

HYSTEOSALPINGOGRAPHY IN INFERTILITY: A USEFUL OR OBSOLETE DIAGNOSTIC TOOL?

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ABSTRACT

INTRODUCTION: In the evaluation of infertile women, one of the first steps is the evaluation of tubal patency.

OBJECTIVES: to assess whether hysterosalpingography remains a useful diagnostic tool in the evaluation of tubal obstruction.

METHODS: literature review at PUBMED, in addition to the articles retrieved through a search in databases, textbooks and reference articles of the reviewed articles.

RESULTS: The performance of hysterosalpingography is affected by factors such as the underlying pathology and the training and experience of the practitioner performing and interpreting the images. Hysterosalpingography is most useful for predicting tubal occlusion.

CONCLUSION: despite the imminence of other methods for the evaluation of tubal patency in infertile patients, hysterosalpingography remains a useful diagnostic tool with excellent accuracy for the diagnosis of tubal obstruction.

KEYWORDS: HYSTEOSALPINGOGRAPHY, INFERTILITY, TUBAL OBSTRUCTION, ULTRASONOGRAPHY, MAGNETIC RESONANCE IMAGING, HYSTEOSALPINGOGRAPHY

INTRODUCTION

It is estimated that between 40 and 80 million couples suffer from infertility in the world, and the prevalence may vary depending on the definition used and the location evaluated, ranging from 0.6 to 32.6% of the population^{1,2}, as shown in figure 1.

The World Health Organization (WHO) estimates that 10 to 15% of the population is diagnosed with infertility.



Figure 1. Prevalence of primary infertility in 2010 among women aged 20 to 44 years².

With the insertion of women in the labor market and the search of couples for financial stability, it is known that the

beginning of the constitution of offspring is postponed. Thus, with the advancement of technology in assisted reproduction, the demand for specialized services and treatments increases.

Women's fertility declines gradually with age, but significantly after age 37. Given declining fertility and increased risk of pregnancy loss, women over age 35 should receive an evaluation after six months of unsuccessful attempts to conceive or sooner if clinically indicated.³

The causes of infertility can be divided into three groups: female anatomical factors, female hormonal factors and male factors (figure 2)⁴.

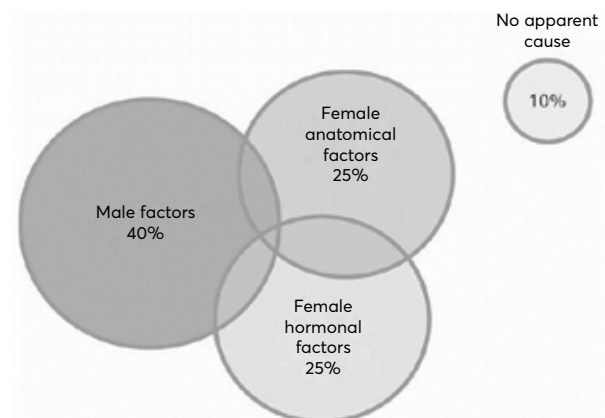


Figura 2: causas de infertilidade e sua distribuição



In the investigation of the infertile couple after a complete clinical history, ruling out male factors and anovulatory factors, one of the next steps is the assessment of tubal patency.

Tubal alterations can be identified in 20 to 36% of women investigated for infertility, which has implications for clinical management and, therefore, the evaluation of the fallopian tubes is indispensable.³

The gold standard for this evaluation remains laparoscopy with chromotubation and direct visualization. However, it requires general anesthesia, is a more invasive procedure and has a greater potential for complications.

Hysterosalpingography (HSG) is widely used in the study of human infertility, where it represents 85% of its indications. It is also indicated in the diagnosis and treatment control of many other gynecological conditions, such as: fibroids, with HSG performance before and after myomectomies; intrauterine synechiae, to control results; reparative surgeries on the tubes, among others. However, it is a painful procedure, exposes the patient to ionizing radiation and has the potential to cause allergic reactions.

With the advent of other post-ultrasonography (US) diagnostic methods, three-dimensional US, computed tomography, and also magnetic resonance imaging, it has become extremely important to critically analyze the role of HSG today, confronting it and situating it in relation to the above methods.

Can HSG, therefore, still be considered the best method for visualizing and evaluating the fallopian tubes?

METHODS

A literature review was carried out at PUBMED, in addition to the articles retrieved through a search in databases, textbooks and reference articles of the reviewed articles shown in table 1.

Year	Author	Study	Patients	Results	Conclusions
2021	Mattos LA ⁵	meta-analysis of seven articles and report of 10 cases comparing HSG MRI with HSG	247 patients + 10 patients	73 to 100% similarity between studies	HSG MRI seems promising, with results similar to HSG (73 to 100% similarity between studies), and the possibility of analyzing pelvic anatomy
2021	Melcer Y ⁴	Systematic review and meta-analysis evaluating the accuracy of HyCoSy comparing four studies with HSG and two studies with chromotubation.	622 fallopian tubes	Sensitivity 99% and specificity 91% (95%CI)	HyCoSy high accuracy rate similar to standard tests

2021	Li YZ ⁷	Meta-analysis of the evaluation of the diagnostic performance of HSG MRI compared with HSG for evaluation of tubal occlusion	101 patients 198 fallopian tubes	91% sensitivity (95% CI), 100% specificity (95% CI)	HSG MRI for serving to assess tubal occlusion
2022	Alcazar JL ⁴	Meta-analysis diagnostic accuracy 2D and 3D HyCoSy US with laparoscopy with chromotubation infertility tubal evaluation	2081 women 4031 fallopian tubes	2D HyCoSy S 86% and E 94% 3D HyCoSy S 95% and E 89%	non-significant difference concludes 2D has similar diagnostic performance to 3D
2017	Armstrong SC ⁸	Review to seek basis for diagnosis and prognosis in investigation for infertility.			TVUS should be offered to all women with symptoms / Hysteroscopy should be suggested when intrauterine pathology is suspected.
2016	Wang Y ⁹	Systematic review and 3D or 4D HyCoSy meta-analysis	1153 women 2259 fallopian tubes	92% sensitivity 91% specificity	3D/4D HyCoSy is an accurate test to diagnose tubal patency in infertile women
2016	Alcazar JL ⁴	meta-analysis to assess diagnostic accuracy of 3dHyCoSy when compared with laparoscopy and HSG	489 women 970 fallopian tubes	98% sensitivity 90% specificity	3D HyCoSy is an accurate test to diagnose tubal patency in infertile women
2015	Yu J ¹⁰	meta-analysis to assess 3D HyCoSy diagnostic efficacy	1037 fallopian tubes	92% sensitivity 95% specificity	3-D HyCoSy had good diagnostic performance in detecting tubal occlusion.

2015	Briceag I ¹¹	literature review 67 articles on the management of tubal infertility, four using medical history data, 21 HSG diagnosis, 14 different US articles, eight exploratory laparoscopies and 20 different treatment modalities articles.		Implementing tubal surgery prior to any IVF cycle will reduce the costs associated with achieving a viable pregnancy in cases of tubal factor sterility by up to 30%
2012	Broeze KA ¹²	meta-analysis to compare tubal patency assessment methods: anti-chlamydia antibodies, HSG and laparoscopy.	4883 women	area under the ROC curve 0.63 for CAT with addition of HSG 0.74 Combining patient characteristics with CAT and HSG results provides the best diagnostic performance for bilateral tubal pathology.
2011	Broeze KA ¹³	meta-analysis to assess the impact of individual characteristics of the infertile patient on the diagnostic performance of HSG. Using laparoscopy as a reference.	seven studies with 4521 women	In women without risk factors, 538% compared with 561% in women with risk factors (P = 0.005). For sensitivity was lower in patients without risk factors / sensitivity of HSG decreases with age
				bilateral tubal pathology, these rates were 13% versus 47% (P = 0.01). For bilateral tubal pathology, HSG sensitivity decreased with age [factor 0.93 per year (P = 0.05)].
1997	Mol BW ¹	meta-analysis evaluating the diagnostic ability of CAT to predict tubal pathology	2729 patients	area below the CAT ROC (elisa or immunofluorescence) similar to HSG diagnostic efficacy of HSG-like CAT
1997	Maas JW ¹⁴	meta-analysis probability of pregnancy after normal versus abnormal HSG findings	3277 patients	15% of women with abnormal HSG and 32% of women with normal HSG became pregnant HSG has a low prognostic value, the outcome of HSG does little to predict the occurrence of pregnancy. However, when HSG shows bilateral obstruction, the chance of becoming

					pregnant is minimal.
1995	Swart P ¹⁵	meta-analysis of HSG in the diagnosis of tubal patency and peritubal adhesions using laparoscopy with chromotubation as the gold standard	20 studies with 4179 patients	Sensitivity 65% Specificity 83% (with great heterogeneity between studies) for tubal obstruction	useful for tubal obstruction / unreliable for peritubal adhesions
2014	Maheux-Lacroix ¹⁶	systematic review and meta-analysis	1551 women 2740 fallopian tubes	sono-HSG with doppler 95% Sensitivity 93% HSG 94% Specificity 92% Doppler use increases S and E. They found no benefit of contrast medium over saline with respect to the diagnostic accuracy of sono-HSG.	sono-HSG should replace HSG in the initial evaluation of subfertile couples.

HSG MRI – magnetic resonance hysterosalpingography, HSG- hysterosalpingography, Sono-HSG- HyCoSy – Hysterosonosalingography with contrast, CAT – anti-chlamydia antibody, S- sensitivity, E - specificity

There is a great heterogeneity of studies and samples of meta-analyses.

DISCUSSION HYSTEROSALPINGOGRAPHY

The HSG is a diagnostic radiographic tool used to assess the endocervical canal, the endometrial cavity, luminal involvement, and the patency of the fallopian tubes by injecting radiopaque contrast through the cervical canal. HSG is mainly used in the evaluation of female infertility¹⁷.

HSG can diagnose, with some accuracy, proximal or distal obstruction, salpingitis isthmica nodosa; and may suggest the presence of fimbrial phimosis or peritubal adhesions. Findings that suggest proximal obstruction deserve a second evaluation to rule out the possibility of artifacts resulting from myometrial/tubal contraction or catheter malposition.

However, this method has some disadvantages, such as radiation exposure, use of iodinated contrast, low contrast resolution and limited evaluation of other pelvic structures, in addition to localized changes beyond the tubal and uterine lumen that may be associated with infertility.

The first description of HSG was started by Rubin in 1919,

with intracervical oxygen insufflation and x-ray to evaluate the presence of pneumoperitoneum⁴. In patients with patent fallopian tubes, the gas would establish a pneumoperitoneum identical to that produced when injected by puncture. direct abdominal. In patients with tubal obstruction it was not possible to obtain such a result.

With the advent of iodinated contrasts the technique was improved.

Hysterosalpingography technique

The HSG consists of the injection of an opaque contrast to the X-rays, through a special cannula placed in the uterine cervix. The injection will outline the cervical-body cavities, the tubal cavities until the diffusion of contrast in the pelvic cavity, when the tubes are permeable¹⁷ (figure 3). The progression of the contrast must be monitored by the fluoroscope and the images are gradually selected on the serigraph.

A hysterosalpingogram is said to be normal when the cervico-body cavities regularly fill with contrast, exhibiting normal anatomical patterns, followed by filling of the fallopian tubes and diffusion of the contrast into the peritoneal cavity.



Figure 3: HSG with normal uterine morphology.

To perform it, you need: a good X-ray machine with a serigraph, cervical cannulas and contrast. HSG requires the presence of a radiologist familiar with this type of exam or a specialized technician duly trained for it, while the manipulation of instruments, such as placement of the cannula and progressive injection of contrast, should preferably be performed by a gynecologist who would order the exact moment of capturing the images.

Currently, water-soluble contrast agents are used, which are reabsorbed and eliminated by the kidneys in a short time.

It takes an average of 10 minutes, involves approximately 90 seconds of fluoroscopic time and has an average radiation exposure to the ovaries of 1-2rads.

It is performed between day 5 and 10 of the menstrual cycle, after menstrual flow has ceased to reduce infection and

the risk of removing an egg from the fallopian tubes. The iodinated contrast medium is instilled through a catheter (figure 4-7) placed in the uterus, 10 to 30 ml is the usual dose.



figure 4-7: Different types of cannulas used to perform HSG

Pain represents the most frequent complaint of patients. Usually, anti-inflammatory medication is administered one hour before the procedure, with good tolerability.

Contraindications for performing the procedure include suspected pregnancy, presence of active pelvic inflammatory disease and history of allergy to iodinated contrast.¹⁷

HSG has been referred to by some gynecologists as a therapeutic process, since there are cases of pregnancies that follow this examination¹¹. HSG in infertile women does not improve clinical pregnancy rates when compared to expectant management in heterosexual couples and should not be offered as a therapeutic procedure⁴.

Oil-soluble contrast media have a therapeutic effect compared to water-soluble media and this effect is greater for patients who have been diagnosed with unexplained infertility. New techniques for assessing tubal permeability support the hypothesis that tubal "plugs" may be involved in proximal tubal blockage.¹⁸ However, fat-soluble contrasts have been largely replaced by water-soluble ones, as they cause less pain and less possibility of allergic reactions.

HSG and Laparoscopy

Direct visualization by laparoscopy, with a chromotubation test, remains the gold standard in the diagnosis of tubal factor infertility². It requires general anesthesia for its performance and, as it is an invasive test, it has the potential for complications. It allows confirmation of tube patency, visualization and diagnosis of tubal abnormalities¹⁶ (figure 8). This exam allows, during the same surgical time, the correction of some abnormalities, release of adhesions, correction of fimbrial phimosis and the treatment of foci of endometriosis.

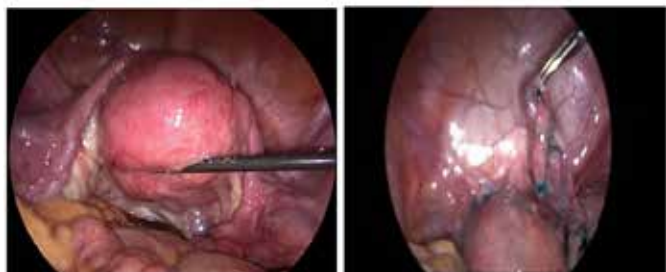


Figure 8: Tubes of usual appearance visualized by laparoscopy with chromotubation.

Data suggest that active implementation of tubal surgery prior to any IVF cycle will reduce the costs associated with achieving a viable pregnancy in cases of tubal factor sterility by up to 30%¹¹.

HSG and Anti-Chlamydia antibodies

The detection of anti-chlamydia antibodies (CAT) is associated with the presence of tubal pathology. Moore et al¹⁹ in 1982 compared HSG, ACC and laparoscopy findings of 182 patients, showing that the presence of CAT correctly classified 72% of infertile patients, HSG 76% and a combination of both 85%. No patient with normal tubes was positive for chlamydia antibodies. The use of anti-chlamydia antibodies is as accurate as HSG for predicting tubal pathology.

Another meta-analysis showed that the addition of CAT to HSG increases the predictive performance of 74% for any tubal pathology and 76% for unilateral pathology. The combination of individual patient factors, with the use of CAT and HSG results in a better diagnostic performance¹².

HSG and MRI

MRI allows excellent characterization of a wide variety of pelvic diseases, including those related to infertility, such as Mullerian anomalies, adenomyosis, leiomyomas, pelvic inflammatory disease, and endometriosis. However, MRI is not able to assess whether the fallopian tubes are obstructed or not, nor to detail their appearance. It can only determine if there is tubal dilatation.

HSG by MRI was suggested for visualization of the fallopian tubes, with the advantage of visualizing the pelvic anatomy and not using ionizing radiation (figure 9).

HSG by MRI seems to be promising, with similar results to HSG (73 to 100% similarity between studies) in a meta-analysis with 257 patients, with a similar test time and good tolerability.⁵

Another meta-analysis showed a sensitivity of 91% (95% CI) and specificity of 100% (95% CI), when evaluating 198 uterine tubes, also proving to be a useful test for evaluating tubal obstruction.

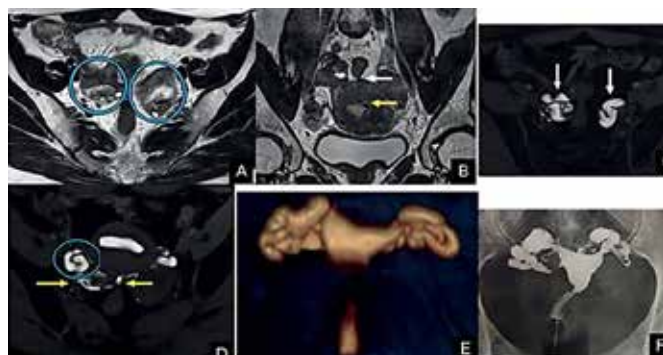


Figure 9: MRI reconstruction of HSG (1) and HSG (2) showing bilateral hydrosalpinx⁵

Ultrasound

Transvaginal US should be the initial investigation for uterine abnormalities. In addition to easy access, it can identify fibroids, suggest malformations, ovarian and endometrial pathologies.

Transvaginal US should be offered to all infertile women with symptoms or signs of anatomic pelvic pathology. It should not be routinely suggested for patients without symptoms of pelvic pathology.⁴

Hysterosonosalpingography

Hysterosonosalpingography (Sono-HSG) and more recently Sono-HSG with contrast (HyCoSy) in terms of accuracy and effectiveness have had promising results (figure 10). By not using iodinated contrast, it has the benefit of not being exposed to radiation and less chance of allergic reaction.

Melcer et al⁶ in a 2021 meta-analysis involving 622 fallopian tubes, estimated a sensitivity of 99% and specificity of 91%, with an extremely low negative predictive value (0.6%), demonstrating a high accuracy of the method, similar to the methods (HSG and laparoscopy with chromotubation). Sonohysterography contrast media are not yet widely available and used.



Figure 10: representation of contrast injection in Sono-HSG

Alcázar⁴ compared Sono-HSG with contrast (HyCoSy) 2D or with 3D/4D and, despite the heterogeneity of studies and samples, demonstrated that both have similar diagnostic performance. Figure 11 represents a 3D Sono-HSG using contrast. No benefit of saline contrast medium in relation to the diagnostic accuracy of Sono-HSG has yet been found.

Among the benefits of Sono-HSG, the fact that it is not exposed to radiation, anesthesia, does not involve the use of iodinated contrast media, in addition to the possibility of evaluating the pelvic anatomy (ovaries and uterus), Sono-HSG has been suggested as a test fundamental to female infertility.⁴

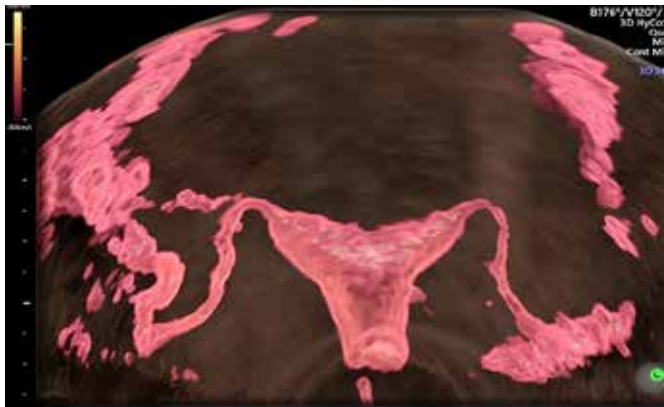


Figure 11: HyCoSy 3D using contrast (Courtesy of Dr Felipe Bassols)

Hysteroscopy

HSG is still a useful screening test for evaluating the uterine cavity. If an HSG demonstrates intrauterine abnormalities, hysteroscopy should be considered to establish a definitive diagnosis and treatment. Both procedures must be complementary to each other. Hysteroscopy is the gold standard for intrauterine pathology⁴.

In a prospective study of 336 women undergoing HSG and diagnostic hysteroscopy, the ability of HSG to detect intrauterine pathology reports a low specificity (35%) despite good sensitivity (98%).⁴

Common misdiagnoses of HSG were identifying cervical stenosis as severe intrauterine adhesions, endometrial polyps as submucosal fibroids, and submucosal fibroids as endometrial polyps.

Because it has a negative predictive value of 92%, HSG is a useful screening test for evaluating the uterine cavity. If an HSG demonstrates intrauterine abnormalities, hysteroscopy should be considered to establish a definitive diagnosis and treatment. Both procedures must be complementary to each other.

CONCLUSION

The performance of the HSG is affected by factors such as the underlying pathology, the training and experience of the professional performing and interpreting the images. HSG is most useful for predicting tubal occlusion.

In a meta-analysis with 4179 infertile patients when compared to laparoscopy, HSG has a sensitivity of 65% and specificity of 83% for the identification of tubal factor, with values that vary widely according to authors⁴. HSG appears to be of little use for identifying peritubal adhesions.

In another meta-analysis with 1551 patients and 2740 fallopian tubes comparing HSG or sono-HSG with laparoscopy as a standard, the sensitivity and specificity estimates for HSG in identifying tubal occlusion were 0.94 (95% CI 0.47-0.99) and 0.92 (95% CI 0.87-0.95), respectively.¹⁹

However, the authors themselves suggest variable methodological quality between studies, in addition to not distinguishing between proximal and distal obstruction²⁰.

Individual patient characteristics interfere with the diagnostic capacity of HSG. In women with no risk factors for tubal pathology (no history of PID, endometriosis, etc.) sensitivity was lower, possibly due to false-positive results at laparoscopy.²¹ HSG is a useful screening test for tubal patency for all infertile couples.

When assessing the prognostic value of hysterosalpingography (HSG) and the likelihood of pregnancy after normal versus abnormal HSG findings, among women with abnormal HSG 15% and 32% of women with normal HSG became pregnant. The OR was 3 (95% CI: 2.3-3.4). Sensitivity of 63% and a specificity of 62%. OR were 2 (95% CI: 1.5-2.6) for unilateral obstruction and 19 (95% CI: 7.5-46.5) for bilateral. Thus, in general, HSG has a low prognostic value, the outcome of HSG does little to predict the occurrence of pregnancy²²⁻²⁴. However, when HSG shows bilateral obstruction, the chance of becoming pregnant is minimal.

FINAL CONSIDERATIONS

It is estimated that 10 to 15% of women suffer from infertility and undergo various imaging methods during the diagnostic investigation. Despite technological development with improvement of diagnostic techniques, HSG remains an integral part of gynecological investigation and its value has not been underestimated, especially for the assessment of tubal permeability²⁰. In the vast majority of studies analyzed, it is considered a standard exam due to its high diagnostic accuracy, which is already well established, defining diagnoses and leading to the institution of a well-defined therapy.

It should still be part of the gynecologist's arsenal, together with transvaginal US, as a screening test to investigate female anatomical factor infertility. HSG remains a useful diagnostic tool for the practitioner who will initiate the investigation of infertility when considering the possibility of tubal factor in a patient.

If tubal infertility is suspected, in women with no known comorbidities, HSG should be offered as an initial screening test, which may be replaced by sono-HSG with contrast or MRI-HSG, if available.

In infertile patients with a history of PID, history of ectopic pregnancy, presence of CAT, laparoscopy with chromotubation may be suggested initially for diagnostic and therapeutic management.

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