endometrial thickness for the malignant lesion is 10-20mm.

The mean thickness of atrophic endometrium, endometrial polyp, hyperplastic endometrium, and endometrial cancer were 2.5mm 12.3 mm. 13.6mm and 18.8 mm respectively and there was a statistically significant difference between endometrial thickness and different histopathological findings.

Erkan et al.⁽¹⁴⁾ found a median endometrial thickness of 5mm, 8.5mm 6mm for benign, hyperplastic, and carcinomatous endometrium respectively, and postulated 3mm point. This was revised later by **Bender**⁽¹⁵⁾ studied 242 patients with abnormal uterine bleeding (age range 45-86 years). They found the mean endometrial thickness for benign, hyperplastic, and malignant endometrium to be 3.38mm, 6.09mm, and 8.96mm; respectively.

It has been shown that 70% of curettages performed for postmenopausal bleeding could have been avoided if an endometrium less than 5mm had been demonstrated vaginosonographically⁽¹⁶⁾.

After histopathological examination of the endometrium, most cases showed atrophic endometrial changes 34.1%.

Coincided to this study the work of **Karmarkar et al.**⁽¹⁶⁾ reported that atrophic endometrium was recorded in histological findings (32%). Also, to this review in the work of **Dawood et al.**⁽¹⁷⁾ in which the commonest reason for PMB was atrophic endometritis 33 (21.2%). The general rate of different genital tract malignancies was 25 (16.0%).

In the work of **Kim et al.**⁽¹⁸⁾ in which the endometrial histopathologic discoveries of 174 ladies, atrophic endometrium was additionally the most widely recognized finding (30.5%).

In the work of **Singh et al.**⁽¹⁹⁾ dominant part (38.33 %) of patients had atrophic endometrium.

Against this was the work of **Keirse**⁽²⁰⁾ in which atrophic endometrium was the second most regular finding. It was analyzed in 11-9% of the cases.

In this study the second regular cause of postmenopausal bleeding was endometrial polyp 26.7% of cases this was in a line with the work of **Keirse**⁽²⁰⁾ in which endometrial polyp was likewise the second normal finding and was discovered in 21-7 % of cases. Against this was the work of **Singh et al.**⁽¹⁹⁾ in which endometrial polyp was (10 %) of patients.

In this study, the third regular cause of postmenopausal bleeding after atrophic endometrium and the endometrial polyp was endometrial hyperplasia which represented 25% of cases then endometrial cancer which represented 14.2% of cases.

Similar to this study the work of **Singh et al.**⁽¹⁹⁾ in which endometrial hyperplasia was distinguished in 14 (23.33 %) out of which 11 had basic hyperplasia while 3 had atypical hyperplasia. Endometrial malignancy was identified in 8 (13.33 %) patients.

In the work of **Kim et al.**⁽¹⁸⁾ endometrial cancer was affirmed in 28 cases (16.1%), and endometrial hyperplasia was analyzed in 17 cases (9.8%).

Against this review the work of **Karmarkar et al.**⁽¹⁶⁾ in which Endometrial adenocarcinoma was found in 3.64% of cases

In this study, the range of endometrial thickness was 1mm to 20 mm with a mean of 10.4mm which coincided with **Famuyide et al.**⁽²¹⁾. Where the scope of endometrial estimations was 4.2 to 28mm (mean = 10.0mm). Additionally, in the work of **Turnbull et al.**⁽²²⁾ over a 52-month time frame, 4148 ladies were researched for postmenopausal vaginal bleeding. 588 (14.2%) ladies were found to have endometrial thickness estimations of equivalent to or more noteworthy than 10 mm on transvaginal ultrasonography.

In this study there was a highly statistically significant increase in the frequency of E.C cases had ET more than 10mm similar to this review is the study of **Bruchim et al.**⁽²³⁾ in which the mean endometrial thickness was significantly lower in absence of endometrial carcinoma (9.6 + 4.3mm) than in its presence (13.5 + 7.7mm).

CONCLUSIONS

Transvaginal sonography evaluation of endometrial thickness is not sensitive enough to detect cancer of the endometrium and therefore couldn't replace the histological evaluation of the endometrial tissue in women with postmenopausal bleeding.

Further studies will need transvaginal sonographic morphology and echogenicity of endometrium in addition to endometrial thickness measurement to detect endometrial lesions.

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