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A grayscale ultrasound image of the endometrium, showing a curved, layered structure with a darker, more echogenic area on the right side, likely representing the endometrial lining and a polyp.

The diagnostic accuracy of endometrial thickness to exclude polyps in women with postmenopausal bleeding

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Abstract

Objective: To determine the accuracy of endometrial thickness measurement with transvaginal ultrasound (TVU) to diagnose endometrial polyps in women with postmenopausal bleeding (PMB) in whom a carcinoma has been ruled out.

Methods: In women with PMB endometrial thickness was measured with TVU. If endometrial thickness was > 4 mm, office hysteroscopy was performed. At hysteroscopy, the uterine cavity was assessed for the presence of polyps. Women with malignancy were excluded. We used Receiver Operating Characteristics (ROC) analysis to assess the capacity of TVU endometrial thickness measurement to diagnose endometrial polyps. Findings at hysteroscopy were considered to be the reference standard.

Results: We included 178 women with PMB and endometrial thickness > 4 mm. Hysteroscopy showed an endometrial polyp in 90 women (50%). The ROC analysis revealed that endometrial thickness had an area under the curve of 0.64 in the diagnosis of endometrial polyps.

Conclusion: In women with PMB in whom carcinoma has been ruled out, measurement of endometrial thickness with TVU is not useful in the diagnosis of endometrial polyps.

Introduction

Postmenopausal bleeding (PMB) is often caused by abnormalities of the endometrium, whether they are benign or malignant. At present, transvaginal ultrasound (TVU) is used as a first step in the evaluation of women with PMB.^{1,3} The probability of malignant pathology is strongly reduced in the presence of a distinct endometrial ultrasound with an endometrial thickness ≤ 4 mm.⁴ Endometrial sampling is not recommended below this cut-off value, but it is warranted to rule out malignancy above this cut-off value.⁵

The diagnostic approach is less clear with respect to benign disease. The prevalence of endometrial polyps in women with PMB and endometrial thickness > 4 mm is estimated to be approximately 40%.⁶ The majority of gynaecologists advocate removal of endometrial polyps. Removal of such polyps might reduce the probability of recurrent bleeding and allow histological assessment of the removed polyp.⁷ From that point of view, it would be important for TVU to diagnose endometrial polyps so that a selective hysteroscopy could be undertaken with the intention of removing the polyps.

The role for measuring endometrial thickness in order to exclude endometrial carcinoma is clearly established. However, it is unclear whether measurement of endometrial thickness is clinically useful for predicting the presence or absence of endometrial polyps. In pre-menopausal women, a thin endometrium has been shown to reduce the probability of intrauterine abnormalities such as polyps, but did not exclude them.⁸ No such data are available for symptomatic postmenopausal patients. Therefore the aim of the present study was to determine the accuracy of TVU endometrial thickness measurement in the diagnosis of endometrial polyps in women with PMB.

Material and Methods

The study was performed between January 1st 2002 and July 1st 2005 in the St. Antonius Hospital, a university-affiliated teaching hospital in Nieuwegein, The Netherlands. The St. Antonius Hospital has a fixed local protocol for the diagnostic work-up of women with PMB. This protocol includes TVU measurement of endometrial thickness and office hysteroscopy in women with endometrial thickness > 4 mm. Consecutive women undergoing office hysteroscopy are documented in a database. Women who underwent hysteroscopy in the study period because of PMB were identified from this database. The medical files of these women were reviewed to obtain information about endometrial thickness, hysteroscopic findings and histology results. This study was limited to women with endometrial thickness > 4 mm or endometrial thickness not measurable.

The work-up was started with TVU which was performed by a gynaecologist or gynaecological resident to measure endometrial thickness. TVU was performed with 5 MHz vaginal probe transducers (UST 984-5) connected to an Aloka SSD 900 scanner (Aloka, Tokyo, Japan). The thickness of the endometrium was measured from a longitudinal sonogram through the thickest area of the endometrium. The endometrial stripe was scanned longitudinally from right to left until the thickest point was found, and this thickness was measured. The measurements of endometrial thickness included both layers. When the endometrial layers were separated by intracavitary fluid, each layer was measured and the sum was recorded. In case the endometrium was too ill-defined to allow a reliable measurement result, this was recorded as “endometrial thickness not measurable”. Furthermore, intracavitary pathology could be suspected on TVU, by a focal or circumscribed isoechogetic lesion of the endometrium. In case of endometrial thickness > 4 mm or in case of endometrial thickness not measurable, patients were scheduled for a hysteroscopy.

Hysteroscopy was performed in an office setting using a 5.5 mm continuous flow hysteroscope (3 mm telescope and 5.5 mm operative with 5 French channel sheaths; (Olympus®, Olympus America Inc., Melville, NY) by a gynaecologist with expertise in hysteroscopy or by a resident under direct supervision of this gynaecologist. The hysteroscopist was aware of the results of the TVU. Hysteroscopy was performed using a vaginoscopic approach, without speculum, tenaculum or local anaesthetics. During hysteroscopy the uterine cavity was described in a standard way, which included a description of polyps, submucous myomas, suspicion of malignancy, normal endometrium or atrophy. A polyp was defined as a benign, localized overgrowth of endometrial tissue covered by epithelium. Polyps could be sessile or pedunculated and they could be single (i.e. one polyp) or multiple (i.e. at least two polyps). In case of abnormalities in the uterine cavity, these abnormalities were resected or a biopsy was taken and the material was sent for pathological examination. Hysteroscopic findings and histology results were combined for final diagnosis. Patients with final diagnosis of malignancy were excluded. The STARD (Standards for Reporting of Diagnostic Accuracy) initiative checklist was used to report the results of the study.⁹

Statistical analysis

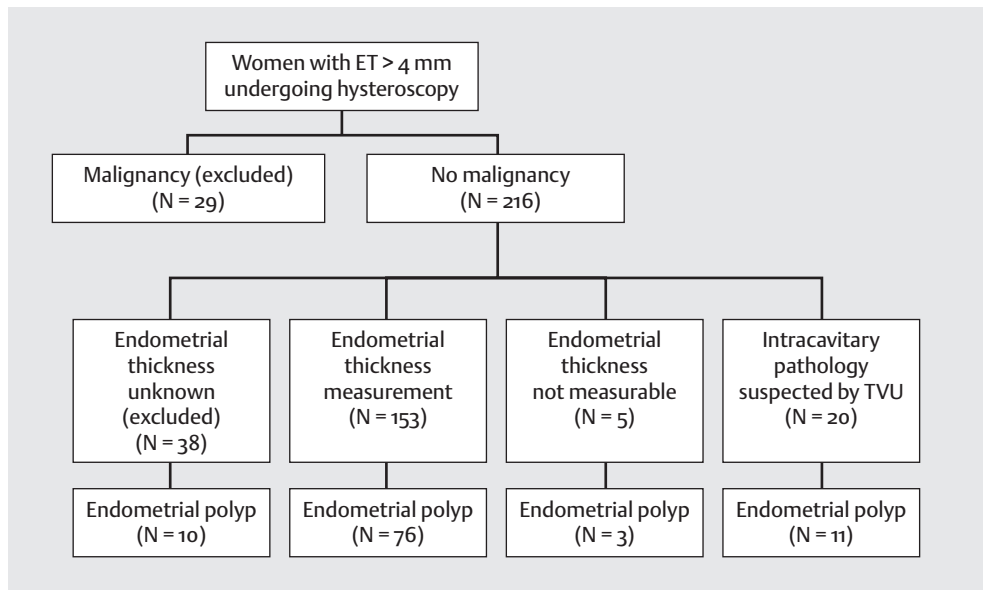
In the analysis, endometrial thickness was related to the final disease status (i.e. the presence of a benign polyp or not). We categorized the results of endometrial thickness and tabulated them against the presence or absence of polyps. Endometrial thickness that could not be measured was considered as a separate category, as was suspicion of intracavitary pathology, based on the TVU image. Likelihood ratios (LRs) with 95% confidence intervals (95% CIs) were calculated for different ranges of endometrial thickness, as well as for the diagnostic categories “suspicion of intracavitary pathology” and “endometrial thickness not measurable”. We performed Receiver Operating Characteristics (ROC) analysis to assess the discriminative

capacity of endometrial thickness for the presence of benign polyps. The area under the ROC curve (AUC) reflects the diagnostic accuracy of a test, incorporating sensitivity and specificity for all possible thresholds, thus allowing detection of an optimal cut-off point for further clinical management. An AUC of 0.5 indicates no discriminative capacity whereas an AUC of 1 indicates perfect discriminative capacity. Statistical analysis was performed with SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

Results

Two hundred forty-five women underwent office hysteroscopy for PMB. At hysteroscopy, 29 of the 245 women were diagnosed with endometrial carcinoma, leaving 216 women with a benign diagnosis. Among these 216 women, there were 100 women in whom hysteroscopy showed an endometrial polyp. In 38 of these 216 women, endometrial thickness was unknown, thus these women were excluded from further analysis. Endometrial thickness was recorded in 153 women. Endometrial thickness was not measurable in five of the 153 women and intracavitary pathology was suspected on TVU in 20 women (Figure 1).

Figure 1. Flow Chart



Endometrial polyps were found in three women in whom endometrial thickness was not measurable (n=5), in 11 patients in whom intracavitary pathology was suspected (n=20) and in 76 women with recorded endometrial thickness (n=153). ROC analysis was performed us-

ing the 153 women with recorded endometrial thickness. Women with endometrial thickness not measurable, and women with suspected intracavitary pathology on TVU were analyzed as separate categories. Table 1 shows the likelihood for different TVU results. The LRs varied between 0.6 and 1.2, indicating poor diagnostic performance of TVU. Endometrial thickness not measurable showed a sensitivity of 3% (95% CI 1.1-93%) and specificity of 98% (92.1-99.4%). For TVU suspicion of intracavitary pathology the sensitivity was 12% (95% CI 7.0-20.6%) and specificity 90% (95% CI 81.7-94.5%).

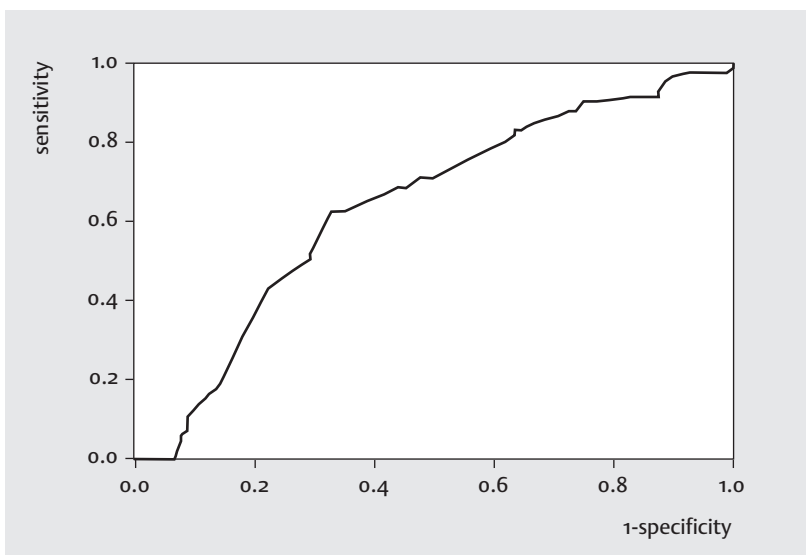
Table 1. Diagnostic value of endometrial thickness measured via TVU in the detection of endometrial polyps as established at hysteroscopy

Endometrial thickness (mm)	No. of patients	No. of patients (%) with endometrial polyp at hysteroscopy	LR (95% CI) for endometrial polyp
5-8	70	24 (34%)	0.68 (0.46-1.0)
9-12	45	29 (64%)	1.28 (0.86-1.9)
>12	38	23 (61%)	1.20 (0.76-1.9)
Not measurable	5	3 (60%)	1.19 (0.29-4.9)
Polyp suspected on TVU image	20	11 (55%)	1.09 (0.55-2.2)

CI, confidence interval; LR, Likelihood Ratio

Figure 2 shows the ROC curve for endometrial polyps. The AUC was 0.64, confirming the poor diagnostic performance that was derived from the LRs.

Figure 2. ROC analysis of diagnostic value of endometrial thickness for detection of endometrial polyps



Discussion

This study shows that endometrial thickness measured with TVU is not helpful in the diagnosis of endometrial polyps in women with PMB. Whereas in women with PMB a cut-off value of the endometrial thickness of 4 mm identifies women at low risk for endometrial carcinoma, no such cut-off level of endometrial thickness could be identified for endometrial polyps. Both the ROC analysis and likelihood ratios indicated poor discriminative capacity.

A limitation of this study is that data were collected retrospectively. Although the protocol in our clinic is to measure endometrial thickness in case of PMB, and all women with endometrial thickness > 4 mm undergo office hysteroscopy, it is possible that not all women with an endometrial thickness > 4 mm had had an office hysteroscopy. Alternatively, they could either have had an outpatient endometrium sampling (Pipelle) without hysteroscopy or they could have been scheduled for an inpatient hysteroscopy under general anaesthesia. In 2004, we recorded all women that visited the outpatient department of our clinic because of PMB. Based on unpublished data from this database, 5% of the women with endometrial thickness > 4 mm did not have an office hysteroscopy. Because this 5% is rather low, and because the choice for not having an office hysteroscopy is rather random, we feel that it is unlikely that these drop-outs have affected our results.

Another limitation of this study is the fact that the hysteroscopist was aware of the sonographic findings. Women with thicker endometrium or women with suspicion of intracavitary pathology at TVU might therefore be evaluated more thoroughly at hysteroscopy than women with thinner endometrium. However, the definition of a polyp was well described in this study, and it seems unlikely that polyps might have been missed in case of thinner endometrium. Furthermore, the pathologist who was unaware of the TVU findings made the final diagnosis of a polyp. Finally, if such a bias were to be present, it would lead to an overestimation of accuracy. Thus, the poor discriminative capacity that we found might even be an overestimation of the accuracy.

According to current guidelines the work-up of women with PMB focuses on exclusion of endometrial carcinoma, and the work-up starts with measurement of endometrial thickness via TVU. In cases of endometrial thickness > 4 mm, further evaluation of the endometrium is required to exclude malignancy using either hysteroscopy with endometrial biopsy or by blind office endometrial sampling.^{1,3} In cases where malignant pathology has been excluded by office endometrial sampling (e.g. Pipelle), significant benign pathology (i.e. endometrial polyps) may have been overlooked. Imaging of the distended uterine cavity is required to most accurately diagnose focal lesions such as endometrial polyps, and the techniques most often employed are hysteroscopy or Saline Infusion Sonography (SIS). Hysteroscopy or SIS

with the aim of detecting endometrial polyps can be incorporated in the diagnostic work-up at first episode of bleeding or in case the bleeding persists or recurs.^{1,3,10} Hysteroscopy has the advantage of allowing simultaneous removal of polyps at the time of diagnosis, although data regarding the efficacy of polypectomy in treating PMB are scarce.¹¹ Therefore it is still questionable if the removal of polyps reduces the probability of recurrent bleeding and from this point of view it can be questioned if the diagnosis of endometrial polyps is important.

Although data regarding efficacy of polypectomy are scarce, polyps are a frequent finding in the work-up of women with PMB. The prevalence of polyps in women with PMB and an endometrial thickness of more than 4 mm has been reported to be as high as 40%, a finding that was confirmed in this study.^{6,12} Conventional TVU is available to most gynaecologists but SIS or outpatient hysteroscopy may not be. In current practice hysteroscopy or SIS are often performed in case of PMB and endometrial thickness > 8 mm or suspicion of intracavitary pathology on TVU.¹

This study addressed the question of whether endometrial thickness measurement via TVU, with its established role in the diagnostic work up of PMB to exclude endometrial carcinoma, could also provide useful information about the presence or absence of the most likely benign intrauterine pathology, endometrial polyps. If so, subsequent testing via hysteroscopy or SIS could be employed to confirm or refute the diagnosis of an endometrial polyp in appropriate women. However, our study demonstrates that TVU endometrial thickness measurement has poor discriminative ability for detecting or excluding endometrial polyps and thus is not clinically useful in the diagnosis of such benign focal pathology.

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