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ORIGINAL ARTICLE

Dilatation and curettage fails to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding

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Objective. To determine the prevalence of focally growing lesions in the uterine cavity in women with postmenopausal bleeding and endometrium ≥5 mm and the extent to which such lesions can be correctly diagnosed by D&C.
Methods. In a prospective study, 105 women with postmenopausal bleeding and endometrium ≥5 mm at transvaginal ultrasound examination underwent diagnostic hysteroscopy, D&C and hysteroscopic resection of any focally growing lesion still left in the uterine cavity after D&C. Twenty-four women also underwent hysterectomy. If the histological diagnosis differed between specimens from the same patient, the most relevant diagnosis was considered the final one.
Results. Eighty percent (84/105) of the women had pathology in the uterine cavity, and 98% (82/84) of the pathological lesions manifested a focal growth pattern at hysteroscopy. In 87% of the women with focal lesions in the uterine cavity, the whole or parts of the lesion remained *in situ* after D&C. D&C missed 58% (25/43) of polyps, 50% (5/10) of hyperplasias, 60% (3/5) of complex atypical hyperplasias, and 11% (2/19) of endometrial cancers. The agreement between the D&C diagnosis and the final diagnosis was excellent (94%) in women without focally growing lesions at hysteroscopy.
Conclusion. If there are focal lesions in the uterine cavity, hysteroscopy with endometrial resection is superior to D&C for obtaining a representative endometrial sample in women with postmenopausal bleeding and endometrium ≥5 mm.

Key words: dilatation and curettage; endometrial pathology; hysteroscopy; postmenopausal bleeding; ultrasound

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Between 5 and 15% of women with postmenopausal bleeding have endometrial carcinoma (1, 2). Therefore, these women need to be examined. Transvaginal ultrasound with measurement of endometrial thickness can be used to discriminate between normal and pathological endometrium if a cut-off level of 5 mm is used, values ≥5 mm indicating pathology (3). Women with postmenopausal bleeding and endometrium ≥5 mm should undergo endometrial sampling, because pathological endometrium is found in about 60% of these women (4). Traditionally, dilatation and curettage (D&C) has been the method of choice for obtaining an endometrial sample. However, in two studies comprising both pre- and post-menopausal women with abnormal uterine bleeding, 40–90% of polyps and 43–66% of hyperplasias were missed by D&C (5, 6). There are studies indicating that both polyps and hyperplasia are risk factors for devel-

Abbreviations:
D&C: dilatation and curettage; HRT: hormone replacement therapy; CL: confidence limits; ROC-curve: receiver operating characteristic curve.

oping endometrial carcinoma (7, 8). Thus, D&C might not be the best method of investigating women with postmenopausal bleeding, unless focally growing lesions – such as polyps – can be excluded.

The aim of this study was to determine the prevalence of focally growing lesions in the uterine cavity and the extent to which focally growing lesions can be diagnosed and removed by conventional D&C in women with postmenopausal bleeding and endometrium ≥5 mm at transvaginal ultrasound examination.

Patients and methods

The Ethics Committee of the Medical Faculty at Lund University, Sweden, approved of the study. Consecutive postmenopausal women presenting at the clinic with postmenopausal bleeding underwent transvaginal ultrasound examination by one of two examiners (EE, LV). A woman was considered to be postmenopausal, if she reported a period of at least 12 months of amenorrhea after the age of 40 years, provided that the amenorrhea was not explained by medication or disease. A postmenopausal bleeding was defined as any vaginal bleeding in a postmenopausal woman not on hormone replacement therapy (HRT), or as an unscheduled bleeding in a postmenopausal woman on HRT. The age at menopause was determined retrospectively on the basis of the woman's information on her last menstrual period. The median age of the women was 66 years (range 43–88), and the median time elapsed since menopause was 16 years (range 1–47). Twenty-eight women (27%) used combined oral HRT, 22 (21%) used locally administered estrogens, and three women (3%) were on tamoxifen treatment. One hundred and five women whose endometrium measured ≥5 mm at ultrasound examination (the 'double layer measurement technique' was used) (9) consented to take part in the study. Under general anesthesia they underwent hysteroscopy and D&C by the gynecologic surgeon of the team (AR) within six weeks of the ultrasound examination. The ultrasound equipment used was a Sequoia Ultrasound system (Acuson Inc., Mountain View, CA, USA) with a 4 to 7.5 MHz transvaginal transducer.

Hysteroscopy was carried out using a 10 mm Storz resectoscope (Karl Storz, Tuttingen, Germany). The uterine cavity was distended with glycine ethanol up to a pressure of 100 mmHg. Any focally growing lesion in the uterine cavity was identified by the hysteroscopist, and its presence was noted in the research protocol. Then the hysteroscope was removed, and D&C was carried out including 'fishing' for polyps with a forceps. The hysteroscope was then reinserted into the uterine cavity, and any localized lesion still left in the cavity was removed under hysteroscopic control. If the endometrial curettage was very scant, a piece of the endometrium was resected even when no focal lesion had been detected in the cavity. The hysteroscopist had no knowledge of the ultrasound findings when performing the hysteroscopy.

The curettage from the cervix and the corpus uteri, and any resected tissue, were placed in separate containers with 10% formaldehyde and sent for separate histological analysis by the pathologist of the team (LS). A predetermined classification system for histological diagnosis was used: insufficient material, normal endometrium (proliferative endometrium, secretory endometrium, mixed hormonally induced changes, and atrophic endometrium), benign pathological endometrium (simple hyperplasia, complex hyperplasia, focal hyperplasia, endometrial polyp, submucous myoma, and adenofibroma), premalignancy/malignancy (complex hyperplasia with atypia, endometrial carcinoma, and adenosarcoma). The final diagnosis of each woman was made on the basis of the histological diagnosis of the curettage specimen, any resected material, and the hysterectomy specimen when present. If the diagnosis differed between the specimens, the most relevant diagnosis was considered the final one. Premalignancy/malignancy in any specimen was considered the final diagnosis.

Receiver operating characteristic curves (ROC-curves) (10) were plotted to define the cut-off value for endometrial thickness as measured by transvaginal ultrasound that best discriminated between focal and non-focal lesions seen at hysteroscopy.

The Chi-squared test with continuity correction was used to compare unpaired categorical data, and the Mann-Whitney test was used to compare continuous unpaired data. Exact confidence limits (95% CL) were calculated using the binomial distribution. p-values<0.05 were considered statistically significant. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, USA, 1996) and the StatXact-3 statistical program (Cytel Software Corporation, Cambridge, Massachusetts, USA, 1995).

Results

At hysteroscopy, 83% (95% CL 74–90%; 87/105) of the women had focally growing lesions. According to the hysteroscopist the whole or parts of the focal lesion remained in the uterine cavity after D&C in 75 of 86 women (87%, 95% CL 78–93%) with focally growing lesions. Rehysteroscopy failed

in one woman because of technical problems, it was suboptimal in six women (technical problems, $n=2$; blood disturbing the view, $n=4$). It was successfully performed in 98 women. Seventy-four of the 75 women had their remaining focal lesions hysteroscopically resected, but in one woman a lesion judged to be a submucous myoma was left *in situ*. In 18 women (17%), hysteroscopy revealed a smooth endometrial cavity without any focally growing lesions. In 16 of these 18 women hysteroscopic resection was carried out because the D&C specimen was judged to be too scant for a histological diagnosis to be made. In all, 92% (97/105) of the women underwent hysteroscopic resection.

Twenty-four women subsequently underwent abdominal hysterectomy, 22 because of premalignancy/malignancy in the specimen obtained at D&C or hysteroscopic resection, one because of a large submucous myoma, and one because of discrepancy between the ultrasound diagnosis and the diagnosis obtained at hysteroscopic resection. In the latter case, the ultrasound diagnosis suggested malignancy, but the histological diagnosis of the resected material was adenofibroma. The hysterectomy specimen showed adenosarcoma. Two women with complex atypical hyperplasia did not undergo hysterectomy because of poor health but were treated with gestagen therapy.

The agreement between the diagnosis made on the basis of the D&C specimens and the final diagnosis is shown in Table I. Eighty percent (95% CL 71–87%; 84/105) of the women had endometrial pathology. The diagnosis made on the basis of the D&C specimen agreed with the final diagnosis in 50% (52/105) of the women. D&C failed to diagnose 58% (95% CL 42–73%; 25/43) of polyps, 50% (95% CL 19–81%; 5/10) of hyperplasias/focal hyperplasias, 60% (95% CL 15–95%; 3/5) of complex atypical hyperplasias, 11% (95% CL 1–33%; 2/19) of endometrial cancers, and the adenosarcoma. The final pathological diagnosis, and the corresponding pathological diagnosis made at D&C, hysteroscopic resection and hysterectomy in the six women with a premalignancy/malignancy missed by D&C are shown in Table II. In one woman with complex atypical hyperplasia in the hysteroscopically resected specimen, the hysterectomy specimen showed simple hyperplasia, the atypical cells probably having been completely removed by hysteroscopic resection (Table II).

The median endometrial thickness in women whose polyps were removed by D&C was 8.5 mm *vs.* 10.0 mm in women whose polyps remained in the uterine cavity after D&C ($p=0.62$; the Mann-Whitney test). If the histological diagnoses were classified as normal endometrium, benign pathol-

Table I. Agreement between the diagnosis made on the basis of the D&C specimen and the final histological diagnosis

	Final diagnosis								
D&C-diagnosis	Insufficient sample	Normal endometrium	Endometrial cancer	Adenosarcoma	Complex atypical hyperplasia	Hyperplasia/ focal hyperplasia	Endometrial polyp	Submucous myoma	**Total**
Insufficient sample	4	11	1	1		1	10	2	30
Normal endometrium		6			1	4	12	2	25
Endometrial cancer			17						17
Adenosarcoma									
Complex atypical hyperplasia					2				2
Hyperplasia/focal hyperplasia			1		2	5	3	2	13
Endometrial polyp							18		18
Submucous myoma								0	0
Total	4	17	19	1	5	10	43	6	105

Table II. Description of premalignancies/malignancies missed by D&C

Hysteroscopic findings	Pathological diagnosis at D&C	Pathological diagnosis at hysteroscopic resection	Pathological diagnosis at hysterectomy	Final pathological diagnosis
No focal lesion	Proliferative endometrium	Complex atypical hyperplasia	Simple atypical hyperplasia	Complex atypical hyperplasia
Focal lesion	Complex hyperplasia	Complex atypical hyperplasia	Simple hyperplasia	Complex atypical hyperplasia
Focal lesion	Complex hyperplasia	Complex atypical hyperplasia	Simple hyperplasia	Complex atypical hyperplasia
Focal lesion	Simple hyperplasia	Complex atypical hyperplasia	Adenocarcinoma	Adenocarcinoma, stage 1B
Focal lesion	Insufficient material	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma, stage 1B
Focal lesion	Insufficient material	Adenofibroma	Adenosarcoma	Adenosarcoma

Table III. Agreement between diagnoses made on the basis of D&C specimens and final diagnoses in relation to presence or absence of focally growing lesions at hysteroscopy

D&C diagnosis	Final diagnosis			
	Normal endometrium/ insufficient material	Benign pathology	Premalignancy/ malignancy*	
Focal lesion at hysteroscopy (n=87)				
Normal endometrium/insufficient material	5	31	2	
Benign pathology	0	27	3	Agreement: 0.59
Premalignancy/malignancy*	0	0	19	
No focal lesion at hysteroscopy (n=18)				
Normal endometrium/insufficient material	16	0	1	
Benign pathology	0	1	0	Agreement: 0.94
Premalignancy/malignancy*	0	0	0	

*Complex atypical hyperplasia, endometrial cancer, adenosarcoma.

ogy, and premalignancy/malignancy, the agreement between the diagnosis made on the basis of the D&C specimen and the final diagnosis was 59% in women with focally growing lesions at hysteroscopy *vs*. 94% in women without focally growing lesions at hysteroscopy (p=0.004, the Chi-squared test; Table III). One or more focally growing lesions were found at hysteroscopy in 96% (24/25) of the premalignancies/malignancies, 98% (42/43) of the polyps, all (6/6) submucous myomas, all (10/10) hyperplasias, 29% (5/17) of the normal endometria, but in none (0/4) of the insufficient samples.

The ROC-curve showed that the best cut off value to predict the presence of focally growing lesions at hysteroscopy was 10 mm, values ≥10 indicating focal lesions (sensitivity 66%, specificity 85%). At endometrial thickness ≥10 mm, 57 of 59 women (97%; 95% CL 88–100%) had focally growing lesions at hysteroscopy. The corresponding figures at endometrial thickness 5–9 mm were 30 of 46 (65%; 95% CL 50–79%).

Discussion

In our study, 80% of the women with postmenopausal bleeding and endometrium ≥5 mm had pathological endometrium. This is more than the 60% reported in the Nordic multicenter study by Karlsson and colleagues comprising 1168 women (4). The discrepancy is likely to be explained by Karlsson and colleagues using D&C as golden standard, whereas we performed hysteroscopic resection in almost all patients.

All pathological endometrial lesions except two manifested a focal growth pattern at hysteroscopy. Focal growth of most pathological lesions is likely to explain the poor agreement (50%) between the diagnosis made on the basis of the D&C specimen and the final diagnosis. Rehysteroscopy after D&C revealed focally growing lesions to remain totally or partly *in situ* in 87% of the women. These findings are in agreement with the findings of Englund and co-workers, who reported that the uterine cavity was satisfactorily emptied in only 35% of women undergoing D&C (11). Our results showed that in women with focally growing lesions at hysteroscopy, agreement between the D&C diagnosis and the final diagnosis was unacceptably poor (59%), whereas in women without focal lesions, the agreement was excellent (94%).

An important conclusion drawn from our results is that that one should never accept an insufficient D&C specimen in a woman with postmenopausal bleeding and an endometrium ≥10 mm. Almost all these women have focally growing lesions at hysteroscopy, and D&C seems to be a reliable diagnostic tool only if there are no focally growing lesions in the uterine cavity. On the other hand, the excellent agreement between the D&C diagnosis and the final diagnosis in women with a smooth uterine cavity mainly reflects agreement in normal results.

About half of the benign pathological lesions were missed by D&C. This is in agreement with previously reported results from study populations comprising both pre- and post-menopausal women (5, 6). We believe that it is important to correctly diagnose and remove benign pathology. Firstly, because benign pathology might be the cause of the postmenopausal bleeding. It might continue to give the patient symptoms, resulting in repeated diagnostic procedures, if it is not properly removed. Secondly, because there are studies indicating that both polyps and hyperplasia are risk factors for developing endometrial cancer (7, 8). Sixty percent (3/5) of the complex atypical hyperplasias, 11% (2/19) of the endometrial cancers, and one adenosarcoma were also missed by D&C (Table I). These figures might seem high, but not

unrealistic, because in four of the six cases where a premalignancy/ malignancy was missed by D&C the hysteroscopist found small and well delineated focal lesions. In the fifth case no focal lesion was seen at hysteroscopy, but hysteroscopic resection was performed because of scant D&C material, indicating that only minute pathological changes were present. The sixth case was an adenosarcoma, that looked highly malignant at hysteroscopy. Despite several resected biopsies at hysteroscopy, the correct diagnosis was not made until hysterectomy had been done. In a retrospective study comprising women of all ages undergoing D&C routinely before hysterectomy, Stovall and colleagues reported D&C to miss 7% (2/30) of endometrial cancers (5). This is in agreement with our results. There is a possibility of operator bias in the study by Stovall and coworkers, because the D&C was not an essential part of the diagnostic work-up, and therefore D&C might not have been thoroughly performed. In our study, operator bias also cannot be completely excluded. To avoid operator bias, it would be necessary to use two different gynecologic surgeons, one performing the D&C and the other performing the hysteroscopic resection. Nevertheless, our results and those of others (5, 6) suggest that both benign and malignant pathology may quite frequently be missed by D&C, even though the exact magnitude of this problem must be determined in a larger series of patients, where operator bias has been reduced to a minimum.

Two recently published retrospective studies have shown that hysteroscopy prior to hysterectomy because of endometrial carcinoma stage IA or IB might lead to dissemination of malignant cells (12, 13), positive peritoneal cytology being significantly associated with hysteroscopy (12, 13). All women with endometrial malignancy in our study underwent hysteroscopy and hysteroscopic resection, but no woman with endometrial carcinoma of stage 1A or 1B had positive peritoneal cytology. Only one woman with deep myometrial invasion, stage 3A, did. In a retrospective study of women with endometrial carcinoma stage IA or IB, there was no difference in the disease free 5-year survival between women who had undergone hysteroscopy before laparotomy ($n=135$) and those who had not ($n=127$) (14), nor was there a higher prevalence of positive peritoneal cytology in women who had undergone hysteroscopy before to laparotomy (14). To the best of our knowledge, there are no randomized trials comparing peritoneal dissemination of malignant cells, disease free survival, or endometrial cancer mortality between women with stage IA or IB endometrial cancer who have undergone or not undergone hysteroscopy before laparotomy. Thus, there is no strong evidence that hysteroscopy has a negative effect on prognosis in women with endometrial malignancy. We believe that hysteroscopy can be used in the management of women with postmenopausal bleeding, until more knowledge is achieved.

The results of this study show that most pathological lesions in the uterine cavity manifest a focal growth pattern, and that hysteroscopic resection is superior to D&C as a diagnostic tool in women with focally growing lesions. Office hysteroscopy or hydrosonography (infusion of saline into the endometrial cavity during ultrasound scanning) can be used as a first step of investigation to disclose the presence of focal lesions in the uterine cavity (1, 15, 16). Operative hysteroscopy should be considered in all women with postmenopausal bleeding and endometrium ≥ 5 mm, if focal lesions are present.

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References

1. O'Connell LP, Fries MH, Zeringue E, Brehm W. Triage of abnormal postmenopausal bleeding: a comparison of endometrial biopsy and transvaginal sonohysterography *versus* fractional curettage with hysteroscopy. Am J Obstet Gynecol 1998; 178: 956–61.
2. Danero S, Ricci MG, La Rosa R, Massafra C, Franchi F, Pitino C et al. Critical review of dilatation and curettage in the diagnosis of malignant pathology of the endometrium. Eur J Gynaecol Oncol 1986; 7: 162–5.
3. Smith Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. JAMA 1998; 280: 1510–17.
4. Karlsson B, Granberg S, Wikland M, Ylostalo P, Torvid K, Marsal K et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding – a Nordic multicenter study. Am J Obstet Gynecol 1995; 172: 1488–94.
5. Stovall TG, Solomon SK, Ling FW. Endometrial sampling prior to hysterectomy. Obstet Gynecol 1989; 73: 405–9.
6. Valle RF. Hysteroscopic evaluation of patients with abnormal uterine bleeding. Surg Gynecol Obstet 1981; 153: 521–6.
7. Sherman AI, Brown S. The precursors of endometrial carcinoma. Am J Obstet Gynecol 1979; 135: 947–56.
8. Pettersson B, Adami HO, Lindgren A, Hesselius I. Endometrial polyps and hyperplasia as risk factors for endometrial carcinoma. A case-control study of curettage specimens. Acta Obstet Gynecol Scand 1985; 64: 653–9.
9. Sladkevicius P, Valentin L, Marsal K. Endometrial thickness and Doppler velocimetry of the uterine arteries as discriminators of endometrial status in women with post-

menopausal bleeding: a comparative study. Am J Obstet Gynecol 1994; 171: 722–8.
10. Richardson DK, Schwartz JS, Weinbaum PJ, Gabbe SG. Diagnostic tests in obstetrics: a method for improved evaluation. Am J Obstet Gynecol 1985; 152: 613–18.
11. Englund S, Ingelman-Sundberg A, Westin B. Hysteroscopy in diagnosis and treatment of uterine bleeding. Gynecologia 1957; 143: 217–22.
12. Zerbe MJ, Zhang J, Bristow RE, Grumbine FC, Abularach S, Montz FJ. Retrograde seeding of malignant cells during hysteroscopy in presumed early endometrial cancer. Gynecol Oncol 2000; 79: 55–8.
13. Obermair A, Geramou M, Gucer F, Denison U, Graf AH, Kapshammer E et al. Does hysteroscopy facilitate tumor cell dissemination? Incidence of peritoneal cytology from patients with early stage endometrial carcinoma following dilatation and curettage (D & C) *versus* hysteroscopy and D & C. Cancer 2000; 88: 139–43.
14. Obermair A, Geramou M, Gucer F, Denison U, Graf AH, Kapshammer E et al. Impact of hysteroscopy on disease-free survival in clinically stage I endometrial cancer patients. Int J Gynecol Cancer 2000; 10: 275–9.
15. Parsons AK, Lense JJ. Sonohysterography for endometrial abnormalities: preliminary results. J Clin Ultrasound 1993; 21: 87–95.
16. Widrich T, Bradley LD, Mitchinson AR, Collins RL. Comparison of saline infusion sonography with office hysteroscopy for the evaluation of the endometrium. Am J Obstet Gynecol 1996; 174: 1327–34.

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