

# Measurement of Endometrial Thickness by Trans-vaginal Ultrasound and its Correlation with Body Mass Index and Endometrial Biopsy Results in Post-Menopausal Bleeding

Original  
Article

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## ABSTRACT

**Objectives:** To assess the correlation between endometrial thickness as measured through transvaginal ultrasound and body mass index (BMI), with the findings of subsequent histopathological examinations in instances of bleeding after menopause.

**Study Design:** An observational study.

**Subjects and Methods:** This study included 95 women experiencing bleeding post-menopause. These participants were selected from the outpatient departments of obstetrics and gynecology at Benha University Hospital. Based on the findings, participants were divided into two categories: a malignant group of 13 and a benign group of 82.

**Results:** There was a notable difference in the average endometrial thickness between the groups, with the malignant group presenting an average thickness of 28.54mm ( $\pm$  5.19) and the benign group showing 14.4mm ( $\pm$  6.07). A significant direct relationship was observed between BMI and the thickness of the endometrium. The Receiver Operating Characteristic (ROC) curve for endometrial thickness indicated its utility in malignancy prediction, presenting a threshold value of >21.18mm with an 85.73% specificity. Similarly, the ROC curve for BMI identified a predictive cutoff value of >32.57 with an 86.59% specificity. Logistic regression was utilized to predict malignancy, indicating a significant association between endometrial thickness and cancer risk in both univariate and multivariate analyses.

**Conclusion:** The study identified that endometrial thickness greater than 21.18 mm and a BMI exceeding 32.57 serve as critical indicators for detecting endometrial disorders and cancers. Furthermore, it underscores the connection between obesity and the risk of endometrial carcinoma.

**Key Words:** Body mass index; endometrial biopsy; endometrial thickness; post-menopausal bleeding; trans-vaginal ultrasound.

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## INTRODUCTION

Menopause is characterized by a range of mental and bodily transformations that a woman undergoes after her menstrual periods come to an end, originating from the Greek words "men" meaning month and "pause" indicating a stop<sup>[1]</sup>. Episodes of bleeding that resume 12 months following a woman's final regular menstrual cycle are referred to as postmenopausal bleeding<sup>[2]</sup>.

Bleeding after menopause can stem from both non-cancerous and cancerous conditions. Potential reasons include alterations in the structure of the reproductive system, infections, hormonal imbalances, cancers, and overall health issues<sup>[3]</sup>. The primary factors behind sporadic bleeding in women who have gone through menopause are often thinning of the vaginal or uterine lining and hormone treatments; meanwhile, endometrial cancer is responsible for about 10% of cases of bleeding post-menopause<sup>[4]</sup>.

Transvaginal ultrasound plays a crucial role in customizing endometrial biopsy techniques for individuals or decisively eliminating the need for additional assessments in women with a minimal likelihood of developing endometrial cancer<sup>[5]</sup>. It has been discovered through transvaginal sonography that women with an endometrial thickness of less than 5mm are at a reduced risk of cancer. However, this risk escalates with an increase in endometrial thickness, making ultrasound a valuable tool in distinguishing between patients at lower risk and those at higher risk<sup>[6]</sup>.

Endometrial biopsy stands as the gold standard for identifying abnormalities in endometrial tissue among patients experiencing postmenopausal bleeding, offering high levels of sensitivity<sup>[7]</sup>. Being over the age of 40 is broadly recognized as a risk factor for endometrial disorders and serves as a criterion for recommending a biopsy in women presenting with unusual bleeding patterns.

The prevalence of endometrial hyperplasia and cancer is higher in older women compared to younger ones, yet the most significant risk factor is the duration of exposure to estrogen without progesterone counterbalance<sup>[8]</sup>.

The Body Mass Index (BMI) serves as a highly reliable measure for identifying obesity as a significant risk factor for endometrial cancer<sup>[9]</sup>. An elevated BMI is associated with a heightened risk of developing endometrial cancer. It is estimated that in societies with higher levels of wealth, obesity accounts for approximately 40% of cases of endometrial cancer<sup>[10]</sup>.

This study aimed to correlate the endometrial thickness measurement by transvaginal sonography and BMI with subsequent histopathological studies in cases of postmenopausal bleeding.

## **SUBJECTS AND METHODS**

### ***Participants and Procedures***

This observational study was conducted at the obstetrics and gynecology outpatient clinics of Benha University Hospital, starting from May 2022 until the study's conclusion. The research focused on postmenopausal women who met the specified criteria and agreed to participate during the study period. Eligible participants were postmenopausal women experiencing bleeding one year after their last menstruation, with an endometrial thickness of 5mm or more as measured by Transvaginal Ultrasound (TVUS), and a BMI of 25 or higher.

Individuals were excluded from the study if they had any condition that could cause abnormal uterine bleeding (AUB), including systemic diseases like diabetes mellitus, hypertension, renal or liver disease, and sickle cell disease. Other exclusion criteria encompassed women undergoing hormone replacement therapy or Tamoxifen treatment, those on anticoagulant medication, presence of an adnexal mass as detected by TVUS, clear causes of cervical or vaginal bleeding such as ulcers, and those with incomplete medical records.

Each participant underwent a comprehensive evaluation process that included the following steps

### ***Medical History Assessment***

The study collected detailed medical histories from all participating women. This included their age, the age at which they reached menopause, the number of children they had given birth to (parity), their current experiences of bleeding, any previous uterine curettage procedures, and any family history of similar conditions.

### ***Physical Examination***

Participants underwent a thorough physical examination. This included an evaluation of the external genital area, a bimanual pelvic exam to assess the size, position, and mobility of the uterus, the presence of any tenderness, cervical or adnexal masses, and a speculum examination using a Cusco's speculum.

### ***BMI Calculation***

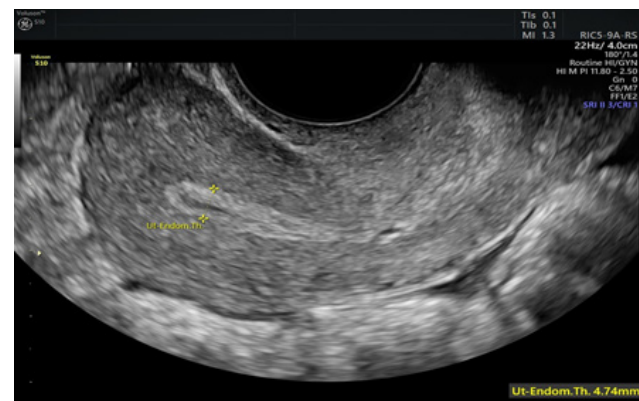
The BMI was calculated for each participant using the formula: BMI = weight in kilograms divided by height in meters squared.

### ***Laboratory Tests***

Blood tests conducted for each participant included a Complete Blood Count (CBC), International Normalized Ratio (INR), liver function tests (SGOT, SGPT), serum creatinine levels, and fasting and postprandial blood sugar levels.

### ***Imaging***

A Transvaginal ultrasound using a two-dimensional ultrasonography machine equipped with a 3.5 MHz transvaginal probe was performed (Figure 1).



**Fig. 1:** Trans vaginal ultrasound measurement of endometrial thickness measured 4.74 mm in postmenopausal woman

The endometrium was imaged from one end of the uterus to the other in the sagittal plane, and the thickness of the endometrium was measured between the basal layers of the anterior and posterior uterine walls. The measurement was adjusted by subtracting the fluid diameter when applicable.

### ***Biopsy Procedure***

A conservative dilatation and curettage procedure was performed using a sharp-ended curette. The procedure

started at the uterus's fundus, followed by the posterior and anterior walls, the right and left lateral walls, and concluded at the fundus again. The collected specimen was then preserved in 10% formalin for histopathological examination.

**Statistical Analysis**

The study's data was carefully processed and analyzed using IBM SPSS Statistics software, Version 25.0. The Shapiro-Wilk test checked data distribution, employing mean and standard deviation for normally distributed data, and median and range for skewed data, with non-numerical data summarized by frequencies and percentages. Analytical techniques included the Student's T-test for mean differences between two groups, the Mann-Whitney U test for non-parametric variable differences, and the Chi-Square test for relationships between qualitative variables. Correlation analysis assessed quantitative variable associations, while ROC Curve analysis evaluated diagnostic measure accuracy, identifying optimum cutoff points for high, moderate, and low accuracy levels. Logistic regression analysis predicted risk factors for categorical outcomes using odds ratios to measure exposure and outcome associations, considering a *p-value* of less than 0.05 at a 95% confidence interval as statistically significant.

**RESULTS**

Histopathological analysis revealed that specimens from the malignant group exhibited endometrial carcinoma and atypical hyperplasia, whereas the benign group's specimens displayed hyperplasia or nonspecific findings (Table 1).

**Table 1:** Comparison between malignant and benign groups as regard histopathological findings

Malignant group n=13		Benign group n=82	
Endometrial carcinoma	10(76.9%)	Hyperplasia	69(84.2)
Hyperplasia with atypia	3(23.1%)	Non specific finding	13(15.8%)

ROC - Receiver Operating Characteristic, AUC - Area Under the Curve, CI - Confidence Interval

The ROC curve analysis for endometrial thickness indicated a cutoff value of over 21.8mm for predicting malignancy, with a specificity of 85.73% (Table 2).

**Table 2:** ROC curve analysis of endometrial thickening and relation to malignancy

AUC	95% CI	<i>p</i>	Cut off	Sensitivity (%)	Specificity (%)
0.932	0.882-0.981	<0.001*	21.18	100	85.73

ROC - Receiver Operating Characteristic, AUC - Area Under the Curve, CI - Confidence Interval

Similarly, the ROC curve for BMI identified a cutoff value of over 32.57 for malignancy prediction, with a specificity of 86.59% (Table 3).

**Table 3:** ROC curve analysis of BMI and relation to malignancy

AUC	95% CI	<i>p</i>	Cut off	Sensitivity (%)	Specificity (%)
0.687	0.498-0.876	0.031*	32.57	64.54	86.59

ROC - Receiver Operating Characteristic, BMI - Body mass index, AUC - Area Under the Curve, CI - Confidence Interval

A significant correlation was observed between BMI and several factors including endometrial thickness, gravidity, hemoglobin levels, Alanine Transaminase (ALT), International Normalized Ratio (INR), and platelet counts, whereas no significant correlations were found with the remaining measured parameters (Table 4).

**Table 4:** Spearman correlation of BMI and other studied parameters

	BMI	
	r	p
Age	0.154	0.136
Endometrial Thickness	.289	0.005*
Gravidity	.225	0.028*
Parity	-0.031	0.765
Duration of PMB	0.069	0.508
HGB	-.208	0.044*
Creatinine	-0.059	0.569
ALT	.225	0.028*
AST	0.155	0.134
INR	.246	0.016*
Platelet	-.236	0.021*
WBX	-0.055	0.595
FBS	-0.019	0.854
RBS	-0.079	0.444
SBP	0.145	0.161
DBP	-0.011	0.912

BMI - Body Mass Index, r - Pearson correlation coefficient, PMB - Postmenopausal Bleeding, HGB - Hemoglobin, ALT - Alanine Transaminase, AST - Aspartate Aminotransferase, INR - International Normalized Ratio, WBX - White Blood Cells, FBS - Fasting Blood Sugar, RBS - Random Blood Sugar, SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure

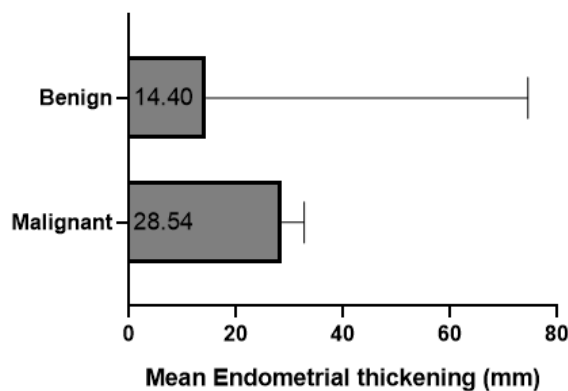
Logistic regression analysis aimed at predicting malignancy showed that endometrial thickness was associated with an increased risk of malignancy in both univariate and multivariate analyses. However, factors such as age, gravidity, parity, BMI, hemoglobin levels, and platelet counts demonstrated significant correlation only in univariate analysis (Table 5).

**Table 5:** Logistic regression analysis of possible related markers of malignancy

	Univariable			Multivariable		
	p	OR	95% C.I	p	OR	95% C.I
Age	0.035*	0.861	0.749-0.989			
BMI	0.045*	0.876	0.769-0.997			
Endometrial Thickening	<0.001*	0.784	0.701-0.876	<0.04*	0.786	0.701-0.88
Gravidity	0.001*	0.352	0.187-0.66			
Parity	0.004*	0.401	0.216-0.744			
duration	0.390	0.868	0.628-1.198			
HGB	<0.001*	3.541	1.88-6.667			
Creatinine	0.396	0.077	0-28.616			
ALT	<0.001*	0.912	0.868-0.957			
AST	<0.001*	0.898	0.846-0.952			
Platelet	<0.001*	1.112	1.062-1.164			
Wbc	0.771	1.047	0.769-1.424			
FBS	0.123	1.041	0.989-1.095			
RBS	0.615	0.975	0.885-1.074			
SBP	0.451	1.024	0.962-1.088			
DBP	0.788	0.990	0.92-1.064			

OR - Odds Ratio, C.I - Confidence Interval, BMI - Body Mass Index, HGB - Hemoglobin, ALT - Alanine Transaminase, AST - Aspartate Aminotransferase, WBC - White Blood Cells, FBS - Fasting Blood Sugar, RBS - Random Blood Sugar, SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure

Medical histories indicated a higher number of pregnancies (gravidity) in the malignant group. Notable differences were observed between the two groups in terms of average endometrial thickness—28.54mm (± 5.19) in the malignant group versus 14.4mm (± 6.07) in the benign group (Figure 2).



**Fig. 2:** Mean endometrial thickening differences between the malignant and benign cases

**DISCUSSION**

In this research, notable disparities were observed in the average thickness of the endometrium between

the malignant group (28.54mm ± 5.19) and the benign group (14.4mm ± 6.07). These findings align with those of Opolskiene et al.<sup>[11]</sup>, who noted that individuals with malignant endometrial conditions had a significantly thicker endometrium (median of 16.2 mm) compared to those with benign conditions (median of 9.6 mm). Similarly, Mohamed et al.<sup>[12]</sup> found a considerable difference in endometrial thickness between benign (11.14±4.73 mm) and malignant groups (26.81±9.16 mm), highlighting a marked increase in thickness in cases of malignancy.

Additionally, our study demonstrated a significant positive association between BMI and endometrial thickness, corroborating the findings of Mohamed et al.<sup>[12]</sup>, who also identified a positive correlation between these two factors. This is further supported by Crosby et al.<sup>[13]</sup>, who found a link between endometrial thickness and BMI. However, Van den Bosch et al.<sup>[14]</sup> reported no relationship between endometrial thickness, weight, or BMI after adjusting for age, suggesting that age significantly influences the analysis and may act as a confounding factor.

Our study's biopsy histopathology revealed 13.7% malignant and 86.3% benign cases. Of the malignancies, 76.9% were endometrial carcinoma and 23.1% were hyperplasia with atypia, while the benign cases mostly showed hyperplasia (84.2%) or nonspecific findings (15.8%). In contrast, Mohamed et al.<sup>[12]</sup> primarily found endometrial hyperplasia without atypia (30%), followed by various other conditions, with obesity being a common factor among subjects. Their study also noted endometrial polyps in 17.8% of benign cases but none in malignant ones, indicating polyps were not a significant marker of malignancy.

Our study's outcomes show variations when compared to other research, largely due to differences in the number of participants and the criteria for inclusion. For instance, Yaman et al.<sup>[15]</sup> analyzed 213 instances of postmenopausal bleeding and discovered that 42 cases (19.7%) were malignant, while 109 cases (51.17%) had benign lesions such as polyps and hyperplasia, and 62 cases (29.1%) exhibited atrophic changes. Similarly, Opolskiene et al.<sup>[11]</sup> evaluated 261 instances of postmenopausal bleeding, identifying malignancy in 63 cases (24%) and benign lesions in 198 cases (76%).

In their comprehensive review and meta-analysis concerning the cancerous potential of endometrial polyps, Lee et al.<sup>[16]</sup> found that symptoms of vaginal bleeding and a postmenopausal status in women with endometrial polyps were associated with a heightened risk of endometrial cancer. Costa-Paiva et al.<sup>[17]</sup> also observed a higher prevalence of endometrial cancer in women presenting with endometrial polyps and postmenopausal bleeding, further emphasizing the significance of these factors in assessing the risk of malignancy.

The ROC curve analysis identified a cutoff value for endometrial thickness at over 21.18mm to predict malignancy with 85.73% specificity. Research typically points to a 4- or 5-mm threshold as indicative of increased cancer risk, noted for its high sensitivity<sup>[12]</sup>. Studies reveal that thickness beyond 17 mm correlates strongly with malignancy, offering 90% sensitivity and 80% accuracy. Karasu *et al.*<sup>[18]</sup>, in their study of 287 women with postmenopausal bleeding, determined a 4 mm cutoff via transvaginal ultrasound, yielding a 99% negative predictive value for endometrial cancer, with actual cancer detection in 27 cases. This aligns with Evans *et al.*<sup>[19]</sup>, who found a 4.5 mm thickness to provide 90.9% sensitivity and 79.1% specificity, suggesting its effectiveness as a diagnostic measure against uterine curettage findings.

Phillip *et al.*<sup>[20]</sup> observed discrepancies between imaging and pathological results, with half of the endometrial cancer cases showing thickness between 3 and 4 mm, and 70% of cases over 5 mm being benign. Schramm *et al.*<sup>[21]</sup> noted a median endometrial thickness of 14.3 mm in cancer patients versus 9.0 mm in non-cancerous cases, indicating no ideal threshold for both high sensitivity and specificity. Park *et al.*<sup>[22]</sup> identified an 8 mm threshold as highly effective for early cancer detection, indicating a good prognosis for patients, including those with endometrial hyperplasia or clear and mixed cell carcinoma. Recent research showed a 3 mm endometrial thickness yields a 97% sensitivity and 45.3% specificity for cancer detection, highlighting the effectiveness of endometrial thickness measurement as a screening tool for endometrial cancer in postmenopausal women<sup>[23]</sup>.

The analysis of the ROC curve for BMI demonstrated a cutoff value of over 32.57 for predicting endometrial cancer with an 86.59% specificity. This finding aligns with Zaki *et al.*<sup>[24]</sup>, who identified a high BMI as a significant indicator for assessing the risk of endometrial cancer in Egyptian women with postmenopausal bleeding (PMB). Similarly, Lukanova *et al.*<sup>[25]</sup> observed that obese women (BMI  $\geq$  30) faced a 36% increased risk of cancer compared to those with a normal BMI range (18.5-25), particularly noting the endometrium as the most obesity-associated cancer site. These results concur with the International Agency for Research on Cancer's assessment, which categorizes the link between obesity and endometrial cancer as 'strong or compelling,' with obese women having a relative risk (RR) two to three times greater than non-obese women<sup>[26]</sup>, underscoring the significant correlation between high BMI and endometrial cancer risk.

In this research, logistic regression was utilized to estimate the likelihood of malignancy, revealing that endometrial thickness is a significant predictor of cancer risk in both univariate and multivariate analyses. However, factors such as age, number of pregnancies, number of live births, BMI, hemoglobin levels, and platelet count were significant only in the univariate analysis. In a

related study involving 142 women with postmenopausal bleeding, Salman *et al.*<sup>[27]</sup> found that those with malignant endometrial conditions were generally older (average ages of 53.8 vs 65.3 years,  $P=0.001$ ) and had higher BMIs (27.9 kg/m<sup>2</sup> vs 30.6 kg/m<sup>2</sup>,  $P=0.028$ ). Additionally, women with endometrial cancer experienced a slightly longer duration of menopause, and the endometrial thickness measured via transvaginal ultrasound was significantly greater in cancer patients (26.0 $\pm$ 6.0 mm) compared to those without cancer (8.8 $\pm$ 2.2 mm).

## CONCLUSIONS

Transvaginal sonography (TVS) proves to be an effective tool for identifying endometrial abnormalities and early stages of endometrial cancer. The ability to detect these conditions early, especially in patients without specific symptoms like vaginal bleeding, can lead to favorable outcomes. The study identified optimal cutoff values for endometrial thickness (>21.18 mm) and BMI (>32.57) as critical indicators for the presence of endometrial pathologies and cancer, emphasizing the strong link between obesity and the risk of developing endometrial carcinoma.

## CONFLICT OF INTERESTS

There are no conflicts of interest.

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