Original Article

Transvaginal Ultrasonography and Saline Infusion Sonography Compared to Hysteroscopy for Diagnosis of Intracavity Lesion: A 4-Year Experience in Suburban Referral Hospital

Phaliwong P, MD[1], Luangdansakul W, MD[2], Bhamarapravatana K, PhD[3], Suwannarurk K, MD[4]

[1] Reproductive Medicine Unit, Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Bangkok, Thailand

[2] Fetomaternal Medicine Unit, Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Bangkok, Thailand

[3] Department of Preclinical Science, Faculty of Medicine, Thammasat University Hospital, Bangkok, Thailand

[4] Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University Hospital, Bangkok, Thailand

Objective: To evaluate the accuracy of transvaginal ultrasonography (TVS) and saline infusion sonography (SIS) in use for the diagnosis of endometrial polyps and submucous myoma compared to hysteroscopy. Histopathology was considered as the gold standard for final diagnosis.

Materials and Methods: The present retrospective study was conducted at Bhumibol Adulyadej Hospital, Bangkok, Thailand between January 2014 and December 2017. Medical records of 150 patients who attended for hysteroscopy and histopathological diagnosis were reviewed. The accuracy of TVS and SIS for the diagnosis of endometrial polyps and submucous myoma were determined.

Results: Out of 150 enrolled cases, endometrial polyp was the most frequent hysteroscopic finding in participants of the present study (92/150). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of TVS, SIS, and hysteroscopy compared to pathologic reports for detection endometrial polyps were 71.7% versus 93.5% versus 97.8%, 38.5% versus 52.2% versus 68.2%, 80.5% versus 88.7% versus 92.8%, 27.8% versus 66.7% versus 88.2%, and 64.4% versus 85.2% versus 92.1%, respectively. The sensitivity, specificity, PPV, NPV, and accuracy of TVS, SIS, and hysteroscopy for detection of submucous myoma were 81.6% versus 92.1% versus 94.7%, 66.7% versus 86.9% versus 100%, 77.5% versus 92.1% versus 100%, 72.0% versus 86.9% versus 90.9%, and 75.4% versus 90.2% versus 96.6%, respectively. The kappa value from TVS, SIS, and hysteroscopy when the histopathologic reports were overall intrauterine abnormalities, endometrial polyps and submucous myoma were 0.45/0.43/0.72, 0.77/0.76/0.89, and 0.92/0.92/1.00, respectively.

Conclusion: Sensitivity, specificity, PPV, NPV, accuracy, and kappa value of SIS for detecting endometrial polyps and submucous myoma were better than TVS.

Keywords: Ultrasonography, Saline infusion sonography, Hysteroscopy, Accuracy

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Correspondence to:

Phaliwong P.

Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Royal Thai Air, 171 Phahonyothin Road, Khlong Thanon, Sai Mai, Bangkok 10220, Thailand.

Phone: +66-2-5347314, **Fax**: +66-2-5347000

Email: p_phaliwong@yahoo.com

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Women with intrauterine abnormalities such as endometrial polyp or submucous myoma largely presented with abnormal uterine bleeding (AUB), infertility, or recurrent pregnancy loss[1]. A differential diagnosis between endometrial polyp and submucous myoma is important for appropriate treatment. Submucous myoma patients require surgical intervention while patients with endometrial polyp have multiple treatment options, namely expectant management, medical, and surgical treatment[2-5].

Many methods are currently used for intrauterine abnormalities assessment, namely transvaginal ultrasonography (TVS), endometrial biopsy, saline

infusion sonography (SIS), and hysteroscopy (HY). TVS is currently the default and basic method for the examination of pelvic organs in women including intrauterine pathologies. Most hospitals in Thailand have TVS equipment and two-dimensional (2D) ultrasonography. SIS refers to a procedure in which transcervical fluid is instilled into the uterine cavity to provide enhanced endometrial visualization during a transvaginal ultrasound examination[6]. This method is easy and inexpensive. HY is considered the gold standard for endoscopic evaluation of the uterine cavity[7]. In Thailand, HY could only be performed at selected, large hospitals.

The present study was to examine the accuracy of TVS, SIS, and HY for the diagnosis of endometrial polyp and submucous myoma compared to histopathological diagnosis. The results suggested that SIS, which is a less invasive and more readily available method, could be a suitable choice for rural hospital operation with limited resources.

Materials and Methods

The present retrospective study was conducted in Bhumibol Adulyadej Hospital (BAH), Bangkok, Thailand. It was approved by the Institutional Review Board of Bhumibol Adulyadej Hospital (IRB 50/61). Data were reviewed from medical records kept in BAH computerized databases. Data from all patients with hysteroscopic surgery with histopathological diagnosis between January 2014 and December 2017 were collected. The inclusion criteria for the present study were women who 1) had abnormal TVS either or SIS, 2) underwent TVS no more than three months before SIS, and 3) had final HY and histopathologic reports. Exclusion criteria included women who did not complete all three diagnostic tests, which are the TVS, SIS, and HY with pathological analysis. Demographic data collected from medical records included age, body mass index (BMI), symptoms, hysteroscopic findings, TVS, SIS, and histopathological reports.

TVS (2D TVS) was performed on each patient's first visit (GE, Voluson, E6) by a qualified gynecologist. A 9 MHz vaginal probe was used for endometrial thickness measurement. Any focal abnormalities were recorded. Patients with endometrial thickness less than 4 mm were excluded from the present study.

SIS was performed during the proliferative phase of menstrual cycle, which is within 10 days of menstrual cessation, and the earliest time without vaginal bleeding in pre- and post-menopausal women, respectively by an expert gynecologist. Under aseptic technique, Foley's catheter no. 8F was inserted into the endometrial cavity followed by a balloon inflation with 1 to 1.5 milliliter of normal saline. Ten to twenty milliliters of normal saline was injected into the endometrial cavity until enough distention was achieved. Results of the TVS and SIS were classified by using the following criteria, thickened endometrial was defined as a full endometrial wall thickness of more than 14, 8, and 5 mm in pre-menopause, post-menopause with and post-menopause without hormone replacement therapy, respectively[8]. Endometrial polyp was defined as a hyperechogenic lesion with a pedunculated attachment to the endometrium as represented in Figure 1 and 2. Submucosal myoma was defined as a lesion of mixed echogenicity disrupting the endometrial continuity as showed in Figure 3 and 4[9].

Participants who had either abnormal TVS or SIS results were counselled to undergo HY for histopathological diagnosis. The investigation procedure was performed by a certified reproductive medicine specialist. HY was performed with a 5 mm Hopkins II straight forward and 30° telescope (Karl Storz, Germany). The patients were placed in the dorsal lithotomy position under general anesthesia. The distension media in HY was 1.5% glycine. Distension media irrigation was performed at the rate of 100 to 200 ml/minute. The pressure of irrigation was around 50 to 100 mmHg. Two hundred microgram misoprostol vaginal tablet was inserted vaginally six hours before the procedure. During the hysterocope insertion, endocervical canal and uterine cavity were visualized. Normal uterine cavity, endometrial hyperplasia, endometrial polyp, and submucous myoma were evaluated, as presented in Figure 5 and 6. Hysteroscopic polypectomy or myomectomy were performed for endometrial polyp or submucous myoma, respectively. The electrocautery was set at 80 watt in a unipolar cutting mode. Uterine curettage was performed if there was no focal endometrial abnormality. Endometrial specimens were sent for histopathologic diagnosis. Histopathologic reports were considered the reference standard for the final diagnosis.

Statistical analysis

Descriptive statistics were used to analyze patient demographic data. Continuous data were expressed as mean and standard deviation (SD). Categorized data were expressed as number and percentage. Pearson chi-square and Fisher's exact test were used in data analysis when appropriate. The p-value of 0.05 or

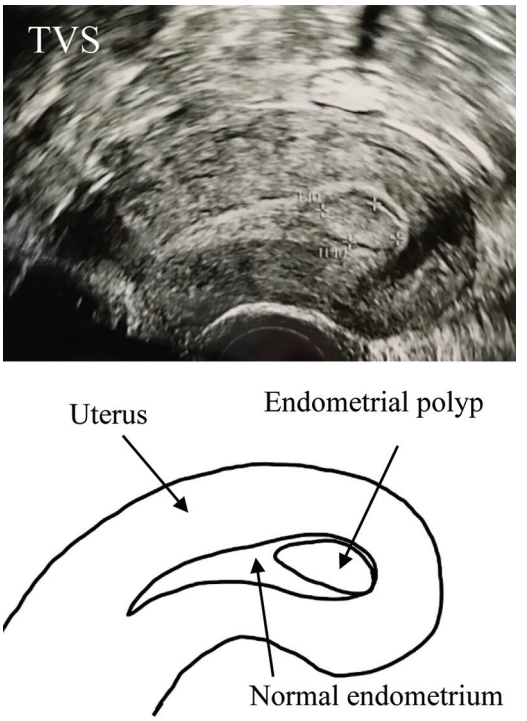

Figure 1. Endometrial polyp size 15×11 mm at posterior wall of uterine cavity demonstrated by using TVS.

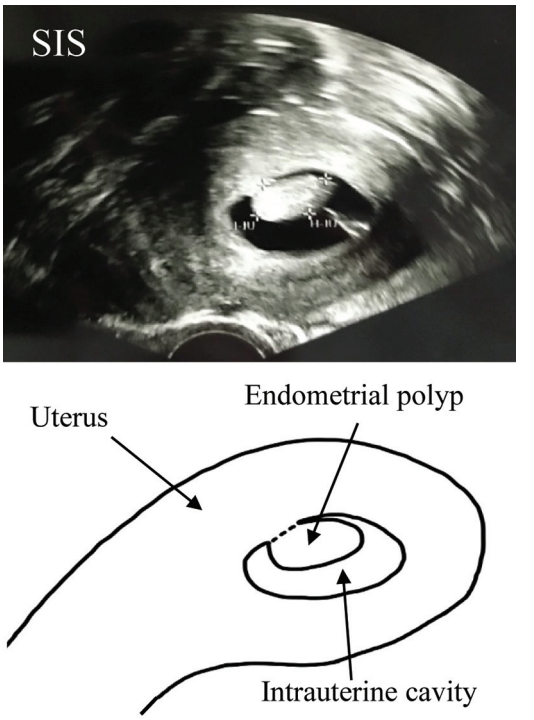

Figure 2. Endometrial polyp size 15×11 mm at posterior wall of uterine cavity demonstrated by using SIS, longitudinal view.

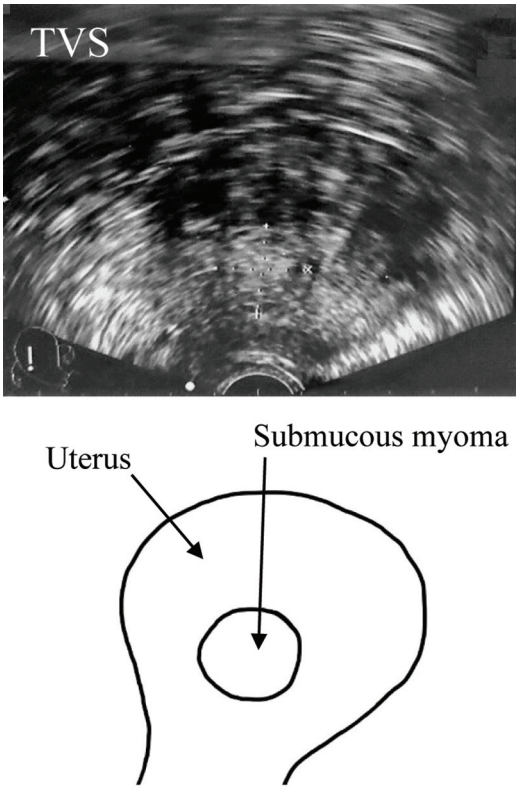

Figure 3. TVS demonstrating a 23×18 mm submucous myoma, protruding from the posterior uterus wall.

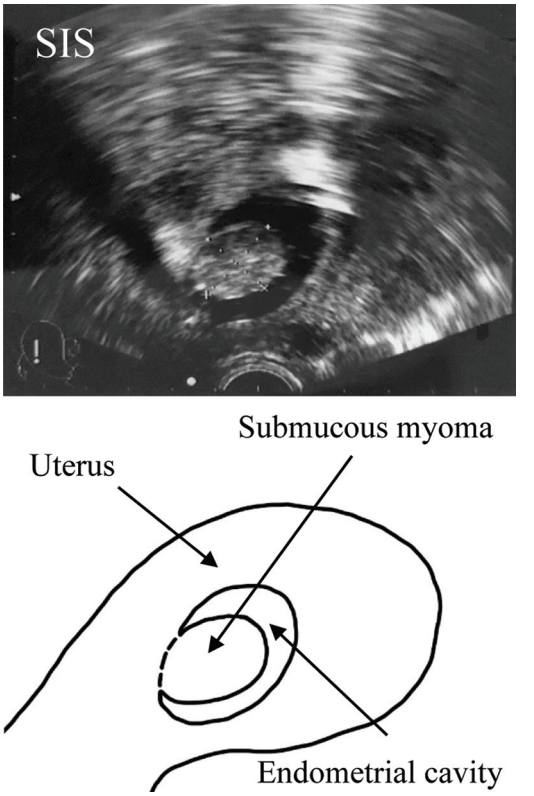

Figure 4. SIS, sagittal view, demonstrating a 23×18 mm submucous myoma, protruding from the posterior uterus wall.

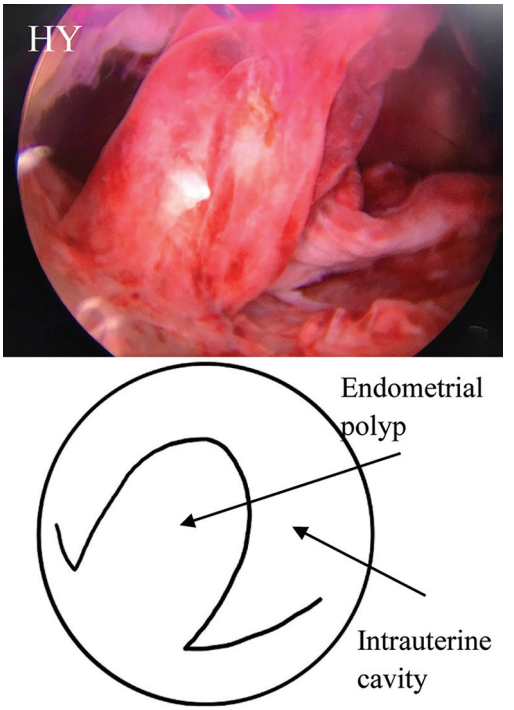

Figure 5. Endometrial polyp size 15×11 mm at posterior wall of uterine cavity demonstrated by using hysteroscopy.

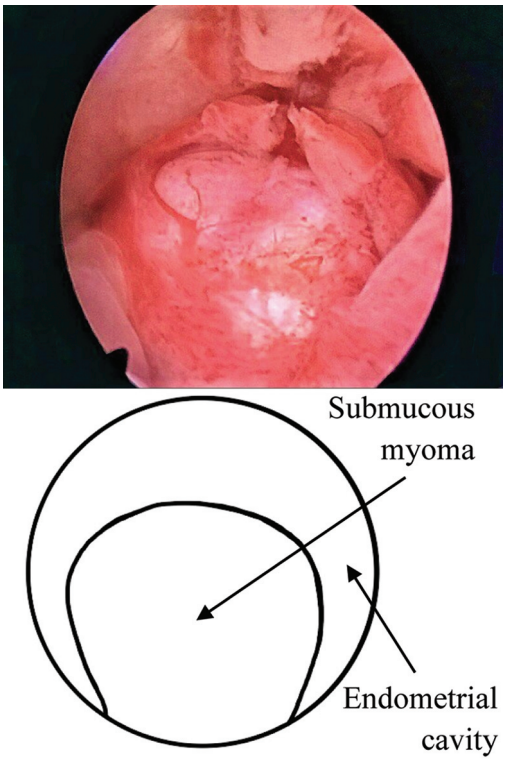

Figure 6. Hysteroscopy demonstrating a 23×18 mm submucous myoma, protruding from the posterior uterus wall.

Table 1. Demographic and clinical characteristics of the study cohort

Baseline characteristics	n=150 n (%)
Age (year); mean±SD	41.1±10.6
BMI (kg/m^2); mean±SD	23.5±4.4
Symptoms	
Infertility	23 (15.3)
• Primary	16 (10.7)
• Secondary	7 (4.6)
AUB	127 (84.7)
• Premenopausal bleeding	115 (76.7)
• Postmenopausal bleeding	12 (8.0)

SD=standard deviation; BMI=body mass index; AUB=abnormal uterine bleeding

less was considered to be statistically significant. Analysis was performed using the PASW Statistics software, version 18 (SPSS Inc., Chicago, IL, USA). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR–) for TVS, SIS and HY were calculated. The Cohen kappa statistic was used to evaluate the inter-rater reliability of TVS, SIS and HY.

Results

During the study period, 150 medical records were examined. There were 127 and 23 cases in the AUB and infertility groups, respectively. The mean age of women participating in the present study was 41.1 years old. The demographic characteristics are presented in Table 1.

Comparison of TVS, SIS, and hysteroscopic results with histopathologic reports especially normal and thickened endometrium, percent false negative over false positive from TVS and SIS in the present study were 73.7/50.5 and 21.4/100.0, respectively, with statistical difference ($p \leq 0.001$). While the diagnosis of endometrial polyps and submucous myoma were corrected, the TVS, SIS, and hysteroscopic results with pathologic reports were 80.5/77.5, 88.7/92.1 and 92.8/100 percent, respectively, with statistical significance ($p<0.001$) as presented in Table 2.

The comparisons of sensitivity, specificity, PPV, NPV, and accuracy of TVS, SIS, and HY are presented in Table 3. In cases where the histopathologic reports indicated endometrial polyps, the sensitivity of TVS, SIS, and HY were 71.7, 93.5, and 97.8, respectively.

Table 2. TVS, SIS, and HY results compare to histopathologic reports

Methods	Findings	Histopathologic reports; n (%)			
		Negative (n=20)	Polyp (n=92)	Myoma (n=38)	Total (n=150)
TVS*	Normal EM	5 (26.3)	14 (73.7)	0 (0.0)	19
	Thickened EM	3 (33.3)	5 (55.6)	1 (11.1)	9
	Polyp	10 (12.2)	66 (80.5)	6 (7.3)	82
	Myoma	2 (5.0)	7 (17.5)	31 (77.5)	40
SIS*	Normal EM	11 (78.6)	3 (21.4)	0 (0.0)	14
	Thickened EM	1 (100)	0 (0.0)	0 (0.0)	1
	Polyp	8 (8.2)	86 (88.7)	3 (3.1)	97
	Myoma	0 (0.0)	3 (7.9)	35 (92.1)	38
HY*	Normal EM	15 (100)	0 (0.0)	0 (0.0)	15
	Thickened EM	0 (0.0)	2 (100)	0 (0.0)	2
	Polyp	5 (5.2)	90 (92.8)	2 (2.0)	97
	Myoma	0 (0.0)	0 (0.0)	36 (100)	36

TVS=transvaginal ultrasonography; SIS=saline infusion sonography; HY=hysteroscopy; EM=endometrium; Polyp=endometrial polyp; Myoma=submucous myoma

* The result is significant at $p<0.001$

Table 3. Comparison of diagnostic parameters of TVS, SIS, and HY (histopathologic results as gold standard)

Methods	Diagnostic parameters						
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	LR+	LR–
TVS							
Overall	89.2	25.0	88.6	26.3	80.7	1.2	0.4
• 95% CI	82.6 to 93.9	8.7 to 49.1	85.6 to 90.9	12.6 to 46.9	73.4 to 86.7	0.9 to 1.5	0.2 to 1.1
Polyp	71.7	38.5	80.5	27.8	64.4	1.2	0.7
• 95% CI	61.4 to 80.6	20.2 to 59.4	74.8 to 85.2	17.6 to 40.9	55.1 to 73.0	0.8 to 1.6	0.4 to 1.3
Myoma	81.6	66.7	77.5	72.0	75.4	2.5	0.3
• 95% CI	65.7 to 92.3	46.0 to 83.5	66.4 to 85.7	55.6 to 84.1	63.1 to 85.2	1.4 to 4.3	0.1 to 0.6
SIS							
Overall	97.7	55.0	93.4	78.6	92.0	2.2	0.0
• 95% CI	93.4 to 99.5	31.5 to 76.9	89.7 to 95.8	52.8 to 92.3	86.4 to 95.8	1.3 to 3.5	0.0 to 0.1
Polyp	93.5	52.2	88.7	66.7	85.2	1.9	0.1
• 95% CI	86.3 to 97.6	30.6 to 73.2	83.6 to 92.3	45.7 to 82.6	77.4 to 91.2	1.3 to 3.0	0.0 to 0.3
Myoma	92.1	86.9	92.1	86.9	90.2	7.1	0.1
• 95% CI	78.6 to 98.3	66.4 to 97.2	80.2 to 97.1	68.9 to 95.2	79.8 to 96.3	2.5 to 20.4	0.0 to 0.3
HY							
Overall	100	75.0	96.3	100	96.7	4.0	0.0
• 95% CI	97.2 to 100	50.9 to 91.3	92.4 to 98.2	100 to 100	92.4 to 98.9	1.9 to 8.6	0.0 to 0.0
Polyp	97.8	68.2	92.8	88.2	92.1	3.1	0.0
• 95% CI	92.3 to 99.7	45.1 to 86.1	87.5 to 95.9	64.9 to 96.8	85.5 to 96.3	1.7 to 3.7	0.0 to 0.1
Myoma	94.7	100	100	90.9	96.6	0.0	0.0
• 95% CI	82.3 to 99.4	83.2 to 100	100 to 100	72.2 to 97.5	88.1 to 99.6	0.0 to 0.0	0.0 to 0.2

PPV=positive predictive value; NPV=negative predictive value; LR+=positive likelihood ratio; LR–=negative likelihood ratio; TVS=transvaginal ultrasonography; SIS=saline infusion sonography; HY=hysteroscopy; Overall=overall detection; Polyp=endometrial polyp; Myoma=submucous myoma; CI=confidence interval

Table 4. Comparison of inter-rater reliability using kappa statistics of TVS, SIS, and HY (histopathologic results as gold standard)

Intrauterine pathologies	Methods	Kappa value#	95% CI
Overall detection*	TVS	0.45	0.32 to 0.56
	SIS	0.77	0.67 to 0.86
	HY	0.92	0.86 to 0.97
Polyp*	TVS	0.43	0.29 to 0.58
	SIS	0.76	0.65 to 0.85
	HY	0.92	0.83 to 0.97
Myoma*	TVS	0.72	0.57 to 0.84
	SIS	0.89	0.79 to 0.97
	HY	1.00	1.00 to 1.00

TVS=transvaginal ultrasonography; SIS=saline infusion sonography; HY=hysteroscopy; Polyp=endometrial polyp; Myoma=submucous myoma; CI=confidence interval

Interpretation of Cohen's kappa[10], * The result is significant at p<0.001

Specificity of the three techniques were 38.5, 52.2, and 68.2, respectively. NPV and the accuracy of the three interventions were 27.8/64.4, 66.7/85.2 and 88.2/92.1 percent, respectively. Ninety percent PPV of all three techniques were similar.

When the histopathologic reports were submucous myoma, the sensitivity of TVS, SIS, and HY were 81.6, 92.1, and 94.7 percent, respectively. The specificity, NPV and the accuracy were nearly 100 percent in SIS and hysteroscopic techniques. PPV of the three methods were 77.5, 92.1, and 100, respectively. Positive likelihood ratio of SIS technique was high.

While the hysteroscopic reports were overall intrauterine abnormalities, the sensitivity of TVS, SIS, and HY were 89.2, 97.7, and 100 percent, respectively. The specificity over NPV of the three techniques were 25.0/26.3, 55.0/78.6, and 75.0/100, respectively. The accuracy of TVS, SIS, and HY were 80.7, 92.0 and 96.7 percent, respectively. PPV of all three methods were around ninety percent.

Comparison of inter-rater reliability by using kappa statistics of TVS, SIS, and HY are presented in Table 4. When the pathologic reports indicated overall intrauterine abnormalities, endometrial polyps, and submucous myoma, the kappa value from TVS, SIS, and HY were 0.45/0.43/0.72, 0.77/0.76/0.89, and 0.92/0.92/1.00, respectively.

Discussion

The present study evaluated the accuracy of TVS and SIS for detection of intrauterine pathology compared to HY. HY has been accepted as the common standard method for the evaluation of the intrauterine cavity[11].

In this investigation, intrauterine abnormalities of women with AUB and infertility from HY were 86.7% (130/150). The most common abnormalities were endometrial polyps at 61.3 percent (92/150). The result was similar to what reported in previous literatures that the endometrial polyps were the most frequent lesion in AUB and infertile women, found in 51.7 and 6.0 percent, respectively in studies by Fatemi et al[12] and Chawla et al[13]. Fatemi et al[12] reported the prevalence of unsuspected intrauterine abnormalities in 678 unselected, asymptomatic, infertile women with a regular indication for a first in vitro fertilization (IVF)/intra-cytoplasmic sperm injection (ICSI) treatment underwent office HY. Fatemi's work was a randomized controlled trial. The participants were Dutch women. Most intrauterine abnormalities were endometrial polyp at six percent. Chawla et al[13] evaluated the accuracy of SIS for evaluation of uterine cavity abnormalities in 60 pre-menopausal and post-menopausal women. Both groups were presented with AUB and took HY as the gold standard. Chawla's work was a prospective study done in India. The results showed the most uterine cavity abnormalities were endometrial polyps in 51.7 percent of patients.

Endometrial polyp

In the present study, sensitivity and specificity of TVS, SIS, and HY were 71.7 and 38.5, 93.5 and 52.2, and 97.8 and 68.2 percent, respectively, for the detection of endometrial polyps. Imaging of endometrial polyps on TVS may appear as non-specific endometrial thickness or as focal masses within the endometrium cavity. Endometrial polyp may have the same echogenicity as the surrounding endometrium with smooth borders[14]. Endometrial polyps were some of the most frequent misdiagnosed pathologies by ultrasonography[15]. SIS is a very useful adjunct to the conventional TVS, implying that the detection rate of endometrial polyp increased significantly on the addition of SIS to TVS. SIS decreased false-negative results of endometrial polyp. From the authors' TVS findings, in submucous myoma, normal and thickened endometrium patterns, SIS increased accurate diagnosis rate of endometrial polyps to 57, 79, and 100 percent, respectively. SIS increased the true positive reports for endometrial polyp at 30 percent (66/86). The diagnostic efficacy of SIS is superior to that of TVS for the diagnosis of endometrial polyps. The present study observation

was supported by the finding of Bittencourt et al[16] and Vathanan et al[17]. The Bittencourt et al[16] studied 1,398 patients from Brazil in 2017. It was a systematic meta-analysis work published between 2015 and 2016. The pooled sensitivity and specificity of 2D SIS in detecting endometrial polyps were 93 and 81 percent, respectively. Vathanan's work[17] studied 223 patients from North West London. His work was a retrospective observational study. For endometrial polyps, sensitivity, specificity and NPV of SIS were better than that of TVS (95 versus 60.5, 97.2 versus 97, 94.4 versus 68.7 percent, respectively). In the current study, the kappa value from TVS, SIS, and HY for the detection of endometrial polyps were 0.43, 0.76, and 0.92, respectively. The interpretation of kappa value suggested that HY was the most reliable diagnosis method for endometrial polyps and TVS was the least reliable procedure for endometrial polyps.

For HY, the false negatives in the detection of endometrial polyps in the thickened endometrium in the present investigation consisted of two cases (100%). There were five (5.2%) false positives for diagnostic endometrial polyp in endometrial polyp. Because the operation was done in the middle to late proliferative phase of menstrual cycle, the characteristic of endometrial findings such as the endometrial fold may be mistaken by a physician as small endometrial polyps.

Submucous myoma

In the present study, submucous myoma was found at 25.3 percent (38/150). The sensitivity, specificity, NPV, and accuracy of TVS, SIS, and HY were similar at around ninety percent. The results from the current study were comparable to the result from work by Bittencourt et al[16], Maheux-Lacroix et al[18], and Vathanan et al[17]. Bittencourt et al's work[16] demonstrated the pooled sensitivity and specificity in the detection of submucous myoma from 2D-SIS at 94 and 81 percent, respectively. Maheux-Lacroix et al's work[18] showed the percentage of sensitivity and specificity for submucosal leiomyomas diagnosis on TVS and SIS were 69/94 and 98/97, respectively. Vathanan et al's work[17] reported the percentage of sensitivity, specificity, PPV, and NPV for submucous myoma from TVS and SIS at 57.1/96.5, 93.4/100, 84.2/100, and 78.1/97.9, respectively. The results from these three studies were comparable. In the present investigation, the value of kappa from TVS, SIS, and HY for diagnosing submucous myoma were 0.72, 0.89, and 1.00, respectively. SIS and HY had strong values almost perfect for submucous myoma detection, while TVS showed only moderate reliability.

Submucous myoma and endometrial polyp (overall detection)

The sensitivity, specificity, and accuracy of TVS for detection of overall intrauterine abnormalities in the present study were 89.2, 25.0, and 80.7 percent, respectively. The combination of SIS and TVS showed higher accuracy (92.0%) in the detection of abnormalities in uterine cavity. The performance of SIS in the current study was compared to the results from Seshadri et al's work[19] and Nieuwenhuis et al[1]. The percentage of sensitivity and specificity of 2D-SIS in present study, Seshadri et al's work and Nieuwenhuis's former were 97.7/88/90.9 and 55.0/94/96.3, respectively[19]. The results from the present study were similar to the previous study of Seshadri et al and Nieuwenhuis et al that SIS also had a high sensitivity in the detection of all intrauterine abnormalities. The kappa statistic results of TVS, SIS, and HY for diagnosed overall intrauterine abnormalities were 0.45, 0.77, and 0.92, respectively. HY was an almost perfect tool for general diagnosis of intrauterine pathologies due to its reliability. SIS was shown to be a more reliable tool than TVS for overall detection of intrauterine abnormalities in moderate level.

The diagnostic values for detection of intrauterine abnormalities of SIS was similar to that of HY and superior to that of conventional TVS. The images obtained by SIS are visualized in three-dimensions. Intrauterine normal saline injection helps to enhance visualization of the uterine cavity and may help discriminate between endometrial polyps and submucous myomas. The images from conventional TVS were two-dimensions. SIS enhanced detection and classification of focally intracavitary lesions could potentially result in improving patient outcomes. A better treatment could reduce morbidity from unnecessary hysteroscopic surgery or undetected abnormalities. SIS could be used very accurately to measure the size, location, type assessment, and classification of submucous myomas. These parameters are very important for the planning of hysteroscopic surgery. Another advantage of an accurate imaging diagnosis is the potential to omit an unnecessary surgical procedure and therapeutic diagnosis[1].

In the present study, there were no endometrial hyperplasia and intrauterine adhesion (Asherman's

syndrome) because they underwent endometrial sampling or evacuation and were managed by general gynecologist.

The limitations in the present study were the retrospective collection data and the relatively small number of women that underwent TVS, SIS, and HY with histopathologic results. HY needs high cost of hysteroscope, which was the problem of major institutes in Thailand. This procedure also needs an operation room. However, there was minimal missing data in the present study, and the number of the study cases were enough for sample size to complete the statistical significance.

Conclusion

In conclusion, the addition of SIS to TVS improved the sensitivity, specificity, PPV, NPV, accuracy, and inter-rater reliability significantly for detection of the intrauterine abnormalities. SIS showed excellent correlation with HY and pathologic diagnosis. It should be performed as an initial diagnostic test. It can replace a less accurate method such as TVS or an expensive and invasive methods such as HY. The adoption of SIS would reduce a considerable number of cases of unnecessary hysteroscopic procedures. In general practice, SIS might be considered as a gold standard where HY is not available due to high accuracy. The use of HY is appropriate for cases when SIS is not conclusive, or for a definite treatment in patients with intrauterine pathologies as confirmed by SIS.

What is already known on this topic?

Intrauterine abnormalities led the women to seek physician care with AUB and infertility. Many methods are currently used to diagnose intrauterine abnormalities, namely TVS, endometrial biopsy, SIS, and HY. TVS is an easy basic gynecological diagnostic tool. SIS refers to a procedure in which transcervical fluid is instilled into the uterine cavity to provide enhanced endometrial visualization during a transvaginal ultrasound examination. This method is easy and less invasive. It is the method of choice in most state hospitals in Thailand. HY is quickly becoming the standard of treatment in AUB. It gives a more complete visualization of the endometrium pathology that leads to either biopsy or excision of the entire pathology.

What this study adds?

SIS showed excellent correlation with HY and pathologic diagnosis. It should be the initial diagnostic test concurrent to TVS. SIS has comparable efficacy to HY. In situations with limited resources, SIS may be an adequate substitute to the HY.

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Conflicts of interest

The authors declare no conflict of interest.

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