A Study of Endometrial Pathology by Transvaginal Color Doppler Ultrasonography and its Correlation with Histopathology in Post-menopausal Women

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Abstract

Objective: Endometrial carcinoma is the most common gynaecological malignancy. Approximately 80% of endometrial carcinoma occur in post-menopausal women. Present study aimed to evaluate the role of transvaginal ultrasonography and colour flow imaging in diagnosing endometrial pathologies especially endometrial carcinoma and later its confirmation by histopathology.

Methods: 38 women presenting with history of at least 6 months amenorrhoea followed by bleeding per vaginum were included in the study. Transvaginal colour Doppler (TVS) followed by fractional curettage was done in all cases and cervical biopsy was done in selected cases. Uterine size, endometrial thickness and blood flow indices (RI, PI) were measured. Analysis of data was done using ‘z’ test and ‘t’ test.

Results: Out of 38 women maximum number of cases (39.47%) were between 50 – 55 years. Using 4 mm of endometrial thickness as cut off value for discriminating normal and abnormal endometrium, sensitivity, specificity, PPV and NPV were 94.12%, 50%, 95.12% and 50% respectively (p < 0.05). No case of endometrial carcinoma was detected when the endometrium was <4 mm, making the sensitivity as 100%, NPV 100%, specificity 13.33% and PPV 23.53%. Using RI = 0.81 as cut off value for discriminating benign and malignant endometrium, sensitivity was 62.5%, specificity 53.33%, PPV – 26.3% and NPV as 84.2%.

Conclusion: Transvaginal sonographic (TVS) evaluation of endometrial thickness (ET) is a reliable method of screening women with post-menopausal bleeding. Conservative approach may be offered to women showing ET of less than 4 mm and high impedance to flow in uterine and endometrial vessels.

Keywords
endometrial pathology, post-menopausal women, endometrial thickness (et), transvaginal colour doppler, histopathology

Introduction
Endometrial carcinoma is the most common
gynaecological malignancy. It is the seventh leading cause of death from malignancy in women, yet also the one with best survival statistics. There has been a steady increase in incidence over recent years which may be related to increased longevity, increased cholesterol in the diet, exogenous estrogen supplementation and probably better diagnostic methods.

Approximately, 80% of endometrial carcinoma occur in postmenopausal women, with bleeding as the initial symptom in 90% of cases. To diagnose endometrial pathology these women are subjected to diagnostic curettage. However, diagnostic curettage is an invasive procedure and not without danger in the elderly. The false negative rate for curettage is 2-6% because curettage may not empty the uretine cavity completely. Therefore, non invasive technique like ultrasonography is being utilized nowadays to detect endometrial carcinoma. Recently transvaginal colour and pulsed Doppler ultrasound has increased the reliability of ultrasonographic diagnosis of women with certain endometrial pathologies. It is able to detect subtle changes in the endometrium and it has been observed that endometrial thickness <4 mm is usually associated with normal morphology. This would help in selecting those patients who require diagnostic curettage, thus preventing an unnecessary operation. It also helps in localizing the tumour prior to diagnostic curettage thereby minimizing the chances of missing the lesion.

Mode of treatment and 5 year survival with endometrial carcinoma depends on the depth of myometrial invasion which can also be detected by transvaginal ultrasonography. The distinction between benign and malignant conditions is based on the detection of tumoral blood vessels that exhibit low impedance and high diastolic blood flow. Correlation between ultrasound estimated endometrial thickness and pathologically confirmed thickness may be as close as one millimeter. Ultrasound being non invasive and painless is highly acceptable to the atients.

Present study aimed to evaluate the role of transvaginal ultrasonography and colour flow imaging in diagnosing endometrial pathologies, especially endometrial carcinoma and later its confirmation by histopathology.

Material and Methods

38 women presenting with history of at least 6 months amenorrhoea followed by bleeding per vaginum were included in this study after informed consent.

Transvaginal color Doppler Sonogrpahy followed by fractional curettage was done in all cases and cervical biopsy was done in some selected cases. Besides, uterine size and endometrial thickness measurement, blood flow indices were measured like Pulsatility Index (PI) and Resistance Index (RI). Statistical analysis was done using ‘Z’ test and ‘t’ test.

Observation

38 women with post-menopausal bleeding were investigated with the aim to study the relationship between transvaginal ultrasonography, color Doppler imaging and histological changes in the endometrium.

Maximum number of cases were between 50-55 years i.e. 15 cases (39.47%). Median age was 52 years and ranged from 46 to 76 years. In the study group maximum number of 25 cases (65.79%) were more than para 4. Median was 5 and parity ranged from nulliparity to parity 10.

In post-menopausal women, normal length of uterus is usually between 4-6 cm; with 6 cm taken as the cut off value, 35 cases (92.1%) had bulky uterus (>6 cm in size) whereas only 3 cases (7.89%) had normal sized uterus. In our study, duration of menopause ranged from 6 months to 25 years with median as 2 years.

Correlation of Ultrasound with Histopathology Report

The category normal endometrium comprised the histologic diagnosis of atrophic endometrium and those reported as insufficient sample. The category abnormal endometrium included hyperplasia, proliferative endometrium, endometritis and endometrial carcinoma.

Table 1 shows that no case of abnormal endometrium was found when the size of uterus small i.e. < 6 cm whereas 34 cases of abnormal endometrium and one case of normal endometrium was found when the size of uterus was bulky i.e. >6 cm. Correlation between the size of uterus and endometrial pathology was highly significant.

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| Mean of Malignant endometrium = 16.36±7.1 mm, t = 3.4 (p<.01) significant |

Table 2 depicts that out of 38 patients, 4 cases had endometrium measuring less than 4 mm of which one each
were of atrophic, proliferative, hyperplastic endometrium and insufficient sample as reported on histopathological examination. Thus, when endometrial thickness was more than 4 mm, incidence of endometrial carcinoma was high which was even more when endometrial thickness was >10 mm. Using Z test, significant difference was found between the mean of benign and malignant endometrium.

Table 3 shows that using 4 mm of endometrial thickness as cut off value for discriminating normal and abnormal endometrium, sensitivity was 94.12%, specificity 50%, positive predictive value 95.12%, and negative predictive value 50%. Using ‘Z’ test, we found significant correlation between endometrial pathology and endometrial thickness.

Above table depicts that no case of endometrial carcinoma was detected when the endometrium was <4 mm thick, making the sensitivity of the study 100% and negative predictive value 100% with specificity 13.33% and positive predictive value 23.53%.

26 cases with benign endometrium had >4 mm of endometrial thickness and all the 8 cases of endometrial carcinoma had more than 4 mm thick endometrium. Thus using endometrial thickness we can exclude malignant endometrium with confidence but cannot differentiate between benign and malignant endometrium when endometrial thickness (ET) is > 4 mm (p < 0.05).

Using PI = 1.83 as cut off value for discriminating between benign and malignant endometrium, sensitivity was 75%, specificity 56.67%, positive predictive value 31.56% and negative predictive value 89.47% using ‘t’ test, no significant difference was observed between mean PI values of benign and malignant endometrium. Benign endometrium was associated with high mean RI value (0.95±0.21) ranging from 0.57 to 1.8 indicating high resistance to blood flow in uterine artery whereas malignant endometrium was associated with low value of mean RI (0.77±0.14) ranging from 0.55 to 0.96 suggesting a low resistance to blood flow in uterine artery in presence of malignancy. Using ‘t’

### Table 1
<table>
<thead>
<tr>
<th>Size of uterus (cm)</th>
<th>No. of women</th>
<th>Normal Endometrium</th>
<th>Abnormal Endometrium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>&lt;6</td>
<td>3</td>
<td>3</td>
<td>7.89</td>
</tr>
<tr>
<td>&gt;6</td>
<td>35</td>
<td>1</td>
<td>92.10</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>

Z = 5.4 (p<0.001), highly significant.

### Table 2
<table>
<thead>
<tr>
<th>Endometrial thickness in relation to various Histopathological Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women</td>
</tr>
<tr>
<td>ET (mm)</td>
</tr>
<tr>
<td>&lt;4</td>
</tr>
<tr>
<td>&gt;4</td>
</tr>
<tr>
<td>4-10</td>
</tr>
<tr>
<td>10-20</td>
</tr>
<tr>
<td>&gt;20</td>
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</tbody>
</table>

Mean of Benign endometrium = 9.2±67 mm
test, we observed significant difference between mean RI values of benign and malignant endometrium.

Table 5 shows that using RI = 0.81 as cut off value for discrimination between benign and malignant endometrium, sensitivity was 62.5% specificity = 53.33%, positive predictive value = 26.3% and negative predictive value was 84.2%.

Discussion

It is well known fact that cancer does not develop suddenly from normal but is preceded by various histological changes such as hyperplasia. If these changes are recognized and treated early then it will be possible to decrease significantly the frequency of invasive cancer. An effort has been made to predict the efficacy of transvaginal color Doppler sonography in discriminating between benign and malignant endometrium and whether ultrasonographic evaluation could help avoid an unnecessary curettage in these patients.

Results of previous studies have shown that endometrial thickness is a reliable method of detecting pathological changes in the endometrium. The maximum thickness of the atrophic endometrium as measured histologically in the previous studies is 3 mm. Based on these findings, we have chosen cut off limit of 4 mm of endometrial thickness for discriminating between normal and abnormal endometrium or between benign and malignant endometrium.

The maximum number of cases (50%) with benign endometrium were immediately postmenopausal whereas those with malignant endometrium were usually more than 10 years postmenopausal. Thus endometrial carcinoma in the present study was found to be more common after 10 years of attaining menopause. This is in accordance with Novak’s Gynaecology (12th Ed. 1996)\(^3\), that peak incidence of endometrial cancer occurs 10-15 years after average age of menopause.

In the present study, we observed significant difference
between the mean endometrial thickness in cases with benign endometrium i.e. 9.2 mm (S.D. = 4.67 mm) and in cases with malignant endometrium i.e. 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.

With <4 mm of endometrial thickness we found one case each of atrophy, proliferative endometrium and those reported as insufficient sample and one case of atypical hyperplasia associated with pyometra which could be the reason for compression of endometrium.

It was found that an atrophic endometrium was generally no more than 1 mm and should not exceed 3 mm. In another study it was found that the endometrium of less than 4 mm thickness as seen ultrasonography was well correlated with endometrial characteristics of decreased estrogen stimulation.

In the present study, 75% cases with endometrial thickness more than 20 mm were diagnosed as endometrial carcinoma. Thus, incidence of endometrial carcinoma was high when endometrium was >20 mm thick.

Using 4 mm of endometrial thickness as a cut off value for discriminating between normal and abnormal endometrium; sensitivity and positive predictive value were 91% and 94% respectively in our study. Using ‘Z’ test significant correlation was found between endometrial pathology and endometrial thickness (p<0.01).

No case of endometrial cancer was found when endometrium was less than 4 mm thick. Using 4 mm of endometrial thickness as cut off value, we observed high values of sensitivity (100%) and negative predictive value (100%), so endometrial thickness can be used as a reliable method for excluding malignancy in <4 mm endometrial thickness but cannot differentiate between benign and malignant endometrium.

One study reported sensitivity of 91% and specificity 100% using 5 mm as cut off value. Whereas another study reported sensitivity of 100%, specificity of 61%, positive predictive value 39% and negative predictive value 100%.

Thus, taking normal and abnormal endometrium into consideration, the predictability of endometrial thickness is high but when we take benign and malignant endometrium, the predictability is low.

Using cut off value of Pulsatility Index (PI) as 1.83 (median) for discriminating between benign and malignant endometrium, we observed that PI presented high values of sensitivity 75% and negative predictive value (NPV) 89.47 can be used for discriminating benign and malignant endometrium.

In the present study we observed sensitivity 62.5% specificity 53.3% PPV 26.8% and NPV 84.2% using RI of 0.81 (median) as cut off for discriminating between benign and malignant endometrium.

Table 6 depicts that endometrial thickness showed highest values of sensitivity and negative predictive value i.e. 100% as compared to Pulsatility Index and Resistive Index. Thus endometrial thickness is a reliable method of screening the women with postmenopausal bleeding, as histological examination might not be needed in patients with an endometrial thickness of 4 mm or less as measured by transvaginal ultrasound throughout the whole cavity.

Among blood flow indices Pulsatility Index appeared to be more reliable than Resistive Index and carried a sensitivity of 75%, specificity 36.67%, PPV 31.58% and NPV 89.47%.

Conclusion

Transvaginal ultrasound evaluation of endometrial thickness is a reliable method of screening women with postmenopausal bleeding. Colour Doppler can detect
neovascularization and decreased pulsatility index and resistive index in uterine and endometrial vessels in malignant conditions.

Thus, a conservative approach may be offered to women with post menopausal bleeding showing endometrial thickness of <4 mm and high impedance to flow in the uterine artery, thereby avoiding the need for curettage in large number of women.

References


