

Comparison of Transvaginal Sonography and Saline Contrast Sonohysterography in Women with Abnormal Uterine Bleeding: Correlation with Hysteroscopy and Histopathology

Muhammad Aslam, Lubna Ijaz, Shamsa Tariq, Kausar Shafqat, Meher-un-Nisa, Rubina Ashraf, Tahira Kazmi

Department of Obstetrics and Gynecology, Rawalpindi Medical College, Unit-I, Holy Family Hospital, Rawalpindi, Pakistan

Abstract :

Background: Transvaginal ultrasound is used conventionally as initial investigation of patients with abnormal uterine bleeding but saline contrast sonohysterography is a better technique to reliably distinguish focal from diffuse endometrial lesions. This study was performed to compare the ability of transvaginal ultrasonography and saline infusion sonohysterography as initial modality for the diagnosis of endometrial abnormalities in women with abnormal uterine bleeding.

Patients and Methods: In a prospective study, 100 women with abnormal uterine bleeding were submitted to sequential examination by transvaginal ultrasound, and sonohysterography. The presence of focal endometrial lesions and the type of lesion (endometrial hyperplasia, polyp, submucous myoma, or malignancy) were noted. Predictive values were calculated by correlating the results with final diagnosis reached by hysteroscopy and endometrial biopsy.

Results: The sonohysterography had 92.9% sensitivity and 89.7% specificity compared to 71.4% sensitivity and 67.7% specificity achieved by transvaginal sonography. There was 91% agreement between saline contrast sonohysterography and hysteroscopy as compared to 69% for TVS ($p = 0.002$). The diagnostic performance of sonohysterography for 3 main endometrial abnormalities (i.e. endometrial hyperplasia, polyps and submucous myoma) was better than transvaginal sonography. The best results were seen in cases of submucous myoma where sensitivity and specificity of sonohysterography reached to 100% as compared to TVS (61.55 and 97.7% respectively).

Conclusion: Our results have substantiated that sonohysterography is a better tool than transvaginal sonography for the assessment of endometrial intra-cavity lesions. By providing accurate differentiation between focal and diffuse endometrial lesions, it can help in decision making regarding selection of cases for hysteroscopy and directed biopsy. We recommend that saline contrast sonohysterography should be used as an initial investigation in cases of abnormal uterine bleeding.

Keywords: Ultrasound, transvaginal sonography, sonohysterography, hysteroscopy, abnormal uterine bleeding.

Correspondence:

*Prof. Muhammad Aslam
College of Medicine, Qassim University
Buraydah, Saudi Arabia.
Email: professoraslam@hotmail.com*

Introduction

Abnormal uterine bleeding (AUB) is a common gynecologic complaint in women attending outpatient department.⁽¹⁾ The causes may vary from simple dysfunctional uterine bleeding without any organic cause to the endometrial cancer. The cases of AUB usually need thorough investigation to rule out organic causes especially at perimenopausal and postmenopausal age when the risk of endometrial carcinoma is 10% to 15%.⁽²⁻⁴⁾ Hysteroscopy with directed biopsy, over the years, has assumed the role of reference standard investigation for AUB because it is an accurate method for diagnosing and treating endometrial abnormalities, however, its invasive nature and high cost preclude its use as a primary diagnostic procedure in patients with AUB.⁽⁵⁾

Transvaginal sonography (TVS) plays an important role as the initial modality for evaluation of AUB,^(1,6,7) but its ability for screening the lesions within the endometrial cavity is limited. The finding of a thickened central endometrial complex seen on TVS is often non-specific and may be caused by an endometrial polyp, submucosal fibroids, endometrial hyperplasia, carcinoma, or cystic atrophy. Focal lesions are underdiagnosed at TVS because of limitations of the double-layer thickness evaluation.^(3,8,9)

Saline contrast sonohysterography (SHG) is a technique in which the endometrial cavity is distended with saline during ultrasonic examination and it permits single layer evaluation of the endometrial lining and enables the sonologist to reliably distinguish focal from diffuse endometrial pathologic conditions. Several studies in recent literature have indicated that SHG can improve the specificity of TVS in differentiating endoluminal masses from more diffuse endometrial thickening.⁽¹⁰⁻¹⁶⁾

This study was performed to compare the ability of transvaginal ultrasonography and saline infusion sonohysterography as initial modality for the diagnosis of endometrial abnormalities in women with AUB by correlating the results with hysteroscopy and endometrial biopsy.

Methods

This prospective study was conducted at Unit-I, Holy Family Hospital, Rawalpindi, Pakistan which is a tertiary care hospital. The study was approved by the research ethics committee at the

hospital, and informed consent was obtained from all patients.

Over a period from August 2003 to July 2004, three hundred and forty eight women were seen in our institution with AUB. We included only the patients with vaginal bleeding that was marked enough to warrant further diagnostic evaluation. The patients who did not undergo the sequential evaluation by all three modalities (TVS, SHG, and hysteroscopy-biopsy) were excluded.

The patient's ages ranged from 25 to 68 years (mean age, 38.3 ± 9.6 years). Eighty eight women were premenopausal and 12 were postmenopausal. All 100 patients were first evaluated on the same day with TVS followed by SHG. All hysteroscopies with biopsies were scheduled within 14 days of this examination. The mean interval from TVS and SHG to hysteroscopy was 4.8 days (range, 2–14 days). Hysterectomy was performed in ten patients within 4 weeks.

All TVS examinations were performed on an ultrasound imager (model AU3 Partner, from ESAOTE Biomedica German) with 6.5 MHz linear array transvaginal transducer. TVS was used to examine both ovaries and the uterus. The uterus was scanned in the sagittal and coronal planes for the presence of myometrial masses, and the endometrium was examined for an endometrial pathology. The double-layer endometrial thickness was measured at the widest point between the endometrial-myometrial interfaces in the sagittal plane by using electronic callipers. The presence of focal endometrial thickening or a focal mass was noted.

Saline contrast sonohysterography was performed by placing the patient in the dorsal lithotomy position, and placing a speculum into the vagina to expose the cervix. The external os was cleansed with povidon-iodine solution. A 6 F balloon catheter was inserted through the cervix and the balloon was inflated with 2-6 ml of the saline to seal the external os tightly to prevent any leakage into the vagina. The transvaginal ultrasound probe was inserted and approximately 10 ml of sterile saline solution was injected slowly through the catheter under direct sonographic visualization. Multiple sagittal and coronal images were then obtained. The endometrial cavity was examined for the presence of polyps, submucous fibroids, focal endometrial thickenings or other pathologic conditions. On both ultrasound techniques, the endometrium was regarded as

abnormal if it was equal to or thicker than 8 mm in the premenopausal period, and equal to or thicker than 5 mm in the postmenopausal period.^(17,18)

After TVS and SHG procedure, all patients underwent hysteroscopy with directed biopsy or endometrial sampling performed by one of the authors who were kept blinded to the TVS-SHG findings. The appearance of the endometrium (atrophic, proliferative, secretory, or hyperplastic) and the presence of polyps, fibroids, synechiae or carcinoma were recorded. The finding of an atrophic, proliferative or secretory endometrium without other abnormalities at examination was considered to indicate a normal uterus. Directed biopsy of any abnormal area was performed through the 3-mm operating channel. Endometrial sampling was done in rest of the cases using a small curette. All specimens were immediately placed into a 10% neutral buffered formalin solution and sent for histopathologic evaluation. Ten patients were later treated by hysterectomy and their uteri sent for histopathology. The pathologists were blinded to the TVS and SHG findings. A final pathologic diagnosis was made by using the results of the surgical procedures and histopathologic analysis.

The accuracy of TVS and SHG for detection of specific diseases was determined by correlating the results with final diagnosis.

Sensitivity, specificity, and positive and negative predictive values for predicting endometrial disease were then calculated. Ninety five percent CIs for sensitivity, specificity, and positive and negative predictive values were calculated by using the Wilson method.⁽¹⁹⁾ McNemar's χ^2 test was used to compare the diagnosis rate. Statistical significance was defined as a probability value of < 0.05 .

Results

The tolerance of the SHG procedure was excellent, and all examinations were completed successfully. In few patients, some endovaginal reflux of saline was noted during injection. Some patients complained of pelvic discomfort during examination and injection was stopped temporarily in two patients because of patient's complaint of crampy pelvic pain. Both procedures were resumed after analgesic injection and tolerated by the patients.

Table (1) shows the final hysteroscopic-histopathologic diagnosis in 100 cases and its comparison with TVS and SHG findings. Our final results confirmed endometrial hyperplasia in 16, submucosal myoma in 13, endometrial polyp in 10, chronic endometritis in 3, uterine synechiae in two and endometrial cancer in one case. Fifty five cases were found to have normal uteri.

Table (1). Diagnoses of the 100 Patients with AUB provided by three investigation modalities

Diagnosis	Hysteroscopic-Histopathologic diagnosis Number of Patients	TVS diagnosis Number of Patients	SHG diagnosis Number of Patients
Normal uterus	55	53	55
Endometrial hyperplasia	16	28	20
Submucosal myoma	13	9	13
Endometrial polyp	10	10	10
Chronic Endometritis	3		
Adhesions	2		2
Endometrial cancer	1		
Total	100	100	100

**The finding of an atrophic, proliferative or secretory endometrium without other abnormalities at examination was considered to indicate a normal uterus*

Table (2). Diagnostic Performance of TVS and SHG.

Test	Sensitivity	Specificity	PPV	NPV	DA	Likelihood Ratio	
						Positive	Negative
TVS	71.43 (54.94 to 83.67)	67.7 (55.61 to 77.79)	54.35 (40.18 to 67.84)	81.48 (69.16 to 89.61)	69 (59.94-78.06)	2.22 (1.47-3.33)	0.42 (0.25-0.72)
SHG	92.86 (80.99 to 97.54)	89.65 (79.21 to 95.17)	86.67 (73.82 to 93.74)	94.54 (85.14 to 98.12)	91* (85.44-96.61)	8.98 (4.19-19.24)	0.07 (0.03-0.24)

* $p = 0.002$

Note: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy (DA) data are percentages. All numbers in parentheses are 95% CIs.

Eight cases diagnosed as normal on TVS showed various endometrial abnormalities on SHG, and 10 cases showing endometrial abnormalities on TVS were found normal on SHG evaluation. The discrepancy between TVS and final diagnosis was present in 27 cases. The 15 false negative diagnoses included 5 submucosal myoma, 3 endometrial polyps, 3 chronic endometritis, 2 uterine synechiae, and one case of endometrial hyperplasia and carcinoma each. False positive diagnosis was made in 12 cases which included 10 endometrial hyperplasia, and one case of endometrial polyp and myoma each. The diagnostic discrepancy was seen in only 9 cases evaluated by SHG. Six false negative results included 3 chronic endometritis, and one case of endometrial polyp, uterine synechiae and endometrial carcinoma each. Three cases of normal endometrium were falsely diagnosed as hyperplasia on SHG.

Diagnostic performance of TVS and SHG in comparison to final hysteroscopic- histopathologic diagnosis is indicated in Table (2).

The SHG was more sensitive and specific as compared to TVS alone. The sensitivity and specificity of TVS were 71.4% and 67.7%, respectively as compared to sensitivity and specificity of SHG which were 92.9% and 89.7% respectively. The positive predictive value of SHG was 86.7% as compared to 54.4% for TVS. The diagnostic accuracy of SHG (91%) was significantly better than that of TVS (69%) with a $p = 0.002$. The positive and negative likelihood ratios for SHG were 8.98 and 0.07 respectively as compared to 2.22 and 0.42 respectively for TVS.

We further studied the diagnostic performance of TVS and SHG for 3 main endometrial abnormalities i.e. endometrial hyperplasia, polyps and submucous myoma and our results are tabulated in Table (3).

Table (3). Diagnostic Performance of TVS and SHG in identifying various causes

Diagnosis Test performance	Endometrial hyperplasia		Endometrial polyp		Submucous myoma	
	TVS	SHG	TVS	SHG	TVS	SHG
Sensitivity	81.25 (56.99 to 93.40)	93.75 (71.67 to 98.88)	70 (39.67 to 89.22)	90 (59.58 to 98.21)	61.54 (35.52 to 82.29)	100 (77.19 to 100)
Specificity	73.68 (61.02 to 83.35)	91.23 (81.05 to 96.19)	95.35 (84.54 to 98.71)	98.11 (90.05 to 99.66)	97.67 (87.94 to 99.58)	100 (93.12 to 100)
PPV	46.43 (29.53 to 64.18)	75 (53.12 to 88.81)	77.78 (45.25 to 93.67)	90 (59.58 to 98.21)	88.89 (56.50 to 98.01)	100 (77.19 to 100)
NPV	93.33 (82.14 to 97.70)	98.11 (90.05 to 99.66)	93.18 (81.77 to 97.65)	98.11 (90.05 to 99.66)	89.36 (77.40 to 95.36)	100 (93.12 to 100)
DA	75.34 (65.45-85.23)	91.78* (85.48-98.08)	91.57 (82.70-98.44)	96.83 (92.50-101.15)	89.29 (81.18-97.39)	100.00†
Likelihood Ratio Positive	3.09 (1.88-5.06)	10.69 (4.58-24.92)	15.05 (3.66-61.82)	47.7 (6.77-336.05)	26.46 (3.64-192.45)	∞
Negative	0.25 (0.09-0.71)	0.07 (0.01-0.46)	0.31 (0.12-0.81)	0.10 (0.02-0.65)	0.39 (0.2-0.78)	0

* $p = 0.096$, † $p = 0.008$

Note – Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy (DA) data are percentages. All numbers in parentheses are 95% CIs.

The sensitivity and specificity of SHG for diagnosing these lesions is better than those of TVS. Out of 16 cases of endometrial hyperplasia, 15 were correctly diagnosed on SHG in comparison to 13 diagnosed by TVS. The diagnostic accuracy of SHG versus TVS for diagnosing endometrial hyperplasia was 91.8% and 75.3% ($p = 0.096$). The positive likelihood ratio of TVS vs. SHG was 3.1 vs. 10.7. The negative likelihood ratio TVS vs. SHG was 0.25 vs. 0.07. The best results were seen in cases of submucous myoma where sensitivity and specificity of SHG reached to 100% as compared to TVS (61.55 and 97.7% respectively). In all 13 cases, submucous myomas were correctly located by SHG compared to 8 cases by TVS. In 5 cases of submucous myomas, TVS was unable to diagnose the location of myoma correctly. Diagnostic accuracy of SHG vs. TVS for submucous myoma was 100 vs. 89.3% ($p = 0.008$). The diagnostic accuracy was comparable in cases of endometrial polyps (91.6% for TVS vs. 96.9% for SHG) but SHG showed a positive likelihood ratio of 47.7 as compared to 15.05 for TVS.

Discussion

Transvaginal ultrasonography has been used extensively in the evaluation of patients with AUB. Many previous studies in the literature have substantiated that TVS was quite a sensitive method to evaluate the abnormal uterine bleeding. The diagnostic accuracy of TVS varies depending upon the expertise of the investigators, the sensitivity being 87% (range 24–96%) and the specificity 82% (range 29–93%).^(14,20,21) Our study results have indicated 71.4% sensitivity, 67.7% specificity, 54.4% PPV and 81.5% NPV of TVS for investigating AUB.

Despite the wide spread use of TVS for initial evaluation of AUB, the number of studies in the literature is growing which indicate that TVS has its limitations in depicting small nodular lesions, which are isoechoic within the endometrium, and even a normal thickness endometrium may be seen to represent endometrial hyperplasia.⁽²⁰⁻²³⁾ Similarly, TVS also cannot differentiate submucosal from intramural leiomyoma in many instances, which is an important distinction for selection of cases for hysteroscopic resection of these lesions.^(24,25) Our study results indicate that out of 13 cases of submucous myomas, 5 were misinterpreted as

interstitial by TVS but correctly located by SHG. This study has also indicated that 8 cases diagnosed as normal on TVS showed various endometrial abnormalities on SHG, and 10 cases showing endometrial abnormalities on TVS were found normal on SHG evaluation. These results are in agreement with the study by Laifer-Narin et al.⁽²²⁾ who claim that 14% of 114 patients showing normal TVS findings revealed abnormalities on SHG.

There are many advantages of using saline contrast sonohysterography as an initial evaluation test in abnormal uterine bleeding. Owing to its ability to demonstrate small endometrial lesions and its reliability to differentiate between focal and diffuse endometrial lesions, HSG can be used as a method of choice to evaluate patients with abnormal uterine bleeding. The sensitivity and specificity of SHG have been reported to be as high as 85-91% and 83-100%, respectively.^(3,14,16,26) Our result have shown 92.9% Sensitivity, 89.7% Specificity, 86.7% PPV, and 94.5% NPV for SHG to diagnose intra-cavity endometrial lesions. Overall Diagnostic accuracy was 91%. Similar high accuracy rates ranging from 84% to 96% have been reported by other studies.^(11,26,27)

Three commonly seen lesions in cases of AUB are submucous myoma, endometrial polyps and hyperplasia. There have been several reports of the diagnostic value of SHG in differentiation of these diseases. Epstein et al.⁽¹¹⁾ has reported an almost perfect agreement (96%) between saline contrast sonohysterography and hysteroscopy in the diagnosis of focally growing lesions. Saline contrast sonohysterography and hysteroscopy both had a sensitivity of approximately 80% with regard to diagnosing endometrial polyps (false-positive rates of 24% and 6%, respectively), whereas conventional ultrasound missed half of the polyps (sensitivity, 49%; false-positive rate, 19%). Kamel et al.⁽²⁸⁾ in a study of 106 patients with AUB has achieved 93.3% sensitivity, 94.6% positive predictive value and 93.3% diagnostic accuracy in the detection of endometrial polyps by SHG. Soares et al.⁽²⁹⁾ has reported 100% sensitivity, 100% positive predictive value and 100% diagnostic accuracy for polypoid lesions, including endometrial polyps, fibroids and endometrial hyperplasia. Nanda et al.⁽³⁰⁾ reported 100% sensitivity of SHG in detecting endometrial polyps. Leone et al.⁽²⁵⁾ correctly diagnosed all 48 cases of submucosal fibroids using SHG. The data and results from the

present study are in agreement with the above-mentioned published reports and the accuracy of SHG in differentiating submucosal from intramural fibroids was found to be 100% in the present study.

The most worrisome cause of AUB, in the minds of patient and clinician both, is endometrial carcinoma especially at menopausal age. In the present study only one case of endometrial carcinoma was detected and it was misdiagnosed as endometrial hyperplasia on TVS and SHG both. Our retrospective review of this case indicated a very small lesion associated with adenomatous hyperplasia detected on endometrial biopsy. Epstein *et al.*¹¹ has reported that hysteroscopy is superior to both HSG and TVS for discriminating between benign and malignant lesions (sensitivity, 84%, 44%, and 60%; false-positive rate, 15%, 6% and 10%, respectively). However, neither hysteroscopy nor saline contrast sonohysterography can reliably discriminate between all the benign and malignant focal lesions and biopsy is usually indicated to further evaluate such lesions. Dubinsky *et al.*³¹ established criteria for classifying benign and suspicious lesions seen on SHG. Their results for detecting endometrial carcinoma with SHG had a sensitivity of 89%, specificity of 46%, PPV of 16% and NPV of 97%. These criteria were highly predictive for benign processes, particularly endometrial thickening. However, because many pathologic conditions had a suspicious appearance, the positive predictive value of SHG for carcinoma was low.

Most endometrial abnormalities, including carcinoma, appear as a focal mass on ultrasonography; therefore, women with multifocal or sessile lesions should undergo a hysteroscopic guided biopsy. The SHG is useful in identifying benign pathologic conditions of the endometrium and can help in the triage for hysteroscopic versus nondirected endometrial biopsy.

There were no procedural failures in the present study, but a failure rate of 2.9% to 6% is mentioned in the literature which is mainly due to cervical stenosis commonly present in postmenopausal patients.⁽³²⁻³⁴⁾ Majority of our study population (88%) were premenopausal and their cervixes were easy to catheterise. Similarly we did not encounter any complication related to SHG. Complications of SHG, in the literature are exceptional and include vasovagal syncope, endometrial shearing with catheter,

bleeding, infection, perforation (due to instrumentation) and theoretical risk of spreading of carcinoma. Dubinsky *et al.*⁽³¹⁾ found two cases of endometritis after SHG in their study ($n=89$ patients). The risk of infection following SHG is estimated to be 1%.⁽¹⁰⁾

One of the limitations of our study was that we did not consider any other aspects of SHG examinations as a screening method, including its cost-effectiveness, time spent, patient's preference, patient's discomfort and the effects on treatment. Some studies in the literature are seen to address these issues.^(1,35) These studies are small in number and further work in this regard is needed in the future.

Conclusion

Our results have substantiated that SHG is a better tool as compared to TVS for the assessment of endometrial intra-cavity lesions. By providing accurate differentiation between focal and diffuse endometrial lesions, it can help in decision making regarding selection of cases for hysteroscopy and directed biopsy. We recommend that saline contrast sonohysterography should be used as an initial investigation in cases of abnormal uterine bleeding.

References

1. Dubinsky TJ. Value of sonography in the diagnosis of abnormal vaginal bleeding. *J Clin Ultrasound* 2004; 32(7):348-53.
2. Holst J, Koskela O, von Schoultz B. Endometrial findings following curettage in 2018 women according to age and indications. *Ann Chir Gynaecol* 1983; 72:274-7.
3. 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.
4. Karlsson B, Granber S, Hellberg P, Wikland M. Comparative study of transvaginal sonography and hysteroscopy for the detection of pathologic endometrial lesions in women with postmenopausal bleeding. *J Ultrasound Med* 1994;13:757-62.
5. Abu-Ghazze Y, Shakoury WA, Barqawi R. Comparative study of Transvaginal Hysterosonography and Biopsy for the evaluation of post-menopausal bleeding. *Ann Saudi Med* 1999;19(2):116-9.

6. Dubinsky TJ, Parvey HR, Maklad N. The role of transvaginal sonography and endometrial biopsy in the evaluation of peri and postmenopausal bleeding. *AJR Am J Roentgenol* 1997;169:145-9.
7. Fleischer AC. Sonographic assessment of endometrial disorders. *Semin Ultrasound CT MR* 1999;20:259-66.
8. Bree RL, Bowerman RA, Bohm-Velez M, Benson CB, Doubilet PM, DeDreu S, et al. US evaluation of the uterus in patients with postmenopausal bleeding: a positive effect on diagnostic decision making. *Radiology* 2000; 216:260-64.
9. Davis PC, O'Neill MJ, Yoder IC, Lee SI, Mueller PR. Sonohysterographic findings of endometrial and subendometrial conditions. *Radiographics* 2002; 22:803-16.
10. Dueholm M, A. Forman, Jensen ML, Laursen H, Karacht P. Transvaginal sonography combined with saline contrast sonohysterogram in evaluating the uterine cavity in premenopausal patients with abnormal uterine bleeding. *Ultrasound Obstet Gynecol* 2001;18:54-61.
11. Epstein E, Ramirez A, Skoog L, Valentin L. Transvaginal sonography, saline contrast sonohysterography and hysteroscopy for the investigation of women with postmenopausal bleeding and endometrium > 5 mm. *Ultrasound in Obstet Gynecol* 2001;18:157.
12. Fong K, Causer P, Atri M, Lytwyn A, Kung R. Transvaginal US and Hysterosonography in postmenopausal women with breast cancer receiving Tamoxifen: Correlation with Hysteroscopy and Pathologic Study. *Radiographics*. 2003;23:137-50.
13. Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for investigation of abnormal uterine bleeding in premenopausal women. *Acta Obstet Gynecol Scand* 2003;82:493-504.
14. Ryu J, Kim B, Lee J, Kim S, Lee SH. Comparison of transvaginal ultrasonography with hysterosonography as a screening method in patients with abnormal uterine bleeding. *Korean J Radiol* 2004;5:39-46.
15. Milingos S, Kallipolitis G, Stefanidis K, Sklia J, Makris N, Loutradis D et al. Saline contrast hysterosonography in infertile patients and in women with abnormal uterine bleeding. *Eur J Gynecol Oncol* 2005;26:564-70.
16. Alborzi S, Parsanezhad ME, Mahmoodian N, Alborzi S, Alborzi M. Sonohysterography versus transvaginal sonography for screening of patients with abnormal uterine bleeding. *Internat J Gynecol Obstet* 2007;96:20-3.
17. Dueholm M, E. Lundorf E, Olesen F. Imaging techniques for evaluation of the uterine cavity and endometrium in premenopausal patients before minimally invasive surgery. *Obstet. Gynecol. Surv* 2002;57:389-403.
18. Getpook C, Wattanakumtornkul S. Endometrial thickness screening in premenopausal women with abnormal uterine bleeding. *J. Obstet. Gynaecol. Res* 2006;32:588-92.
19. Agresti A, Coull BA. Approximate is better than "exact" for interval estimation of binomial proportions. *Am Stat* 1998;52:119-26.
20. Bree RL. Ultrasound of the endometrium: facts, controversies, and future trends. *Abdom Imaging* 1997;22:557-68.
21. Lalchandani S, Phillips K. Evaluation of endometrial cavity—investigation options. *Rev Gynaecol Prac* 2003;3:165-70.
22. Laifer-Narin S, Ragavendra N, Parmenter EK, Grant EG. False normal appearance of the endometrium on conventional transvaginal sonography: comparison with saline hysterosonography. *Am J Roentgenol* 2002;178:129-33.
23. Saidi MH, Sadler RK, Theis VD, Akright BD, Farhart SA, Villanueva GR. Comparison of sonography, sonohysterography, and hysteroscopy for evaluation of abnormal uterine bleeding. *J Ultrasound Med* 1997;16:587-91.
24. Becker E Jr, Lev-Toaff AS, Kaufman EP, Halpern EJ, Edelweiss MI, Kurtz AB. The added value of transvaginal sonohysterography over transvaginal sonography alone in women with known or suspected leiomyoma. *J Ultrasound Med* 2002;21:237-47.
25. Leone FPG, Lanzani C, Ferrazzi E. Use of strict sonohysterographic methods for preoperative assessment of submucous myomas. *Fertil Steril* 2003;79:998-1002.

26. Wongsawaeng W. Transvaginal ultrasonography, sonohysterography and hysteroscopy for intrauterine pathology in patients with abnormal uterine bleeding. *J Med Assoc Thai* 2005;88:77-81.
27. Ragni G, Diaferia D, Vegetti W, Colombo M, Arnoldi M, Crosignani PG. Effectiveness of Sonohysterography in Infertile Patient Work-Up: A Comparison with Transvaginal Ultrasonography and Hysteroscopy. *Gynecol Obstet Invest* 2005;59:184-8.
28. Kamel HS, Darwish AM, Mohamed SA. Comparison of transvaginal ultrasonography and vaginal sonohysterography in the detection of endometrial polyps. *Acta Obstet Gynecol Scand* 2000;79:60-4.
29. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. *Fertil Steril* 2000;73:406-11.
30. Nanda S, Chadha N, Sen J, Sangwan K. Transvaginal sonography and saline infusion sonohysterography in the evaluation of abnormal uterine bleeding. *Aust NZ J Obstet Gyneacol* 2002;42:530-34.
31. Dubinsky TJ, Stroehlein K, Abu-Ghazze Y, Parvey HR, Maklad N. Prediction of Benign and Malignant Endometrial Disease: Hysterosonographic-Pathologic Correlation. *Radiology* 1999;210:393-7.
32. Gaucherand P, Piacenza JM, Salle B, Rudigoz RC. Sonohysterography of uterine cavity: preliminary investigations. *J. Clin. Ultrasound* 1995;23:339-48.
33. Lev-Toof A, Toaf ME, Liv JB, Merton DA, Goldberg BB. Value of sonohysterography in the diagnosis and management of abnormal uterine bleeding. *Radiology* 1996;201:179-84.
34. Schwärzler P, Conci H, Bösch H, Berlinger A, Wohlgenannt K, Collins WP *et al*. An evaluation of sonohysterography and diagnostic hysteroscopy for the assessment of intrauterine pathology. *Ultrasound Obstet. Gynecol* 1998;11:337-42.
35. Bree RL, Carlos RC. US for Postmenopausal Bleeding: Consensus Development and Patient-centered Outcomes. *Radiology* 2002;222:595-8.