Thickened Endometrium in Asymptomatic Postmenopausal Women: Is Biopsy Mandatory?

SOHA SIAM, M.D. and AZZA A. ABD EL-HAMEED, M.D.
The Departments of Obstetrics and Gynecology, Faculty of Medicine, Zagazig University, Egypt

Abstract

Objectives: To evaluate the value of endometrial sampling and histopathology for asymptomatic postmenopausal women with endometrial thickness ≥5mm.

Population: Two hundred sixty one asymptomatic postmenopausal women with thick endometrium ≥5mm accidentally discovered during investigations for reasons other than vaginal bleeding.

Method: Cases with confirmed thick endometrium ≥5mm by TVS underwent outpatient endometrial sampling by chairman curette and sent for histopathology.

Results: The TVS findings (endometrial thickening of 5mm or more) were associated with normal endometrium in 237 (90.8%) cases. Abnormal endometrial pathology was detected in 24 (9.1%) cases, it was; simple hyperplasia in 19 (7.2%) cases and complex hyperplasia in three (1.1%) case, endometrial cancer in two (0.7%) cases. Validity tests to predict abnormal endometrium at different cut off values for endometrial thickness shows that cut off values of 5 and 6mm had the highest sensitivity while that of 11 and 12mm had the highest specificity.

Conclusion: Although endometrial thickness was significantly higher in asymptomatic postmenopausal women with abnormal endometrial histopathology, there is no cut off value that has accepted both sensitivity and specificity and the need for further evaluation for these cases is not routinely advised.

Key Words: Thick endometrium – Postmenopausal women – Endometrial sampling.

Introduction

ENDOMETRIAL cancer is the most common gynecological malignancy and the fourth most frequent site of malignant neoplasm in females in most western countries [1].

TVS is an excellent non invasive diagnostic method for determining endometrial pathologies. A relationship between endometrial thickness (as measured by TVS) and endometrial malignancy has been shown in different studies [2].

The endometrium of postmenopausal women is thin and atrophic, usually less than 10mm in total thickness, occasionally small amount of intraluminal fluid may be present [3]. In cases presenting with postmenopausal bleeding, the fining of thin endometrial (<5mm) rules out about 99% of endometrial cancer, however, in many situations with endometrial thickness >5 and postmenopausal bleeding, no endometrial pathology found. That is to say many women will be exposed to unnecessary D and C or hysteroscopy which carry potential risks [4].

It has been suggested that screening of asymptomatic endometrial cancer by transvaginal ultrasound before the onset of clinical symptoms, i.e., postmenopausal bleeding, leads to an earlier diagnosis [5]. As in other malignancies, it can be hypothesized that an earlier diagnosis leads to a lower stage of disease, a less radical surgery, a therapy with less side effects and, subsequently, a better prognosis of the affected patients [6].

The aim of this study: Is to determine the value of further management (through endometrial sampling and histopathology) of increased endometrial thickness in postmenopausal women subjected to pelvic scans for reasons other than vaginal bleeding.

Patients and Methods

This cross sectional study was performed at Obstetrics and Gynecology department, Zagazig University Hospitals from June 2008 to October 2010.

The study was approved by the hospital ethics committee and informed consent was obtained from all participants.
Two hundred sixty one women included in the study met the following inclusion criteria: menopause duration of at least one year, no history of vaginal bleeding since menopause, TVS with evidence of endometrial thickness ≥5mm, no other pelvic or uterine masses.

Exclusion criteria includes; history of HRT, Tamoxifen, Raloxifene for the last year, endometrial procedures done within the last year (biopsy or D&C), known uterine lesions proved by histopathology within the last year.

All patients were subjected to, history taking (age, occupation, smoking, parity, history of HRT and Medical history). Duration since menopause is also recorded.

Clinical examination with special attention to BMI, blood pressure, any suspected pelvic or pelvis-abdominal masses.

Ultrasound examinations were performed using medical system (GE healthcare, Voluson 730 pro V, Austria) equipped with a multi frequency 5-7.5-MHz abdominal and TVS probes. Examination was performed by an expert examiner blind to the initial TVS results.

All women were examined in the lithotomy position with an empty bladder.

Uterine dimensions were measured in the mid-sagittal plane, so that the endometrium was visible from fundus to cervix. The double layer endometrial thickness was measured within 1cm from the uterine fundus or at its widest point in cases of asymmetrical endometrial appearance [7].

Endometrial sampling was done for all cases as an outpatient procedure using Chairman Curette without anesthesia. Samples were taken from anterior, posterior uterine wall and uterine fundus and sent for histopathological examination.

The main outcome measure was finding of abnormal endometrium (endometrial cancer or endometrial hyperplasia).

Statistical analysis:

Statistical calculations were performed using SPSS versions 12.2 and 16.0 (SPSS Inc., Chicago, IL., USA). Data represented as mean, standard deviation, number, percentage, student t-test was used, and evaluation of predictive power was done by measuring sensitivity, specificity, positive predictive value and negative predictive value. p-value, less than 0.05 was considered to be statistically significant.

Results

The demographic data of the studied group was illustrated in Table (1). The mean age (mean ±S.D.) was 56.0±7.0 years (range: 43-73 years); body mass index BMI (kg/m²) was 23.2±3.4 (from 21-36); the average years since menopause were 10.2±8 (range 1-27); and parity 5 ±2.13 (range zero-8).

The TVS findings (endometrial thickening of 5mm or more) were associated with normal endometrium in 237 (90.8%) cases. Abnormal endometrial pathology was detected in 24 (9.1%) cases, it was; simple hyperplasia in 19 (7.2%) cases and complex hyperplasia in three (1.1%) case, endometrial cancer in two (0.7%) cases (Table 2).

The mean endometrial thickness was 11.7±1.6mm (range: 8-17mm) in simple hyperplasia cases, 13.4±1.2 in the complex hyperplasia cases, 16mm & 17mm in the endometrial cancer cases.

Cases with abnormal endometrial finding had significantly higher age, lower parity and increased mean endometrial thickness measured by TVS than those with normal endometrium (Table 3).

Table (4) shows validity tests to predict abnormal endometrium at different cut off values for endometrial thickness, cut off values of 5 and 6mm had the highest sensitivity while that of 11 and 12mm had the highest specificity. At cut off value 5mm, specificity and NPV was 0% as all our cases had endometrial thickness ≥5mm.

![Fig. (1): Flow chart of the study population.](image-url)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(Mean±S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>56.0±7.0</td>
</tr>
<tr>
<td>Parity</td>
<td>5±2.13</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2±3.4</td>
</tr>
<tr>
<td>Duration since menopause</td>
<td>10.2±8</td>
</tr>
</tbody>
</table>
Table (2): Histopathology of the obtained specimens.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>237 (90.8%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>24 (9.1%)</td>
</tr>
<tr>
<td>Simple endometrial hyperplasia</td>
<td>19 (7.2%)</td>
</tr>
<tr>
<td>Complex endometrium hyperplasia</td>
<td>3 (1.1%)</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>2 (0.7%)</td>
</tr>
</tbody>
</table>

Table (3): Comparison between those with normal and abnormal endometrial findings.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal endometrium N=237 (90.8%)</th>
<th>Abnormal endometrium N=24 (9.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.4±6.2</td>
<td>59.6±6.82**</td>
</tr>
<tr>
<td>Parity</td>
<td>5.2±2.64</td>
<td>3.8±2.4*</td>
</tr>
<tr>
<td>BMI</td>
<td>23.1±4.2</td>
<td>23.7±4.51</td>
</tr>
<tr>
<td>Duration since menopause</td>
<td>10.1±7.8</td>
<td>10.8±7.23</td>
</tr>
<tr>
<td>Endometrial thickness</td>
<td>7.8±1.6</td>
<td>12.8±2.11**</td>
</tr>
</tbody>
</table>

* = Significant p<0.05.
** = Highly significant p<0.005.

Table (4): Sensitivity, specificity, PPV and NPV of endometrial thickness measured by TVS at different cutoffs levels to predict abnormal endometrium.

<table>
<thead>
<tr>
<th>Endometrial thickness (mm)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>100</td>
<td>0.0</td>
<td>9.2%</td>
<td>0.0</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>8.68</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>7</td>
<td>91.66</td>
<td>40.5</td>
<td>13.9</td>
<td>97.96</td>
</tr>
<tr>
<td>8</td>
<td>79.16</td>
<td>51.05</td>
<td>14.07</td>
<td>90.03</td>
</tr>
<tr>
<td>9</td>
<td>66.66</td>
<td>56.1</td>
<td>13.3</td>
<td>94.3</td>
</tr>
<tr>
<td>10</td>
<td>62.5</td>
<td>72.15</td>
<td>8.06</td>
<td>95</td>
</tr>
<tr>
<td>11</td>
<td>54.1</td>
<td>85.65</td>
<td>6.01</td>
<td>94.86</td>
</tr>
<tr>
<td>12</td>
<td>54.1</td>
<td>95.35</td>
<td>5.4</td>
<td>95.35</td>
</tr>
</tbody>
</table>

Discussion

In asymptomatic women (without AUB), the value of measurement of endometrial thickness has not been documented. A clinical dilemma arises when discovering thick endometrium in those women [8].

A guideline by the Austrian Society of Gynecology and Obstetrics (OEGGG) and the Austrian Society of Gynecologic Oncology (AGO) recommends endometrial sampling in cases of a postmenopausal bleeding or an endometrial thickness ≥11mm in asymptomatic women [9].

In our study, we use the 5mm as cutoff value for investigating asymptomatic postmenopausal women for the following:

- The risk of endometrial cancer in even asymptomatic postmenopausal women (vaginal bleeding) and ET <5mm is very low (0.1-1%).
- Almost all women with endometrial cancer have an ET ≥5mm.
- When a cut-off value of 5mm is used, the sensitivity of detecting endometrial cancer (using TVS) is comparable with that of the endometrial biopsy [10].

Why do we use an ET cut-off of 5mm rather than 4mm?

Smith-Bindman and colleagues [11] found that lowering the ET cut-off to 4mm causes only a little decrease in the sensitivity, but a substantial decrease in the specificity (which means more false positive results) for cancer detection [11].

Our study included asymptomatic postmenopausal women with thick endometrium to evaluate importance of further management of such group of women (by endometrial sampling and histopathology).

Some studies found that asymptomatic patients with endometrial cancer have a better prognosis than those presents after the onset of a postmenopausal bleeding. However, these studies are few [6,12-14].

Endometrial sampling is a simple office procedure which is less invasive than D&C to sample small areas of the endometrium, but it is not known whether this technique is as reliable as D&C in postmenopausal women without focal lesions [18]. This office-based procedure may miss up to 18% of focal lesions of the endometrium including polyps and fibroids [16].

In this study abnormal endometrial pathology was detected in 24 (9.1%) cases, which was simple hyperplasia in 19 (7.2%) cases, complex hyperplasia in three (1.1%) cases, endometrial cancer in two (0.7%) cases. Endometrial thickness was significantly higher in cases with abnormal histopathology of the endometrium than those with normal histopathology.

Gambacciani and colleagues [17] reviewed 850 postmenopausal women referred for hysteroscopy, of which 148 was asymptomatic (bleeding free), and with endometrial thickness >5mm, endometrial abnormality was found in 6.8%, which were en-
dometrial hyperplasia in 8 cases (5.4%), complex hyperplasia in one (0.7%) and endometrial cancer in one case (0.7%). In 93.2%, TVS (endometrial thickness cutoff >5mm) was falsely positive, so that most of these women referred to hysteroscopy were subjected to this unnecessary, invasive procedure. Really, in most of the women examined by hysteroscopy exclusively due to ultrasound indication (endometrial thickness: >5mm), the histological evaluation of endometrial specimens revealed atrophy to normal endometrium [17].

In a sub study of the PEPI trial, 53% of the women with normal biopsies had an endometrial thickness of at least 5mm [18]. In a another prospective, multicenter study to compare TVS and endometrial biopsy in postmenopausal women on HRT, The range of endometrial thickness in women with a histologically normal endometrium was 1.0-25.0mm [19].

In this study no single cut off value which had accepted both sensitivity and specificity, value of 6mm had the highest sensitivity and NPV (100% for both), while value of 11 and 12mm had the highest specificity (85.65 and 95.35% respectively). PPV was low at different cut off values, this means that there are high false positive results.

In a study performed by Aboul Foutoh et al. [20]; when they considered an endometrial thickness of 5mm as a cut off value for prediction of endometrial malignancy they found that it had 100% sensitivity, 51.9% specificity, 60.9% positive predictive value, 100% negative predictive value, when raising the cut off value to 8 mm it was found to have 100% sensitivity, but with much higher specificity, positive predictive value and negative predictive value (80.4%, 73.7% and 100% respectively).

It is of importance to mention that, our study was not performed to evaluate the advantages of a transvaginal ultrasound in the screening of endometrial cancer.

Conclusion: Although endometrial thickness was significantly higher in asymptomatic postmenopausal women with abnormal endometrial histopathology, there is no cut off value that has accepted both sensitivity and specificity and the need for further evaluation for these cases is not routinely advised.

References


