Cancer of the endometrium is the most common type of gynecologic cancer in the United States. Vaginal bleeding is the presenting sign in more than 90% of postmenopausal women with endometrial carcinoma. Most women with postmenopausal vaginal bleeding (PMB) experience bleeding secondary to atrophic changes of the vagina or endometrium. Depending on age and risk factors, 1% to 14% of women with PMB will have endometrial cancer, although most studies suggest it is in the 3% to 7% range.

**Histologic evaluation.** For much of the last half of the twentieth century, dilatation and curettage (D&C) with review of pathology was the cornerstone of diagnosis. As early as 1975, researchers realized that by doing prehysterectomy D&Cs, up to 50% of the uterine cavity went unsampled with these blind procedures.2 Reusable metal cannulas attached to a suction machine allowed sampling to move into the office. In the 1980s, disposable suction piston devices (Pipelle was the original brand name) were introduced and, because they were noted to have similar diagnostic yield as metal cannulae while causing less patient discomfort, became widely employed for endometrial sampling in the United States. A widely publicized study of women with known carcinoma using the Pipelle device for endometrial sampling found cancer in 39 out of 40 of such women, thus claiming 97.5% accuracy and resulting in Pipelle and similar devices becoming the standard approach to diagnosis of women with any abnormal uterine bleeding, including PMB.3 A subsequent study of 65 women with known carcinoma missed 11 out of 65, or 16%, of the cancers.4 Of note, on opening the uteri, it was found that all those missed cancers occupied less than 50% of the surface area of the endometrial cavity.

Finally in 2012, the American College of Obstetricians and Gynecologists (ACOG), although stating that an office endometrial biopsy represents the first-line procedure for tissue sampling, acknowledged that when a cancer occupies less than 50% of the surface area, it may be missed using this diagnostic technique and that a positive test is more accurate for ruling in disease than a negative test is for ruling it out; “therefore, these tests are only an endpoint when they reveal cancer or atypical complex hyperplasia.”5 This represents a major shift in how blind endometrial sampling should be viewed.
**Transvaginal ultrasound.** The earliest reports comparing transvaginal ultrasound (TVU) with endometrial sampling in women with PMB consistently found that an endometrial thickness 4 mm to 5 mm or less reliably excluded endometrial cancer. Since that time, a number of confirmatory multicenter studies have been performed. Accordingly, ACOG in 2009 stated that when TVU images a thin, distinct endometrial echo 4 mm or less, the risk of malignancy is 1 in 917, and therefore, endometrial sampling is not required. Thus the initial evaluation of women with PMB may begin with a TVU, and if sufficiently distinct and thin, no further workup is necessary. In fact, if one does attempt endometrial sampling in such women, often no tissue is present, and if present, it is often insufficient for histologic evaluation.

**Limitations of transvaginal ultrasound.** Transvaginal ultrasound does not adequately image the endometrial cavity in all women with PMB. An axial uterus, obesity, coexisting myomas, adenomyosis, or previous uterine surgery can preclude satisfactory endometrial evaluation. Failure to adequately identify a thin, distinct endometrial echo in a postmenopausal woman with bleeding should trigger an alternative method of evaluation. Endometrial fluid, which may result from atrophic changes or cervical stenosis, may be identified when TVU is performed in women with PMB. When present, such fluid should not be included in the measurement of endometrial thickness.

**Alternative evaluation.** When alternative evaluation is necessary, saline infusion sonohysterography (SIS) or hysteroscopy, preferably in an office setting, is appropriate. Saline infusion sonohysterography involves instillation of a small amount of saline through a special catheter under ultrasound guidance. By distending the endometrial cavity, SIS highlights the endometrial contents, revealing causes of PMB, including endometrial polyps, intracavitary (submucosal) fibroids, and diffuse endometrial abnormalities suggestive of hyperplasia or cancer. A sonohysterogram demonstrating uniformly smooth endometrial surfaces without intracavitary masses provides reassurance that organic pathology is not present. An alternative to SIS involves using new disposable office hysteroscopes that facilitate direct endometrial visualization in the office setting.

**Postmenopausal women without bleeding.** As use of TVU in postmenopausal women has grown, some clinicians have inappropriately extrapolated this information to assume that a thick endometrial echo, discovered incidentally, is abnormal and requires investigation. One prospective study in an unselected asymptomatic population of postmenopausal Danish women revealed that 13% had a benign endometrial polyp on sonohysterography. In another study, operative hysteroscopy was performed in 82 asymptomatic postmenopausal women in whom TVU had a thick endometrial echo suspected to be a polyp, with no cases of endometrial carcinoma or complex hyperplasia identified. Perioperative complications occurred in 3.6% of these women (two perforations, one difficult intubation).

What is the risk of malignancy in such cases? A multicenter trial in Italy removed 1,152 polyps from asymptomatic postmenopausal women diagnosed by sonohysterography and reported one grade 1 carcinoma in a polyp, although three other women had a malignancy that was focal in nature and had appeared polypoid on sonohysterography. Thus, the overall incidence of any cancer in this cohort of asymptomatic women was 1 in 288. A German study found that 5-year survival was similar for endometrial cancers discovered incidentally and those treated within 8 weeks of their clinical postmenopausal bleeding presentation. Accordingly, when TVU identifies an incidental finding of a homogeneous-appearing endometrial echo greater than 4 mm
in a postmenopausal woman without bleeding, further evaluation is not routinely indicated. However, individualized assessment based on patient characteristics and risk factors such as obesity, diabetes, or hypertension is always appropriate and represents good clinical judgment.

As more women have undergone endometrial ablation, clinicians are encountering more menopausal patients with bleeding after ablation. Unfortunately, evaluating such women can be challenging because in some cases, adequate endometrial biopsy, sonohysterogram, or hysteroscopy is not feasible because of iatrogenic scarring. There are no data on how to proceed in such instances, and decision making is done on a case-to-case basis.

To summarize, postmenopausal bleeding mandates evaluation. If TVU reveals a distinct, thin (≤ 4 mm) endometrial echo in women of average risk, this represents a sufficient initial evaluation. If an initial evaluation is done with blind endometrial sampling, unless the result is positive (endometrial cancer or complex atypical hyperplasia), the evaluation is not complete. After either approach to initial evaluation of PMB, if bleeding persists, alternative evaluation should be undertaken: SIS or hysteroscopy, preferably in an-office setting. Finally, a thick endometrial echo found incidentally in a nonbleeding woman is more prevalent than previously appreciated and need not trigger additional evaluation unless significant comorbid risk factors (ie, obesity, diabetes, or hypertension) are present.

References


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This *Practice Pearl*, developed by the author, provides practical information on current controversial topics of clinical interest. It is not an official position of The North American Menopause Society (NAMS). Clinicians must always take into consideration the individual patient along with any new data published since the publication of this statement. The *Practice Pearl* series is coordinated by the NAMS *Practice Pearl* Task Force, edited by Dr. Andrew Kaunitz, and approved by the NAMS Board of Trustees.

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