At what thickness is the endometrial stripe cause for concern in a woman who has postmenopausal bleeding?

4 mm That is the cutoff recommended by ACOG. However, the authors of this systematic review and meta-analysis propose a new cutoff: 3 mm.

Timmermans A, Opmeer BC, Khan KS, et al. Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding. Obstet Gynecol. 2010;116(1):160–167.

EXPERT COMMENTARY

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Since transvaginal ultrasonography (TVS) was introduced in the 1980s, it has been increasingly utilized to evaluate postmenopausal vaginal bleeding. In August 2009, ACOG reissued a Committee Opinion on the use of TVS in this setting.[1] Based on the very high negative predictive value of TVS, ACOG recommended a cutoff of 4 mm for endometrial thickness: That is, endometrial stripes 4 mm or thinner require no endometrial sampling; only those thicker than 4 mm require a biopsy.[2]

How can we interpret this study, which recommends changing that cutoff to 3 mm?

Meta-analysis focused on *individual* patient data

Timmermans and coworkers employed an unusual statistical approach in their meta-analysis: Rather than use entire datasets from each study included in their analysis, they attempted to obtain individual patient data. They identified 74 investigations that reported endometrial thickness and endometrial carcinoma rates in women who experienced postmenopausal bleeding. They obtained individual data from 13 of these studies, representing 2,896 women. Using a sophisticated receiver operator characteristic (ROC) curve analysis, they calculated summary estimates of the sensitivity and specificity of TVS in diagnosing endometrial cancer in this population. They found the diagnostic accuracy of TVS to be lower than the accuracy demonstrated in the most frequently cited meta-analysis in the literature.[3]

TVS accurately predicted the presence of endometrial cancer in women who had postmenopausal bleeding with different rates of sensitivity and specificity, depending on the cutoff used:

- **5 mm**—sensitivity, 90.3% (95% confidence interval [CI], 80.0%–95.5%); specificity, 54% (95% CI, 46.7%–61.2%)
- **4 mm**—sensitivity, 94.8% (95% CI, 86.1%–98.2%); specificity, 46.7% (95% CI, 38.3%–55.2%)

WHAT THIS EVIDENCE MEANS FOR PRACTICE

The preponderance of data supports the continued use of 4 mm as a cutoff for endometrial sampling: That is, only women who have postmenopausal bleeding and an endometrial stripe thicker than 4 mm need to undergo endometrial biopsy.

It is important to take other variables into account to improve our diagnostic accuracy without increasing the rate of unnecessary endometrial sampling. These variables include consideration of:

- the patient's history and other characteristics[5]
- the persistence of postmenopausal bleeding[4]
- cervical cytology.[6]

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FAST TRACK

ACOG recommends endometrial sampling only when the endometrial stripe is thicker than 4 mm

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- **3 mm**—sensitivity, 97.9% (95% CI, 90.1%–99.6%); specificity, 35.4% (95% CI, 29.3%–41.9%).

Sensitivity and specificity are integrally related; we increase sensitivity at the expense of specificity. Are we willing to increase our detection of true positive test results by also increasing the false-positive rate? The authors suggest that in the setting of a potential cancer diagnosis, clinicians should aim for 100% sensitivity—and they push for a 3-mm cutoff for that reason. However, if we shift to a 3-mm cutoff, considerably more women who do *not* have endometrial cancer will undergo biopsy. We must also be mindful of the false-negative rate of endometrial sampling and of the fact that not all women can be sampled, because of cervical stenosis or technical difficulties.

Strengths and weaknesses of the study

One strength of this analysis is that the investigators used the exact endometrial thickness for each patient rather than pooled data. Because of this requirement, however, only 13 of 74 studies of endometrial thickness and the endometrial cancer rate were able to provide data. Had all 74 publications provided data, many more patients would have been represented in the meta-analysis. Instead, bias was introduced because the small subset of patients whose individual data was available may not represent the entire population. The 95% confidence intervals for sensitivity and specificity reflect the small sample size.

This study also has a number of minor limitations. For example, it fails to address the fact that not all TVS studies are optimal studies. It can be difficult to measure the endometrial stripe when fibroids are present, when the patient has a history of uterine surgery, or when she is obese. Uterine position also can affect imaging.

In addition, the technology of TVS has improved significantly over the past two decades, making comparison of older studies (as early as 1995) to more modern studies (as recent as 2008) difficult to justify.

Timmermans and colleagues fail to provide information on the adequacy of TVS in assessing the endometrial stripe. Nor do they provide details on the histologic type of cancer in women who had thin endometrial stripes. The latter data would have been interesting because patients who have rare "type 2" endometrial cancers are more likely to exhibit endometrial stripes thinner than 4 mm.[4]

References

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Patients who have rare "type 2" endometrial cancers are more likely to exhibit endometrial stripes thinner than 4 mm