

Accuracy of hysteroscopy made by young residents in detecting endometrial pathologies in postmenopausal women

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Summary

Purpose of investigation: The aim of the study was to analyze the diagnostic value of hysteroscopy made by young residents in evaluating uterine cavity compared to experienced hysteroscopists with histological diagnosis as reference in postmenopausal women, with particular attention to endometrial hyperplasia and cancer. **Materials and Methods:** A total of 600 postmenopausal women that underwent diagnostic hysteroscopy (DH) between January 2011 and December 2013 were evaluated. The authors compared the first 200 hysteroscopic findings of each young resident with those of seniors that supervised all the procedures, regarding the same patients. Subsequent histological evaluation was obtained by operative hysteroscopy or endometrial biopsy. Residents' and seniors' data were compared with the final histological diagnosis established by anatomopathologist. **Results:** No adverse effects such as vaso-vagal reactions or uterine perforations in DH neither in operative hysteroscopic procedures were reported. Hysteroscopy made by residents had 60%, 9.09%, and 70.4% sensitivity (SE) and 97.1%, 98.8%, and 99.1% specificity (SP) in detecting hyperplasia without atypia, hyperplasia with atypia, and endometrial cancer, respectively. On the other hand, DH made by seniors resulted in 85%, 72.7%, and 96.3% SE and 99.8%, 99.8%, and 100% SP, in detecting the same three histological findings. **Conclusion:** Outpatient hysteroscopy made by residents at their endoscopic experience beginning has good accuracy in detecting clear endometrial malignant lesions, unlike in detecting premalignant lesion as hyperplasia with atypia. This could signify that more than 200 hysteroscopies are necessary for a resident to well recognize premalignant and malignant lesions.

Key words: Diagnostic hysteroscopy; Postmenopausal women; Endometrial cancer; Endometrial hyperplasia; Residents.

Introduction

Endometrial carcinoma (EC) is the sixth commonest female malignancy worldwide and it represents 5% of all women cancer; 288,000 new cases were registered in 2010 [1]. This carcinoma accounted for 4.8% of new cancer diagnosis among women between 2003 and 2005 in Italy; in the same country the mean annual number of endometrial cancer cases was 25.4 on 100,000 women [2].

Abnormal uterine bleeding (AUB) in menopause occurs in almost 90% of affected patients and is the most common first-presenting symptom. Ten percent of postmenopausal women presents AUB, [3] but only 10-15% of these women have endometrial cancer.

Actually no satisfactory screening method has been validated for EC; nevertheless this carcinoma is usually diagnosed at early stages because most women who experience AUB quickly consult with gynecologist.

Over the last few years many methods were developed for evaluating the uterine cavity. The first-line examination is worldwide considered transvaginal sonography (TVS) because of its simplicity and its good accuracy for most uterine abnormalities. However there are conflicting data about its diagnostic accuracy in case of endometrial cancer. Diagnostic hysteroscopy (DH) is considered second-

line examination, but its advantage of allowing direct and dynamic visualization of the endometrium and the uterine cavity made it the gold standard in the management of AUB [4-6]. It can be performed as an office procedure without anesthesia and with minimal morbidity. Moreover, the possibility to perform focused biopsy improves its diagnostic accuracy [7].

Previous trials have evaluated the accuracy of hysteroscopy [8, 9] and have also compared it with other diagnostic techniques as transvaginal ultrasound, sonohysterography, and magnetic resonance imaging.

DH is a simple technically procedure, but the interpretation of anatomical features can be not so easy. To date there are no satisfactory data regarding the significance of this important diagnostic instrument in non-experienced hands.

The purpose of this study was to evaluate the diagnostic accuracy of hysteroscopy made by young residents in the assessment of uterine cavity in postmenopausal women, using the final histologic finding as reference.

Materials and Methods

Postmenopausal patients referred to the hysteroscopic service of the Department of Woman and Child Health, Obstetrics and Gynaecology Clinic, University of Padua, from January 2011 to December 2013 were enrolled in an observational longitudinal study. All women were referred to hysteroscopy for AUB or a suspected finding on ultrasonography (endometrial thickening, endometrial

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Table 1. — Sensitivity, specificity, positive, and negative predictive values (PPV and NPV) and positive and negative likelihood ratio (LR + and LR -) of hysteroscopies made by residents (R) and by seniors (S) with histology as reference.

	Negative		Hyperplasia without atypia		Hyperplasia with atypia		Cancer	
	R %	S %	R %	S %	R %	S %	R %	S %
Sensitivity	97.32	100.00	60.00	85.0	9.09	72.73	70.37	96.30
Specificity	74.36	89.74	97.14	99.82	98.81	99.83	99.13	100.00
PPV	96.21	98.49	60.00	97.14	12.50	88.89	79.17	100.00
NPV	80.56	100.00	97.14	98.94	98.31	99.49	98.61	99.83
LR +	3.80	9.75	21.00	476.0	7.65	428.36	80.64	-
LR -	0.04	0.00	0.41	0.15	0.92	0.27	0.30	0.04

Table 2. — Concordance between hysteroscopic features and histological diagnosis among residents.

		Hysteroscopic findings by residents				Total
		Negative	Hyperplasia without atypia	Hyperplasia with atypia	Cancer	
Histological diagnosis	Negative	508 (97.3%)	12 (2.3%)	1 (0.2%)	1 (0.2%)	522 (100%)
	Hyperplasia without atypia	10 (25.0%)	24 (60.0%)	5 (12.5%)	1 (2.5%)	40 (100%)
	Hyperplasia with atypia	6 (54.5%)	1 (9.1%)	1 (9.1%)	3 (27.3%)	11 (100%)
	Cancer	4 (14.8%)	3 (11.1%)	1 (12.5%)	19 (70.4%)	27 (100%)
	Total	528 (88%)	40 (6.7%)	8 (1.3%)	24 (4.0%)	600 (100%)

polyps or any other suspected irregularity) performed by the referring gynecologists.

For the study the authors selected the first 200 hysteroscopies performed by three young residents that had attended the hysteroscopic service at least three months prior to the beginning of the procedures.

All diagnostic outpatient hysteroscopies were performed in a dedicated room without sedation using a 2.9 mm-diameter hysteroscope with a continuous-flow and a 30° fore-oblique lens and a normal saline solution was used as the distention medium. Neither preoperative cervical ripening nor a cervical block was performed. No systemic drugs were given to women before the procedure. The hysteroscope was guided through the vagina, the endocervical canal, and the uterine cavity without using a speculum nor a tenaculum.

For the data analysis, the authors firstly considered endometrial features described by the young residents without considering the final diagnosis made by two experienced hysteroscopists that supervised all the procedures. Then they compared seniors' hysteroscopic results of the same patients with those of the residents.

Hysteroscopic findings were divided in negative (atrophy, non-malignant lesions as endometrial polyps, and synechiae), hyperplasia without atypia (endometrium thickened diffusely or in polypoid appearance, that represents glandular-stromal growth with mucosal edema and increased vascularization), hyperplasia with atypia (dishomogeneous glandular-stromal growth with increased glandular-stromal ratio, and increased vascularization) or cancer (irregular friable polypoid formations with dilated and tortuous vessels, necrosis or bleeding).

The authors collected data regarding patient's age and body mass index. Menopause was defined as spontaneous cessation of menses for 12 consecutive months or more. AUB was considered any uterine bleeding thereafter.

For all patients, an office endometrial biopsy by stainless steel Novak curette or resectoscopy (i.e., polyp removal or focal endometrial resection) was performed, enabling histological diagnosis and appropriate therapy.

Histological diagnosis was considered the gold standard to define hysteroscopy efficacy in diagnosing all the endometrial le-

sions. Histological results were grouped into the same categories of DH findings: negative, hyperplasia without atypia, hyperplasia with atypia, and EC.

The authors calculated the sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV), and positive and negative likelihood ratios (LR + and LR -) for each hysteroscopic finding revealed by young residents and seniors.

Results

A total of 600 hysteroscopic findings were evaluated, 200 for each young resident. The mean age of women was 61.37 years and the mean body mass index was 25.97 kg.

No adverse effects such as vaso-vagal reactions or uterine perforations in DH neither in operative hysteroscopic procedures were reported.

The most common hysteroscopic descriptions, observed in 528 cases among residents and in 530 cases among seniors, were negative findings. The young residents registered 40 cases of hyperplasia without atypia, eight cases of hyperplasia with atypia, and 24 cases of EC at DH. On the other hand, the seniors described 35 cases of hyperplasia without atypia, nine cases of hyperplasia with atypia, and 26 cases of EC at the same DHs.

The histological results revealed 522 negative findings, 40 cases of hyperplasia without atypia, 11 cases of hyperplasia with atypia, and 27 cases of cancer.

SE, SP, PPV, and NPV and LR + and LR - for each hysteroscopic finding are shown in Table 1, distinguished in residents and seniors.

Concordance between hysteroscopic features and histological diagnosis is shown in Table 2 for the young residents and in Table 3 for the seniors.

Table 3. — Concordance between hysteroscopic features and histological diagnosis among seniors.

		Hysteroscopic findings by seniors				Total
		Negative	Hyperplasia without atypia	Hyperplasia with atypia	Cancer	
Histological diagnosis	Negative	522 (100%)	0 (0%)	0 (0%)	0 (0%)	522 (100%)
	Hyperplasia without atypia	5 (12.5%)	34 (85%)	1 (2.5%)	0 (0%)	40 (100%)
	Hyperplasia with atypia	2 (18.2%)	1 (9.1%)	8 (72.7%)	0 (0%)	11 (100%)
	Cancer	1 (3.7%)	0 (0%)	0 (0%)	26 (96.3%)	27 (100%)
	Total	530 (88.3%)	35 (5.8%)	9 (1.5%)	26 (4.3%)	600 (100%)

Hysteroscopy made by residents demonstrated a high SE and SP in recognising atrophy and benign lesion, such as polyps and synechiae.

Noteworthy is that hyperplasia without atypia was diagnosed in 40 cases, of which only 24 cases had been suspected by the young residents and the other 16 cases were not suspected during the procedures. Similarly, hyperplasia with atypia was confirmed in 11 cases, of which only one case had been suspected by the young residents and the other ten cases were not suspected (Table 2). These results demonstrated a low SE, PPV, and LR+ in suspecting atypical hyperplasia among young residents (Table 1). On the other hand, the residents hysteroscopic findings were not suspicious for malignancy in eight cases proved by histological examination, but they were diagnostic for cancer in 19 patients (Table 2). Therefore the authors found a good SP and VPV but low SE and PPV among residents in diagnosing cancer (Table 1).

Experienced hysteroscopists demonstrated a high SE and SP in recognising all hysteroscopic findings. In particular, hyperplasia without atypia was diagnosed in 40 cases, of which 34 cases had been suspected by the seniors and hyperplasia with atypia was suspected in eight out of 11 cases. Of 27 women with cancer, 26 of them were immediately diagnosed by seniors at DH (Table 3). Therefore these data revealed a SE, SP, PPV, and NPV higher than those of residents in detecting hyperplasia with and without atypia and cancer (Table 1).

Discussion

The most common malignant carcinoma of the female genital tract is nowadays EC. AUB in menopause occurs in almost 90% of affected patients and is the most common first-presenting symptom [3]. Therefore differentiation of benign from malignant causes of postmenopausal bleeding is very important. Actually no satisfactory screening method has been validated for EC diagnosis.

In the past, the common practice to evaluate postmenopausal bleeding was dilatation and curettage. Over the last few years many other methods have been developed for evaluating the uterine cavity. Nowadays the first-line examination is worldwide considered TVS because of its simplicity and its good accuracy for most uterine abnormalities [4, 5].

However there is still discussion over the best cut-off value for endometrial thickness that should guarantee conservative management. After the menopause endometrium undergoes atrophic changes due to estrogenic lack and many cut-off values for pathological endometrial thickness have been proposed.

Almost every guideline refers to a meta-analysis performed in 1998 by Smith-Bindman *et al.* in which they suggested that cut-off value for endometrial thickness that recommended further investigations in women with postmenopausal bleeding is beyond five mm; below this range they proposed a conservative management [10].

Previous studies in fact have shown that the risk of malignancy decreases to one in 1,000 when endometrial thickness is < four mm in a postmenopausal women with bleeding [11].

Chandavarkar *et al.* underlined that type 2 EC may not always induce a thickened endometrium because it does not usually develop from hyperplasia, therefore postmenopausal bleeding requires endometrial direct evaluation despite endometrial thickness [12, 13]. They also underlined that type 2 tumors are more aggressive, because they metastasize far more rapidly. Hence they recommended that women be counselled that the risk of cancer in symptomatic women with endometrial thickness \leq four mm is very low, but EC cannot be completely excluded, especially when there is persistent bleeding.

As a result of findings of Litta *et al.* in 220 postmenopausal women with AUB, transvaginal ultrasonography alone is inadequate to rule out EC and outpatient hysteroscopy with biopsy is mandatory in all of these [14].

The importance of incidentally detected thick endometrium in asymptomatic postmenopausal women is still controversial. A systematic review published in 2012 reported a mean endometrial thickness in menopause of 2.9 mm in 2,952 studied women and found out no valid cut-off to suggest histological examination in asymptomatic women [15].

DH is considered second-line examination, but its advantage of allowing direct and dynamic visualization of the endometrium and the uterine cavity made it the gold standard for evaluating them. Furthermore biopsy may improve its diagnostic accuracy [7, 16].

Both TVS and DH are accessible office procedures for the diagnosis of abnormal intrauterine pathologies. Direct

visualization of uterine cavity allows in deciding if further surgical procedures are needed and which technical approach is the most appropriate. After DH, to solve the problem, a resective hysteroscopy could be necessary in case of polyps or confined hyperplasia; a radical surgery in case of cancer or a radical endometrial resection by hysteroscopy as an alternative to hysterectomy in selected patients with atypical focal endometrial lesions [17].

Hysteroscopy can be performed as an office, safe procedure without anesthesia, because it is usually well-tolerated and has minimal morbidity. Cervical preparation before hysteroscopy is not used because there are not evidences of benefit in terms of pain reduction. Procedural pain is significantly reduced with the use of small-diameter hysteroscope, through a vaginoscopic approach, and with the use of sterile sodium chloride solution as the distention medium, because it seems to reduce incidence of vasovagal episode [18]. It was even demonstrated that office-based hysteroscopic polypectomy using a five mm-diameter hysteroscope could be a safe and a well-tolerated procedure [19]. In case of operative hysteroscopy, when a resectoscopic approach is necessary in high-risk patient, spinal anesthesia can be performed to reduce the risks associated to anesthesia [20].

In this study, hysteroscopic visualization of uterine cavity by young residents showed good accuracy in detecting overall atrophy and benign uterine cavity abnormalities, such as polyps and synechiae. The calculated SE and SP are comparable with senior and with others in literature [8, 16, 21].

Endometrial hyperplasia diagnosis may not be obvious especially in early stages of the disease. Other published studies evaluating endometrial hyperplasia reported a SE, SP, PPV, and NPV of 61.6%, 95.2%, 79.4%, and 89.3%, respectively [22], and 56.5%, 91.6%, 72.2%, and 84.6%, respectively [16]. These results are similar to seniors findings in this study. On the other hand, results of residents, especially for hyperplasia with atypia, are not in line with the aforementioned findings. In the latter, only about two-thirds of the cases of hyperplasia were correctly confirmed by histology, but in less than one-third of the cases, it was not well-recognized during DH. Lower SE and PPV of hysteroscopy made by residents in recognizing hyperplasia with or without atypia can be explained by the resident's tendency to overestimate malignant lesion in order to avoid unrecognizing cancer.

The main objective in postmenopausal women, especially if they presented with AUB, is to detect or rule out EC. Regarding the present findings, this cancer can be detected by residents with no high SE, but with very good SP. These results are consistent with others in literature. Rokita *et al.* reported a SE of 61% and a SP of 90% [23] and Lo *et al.* revealed a SE of 58.8% in detecting cancer at hysteroscopy not made by residents [7]. Elfayomy *et al.*'s data also showed a SE of 50% and SP of 94.2% [16].

All this data are concordant with opinion in the literature that reported a high accuracy in differentiating benign and malignant endometrial pathologies, but a limited role of DH in revealing hyperplasia, cancer or both [24, 25].

Conclusions

The results of the present study confirm the opinion that hysteroscopy has great accuracy in diagnosing focal pathology and especially in distinguishing benign and malignant endometrial pathologies.

According to the authors' experience, outpatient hysteroscopy made by residents in their endoscopic practice beginning has good accuracy in detecting clear endometrial malignant lesions, but not as good an accuracy in detecting premalignant lesion as hyperplasia with atypia. DH accuracy in expert-hands is not comparable to that in residents-hands during their first procedures. This could signify that more than 200 hysteroscopies are necessary for a resident to well recognize premalignant and malignant lesions.

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