

# Hysterosalpingo-foam sonography (HyFoSy) in the evaluation of tubal patency

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## ABSTRACT

Women's infertility represents a public health issue as the birth rate in many countries is more and more diminished. At present, there are many investigation procedures for tubal patency with high accuracy that dictate the further management of infertility cases: hysterosalpingography, hysterosalpingo-contrast sonography, chromopertubation testing during laparoscopy (dye test), magnetic resonance-hysterosalpingography. The traditional gold standard in fertility investigation is represented by laparoscopy with chromopertubation testing, which carries the risk of surgical and anesthesia complications, being a procedure performed as inpatient and the costs are elevated. As ultrasonographic techniques advanced, there has been developed hysterosalpingo-foam sonography, a minimally invasive diagnostic procedure, with imperceptible risks or complications, which simultaneously imports valuable information about the uterine cavity and the tubal patency to the sonographer. Our aim in this paper is to present the statistical results existing in the literature concerning the accuracy of hysterosalpingo-foam sonography (HyFoSy) in relation to the other examination methods, as well as its advantages.

**Keywords:** infertility, tubal patency, HyFoSy, hysterosalpingo-contrast sonography

## INTRODUCTION

For many years hysterosalpingography has been used as a fundamental evaluation procedure in women's fertility investigation. Hysterosalpingography (HSG) represents a fluoroscopic procedure with the role to evaluate the uterine cavity, fallopian tubes patency as well as adjacent peritoneal cavity after injecting contrast substance transcervically (1,2). Besides its use in infertility evaluation (intra-cavitary lesions, uterine synechiae, septum or fallopian tube obstruction), hysterosalpingography can also identify congenital uterine abnormalities and it is also useful in certain treatment plan establishments before therapeutic hysteroscopy (2,3).

The main contraindications for this procedure consist in pregnancy, active pelvic infection, vaginal bleeding and iodinated contrast allergy (3).

Results were extremely reliable. A meta-analysis published by Maheux-Lacroix et al. (4) in 2014 affirms that the pooled estimates for HSG sensitivity in diagnosing tubal occlusion were 0.94 (95% CI 0.47-0.99) and for the specificity were 0.92 (CI 0.87-0.95). Regarding uterine pathology, a sensitivity of 98% and a specificity of 35% of HSG have been reported in a study including 336 women (5).

Since 2000, an article by Kiyokawa et al. (6) has proposed the use of saline infusion 3D hysterosalpingo-contrast sonography (3D-HyCoSy) as a routine procedure in the fertility protocol used in the initial evaluation of women's fertility without the need of hospitalization. The results concerning the uterine cavity assessment were superior compared to X-ray hysterosalpingography (XHSG) and the ones regarding the tubal patency were acceptable.

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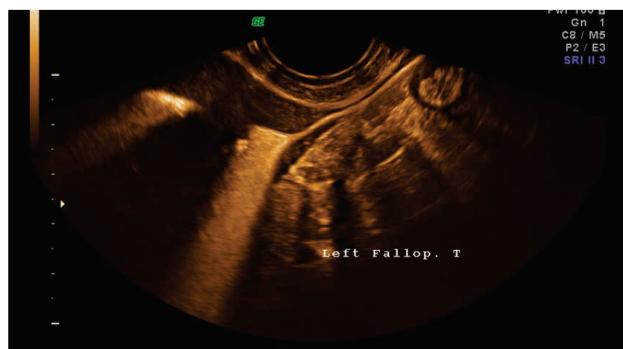
An argument in favor of 3D-HyCoSy was the better tolerance as well as the diminished examination time. In addition, this technique was less invasive, feasible, adequate for infertility evaluation and its cost was reduced.

A year later, a prospective randomized multi-center study published by Boudghène et al. (7) compares the efficacy of identifying tubal patency of saline infusion HyCoSy and air-filled albumin microspheres (Infoson) HyCoSy. The results of Infoson HyCoSy, a positive ultrasound contrast agent, in tubal permeability determination were superior to saline infusion HyCoSy and similar to those after the same population was explored using iodinated contrast agent during hysterosalpingography. The advantage of HyCoSy was the absent exposure to iodinated contrast agent and to ionizing radiation during an invasive procedure as conventional hysterosalpingography. Starting with 2007, a non-toxic gel has been introduced in tubal patency evaluation as contrast medium in HyCoSy (8).

The purpose of our study is to sustain the use of hysterosalpingo-foam sonography (HyFoSy) in the evaluation of infertile women as a routine procedure in the infertility protocol. We have an almost 700 cases experience and in the last 8 years HyFoSy is the only method that we have used for infertility investigation (Figures 1-4).



**FIGURE 1.** Transversal HyFoSy 2D sepia color image of the uterus and both fallopian tubes emergences



**FIGURE 2.** HyFoSy image of the left fallopian tube using sepia color mode



**FIGURE 3.** HyFoSy image of a left sinusoidal pattern fallopian tube using sepia color mode



**FIGURE 4.** HyFoSy image in Sepia mode of the left ovary with paraovarian effusion of the contrast substance

**MATERIAL AND METHODS**

In the present paper we performed a literature search, using PubMed and Uptodate data bases and we used the terms ‘hysterosalpingo-contrast sonography’ and ‘foam’, respectively ‘chormopertubation’, ‘hysterosalpingography’ to identify articles comparing the different methods for tubal patency testing. The search included articles dating from 2010 until November 2021. The abstracts have been screened to select the most relevant articles. We included retrospective studies, prospective studies and meta-analyses.

**RESULTS**

The initial search returned 37 articles and we selected the most relevant studies comparing different methods of tubal patency diagnosis. We selected studies comparing saline infusion HyCoSy with HyFoSy respectively SonoVue-HyCoSy, HyFoSy with diagnostic laparoscopy with chromopertubation testing and HyFoSy with magnetic resonance - hysterosalpingography.

**Contrast agents HyCoSy vs saline infusion HyCoSy**

A retrospective study on 42 infertile patients in a university hospital published by Lanzani et al. (9) in

2008 compared the detecting ratio of tubal permeability regarding the use of SonoVue HyCoSy as well as saline infusion or hydro HyCoSy. They used hysterosalpingography and chromolaparoscopy as references tests. The authors concluded that SonoVue-HyCoSy has been more accurate concerning the evaluation of tubal patency.

Other studies present results in favor of hysterosalpingo- foam sonography (10,11). The results are summarized in Table 1.

In addition, the authors emphasize the advantage of contrast agents used HyCoSy, more specifically the advantage of second-generation contrast medium that do not necessitate a prolonged method learning period, as the positive contrast medium presents a longer persistence in the uterine cavity and fallopian tubes, easing the sonographer's examination and presenting a higher diagnosis accuracy, fact sustained by a prospective study in 2005 by Tamási et al. (12) in which the importance of the sonographer is highlighted as the authors reveal that their experience and diagnostic precision had an increase in time.

#### HyFoSy vs diagnostic laparoscopy with chromopertubation testing

Certain studies (8,13) have demonstrated the fact that HyFoSy has been a real use in the tubal permeability evaluation. Compared to diagnostic laparoscopy with chromopertubation testing, HyFoSy presents the advantage of an outpatient procedure with high standard accuracy, with minimal discomfort and easy feasibility. Thus, using HyFoSy the patients do not present surgical complications, are not exposed to the anesthesia risk, do not depend of a waiting list for the procedure and the costs are significantly reduced.

HyFoSy vs magnetic resonance-hysterosalpingography

A recently published meta-analysis by Chen et al. (14) including 24 articles, respectively 1340 patients, has concluded that, concerning the tubal patency diagnosis degree of accuracy, HyFoSy and magnetic resonance-hysterosalpingography presented similar results (Table 2). The results regarding the 3D and 4D gel-HyCoSy specificity was statistically significant ( $p = 0.005$ ).

#### DISCUSSION

In the last years, HyFoSy has gained popularity in the women's infertility evaluation due to the fact that tubal obstruction is one of the most frequent pathologies in women of childbearing age, preventing them from completing their family (15). HyFoSy is a minimally invasive evaluation method that presents the main advantages of avoiding hospitalization as well as surgery and anesthesia risks as there are in cases of laparoscopic chromopertubation testing or irradiation and possible allergic reactions due to iodinated contrast substances as in cases of hysterosalpingography; in addition, compared to magnetic resonance-hysterosalpingography the costs are diminished and HyFoSy is more accessible to patients.

Furthermore, there is evidence that some women with infertility have spontaneously conceived within the first year after undergoing a 4D-HyCoSy examination. A retrospective study Liu et al. (16) relate that in their database 40.9% of the infertile women who were performed a 4D-HyCoSy conceived spontaneously in the first 12 months after the procedure. Also, their results have shown 21.5% spontaneous conception in the first 3 months.

Regarding possible complications, the primary complication is represented by pain. A study conducted in 2014 (17) compared pain scores during HyFoSy and hysterosalpingography, the results de-

TABLE 1. Hydro-HyCoSy vs other contrast agents HyCoSy study results

Article	Used procedure	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Lanzani et al. (2008)	Hydro-HyCoSy	91	71	55	95
	SonoVue-HyCoSy	87	84	69	85
Ludwin et al. (2017)	Hydro-HyCoSy	86.8	93	30	99.5
	HyFoSy	96.88	94	71	99.6
Piccioni et al. (2017)	Hydro-HyCoSy	50	66.6	Not specified	Not specified
	HyFoSy	87.5	100	Not specified	Not specified

TABLE 2. HyFoSy vs magnetic resonance-hysterosalpingography study results

Used procedure	Pooled sensitivity (%)	Pooled specificity (%)
HyFoSy 3D, respectively 4D	95, respectively 100 (95% CI, 87%-91%)	94, respectively 82 (95% CI, 91%-94%)
Magnetic resonance-hysterosalpingography	100 (95 % CI, 98-100%)	82 (95 % CI, 74-89%)

scribing a lower pain score during HyFoSy. An observational study conducted in 5 Spanish centers including 915 patients who underwent HyFoSy for infertility published in 2021 (18) relates 8 cases in which the procedure could not be performed due to impossibility of introducing the intracervical catheter; concerning pain score they used visual analogue score (VAS) ranging from 0 to 10, 0 describing the absence of pain or discomfort and 10 describing severe pain. The median VAS score in this group of patients was 2. In this study, 62.2% of patients described mild pain during the procedure, 35.8% related moderate pain and only 2% experienced severe pain. The same study relates 3 cases of side effects: 2 vagal episodes during the procedure and one mild urinary infection. Another pain-related study published in 2015 (19) reveals the fact that

median pain VAS score was 3.6 (95% CI, 3.0-4.0) during HyFoSy while for transvaginal ultrasound it was 1.5 (95% CI, 1.2-1.7).

## CONCLUSIONS

In conclusion, hysterosalpingo-foam sonography represents an easy, feasible, well-tolerated, cost reduced procedure that presents results comparable with other current diagnosis methods for tubal patency, does not expose the patient to unnecessary risks (surgical, anesthesia, contrast substances, ionizing radiation) and could slowly replace the actual gold standard for tubal permeability evaluation respectively laparoscopy with chromopertubation testing.

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