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## Postmenopausal endometrial thickness guidelines

Number 734 ( (Replaces Committee Opinion Number 440, August 2009)Committee on Gynecological PracticeThis committee opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice in collaboration with Catherine Cansino, MD, MPH. SUMMARY: Endometrial cancer is the most common type of gynecological cancer in the United States. Vaginal bleeding is the presenting sign in more than 90% of postmenopausal women with endometrial carcinoma. Clinical risk factors for endometrial cancer, including, but not limited to, age, obesity, use of non-opposite estrogens, specific medical comorbidities (e.g., polycystic ovary syndrome, type 2 diabetes mellitus, atypical glandular cells when screening for cervical cytology) and family history of gynecological malignancy should also be considered when assessing postmenopausal bleeding. The clinical approach to postmenopausal bleeding requires prompt and effective evaluation to rule out or diagnose endometrial carcinoma and endometrial intraepithelial neoplasia. Transvaginal ultrasound is usually sufficient for an initial assessment of postmenopausal bleeding if ultrasound images reveal a thin endometrial echo (less than or equal to 4 mm), since an endometrial thickness of 4 mm or less has a negative predictive value greater than 99% for endometrial cancer. Transvaginal ultrasound is a reasonable alternative to endometrial sampling as the first approach in evaluating a postmenopausal woman with an initial episode of bleeding. If blind sampling does not reveal endometrial hyperplasia or malignancy, other tests, such as dilation and curettage hysteroscopy, are warranted in the assessment of women with persistent or recurrent bleeding. An endometrial measurement greater than 4 mm that is incidentally discovered in a postmenopausal patient without bleeding does not need to systematically initiate evaluation, although an individualized assessment based on patient characteristics and risk factors is appropriate. Transvaginal ultrasound is not an appropriate screening tool for endometrial cancer in postmenopausal women without bleeding. The American College of Obstetricians and Gynecologists makes the following recommendations and conclusions: The clinical approach to postmenopausal bleeding requires rapid and effective evaluation to rule out or diagnose endometrial carcinoma and endometrial intraepithelial neoplasia. Transvaginal ultrasound is appropriate for an initial assessment of postmenopausal bleeding if ultrasound images reveal a thin endometrial echo (less than or equal to 4 mm), as an endometrial thickness of 4 mm or has a negative predictive value of more than 99% for endometrial cancer. Transvaginal ultrasound is a reasonable alternative to endometrial sampling as the first approach in evaluating a postmenopausal woman with an initial episode of bleeding. Transvaginal ultrasound may be useful in women's triage that endometrial office sampling was performed but the tissue was insufficient for diagnosis. Failure to adequately identify a thin and distinct endometrial echo in a postmenopausal woman with bleeding should trigger sonohysterography, office hysteroscopy, or endometrial sampling. If blind sampling does not reveal endometrial hyperplasia or malignancy, other tests, such as dilation and curettage hysteroscopy, are warranted in the assessment of women with persistent or recurrent bleeding. An axial uterus, obesity, coexisting myomas, adenomyosis, or previous uterine surgery may contribute to difficulty by obtaining reliable transvaginal ultrasound evaluation of endometrial thickness and texture. Since rare cases of endometrial carcinoma (particularly type II) may present with an endometrial thickness of less than 3 millimetres, persistent or recurrent uterine bleeding should prompt a histological evaluation of the endometrium regardless of endometrial thickness. An endometrial measurement greater than 4 mm that is incidentally discovered in a postmenopausal patient without bleeding does not need to systematically initiate evaluation, although an individualized assessment based on patient characteristics and risk factors is appropriate. Endometrial cancer is the most common type of gynecological cancer in the United States. In 2017, an estimated 61,380 new cases of uterine cancer were diagnosed and approximately 10,920 deaths occurred 1. Most cases of uterine cancer (92%) occur in the endometrium and are called endometrial cancer. Vaginal bleeding is the presenting sign in more than 90% of postmenopausal women with endometrial carcinoma 2. Postmenopausal vaginal bleeding is usually caused by atrophic changes in the vagina or endometrium. Depending on age and risk factors, 1-14% of women with postmenopausal bleeding will have endometrial cancer 3 4 5 6. The clinical approach to postmenopausal bleeding requires prompt and effective evaluation to rule out or diagnose endometrial carcinoma and endometrial intraepithelial neoplasia. This committee opinion describes the use of transvaginal ultrasound for the evaluation of women with postmenopausal bleeding as well as the approach to the incidental finding of a thickened endometrial echo in an asymptomatic postmenopausal woman. Endometrial thickness is measured as the maximum anterior-posterior thickness of the endometrial echo on a long-axis transvaginal view of the uterus. Early reports comparing transvaginal ultrasound with endometrial sampling consistently found that an endometrial thickness of 4-5 millimetres or less in women with bleeding reliably excluded endometrial cancer 7 8 9. Since then, a number of multicenter confirmation trials have been completed Table 1. Transvaginal ultrasound is suitable for an initial assessment of postmenopausal bleeding if ultrasound images reveal a thin endometrial echo (less than or equal to 4 mm), as an endometrial thickness of 4 mm or or has a negative predictive value of more than 99% for endometrial cancer. Ultrasound to measure endometrial echo should be offered as an initial evaluation only to women with postmenopausal bleeding for whom no further evaluation would be required if a thin echo is found. Persistent or recurrent bleeding should trigger further assessment. Transvaginal ultrasound is a reasonable alternative to endometrial sampling as the first approach in evaluating a postmenopausal woman with an initial episode of bleeding. Ultrasound should only be used for patients with a previous probability of cancer and hyperplasia low enough that no further testing is required after a normal ultrasound. Endometrial sampling is also a reasonable first approach for women with postmenopausal bleeding 10. This initial assessment does not require the completion of both tests. Clinical risk factors for endometrial cancer, including, but not limited to, age, obesity, use of non-opposite estrogens, specific medical comorbidities (e.g., polycystic ovary syndrome, type 2 diabetes mellitus, atypical glandular cells when screening for cervical cytology) and family history of gynecological malignancy should also be considered when assessing postmenopausal bleeding. A retrospective cohort study of 4,383 women in Hong Kong assessed endometrial cancer detection rates based on different threshold levels and concluded that the predetermined threshold for further assessment should be based on available resources, comorbidities and acceptable detection rates 11. Endometrial sampling should be the first-line test for women with higher-risk postmenopausal bleeding (based on clinical risk factors or clinical presentation) of endometrial cancer and endometrial intraepithelial neoplasia. Table 2 shows the number of cases of endometrial cancer missed by transvaginal ultrasound based on different thresholds. Using an endometrial echo of 4 mm as a cut value, transvaginal ultrasound has an extremely high negative predictive value (above 99%). However, a thickened endometrial echo is not a diagnosis of a particular pathology. Even with an extremely high probability that a woman with a negative screening test result really does not have the condition, a thin endometrial echo does not rule out all the possibilities of the disease. In addition, a thin endometrial echo does not reliably rule out type II endometrial cancer (uterine papillary, mucinous and clear) 12. Repeated episodes of bleeding and continuous postmenopausal bleeding require histological evaluation even in women with an apparent thin endometrial echo 10. Given its ease of performance, ambulatory endometrial sampling with disposable devices is the primary method of choice for histological evaluation. If blind sampling does not reveal endometrial hyperplasia or malignancy, other tests, such as dilation and curettage hysteroscopy, are warranted in the assessment of women without recurrent bleeding 10. It is not possible to complete a significant transvaginal ultrasound examination with a reliable measurement of endometrial thickness in all women 13 14. The thickest part of the endometrium must be measured perpendicular to its longitudinal plane in the anteroposterior diameter, representing the distance between the echogenic boundaries Figure 1 15. An axial uterus, obesity, coexisting myomas, adenomyosis, or previous uterine surgery may contribute to difficulty by obtaining reliable transvaginal ultrasound evaluation of endometrial thickness and texture. Failure to adequately identify a thin and distinct endometrial echo in a postmenopausal woman with bleeding should trigger sonohysterography, office hysteroscopy, or endometrial sampling 10. In addition, endometrial fluid, when present, should not be included in the measurement of endometrial thickness. If an abnormal endometrium is identified, endometrial sampling is warranted. Sampling of endometrial tissue resulting in insufficient diagnostic results is common. In a study of 97 consecutive women with postmenopausal bleeding evaluated by transvaginal ultrasound and endometrial biopsy, a pipelle biopsy could be performed in only 82% of women (n=45) with an endometrial thickness of less than 5 millimeters 16. Of these women, an adequate sample for diagnosis was obtained in only 27%. There was no correlation between sample adequacy and parity or cavity length. In a meta-analysis of studies on women with postmenopausal bleeding, the range of sampling failure (e.g., inadequate sample or inability to perform biopsy) with biopsy was 0-54% 17. The associated sample size-weighted failure rate specifically with pipelle biopsy was 10.4% 17. Transvaginal ultrasoundography may be useful in triage of women in whom endometrial office sampling was performed but the tissue was insufficient for diagnosis 18. In one study, 29.8% of the women assessed for abnormal uterine bleeding had an insufficient endometrial sample (none had endometrial hyperplasia or cancer after two-year follow-up). No further evaluation is required after an insufficient endometrial biopsy if the following transvaginal ultrasound demonstrates a thin echo in a woman with postmenopausal bleeding in whom bleeding stopped Table 1. Since rare cases of endometrial carcinoma (particularly type II) may occur with an endometrial thickness of less than 3 millimetres, persistent or recurrent uterine bleeding should prompt a histological assessment of the endometrium regardless of endometrial thickness transvaginal ultrasound to rule out pathology in postmenopausal women with bleeding should not be extrapolated to asymptomatic postmenopausal women without bleeding. In 1,750 postmenopausal women without bleeding who were examined for a selective study of estrogen receptor modulator, an endometrial thickness of 6 millimeters or less had a negative predictive value of 99.94% to rule out malignancy (only one case of cancer cancer 1,750 women) and a negative predictive value of 99.77% for complex hyperplasia (only four cases in 1,750 women) 19. Among 42 women with endometrial thickness of more than 6 millimeters, there was one case of adenocarcinoma and no cases of hyperplasia (positive predictive value of 2.4%). In another study, 82 asymptomatic postmenopausal women had an incidental ultrasonographic finding of a thick endometrial echo suspected to be a polyp 20. All women underwent operative hysteroscopy. Of these women, a benign polyp was found in 68, submucosal myoma in 7, atrophic endometrium in 6, and proliferating endometrium in 1. A polyp contained simple hyperplasia. There were no cases of endometrial carcinoma or complex hyperplasia. The total complication rate was 3.6% (two perforations, difficult intubation). An asymptomatic population of postmenopausal Danish women who were randomly selected from a marital status reported that 13% had a nonbleeding polyp detected by 21. A retro multicenterography test in which 1,152 polyps were removed from asymptomatic postmenopausal women diagnosed by sonohysterography reported a case of stage 1 22 category 1 carcinoma. The incidence of any cancer in this trial of asymptomatic women was 1 in 298. A retrospective study of 190 postmenopausal women with symptomatic endometrial carcinoma and 123 asymptomatic women with suspicious endometrium detected by transvaginal ultrasound found no prognostic benefit in terms of 5 years survival between women with cancer discovered incidentally and those treated within 8 weeks of their clinical presentation of postmenopausal bleeding 23. An endometrial measure greater than 4 millimeters that is incidentally discovered in a postmenopausal patient without bleeding does not need to systematically initiate evaluation, although an individualized assessment based on patient characteristics and risk factors is appropriate. Thus, transvaginal ultrasound is not an appropriate screening tool for endometrial cancer in postmenopausal women without bleeding. American Cancer Society. Cancer Facts and Figures 2017. Atlanta (GA): ACS; 2017. Article Locations: Goldstein RB, Bree RL, Benson CB, Benacerraf BR, Bloss JD, Carlos R, et al. Evaluation of the woman with postmenopausal bleeding: Society of radiologists in ultrasound-sponsored consensus conference statement. J Ultrasound Med 2001;20:1025-36. Article Locations: Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, et al. Endomeginal ultrasound to rule out endometrial cancer and other endometrial abnormalities. JAMA 1998;280:1510-7. 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