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Original Research Article

Role of transvaginal ultrasound in assessment of endometrial pathology in patients with post-menopausal bleeding

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ABSTRACT

Background: Post-menopausal bleeding (PMB) is the most distressing problem in females Endometrial thickness (EMT) as assessed by transvaginal ultrasound (TVS) aids in diagnosing endometrial pathology. This study analyses usefulness of TVS as a diagnostic tool in the evaluation of PMB.
Methods: A prospective study was conducted in 100 patients. Correlation of EMT by TVS was compared with gold standard of histopathological examination (HPE) of the endometrium by fractional curettage (FC).
Results: Mean age was 56.9±8.03 years and mean parity status was 2.83±1.45. Mean duration after menopause to presentation of bleeding per vaginum was 5.7±3.85 years. As per the receiver operating characteristic curve (ROC) analysis, an EMT of 10.8 mm had a high negative predictive value (99.1%) for malignancy with moderate specificity (62.79%) and high sensitivity (92.3%).
Conclusions: TVS can be easily performed and is less expensive and a useful diagnostic tool in the evaluation of PMB with a cut off value of 10.8 mm EMT gives a high sensitivity (92.3%) and moderate specificity (62.79%).

Keywords: Carcinoma endometrium, Endometrial thickness, Postmenopausal bleeding, Transvaginal ultrasound

INTRODUCTION

Menopause is said to have occurred after 12 consecutive months of amenorrhea for which no pathological cause is found. The cessation of follicular function results in negligible amounts of oestrogen which is insufficient to stimulate the endometrium leading to amenorrhea. The average age of menopause is 51 years in western population and 48.3 years in Indian population.[1] Postmenopausal bleeding (PMB) can be multifactorial. It may be due to endometrial or endocervical polyp, sub mucus myoma, endometrial hyperplasia (adenomatous /atypical), anovulatory endometrium, uterine carcinoma (endometrium or cervix).[1-3] The most common cause of postmenopausal bleeding is found to be atrophic endometrium and hormone replacement therapy.[4] The basic pathology in PMB being endometrial hyperplasia induced by oestrogen. Post-menopausal women continue to have measurable levels of estrone and estradiol even though the production of progesterone completely ceases after menopause, thereby providing a hormonal milieu for unopposed stimulation of endometrium by oestrogen. This may lead to the risk of endometrial hyperplasia and carcinoma which commonly presents with PMB. Postmenopausal bleeding needs evaluation urgently as 5-15% cases are caused by carcinoma endometrium or cervix.[5]

Fractional curettage, an invasive technique was considered as gold standard for evaluation of PMB, but is uncomfortable and associated with anesthetic risk especially in this population with high prevalence of diabetes, hypertension and obesity.[6-8]

Transvaginal ultrasound (TVS) has been established as the first step in the evaluation of PMB.[9,10] In addition to evaluation of endometrial thickness, TVS also provides information regarding other causes like polyp, myoma

and adnexial pathology etc. Endometrial thickness of normal atrophic uterus of a postmenopausal woman does not exceed 4- 5 mm.[11-13]. Endometrial thickness of <4mm correlated with atrophic endometrium in 289 patents with post menopausal bleeding in a study by Guner et al.[14] 74.8% of patients had a positive predictive result, 25.2% had endometrial thickness of 6.1±3.7mm but tissue was insufficient for diagnosis and concluded that a cut off value of <4mm for endometrial thickness had a negative predictive accuracy of 100%14. Similarly endometrial thickness of <4mm had higher negative predictive value in postmenopausal bleeding in studies by Ciatto et al and Gull et al.[15,16]

A study by Conoscenti et al, trans-vaginal sonography showed sensitivity, specificity, positive predictive and negative predictive value of 55%, 96.1%, 68.75% and 93.2% respectively in detecting pre-malignant and malignant endometrial pathology.[13] Thus a vast majority of patients with PMB can be managed expectantly with reassurance. The value of an approach to distinguish such patients from those of with organic pathology by a safe, painless and convenient method is obvious. Higher values of EMT indicate endometrial hyperplasia or endometrial carcinoma.[16,17]

This study is aimed at comparing the endometrial thickness as measured by TVS with histopathology of the endometrium in patients with PMB and to define a cut off value of EMT by plotting a Receiver Operating Characteristic curve (ROC) for identifying patients at risk for malignancy.

METHODS

This is a prospective study with a diagnostic tool evaluation performed in a tertiary care referral centre, Sree Avittam Thirunal Hospital, Trivandrum Kerala, South India. Prospective postmenopausal patients with bleeding per vaginum who attended the hospital for evaluation between June 2014 and December 2014 were recruited for the study.

Inclusion criteria were any patient with PMB with no palpable pathology by thorough clinical examination. The exclusion criteria were as follows.

- Patients unwilling to participate
- Patients with bleeding per vaginum within 1 year of amenorrhea
- Patients on oral anticoagulants/ antithrombotic therapy
- Patients with hematological disorders
- Patients with obvious uterine and adenexal pathology

During the study period a total of 165 patients presented with post-menopausal bleeding of which 109 patients who satisfied the inclusion criteria were included. After detailed history and thorough clinical examination, TVS was done for all patients to assess the endometrial thickness and morphology and exclude uterine and adenexal pathology, Fractional curettage was done for all study patients and curettings were sent for histopathological examination. Histopathology was classified as Proliferative endometrium, Atrophic endometri-um, Secretary endometrium, Simple hyperplasia, Atypical hyperplasia and Carcinoma endomte-rium.[18,19]

Data was analyzed using standard statistical methods. A Receiver operating Characteristic curve (ROC) was plotted to obtain the cut off value of endometrial thickness assessed by TVS. The sensitivity, specificity, positive predictive value, and negative predictive value were assessed.

RESULTS

A total of 109 patients were included in the analysis. Mean age was 56.9±8.03 years (age range 46- 84 years) and the mean parity status was 2.83±1.45 and mean duration after menopause to PMB was 5.73±3.85 years. 22.01% of patients were hypertensive, 17.43% were having diabetes mellitus and 58% were obese.

Histopathology observations

Majority of the patients had atrophic endometrium (35.78%). Simple hyperplasia and atypical hyperplasia were seen in 8.26% and 10.09% patients respectively. Carcinoma endometrium was reported in 4.59% of patients and proliferative endometrium in 27.52% and secretary endometrium was reported in 4.59%.

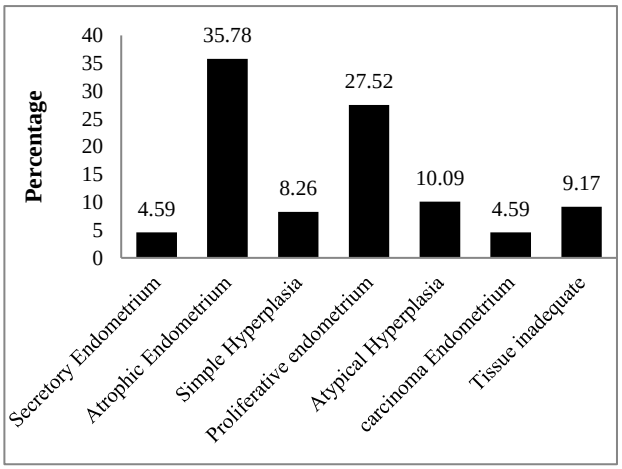

Figure 1: Distribution of histopathological changes in the endometrium.

Highest mean endometrial thickness was observed in atypical hyperplasia and carcinoma endometrium and lowest endometrial thickness in those with atrophic endometrium. A receiver operating characteristic (ROC) curve was plotted with the endometrial thickness by TVS as a variable against the occurrence of atypical hyperplasia and adenocarcinoma to identify the positive

predictive value, negative predictive value, sensitivity and specificity (Table 1).

Table 1: Correlation between EMT by TVS and histopathology.

Histopathology of endometrium	Endometrial Thickness (mm)	Mean±SD (mm)
Simple hyperplasia	11-15	13.33±1.63
Secretory endometrium	9-14	11.33±2.14
Proliferative endometrium	4.9-27	13.47±5.14
Atrophic endometrium	2.5- 8	5.88±1.17
Atypical hyperplasia	7.5 -22	14.21±5.29
Carcinoma endometrium	12-18	14.75±2.50

Table 2: The ROC curve analysis.

Variable	EMT
Classification variable	CA
Sample size	99
Positive group [a]	13 (13.13%)
Negative group [b]	86 (86.87%)
Disease prevalence (%)	7
Area under the ROC curve (AUC)	0.788
Standard Error [a]	0.0517
95% Confidence interval [b]	0.694 to 0.864
z statistic	5.568
Significance level P (Area=0.5)	<0.0001
Youden index J	0.5510
Associated criterion	>10.8
Sensitivity	92.31
Specificity	62.79

[a]CA = 1, [b]CA = 0; [a] DeLong et al, [b] Binomial exact

Endometrial thickness of 10.8 mm by TVS as a cut off value to identify malignant endometrial pathology, from ROC had 92.3% sensitivity and 62.8% specificity. Moreover, the negative predictive value (99.1%) whereas the positive predictive value was 15.7%.

Table 3: Criterion values and coordinates of the ROC curve.

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR	+PV	-PV
≥2.5	100.00	75.3 - 100.0	0.00	0.0 - 4.2	1.00		7.0	
>7	100.00	75.3 - 100.0	41.86	31.3 - 53.0	1.72	0.00	11.5	100.0
>7.5	92.31	64.0 - 99.8	43.02	32.4 - 54.2	1.62	0.18	10.9	98.7
>10.8	92.31	64.0 - 99.8	62.79	51.7 - 73.0	2.48	0.12	15.7	99.1
>11	76.92	46.2 - 95.0	70.93	60.1 - 80.2	2.65	0.33	16.6	97.6
>12	61.54	31.6 - 86.1	76.74	66.4 - 85.2	2.65	0.50	16.6	96.4
>13	53.85	25.1 - 80.8	80.23	70.2 - 88.0	2.72	0.58	17.0	95.8
>14	38.46	13.9 - 68.4	87.21	78.3 - 93.4	3.01	0.71	18.5	95.0
>15	30.77	9.1 - 61.4	89.53	81.1 - 95.1	2.94	0.77	18.1	94.5
>16	15.38	1.9 - 45.4	89.53	81.1 - 95.1	1.47	0.95	10.0	93.4
>17.2	15.38	1.9 - 45.4	91.86	83.9 - 96.7	1.89	0.92	12.5	93.5
>18	7.69	0.2 - 36.0	94.19	87.0 - 98.1	1.32	0.98	9.1	93.1
>20	0.00	0.0 - 24.7	94.19	87.0 - 98.1	0.00	1.06	0.0	92.6
>32	0.00	0.0 - 24.7	100.00	95.8 - 100.0		1.00		93.0

DISCUSSION

Exclusion of carcinoma endometrium as the cause of PMB is the primary aim of evaluation in PMB patients. Fractional curettage is an invasive procedure and requires anesthesia and inherent risks of it. TVS has been suggested as a screening modality in patients with PMB. Increased endometrial thickness increases the risks of having malignancy.

Mean age of the population studied was 56.87±8.03 years, comparable to a previous study by Kaur et al.[20] The most common cause for PMB was atrophic endometrium (35.78%) followed by proliferative endometrium (27.59%) similar to the previously reported study. 31.4% each had atrophic and proliferative endometrium. Adenocarcinoma occurred in 4.5% of patients with PMB comparable to 5.71% observed by Kaur et al.[20]

Mean endometrial thickness was maximal in carcinoma endometrium i.e. 14.75±2.50 mm followed by atypical hyperplasia 14.21±5.29 mm. But Higher values 29.5±3.54 mm and 16.45±3.98 mm respectively were reported by Kaur et al. Proliferative endometrium and simple hyperplasia showed endometrial thickness of 13.47±5.14 mm and 13.33±4.63 mm respectively similar to the observations by Kaur et al.[20]

The receiver operating Characteristic curve (ROC) plotted using endometrial thickness against endometrial carcinoma and atypical hyperplasia. A cut off value of 10.8mm was identified. This cutoff had a high negative predictive value (99.1%) and low positive predictive value. sensitivity and specificity were 92.3% and 62.79% respectively. Previous report by Kaur et al showed a cut off value of 4 mm with a sensitivity and specificity 100% and 72.73% respectively. The positive predictive value was 87.5% and negative predictive value of 100%. Bindman SR et al reported that the risk of endometrium carcinoma is 6.7% if the endometrium is more than 11 mm thick and is 0.002% if the endometrium is below 11 mm.[21]

CONCLUSION

The thickness of endometrium as assessed by Transvaginal ultrasound (TVS) may be helpful in identifying the cause of post-menopausal bleeding (PMB). As per the ROC analysis of this study the endometrial thickness of 10.8 mm has a high negative predictive value (99.1%) for malignancy with moderate specificity (62.79%) and high sensitivity (92.3%).

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