Transvaginal sonography combined with saline contrast sonohysterography to evaluate the uterine cavity in patients with abnormal uterine bleeding and postmenopausal endometrium more than 5 mm

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Summary

Objectives: To determine whether saline contrast sonohysterography (SCSH) gives additional information to that obtained by transvaginal sonography (TVS) for predicting endometrial abnormality in premenopausal, menopausal and postmenopausal patients with abnormal uterine bleeding and postmenopausal patients with endometrial thickness > 5 mm.

Methods: This was a prospective study at the Ege University Obstetrics and Gynecology Clinic in Izmir, Turkey. Patients presenting with abnormal bleeding related to uterine pathologies, postmenopausal patients with endometrial thickness more than 5 mm and scheduled for surgical treatment were prospectively included in our study conducted between 1 July, 2000 and 31 January, 2002. The uterine cavity was first evaluated with TVS in 53 premenopausal, menopausal, postmenopausal patients with abnormal uterine bleeding and postmenopausal patients whose endometrial thickness was > 5 mm measured by conventional ultrasound examination. SCSH was carried out later with the intention of establishing further surgical management (hysterectomy). Twenty of the patients had operative hysterectomy within the 1.5 year period of time. The presence of focally growing lesions and the type of lesion (endometrial polyp, submucous myoma, malignancy or unclear focal lesion) were noted at ultrasound examination and at hysteroscopy, and then hysterectomy material was examined by Ege University's Pathology Department which provided a detailed evaluation of the uterine cavity.

Results: Based on normal endometrial morphology alone, the results for detection of an abnormal uterine cavity were as follows: sensitivity of TVS 0.94, SCSH 0.97; specificity of TVS 0.56, SCSH 0.62; positive predictive value of TVS 0.79, SCSH 0.81; negative predictive value of TVS 0.83, SCSH 0.93. Transvaginal sonography combined with SCSH was superior to TVS for detection of intracavitary abnormalities. When normal endometrial morphology was combined with an endometrial thickness of < 12 mm for evaluation of all abnormalities including hyperplasia, the diagnostic potential of TVS or SCSH was almost unchanged. Transvaginal sonography missed 24% of the polyps.

Conclusions: Sonohysterography was a sensitive tool and was superior to TVS used alone for evaluation of the uterine cavity in patients who underwent operative surgery for abnormal uterine bleeding.

Key words: Saline contrast sonohysterography; Transvaginal sonography; Abnormal uterine cavity.

Introduction

Transvaginal sonographic assessment of the endometrium, which is usually based on measurement of endometrial thickness, may represent an adequate, non-invasive technique [1]. Several studies have shown a relationship between endometrial thickness, as measured by transvaginal sonography (TVS), and endometrial pathology in postmenopausal women. However, the different values given in the literature must be taken into consideration when selecting a cut-off point for endometrial thickness. Most authors recommend the use of a low cut-off point such as 4-5 mm as this provides a high sensitivity. Yet the specificity is reduced, which leads to many unnecessary curettage procedures. These procedures are performed in an attempt to avoid missing an endometrial carcinoma. Between 10% and 15% of women with postmenopausal bleeding have endometrial carcinoma and the risk of finding endometrial pathology increases with increasing endometrial thickness as measured by transvaginal ultrasound [2]. Up to 80% of women with postmenopausal bleeding and endometrial thickness > 5 mm have endometrial pathology and most pathological lesions have a focal growth pattern [3]. In pre- and perimenopausal patients with abnormal bleeding, the diagnostic potential of TVS in experienced hands has been found to be in line with that of hysteroscopy, but not when less experienced operators performed the examination [4]. It is crucial to rule out focal lesions in the uterine cavity, because these need to be hysteroscopically resected, since dilatation and curettage (D&C) and other blind endometrial sampling techniques fail to detect most focally growing lesions. Furthermore, D & C is an invasive procedure associated with some morbidity and limited sensitivity. Various techniques can be used in the diagnostic work up of women with postmenopausal bleeding in addition to transvaginal ultrasound [4-10]. At conventional transvaginal ultrasound examination focal lesions in the uterine cavity may be suspected, but confirmation by saline contrast sonohyste-

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rography (SCSH), which involves instillation of saline into the uterine cavity during scanning, improves the accuracy. SCSH is an additional but more invasive method for the sonographic differentiation of the endometrium [5]. Our study employing this method achieved a better differentiation of intracavitary abnormalities than by the use of TVS alone like previous other studies [11]. It has been recommended that the use of SCSH should be as a supplement to TVS only for patients with increased (> 5 mm) endometrial thickness [6]. The aim of our study was to investigate in a prospective manner whether evaluation of endometrial morphology would improve the accuracy of TVS for detecting sonomorphology of the endometrium and endometrial pathology including carcinomas. Diagnostic hysteroscopy can detect focal lesions in the uterine cavity, and a preliminary histological diagnosis can be made. Hysteroscopy with biopsy has become the gold standard for evaluation of the uterine cavity, as a reliable and safe method in routine outpatient settings [12]. When TVS was combined with saline contrast in the uterine cavity (SCSH), the diagnostic accuracy was markedly improved and was found to equal that of hysteroscopy when performed by skilled investigators. In our study the diagnostic potential of TVS, and that of TVS combined with saline contrast, were compared with the findings at hysterectomy in a group of pre-, peri- and postmenopausal patients. Our aim was to evaluate whether SCSH improved the diagnostic accuracy of TVS for identification of the uterine cavity. The aims of our study were firstly to determine the ability of transvaginal ultrasound with and without saline infusion to detect focally growing lesions in the uterine cavity, and secondly to determine the ability of conventional transvaginal ultrasound, SCSH, and hysteroscopy to discriminate between endometrial polyps, submucous myomas, and endometrial cancer [13].

Methods

The study was carried out at Ege University Obstetrics and Gynecology Clinic, between 1 July, 2000 and 31 January, 2002. A total of 53 women were referred to our clinic due to bleeding disorders during this period, and met the inclusion criteria. One registrar and a consultant with routine experience in transvaginal ultrasound who had performed SCSH before were involved. Patients were recruited if they had abnormal uterine bleeding (menorrhagia, metrorrhagia, and menometrorrhagia), were premenopausal (defined as being within 1 year of arrest of bleeding), menopausal or postmenopausal and were between the ages of 40 and 71 years. By this selection we tried to avoid patients with endometrial cancers because SCSH has a theoretical but not proven risk of spreading endometrial cancer by transport of endometrial cells through the Fallopian tubes. Patients under 45 years of age 35 years of age had a negative chlamydia test. Those using an intrauterine contraceptive device agreed to have it removed prior to recruitment into the study. Moreover, patients with serious cardiopulmonary disease which required cardiac surveillance and those in whom pregnancy or infection-related bleeding disorders were suspected, were excluded. Abnormal uterine bleeding caused by cervical factors was diagnosed by colposcopy prior to the consultation. In each patient, the gynecological history was taken, the procedures explained and consent obtained. Bimanual palpation of the pelvis was performed with patients in the dorsal lithotomy position. Transvaginal sonography was performed using a 5-7.5-MHz transvaginal transducer (Hondex HS-370, JAPAN). Measurement of the endometrium included both endometrial layers (double layer). The contours of the endometrial cavity were studied from the internal os to the fundus in the longitudinal and transverse planes. The midline echo was considered to be normal when a straight regular endometrial lining, with well-defined margins and without echodense foci, was found [14]. When the midline echo was disturbed, polyps were defined as echogenic masses with a fairly homogeneous texture without disruption of the myometrial-endometrial interface, while submucous myomas had an inhomogeneous texture with possible continuity with the myometrium. Myomas disturbing the midline echo or exceeding a diameter of 15 mm in the myometrium were counted [15-17]. The investigators classified the quality of the examinations as sufficient or insufficient for evaluation of the uterine cavity. Before SCSH, the presence or absence of abnormalities was recorded, and all abnormalities were described. Following TVS, SCSH was performed by the same investigator.

Saline contrast sonohysterography (SCSH):

A small flexible sterile catheter (embryo transfer catheter) mounted with a 50-ml syringe was introduced into the uterine cavity. During instillation of isotonic saline, the pressure was manually adjusted until sufficient for expansion of the uterine cavity. Concomitantly, the distension was observed by transvaginal sonography (with the above equipment) and continued until the entire uterine cavity was clearly visible [16]. The uterine cavity was evaluated in the sagittal and coronal views and pictures were taken for documentation. Findings at SCSH were noted according to a standard form. A normal finding implied the presence of a straight regular endometrial lining without echodense foci and projections from the myometrium [17]. Again the investigators noted the quality of the examination. Finally the patients were asked whether they had experienced discomfort during SCSH (yes or no). Less than 10 min was required to complete each examination.

Endometrial sampling:

Endometrial sample specimens were obtained with dilatation and curettage (D&C). Samples were always obtained prior to hysterectomy. With normal findings at SCSH, no endometrial sample was taken when a sufficient normal sample had been obtained within the last year. In 21 patients SCSH was followed by endometrial sampling only. Endometrial material was sent for pathological examination. The presence and size of abnormalities and the percentage of myomas in the uterine cavity were described at hysterectomy. The operative procedures were performed after pathological examination. Hysterectomy was performed in 20 patients, while 12 patients did not have dilatation and curettage (D&C) performed because two of them did not want the procedure and ten had no abnormal findings at TVS and SCSH.

Analysis:

Findings at TVS and SCSH were analyzed in two ways.

1) Normal endometrial morphology alone, i.e., a straight regular endometrial lining with well-defined margins and with no echodense foci irrespective of the endometrial thickness. (TVS or SCSH were combined with endometrial samples as the standard for diagnosis of hyperplasia or malignancies).

2) Normal endometrial morphology and thickness, i.e., a straight regular endometrial lining with well-defined margins and with no echodense foci and endometrial thickness < 12 mm (TVS or SCSH was used for exclusion of all abnormalities including hyperplasia and endometrial cancer) [18-20]. Sensitivity, specificity and positive and negative predictive values of TVS and SCSH were calculated with findings at hysterectomy. We used the Exact Binominal Confidence Interval Method to find confidence intervals.

Results

The age distribution of patients ranged from 40 to 71 years old (mean age of all patients was 47 years). Forty-eight patients (91%) did not complain of pain during the examination, while acceptable discomfort was reported in five (9%) patients. Fifty-three patients met the inclusion criteria during the study period. In three cases SCSH was inconclusive. Twenty patients underwent operative hysterectomy and 21 patients underwent endometrial sampling only.

No patient had endometrial cancer, and only three patients with operative surgery had hyperplasia. Samples with no abnormalities showed the endometrium to be secretory or proliferative in 21 out of 53 cases. In 11% of the patients ovarian cysts with a diameter of > 4 cm were found. No ovarian malignancies were found. Hysterectomy was performed in 20 patients, while 12 patients did not have dilatation and curettage (D&C) performed because two of them did not allow the procedure and ten had no abnormal findings at TVS and SCSH (Table 1).

Table 1. — *Number of patients with various abnormalities in the groups with surgical follow-up (operative hysterectomy), saline contrast sonohysterography with endometrial samples, and saline contrast sonohysterography without endometrial samples.*

	Submucous myomas	Polyps	Hyperplasia	Endometrial cancer	Other	No abnormality	Total
Operative hysterectomy	11	2	1*	0	0	6	20
SCSH+ endometrial sample	2	1	2	0	1	15	21
SCSH + no endometrial sample	1	1	0	0	0	10	12
Total number	14	4	3	0	1	31	53

*1 with atypia; SCSH, saline contrast sonohysterography.

Transvaginal sonography and saline contrast sonohysterography vs operative follow-up: In 20 out of 53 patients TVS was followed by operative hysterectomy (Table 2).

The assessments of diagnostic potential were based on the findings at operative follow-up as the gold standard [20]. Equivocal sonographic findings were classified as abnormal in the evaluation of diagnostic potential. The discrepancies between findings at TVS and at operative follow-up are listed in Table 3. In two patients polyps were not identified at TVS, whereas one false-positive finding occurred. The diagnostic sensitivity for detection of polyps at TVS was poor [21].

Table 2. — *Diagnostic potential of transvaginal sonography for diagnosis of polyps and submucous myomas compared with hysterectomy.*

Findings at transvaginal sonography	Findings at hysterectomy Uterine cavity		
	Abnormal	Normal	Total
Abnormalities	10	1	11
No abnormalities	1	4	5
Possible abnormality	3	1	4
Total	14	6	20
Sensitivity (95% CI)	0.714 (0.4190-0.9161)		
Specificity (95% CI)	0.833 (0.3588-0.9958)		
Positive predictive value (95% CI)	0.909 (0.5872-0.9972)		
Negative predictive value (95% CI)	0.556 (0.2120-0.8630)		

Abnormalities at hysterectomy; CI, confidence interval.

Table 3. — *Disagreement between transvaginal sonography and hysterectomy.*

False results at TVS (n)	Findings at sonography	Findings at SCSH	Hysterectomy results	Endometrial pathology results
False negative				
3	Normal	Polyp	Polyp	Polyp
1	Normal	Normal	Polyp	Menstruation
1	Normal	Polyp	Submucous myoma	Myoma
1	Intramural myoma	Intramural myoma	Submucous myoma	Proliferative
1	Normal	Submucous myoma	Submucous myoma	Myoma
False positive				
1	Submucous myoma	Submucous myoma	Intramural myoma	Secretory, proliferative
1	Submucous myoma	Intramural myoma	Intramural myoma	Menstruation, proliferative

Two polyps and 2 submucous myomas were not found at vaginal sonography. Equivocal sonograms are not included. TVS, transvaginal sonography; SCSH, saline contrast sonohysterography.

Findings at SCSH and at operative follow-up were compared (Table 4). Findings at SCSH were classified as normal or abnormal including equivocal results. Saline contrast sonohysterography detected all abnormal cavities except one. In this patient a myoma of 10 mm in diameter was found on pathologic examination by hysterectomy. The sensitivity and negative predictive value for SCSH in the detection of the normal/abnormal uterine cavity were 0.857 and 0.667, respectively (Table 4). This implies that SCSH detected almost all abnormalities. The lower specificity (0.667) in this population of mostly abnormal cavities was mainly a consequence of small irregularities in the uterine cavity being assessed as polyps or myomas with slight impressions in the uterine cavity. The sensitivity of SCSH and TVS and the negative predictive values had almost the same values as seen in Tables 2 and 4, in which sonograms were considered

Table 4. — *Diagnostic potential of saline contrast sonohysterography for diagnosis of polyps and submucous myomas compared with hysterectomy.*

Findings at saline contrast sonohysterography	Findings at hysterectomy - Uterine cavity		
	Abnormal	Normal	Total
Abnormalities	12	1	13
No abnormalities	1	3	4
Possible abnormality	1	2	3
Total	14	6	20
Sensitivity (95% CI)	0.857 (0.5719-0.9822)		
Specificity (95% CI)	0.667 (0.2228-0.9567)		
Positive predictive value (95% CI)	0.857 (0.5719-0.9822)		
Negative predictive value (95% CI)	0.667 (0.2228-0.9567)		

Abnormalities at hysterectomy; CI, confidence interval (Calculated by using Exact Binominal Confidence Interval Method).

normal when a straight regular endometrial lining was seen independent of the endometrial thickness. The specificities, however, were lower as only a small number of patients had an endometrial thickness of < 12 mm and no abnormalities after TVS and SCSH. No significant differences were found between TVS and SCSH in identification of the normal uterine cavity (Table 4).

Patients with equivocal results of SCSH, or disagreement between SCSH and findings at operative hysterectomy, and the corresponding pathologic findings are listed in Table 5.

Table 5. — *Disagreement between saline contrast sonohysterography and hysterectomy* (n = *20).*

False/equivocal results at SCSH (n:20)	Findings at SCSH	Hysterectomy results	Endometrial pathology results
False negative			
1	Normal cavity, multiple intramural myoma	Multiple intramural myomas	Proliferative
False positive			
1	Polyp	Normal	Secretory or proliferative
1	Polyp	Normal	Hyperplasia, simple
2	Myoma	Normal	Secretory or proliferative
1	Myoma	Normal	Dysfunction, normal
Equivocal results			
1	Possible polyp	Normal	Secretory or proliferative
1	Possible polyp	Normal	Dysfunction, normal
2	Possible polyp	Polyp	1 polyp, 1 secretory
1	Possible intramural myomas	Normal	Proliferative

Transvaginal sonography vs saline contrast sonohysterography:

For detection of any abnormality in the uterine cavity SCSH showed a higher sensitivity than TVS. In 14 cases of abnormal cavities at operative follow-up, two cases were falsely abnormal at TVS and truly abnormal at SCSH, while no cases were false normal at SCSH and normal at TVS. In five cases there were difficulties in discrimination between myomas and polyps, and uncertainty in the detection of two abnormalities in the same patient (Table 6).

In Table 7 findings at TVS and SCSH were again evaluated against findings at subsequent operative hysterectomy, but with hyperplasia included as an abnormality and an endometrial thickness of 12 mm counted as an abnormal finding at TVS and SCSH.

When the results of gold standard hysterectomy are considered, ten of the 14 abnormal cases were found by TVS while 13 were found by SCSH. SCSH was found to be more reliable in measuring normal uterine cavities.

Table 6. — *Saline contrast sonohysterography vs operative hysterectomy; patients with disagreement between findings of polyps vs myomas.*

Polyp vs myoma at SCSH (n)	Findings at SCSH	Hysterectomy results	Pathology results
1	Polyp	Myoma	Myoma
1	Polyp	Myoma	Secretory, normal
1	Myoma	Polyp	Polyp
1	Myoma	Polyp	Polyp
1	Myoma	Polyp	Dysfunction, normal

There was disagreement between findings of polyps vs myomas at saline contrast sonohysterography and at hysterectomy in five patients. Two findings of polyps at SCSH were found to be myomas at microscopic examination. In three patients, myomas were found at SCSH, but at hysterectomy polyps were discovered. SCSH, saline contrast sonohysterography.

Table 7. — *Diagnostic potential of transvaginal ultrasound and saline contrast sonohysterography compared with hysterectomy when hyperplasia was included as an abnormality and an endometrial thickness of* ≥ *12 mm was considered an abnormal finding at TVS and SCSH.*

	Hysterectomy	
	Abnormal cavity	Normal cavity
Transvaginal sonography (*n* = 20)		
Abnormalities at TVS	11	2
No abnormalities at TVS	3	4
Sensitivity (95% CI)	0.943 (0.8084-0.9930)	
Specificity (95% CI)	0.556 (0.3076-0.7847)	
Positive predictive value (95% CI)	0.795 (0.6354-0.9070)	
Negative predictive value (95% CI)	0.833 (0.5159-0.9791)	
Saline contrast sonohysterography (*n* = 20)		
Abnormalities at SCSH	13	1
No abnormalities at SCSH	1	5
Sensitivity (95% CI)	0.968 (0.8378-0.9992)	
Specificity (95% CI)	0.619 (0.3844-0.8189)	
Positive predictive value (95% CI)	0.805 (0.6513-0.9118)	
Negative predictive value (95% CI)	0.929 (0.6613-0.9982)	

TVS, transvaginal ultrasound; SCSH, saline contrast sonohysterography; CI, confidence interval.

Discussion

In this prospective study TVS and SCSH were used to examine the uterine cavity in a population of patients with premenopausal and postmenoausal bleeding disorders. Both methods were compared to hysterectomy as the gold standard. While TVS was the less invasive of the two procedures, SCSH displayed a higher diagnostic potential. Thus, SCSH showed a higher accuracy than TVS for detection of an abnormal cavity. Moreover, midline echo could not be described as definitely abnormal or normal in 24% of the patients during TVS. In these cases the uterine cavity had to be examined in another way. Finally, TVS displayed a negative predictive value of 0.833, and in patients scheduled for surgery, routine use of TVS without further investigations might leave a significant number of abnormalities undiagnosed.

Saline contrast sonohysterography displayed a high sensitivity for diagnosis of abnormalities in the uterine cavity, in accordance with previous studies [20-23]. In addition, a high negative predictive value was found. Thus routine use of this method even in non-expert hands implies a low number of undiagnosed lesions. A normal sonogram combined with an endometrial thickness of < 12 mm excluded even abnormalities such as hyperplasia, but the small number of patients with hyperplasia made the benefits and evidence limited for exclusion of this abnormality. The main disadvantage of SCSH was that small irregularities caused by blood clots or endometrial protrusions were frequently interpreted as polyps. In addition slight projections of myomas in the intramural portion of the uterus were seen at SCSH. These factors may have contributed to the relatively low specificity for SCSH. Moreover, detailed mapping of more than one lesion was difficult, and the capacity of SCSH for discrimination between polyps and myomas was poor. For patients with disagreement whether findings of polyps or myomas the same examiner performed both TVS and SCSH. The study design eliminated the difference within patients caused by differences in skill between observers. Transvaginal sonography was compared to SCSH in all patients referred for abnormal bleeding. In accordance with other studies polyps or myomas were diagnosed in 35% of cases [17]. At least three false-negative findings occurred at subsequent SCSH, when the midline echo was found to be normal at TVS. Nevertheless SCSH is an invasive method which had a 15% false-positive rate in the referred population. Moreover, only a few submucous myomas, but several polyps were missed. Thus, the efficacy of TVS combined with endometrial samples as a diagnostic procedure in premenopausal patients with abnormal bleeding might be related to the clinical importance of finding polyps, which are rarely malignant in premenopausal patients. Efficient removal of polyps requires hysteroscopy and is not achieved by curettage alone [24]. No controlled trial has been performed, but retrospective data suggest hysteroscopic removal of polyps to be effective in the treatment of bleeding abnormalities. In infertile patients removal of small polyps did not seem to improve fertility, and detection of small polyps might be clinically unimportant. Nevertheless, it seems rational to remove polyps by hysteroscopy until control trials have been performed. Thus in relatively inexpert hands the higher diagnostic accuracy of SCSH at the expense of a few unnecessary hysteroscopies and slight patient discomfort may motivate the combined use of TVS with SCSH in a population of patients referred with abnormal bleeding. In conclusion, especially when surgical treatment is planned, SCSH is superior to TVS. Normal findings at TVS reduce intervention rates but fail to eliminate particularly polyps, while submucous myomas seem to be identified. The use of TVS without SCSH would leave 21% of polyps undiagnosed in patients referred for abnormal uterine bleeding. Thus, SCSH was found to be a very sensitive tool for prediction of an abnormal uterine cavity, and routine use of this method as an alternative to diagnostic hysteroscopy in the primary investigation of patients with bleeding disorders would potentially lead to two in three hysteroscopies being avoided.

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