

Transvaginal sonography, sonohysterography, and hysteroscopy for investigation of focal intrauterine lesions in women with recurrent postmenopausal bleeding after dilatation & curettage

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Abstract

Purpose To determine the diagnostic accuracy of different diagnostic methods (blind dilatation & curettage (D&C), transvaginal ultrasonography (TVS), sonohysterography (SH), and hysteroscopy) compared with gold standard (hysteroscopic biopsy's histopathologic result) in diagnosis of focal intrauterine lesions of recurrent postmenopausal bleeding.

Methods 36 postmenopausal women with recurrent vaginal bleeding after a normal D&C results were enrolled into the study. TVS, SH, hysteroscopy were performed on all patients. Outcomes of blind D&C, TVS, SH, and hysteroscopy were compared with results of gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios (LR) were calculated.

Results Blind D&C sensitivity, specificity, PPV, and NPV were 47, 68, 57, 59%, respectively in comparison with gold standard. Blind D&C fails to diagnose 70% of all focal intracavitary lesions. TVS sensitivity, specificity, PPV, NPV were 63, 78, 89, 41%, respectively. SH yielded better results; with 93% sensitivity, 56% specificity, 86% PPV, and 71% NPV. Hysteroscopy sensitivity, specificity, PPV, and NPV were 100, 44, 84, 100%, respectively.

Conclusions In experienced hands, SH can be an initial evaluation method of uterine cavity for detecting focal lesions in women with recurrent postmenopausal bleeding.

Keywords Transvaginal ultrasonography · Sonohysterography · Hysteroscopy · Postmenopause · Dilatation & curettage

Introduction

Up to 80% of women with postmenopausal bleeding and endometrial thickness greater than 5 mm have endometrial pathology and most of the pathological lesions have a focal growth pattern [1, 2]. The high incidence of organic pathology, including malignancy in this age group makes early diagnosis mandatory.

Traditionally, D&C has been the method of choice for obtaining an endometrial sample. However, it is a blind procedure and histologic examination of 50 hysterectomy specimens after curettage showed that in 60% less than half of the endometrial lining was reached with the curette and in 16% less than one-fourth [3]. Thus, D&C might not be the best method of investigating women with abnormal uterine bleeding [4].

TVS is a quite sensitive, simple, and noninvasive method that has been used in the screening for uterine cavity pathologies in gynecologic practices [5, 6]. However, evaluation of the uterine cavity is limited. Small structural abnormalities can be missed and the exact localization of the lesion relative to the uterine cavity or the nature of the lesion always cannot be clearly assessed with TVS [7, 8].

SH is a simple, minimally invasive and effective ultrasound procedure that can be used to evaluate these abnormalities [9, 10]. It is mainly indicated in the cases of

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irregular endometrial echoes not adequately visualized by TVS. When endometrial lesions such as polyps, submucosal fibroids, and focal endometrial hyperplasia are suspected in symptomatic patients, it can provide the diagnosis and an unnecessary diagnostic hysteroscopy can be avoided [11].

Hysteroscopy has the advantage of directly visualizing the uterine cavity and endometrium allowing biopsy to be taken immediately from the suspected abnormality under direct vision but it does not give any information regarding adnexa and myometrium [12]. However, hysteroscopy is an invasive procedure that is associated with discomfort and is generally performed under local or general anesthesia. It is an operator-dependent technique and its sensitivity is therefore not as optimal as that of a histological examination [13]. Diagnostic hysteroscopy combined with histological examination of an endometrial biopsy is considered the 'gold standard' in the diagnosis of intrauterine abnormalities [14, 15].

In this study, we aimed to show diagnostic accuracy of blind D&C, TVS, SH, and hysteroscopy in comparison with gold standard (hysteroscopic biopsy's histopathologic result) for evaluation of focal intrauterine lesions in postmenopausal women with recurrent bleeding after D&C.

Materials and methods

The study was conducted at our hospital's gynecology department between March 2006 and March 2007. The study was approved by the ethic's committee of our hospital. Exclusion criteria were: history of endometrial carcinoma and hyperplasia with atypia, abnormal cervical cytology results, history of tamoxifen treatment and present use of postmenopausal hormone treatment.

Women with postmenopausal bleeding and endometrial thickness greater than 5 mm at TVS are evaluated with D&C in our department. But sometimes despite no recognizable endometrial pathology on D&C result, postmenopausal patients can experience recurrent vaginal bleeding. All patients having D&C and recurrent symptoms after D&C were included in our study. During our study period 53 patients with recurrent vaginal bleeding despite normal D&C pathology result had applied to our clinic. All the D&C procedures were performed by the same fourth year gynecology resident. But only 36 of them accepted to undergo all steps of the study and signed informed consent. Remaining 17 patients were not included in the study. After recruitment TVS, SH, and hysteroscopy were performed consecutively to 36 patients.

The participants were then examined by a gynecologist who is experienced in gynecologic ultrasound examination and who is blind to D&C results. For TVS, Diasonics

Synergy (General Electric, Norway) ultrasonography machine with 6.5 MHz transvaginal probe was used. The uterus was visualized longitudinally and axially, and measurement of myometrial and endometrial thickness and echogenicity were noted. Gross lesions of the myometrium, endometrium, and adnexa were noted. In postmenopausal women, we considered endometrium measuring less than 5 mm in double-layer thickness at TVS and less than 2.5 mm in single-layer thickness at SH as normal. The focal lesions were classified by the ultrasound examiner as polyp or submucous myoma. At conventional ultrasound examination, an endometrial polyp was suggested if a hyperechoic line surrounded the central endometrial complex and if the endometrium had a fairly homogenous echogenicity with or without cystic spaces. A submucous myoma was suggested at conventional ultrasound examination if a submucosal mass is continuous with the myometrium and with echogenicity similar to myometrium bulged into the endometrium. Colour or power Doppler sonography technique was not used in the present study.

SH was carried out by a second gynecologist who was experienced in gynecologic ultrasound examination and who was not told about the data of TVS. After an open sided vaginal speculum was inserted, the vagina and cervix were cleaned with an antiseptic solution. An intrauterine insemination catheter or Karman canula was then inserted into the cervical canal. The speculum was then removed. While the uterus was visualized with the transvaginal ultrasonographic probe, approximately 10 ml of sterile isotonic saline solution was slowly injected into the intrauterine cavity with a 50-ml syringe until the intrauterine cavity was clearly observed. In case of a patulous cervix, if the saline solution flowed back out of the uterus, more saline solution was continuously infused. Longitudinal and axial views of the uterus were obtained by transvaginal ultrasonography during saline solution instillation. Deformations of the central echo line, variability of endometrial echogenicity or circumscribed changes in the echogenicity of the uterine wall that impinge on the cavity were noted. At SH, endometrial polyp appeared as a well-defined, homogenous, polypoid lesion isoechoic to endometrium with preservation of endometrial-myometrial interface. At SH, we can also distinguish between intramural and submucosal myomas. Submucosal myomas were usually broad-based, hypoechoic, well-defined solid masses with shadowing and overlying layer of echogenic endometrium that distort the endometrial-myometrial interface.

An experienced hysteroscopist who is a gynecologist performed all hysteroscopies in the study. He performed ultrasonographic examination before hysteroscopic procedure for all patients also. The ultrasound examiner and the hysteroscopist were unaware of each other's ultrasonographic findings to prevent bias. Hysteroscopy was

performed under general anesthesia in all patients because of anesthesia consultation and preoperative preparations hysteroscopic procedure could be performed the following day. After preparing the cervix with an antiseptic solution, a 5-mm hysteroscope was advanced under direct visualization into the uterus. Any masses found were measured and recorded on a separate data sheet. Hysteroscopic-directed endometrial sampling was performed in all women. If masses were detected, operative hysteroscopy was applied in the same session and all of the specimens were examined by the same pathologist.

The histopathologic findings (gold standard) of hysteroscopy-guided endometrial biopsies were compared with the results obtained from blind D&C, TVS, SH and hysteroscopy separately. Polyp and submucosal myoma were considered as pathologic results whereas proliferative, secretory, atrophic endometrium and hyperplasia without atypia were regarded as normal results. There was no complication before and during the study.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive LR [sensitivity/

$(1 - \text{specificity})$], negative LR [$(1 - \text{sensitivity})/\text{specificity}$], and relative risk $[\text{RR} = (a/a + b)/(c/c + d)]$ were calculated by comparing the results of each method with those obtained by gold standard for detecting focally growing lesions in the uterine cavity. The diagnostic accuracy was calculated for each of the procedure separately.

Results

36 women (aged 46–70 years) with recurrent postmenopausal bleeding after D&C were enrolled into our study.

The endometrial thickness measured on TVS was less than 5 mm in 3 patients (8%), 5–10 mm in 16 patients (44%), and greater than 10 mm in 17 patients (47%).

The results of blind D&C were compared with the gold standard (Table 1). In ten patients, results of blind D&C were ‘insufficient material’ because of technical problems.

Documentation of other diagnostic procedure’s results in this group of patients was shown on (Table 2). Blind D&C demonstrated 47% sensitivity and 68% specificity in diagnosing focal intracavitary abnormalities. PPV was 57% and NPV was 59% (Table 3). Blind D&C missed 15 polyps (65% of all polyps) and all submucous myomas. One polyp has been removed completely by blind D&C and it has not been determined by the other procedures.

The results of TVS were compared with the gold standard (Table 4). TVS detected intrauterine lesions with sensitivity of 63%, specificity of 78%, PPV of 89%, and NPV of 41%. TVS failed to identify ten patients with intrauterine pathologic conditions (polyps). Two of the normal patients were overdiagnosed as polyp.

In the present study, SH was found to have sensitivity of 93%, specificity of 56%, PPV of 86%, NPV of 71%, and

Table 1 Comparison of blind D&C with gold standard (hysteroscopic histologic diagnosis)

	Gold standard			Total
	Normal	Polyp	Myoma	
D&C				
Normal	3	10	4	17
Polyp	1	8		9
Insufficient material	5	5		10
Total	9	23	4	36

D&C Dilatation and curettage

Table 2 Documentation of patients with ‘insufficient material’ results after D&C

Patients with ‘insufficient material’ results after D&C	TVS results	SH results	Hysteroscopic results	Gold standard results
Case 1	Irregular endometrium	Polyp	Polyp	Polyp
Case 2	Irregular endometrium	Polyp	Polyp	Polyp
Case 3	Polyp	Polyp	Polyp	Polyp
Case 4	Polyp	Polyp	Polyp	Polyp
Case 5	Hyperechodense endometrium	Polyp	Myoma	Normal
Case 6	Irregular endometrium	Thick endometrium	Polyp	Polyp
Case 7	Hyperechodense endometrium	Polyp	Polyp	Normal
Case 8	Irregular endometrium	Thick endometrium	Normal	Normal
Case 9	Irregular endometrium	Thick endometrium	Polyp	Normal
Case 10	Irregular endometrium	Thick endometrium	Normal	Normal

D&C Dilatation and curettage

TVS Transvaginal ultrasonography

SH Sonohysterography

Table 3 Comparison of each procedure with gold standard (hysteroscopic histologic diagnosis) and sonohysterography with hysteroscopy

	Sensitivity (100%)	Specificity (100%)	PPV (100%)	NPV (100%)	Accuracy	RR	+LR	–LR
Hysteroscopy/Gold standard	1.00	0.44	0.84	1.00	0.86	–	1.80	0.0
Sonohysterography/Gold standard	0.93	0.56	0.86	0.71	0.83	3.02	2.08	0.13
Trans vaginal sonography/Gold standard	0.63	0.78	0.89	0.41	0.67	1.52	2.83	0.47
Blind D&C/Gold standard	0.47	0.68	0.57	0.59	0.58	1.40	1.49	0.78
Sonohysterography/Hysteroscopy	0.88	0.75	0.97	0.43	0.86	1.69	3.50	0.16

D&C Dilatation and curettage

PPV Positive predictive value

NPV Negative predictive value

RR Relative risk

+LR Positive likelihood ratio

–LR Negative likelihood ratio

Table 4 Comparison of TVS with gold standard (hysteroscopic histologic diagnosis)

	Gold standard			Total
	Normal	Polyp	Myoma	
TVS				
Normal	7	10	–	17
Polyp	2	11	1	14
Myoma	–	2	3	5
Total	9	23	4	36

TVS Transvaginal ultrasonography

diagnostic accuracy of 83%. In 26 patients, a diagnosis of endometrial polyp was established with SH (Table 5). The diagnosis was confirmed histopathologically in 20 of them. Normal secretory endometrium was found in the remaining four women and pedunculated submucous myoma was found in the other two women. Two polyps were missed because of too small size and one polyp was misdiagnosed as submucous myoma because of large peduncle. Sensitivity and PPV were higher with SH in comparison to TVS for detection of focal intracavitary abnormalities.

In Table 6 hysteroscopy and hysteroscopic histopathologic results were compared. Hysteroscopy detected intrauterine lesions with sensitivity of 100%, specificity of 44%, PPV of 84%, and NPV of 100%. Therefore, hysteroscopy identified all 27 women with intracavitary masses but also identified five patients as having intracavitary pathologic conditions when they actually had normal cavities. Four of these false positive findings on hysteroscopy were found to be endometrial folds or endometrium dislodged from the basalis layer. Pathologic results of two cases were ‘secretory endometrium’ and other two cases were endometrial hyperplasia without atypia. One of false positive findings on hysteroscopy was found to be submucous myoma and pathologic result did not confirm this diagnosis.

Table 5 Comparison of SH with gold standard (hysteroscopic histologic diagnosis)

	Gold standard			Total
	Normal	Polyp	Myoma	
SH				
Normal	5	2	–	7
Polyp	4	20	2	26
Myoma	–	1	2	3
Total	9	23	4	36

SH Sonohysterography

Table 6 Comparison of hysteroscopy with gold standard

	Gold standard			Total
	Normal	Polyp	Myoma	
Hysteroscopy				
Normal	4	–	–	5
Polyp	4	23	–	27
Myoma	1	–	4	4
Total	9	23	4	36

When SH findings were compared with hysteroscopy, the sensitivity and specificity of SH were found to be 88 and 75%, respectively. The PPV and NPV were 97 and 43%, respectively (Table 7). One polyp result of SH could not be confirmed with hysteroscopy and its pathologic result was endometrial hyperplasia without atypia. There were eight false negative results with SH. Four small polyps were missed and in remaining four cases the two techniques disagreed about whether the structure was a polyp or a myoma. Diagnostic accuracy of SH was found to be 86% and positive likelihood ratio was 3.5 when compared with hysteroscopy.

When we look at the final results of 36 patients with recurrent postmenopausal bleeding on the hysteroscopic-directed

Table 7 Comparison of SH with hysteroscopy

	Hysteroscopy			Total
	Normal	Polyp	Myoma	
SH				
Normal	3	4		7
Polyp	1	22	3	26
Myoma		1	2	3
Total	4	27	5	36

SH Sonohysterography

pathology (gold standard), 75% of patients have focal intrauterine lesions (polyps and myomas) and 85% of focal intrauterine lesions were endometrial polyps.

Discussion

Our study compared four modalities in postmenopausal recurrent bleeding. Our results indicate that the SH is superior to blind D&C and TVS, and it is as effective as hysteroscopy in diagnosing intrauterine focal lesions in postmenopausal recurrent bleeding.

One of our study limitations is small number of study group. The reason was difficulty in finding patients who were postmenopausal, with normal D&C pathology result, experiencing recurrent vaginal bleeding and accepting all steps of the study. D&C arm of the study was retrospective and there were no detailed ultrasound reports before blind D&C. This seems like a limitation but it was obligatory since we studied postmenopausal women with recurrent bleeding after a blind D&C.

Several investigators have shown that the D&C fails to diagnose approximately half of all benign pathological lesions and sometimes endometrial cancer as well. The procedure commonly (38–100%) leaves all or part of the lesions within the uterine cavity [3, 16–18]. An important drawback of this procedure is being performed blindly. D&C may obtain tissue from adjacent endometrium and miss a mobile polyp that may be deflected by the biopsy catheter. Pedunculated polyps can be too mobile to be found and sessile polyps can be torn in so many pieces that they would not be recognizable [19]. Moreover, there is a threefold increased risk for polyps to regrow when they are removed by D&C as compared to hysteroscopic resection [20]. Especially, in postmenopausal women, D&C technically can be difficult and sampling can be insufficient like in our ten patients which decrease diagnostic accuracy of this method. It is postulated that the D&C alone should no longer be the sole means of diagnosing endometrial pathology which is supported by our study also. We found that

the blind D&C missed 70% of focal intracavitary lesions in comparison with hysteroscopic histopathologic results. These findings are compatible with the findings of Epstein and co-workers who reported that in women with focally growing lesions agreement between the D&C diagnosis, and the final diagnosis was unacceptably poor (59%) [4].

TVS did not allow a clear differentiation between endometrial polyps and hyperplasias, and abnormal endometrial growths [15]. In the present study, we missed ten endometrial polyps on TVS. These small polyps were masked by a very hyper-echo-dense endometrium. Goldstein et al. [21] found that small structural abnormalities can be easily missed and it is not possible always to differentiate endometrial and myometrial abnormalities on TVS. TVS is helpful in assessment of cases with abnormal uterine bleeding, however, polyps are often missed particularly when cervical or cornual in location. Furthermore, it cannot differentiate endometrial thickening from polyps in most cases [22]. In the present study, two normal cases were overdiagnosed as polyp due to this reason. Some authors have reported that TVS is more precise than hysteroscopy in mapping and measuring submucous myomas but frequently fails to distinguish submucous myomas from polyps [23]. In this study, two polyps and one submucous myoma were misdiagnosed by TVS. In the present study, TVS has a lower sensitivity (63%) for detecting focal intrauterine pathology compared with SH and hysteroscopy. In the literature conventional TVS, without the use of SH, will only have a sensitivity of 60–78% with regard to detection of focally growing lesions making it a poor screening tool [24–26]. We did not use colour or power Doppler ultrasound. This technique is superior to conventional ultrasound to show endometrial polyps when radial flow is present but since Doppler ultrasound cannot be available in every department we preferred to use conventional ultrasonography.

SH is easy to learn, well tolerated by the patient, less expensive in comparison to outpatient hysteroscopy and can be performed quickly [18, 27]. However, it is important to emphasize that SH cannot reliably discriminate between benign and malignant focal lesions [26]. In postmenopausal women where the endometrium cannot be visualized, endometrial pathology—and even endometrial cancer—is not an uncommon finding [3]. SH can be very helpful where the endometrium is difficult to measure as it will assist the practitioner in visualizing the endometrium and in most cases make endometrial measurement possible [18]. In contrast to hysteroscopy, SH is able to distinguish not only the endometrium but also myometrium. Therefore, SH is more suitable than hysteroscopy for classifying the degree of the extension of myomas [25]. Important information is also obtained by adnexal evaluation [28]. We have found that the diagnostic accuracy of SH was not different from that of

hysteroscopy (Table 3). In a recent systematic review and meta-analysis of 24 studies, SH was found to be both feasible and accurate in the evaluation of the uterine cavity in pre and postmenopausal women [29]. They concluded that SH in combination with an aspiration biopsy in selected cases can become the standard diagnostic procedure in pre and postmenopausal women complaining of abnormal uterine bleeding. Our data correspond to those in the literature in which SH had 93% sensitivity and a PPV of 86% for diagnosing intracavitary abnormalities. In our study, two polyps were missed by SH. It is suggested that a thick endometrium obscures a complete view of the uterine cavity, which would especially hamper accurate detection of endometrial polyps [29]. In our series, we found four false positive cases in SH. These false positive results may be explained as misinterpretation of endometrial folds. Wolman et al. [30] stated that the endometrial folds might become thickened during the secretory phase of the cycle and simulate small, single or even multiple endometrial polyps. In our study, one polyp and two myomas were misdiagnosed by SH. Consistently distinguishing between large polyps and pedunculated myoma was difficult with SH. Both these pathologic conditions, however, can be treated with hysteroscopic resection. Therefore, the treatment does not change if they are confused with each other [28]. Widrich et al. [28] compared SH with office hysteroscopy, and concluded that there was no difference in the procedures in detecting endometrial polyps, myomas, snechia, hyperplasia, endometrial cancer or normal uterine cavities. We compared hysteroscopy and SH, and found 86% diagnostic accuracy to detect intracavitary abnormalities. SH is less painful than hysteroscopy. SH may be useful for gynecologists who do not perform hysteroscopy. Moreover, SH may be used as an initial test to triage patients with abnormal uterine bleeding for diagnostic or operative hysteroscopy.

Disadvantages of SH compared with hysteroscopy are that multiple myomas may obscure the view and patients with severe Asherman's syndrome cannot be assessed [28, 31]. The high sensitivity and PPV of SH make it a good predictor of the necessity and type of the surgical intervention.

Although hysteroscopy is very sensitive, it generally requires operating room setting and local or general anesthesia. These requirements increase the risk and cost [12]. In our study, we performed hysteroscopy under general anesthesia. Hysteroscopy under general anesthesia is easier to perform and is more accurate than office hysteroscopy [26].

We chose to perform both diagnostic and operative hysteroscopy in the same session. For this reason, general anesthesia was more suitable for our study.

Even though magnification with hysteroscopy allows excellent visualization of the small details in the uterine

cavity, the correct interpretation of these details is difficult and requires a great deal of experience [12]. Hysteroscopic polypectomy is regarded as the optimal therapy and removal of the endometrial basalis layer in the endometrial polyp origin area prevents persistence or recurrence of endometrial polyps [32].

In hysteroscopy, not every structure with a polypoid appearance meets the pathologic criteria of a polyp [28]. In our series, we found five patients with false positive diagnosis. These were thickened endometrial folds and fragments of endometrium that were mistakenly identified as abnormal anatomic structures on hysteroscopy. In present study, a high sensitivity (100%) and NPV (100%) of hysteroscopy were found in comparison to hysteroscopic histologic examination (gold standard).

D&C alone will miss benign intrauterine focal pathology such as polyps and submucous fibroids. TVS alone will occasionally miss important endometrial pathology. We recommend SH as a tool in the diagnostic evaluation of postmenopausal women with recurrent vaginal bleeding. SH is almost as good as hysteroscopy at detecting focally growing lesions in the uterine cavity. Preoperative use of SH may assist in choosing the best conservative surgical treatment for the patient. Endometrial biopsy would then be reserved for patients with a symmetrically thickened endometrium whereas hysteroscopically directed biopsy or resection would be reserved for patients with focal endometrial thickening or an intraluminal mass. SH reduce unnecessary procedures, however, hysteroscopy and endoscopic biopsies remain as the decisive diagnostic tests for intracavitary lesions.

Conflict of interest statement None.

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