



Diagnostic accuracy of endometrial thickness for the detection of intra-uterine pathologies and appropriateness of performed hysteroscopies among asymptomatic postmenopausal women



L. Giannella^{a,*}, K. Mfuta^a, T. Setti^a, F. Boselli^b, E. Bergamini^a, L.B. Cerami^a

^a Local Health Authority of Reggio Emilia, Division of Obstetrics and Gynaecology, Cesare Magati Hospital, Scandiano, Italy

^b Mother–Infant Department, Institute of Obstetrics and Gynaecology, University of Modena and Reggio Emilia, Modena, Italy

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ABSTRACT

Objective: To measure the diagnostic accuracy of endometrial thickness for the detection of intra-uterine pathologies among asymptomatic postmenopausal women, and to test the diagnostic accuracy and appropriateness of performed hysteroscopies.

Study design: Prospective study of 268 asymptomatic postmenopausal women with endometrial thickness ≥ 4 mm referred to diagnostic hysteroscopy. The diagnostic accuracy of various endometrial thickness cut-off values was tested. Histological and hysteroscopic results were compared to measure the diagnostic accuracy of outpatient hysteroscopies.

Results: No endometrial thickness cut-off values had optimal diagnostic accuracy [positive likelihood ratio (LR+) > 10 and negative likelihood ratio (LR-) < 0.1]. The best endometrial thickness cut-off value for the detection of all intra-uterine pathologies was ≥ 8 mm (LR+ 10.05 and LR- 0.22). An endometrial thickness cut-off value ≥ 10 mm did not miss any cases of endometrial cancer. The success rate of diagnostic hysteroscopy was 89%, but 97% of these revealed a benign intra-uterine pathology. The diagnostic accuracy of hysteroscopy was optimal for all intra-uterine pathologies, except endometrial hyperplasia (LR- 0.52).

Conclusion: Using an endometrial thickness cut-off value ≥ 4 mm, only 3% of performed hysteroscopies were useful for the detection of pre-malignant or malignant lesions. Despite the finding that endometrial thickness did not show optimal diagnostic accuracy, using the best cut-off value (≥ 8 mm) may be helpful to decrease the number of false-positive results. No cases of endometrial cancer were diagnosed in asymptomatic postmenopausal women with endometrial thickness < 10 mm.

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Introduction

The incidental finding of a thickened endometrium is common among postmenopausal women. Although there are endometrial thickness cut-off values to discriminate between postmenopausal women with vaginal bleeding at high and low risk for intra-uterine pathologies, no recommendations exist regarding the clinical management of asymptomatic postmenopausal women [1].

The lack of clear guidelines about good clinical practice has resulted in many physicians using the same clinical recommendations for both symptomatic and asymptomatic postmenopausal

women. This has led to indiscriminate use of unnecessary assessments with considerable physical and psychological discomfort.

It has been shown that the risk of malignancy is higher among postmenopausal women with vaginal bleeding and endometrial thickness of 4 mm [2,3], and Menzies et al. observed the same risk of cancer among asymptomatic postmenopausal women with endometrial thickness of 15 mm [4]. These results suggest that the incidence of endometrial cancer is significantly lower in asymptomatic postmenopausal women compared with symptomatic postmenopausal women. Indeed, some studies have reported a malignancy rate of 0% among asymptomatic postmenopausal women with a thickened endometrium [5,6]. Likewise, it has been reported that approximately 90% of women with endometrial cancer experience vaginal bleeding, and a malignancy may occur without signs or symptoms in 20% of cases [7,8].

Previous studies have found that endometrial thickness is a non-optimal tool to identify asymptomatic postmenopausal

* Corresponding author at: Division of Obstetrics and Gynaecology, Cesare Magati Hospital, Viale Martiri della Libertà 6, 42019 Scandiano, Reggio Emilia, Italy. Tel.: +39 0522850312; fax: +39 0522850415.

E-mail address: lucazeta1976@libero.it (L. Giannella).

women at high or low risk for endometrial pathology or malignancy [9,10].

As such, this study aimed to measure the diagnostic accuracy of endometrial thickness for the detection of all intra-uterine pathology among asymptomatic postmenopausal women. Furthermore, the study tested the diagnostic accuracy and appropriateness of outpatient hysteroscopies.

Materials and methods

This observational prospective study included 268 asymptomatic postmenopausal women with endometrial thickness ≥ 4 mm referred to diagnostic hysteroscopy. The study was performed at Cesare Magati Hospital, Italy from January 2008 to February 2013. The provincial ethical committee approved the study and each woman gave informed consent.

Exclusion criteria were: vaginal bleeding; treatment with tamoxifen, hormone replacement therapy or anticoagulants; and oncological disease. Postmenopausal status was defined as the absence of menstruation for at least 12 months after 40 years of age, with any pathological cause of amenorrhoea excluded.

On the day of hysteroscopic examination, each woman completed a questionnaire regarding her medical history. Women who met the inclusion criteria were subjected to transvaginal ultrasound before hysteroscopy; this was performed by an experienced sonographer, and the surgeon was blinded to the ultrasound findings. Only asymptomatic postmenopausal women with endometrial thickness ≥ 4 mm were included in the study. When it was not possible to perform a hysteroscopy, these women were excluded from the study.

All diagnostic hysteroscopies were performed without anaesthesia in an outpatient setting, using a saline solution as the distension medium and a 3.5-mm diagnostic single-flow sheath with a viewing angle of 30°. Ultrasound examination was performed using a 5–9 MHz vaginal transducer, and the thickest part of the anteroposterior bilayer endometrium was measured in the sagittal plane.

All hysteroscopic findings were confirmed by a definitive histological diagnosis which was considered as the reference standard. The following criteria were used, based on the hysteroscopic appearance: (1) women without any intra-uterine lesions (atrophy) underwent Vabra endometrial sampling; (2) women with suspected pre-malignant or malignant lesions underwent a targeted biopsy and random biopsies of each uterine wall; (3) women with polyps or myomas underwent intra-uterine lesion resection; and (4) based on the progression rate of endometrial hyperplasia to endometrial cancer [11], all women with atypical endometrial hyperplasia, and all women with intra-uterine malignant lesions, underwent a hysterectomy which represented the reference standard as the definitive histological

finding; this was done in order to avoid several underdiagnoses as reported in the literature [12].

Patient characteristics taken into account were age, age at menarche, age at menopause, parity, body mass index [BMI = weight (kg)/height²(m²)], hypertension and diabetes. Histological and hysteroscopic findings were compared to measure the diagnostic accuracy of hysteroscopy for intra-uterine pathologies. Likewise, different endometrial thickness cut-off values were tested to measure their diagnostic accuracy for intra-uterine lesions. Finally, the appropriateness of hysteroscopies was determined based on the number of negative hysteroscopies (atrophy), unrecognized benign lesions (polyps, myomas, endometrial hyperplasia without atypia), unrecognized pre-malignant lesions (atypical endometrial hyperplasia) and unrecognized endometrial cancers. Overall, unnecessary hysteroscopies were represented by negative hysteroscopies (atrophy) and unrecognized benign lesions.

Categorical variables were evaluated using Chi-squared test, and one-way analysis of variance was used to test the difference between the means of several subgroups of a variable. The diagnostic test was used to calculate test characteristics such as sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR-), and positive and negative predictive values (PPV and NPV) from a 2 × 2 table. Given that LR+ is given by the mathematical formula (sensitivity)/(1-specificity), LR+ would be $+\infty$ in cases with specificity of 100%. In the latter case, its value has not been reported. Finally, a receiver operating characteristic (ROC) curve analysis was performed by dividing the sample into women without intra-uterine pathologies (atrophy) and women with intra-uterine pathologies (myoma, polyp, hyperplasia or cancer).

Statistical analyses were performed using MedCalc (MedCalc Software, Mariakerke, Belgium). $p < 0.05$ was considered to indicate statistical significance.

Results

In total, 268 asymptomatic postmenopausal women with endometrial thickness ≥ 4 mm referred to diagnostic hysteroscopy were evaluated. Two hundred and eighty-eight women with postmenopausal vaginal bleeding, 28 women receiving hormone replacement therapy, 32 women with a cervical canal stenosis that made outpatient hysteroscopy impracticable, 52 women receiving tamoxifen, and 57 women with endometrial thickness < 4 mm were excluded from this study.

Histological examination revealed endometrial atrophy in 156 (56.8%) women, endometrial polyps in 92 (34.4%) women, submucosal myomas in 12 (4.5%) women, endometrial hyperplasia in eight (2.9%) women (two cases of complex hyperplasia with atypia, three cases of complex hyperplasia without atypia and three cases of simple hyperplasia without atypia), and endometrial

Table 1
Patient characteristics and intra-uterine findings of study participants.

Intra-uterine findings	Patient characteristics									
	Age (years)	Age at menarche (years)	Age at menopause (years)	Body mass index (kg/m ²)	Parous n = 254	Nulligravid n = 14	Diabetic n = 21	Not diabetic n = 247	Hypertensive n = 147	Not hypertensive n = 121
Atrophy	63.6	12.3	50.7	26.8	144 (56.6%)	8 (57.2%)	12 (57.1%)	140 (56.7%)	68 (46.2%)	84 (69.4%)
Polyp	63	12.6	51	29.3	92 (36.2%)	0 (0%)	4 (19.1%)	88 (35.6%)	60 (40.8%)	32 (26.4%)
Myoma	61.6	12.6	50.3	27.6	12 (4.8%)	0 (0%)	0 (0%)	12 (4.9%)	8 (5.4%)	4 (3.3%)
Hyperplasia	69	11.5	54.5	28	4 (1.6%)	4 (28.5%)	4 (19.1%)	4 (1.6%)	8 (5.4%)	0 (0%)
Cancer	64	12.2	52.2	29.7	2 (0.8%)	2 (14.3%)	1 (4.7%)	3 (1.2%)	3 (2.2%)	1 (0.9%)
p-Value	0.37 ^a	0.29 ^a	0.19 ^a	0.13 ^a		$< 0.0001^b$		0.0001 ^b		0.0011 ^b

^a Using one-way analysis of variance.

^b Using Chi-squared test.

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