Power doppler versus saline infusion sonography in the diagnosis of endometrial polyps in patients who present with abnormal uterine bleeding*

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ABSTRACT

Objective: To compare the diagnostic performance of Power Doppler versus Saline Infusion Sonography (SIS) in the diagnosis of endometrial polyps in patients who present with abnormal uterine bleeding using histopathological confirmation.

Methods: This is a 2-year cohort study involving non-pregnant patients with abnormal uterine bleeding examined prospectively and subjected to both transvaginal sonography with power Doppler and SIS. Single-vessel pattern/comma-like patterns on power Doppler were considered positive. Results were compared to the gold standard histopathological examination obtained by endometrial biopsy, curettage, or hysteroscopic resection of endometrial polyp.

Results: A total of 42 patients completed the study and were included in the final analysis. Thirty-five (35) patients had confirmed endometrial polyp by histopathology. Power Doppler was positive in 32 of these patients. SIS, on the other hand was positive in 16 patients. The results are as follows: sensitivity 89%, specificity 83%, and positive and negative predictive values 97% and 56% respectively for power Doppler. For SIS, on the other hand, sensitivity 46%, specificity 86%, positive and negative predictive values of 94% and 24% respectively.

Conclusion: Power Doppler is as useful in identifying patients with endometrial polyps and can be used in place of the traditional test SIS. Its diagnostic accuracy is better than SIS.

Keywords: Saline Infusion Sonography, Power Doppler, and Endometrial Polyp

INTRODUCTION

Abnormal uterine bleeding (AUB) affects 10 to 30 percent of reproductive-aged women and up to 50 percent of peri-menopausal women *(Haynes, 1977; Prentice, 2000)*. It can often be as subtle as post-coital bleeding, inter-menstrual bleeding, or a more pronounced, bothersome presentation such as post-menopausal bleeding and menorrhagia. In patients with abnormal uterine bleeding, transvaginal ultrasound (TVS) is the first line in the diagnostic approach to exclude endometrial pathology. It is a safe, non-invasive, and inexpensive initial diagnostic test that is useful for informing subsequent investigation and directing clinical management. If a thickened endometrium suggests endometrial pathology, then other diagnostic procedures such as saline infusion sonography (SIS), hysteroscopy or tissue sampling is done depending on other clinical data.

Thickened endometrium with a most likely diagnosis of endometrial polyp as the cause of the AUB, can be further investigated by the use of SIS in most settings. It is a well-known procedure in which diagnostic power of TVS is enhanced by the instillation of sterile saline solution in the uterine cavity, as a contrast medium. It allows a better visualization of the endometrial cavity for the detection of intra-cavitary lesions. However, being an invasive procedure SIS is considered as a minimally invasive test that entails patient discomfort and added complication as well as increased cost.

Power Doppler, on the other hand, is a relatively new technology with various advantages over conventional ultrasound. Power Doppler is based on the amplitude of the Doppler signal and is more sensitive to low velocity blood flow that is characteristic of the vasculature of polyp. These features make power Doppler advantageous for blood flow mapping since it depicts more clearly and reliably the vascular architecture of pathologic lesions in the endometrium.[1]

This study aims to determine the diagnostic accuracy of using power Doppler ultrasound technology in determining presence of endometrial polyps compared to SIS.

OBJECTIVES

To compare the diagnostic performance of Power Doppler and Saline Infusion Sonography (SIS) in the diagnosis of Endometrial Polyps in patients who present with abnormal uterine bleeding using histopathological confirmation.

* 2014 Winner, POGS Fellow's Research Paper Contest

Specific Objectives

1. To compute for the sensitivity and specificity of power Doppler ultrasound versus saline infusion sonography.
2. To compute for the positive and negative predictive values of power Doppler ultrasound versus saline infusion sonography.
3. To compute for the likelihood ratios of power Doppler ultrasound versus saline infusion sonography.

REVIEW OF RELATED LITERATURE

Polyps are common, and their prevalence ranges from 10 to 30 percent in women with abnormal uterine bleeding (AUB) in the reproductive age group *(Bakour, 2000; Goldstein, 1997)*. Among women undergoing endometrial sampling of thickened endometrium, the prevalence of endometrial polyps is 10 to 24 percent *(Stewart, 2010)*. More than 70 percent of women with endometrial polyps will complain of menorrhagia or metrorrhagia *(Preutthipan, 2005; Reslova, 1999)*. In a study by Anastasiadis, et al in 2000, the prevalence of endometrial polyps was 8.9% in women aged 20-85 years old complaining of abnormal uterine bleeding. It is thought that stromal congestion within the polyp leads to venous stasis with apical necrosis and eventual bleeding *(Jakab, 2005)*.

Power Doppler is a novel advancement in ultrasound technology. Its utility is based solely on its ability to detect low velocity blood flow and hence, its value in identification of endometrial lesions. The vascular pattern of endometria polyps show a feeding vessel beginning from the base and going through the central part of the endometrium referred to by *Timmerman et al*. as the **"pedicle artery sign"** and by *Alcaraz et al*. as the **"single-vessel pattern"**.[2] With the expertise of our sonologists and the knowledge of the distinct vascular patterns in polyps and myomas, we were able clearly delineate the presence of endometrial polyps.

Using transvaginal sonography (TVS), an endometrial polyp may appear as a nonspecific endometrial thickening or as round or elongated focal masses within the endometrial cavity. Sonolucent cystic spaces corresponding to dilated endometrial glands may be seen within some polyps In premenopausal women, polyps were the pathology most likely to be missed, according to one literature review. TVS identified only 275 of 344 polyps in this population — a sensitivity of 80%.[5] The high index of suspicion then on ultrasound as to the presence of an endometrial pathology needs to be further strengthened by another test.

As for the diagnosis of endometrial polyp, saline infusion sonography (SIS) is often used. SIS can be utilized to accurately evaluate the myometrium, endometrium, and endometrial cavity. This constitutes one of the most significant advances in ultrasonography of the past decade. SIS can provide a wealth of information about the uterus in patients with abnormal bleeding. It offers an exquisite view of the endo-myometrial complex that cannot be obtained with TVS alone.[5] Interpreting SIS images requires experience, correlation with the menstrual history, and careful scanning. In premenopausal women, SIS has an overall sensitivity of 94% and a specificity of 85%.[10] It provides a more comprehensive view of the pelvic anatomy than TVS alone, with more concentrated visualization of the endometrium. Whereas these frequently create nondescript distortion or thickening of the endometrial lining when imaged with TVS, SIS typically permits detection of intracavitary masses as well as differentiation of lesions as being endometrial, submucosal, or intramural. However, it can pose some technical difficulties.[5] Other limitations of SIS include the inability to thread the catheter, iatrogenic introduction of air bubbles into the uterus, and the inability to maintain distension in patients with a patulous cervix.

AP Cil, et al. in 2010, focused on a comparison of power Doppler flow mapping characteristics of endometrial polyps and submucosal fibroids and analysis whether two different power Doppler characteristics, *single-vessel pattern* and *rim-like vessel* pattern, can help to differentiate these focal endometrial lesions. Included in their study were patients suspected of having endometrial polyps or submucosal myomas on SIS. Subjects were examined prospectively by TVS and power Doppler. Single-vessel pattern and rim-like vessel pattern were considered to be characteristic of endometrial polyps and submucosal fibroids, respectively. Suspected diagnoses of the lesions according to vascular Doppler characteristics were compared with the final diagnosis following histopathological examination. Included in the final analysis were 49 patients with histological confirmation of the type of endometrial lesion: 32 with endometrial polyps and 17 with submucosal fibroids. The sensitivity, specificity and positive and negative predictive values for single-vessel pattern in diagnosing endometrial polyps were 81.2%, 88.2%, 92.9% and 71.4% and for rim-like pattern in diagnosing submucosal fibroids they were 70.6%, 100%, 100% and 86.5%, respectively. They concluded that power Doppler flow mapping is a valuable tool in the diagnosis of focal endometrial pathology and was also useful in distinguishing submucosal fibroids and endometrial polyps. Based on a comprehensive literature search, there were no journals elucidating the utility of power Doppler compared to SIS in identification of patients with endometrial polyp.

The gold standard of this study is the tissue diagnosis

or confirmation of an endometrial polyp. There have been many advances in sampling of the endometrium. No technique surpasses the sensitivity and specificity of hysteroscopy with directed biopsy.[8] Owing to its superior diagnostic potential, hysteroscopy, even when performed in the office, leads to precise diagnosis and appropriate management of intrauterine pathologic conditions. However, for physicians who are untrained or lacking the equipment to perform diagnostic hysteroscopy with directed biopsy, simple in-office endometrial sampling techniques with no visual control provide a means to obtain reasonably reliable samples with negligible patient discomfort. Numerous studies have shown that the endometrium is adequately evaluated with office sampling techniques. A sample, which is representative of the lesion, can be obtained in at least 90 percent of patients undergoing a blind procedure.[8] Thus diagnostic dilatation and curettage (D&C) and endometrial biopsy are widely considered to be the method of choice for obtaining samples of endometrium for histologic examination in low-cost settings.

METHODOLOGY AND DATA

Clinical History of Study Population

Between May 2011 to October 2012, seventy two (72) patients who consulted at USTH GYN-OPD with a chief complaint of abnormal uterine bleeding were included in this study after obtaining written informed consent. Age ranged from 20-52 years old, all with sexual contact, pre-menopausalor peri-menopausal with a negative pregnancy test. The AUB characteristics were heavy menstrual bleeding with or without change in duration of menses (39), prolonged menstruation without change in amount (14), intermenstrual bleeding /spotting (16), post-coital bleeding (3). Those with abnormal uterine bleeding suspected of having endometrial pathology on TVS (either as thickened endometrium or visualization of endometrial polyp) were examined prospectively by addition of power Doppler and subsequently, saline infusion sonography with eventual tissue diagnosis of the pathology either by endometrial biopsy, endometrial curettage, or hysteroscopy-guided endometrial sampling.

Two sonographers did the examination, one for the transvaginal ultrasound with power Doppler and another for the saline infusion sonography. Both were blinded to the results of the other test. Power Doppler characteristics and SIS results were noted and once both were completed, they were scheduled for a diagnostic procedure. Of the total 72 patients eligible for the study with abnormal uterine bleeding suspected of having endometrial pathology, 51 were able to undergo both the TVS with power Doppler and SIS. Among the 51 subjects, 42 were able to undergo one of the gold standard tissue diagnostic procedures mentioned earlier.The remaining 9 were not able to undergo any diagnostic procedure and they, as well as those who were not able to complete TVS with power Doppler and SIS, were excluded from the statistical analysis leaving a study population of 42. (Figure 1)

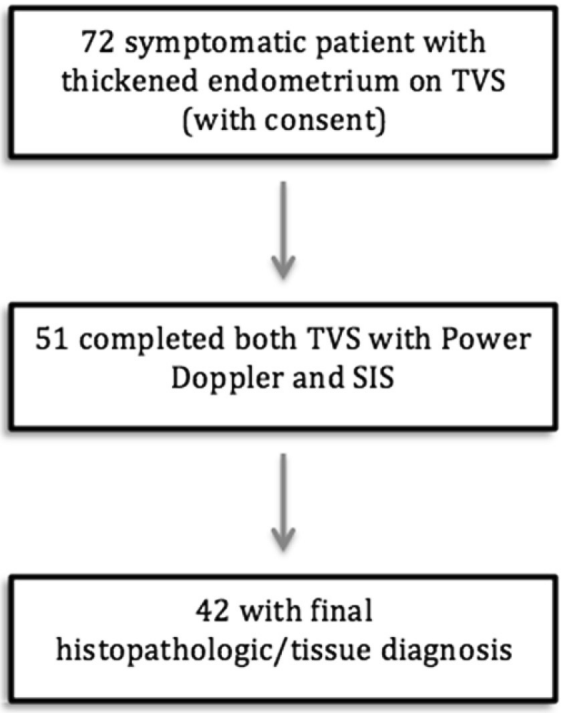

Figure 1. Algorithm for patient selection and methodology

Sonography

TVS was performed in all patients using frequency 3.75 MHz. First, standard B-Mode TVS was performed in order to evaluate endometrial thickness and echogenicity. Attempts were made to scan on days 4-11 (proliferative phase) of the cycle, when the endometrium is at its thinnest phase.

Machine: GE VOLUSON 730 Expert

Power Doppler Sonography

Along with the TVS, power Doppler sonography was done as well to evaluate: the presence or absence of color-coded zones that represent vascularized areas; and the vascular pattern of the endometrium (blood flow mapping). Power Doppler settings were set to achieve maximum sensitivity for detecting low-velocity flow without noise (power doppler gain, 16-17; filter, 2; PRF 0.03-0.1). Similar preset power Doppler ultrasound settings were used for all examinations. However, to optimize flow imaging and minimize noise, adjustments were made to the filter. Single vessel pattern, with a single vessel penetrating from the myometrium into the endometrium was considered to be characteristic of endometrial polyp. This test was done

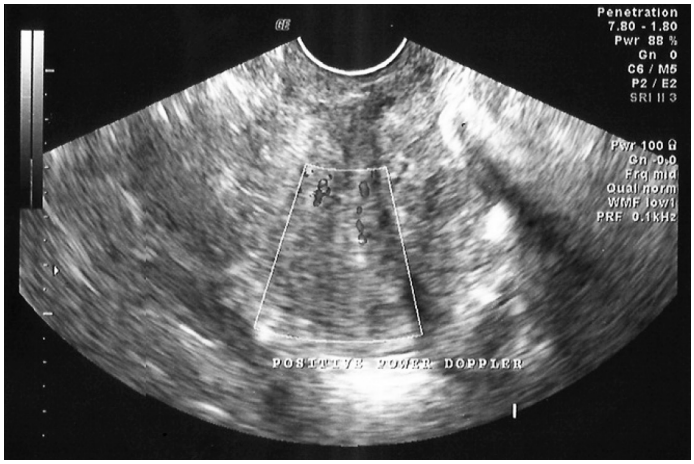

Figure 2. Positive Power Doppler

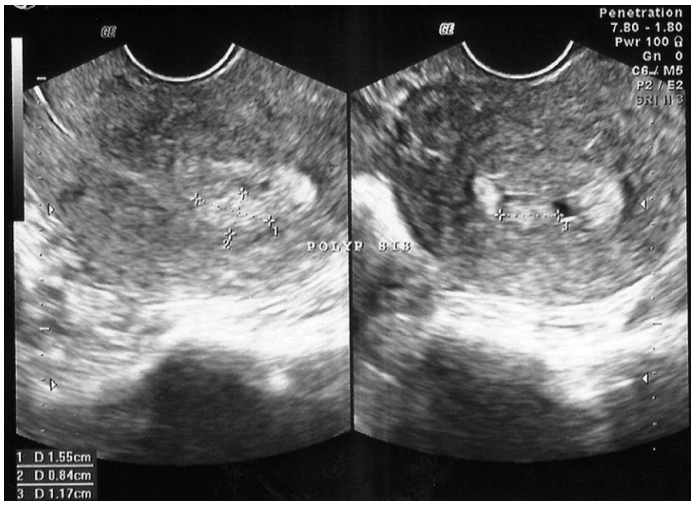

Figure 3. Positive SIS

during the proliferative phase of the cycle as well (as much as possible during the same cycle TVS and power doppler were done).

Saline Infusion Sonography

Subsequent sonohysterography was performed. After cleaning and visualizing the cervix, a sterile F5 feeding tube that has been flushed with sterile saline to eliminate the air is then guided into the endocervical canal. The catheter is advanced passed the external cervical os for a variable distance (ranging 5-7cm). The speculum is then carefully removed, allowing the catheter to remain in place. Transvaginal scanning is then performed during the instillation of sterile saline solution. Total of 10-20 cc is usually sufficient. The examination usually lasts 10-15 minutes.

Management and Histopathological examination

Two (2) patients underwent hysteroscopy, thirteen (13) had endometrial curettage, twenty-seven (27) had endometrial biopsy within 1 month after completion of power Doppler and SIS.

Table 1. Summary of AUB Characteristics

Menstrual Problem	Number of Subjects who presented with the symptom
Heavy menstrual bleeding with/ without change in duration	39
Prolonged menses without change in amount	14
Intermenstrual spotting	16
Post-coital bleeding	3

Table 2. Summary of Patient Demographics

Age	Number
20-30 years old	20
31-40 years old	14
41-50 years old	7
>51 years old	1

DATA ANALYSIS AND DISCUSSION

Data were analyzed using the 2x2 contingency table to determine the sensitivity, specificity, positive and negative predictive values as well a likelihood ratios with 95% confidence interval.

Possible threats to the validity of this study were minimized. We tried to answer the question, “Has there been an independent, blind comparison with a gold standard of diagnosis?”. All study patients have undergone both diagnostic tests being compared (power Doppler and SIS) as well as the reference/ “gold” standard evaluation, which is tissue diagnosis. The reference standard has been applied regardless of the test results.

Sensitivity and Specificity

Power Doppler has a 89 % sensitivity compared to about 46 % for SIS. This means that based on the data gathered, power Doppler correctly identifies 89% of patients with endometrial polyp. About 11% with endometrial polyp go undetected (false negatives). A high sensitivity is clearly important where the test is used to identify a treatable disease. Screening the female population complaining of AUB by TVS with power Doppler is a good test. Power Doppler has a specificity of 83% whereas SIS has 86%. Power Doppler therefore correctly identifies 83% of patients without endometrial polyp that is not significantly different from SIS, which identifies 86% of patients without endometrial polyp. There is a almost the same false positive test result for SIS and almost the

Table 3. Table Data

Subjects	Power Doppler	Saline Infusion Sonography	Tissue Diagnosis
1	(-)	(+)	ACT 11-1346 Endometrial Biopsy: *Secretory Endometrium*
2	(+)	(-)	ACT 11-1627 Endometrial biopsy: *Endometrial polyp*
3	(+)	(+)	ACT 11-1639 Endometrial Biopsy: *Endometrial Polyp*
4	(+)	(-)	ACT 11-1686 Endometrial biopsy: Endometrial Polyp
5	(+)	(-)	ACT 11-1746 Endometrial biopsy: *Simple hyperplasia without atypia*
6	(+)	(+)	ACT 11-1753 Endometrial biopsy: *Endometrial polyp*
7	(+)	(-)	ACT 11-1804 Endometrial biopsy: Endometrial polyp *Chronic endocervicitis*
8	(+)	(+)	ACT 11-1811 Endometrial Curettage: *Functioning Endometrial Polyp* *Secretory Endometrium*
9	(+)	(+)	ACT 11-1823 Endometrial Curettage: *Functioning Endometrial Polyp* *Secretory Endometrium*
10	(+)	(-)	ACT 11-1853 Endometrial Biopsy: *Endometrial Polyp* *Benign endocervical tissues*
11	(+)	(+)	ACT 11-1864 Hysteroscopic resection of polyp: A. *Endometrial polyp* B. *Endocervical polyp with hemorrhage and congestion*
12	(+)	(-)	ACT 11-1873 Endometrial curettage: *Endometrial Polyp with hemorrhage*
13	(+)	(-)	ACT 11-1915 Endometrial Curettage: Endometrial Polyp *Simple Hyperplasia without atypia*

14	(+)	(-)	ACT 11-1935 Endometrial Biopsy: *Endometrial Polyp*
15	(-)	(-)	ACT 11-1952 Endometrial biopsy: *Endometrial Polyp*
16	(-)	(-)	ACT 11-1982 Endometrial Curettage: *Endometrial Polyp* *Chronic cervicitis with squamous metaplasia*
17	(+)	(-)	ACT 11-2050 Endometrial Biopsy: *Endometrial Polyp* *Proliferative endometrium*
18	(-)	(-)	ACT 11-2081 Endometrial biopsy: *Strips of endometrial and endocervical epithelium with mucin*
19	(+)	(+)	ACT 11-2134 Polypectomy with Hysteroscopic resection of polyp: A. *Endometrial polyp* B. *Secretory Endometrium*
20	(+)	(+)	ACT 11-2419 Endometrial Curettage: *Functioning endometrial polyp* *Secretory endometrium*
21	(+)	(+)	ACT 11-2425 Endometrial Curettage: *Functioning Endometrial Polyp* *Secretory Endometrium*
22	(+)	(-)	ACT 11-2462 Endometrial Curettage: *Functioning Endometrial Polyp* *Secretory Endometrium, day 28*
23	(+)	(+)	ACT 11-2527 Endometrial curettage: *Endometrial polyp*
24	(+)	(+)	ACT 12-274 Endometrial biopsy: *Endometrial polyp*
25	(+)	(+)	ACT 12-323 Endometrial biopsy: *Endometrial polyp*
26	(-)	(-)	ACT 12-326 Endometrial biopsy: *Endometrial polyp, proliferative endometrium*
27	(+)	(-)	ACT 12-433 Endometrial curettage: *Endometrial polyp*
28	(+)	(+)	*ACT 12-844* *Endometrial biopsy:* *Endometrial polyp*

29	(+)	(-)	ACT 12-845 Endometrial biopsy: *Endometrial polyp*
30	(+)	(+)	ACT 12-883 Endometrial biopsy: *Endometrial polyp*
31	(+)	(+)	ACT 12-1060 Endometrial biopsy: *Endometrial polyp*
32	(+)	(-)	ACT 12-1251 Endometrial biopsy: *Endometrial polyp*
33	(-)	(-)	ACT 12-1308 Endometrial biopsy: *Functioning endometrial polyp, early secretory endometrium*
34	(-)	(-)	ACT 12-1351 Endometrial biopsy: *Simple hyperplasia without atypia*
35	(+)	(+)	ACT 12-1776 Endometrial biopsy: *Endometrial polyp* *Proliferative endometrium*
36	(-)	(-)	ACT 12-2091 Endometrial curettage: *Simple hyperplasia without atypia* *Chronic endocervicitis with squamous metaplasia*
37	(+)	(-)	ACT 12-2143 Endometrial curettage: *Simple hyperplasia without atypia* *Benign ectocervical tissue fragments*
38	(+)	(-)	ACT 12-2064 Endometrial biopsy: *Endometrial polyp, chronic endocervicitis*
39	(+)	(+)	ACT 12-2093 Endometrial curettage: *Endometrial polyp, proliferative endometrium*
40	(+)	(+)	ACT 12-2156 Endometrial biopsy: *Endometrial polyp*
41	(-)	(-)	ACT 12-2172 Endometrial biopsy: *Simple hyperplasia without atypia*
42	(+)	(-)	ACT 12-2173 Endometrial biopsy: *Endometrial polyp* *Proliferative endometrium*

Table 4. Calculation of Accuracy - Saline Infusion Sonohysterography

SIS	(+) Polyp	(-) Polyp	Total	
(+) Test Outcome	16	1	17	*Positive Predictive Value* 94.11 (71-99)
(-) Test Outcome	19	6	25	*Negative Predictive Value* 24 (9-45)
	35	7	42	*Prevalence* 83.33
	Sensitivity **45.71** (28-63)	*Specificity* **85.71** (42-99)		
Likelihood ratio (positive test) = 3.19 (0.5-20.35) Likelihood ratio (negative test) = 0.63 (0.41-0.97) Odds Ratio = 5.05 Relative Risk = 1.24 Number Needed to Treat = 5.5				

Table 5. Chi-Square Test and Fisher Exact Test – Saline Infusion Sonohysterography

Type of Test	Chi Square	p-value
Pearson Uncorrected	2.392	0.122
Mantel-Haenszel	2.335	0.127

same proportion of women with AUB who go on to have an SIS and are ultimately found to have no underlying endometrial polyp on histopathologic examination.

As discussed above, a test with a high sensitivity but low specificity results in many patients who do not have endometrial polyp but being told of the possibility that they have it and are then subject to further investigation. If the test is highly sensitive (as for power Doppler) and the test result is negative you can be nearly certain that they don't have an endometrial polyp.

Table 6. Calculation of Accuracy - Power Doppler Ultrasound

SIS	(+) Polyp	(-) Polyp	Total	
(+) Test Outcome	32	1	33	*Positive Predictive Value* 96.96 (84-99)
(-) Test Outcome	4	5	9	*Negative Predictive Value* 55.55 (21-86)
	36	6	42	*Prevalence* 85.71
	Sensitivity **88.9** (73-96)	*Specificity* **83.3 (35-99)**		
Likelihood ratio (positive test) = 5.33 (0.88-32.03) Likelihood ratio (negative test) = 0.13 (0.049-0.35) Odds Ratio = 40 Relative Risk = 2.18				

Table 7. Chi-Square Test and Fisher Exact Test–Power Doppler

Type of Test	Chi Square	p-value
Pearson Uncorrected	15.9	0.01
Mantel-Haenszel	15.5	0.01

Predictive Values

When evaluating the power of a diagnostic test to discriminate between those with and without a condition,

we are interested in the test's sensitivity and specificity. When we are faced with a patient and a test result, we need to determine the likelihood that a patient has an endometrial polyp (or does not have it), we are interested in the test's predictive value. Power Doppler has a 97% positive predictive value compared to 94% for SIS. This means that about 97% of patients with positive power Doppler test results will actually have endometrial polyp on histopathologic examination which is almost the same for SIS which is about 94%.

Likelihood Ratio

Power Doppler has a 5.3 likelihood ratio for a positive test as compared to 3.19 likelihood ratio for SIS. The positive likelihood ratio represents the odds ratio that a positive test result will be observed in patients with endometrial polyp compared to the odds that the same result will be observed among patients without the endometrial polyp.

LIMITATION

We acknowledge the limitations of our study, including the small study population and our evaluation of only pathological endometrium. This was an observational study of a pre-selected group and is not therefore clinically relevant to the general population. This study should be carried out in a large patient population including symptomatic and asymptomatic patients with pathological and normal endometria. The true accuracy of a promising diagnostic test is not known until it has been evaluated in one or more independent studies.

CONCLUSION

In conclusion, our study showed that power Doppler flow mapping is a valuable tool for diagnosing focal endometrial pathology and is useful in distinguishing between focal endometrial lesions such as endometrial polyps as much as SIS would if not better. The effectiveness of single-vessel pattern or pedicle artery sign to indicate endometrial polyps is well established by others and confirmed by our study, but future research by different investigators is needed to assess reproducibility and inter- and intra-observer variability.

Although sonohysterography remains the best means with which to diagnose intrauterine endometrial lesions, it is more costly, requires additional materials and is time-consuming compared with power Doppler. In these situations and in those areas where sonohysterography is not available because of lack of catheters or expertise, power Doppler, as a non-invasive, simple and quick procedure, may be helpful in distinguishing these lesions and could improve preoperative planning. ■

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