

## Clinical Opinion

# Should Diagnostic Hysteroscopy be Performed Before In Vitro Fertilization-Embryo Transfer?

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**ABSTRACT** The role of routine uterine cavity evaluation before an in vitro fertilization–embryo transfer (IVF-ET) cycle has not been uniformly accepted. Published trials have demonstrated a relatively high incidence of cavity abnormalities diagnosed at outpatient hysteroscopy in patients with previous IVF-ET cycle failure, the correction of which markedly improves outcomes. The value of performing this procedure before an initial cycle in patients without previous implantation failure has not been definitively confirmed in prospective randomized trials, but would seem logical in an effort to minimize the number of cycles a patient must undergo. The incidence of cavity abnormalities in this population varies. One large series has reported a 22.9% incidence of endometrial cavity abnormalities diagnosed at pre-cycle office hysteroscopy in this patient group. Hysterosalpingography and baseline transvaginal ultrasonography are insufficiently sensitive alternatives. Sonohysterography with infusion of saline solution, in particular with 3-dimensional technology, may be a reasonable alternative to diagnostic hysteroscopy, although relatively few well-designed trials have addressed this issue. There are an insufficient number of prospective randomized trials to clearly demonstrate that surgical removal of all abnormalities improves IVF-ET outcome. However, investigators suggest a benefit for resection of submucosal leiomyomas, adhesions, and at least a subset of polyps. Appropriately designed trials are required before a definitive recommendation can be made. *Journal of Minimally Invasive Gynecology* (2012) 19, 643–646 © 2012 AAGL. All rights reserved.

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The question of whether diagnostic hysteroscopy should be routinely performed before initiating in vitro fertilization–embryo transfer (IVF-ET) cycles has not been definitively answered, although the data are fairly convincing. The topic can be broken down further to the issues of whether (1) diagnostic hysteroscopy should be used routinely before a first cycle, (2) the procedure should be performed only after a failed cycle, (3) hysteroscopy can be replaced by an alternative procedure, and (4) treatment of

all or only a subset of abnormalities has a role in improving cycle outcomes.

## What Is the Evidence?

The question of whether a uterine evaluation should be routinely performed or solely performed after an unsuccessful cycle can be answered from the perspectives of evidence, philosophy, and economics. What is the evidence? A variety of investigators have evaluated the value of this approach in patients before IVF-ET. In an early study, Shamma et al [1] reported on 34 patients with normal findings at hysterosalpingography (HSG) who underwent pre-cycle hysteroscopy, of whom 28 underwent embryo transfer. Significantly lower pregnancy rates were achieved in the patients with abnormal versus normal hysteroscopic findings (8.3% vs 37.5%;  $p = .04$ ) despite similar ages, responses to gonadotropin stimulation, and number of embryos transferred. More

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recently, Karayalcin et al [2] reported on 2500 consecutive office-based diagnostic hysteroscopic procedures performed before IVF, of which 22% revealed endometrial disease including polyps, submucosal myomas, intrauterine adhesions, and septae. It is interesting to note that all patients in that study had normal findings at either baseline ultrasound examination or HSG within 1 month of the procedure. Others are less convinced of the usefulness of this approach. Fatemi et al [3] evaluated a similar population of 678 women before a first IVF-ET cycle with normal findings at baseline transvaginal ultrasound examination, and noted an 11% incidence of endometrial cavity abnormalities at hysteroscopy, with the primary abnormal finding being small uterine polyps. Those authors questioned the usefulness of using this procedure on a routine basis.

Several groups have evaluated patients after previous IVF-ET failure. Oliveira et al [4] reported on 55 patients with a normal uterine cavity at HSG, but had failed 2 previous IVF-ET cycles, each involving transfer of at least 2 good-quality embryos. Forty-five percent had abnormal hysteroscopic findings, which were subsequently corrected. All patients underwent a third cycle. Significantly higher clinical pregnancy rates were achieved in those treated for cavity abnormalities as opposed to those with a normal uterine cavity (52% vs 20%;  $p = .02$ ). These outcomes have been reproduced by others [5,6]. In a meta-analysis of randomized trials, El-Toukhy et al [7] calculated that the likelihood of clinical pregnancy was significantly increased in patients with failed implantation who underwent hysteroscopy and resection of lesions (relative risk [RR], 1.57; 95% confidence interval [CI], 1.29–1.92;  $p < .001$ ). There were no differences in the rate of miscarriage.

With the availability of extremely small-diameter rigid and flexible hysteroscopes with an outer sheath  $<5$  mm, the overwhelming majority of procedures can be performed in an office setting, requiring minimal analgesia and occasional paracervical block [8,9]. The primary barriers in a premenopausal population are cervical stenosis and extreme obesity [8]. In a series of 145 patients undergoing outpatient hysteroscopy before IVF-ET using a rigid 4-mm hysteroscope, El-Mazny et al [6] reported that 95.4% of procedures were successful. The use of flexible hysteroscopes, in my experience, seems to be associated with substantially less discomfort. Insofar as distention medium, Raimondo et al [10] reported no differences in pain or difficulty of procedure when using either CO<sub>2</sub> or normal saline solution in a randomized trial, but believed that CO<sub>2</sub> afforded improved visualization. In contrast, others have suggested that normal saline solution is more tolerable [11]. Investigators have successfully treated minor abnormalities in the same setting, thus avoiding a second operative procedure, which is clearly both time- and cost-effective [12].

The philosophic issue is whether it is appropriate to wait until patients fail 1 or 2 IVF-ET cycles before offering a relatively innocuous office procedure that could result in enhanced outcomes if appropriate abnormalities are treated.

This approach would necessitate screening a large number of patients to select a subset with uterine disease that could be corrected and, thus, prevent a percentage of unsuccessful cycles. The cost of office hysteroscopy (or comparable procedures, as discussed in “Is Hysteroscopy the Only Option?”) must be balanced against the physical, emotional, and financial cost of additional IVF-ET cycles. Needless to say, there is a desperate need for appropriately designed large-scale randomized trials specifically assessing this larger patient population, with appropriate cost analysis.

### Is Hysteroscopy the Only Option?

Are there alternatives to hysteroscopy? As has been previously reported, the correlation between HSG and hysteroscopic findings is poor [1,4,13]. Cunha-Filho et al [14] compared results of hysteroscopy and HSG in infertile patients before intrauterine insemination or IVF-ET. The specificity of HSG was only 41.14%, with a positive predictive value of 47% and a negative predictive value of 70.6%. More recently, Taskin et al [15] have reported that HSG was associated with a sensitivity of 21.6% and false-negative rate of 78.4%, with agreement between the 2 procedures of only 68.9%.

Baseline transvaginal sonography also does not seem to be sufficiently sensitive [2,3]. Grimbizis et al [16] have reported that diagnostic hysteroscopy demonstrated significantly higher sensitivity (97.26% vs 89.04%) and specificity (92% vs 56%) than transvaginal sonography. It would therefore seem that neither HSG nor basic transvaginal sonography are adequate substitutes for hysteroscopy.

Saline infusion sonohysterography (SIS) is a well-tolerated approach to evaluation of the uterine cavity, and has been proposed as an alternative to diagnostic hysteroscopy in infertile patients. In an early prospective randomized trial of 46 women outpatients, SIS and outpatient hysteroscopy were thought to be statistically equivalent in enabling diagnosis of abnormalities when compared with findings at operative hysteroscopy (52% vs 72%; not significantly different) [17]. The mean pain score for SIS was significantly lower. More recently, Tur-Kaspa et al [18] reported on outcomes of SIS as part of the workup in 600 infertile patients, and noted that 16.2% had intracavitary abnormalities; however, they did not compare the results with those at diagnostic hysteroscopy. Two additional studies using SIS have reported that the incidence of abnormalities in infertile patients varies from 30.5% to 32.5% [19,20].

The addition of 3-dimensional (3D) ultrasound technology to SIS is an intriguing adjunct that may enhance accuracy. In a recent observational trial, 180 infertile women with a presumably normal uterine cavity on the basis of findings at HSG and transvaginal ultrasound underwent 2D SIS, 3D SIS, and outpatient hysteroscopy [21]. Both 3D SIS and outpatient hysteroscopy were believed to be similarly effective in enabling diagnosis of intrauterine lesions ( $p = .23$ ), and both were superior to 2D SIS ( $p < .001$ ). A lack of

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