ABSTRACT: The clinical approach to postmenopausal bleeding requires prompt and efficient evaluation to exclude or diagnose carcinoma. Women with postmenopausal bleeding may be assessed initially with either endometrial biopsy or transvaginal ultrasonography; this initial evaluation does not require performance of both tests. Transvaginal ultrasonography can be useful in the triage of patients in whom endometrial sampling was performed but tissue was insufficient for diagnosis. When transvaginal ultrasonography is performed for patients with postmenopausal bleeding and an endometrial thickness of less than or equal to 4 mm is found, endometrial sampling is not required. Meaningful assessment of the endometrium by ultrasonography is not possible in all patients. In such cases, alternative assessment should be completed. When bleeding persists despite negative initial evaluations, additional assessment usually is indicated.

Cancer of the endometrium is the most common type of gynecologic cancer in the United States. In 2008, an estimated 40,100 cases of cancer of the endometrium will occur and an estimated 7,470 deaths (1). Vaginal bleeding is the presenting sign in more than 90% of postmenopausal patients with endometrial carcinoma (2). The majority of patients with postmenopausal vaginal bleeding experience bleeding secondary to atrophic changes of the vagina or endometrium. However, depending on age and risk factors, 1–14% will have endometrial cancer (3–6). Thus, the clinical approach to postmenopausal bleeding requires prompt and efficient evaluation to exclude or diagnose carcinoma.

Transvaginal Ultrasonography

Transvaginal ultrasonography has been explored as an alternative technique to indirectly visualize the endometrium. Endometrial thickness is measured as the maximum anterior–posterior thickness of the endometrial echo on a long-axis transvaginal view of the uterus. The earliest reports comparing transvaginal ultrasonography with endometrial sampling consistently found that an endometrial thickness of less than or equal to 4–5 mm in patients with postmenopausal bleeding reliably excluded endometrial cancer (7–9). Since that time, a number of confirmatory multicenter trials have been completed (see Table 1). Because transvaginal ultrasonography in postmenopausal patients with bleeding has an extremely high negative predictive value, it is a reasonable first approach. An endometrial thickness of greater than 4 mm is not diagnostic of any particular pathology and cannot be relied on to exclude disease.

Biopsy Findings of Tissue Insufficient for Diagnosis

Endometrial tissue sampling resulting in findings insufficient for diagnosis is common. In a study of 97 consecutive patients with postmenopausal bleeding evaluated by transvaginal ultrasonography and endometrial biopsy, in only 82% of the patients with an endometrial thickness of less than 5 mm (n=45) was a Pipelle biopsy able to be performed (10). Of these patients, a sample adequate for diagnosis was obtained in only 27%. There was no correlation with parity or cavity length. In other studies of patients...
with postmenopausal bleeding, the range of sampling failure (ie, inadequate sample or inability to perform the biopsy) with Pipelle biopsy was 0–54% (11).

Transvaginal ultrasonography can be useful in the triage of patients in whom endometrial sampling was performed but tissue was insufficient for diagnosis (12). No further evaluation is necessary following an insufficient endometrial biopsy if subsequent transvaginal ultrasonography demonstrates an endometrial thickness of less than or equal to 4 mm in a woman with postmenopausal bleeding because the incidence of malignancy is rare in these cases (Table 1). However, if bleeding recurs or persists, additional evaluation usually is indicated.

### Postmenopausal Patients Without Bleeding

Whereas several studies have evaluated transvaginal ultrasonography in postmenopausal women with bleeding, there are fewer data on transvaginal ultrasonography endometrial findings in patients without bleeding. In 1,750 postmenopausal women without bleeding being screened for a selective estrogen receptor modulator study, an endometrial thickness of less than or equal to 4 mm had a negative predictive value of 99.94% for excluding malignancy (only 1 case of cancer in 1,750 women) and a 99.77% negative predictive value for complex hyperplasia (only 4 cases in 1,750 women) (13). Among 42 patients with endometrial thickness of greater than 6 mm, there was 1 case of adenocarcinoma and no cases of hyperplasia (positive predictive value = 2.4%).

In another study, 82 asymptomatic postmenopausal women had an incidental ultrasonographic finding suspected to be an intrauterine polyp (14). All underwent operative hysteroscopy. Of these patients, a benign polyp was found in 68, submucosal myoma in 7, atrophic endometrium in 6, and proliferative endometrium in 1. One polyp contained simple hyperplasia. There were no cases of endometrial carcinoma or complex hyperplasia. The total complication rate was 3.6% (two perforations, one difficult intubation).

The significance of an endometrial measurement greater than 4 mm incidentally discovered in a postmenopausal patient without bleeding has not been established. This finding need not routinely trigger evaluation, although an individualized assessment based on patient characteristics and risk factors is appropriate. Transvaginal ultrasonography is not an appropriate screening tool for cancer in postmenopausal women without bleeding.

### Limitations

It is not possible to complete a meaningful transvaginal ultrasound examination with a reliable measurement of endometrial thickness in all patients (15). An axial uterus, marked obesity, coexisting myomas, or previous uterine surgery all can contribute to difficulty in obtaining reliable transvaginal ultrasound assessment of endometrial thickness and texture. Failure to adequately identify a thin, distinct endometrial thickness in a postmenopausal patient with bleeding should trigger some alternative method of evaluation. In addition, when endometrial fluid is present, it should not be included in measuring endometrial thickness.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Endometrial Thickness*</th>
<th>Number of Women</th>
<th>Number of Cases of Cancer</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karlsson 1995†</td>
<td>≤4 mm</td>
<td>1,168</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Ferrazzi 1996‡</td>
<td>≤4 mm</td>
<td>930</td>
<td>2</td>
<td>99.8%</td>
</tr>
<tr>
<td></td>
<td>≤5 mm</td>
<td></td>
<td>4</td>
<td>99.6%</td>
</tr>
<tr>
<td>Gull 2000§</td>
<td>≤4 mm</td>
<td>163</td>
<td>1</td>
<td>99.4%</td>
</tr>
<tr>
<td>Epstein 2001</td>
<td></td>
<td></td>
<td>≤5 mm</td>
<td>97</td>
</tr>
<tr>
<td>Gull 2003¶</td>
<td>≤4 mm</td>
<td>394</td>
<td>0</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Determined by transvaginal ultrasonography


|| Epstein E, Valentin L. Rebleeding and endometrial growth in women with postmenopausal bleeding and endometrial thickness < 5 mm managed by dilatation and curettage or ultrasound follow-up: a randomized controlled study. Ultrasound Obstet Gynecol 2001;18:499–504.

**Recommendations**

- Any vaginal bleeding in a postmenopausal woman requires assessment to exclude malignancy.
- Women with postmenopausal uterine bleeding may be assessed initially with either endometrial biopsy or transvaginal ultrasonography; this initial evaluation does not require performance of both tests.
- When endometrial biopsy is performed and tissue is reported as insufficient for diagnosis, some further investigation is necessary and transvaginal ultrasonography may be performed.
- When transvaginal ultrasonography is performed for patients with postmenopausal bleeding and an endometrial thickness of less than or equal to 4 mm is found, endometrial sampling is not required.
- Endometrial thickness of greater than 4 mm in a patient with postmenopausal bleeding should trigger alternative evaluation (such as sonohysterography, office hysteroscopy, or endometrial biopsy), as should an inability to adequately visualize thickness.
- Meaningful assessment of the endometrium by ultrasonography is not possible in all patients. In such cases, alternative assessment should be completed.
- When bleeding persists despite negative initial evaluations, additional assessment usually is indicated.
- The significance of an endometrial thickness of greater than 4 mm in an asymptomatic, postmenopausal patient has not been established, and this finding need not routinely trigger evaluation.

**References**


Copyright © August 2009 by the American College of Obstetricians and Gynecologists, 409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, posted on the Internet, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher. Requests for authorization to make photocopies should be directed to: Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400.

ISSN 1074-861X