

The use of new and old ultrasound techniques in the assessment of women with postmenopausal bleeding

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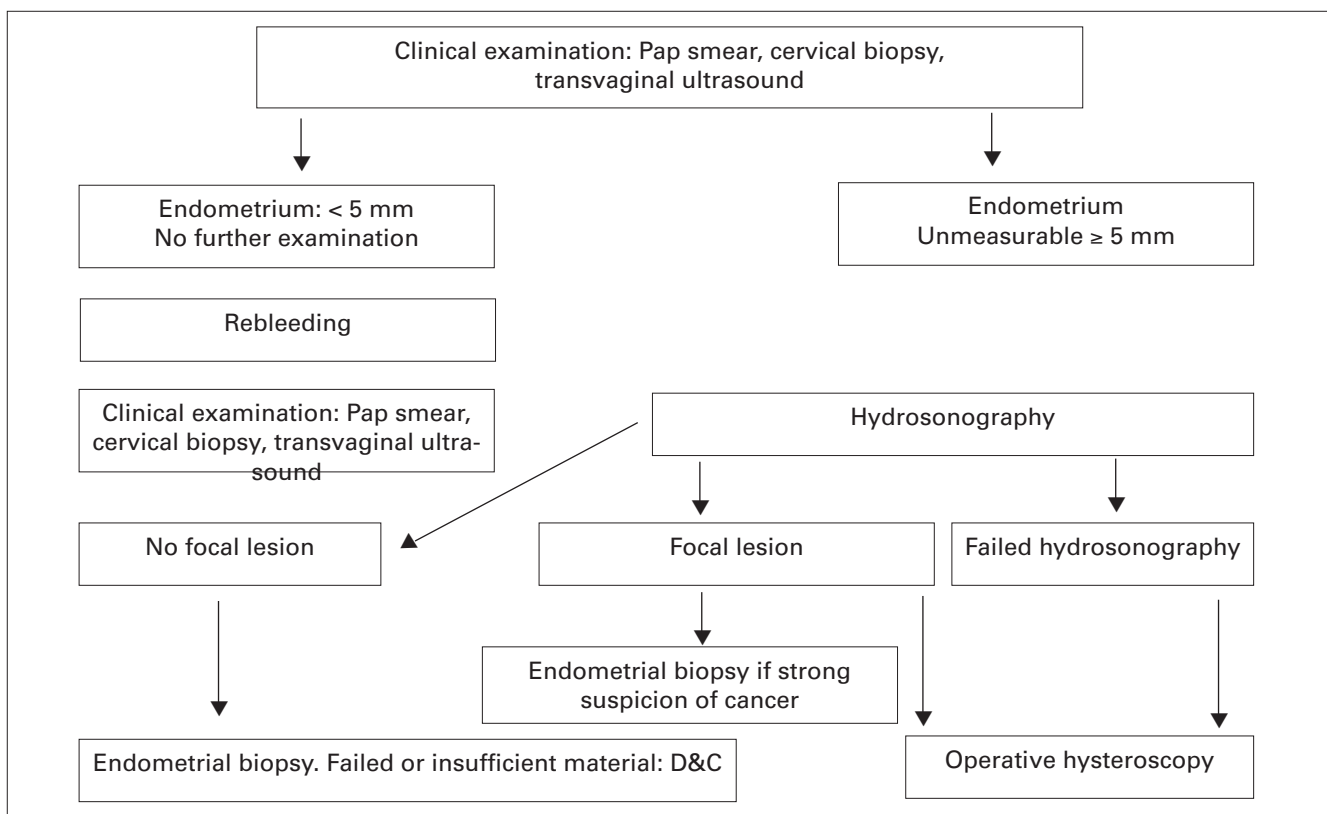


Fig. 1: Simple guidelines for the management of postmenopausal bleeding.



Introduction

Postmenopausal bleeding (PMB) is the most common symptom of the endometrium. Cervical cancer must also not be forgotten, especially in women with a thin endometrium. Therefore, all women presenting with PMB should undergo evaluation with transvaginal ultrasound

to estimate the risk of endometrial cancer, and speculum examination/cervical cytology to rule out cervical pathology. Management strategies using ultrasound as the primary investigation tool have been shown to be more cost effective than those using endometrial biopsy for the investigation of PMB¹. In women with PMB, the primary aim is to estimate the risk of endometrial cancer, since women at low risk of cancer can be managed expectantly, whereas women at high risk must undergo endometrial biopsy.

The secondary goal is to rule out the presence of focal lesions since this is of major importance to determine the

most appropriate biopsy procedure. Finally, in women with an established diagnosis of endometrial cancer ultrasound can be used to assess the extension of the tumour. The focus of this short opinion piece is to discuss the clinical role of both established and novel ultrasound techniques in the assessment of women with PMB.

Established techniques

Measurement of the endometrial thickness (ET) has so far been the most simple and accurate ultrasound technique to estimate the risk of endometrial malignancy in women with PMB. There is solid scientific evidence that transvaginal ultrasound (TVS) examination can reliably distinguish women who are at low risk (ET < 5 mm) from those who are at high risk of endometrial pathology (ET ≥ 5 mm)²⁻⁴. The odds of endometrial cancer is reduced 10-fold after a negative scan, that is if the ET measures < 5 mm⁴. The 5 mm cut-off can be used in all women irrespective of HRT use⁴. A simplified version of the guidelines suggested by the reference group of Ultrasound in Obstetrics and Gynaecology in Sweden is presented in Fig. 1⁵.



Fig. 2: Irregular focal lesion in women with endometrial cancer.

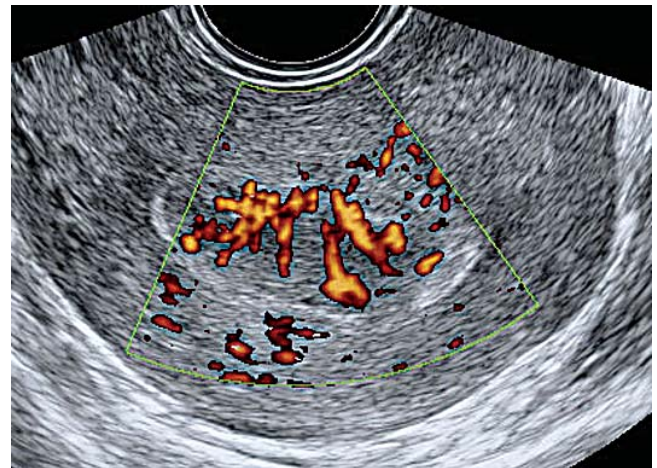


Fig. 3: Multiple vessels in women with endometrial cancer.

It is justifiable to refrain from endometrial sampling in women with PMB and an ET < 5 mm, because the risk of endometrial cancer in these women is very low (0.1–1.0%)⁴. In women with PMB and a thin endometrium, we must not forget to rule out cervical pathology such as cervical cancer as this is twice as common as endometrial cancer in these women⁶. During long term follow-up women with PMB and a thin ET (< 5 mm) at the initial TVS have a persistently increased risk of cervical pathology⁶, whereas the risk of endometrial pathology is the same as for women with no bleeding^{6,7}. In women with repeated bleeding there is an increased risk of both cervical and endometrial pathology^{6,8}, indicating that there is a need for both endometrial and cervical sampling.

Women with an ET \geq 5 mm have a high risk of endometrial pathology and should therefore undergo endometrial biopsy. A large proportion of these women have focally growing pathological lesions in the uterine cavity⁹. Dilatation and curettage (DC) will fail to diagnose and remove half of the benign and 10% of the malignant focally growing lesions^{9–12}. Therefore, women with focal lesions should undergo operative hysteroscopy, whereas simple endometrial biopsy devices can be used in women without focal lesions. In women with a strong suspicion of malignancy, endometrial biopsy should be performed at the time of TVS examination so that women with confirmed cancer can proceed rapidly to hysterectomy.

Saline infusion sonography (SIS) can quickly and accurately^{13–17} detect focal lesions and can therefore help to choose the most appropriate biopsy procedure. The sensitivity of SIS for the detection of focal lesions is 93–100% and the specificity is 85–96%^{13–17}. It is better tolerated, less painful and cheaper than diagnostic hysteroscopy^{16,18,19}.

In women with an unmeasurable or ill defined endometrium, one should not draw the conclusion that the endometrium is thin. According to our own unpublished data, 5% of these women have cancer (Epstein, unpublished). The use of SIS is helpful in this situation as it will help us to see the true appearance of the endometrium and the endometrial cavity.

Novel techniques for risk-estimation of endometrial malignancy in women with PMB

We know that all women with an ET \geq 5 mm are at an

increased risk of cancer. It also is important among these women to quantify the risk, since this will enable us to potentially refrain from invasive procedures in women at high risk of surgery. In addition, it makes it possible to optimise the timing and the type of surgery and we can ask for prompt histological evaluation in those deemed to be high-risk cases.

It is often difficult to differentiate between benign and malignant endometrium based on endometrial grayscale morphology assessment especially in women with an ET < 15 mm²⁰. There are, however, several studies showing that endometrial morphology assessment can be useful in the prediction of endometrial cancer^{20–23}. Endometrial echogenicity and border in combination with ET has been shown to be a better predictor of endometrial cancer than ET measurement alone^{21–23}. The best predictor of cancer at SIS is the finding of an irregular surface focal lesion (sensitivity 89% specificity 67%), Fig. 2²⁰. Assessment of vascular morphology of endometrial vessels can also be used to estimate the risk of endometrial cancer^{20,21,24}. The presence of multiple vessels has a sensitivity of around 80% for the detection of cancer at a specificity of 54–100%, Fig. 3^{21,24}. Irregular vascular branching and areas of densely packed vessels might also be useful in the prediction of malignancy since these phenomena are very uncommon in benign cases²¹.

Vascular indices of areas or volumes make it possible to objectively quantify power Doppler signals. 2D vascularity index (VI) has been reported to be useful in the risk estimation of cancer in women with PMB²⁵. In a selected study population comprising 84 women with known hyperplasia or endometrial cancer, 3D power Doppler vascular indices was found to be significantly higher in malignant than in benign lesions. In addition, the VI was significantly higher in > Stage I endometrial tumours²⁶. More studies are needed to determine the clinical value of power Doppler indices for the prediction of endometrial cancer.

It is still uncertain if endometrial 3D volume measurements have an advantage over ET measurements, for the prediction of endometrial cancer, since studies have shown conflicting results^{27–29}. Volume measurements clearly need to be superior to thickness measurements to have a clinical role since volume measurements are more complicated and require sophisticated equipment. With the present knowledge



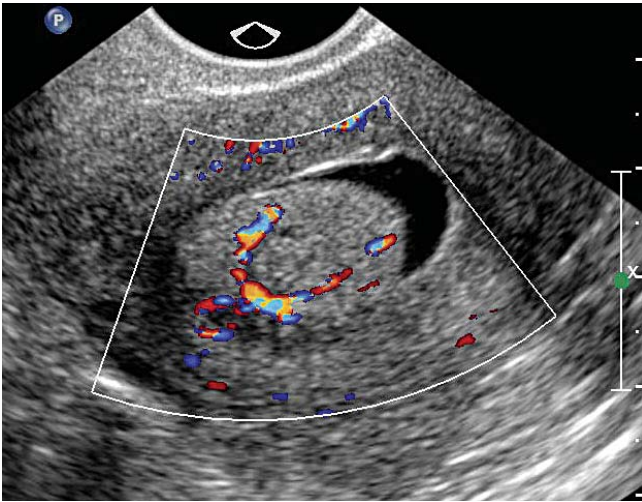


Fig. 4: Smooth polyp with feeding vessel at hydrosonography.

there seems to be no reason to abandon ET measurements.

Can mathematical models improve the risk assessment? We found that a logistic regression model comprising ET, VI and a woman's history of hormone therapy use had an area under the curve (AUC) of 0.88 for the prediction of endometrial cancer²⁵. Oposkiene and co-workers show a slightly better AUC of 0.91 using a logistic regression model comprising only ET and endometrial morphology²¹. Adding Doppler variables did not significantly improve their model's performance. The clinical value of mathematical models needs to be further evaluated in prospective multi-centre studies.

What about reproducibility of ET measurement as compared to endometrial morphology assessment? The inter-observer agreement between two experienced examiners was excellent for ET measurement in our own study with a Kappa value of 0.8³⁰. Opolskiene and co-workers found that the inter-observer agreement between two experienced examiners for endometrial morphology assessment was generally moderate to good, with a kappa value of 0.49–0.78²¹. Assessment of vascular morphology showed a similar reproducibility as previously reported for endometrial thickness measurements^{21,30}.

Novel techniques for the evaluation of the endometrial cavity in women with PMBAs mentioned previously, the secondary goal in the assessment of PMB is to rule out focal lesions. The established ultrasound technique for the assessment of the endometrial cavity is SIS.

Timmerman and co-workers showed that "feeding vessels" are predictive of polyps and focally growing lesions, Fig. 4³¹. The question is can this method replace SIS? The feeding vessel has been reported to have an excellent accuracy for the prediction of polyps^{31,32}. The method however seems to be less good for the over all prediction of focally growing lesions. In our own unpublished material comprising 224 women with PMB, we found a high detection rate (90%), but a lower specificity (48%) indicating that the absence of a feeding vessel will not exclude a focal lesion (Epstein, unpublished). One should be aware that top of the line Doppler equipment is needed for adequate assessment of endometrial vascularity.

Summary

TVS can accurately discriminate women at high or low risk of endometrial cancer using a cut-off 5 mm. Women with an ET

< 5 mm can be managed expectantly but do not forget to rule out cervical cancer. SIS should be performed in all women with PMB with an ET \geq 5 mm to rule out focal lesions. All women with focal lesions should undergo operative hysteroscopy, since these lesions will not be adequately removed or diagnosed with blind sampling procedures. One should suspect endometrial cancer in lesions with multiple vessels, irregular echogenicity, or an irregular surface at SIS.

Desired areas of research and development

- Standardised terminology to describe the endometrium and any intra-cavity lesions during unenhanced and enhanced ultrasound examination should be proposed.
- The clinical value of 3D ultrasound and of vascular indices in the assessment of postmenopausal bleeding needs to be further evaluated.
- The use of mathematical models for the risk estimation of endometrial cancer in women with PMB should be assessed in multi-centre studies.

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