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ASSISTED REPRODUCTION TECHNOLOGIES

Comparison of sonohysterography to hysterosalpingogram for tubal patency assessment in a multicenter fertility treatment trial among women with polycystic ovary syndrome

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Abstract

Purpose To compare saline infusion sonohysterography (SIS) versus hysterosalpingogram (HSG) for confirmation of tubal patency.

Methods Secondary analysis of a randomized controlled trial, Pregnancy in Polycystic Ovary Syndrome II (PPCOS II). Seven hundred fifty infertile women (18–40 years old) with polycystic ovary syndrome (PCOS) were randomized to up to 5 cycles of letrozole or clomiphene citrate. Prior to enrollment, tubal patency was determined by HSG, the presence of free fluid in the pelvis on SIS, laparoscopy, or recent intrauterine pregnancy. Logistic regression was conducted in patients who ovulated with clinical pregnancy as the outcome and HSG or SIS as the key independent variable.

Results Among women who ovulated, 414 (66.9%) had tubal patency confirmed by SIS and 187 (30.2%) had at least one tube patent on HSG. Multivariable analysis indicated that choice of HSG versus SIS did not have a significant relationship on likelihood of clinical pregnancy, after adjustment for treatment arm, BMI, duration of infertility, smoking, and education (OR 1.14, 95% CI 0.77, 1.67, $P = 0.52$). Ectopic pregnancy occurred more often in women who had tubal patency confirmed by HSG compared to SIS (2.8% versus 0.6%, $P = 0.02$).

Conclusions In this large cohort of women with PCOS, there was no significant difference in clinical pregnancy rate between women who had tubal patency confirmed by HSG versus SIS. SIS is an acceptable imaging modality for assessment of tubal patency in this population.

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Introduction

Testing for fallopian tube patency is a standard part of the contemporary infertility evaluation. Hysterosalpingogram and laparoscopy with chromopertubation are the most common methods utilized to evaluate patency of the Fallopian tubes [1]. Historically, laparoscopy with chromopertubation in conjunction with hysteroscopy has been the gold standard in evaluation of tubal patency and the uterine cavity [1]. Compared with laparoscopy, HSG has been demonstrated to be approximately 83% specific for determining tubal patency [2, 3]. Saline infusion sonohysterography (SIS) is a safe, minimally invasive method to evaluate both the patency of the Fallopian tubes and the uterine cavity. It involves instilling sterile saline into the uterine cavity through a small catheter and performing a transvaginal ultrasound. With SIS, visualization of fluid accumulation in the posterior uterine cul-de-sac can be used to determine tubal patency [1]. In recent years, hysterosalpingo-contrast-sonography (HyCoSy), with instillation fluid that has enhanced contrast properties compared to saline, has emerged as a method for evaluating fallopian tube patency. This includes saline-air devices that create a stream of echogenic air bubbles to assess patency [4, 5].

While there are data to demonstrate that the use of contrast sonohysterography is effective in diagnosing tubal patency, very few studies have evaluated the efficacy of SIS without contrast in determining Fallopian tube patency [6–12]. As SIS without contrast is relatively inexpensive, minimally invasive and with no risk of ionizing radiation, it is of clinical value to demonstrate its effectiveness in screening for tubal patency for women who wish to conceive. Drawbacks of SIS include inability to visualize tubal anatomy and to determine if only one or both fallopian tubes are open [13].

The Pregnancy in Polycystic Ovary Syndrome II trial (PPCOS II), conducted by the National Cooperative Reproductive Medicine Network, was a double-blind, prospective, randomized trial of either letrozole or clomiphene citrate for treatment of infertility for anovulatory women with polycystic ovary syndrome (PCOS) [14]. The trial's primary outcome was live birth, and the study revealed a higher live birth rate for women treated with letrozole [15]. Women in the trial were required to have confirmation of tubal patency prior to treatment, and in the vast majority of cases, this was demonstrated by either SIS or HSG [16]. In this secondary analysis, the study objective was to compare SIS versus HSG for confirmation of Fallopian tube patency in women with PCOS undergoing ovulation induction.

Materials and methods

Participants and analytic sample

We performed a secondary analysis of data from the PPCOS II study (ClinicalTrials.gov number, NCT00719186). In the trial, PCOS was defined by a modified Rotterdam criteria: ovulatory dysfunction with either hyperandrogenism (hirsutism or an elevated testosterone level) or polycystic ovaries (defined by > 12 small antral follicles or an increased individual ovarian volume > 10 cm^3), or both [14]. Women recruited into the study were infertile and desired fertility treatment [14]. The institutional review board at each study site approved the study protocol, and each participant provided written informed consent. All pregnancies were followed to completion. The PPCOS II study recruited 750 women with PCOS and their male partners. Female participants were 18–40 years old. Male partners had at least one semen analysis in the past year with a minimum concentration of 14 million sperm per milliliter and evidence of motility. All couples agreed to have regular intercourse with the intent of pregnancy and female partners kept a prospective intercourse journal [14, 16]. Inclusion criteria for the trial included the following parameters for confirming a normal uterine cavity and fallopian tube patency: HSG, SIS with free fluid visualized in the pelvis, combined hysteroscopy and laparoscopy, or an uncomplicated, intrauterine non-IVF pregnancy with live birth and uncomplicated delivery and postpartum course within the past 3 years [16, 17]. The SIS procedures were performed at study sites who preferred technique for tubal patency testing and involved placement of a saline ultrasound catheter followed by instillation of normal saline at time of a transvaginal ultrasound. Accumulation of fluid in the posterior cul de sac was used to affirm patency of at least one fallopian tube. Following ovarian stimulation with either letrozole or clomiphene citrate, ovulation was determined by a serum progesterone level of at least 3 ng/ml or greater [16].

Statistical methods

Prior secondary analyses have evaluated the PPCOS II data in terms of predictive models for ovulation, pregnancy, and live birth as well as male and female weight, smoking, and intercourse frequency [18, 19]. Differences in baseline demographic data and treatment cycle characteristics for participants who ovulated and had tubal patency confirmed by SIS versus HSG were evaluated. Conception was defined by a positive serum human chorionic gonadotropin level. Clinical pregnancy was defined as an intrauterine pregnancy with the

presence of fetal heart motion on ultrasonography. Univariate analyses were conducted with *t* tests used for continuous variables. Chi-square test was used for categorical variables. Bivariate analyses of women who conceived and those with clinical pregnancy were performed to evaluate independent variables in which those positive for either conception or clinical pregnancy differed from those with negative outcomes. Multivariable logistic regression was conducted with conception and live birth as the outcomes and HSG as the independent variable. Likelihood of live birth was estimated with adjustment for parameters based on significant differences in bivariate analyses. The model included treatment arm, body mass index (BMI), length of time attempting conception, smoking, and education. Final models were obtained through stepwise selection. Results were reported as adjusted odds ratio (OR) with 95% confidence intervals (CI). All analyses were performed in SAS version 9.3 (SAS Institute).

Results

In the PPCOS II study, 750 couples were enrolled with 511 women (68.1%) having tubal patency confirmed by SIS and 217 (28.9%) having HSG confirmation of tubal patency. Of the women undergoing HSG, 185 (85,2%) had bilateral tubal patency and 32 (14.7%) had unilateral patency. Seventeen patients underwent laparoscopy with six having both tubes patent and nine having one tube patent. Five patients had a successful intrauterine pregnancy within 3 years prior to enrollment. Of 619 subjects (82.5%) with confirmed ovulation, 414 (66.9%) had tubal patency confirmed by SIS and 187 (30.2%) underwent HSG with at least one patent tube documented (Table 1). Among baseline characteristics of participants who ovulated and who had tubal patency confirmed by either HSG or SIS, the groups differed in body mass index (BMI), with the HSG group having a lower BMI than the SIS

Table 1 Characteristics for PPCOS II participants who ovulated with tubal patency confirmed by SIS versus HSG and for all participants who ovulated

Variable	SIS	HSG	All patients	*P* value*
N	414	187	619**	
Age (year)	28.7 ± 4.2	29.5 ± 4.0	28.9 ± 4.1	0.033
Treatment				0.964
Clomiphene	194 (46.9)	88 (47.1)	288 (46.5)	
Letrozole	220 (53.1)	99 (52.9)	331 (53.5)	
BMI (kg/m^2)	35.3 ± 9.6	32.5 ± 8.3	34.4 ± 9.3	< 0.001
Race				0.416
White	322 (77.8)	145 (77.5)	482 (77.9)	
Black or African-American	58 (14.0)	28 (15.0)	87 (14.0)	
Asian	17 (4.1)	5 (2.7)	23 (3.7)	
American Indian or Alaska Native	2 (0.5)	4 (2.1)	6 (1.0)	
Native Hawaiian or Pacific Islander	1 (0.2)	0 (0.0)	1 (0.2)	
Mixed race	14 (3.4)	5 (2.7)	20 (3.2)	
Ethnic group				0.097
Not Hispanic or Latino	346 (83.6)	166 (88.8)	529 (85.5)	
Hispanic or Latino	68 (16.4)	21 (11.2)	90 (14.5)	
Months attempting conception	42.5 ± 38.7	37.0 ± 31.2	40.2 ± 36.3	0.095
Prior pregnancy	147 (35.5)	72 (38.5)	235(38.0)	0.480
Prior pregnancy loss	89 (21.5)	54 (28.9)	150 (24.2)	0.049
Prior live birth	87 (21.0)	32 (17.0)	129 (20.8)	0.266
AMH (ng/ml)	7.0 ± 5.5	9.0 ± 8.2	7.6 ± 6.5	< 0.001
Total antral follicle count	45.4 ± 25.4	46.6 ± 25.6	45.5 ± 25.3	0.579
Total testosterone (ng/dl)	53.6 ± 29.6	54.6 ± 28.1	53.6 ± 28.8	0.718
Endometrial thickness (mm)	6.5 ± 2.8	6.7 ± 2.7	6.6 ± 2.8	0.524
Estradiol level (pg/ml)	56.0 ± 37.8	57.2 ± 33.6	56.2 ± 36.3	0.719
History of smoking				0.059
Never smoked	243 (58.7)	118 (63.1)	369 (59.6)	
Current smoking	65 (15.7)	16 (8.6)	83 (13.4)	
Quit smoking	106 (25.6)	53 (28.3)	167 (27.0)	
Education				0.551
High school graduate or less	94 (22.7)	36 (19.3)	135 (21.8)	
College graduate or some college	267 (64.5)	123 (65.8)	402 (64.9)	
Graduate degree	53 (12.8)	28 (15.0)	82 (13.3)	
Income				0.010
< $50,000	179 (43.2)	63 (33.7)	248 (40.1)	
≥ $50,000	173 (41.8)	103 (55.1)	286 (46.2)	
Wish to not answer	62 (15.0)	21 (11.2)	85 (13.7)	
Partner sperm concentration (million/ml)	80.4 ± 70.7	82.1 ± 75.7	80.3 ± 71.6	0.791

Values are mean ± standard deviation or *n* (%)

**P* value for significance of difference between SIS vs. HSG groups only

**Includes only 619 patients who ovulated

group. The HSG group also had a higher mean circulating anti-Mullerian hormone (AMH) level compared to the SIS group, was older, and had a higher proportion of women with an income greater than $50,000 per year than the SIS group.

Table 2 summarizes treatment outcomes for patients who had tubal patency confirmed by SIS versus HSG and for all PPCOS II participants. While women with tubal patency confirmed by HSG had higher rates of conception, clinical pregnancy, and live birth, the difference was not statistically significant. The HSG group also had more ectopic pregnancies. Ectopic pregnancies included seven tubal ectopic pregnancies, one heterotopic pregnancy, and two pregnancies of unknown location. Ectopic pregnancy occurred more often in women with tubal patency confirmed by HSG compared to SIS (2.8% versus 0.6%, $P = 0.02$). Among women with unilateral tubal occlusion on HSG (Table 3), the clinical pregnancy rate was 25.0%. Two out of 32 women (6.3%) with unilateral occlusion on HSG were diagnosed with ectopic pregnancy.

Multivariate analysis (Table 4) indicated that choice of HSG versus SIS did not have a significant relationship to the likelihood of clinical pregnancy, after adjustment for treatment arm, BMI, duration of attempting conception, smoking, and education (OR 1.14; 95% CI 0.77–1.67; $P = 0.52$). Likewise, there was no significant impact on likelihood of conception (OR 1.13; 95% CI 0.78–1.64; $P = 0.52$).

Discussion

In this large cohort of women with PCOS, there was no significant difference in conception and clinical pregnancy rates between ovulating study participants who had tubal patency confirmed by SIS versus HSG. These results suggest that SIS is an acceptable imaging modality for assessment of tubal patency in this population. While HSG and SIS are both outpatient procedures that do not require sedation or anesthesia, SIS has the advantage of not exposing a patient to ionizing radiation or iodine-containing contrast as HSG does [1, 20]. SIS can also be easily performed in the clinic, while HSG often requires a dedicated radiology facility. Additionally, SIS allows concomitant visualization of the ovaries and myometrium [1].

As a fallopian tube patency testing modality, HSG has some limitations. One important consideration is that HSG can yield false positive results because of induced proximal tubal occlusion due to tubal spasm, lowering the study's ability to accurately diagnose tubal patency [21]. A meta-analysis conducted in the Netherlands in 1995 evaluated 20 studies comparing HSG to laparoscopy with chromopertubation for diagnosing tubal pathologies. The study, which included 4179 patients, demonstrated that HSG had only 65% sensitivity and 83% specificity for diagnosing tubal occlusion [2]. The authors concluded that proximal tubal occlusion on HSG was often due to tubal spasm or transient collections of debris. Supporting these findings, Hajishafiha et al. (2009) evaluated 40 women who had bilateral proximal obstruction on HSG. When they performed SIS on these patients, they found that 80% had evidence of at least one patent Fallopian tube on SIS [11]. Broeze and colleagues (2011) performed a meta-analysis examining whether patient characteristics such as age, duration of subfertility, and a clinical history without risk factors for tubal pathology were associated with HSG accuracy in diagnosing tubal occlusion, using laparoscopy as the gold standard comparison test. They reported HSG to have a sensitivity and specificity of 53% and 87%, respectively, for any tubal pathology. They also reported HSG to have a sensitivity and specificity of 46% and 95%, respectively, for diagnosing bilateral tubal pathology when compared with laparoscopy [22].

A benefit of HSG is a potential therapeutic effect when HSG was performed with oil-based contrast as

Table 2 Treatment cycle outcomes for PPCOS II participants who ovulated with tubal patency confirmed by SIS versus HSG and for all patients who ovulated

Outcome	SIS *N* (%)	HSG *N* (%)	Another test or no test *N* (%)	All patients *N* (%)	*P* value*
N	414	187	18	619	
Conception	160 (38.7)	87 (46.5)	10 (55.6)	257 (41.5)	0.069
Clinical pregnancy	123 (29.7)	68 (36.4)	7 (38.9)	198 (32.0)	0.105
Pregnancy loss	46 (11.1)	28 (15.0)	5 (27.8)	79 (12.8)	0.182
First trimester loss[a]	44 (10.6)	25 (13.4)	5 (27.8)	74 (12.0)	0.329
Ectopic[b]	3 (0.7)	6 (3.2)	1 (5.6)	10 (1.6)	0.029
Live birth	111 (26.8)	59 (31.6)	5 (27.8)	175 (28.3)	0.232
Days to pregnancy	86.7 ± 46.0	91.7 ± 46.8	98.0 ± 43.8	88.7 ± 46.1	0.436

Values are mean ± standard deviation or *n* (%)

*P value for significance of difference between SIS vs. HSG groups only

[a] Pregnancy loss in the first 12 weeks

[b] Includes seven ectopic pregnancies, one heterotopic pregnancy, and two pregnancies of unknown location

Table 3 Treatment cycle outcomes for PPCOS II participants who had unilateral occlusion on HSG

Outcome	Unilateral occlusion on HSG ($N = 32$)	Both tubes patent on HSG ($N = 185$)	P value*
Ovulation	28/32 (87.5)	159/185 (86.0)	0.814
Conception	11/32 (34.4)	76/185 (41.1)	0.475
Clinical pregnancy	8/32 (25.0)	60/185 (32.4)	0.403
Pregnancy loss	4/32 (12.5)	24/185 (13.0)	0.941
First trimester loss[a]	3/32 (9.4)	22/185 (11.9)	0.681
Ectopic[b]	2/32 (6.3)	4/185 (2.2)	0.193
Live birth	7/32 (21.9)	52/185 (28.1)	0.464
Days to pregnancy			
N	11	71	
Mean ± SD	89.5 ± 53.2	92.0 ± 46.1	0.867

*P value for significance of difference between SIS vs. HSG groups only

[a] Pregnancy loss in the first 12 weeks

[b] Includes seven ectopic pregnancies, one heterotopic pregnancy, and two pregnancies of unknown location

demonstrated by Dreyer et al. (2017) in a recent randomized control trial. In the study, 1119 women were randomly assigned to either HSG with oil contrast (557 women) or water contrast (562 women). Ongoing pregnancy rates were higher in the oil group (39.7%) versus the water group (29.1%) as well as live birth rates (38.8% for oil group versus 28.1% for water contrast, $P < 0.001$) [23]. It is unknown if oil-based contrast was used for any of the HSG procedures performed in this analysis and therefore if any effect can be appreciated.

Maheux-Lacroix et al. (2014) published a systematic review and meta-analysis comparing SIS with HSG in diagnosing tubal occlusion in subfertile women. In total, 28 studies reported SIS results per individual tube and were included in the meta-analysis, representing 1551 women. For diagnosing tubal occlusion, SIS was found to be 92% sensitive and 95% specific. In nine studies (582 women), SIS and HSG were both compared with laparoscopy. For the nine studies that evaluated both modalities, SIS was estimated to be 95% sensitive and 93% specific for diagnosing tubal occlusion, while

Table 4 Likelihood of conception and clinical pregnancy in patients who ovulated who had tubal patency confirmed by SIS or HSG

Variable	Conception		Clinical pregnancy	
	OR (95% CI)	P value	OR (95% CI)	P value
Test performed				
Saline infusion sonography	1.0		1.0	
Hysterosalpingogram	1.13 (0.78, 1.64)	0.522	1.14 (0.77, 1.67)	0.523
treatment				
Clomiphene	1.0		1.0	
Letrozole	1.67 (1.17, 2.37)	0.004	1.51 (1.05, 2.18)	0.028
BMI (kg/m^2)	0.98 (0.96, 0.995)	0.013	0.98 (0.96, 0.995)	0.017
Length of attempting conception (months)	0.99 (0.99, 0.996)	0.001	0.99 (0.98, 0.99)	< 0.001
Prior pregnancy loss				
No	1.0			
Yes	1.55 (1.04, 2.31)	0.032		
History of smoking				
Never smoked	1.0		1.0	
Current smoking	0.40 (0.22, 0.74)	0.003	0.29 (0.14, 0.62)	0.001
Quit smoking	1.52 (1.02, 2.27)	0.039	1.54 (1.03, 2.31)	0.036
Education				
High school graduate or less	1.0		1.0	
College graduate or some college	1.37 (0.89, 2.11)	0.152	1.26 (0.79, 2.00)	0.338
Graduate degree	2.54 (1.40, 4.60)	0.002	2.25 (1.21, 4.18)	0.010

HSG had a sensitivity of 94% and specificity of 92%. The study found no benefit of commercially available contrast media over saline solution with regard to the diagnostic accuracy of SIS [24]. While the sensitivity and specificity of HSG in this study were higher than studies looking at HSG mentioned above, it must be noted that this was a smaller cohort of women evaluated.

The above-noted systematic review and meta-analysis included notable randomized control trials. Dijkman et al. (2000) compared contrast SIS with HSG in evaluating tubal pathology in 100 subfertile women, using laparoscopy/chromopertubation as a reference test. The group found initially that the likelihood ratios of SIS were slightly inferior to those obtained for HSG. However, they surmised that operator experience played a role. After dropping the first 50 SIS cases, the likelihood ratios of diagnosing tubal occlusion were similar between contrast SIS and HSG [25]. Socolov et al. (2009) evaluated the role of SIS with saline with air as a contrast solution versus HSG and laparoscopy/chromopertubation to evaluate tubal patency and the uterine cavity in 95 infertile women. They found that in comparison with laparoscopy, SIS was 81.4% sensitive, whereas HSG was 61.9% sensitive in diagnosing tubal patency. Both had similar sensitivities (87.7% for SIS and 85.3% for HSG) in diagnosing tubal patency. The authors concluded that SIS could be used in combination with HSG in evaluating fertility [26].

Kupesic et al. (2006) evaluated the efficacy of 2D contrast SIS (152 women) and 3D contrast SIS (116 women) in identifying uterine abnormalities and diagnosing tubal patency compared to laparoscopy with chromopertubation. Overall, the group found that 3D contrast SIS with pulsed Doppler was highly sensitive (100%) and specific (99.1%) for diagnosing tubal patency. 2D SIS with pulsed Doppler was also highly sensitive (98.2%) and specific (99.2%). The authors concluded that contrast SIS performed either by 2D or 3D US is a superior screening method evaluating infertile patients and that those that those with uterine cavity defects or nonpatent Fallopian tubes should be directed to operative hysteroscopy and/or laparoscopy [27]. While this study cannot directly compare to our study since we did not use contrast media for SIS, it does demonstrate potential validity for SIS to evaluate for tubal patency. Additionally, in a more recent prospective study, Ludwin et al. (2017) evaluated diagnostic accuracy of 2D/3D hysterosalpingo-foam sonography (HyFoSy) and 2D/3D-high-definition low Doppler (HDF)-HyFoSy in comparison to laparoscopy with dye chromotubation and 2D air/saline-enhanced hysterosalpingo-contrast sonography (HyCoSy). In this study of 132 women (259 Fallopian tubes) undergoing infertility evaluation, 2D-Air/saline-HyCoSy, 2D/3D-HyFoSy, and 2D/3D-HDF-HyFoSy indicated that 46 (17.8%), 27 (10.4%), and 24 (9.2%) of the 259 tubes were occluded, respectively; additionally, inconclusive results were obtained for 8 (3%), 5 (1.9%), and 3 (1.2%) tubes, respectively. Overall, use of 2D/3D-HyFoSy, especially 2D/3D-HDF-HyFoSy, had a significantly higher PPV (48% and 71%, $P < 0.05$ and $P < 0.01$, respectively) and resulted in fewer false positive and inconclusive findings than the use of 2D-air/saline-HyCoSy. The authors concluded that while 2D-Air/saline-HyCoSy is an appropriate initial test, using 2D/3D-HDF-HyFoSy, which has a significantly higher PPV, as a confirmation tool, it may reduce the need for laparoscopy [28].

A series of 1153 SIS procedures revealed adverse side effects in only 8.8% of cases, with adverse effects including pain, vasovagal symptoms, nausea, vomiting, or fever [29]. One randomized trial comparing SIS and HSG found no difference in pain, adverse effects, or procedure duration [30]. SIS has an advantage over HSG because it offers simultaneous evaluation of the ovaries and myometrium. A cost-effectiveness analysis of HSG versus SIS for the evaluation of female fertility would be helpful in resolving the issue of which test is preferable.

Given that SIS can only confirm patency of at least one Fallopian tube, these data indirectly address the question of whether the prognosis for fertility is similar for women with one versus two patent fallopian tubes. One retrospective, case-controlled study examining 62 patients with unilateral tubal occlusion on HSG found that after controlled ovarian stimulation and intrauterine insemination, the cumulative pregnancy rate was similar to that of women with unexplained infertility and bilateral tubal patency by HSG. In this study, women with distal unilateral tubal occlusion had significantly lower pregnancy rates than 115 women with unexplained infertility (19% versus 46.2%) [31]. A more recent study of 38 women with unilateral tubal occlusion demonstrated comparable clinical pregnancy rates between women with unilateral occlusion and unexplained infertility [32].

Strengths of this study include the large and well-characterized patient population and the multicenter nature of the study, which maximizes its generalizability. Although protocols for performance of HSG and SIS were not strictly standardized across sites, each site was an academic medical center and all case report forms were filled out in a standardized manner. Potential weaknesses include the fact that as a secondary analysis, we were not directly evaluating the tubal patency testing modalities and study participants were not randomized to HSG or SIS. Specifically, in this study, women who underwent HSG were older and had lower BMI than those who had SIS, which may have introduced selection bias. Also, conclusions made from this study can only be applied to women with PCOS since that was the study population. Additionally, women with risk factors for fallopian tube pathology may have preferentially undergone HSG and/or laparoscopy adding risk of selection bias. Another potential weakness of our study is that we did not collect data on adverse events related to tubal patency testing, nor did we collect patient satisfaction data. Further studies may examine whether

women identified as being at high risk for tubal factor infertility, such as those with a history of pelvic inflammatory disease or positive chlamydia antibodies, might be better served by HSG or SIS. Additionally, women in our study who underwent HSG ultimately had a higher rate of ectopic pregnancy. This may reflect a bias in that women with increased risk of tubal pathology (and therefore ectopic pregnancy) may have had a selection bias to undergo HSG versus SIS. It is not possible with the data available to assess if this was the case.

In conclusion, in this large cohort of women with PCOS, clinical pregnancy rates did not differ significantly among women who had tubal patency confirmed by SIS versus HSG. Our findings suggest that for infertile women with PCOS, SIS is an acceptable method for determining tubal patency. With the advent of new contrast media, three-dimensional (3D) ultrasound and improved resolution, SIS techniques continue to improve [7, 8, 33]. Wider implications from this study include that SIS can be used for first-line evaluation for women with infertility.

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