

# Evaluation of sonohysterography in detecting endometrial polyps – 241 cases followed with office hysteroscopies combined with histopathological examination

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## Abstract

**Introduction:** Hysteroscopy is considered the ‘gold standard’ procedure in assessing uterine pathology however it is more expensive and invasive method than ultrasonography. An alternative to the diagnostic hysteroscopy is sonohysterography.

**Aim:** To evaluate the usefulness of sonohysterography in detecting endometrial polyps in female patients diagnosed with infertility.

**Material and methods:** We compared the results of sonohysterographic examinations with hysteroscopy combined with histopathological findings.

**Results:** All the 241 sonohysterography examinations were performed successfully. No complications were observed. Forty-three hysteroscopies (17.8%) and six sonohysterography examinations (2.5%) were performed in short total intravenous anesthesia because of a low pain threshold of the patients. After hysteroscopic resection polyps were diagnosed in 74 (30.7%) patients. In 72 cases both saline infusion sonography (sonohysterography, SIS) examination and hysteroscopy confirmed the occurrence of an endometrial polyp. In 7 examinations (4.2%) the diagnosed polyp was not confirmed in sonohysterography (false-positive results). Two SIS procedures (2.7%) did not confirm the occurrence of the polyp (false-negative results). Sensitivity, specificity accuracy and error of sonohysterography in detecting endometrial polyps were 97.3%, 95.8% 96.2% and 3.7%, respectively. Positive and negative predictive values were 91.1% (PPV) and 98.7% (NPV). The agreement between SIS and hysteroscopy combined with histopathological examination was very high ( $K = 0.91$ ).

**Conclusions:** Sonohysterography is a safe and highly sensitive and specific method used in diagnostics of endometrial polyps. Its results closely correspond to those obtained in a hysteroscopic examination and histopathological analysis.

**Key words:** sonohysterography, endometrial polyp, saline infusion sonography, hysteroscopy, infertility, uterus.

## Introduction

The uterus plays an essential role in reproduction. It is a place where spermatozoa are transported, get prepared for fertilization, and then an embryo is implanted and a fetus develops. In 3–10%

of women with fertility disorders a so-called “uterine factor” might be a cause of their reproduction problems [1–3]. This factor includes some congenital and acquired pathologies of the uterus which may disturb spermatozoon migration, implanta-

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tion and may lead to miscarriages and obstetrical problems.

Endometrial polyps include non-malignant hyperplastic tissues of endometrium attached to the uterine wall with a wide base or pedicle. In most cases polyps do not cause any clinical symptoms. If there are such, they include profuse menorrhagia and mid-cycle spotting. Most often they are detected during the diagnostic procedure of abnormal bleeding from the uterine cavity and infertility. After menopause polyps are a risk factor for pathological endometrial hyperplasia [4]. Polyps are believed to have a negative influence on fertility as they might disturb migration of spermatozoa in the uterine cavity and implantation [2]. Endometrial polyps appear in as many as 10–30% of patients with infertility of unknown causes and concomitant endometriosis might increase the likelihood of their occurrence in the uterine cavity in infertile patients [2, 5–7]. A case-control study evaluated the effect of hysteroscopically identified endometrial polyps on endometrium by means of homeobox A 10 (HOXA10) and HOXA11, known molecular markers of endometrial receptivity. Uteri with endometrial polyps demonstrated a marked decrease in HOXA10 and HOXA11 messenger RNA levels, which may impair implantation. These findings suggest a molecular mechanism to support the clinical findings of diminished pregnancy rates in women with endometrial polyps [6, 8]. Decreased levels of mid-secretory insulin-like growth factor-binding protein 1 (IGFBP-1) and glycodelin were associated with the presence of endometrial polyps and both were reversed following hysteroscopic polypectomy [9]. Thus, endometrial polyps might be a direct cause of infertility as well as decreasing chances of becoming pregnant in patients treated for other causes of infertility.

While there is evidence from basic science studies to suggest a detrimental effect of polyps on fertility, the evidence from clinical studies is scarce and conflicting. After removing polyps the percentage of pregnancies in the group of infertile patients increases [10]. However, other authors did not observe such a correlation [11–13]. Transvaginal ultrasonography is a basic examination performed to diagnose intrauterine disorders. If one suspects a polyp, diagnostics should be expanded.

The “gold standard” procedure is hysteroscopy, which makes lesions visible and allows for their removal. With the use of modern endoscopes it is pos-

sible to perform safe hysteroscopy within a short period of time. Thanks to small diameter instruments a specialist does not have to dilate the cervix and apply general anesthesia to perform the treatment [14–18]. Unfortunately, hysteroscopy is a more expensive and more invasive method than ultrasonography. An alternative to diagnostic hysteroscopy could be saline infusion sonography, which is used to evaluate the uterine cavity and patency of Fallopian tubes after application of fluid medium. The advantage of the examination is the possibility of observing the cross section and outline of the uterine cavity as well as a more detailed observation of Fallopian tubes to check whether they are blocked without using some other specialist equipment. The examination is safe and well tolerated by patients [19].

## Aim

The aim of the study was to evaluate the usefulness of sonohysterography in detecting endometrial polyps in female patients diagnosed with infertility.

## Material and methods

### Patients

Two hundred and forty-one infertile patients were included in the study. They underwent diagnostics of infertility in the Gameta Fertility Clinic in Lodz in 2009–2010. A local bioethics committee gave its consent to conduct such a study. The infertility diagnostics included sonohysterography which evaluated patency of Fallopian tubes and hysteroscopy. The infertile patients included in the study were studied routinely prior to intrauterine insemination.

### Methods

Sonohysterography examination was a part of the infertility diagnostic procedure. It was performed with an AlokaProSoundSSD 3500 ultrasonograph, with a 3.8–7.5 MHz vaginal probe. The shape of the uterine cavity was imaged with 25 ml of 0.9% NaCl administered with a Foley catheter. The examinations were performed by one experienced ultrasonographer, who did not perform hysteroscopy. The sonohysterography examinations were performed in the same cycle before the hysteroscopic procedure was performed.

Hysteroscopy was carried out between the sixth and the ninth day of the menstruation cycle, in an

operating theatre, using the following endoscopic instruments: Bettocchhi Karl-Storz 4 mm hysteroscope, Aesculap 2.9 mm diagnostic hysteroscope, Aesculap 1028 AR 7.0 mm resectoscope, source of light Aesculap Axel 180. To obtain a panoramic view, 0.9% NaCl or 5% mannitol was used. After reaching the pressure of 70–100 mm Hg and obtaining the panoramic view of the uterine cavity and tubal outlets, we evaluated the cervical canal of the uterus, the shape and the size of the uterine cave, the endometrium surface (folds, lumps, protrusions, hyperplasia, vessel arrangement), and intrauterine lesions. The diagnosed polyps not bigger than 0.5 cm were removed during a hysteroscopy procedure with a 4 mm hysteroscope. More extensive lesions were removed with a resectoscope. The removed tissue underwent pathological analysis.

### Statistical analysis

When analyzing the sonohysterography procedure results in detecting endometrial polyps, we adopted the hysteroscopic procedure results combined with histopathological examination as referential analysis. For hysterosonography the researchers calculated sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV). The  $\kappa$  coefficient ( $K$ ) confirming the agreement of the results was calculated using the following formula:

$$K = 2 \times \frac{a \times b - b \times c}{[(a + c) \times (c + d) + (c + d) + (a + b) \times (b + d)]}$$

**Table I.** Patients' characteristics

Variable	Number	Percentage
Age, mean $\pm$ SD		32.4 $\pm$ 4.3
Infertility:		
Primary	186	77.2
Secondary	55	22.8
Symptoms:		
None	95	39.4
Dysmenorrhea	54	22.4
Irregular menorrhoea	43	17.8
Hypomenorrhoea	27	11.2
Hypermenorrhoea	22	9.1

where:  $a$  – true-positive results of sonohysterography,  $b$  – false-positive results of sonohysterography,  $c$  – false-negative results of sonohysterography,  $d$  – true-negative results of sonohysterography.

For the purposes of the presented analysis the researchers adopted the following statistical values:  $K < 0.1$  lack of agreement,  $K = 0.11$ – $0.40$  low agreement,  $K = 0.40$ – $0.60$  medium agreement,  $K = 0.61$ – $0.80$  high agreement,  $K = 0.81$ – $1.00$  very high agreement.

### Results

The patients qualified for hysteroscopy were in reproductive age. The mean age was  $32.4 \pm 4.3$ . The majority of the patients were aged 31–25 (40%). Only 4 patients were older than 40 (1.7%). One hundred and eighty-six patients (77.2%) were diagnosed with primary infertility and 55 patients (22.8%) with secondary infertility. Ninety-five patients did not report any symptoms (39.4%) (Table I). Among other patients, symptoms reported included dysmenorrhoea ( $n = 54$ ; 22.4%), irregular menorrhoea ( $n = 43$ , 17.8%), hypomenorrhoea ( $n = 27$ , 11.2%), and hypermenorrhoea ( $n = 22$ ; 9.1%). All the hysteroscopy and sonohysterography procedures were performed with no concomitant complications. Forty-three hysteroscopies (17.8%) and six sonohysterography examinations (2.5%) were performed in short total intravenous anesthesia because of a low pain threshold of the patients.

Endometrial polyps were diagnosed in 74 patients (30.7%). In 72 cases both SIS examination and hysteroscopy confirmed the occurrence of an endometrial polyp. In seven examinations the diagnosed polyp was not confirmed with an endoscopic examination of the uterine cavity (false-positive results). Two SIS procedures did not confirm the occurrence of the polyp (false-negative results). Sensitivity and specificity of sonohysterography in detecting endometrial polyps were 97.3% and 95.8% respectively. The SIS accuracy and error were respectively 96.2% and 3.7%. Positive and negative predictive values were 91.1% (PPV) and 98.7% (NPV). The agreement between SIS and hysteroscopy was very high ( $K = 0.91$ ).

In all the patients with false-positive results the endometrial polyps diagnosed in sonohysterography appeared to be a protruding part of the endometrium localized on the anterior wall of the retroverted uterus just behind the external orifice. None of these findings was bigger than 4 mm. The size of two un-

**Table II.** Anesthesia before sonohysterography and hysteroscopy

Procedure	Non-anesthesia	Anesthesia
Hysteroscopy	198 (82.2%)	43 (17.8%)
Sonohysterography	235 (97.5%)	6 (2.5%)

diagnosed polyps (false-negative results) was 2 mm × 3 mm and they were observed in the area of the tubal ostia (Tables I–III).

## Discussion

For a few years ultrasonography has been a basic diagnostic method used in gynecology. It is a quick and relatively cheap way of diagnosing anomalies of reproductive organs, including pathological states inside the uterine cavity. Thanks to a contrast medium or colorful Doppler used in sonohysterography it is possible to see a contour of the uterine cavity [15, 20]. Moreover, it also allows for confirming the patency of Fallopian tubes. In addition to that, the examination is safe and well tolerated by patients [19]. The SIS procedure makes the whole cross section visible as well as facilitating the observation of the external outline of the uterus. The presented method does not require any extra specialist equipment, except for an ultrasonograph with a transvaginal probe. Such equipment can be found in every gynecological office.

Hysteroscopy can also be performed in an outpatient clinic. Application of thin endoscopes with mini-instruments allows for removing lesions [21]. However, hysteroscopy requires expensive equipment, and such is often used only in obstetric and gynecological wards or one-day fertility clinics.

Endometrial polyps, which in an ultrasonographic examination are seen as oval hyperechogenic structures, are the most common disorders observed in infertile patients. Hysteroscopic examination confirms polyps, not diagnosed before, in as many as every tenth infertile patient [2, 5]. Study material, comprising 2500 hysteroscopic examinations, performed before *in vitro* procedures, confirmed the occurrence of endometrial polyps in 8% of hysteroscopies [22]. For some professionals it is common to carry out a hysteroscopic examination before applying assisted reproductive techniques [3, 23–25]. Such a strategy has not been confirmed in randomized prospective

**Table III.** Comparison of sonohysterography in diagnosing endometrial polyps with hysteroscopic pictures of hysteroscopy (referential method) (*n* = 241)

Variable	Sonohysterography polyp	
	Yes	No
Hysteroscopy polyp:		
Yes	72	2
No	7	160
Sensitivity (%)	97.3	
Specificity	95.8	
False-positive results (%)	4.19	
False-negative results (%)	2.7	
Accuracy (%)	96.27	
Error (%)	3.73	
PPV (%)	91.1	
NPV (%)	98.77	
κ (K)	0.91	

trials. Nevertheless, most clinicians agree that polyps should be removed before initiating assisted reproductive techniques [3, 22, 26, 27]. However, hysteroscopy in the cycle preceding a subsequent *in vitro* fertilization (IVF) attempt nearly doubles the pregnancy rate in patients with at least two failed IVF attempts compared with starting IVF immediately [27].

In our study in all the 241 patients SIS and hysteroscopic examinations were performed successfully. During two SIS procedures the researchers did not diagnose endometrial polyps. The size of two formerly undiagnosed polyps was 2 mm × 3 mm and they were observed in the area of the tubal ostia. It remains controversial whether such disorders disturb fertility [13, 28, 29]. All false positive results concerned the protruding part of the endometrium located on the anterior wall and their size was not bigger than 4 mm. The endometrium might have been damaged when the catheter was placed in the uterine cavity. It is probable that a torn flap of the endometrium resembled an endometrial polyp in the SIS examination. No complications were noted in all the 241 examinations. Only 6 (2.5%) patients required general anesthesia.

Sonohysterography alone is a better-tolerated procedure than an examination including the evaluation of flow of fluid through the Fallopian tubes or traditional hysterosalpingography [30]. It must be

**Table IV.** Sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV) in detecting endometrial polyps

Author	N	Sensitivity	Specificity	PPV (%)	NPV (%)
Schwarzler <i>et al.</i>	177	85.2	87.3	74.2	93.3
Kowalczyk <i>et al.</i>	97	72	96	–	–
Chittacharoen <i>et al.</i>	55	97.8	83.3	97.8	83.3
Kamel <i>et al.</i>	106	93.1	93.9	–	–
Grønlund <i>et al.</i>	66	90.9	100	100	90
Bingol <i>et al.</i>	100	100	93	90	100
Cicinelli <i>et al.</i>	50	58.3	100	100	86.1
Soares <i>et al.</i>	65	100	100	100	100
Cepini <i>et al.</i>	223	91.8	61.2	77.6	83.7
Ludwin <i>et al.</i>	47	100	83	–	–
Erdem <i>et al.</i>	33	100	98	–	–
Nanda <i>et al.</i>	50	100	97	–	–

stressed that all the patients had fallopian tube patency verified, which could be a cause of the greatest discomfort. A narrow cervical canal is often observed in menopausal patients, especially in those who have never given birth. With regard to menopausal patients, as many as 37% did not undergo sonohysterography [31]. The results of our study confirm that SIS can be successfully performed in a group of young patients [32] compared to 50 sonohysterography examinations with hysteroscopic examinations. The sensitivity was 50% and the specificity 100%. Soares *et al.* tried to detect endometrial polyps and hyperplasia. In order to do it they compared 65 sonohysterographic with hysteroscopic examinations and confirmed complete agreement (100% sensitivity, specificity, positive predictive value – PPV, negative predictive value – NPV) [33]. In Cepni's studies the sensitivity was 92.8% and the specificity 87.3% [34]. Bingol *et al.* [35] obtained similar agreement when he compared 100 results of sonohysterographic and hysteroscopic examinations. Other authors confirm high sensitivity and specificity in diagnosing intra-uterine pathologies [36–43] (Table IV).

Sonohysterography is a safe and relatively cheap method which allows for ruling out or confirming endometrial polyps. The findings show that the diagnosis established on the basis of SIS results is almost identical to the one made after performing

a hysteroscopy and pathological analysis. Hysteroscopy is an exceptionally sensitive method which has to be performed in an operating theatre, requiring extra equipment and sometimes anesthesia, which makes it more expensive and slightly more risky. Thus, diagnostic hysteroscopy can be replaced with sonohysterography if an endometrial polyp is suspected. Thanks to sonohysterography the medical professional can decide whether the patient should undergo a surgical hysteroscopy procedure.

## Conclusions

Sonohysterography is a safe and highly sensitive and specific method used in diagnostics of endometrial polyps. Its results closely correspond to those obtained in a hysteroscopic examination combined with histopathological analysis.

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