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The role of Hysterosalpingo-foam sonography in the evaluation of female infertility

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Abstract

Introduction: Assessment of fallopian tube patency represents a fundamental component of the infertility work-up, as tubal factor infertility remains a common cause of female subfertility. Conventional diagnostic methods, such as hysterosalpingography and laparoscopy, are associated with limitations including procedural pain, radiation exposure, invasiveness, and increased costs. Hysterosalpingo-foam sonography has emerged as an ultrasound-based technique for tubal patency assessment, aiming to provide a reliable, well-tolerated, and minimally invasive alternative.

Materials and Methods: A narrative review of the literature was conducted using the PubMed, Scopus, Web of Science, and Google Scholar databases. Studies published between January 2014 and September 2025 were considered, along with one seminal study from 2012 included for its historical relevance. Eligible studies evaluated hysterosalpingo-foam sonography in infertile women, compared it with established diagnostic techniques and reported data on diagnostic accuracy, patient tolerance, safety, or reproductive outcomes. A total of eleven studies met the inclusion criteria and were qualitatively analyzed.

Results: The reviewed studies demonstrated that hysterosalpingo-foam sonography exhibits good diagnostic performance for the assessment of tubal patency, with a high level of agreement with hysterosalpingography and laparoscopy. The technique was consistently associated with lower pain scores and shorter procedure times compared with hysterosalpingography, while avoiding ionizing radiation and iodinated contrast agents. Furthermore, evidence indicates that clinical management based on hysterosalpingo-foam sonography findings results in reproductive outcomes comparable to those achieved following hysterosalpingography-based strategies. Several studies also reported spontaneous pregnancies following the procedure, suggesting a potential tubal flushing effect.

Conclusions: Hysterosalpingo-foam sonography appears to be a reliable, safe, and well-tolerated method for the evaluation of tubal patency in women with infertility. Its diagnostic accuracy, favorable patient experience, and comparable reproductive outcomes support its use as a first-line investigation

in appropriately selected patients. Further research is warranted to refine patient selection criteria and to clarify the potential therapeutic implications of the procedure.

Keywords: HyFoSy, tubal patency, female infertility, hysterosalpingography, ultrasound, reproductive outcomes

Introduction

Female infertility constitutes a common clinical challenge, with tubal factor infertility representing a major contributing cause in a substantial proportion of affected women. Consequently, assessment of fallopian tube patency remains a fundamental component of the initial infertility work-up, guiding subsequent diagnostic and therapeutic decisions. An ideal tubal patency test should be accurate, safe, well tolerated, easily accessible, and cost-effective, while allowing integration into routine outpatient fertility assessment.

Traditionally, laparoscopy with chromopertubation has been regarded as the reference standard for the evaluation of tubal patency. Despite its high diagnostic value and its ability to detect concomitant pelvic pathology, its invasive nature, requirement for general anesthesia, and associated costs limit its routine use as a first-line investigation in infertile women. As a result, hysterosalpingography (HSG) has been widely adopted as the most commonly used initial test for tubal patency assessment. However, HSG exposes patients to ionizing radiation and iodinated contrast media and is frequently associated with procedural discomfort or pain, which may negatively affect patient acceptance [1].

In an effort to overcome these limitations, ultrasound-based techniques have been increasingly incorporated into infertility diagnostics. Hysterosalpingo-contrast sonography (HyCoSy) has emerged as a non-radiating alternative, allowing simultaneous evaluation of the uterine cavity and

tubal patency. Although this technique offers several advantages, its diagnostic accuracy has been reported to vary depending on the contrast medium used and operator experience, and false-positive results related to tubal spasm remain a concern [2]. These limitations have driven the development of improved ultrasound contrast agents and refined imaging techniques.

Hysterosalpingo-foam sonography (HyFoSy) represents a more recent evolution of ultrasound-based tubal patency testing. The technique utilizes a foam contrast agent, most commonly generated from a hydroxyethylcellulose- and glycerol-based gel, which provides enhanced echogenicity and prolonged visualization within the fallopian tubes. This enables real-time assessment of tubal patency using standard transvaginal ultrasonography equipment, without exposure to radiation or iodinated contrast media [3].

The first clinical application of HyFoSy demonstrated the feasibility of the method as an office-based procedure and suggested a favorable safety and tolerability profile [3]. Since then, a growing number of clinical studies have evaluated its diagnostic performance, patient acceptance, and potential role within the infertility work-up. Comparative studies have explored agreement between HyFoSy and established diagnostic modalities, including HSG and laparoscopy, while others have focused on patient-reported pain, procedural efficiency, and clinical outcomes following management decisions based on findings of HyFoSy [1,4].

Table 1. Characteristics and main findings of the studies included in this review

Study (Author, Year)	Study design	Sample size	Comparator / Reference standard	Main outcomes
Emanuel et al (2012)	Prospective observational cohort	73 women	HSG if inconclusive	Highly successful, low discordance with HSG, 19% pregnancy
Dreyer et al (2014)	Randomized controlled trial	40 women	HSG	Lower pain, shorter time
Dreyer et al (2015)	Prospective diagnostic accuracy study	26 women with Essure® device (38 tubes)	HSG	Similar ability to confirm tubal occlusion, lower pain, shorter time
Ludwin et al (2017)	Prospective observational study	132 women (259 tubes)	Laparoscopy & HyCoSy	Significantly higher PPV, fewer inconclusive results, similar NPV
Ramos et al (2021)	Prospective diagnostic accuracy study	106 women	HSG	Concordance with HSG, lower pain
Melcer et al (2021)	Systematic review & meta-analysis	6 studies (622 tubes)	Laparoscopy/HSG	Accurate test for tubal occlusion - on a par with standards tests
van Welie et al (2022)	Multicenter randomized study	1026 women	HSG	Similar live birth outcomes, lower pain
Engels et al (2023)	Multicenter prospective study	799 women	—	Spontaneous pregnancy for 1 in 4 patients within 12 months
Kamphuis et al (2024)	Economic evaluation with RCT	1160 women	HSG	Comparable outcomes, lower costs
Le et al (2024)	Prospective diagnostic accuracy study	447 women (868 tubes)	Laparoscopy	Reliable patency test, no adverse events, VAS scores of no pain
Xydias et al (2025)	Systematic review & meta-analysis	9 studies	HSG/HyCoSy	Moderate concordance with HSG, diagnostically superior to HyCoSy, better tolerability

Abbreviations: HyFoSy = hysterosalpingo-foam sonography; HSG = hysterosalpingography; HyCoSy = hysterosalpingo-contrast sonography; VAS = visual analogue scale; PPV = positive predictive value; NPV = negative predictive value.

Beyond its diagnostic role, interest has also emerged regarding the potential impact of HyFoSy on reproductive outcomes. Similar to observations following HSG, several studies have reported spontaneous pregnancies occurring after the procedure, raising the hypothesis of a possible tubal flushing effect. However, the clinical relevance and underlying mechanisms of this phenomenon remain incompletely understood and warrant careful interpreta-

tion within the broader context of infertility management [5].

Despite the increasing use of HyFoSy in clinical practice, the available evidence remains heterogeneous with respect to study design, patient selection, reference standards, and reported outcomes. Consequently, its precise role within contemporary diagnostic algorithms for female infertility has not been uniformly defined. A comprehensive synthesis of the

existing literature is therefore necessary to clarify the diagnostic value, clinical applicability, and limitations of HyFoSy.

The aim of the present review is to summarize and critically evaluate the available evidence regarding the role of HyFoSy in the evaluation of female infertility, with particular emphasis on diagnostic accuracy, comparison with established techniques, patient tolerance and safety, and reported reproductive outcomes.

Materials and Methods

A narrative review of the literature was conducted using the PubMed, Scopus, Web of Science, and Google Scholar databases. The search strategy included combinations of keywords related to hysterosalpingo-foam sonography and female infertility, such as “HyFoSy”, “hysterosalpingo-foam sonography”, “tubal patency”, “infertility investigation”, “pregnancy outcome”, and “live birth”.

The search was limited to studies published between January 2014 and September 2025 in order to capture contemporary evidence on the clinical application of HyFoSy. In addition, one seminal study published in 2012 was included due to its historical relevance as the first clinical application of the technique.

Eligible studies evaluated HyFoSy in women undergoing infertility assessment and reported data on diagnostic accuracy, comparison with established tubal patency tests, patient tolerance, safety and reproductive outcomes. Following screening and full-text evaluation, a total of eleven studies (ten published between 2014 and 2025 and one published in 2012) were included in the present review.

Results

The included studies varied in terms of study de-

sign, sample size, and reported outcomes. A summary of their main characteristics and findings is presented in Table 1.

The results are presented below according to the main outcome categories.

Diagnostic accuracy of HyFoSy for tubal patency assessment

The diagnostic performance of HyFoSy was evaluated across multiple studies using HSG, HyCoSy, or laparoscopy with chromopertubation as reference standards. Overall, HyFoSy demonstrated good agreement with established diagnostic modalities for the assessment of fallopian tube patency.

In the first pilot study by Emanuel *et al.*, a successful HyFoSy procedure was performed in 92% of the patients, while in 78% of the cases, there was no further need for confirmation by HSG [3]. In only 7% of the patients there was discordance between the two methods [3]. Similarly, in the study by Dreyer *et al.* (2015), which evaluated tubal occlusion following Essure® placement, HyFoSy described an overall accuracy of 97.4% (95% CI 92.3%–100.0%), with a sensitivity of 97.1% (95% CI 84.6%–99.5%) and specificity of 100.0% (95% CI 40.2%–100.0%) [6].

In a prospective diagnostic study, Ludwin *et al.* reported high negative predictive values for HyFoSy, comparable to those of HyCoSy (99.5%), reaching 99% for 2D/3D HyFoSy and 99.6% for Doppler-enhanced HyFoSy ($P > 0.05$) [2]. Notably, HyFoSy demonstrated significantly higher positive predictive values (48% and 71% for 2D/3D and Doppler-enhanced HyFoSy, respectively; $P < 0.05$ and $P < 0.01$) compared with HyCoSy (30.4%) [2]. Consistently, in a prospective study by Ramos *et al.*, HyFoSy findings were concordant with prior HSG results in 72.6% of cases, with only 4.7% total discordance [7]. The inter-test agreement (Cohen’s kappa = 0.57) indicated moderate concordance [7].

A systematic review and meta-analysis by Melcer

et al. reported pooled estimates of sensitivity and specificity of 0.99 (95% CI 0.89–0.99) and 0.91 (95% CI 0.53–0.98), respectively, for the detection of tubal occlusion [8]. The corresponding positive and negative likelihood ratios were 11.5 (95% CI 1.5–87.5) and 0.006 (95% CI 0.0003–0.12), confirming the high diagnostic performance of HyFoSy [8]. In a diagnostic accuracy study by Le et al., HyFoSy also demonstrated a sensitivity of 0.75 (95% CI 0.71–0.79) and specificity of 0.70 (95% CI 0.65–0.74) for the detection of tubal occlusion, compared with laparoscopy [9]. The positive and negative predictive values were 0.76 (95% CI 0.73–0.80) and 0.68 (95% CI 0.64–0.73), respectively [9].

A more recent systematic review by Xydias et al. compared HyFoSy and HyCoSy, reporting pooled sensitivity of 87% and 69%, respectively ($p = 0.074$) and pooled specificity of 95% and 85%, respectively ($p < 0.001$), favoring HyFoSy [10]. When compared with HSG, pooled Cohen's kappa was 0.38, indicating fair-to-moderate agreement [10]. In subsequent analyses using HSG as the reference standard, HyFoSy demonstrated relatively low sensitivity (61%) but high specificity (87%) [10].

Patient tolerance, pain perception, and safety

Patient-reported pain and tolerability were consistently evaluated across multiple studies. In a randomized controlled trial, Dreyer et al. (2014) stated significantly lower pain scores with HyFoSy compared with HSG, with median visual analogue scale (VAS) scores of 1.7 cm versus 3.7 cm, respectively ($p < 0.01$) [1]. The procedure was also statistically significantly shorter with a median of 5.0 minutes (interquartile range: 3.0) for HyFoSy versus 12.5 minutes (interquartile range: 16.0) for HSG [1].

Similar findings were supported by subsequent studies. Dreyer et al. (2015) confirmed significantly lower pain levels during HyFoSy procedures compared with HSG ($p < 0.01$) [6], while Ramos et al., re-

ported that 59.1% of patients experienced no pain during HyFoSy and only 6.6% reported greater pain compared with HSG (OR 6.57, 95% CI 3.11–13.89) [7]. Van Welie et al., in a randomized analysis, described mean VAS scores of 3.1 ± 2.2 for HyFoSy compared with 5.4 ± 2.5 for HSG ($p < 0.001$) [4] and Le et al. demonstrated a median VAS score of 1, with 42.8% of women experiencing no pain (VAS = 0) [9].

These findings are consistent with the systematic review by Xydias et al., which indicated significantly lower pain scores with HyFoSy compared with HSG, with a mean difference of approximately 2.4 points on a 10-point scale ($p < 0.001$) [10], further supporting the superior tolerability of HyFoSy. Across studies, procedure duration was additionally generally shorter for HyFoSy, and the examination was frequently completed without the need for analgesia [1,3,7]. No serious procedure-related adverse events were described across the included studies, supporting the safety of HyFoSy as an outpatient procedure [2,4, 6, 8–10].

Reproductive outcomes and clinical management

Reproductive outcomes following HyFoSy were reported in both randomized and observational studies. In the first pilot study by Emanuel et al., 19% of patients achieved spontaneous pregnancy within a median of 3 months following HyFoSy [3].

In a large multicentre randomized trial, van Welie et al. stated that clinical management based on HyFoSy findings resulted in live birth rates of 46%, compared with 47% for HSG-based management within 12 months of fertility work-up [4]. The difference of -1.2% (95% CI -3.4% to 1.5% ; $p = 0.27$) confirmed the non-inferiority of HyFoSy-guided strategies [4].

In a multicentre observational study, Engels et al. reported that 26.5% of women achieved spontaneous pregnancy within 12 months following HyFoSy, with a median time to pregnancy of

approximately 4 months (95% CI 3.1–4.9) [5]. These findings suggest a possible tubal flushing effect, although its clinical significance remains uncertain.

Economic considerations

Economic evaluation data demonstrated that infertility work-up strategies incorporating HyFoSy were associated with lower overall costs compared with HSG-based strategies [11]. In an economic analysis conducted alongside the FOAM randomized trial, Kamphuis *et al.* indicated that the direct cost of the diagnostic procedure was €136 for HyFoSy compared with €280 for HSG [11].

When subsequent fertility treatment costs were included, the mean total cost per couple was €3307 for the HyFoSy strategy and €3427 for the HSG strategy, corresponding to a mean cost difference of –€119 (95% CI –€125 to –€114) in favor of HyFoSy [11]. Although HyFoSy was associated with slightly lower live birth rates, the incremental cost-effectiveness ratio was estimated at €10,042 saved per additional live birth lost, suggesting that HyFoSy-based diagnostic pathways may represent a cost-efficient alternative in infertility work-up algorithms [11].

Conclusion

Hysterosalpingo-foam sonography represents a reliable and well-tolerated method for the assessment of tubal patency in women undergoing infertility evaluation. The available evidence demonstrates that HyFoSy provides diagnostic accuracy comparable to established techniques, while offering important advantages in terms of patient comfort, safety and avoidance of radiation exposure. Clinical management based on HyFoSy findings, results in reproductive outcomes comparable to those achieved following hysterosalpingography-based strategies, supporting its use as a first-line investigation in appropriately selected patients. Further prospective

studies are warranted to refine its role within infertility diagnostic algorithms and to clarify the potential therapeutic implications of the procedure.

Disclosure of conflicts of interest

The authors report no conflicts of interest.

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