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Correlation of Endometrial Thickness and Histopathological in Women with Post-Menopausal Bleeding

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Abstract

Background: Postmenopausal bleeding is vaginal bleeding that occurring after one years of menopause. When periods have stopped for more than one years in women who are generally over than 45 years old and it is common condition in postmenopausal women ; it can be the presenting symptom of endometrial cancer.

Aim of Study: To assess endometrial thickness by vaginal sonography and correlate it with the cytological pattern evaluated by endometrial sampling and histopatho logical typing of the endometrium.

Patients and Methods: This study was conducted at Obstetrics and Gynecology unit in Bab-Al Sharia University Hospital and Al-Moniera General Hospital from September 2018 to August 2019. The study included 100 patients complaining of postmenopausal bleeding at the outpatient clinic.

Results: ET ≥10 has a sensitivity of 96.1% specificity of 92.3% positive predictive value of 66.3%, negative predictive value of 97% with diagnostic area under the curve of 0.878 in detection of endometrial disorders.

Conclusion: TVS evaluation of ET and uterine size is a reliable method of screening postmenopausal women with PMP. No abnormal endometrium detected in postmenopausal women with endometrial thickness less than 4mm and all causes of endometrial carceinoma have endometrial thickness more than 9mm.

Key Words: *Endometrial thickness – Histopathological – Postmenopausal bleeding.*

Introduction

MENOPAUSE is a physiological event occurring in women at the age of on an average 50. Basically, the approximate age of menopause is 49±3.6 years **[1]**. Postmenopausal bleeding (PMB) is defined as abnormal uterine bleeding occurring after 1 year of permanent cessation of menstruation **[2]**.

For PMB, current guidelines mandate immediate clinical evaluation and Trans-Vaginal Ultrasonograpgy (TVS) assessment followed by D and C or hysteroscopy guided endometrial/endocervical biopsy and subsequent histological evaluation **[1]**.

Vaginal sonography is easy and noninvasive method for early discovering any changes in the endometrium and has been used as a screening method in asymptomatic postmenopausal women before or during hormonal replacement therapy **[3]**.

If the endometrial thickness less than 4mm by transvaginal sonography in women with postmenopausal bleeding this rules out about 99% of endometrial cancers **[4]**.

Many women with postmenopausal bleeding and endometrial thickness ≥4mm do not have any endometrial abnormality, but will still undergo interventional diagnostic procedures such as endometrial biopsy by fractional curettage or hysteroscopic guided endometrial biopsy to exclude any endometrial abnormality **[5]**.

Aim of the work:

The aim of the present study to assess endometrial thickness by transvaginal sonography and correlate it with the cytological pattern evaluated by endometrial sampling and histopathological pattern of the endometrium.

Patients and Methods

This study was conducted at Obstetrics and Gynecology unit in Bab-Al Sharia University Hospital and Al-Moniera General Hospital from September 2018 to August 2019 the study included 100 patients complaining of postmenopausal bleeding at the outpatient clinic.

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Inclusion criteria: Post-menopausal bleeding, defined as lack of menstruation for 1 year in women older than 45 years.

Exclusion criteria: Patients who were taking hormone replacement therapy. Vaginal atrophy is a frequent cause of abnormal bleeding. Evident drug intake that can lead to vaginal bleeding. Vulval or cervical cause of bleeding. General causes that can cause vaginal bleeding.

After a written informed consent all patients will be subjected to do the following: General examination. Abdominal and pelvic examination. Pv and local examination. Complete laboratory analysis.

All women were examined trans-vaginally in the lithotomy position with empty bladder to measurement of endometrial thickness.

Within 1 week after the ultrasound patients underwent endometrial boipsy by fractional curettage for histopathological examination.

Statistical analysis:

Data were statistically described in terms of range, mean ± standard deviation (± SD), median, frequencies (number of cases) and percentages when appropriate. Agreement between US and endometrial sampling diagnosis was done using kappa statistic.

Results

The analyzed data were collected and tabulated and the following results were obtained.

Table (1): Relation between histopathological pattern and degree of bleeding among the study group.

Degree of bleeding	Histopathological pattern								Total		Chi-square test	
	A.E		E.H		E.P		A.C					
	No.	%	No.	%	No.	%	No.	%	No.	%	x^2	*p*-value
Mild	23	41.8	5	16.7	1	16.7	3	33.3	32	32.0	17.933	0.006*
Moderate	31	56.4	21	70.0	5	83.3	3	33.3	60	60.0		
Severe	1	1.8	4	13.3	0	0.0	3	33.3	8	8.0		
Total	55	100.0	30	100.0	6	100.0	9	100.0	100	100.0		

Using: Chi-square test. **p*-value <0.05 significant.
AE: Atrophic endometritis. EH: Endometrial hyperplasia.
EP : Endometrial polyp. AC: Adenocarcinoma of uterus.

Table (2): Comparison between severity of bleeding and the hemoglobin.

Degree of bleeding	Hemoglobin
Mild	12.7±2.2
Moderate	12.5± 1.61
Severe	9.68±2.3
p-value	0.001 (s)

The mean hemoglobin was 11.98±2.12. When we compared between the severity of bleeding and hemoglobin we found there are significant with each other (0.001).

Table (3): Attacks of bleeding among our study.

Items	No.	Percent
1st attack	40	40%
Recurrent attack	60	60%

There were (40%) of patients came by first attack of bleeding and (60%) came to our clinic by recurrent attack.

By Histopathology tests of endometrium we found (55%) had atrophic endometritis, (6%) had endometrial polyp, (30%) had simple endometrial hyperplasia and (9%) had endometrial adenocarcinoma.

Table (4): Relation between histopathological pattern and pelvic examination among the study group.

Pelvic examination	Histopathological pattern								Total		Chi-square test	
	A.E		E.H		E.P		A.C					
	No.	%	No.	%	No.	%	No.	%	No.	%	x^2	*p*-value
Enlarged uterus:												
8-10cm	8	14.5	9	30.0	2	33.3	2	22.2	21	21.0	89.769	<0.001**
10-12cm	1	1.8	3	10.0	0	0.0	3	33.3	7	7.0		
10-14cm	0	0.0	2	6.7	0	0.0	0	0.0	2	2.0		
Enlarged uterus with endocervical polyp	0	0.0	0	0.0	1	16.7	0	0.0	1	1.0		
Normal size uterus/ endocervical polyp	0	0.0	0	0.0	3	50.0	0	0.0	3	3.0		
Normal size uterus	46	83.6	16	53.3	0	0.0	4	44.4	66	66.0		
Total	55	100.0	30	100.0	6	100.0	9	100.0	100	100.0		

Using: Chi-square test. **p-value <0.001 highly significant.
AE: Atrophic endometritis. EH: Endometrial hyperplasia.
EP : Endometrial polyp. AC: Adenocarcinoma of uterus.

Table (5): Frequency and Percentage of endometrial histopathology among study group.

Endometrial pathology	Number	Percent
Atrophic endometritis	55	55%
Endometrial polyp	6	6%
Simple hyperplasia	30	30%
Adenocarcinoma	9	9%

Table (6): Relation between Histopathological pattern and endometrial thickness among group of study.

Endometrial thickness (mm)	Histopathological pattern								Total		Chi-square test	
	A.E		E.H		E.P		A.C					
	No.	%	No.	%	No.	%	No.	%	No.	%	x^2	*p*-value
<4mm	51	92.7	0	0.0	0	0.0	0	0.0	51	51.0	85.158	<0.001**
4-10mm	4	7.3	23	76.7	6	100.0	0	0.0	33	33.0	58.952	<0.001**
11-15mm	0	0.0	7	23.3	0	0.0	2	22.2	9	9.0	15.48	0.002*
16-20mm	0	0.0	0	0.0	0	0.0	6	66.7	6	6.0	64.539	<0.001**
>20mm	0	0.0	0	0.0	0	0.0	1	11.1	1	1.0	10.213	0.017*
Total	55	100.0	30	100.0	6	100.0	9	100.0	100	100.0	–	–

Using: Chi-square test. *p-value <0.05 significant. **p-value <0.001 HS.
AE: Atrophic endometritis. EH: Endometrial hyperplasia.
EP : Endometrial polyp. AC: Adenocarcinoma of uterus.

This table showed endometrial thickness <4mm were 51 patients (92.7%) in atrophic endometritis while no <4mm while there are no cases in the rest Histopathological, there was statistically significant relation between histopathological and endometrial thickness <4mm with p-value (p<0.001 highly statistically), this indicates that the A.E related endometrial thickness <4mm.

This table showed endometrial thickness 4-10mm were 4 patients (7.3%) in A.E, while 23 patients (76.7%) in E.H and 6 patients (100.0%) in E.P, as for the A.C. there are no cases at ET 4-10mm, there was statistically significant relation between histopathological and endometrial thickness 4-10mm with p-value (p<0.001 highly statistically), this indicates that the A.E, E.H and E.P. related endometrial thickness 4-10mm.

This table showed endometrial thickness 11-15mm were 7 patients (23.3%) in E.H., while 2 patients (22.2%) in A.C, as for the A.E and A.C.

there are no cases at ET 11-15mm, there was statistically significant relation between histopathological and endometrial thickness 11-15mm with p-value (p=0.002 statistically), this indicates that the E.H and A.C related endometrial thickness 11-15mm.

This table showed endometrial thickness 16-20mm were 6 patients (66.7%) in A.C, as for the A.E, E.H and E.P there are no cases at ET 16-20mm, there was statistically significant relation between histopathological and endometrial thickness 16-20mm with p-value (p<0.001 highly statistically), this indicates that the A.C related endometrial thickness 16-20mm.

This table showed endometrial thickness >20mm were one patient (11.1%) in A.C, as for the A.E, E.H and E.P there are no cases at ET >20mm, there was statistically significant relation between histopathological and endometrial thickness >20mm with p-value (p=0.017 statistically), this indicates that the A.C related endometrial thickness >20mm.

Table (7): Relation between Histopathological pattern and endometrial thickness "mm" among group of study.

Histopathological pattern	Endometrial thickness (mm)	
	Mean±SD	Range
Atrophic endometritis	2.96±0.85C	2.3-6
Endometrial polyp	7.33±1.03B	6.0-9.0
Endometrial hyperplasia	8.57±2.60B	5.5-14
Adenocarcinoma of uterus	15.67±3.71A	11-22
ANOVA value	142.213	
p-value	<0.001 "highly significant"	

Using: One Way Analysis of Variance; **p-value <0.001
- Values in each row which have different letters are significantly different at (p<0.05).

There was a highly statistically significant difference between Histopathological pattern according to endometrial thickness "mm" with p-value (<0.001). The highest value was found in adenocarcinoma of uterus (15.67±3.71) followed by endometrial hyperplasia (8.57±2.60), as for the Endometrial polyp it was (7.33±1.03), while the lowest value was found in Atrophic endometritis (2.96±0.85).

Table (8): Correlation Histopathological pattern and endometrial thickness "mm" among group of study.

	Endometrial thickness (mm)	
	r-value	p-value
Histopathological pattern	0.762	<0.001**

Using: r-Pearson Correlation Coefficient. **p-value <0.001.

There was a highly statistically significant correlation between Histopathological pattern according to endometrial thickness "mm" with p-value (<0.001).

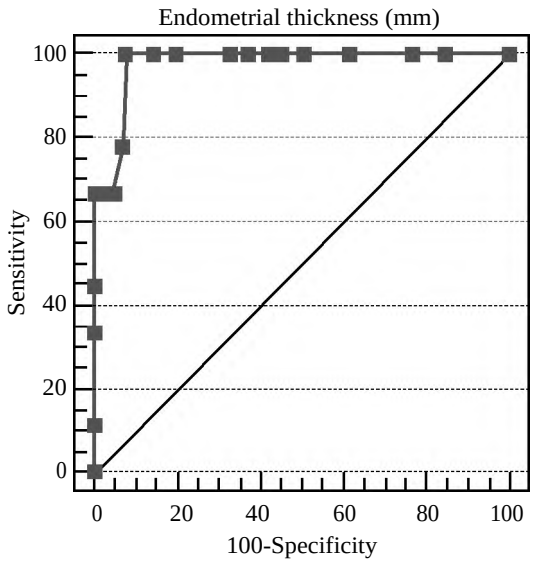

Fig. (1): Receiver-operating characteristic (ROC) curve for prediction malignant "adenocarcinoma of uterus" using the endometrial thickness (mm).

Cut-off	Sen.	Spe.	PPV	NPV	AUC [95% C.I.]
≥10	96.1%	92.3 %	66.3 %	97%	0.878 [0.827-0.897]

Receiver operator characteristics (ROC) curves were indices of endometrial thickness "mm" as predictors of adenocarcinoma of uterus in included patients. Endometrial thickness "mm" indices were significant predictors as denoted by the significantly large area under the curves (AUCs), there was used to define the best cut off value which was ≥10, with sensitivity of 96.1% specificity of 92.3% positive predictive value of 66.3%, negative predictive value of 97% with diagnostic area under the curve of 0.878.

Table (9): Comparison between age values of studied groups in relation to histopathology.

Endometrial pathology	Age (years)
Atrophic endometritis	46.0±8.4C
Simple hyperplasia	48.9±4.4B
Endometrial polyp	51.4±9.1B
Adenocarcinoma	58.5±7.0A
ANOVA test	8.008
p-value	<0.001**

Using: One Way Analysis of Variance. **p-value <0.001
- Values in each row which have different letters are significantly different at (p<0.05).

Also we found there is effect of age variation on the endometrial lesion. Highly significant= (<0.001).

Discussion

Menopause is a physiological event occurring in women at the age of on an average 50. Basically, the approximate age of menopause is 49±3.6 years [1]. Postmenopausal bleeding (PMB) is defined as abnormal uterine bleeding occurring after 1 year of permanent cessation of menstruation [2].

For PMB, current guidelines mandate immediate clinical evaluation and Trans-Vaginal Ultrasonograpgy (TVS) assessment followed by D and C or hysteroscopy guided endometrial/endocervical biopsy and subsequent histological evaluation [1].

Non-invasive TVS, and endometrial biopsy obtained by minimally invasive technique endometrial aspiration via dilatation and curettage for assessment of endometrial pathology in patient presented with PMB.

By histopathological examination of endometrium specimens we found 55% of them had atrophic endometritis, 30% had simple endometrial hyperplasia, 6% had endometrial polyp, and 9% had endometrial adenocarcinoma (AC).

In the current study reported that endometrial histopathology was related to the incidence of bleeding in 457 postmenopausal women observed for 18 months in a health care county in Sweden, with 50% atrophic endometrium, 10% endometrial hyperplasia, 9% polyp, 8% AC, 4% proliferative endometrium, 1 % secretory endometrium and 14% unremarkable endometrium.

Endometrial AC occurs mainly in the postmenopausal period and more than 90% of women are diagnosed at an age >50 years, with a mean age of 63 years. 13 In current study, the mean age of AC group (58.5±7.0 years) was higher than that of other endometrial pathology (46.0±8.4, 48.9±4.4 and 51.4±9.1 years for atrophic endometritis, simple hyperplasia and endometrial polyp respectively) with p<0.001. In accordance with the results of other studies, [6,7,8,11,14,15] increasing ET and older age were associated with a higher prevalence of AC in our cohort of women with PMB.

In postmenopausal women the normal length of uterus is usually between 4-6cm in this study, regard to size of uterus, 21 patients (21.0%) were 8-10cm, 7 patients (7.0%) were 10-12cm and 2 patients (2.0%) were 10-14cm; while one patient (1.0%) were Enlarged uterus with endocervical polyp, as for the Normal size uterus/endocervical polyp were 3 patients (3.0%); additionally, 66 patients (66.0%) were normal size (4-6cm) uterus [11].

Current study showed ET were <4mm in 51 patients (92.7%) in atrophic endometritis while no <4mm while there are no cases in the rest Histopathological, there was statistically significant relation between histopathological and ET <4mm with p-value (p<0.001 highly statistically), this indicates that the atrophic endometritis related ET <4mm.

In agreement with our study found that majority of patients (40%) complaining from atrophic endometrium had ET <4mm. Also mean ET was about 5.97mm in atrophic endometrium and 11.95 mm in carcinomatous endometrium [7,9].

Current study showed at ET 4-10mm, 4 patients (7.3%) in A.E, while 23 patients (76.7%) in E.H and 6 patients (100.0%) in E.P, as for the A.C. there are no cases at ET 4-10mm, there was statistically significant relation between histopathological and ET 4-10mm with p-value (p<0.001 highly statistically), this indicates that the A.E, E.H and E.P. related ET 4-10mm.

In other studies had 46.86% of cases with ET in range of 5-10mm. Out of this secretory endometrium was reported in 17.53% cases. Second common histopathologic pattern was disordered proliferative endometrium (11.51%) [16,17].

Current study showed ET were 11-15mm in 7 patients (23.3%) in E.H., while 2 patients (22.2%) in A.C, as for the A.E and A.C. there are no cases at ET 11-15mm, there was statistically significant relation between histopathological and ET 11-15mm with p-value (p=0.002 statistically), this indicates that the E.H and A.C related ET 11-15mm.

With the thickness range of 11-15mm observed hyperplasia of 2.87% and carcinoma of 0.52% [16].

Current study showed ET were 16-20mm in 6 patients (66.7%) with AC, as for the A.E, E.H and E.P there are no cases at ET 16-20mm, there was statistically significant relation between histopathological and ET 16-20mm with p-value (p<0.001 highly statistically), this indicates that the A.C related ET 16-20mm. ET >20mm were one patient (11.1%) in A.C, as for the A.E, E.H and E.P there are no cases at ET >20mm, there was statistically significant relation between histopathological and ET >20mm with p-value (p=0.017 statistically), this indicates that the A.C related ET >20mm.

Current study showed there was a highly statistically significant difference between Histopathological pattern according to ET "mm" with p-value (<0.001). The highest value was found in AC of uterus (15.67±3.71) followed by endometrial hyperplasia (8.57±2.60), as for the Endometrial polyp it was (7.33± 1.03), while the lowest value was found in Atrophic endometritis (2.96 ±0.85).

In other study mean ET in atrophic endometrium was (2.4-5.3 mm), carcinoma (mean ET 9-32mm), and endometrial carcinoma were the three types of findings (mean thickness 21.1 mm) **[12]**.

In current study, there was a highly statistically significant correlation between Histopathological pattern according to ET "mm" with r=0.762 and p-value (<0.001). This is in concordance with several studies **[1,6,7,8,11,18]**.

In current study, AUC was used to define the best cut off value of ET in prediction of AC at a level of ≥1 0mm, with sensitivity of 96.1 % specificity of 92.3% positive predictive value of 66.3%, negative predictive value of 97% with diagnostic area under the curve of 0.878.

In agreement with our results that reported that the sensitivity, specificity, PPV, and NPV of ET at 10mm were 92.64%, 100%, 100%, and 88.09% **[16]**.

There was statistical significance of sonographic ET as a predictor of endometrial malignant / premaliganat pathological changes. ET > 17mm was significant statistically associated with malignant/ premalignant endometrial pathology with 100% specificity and 25% sensitivity. On the other hand, ET between 10-17mm was significant statistically associated with endometrial pathology, with 100% specificity, while ET<7mm was associated with no endometrial pathology with sensitivity of 88.24% **[12]**.

The benign group's mean ET was 11.14 ± 4.73mm, while the malignant group's was 26.81 ± 9.16mm, suggesting a highly statistically significant discrepancy between the two groups since the endometrium was substantially thicker in the malignant group. With a cutoff value of 90% ET and precision of 80%, malignant pathology was calculated to be greater than 17mm **[12]**.

Endometrial thickness ≥5mm had a sensitivity of 83% and a specificity of 72% for recognizing endometrial carcinoma, which are lower than in symptomatic women **[10]**.

The sensitivity and specificity of TVS for suspecting endometrial pathology at ET <4mm were 87.09 and 75.86%, respectively **[6]**.

Conclusion:

Evaluation of PMB at the earliest is essential for diagnosing endometrial pathology for early intervention. TVS evaluation of ET and uterine size is a reliable method of screening postmenopausal women with PMP. No abnormal endometrium detected in postmenopausal women with endometrial thickness less than 4mm and all causes of endometrial carceinoma have endometrial thickness more than 9mm. Histopathological examination is essential for ruling out malignancy in PMB.

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دراسة العلاقة ما بين سمك بطانة الرحم مع الفحص المعملى للأنسجة فى حالات النزيف ما بعد انقطاع الطمث

خلفية البحث: نزيف ما بعد انقطاع الطمث هو نزيف مهبلى يحدث بعد عام واحد من انقطاع الطمث . عندما توقفت فترات لأكثر من سنة واحدة فى النساء الذين هم عموماً أكثر من ٤٥ سنة، وأنه هو حالة شائعة فى النساء بعد سن الطمث، يمكن أن يكون عرض سرطان بطانة الرحم.

الهدف من البحث: تقييم سمك بطانة الرحم عن طريق التصوير السونوغرافى المهبلى وربطه بالنمط الخلوى الذى يتم تقييمه عن طريق أخذ عينات بطانة الرحم.

المريضات وطرق البحث: أجريت هذه الدراسة فى وحدة أمراض النساء والتوليد فى مستشفى باب الشريعة الجامعى ومستشفى المنيرة العام فى الفترة من سبتمبر ٢٠١٨ إلى أغسطس ٢٠١٩. وشملت الدراسة ١٠٠ مريض يشكون من نزيف ما بعد الطمث فى العيادة الخارجية.

نتائج البحث: ١٠≥ لديه حساسية من ٩٦.١٪ خصوصية ٩٢.٣٪ قيمة تنبؤية إيجابية من ٦٦.٣٪، قيمة تنبؤية سلبية من ٩٧٪ مع منطقة التشخيص تحت منحنى ٠.٨٧٨ فى الكشف عن اضطرابات بطانة الرحم.

الاستنتاج: TCS تقييم ET وحجم الرحم هو وسيلة موثوقة لفحص النساء بعد الطمث مع PMP. لا يوجد بطانة الرحم غير طبيعية الكشف عنها فى النساء بعد الطمث مع سمك بطانة الرحم أقل من ٤ ملم وجميع أسباب الورم الخبيث فى بطانة الرحم لمن لديها سمك بطانة الرحم أكثر من ٩ ملم .