GENERAL GYNECOLOGY

The role of transvaginal ultrasound or endometrial biopsy in the evaluation of the menopausal endometrium

Steven R. Goldstein, MD

All postmenopausal women with vaginal bleeding need endometrial assessment. Disposable suction piston biopsy devices have virtually replaced dilatation and curettage despite little scientific validation. In patients with known carcinoma, false-negative rates with such devices range from 2.5-32.4%. Large prospective studies have shown that an endometrial thickness ≤ 4 mm on transvaginal ultrasound in postmenopausal women with bleeding has a risk of malignancy of 1 in 917. Thus, in postmenopausal patients with bleeding, biopsy is not indicted when endometrial thickness is ≤ 4 mm. The significance of a thick endometrial echo in nonbleeding postmenopausal women has not been validated and need not require automatic tissue sampling.

Key words: Abnormal uterine bleeding, endometrial biopsy, endometrial thickness, postmenopausal bleeding, transvaginal ultrasound

Endometrial assessment is indicated in all postmenopausal women with any vaginal bleeding. Disposable suction piston devices have virtually replaced dilatation and curettage (D&C) despite little scientific validation. Transvaginal (TV) ultrasound (U/S) provides highly magnified images of endometrial contents. There is great confusion about the reliability of a thin distinct endometrial echo on TV U/S, especially in relationship to the reliability of a blind endometrial biopsy with a suction piston device. Significant prospective studies support the notion that a thin distinct endometrial echo ≤ 4 mm in a postmenopausal woman with bleeding will have an incidence of malignancy of about 1 in 1000. The sensitivity of suction piston biopsy done in patients with known carcinoma has reported false-negative rates ranging from 2.5-32.4%. The significance of a thick endometrial echo in nonbleeding postmenopausal women has not been validated. Of postmenopausal women, 10-17% have asymptomatic polyps. The incidence of malignancy in such polyps from reports cited have been 0%, 0%, 0%, and 2.4%. Finally, not all uteri lend themselves to a meaningful TV U/S determination because of things such as coexisting fibroids, axial uterus, preexisting surgery, or morbid obesity, all of which may impair the ability to use TV U/S as a reliable tool.

★ EDITORS' CHOICE ★

It has been almost 20 years since the first reports using TV U/S measurement of endometrial thickness in postmenopausal women with bleeding[1-3] have appeared. Although there have been many significant studies and many publications, it seems that there is still great confusion about the role of TV U/S in clinical treatment of such patients. The high negative predictive value of a thin distinct echo on TV U/S in postmenopausal women who present with bleeding is very different than thick measurements incidentally obtained on TV U/S in women who are asymptomatic (ie, no bleeding since the menopausal transition). This latter scenario has not been validated or adequately studied in a prospective fashion but data that do exist do not support the notion that such nonbleeding patients need to automatically have tissue obtained for histologic examination.

Furthermore, what exactly constitutes postmenopausal bleeding is not so easily defined. Menopause is defined as the final menstrual period. Obviously a woman has no way of knowing that the bleeding episode that has just occurred will be her last. Measurement of follicle-stimulating hormone (FSH) and estradiol levels are notoriously unreliable because, although they may indicate a lack of ovarian response to an increased pituitary FSH at that moment, resumption of some ovarian function in the ensuing months is not uncommon. In other words, the erratic function of the ovaries in late perimenopause often makes it difficult to label a woman's bleeding as definitively "postmenopausal." Generally, menopause has been defined as no bleeding for 12 months as a result of a depletion of ovarian follicles. Thus the patient who presents with clinical signs of menopause, with or without laboratory correlation of FSH levels, and then bleeds after 1 year of no bleeding, must be approached as "endometrial cancer until proven otherwise."

In the United States, cancer of the endometrium is the most common gynecologic cancer. In 2008 the American Cancer Society estimated that 41,520 cases of cancer of the uterine corpus would be diagnosed resulting in 8145 deaths.[4] Vaginal bleeding will be the presenting sign in more than 90% of postmenopausal patients with endometrial carcinoma.[5] The majority of patients with postmenopausal vaginal bleeding actually bleed secondary to atrophic changes of the vagina or endometrium.

From the Department of Obstetrics and Gynecology, New York University School of Medicine, New York, NY.

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However, 1-14% of postmenopausal women with bleeding will have endometrial cancer depending on age and risk factors.[6-9] Thus, the clinical approach to postmenopausal bleeding requires prompt and efficient evaluation to exclude carcinoma.

Women who are not clearly menopausal with abnormal bleeding need evaluation as well. In fact, the American College of Obstetrician and Gynecologists Practice Bulletin No. 14 states that,[10] "There is a distinct increase in the incidence of endometrial carcinoma from ages 30-34 years (2.3/100,000 in 1995) to ages 35-39 (6.1/100,000 in 1995). Therefore based on age alone, endometrial assessment to exclude cancer is indicated in any woman older than 35 years who is suspected of having anovulatory uterine bleeding."

In addition, women < 35 years who have sufficient risk factors (eg, morbid obesity, polycystic ovary syndrome) may also require endometrial evaluation. Much of the evaluation of such nonmenopausal patients is similar to that in menopausal patients. The biggest difference (and this is fundamentally crucial) is that if one uses TV U/S or sonohysterography in women who still have endogenous ovarian function (ie, they are making estrogen) then any U/S evaluation must be timed to the end of the bleeding episode and be done as soon as possible after the bleeding ends when the endometrial thickness will be as thin as possible.[11] In postmenopausal women with no estrogen stimulation and thus no "cycling," U/S evaluation is not time sensitive and can be performed at any time. In the event a patient is on hormone therapy, this will depend on the type of hormone therapy used. In continuous combined hormone therapy there is no cycling and evaluation is not time sensitive. With sequential hormone therapy, there is development of the functionalis of the endometrium by estrogen and then sloughing after the administration of a progestogen. These patients should be evaluated like other cycling patients (ie, as soon as possible after the bleeding ends).

Historical background

Gynecologists have long approached postmenopausal bleeding as "endometrial cancer until proven otherwise." The traditional gold standard for endometrial evaluation was the D&C. First described in 1843,[12] its performance in the hospital became the most common operation performed on women in the world. As early as the 1950s, a review of 6907 curettage procedures[13] found the technique missed endometrial lesions in 10% of cases. Of these, 80% were polyps. A study of curettage before hysterectomy[14] found that in 16% of specimens less than one-quarter of the cavity was curetted, in 60% of specimens less than one-half of the cavity was curetted, and in 84% of specimens less than three-quarters of the endometrial cavity was effectively curetted.

In the 1970s, vacuum-suction curettage devices allowed sampling without anesthesia in an office setting. The most popular was the Vabra (Berkeley Medevices, Berkeley, CA) aspirator. This was 86% accurate in diagnosing cancer.[15] Subsequently, cheaper, smaller, less painful plastic catheters with their own internal pistons to generate suction became popular. One of these, the Pipelle (Unimar; Cooper Surgical, Trumbull, CT) device, had similar efficacy but better patient acceptance when compared with the Vabra.[16]

Pipelle gained widespread acceptance with very little validation. It was first described by Cornier[17] in 1984 in an article entitled "The Pipelle: a disposable device for endometrial biopsy." Subsequently, from 1988-1991, there were 8 articles, of which 7 evaluated Pipelle (often compared with other methods) for timed endometrial biopsy in the luteal phase of the menstrual cycle as part of an infertility evaluation–something no longer used. An article by Kaunitz et al[16] compared Pipelle with Vabra aspiration in 56 patients and found that the final diagnosis was concordant in 50 (89%) of 56. They concluded that Pipelle had similar efficacy to Vabra but much higher patient acceptability (ie, comfort). In 1991 Stovall et al[18] performed Pipelle on 40 patients with known carcinoma in the clinic before their scheduled hysterectomy. They identified endometrial carcinoma in 39 of 40, yielding a sensitivity of 97.5%. These findings were widely advertised throughout the early 1990s and suction devices with their own internal pistons were rapidly adopted as the method of choice for endometrial evaluation. Compared with D&C and the Vabra aspirator such suction piston biopsy instruments were safe, easy, inexpensive, and resulted in less patient discomfort or need for anesthesia or analgesia. It is easy to understand why clinicians rapidly adopted this as the method of choice for endometrial evaluation. The device has become so popular that, although many clinicians may use other brands, the word "Pipelle" has become synonymous with suction piston biopsy instruments just as we often go to the "Xerox" machine (Xerox Corporation, Norwalk, CT) even though our copier may be another brand or we ask for a "Kleenex" (Kimberly-Clark Corporation, Irving, TX) even though our tissue may come from another manufacturer.

Suction piston biopsy devices have several important limitations. First, such devices sample only a small surface of the endometrial cavity. Rodriguez et al[19] did a pathologic study of 25 hysterectomy specimens. The percentage of endometrial surface sampled by the Pipelle device was 4% vs 41% for the Vabra aspirator.

In addition, the sensitivity of such suction piston biopsy devices is quite variable. In other studies, for patients with known malignancies who underwent Pipelle biopsy before hysterectomy, the diagnosis of cancer was missed in 2 (7.6%) of 26[20] and in 12 (32.4%) of 37,[21] not nearly as reliable as the original work by Stovall et al.[18]

The significance of such sampling's limitations is highlighted in another study by Guido et al.[22] They also studied Pipelle biopsy in patients with known carcinoma undergoing hysterectomy. Among 65 patients a Pipelle biopsy provided tissue adequate for analysis in 63 (97%). Malignancy was detected in only 54 (83%) patients. Thus there was a 17% false-negative rate in these patients with