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Evaluation of Endometrial Thickness in Females with Post Menopausal Bleeding

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Abstract
The study evaluated the endometrial thickness in post menopausal bleeding subjects with trans-vaginal /trans-abdominal ultrasonography and further the endometrial thickness was correlated with histopathological findings. This diagnostic study included 50 females who presented with postmenopausal bleeding. All females were subjected to transvaginal ultrasonographic evaluation of the endometrial thickness. These females further underwent dilatation and curettage procedure to obtain endometrial curettings which were subjected to histopathological examination. In the present study 50 females between ages 44 to 68 years were included. Out of the total 50 females who presented with post menopausal bleeding 9 females were diagnosed with endometrial carcinoma , 18 females with endometrial hyperplasia, 16 with benign endometrial glands ,6 with atrophic endometrium and 1 with endometrial polyp on histopathological examination after dilatation and curettage. Mean endometrial thickness was significantly more in cases of malignancy as compared to benign conditions (21.83 vs 11.32 mm; p<0.01). Endometrial thickness was observed to be a significant predictor for malignancy (Area under ROC was 0.844; p-value <0.01) with sensitivity and specificity of 88.9% and 63.4% at a cut-off of 11.7 mm. Although transvaginal sonography endometrial thickness can be used as a screening tool in discriminating normal from abnormal endometrium but cannot differentiate benign from malignant endometrium.

Introduction

Postmenopausal bleeding is defined as bleeding occurring 12 months after cessation of menstruation due to ovarian failure in women not taking hormone replacement therapy. However vaginal bleeding occurring anytime after 6 months of amenorrhea in a woman of menopausal age should be considered as postmenopausal bleeding and investigated.[1]

There has been a steady increase in the incidence of endometrial cancer over recent years. Uterine curettage is mandatory to exclude endometrial cancer in women presenting with post-menopausal bleeding which is the initial presenting symptom in 75 to 90% of the cases .However dilatation and curettage is an invasive procedure associated with morbidity and only 10 % of females are diagnosed with malignancy. Therefore there arises a need for non invasive screening method to diagnose endometrial malignancies which are associated with good prognosis.[2]

Measurement of endometrial thickness by ultrasonography is by far the most convenient, non-invasive method for diagnosis of the endometrial pathologies.

Material and Methods

This diagnostic study comprised of 50 women who presented with postmenopausal bleeding. Women with uterine fibroids, adenomyosis, Carcinoma cervix and any general disease that could affect pelvic blood flow were excluded from the study.

The sonography was performed using Voluson E8 Expert BT09 transvaginal transducer with frequency of 5-7 Mhz after taking .informed consent from the patient Endometrial thickness was measured in longitudinal section from the anterior subendometrial hypoechoic zone (halo) to the opposite side, including two endometrial layers.

Operative procedure of obtaining endometrial curetting was undertaken under short general anesthesia with informed consent and pre-anesthetic check up. The curettings were sent for histopathological examination in 10% formalin solution. The data obtained from ultrasound and Doppler examinations were compared to the results of histopathological study and clinical findings.

Results

The statistical analysis was carried out using statistical Package for social sciences [IBM SPSS version 23]. Mean and standard deviation were calculated for normally distributed data. The endometrial thickness was compared with histopathological findings post dilatation and curettage .Student T test for significance was applied to find the significance of sonographic parameters in detecting endometrial malignancies. All statistical tests were two sided and significance level were taken as of $P < 0.01$.Further ROC curves were used to obtain the ideal cut off for endometrial thickness .Sensitivity and specificity at ideal cut off was determined using ROC curve.

Mean age of the study cases was 52.38 +/- 7.97 years with 82% of the cases between age of 41-60 years. In our study age of females with malignant endometrium was more than that of females with benign endometrium (55.4+/-9.1 as compared to 51.6 +/-7.5). Females with malignant endometrium had more number of years elapsed since menopause (9+/-5.6) whereas those with benign endometrium had less number of mean years elapsed since menopause (6+/-5) (table 1)

Out of total 50 cases, 82% had benign lesions while 18% had malignant lesions.9 females were diagnosed with endometrial carcinoma, 18 females with endometrial hyperplasia, 16 with benign endometrial glands, 6 with atrophic endometrium and 1 with endometrial polyp on histopathological examination after dilatation and curettage (table 2) Mean endometrial thickness was significantly more in cases of malignancy as compared to benign conditions (21.83 vs 11.32 mm; $p<0.01$). (table 3)

Endometrial thickness was observed to be a significant predictor for malignancy (Area under ROC was 0.844; p-value <0.01) with sensitivity and specificity of 88.9% and 63.4% at a cut-off of 11.7 mm. (table 4)

Table 1 Distribution of study cases as per Age group

Age group (yrs)	N	%
41-50	26	52.0%
51-60	15	30.0%
61-70	8	16.0%
> 70	1	2.0%
Total	50	100.0%
Mean age - 52.38 +/- 7.97 years		

Table 2: Distribution of endometrial pathologies

Histopathology	N	%
Adenocarcinoma	9	18.0%
Atrophic Endometrium	6	12.0%
Hyperplasia	18	36.0%
Polyp	1	2.0%
Proliferative Endometrium	14	28.0%
Secretory Endometrium	2	4.0%
Total	50	100.0%

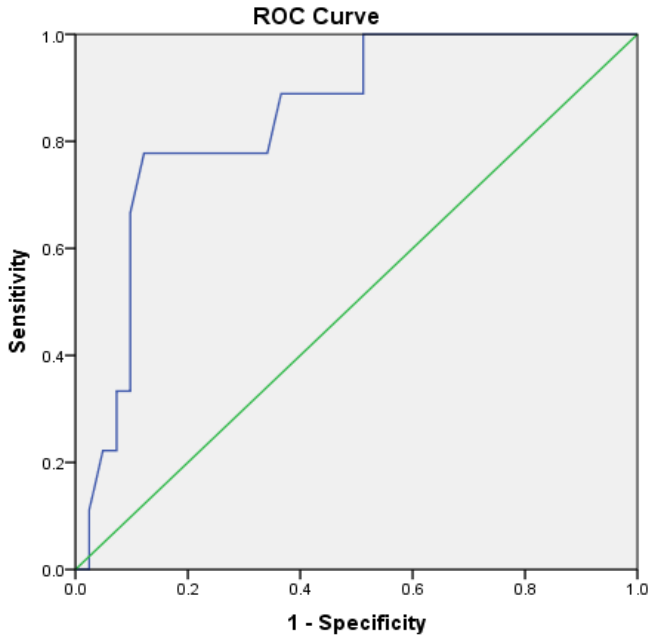
Table 3 Mean endometrial thickness in benign and malignant cases

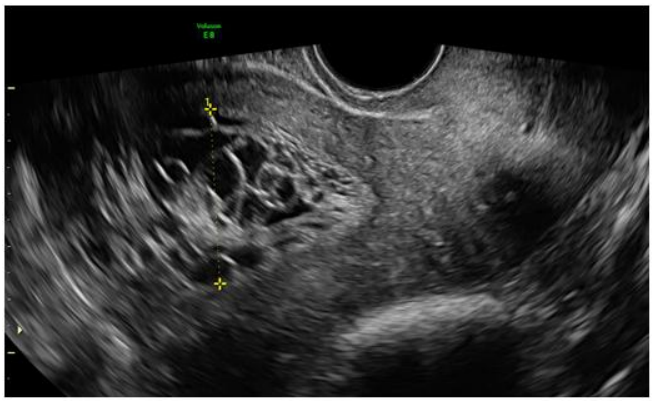
Variables	Diagnosis	N	Mean	SD	p- value
Endometrial Thickness	**Benign**	41	11.32	7.06	**<0.01**
	Malignant	9	21.83	7.79	

Table 3 ROC analysis for endometrial thickness

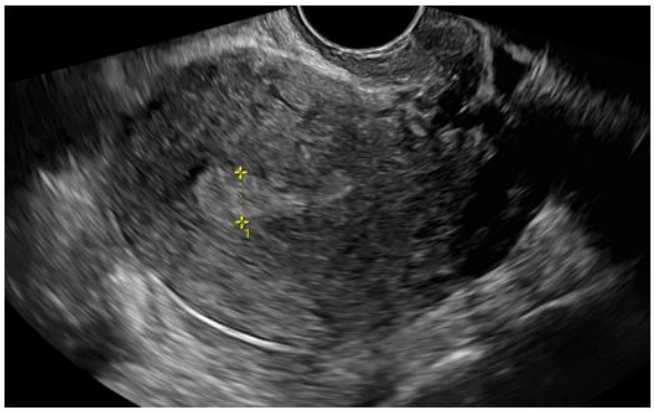
Area Under the Curve					
Test Result Variable(s)	**Area**	**SE**	**p- value**	**95% CI**	
				Lower Bound	**Upper Bound**
ET	0.844	0.065	<0.01	0.717	0.972

Ideal Cut-off	Sensitivity	Specificity
11.7	88.9%	63.4%

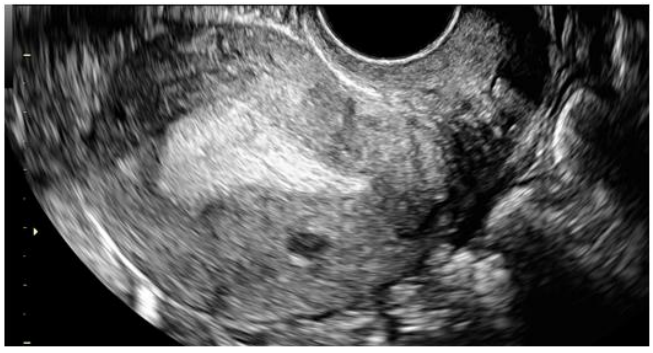




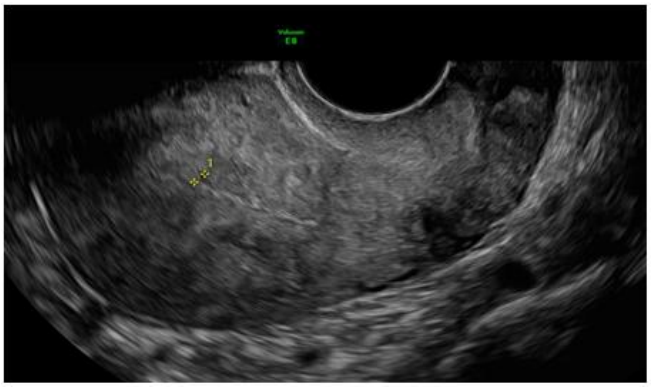
Case 1-A 52 year old female who was diagnosed with malignancy .ET measures 33 mm



Case 2- A 51 year old female who was postmenopausal for last 18 months now was diagnosed with normal endometrial glands .ET measures 9 mm



Case 3 - A 49 year old female who was diagnosed with endometrial hyperplasia on histopathology .ET measures 15 mm



Case 4- A 56 year old female who was postmenopausal for 7 years now presented with an episode of spotting .The endometrial thickness was 3 mm.

Discussion

In India incidence of endometrial cancer is preceeded by cervical and ovarian cancers. In our study Incidence of endometrial carcinoma was 18 % (9 out of 50 females) It is higher as compared to previous studies which have reported an incidence of 10%. Bezeniunka et al[5] nevertheless have reported a 22.6% rate of malignancy in patients with postmenopausal bleeding

Rate of malignancy is variable due to patient characteristics like age, time since onset of menopause. In our study the mean age of females diagnosed with malignant endometrium was higher as compared to females diagnosed with benign endometrium. Howver Develinku et al [6] also have stated that incidence of endometrial cancer increases as patients age increases. In our study females diagnosed with malignant endometrium had more number of mean years elapsed since menopause. Novak's Gynaecology states that peak incidence of endometrial cancer occurs 10-15 years after average age of menopause.

In our study mean endometrial thickness was significantly more in cases of malignancy (21.83 +/- 7.79) as compared to benign conditions (11.32 +/-7.06); Using 'T' test significant correlation was found between endometrial pathology and endometrial thickness ($p<0.01$). These findings are higher than those with Bano et al[7] The mean endometrial thickness in cases with benign endometrium was 9.2 mm (S.D. = 4.67 mm) and in cases with malignant endometrium was. 16.36 (S.D> = 7.1 mm) whereas another study showed mean endometrial thickness as 8 mm ± 9 mm in absence of cancer and 20 mm ± 9 mm in presence of cancer .

The sonographic measurements of endometrium with a thickness of greater than 5mm exhibited 100% sensitivity, 22% specificity, 15% positive predictive value, and 100% negative predictive value in our study. Our findings are in concordance with various studies which have used 3-5 mm endometrial echo as a cut-off value for transvaginal ultrasonography with an extremely high negative predictive value (greater than 99%). The endometrial thickness was observed to be a significant predictor for malignancy (Area under ROC was 0.844; p-value <0.01) with sensitivity and specificity of 88.9% and 63.4% at a cut-off of 11.7 mm. According to the ROC curve the ideal cut off is 11.7 mm which has more specificity as compared to the 3-5 mm cut off used commonly by previous researchers but it comes at the cost of decreased sensitivity.

So we reach a point where if we use ET value 3-5mm we are less likely to miss any malignancy but it will be associated with a high false positive rate. A large number of females will undergo dilatation and curettage and less number of females would be diagnosed with malignancy like in our study. If we use the ideal cut off which is 11.7 mm as provided by the ROC curve we achieve better specificity ie 63.4% however the sensitivity is compromised from 100% to 88.9% .There will be a higher false negative rate at this cut off. In our study if 11.7 mm ideal cut off is used we will miss one case of malignancy in our study.

These considerations underline the fact that ET measurements alone will not decrease unwarranted invasive procedures in about one third to one-half of the cases, due to high false positive results. Using a 5 mm endometrial thickness as a cut-off value is a reliable method to exclude the possibility of malignancy in

postmenopausal bleeding. However it is not diagnostic of any particular pathology.

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