

The value of 3D ultrasound in the management of patients with suspected Asherman's Syndrome

Jaime Cohen, M.D., Alan Copperman, M.D.

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Mt. Sinai School of Medicine, New York, New York.

Alan B Copperman

Reproductive Medicine Associates of New York

635 Madison Ave

10th Floor

New York, NY 10022

acopperman@rmany.com

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3D ultrasound and Asherman's Syndrome

Abstract:

Objective: To assess the value of 3D ultrasound in the management of patients with suspected Asherman's syndrome.

Study Design: A case series of 54 infertile patients who presented to a tertiary care center, between 1998-2004, with suspected Asherman's syndrome and underwent both HSG and 3D ultrasound prior to hysteroscopy. Sensitivity and the ability to attain fertility post-operatively were calculated.

Results: Intra-uterine adhesions (IUA) were demonstrated on 3D ultrasound and HSG in all cases and confirmed by hysteroscopy. However, 3D ultrasound had a sensitivity of 100%, while HSG had a sensitivity of 66.7% for correctly grading the extent of IUA. In 61.1% of cases where HSG results were inconsistent with hysteroscopy, lower uterine segment outflow obstruction was present and HSG misclassified findings as severe Asherman's with complete cavity obstruction. Post-operatively, 90% of patients conceived.

Conclusions: 3D ultrasound provides a more accurate depiction of adhesions and extent of cavity damage than HSG in patients with suspected Asherman's syndrome, particularly when differentiating severe IUA from lower uterine segment outflow obstruction. Therefore, grading systems utilizing HSG to classify severity of disease should be revised to include 3D ultrasound findings.

Introduction:

Asherman's Syndrome is defined by the presence of intrauterine adhesions either partially or completely obliterating the uterine cavity. Although a relatively uncommon diagnosis in the general population, it is often cited as the etiology of pregnancy complications in the infertile population (1). It most often develops after dilation and curettage (D&C) of a recently pregnant uterus; however it can also develop following the secondary removal of placental remnants or post partum hemorrhage, or in fact, after any intra-uterine manipulation. Clinical symptoms associated with the syndrome include menstrual abnormalities, such as hypo or amenorrhea, pelvic pain, infertility, and recurrent pregnancy loss (2). The extent of intrauterine adhesions (IUA) is graded and the severity of disease classified by; extent of cavity obliterated, location of adhesions within the cavity, and the character of the adhesions (3).

The diagnosis of IUA has been traditionally limited to hysterosalpingography (HSG), as this is a simple, safe, inexpensive, sensitive, and minimally invasive procedure that allows for visualization of the uterine cavity. Furthermore, it provides information regarding tubal patency (4,5). However since it is an indirect means for demonstrating the uterine cavity as well as the type, extent and exact location of filling defects the results are often non-specific(4). In addition, another potential drawback of HSG is its inability to characterize the uterine cavity beyond where radiopaque contrast perfuses. Specifically, in cases of lower segment outflow tract obstruction, limited information can be derived from HSG. Therefore hysteroscopy, which allows for direct visualization of the entire cavity, in addition to the ability to biopsy lesions and lyse adhesions, is considered the gold standard for the diagnosis and treatment of IUA (4, 5, 6, 7). Despite its limitations, HSG remains the initial screening tool for detecting IUA and when intrauterine abnormalities are demonstrated, therapeutic hysteroscopic resection of synechiae may be clinically indicated (8).

While investigators have studied the diagnostic accuracy of the transvaginal ultrasound (TVS), the machines utilized were, in most cases, two-dimensional (6, 7, 9, 10, 11, 12). Use of a three-dimensional sonography which allows for interactive visualization through multiplanar reformatting, can provide a more accurate assessment. Therefore, we propose that use of 3D ultrasonography in patients with Asherman's Syndrome will improve both diagnostic and prognostic capabilities when compared to the traditional HSG. The derived images produced by the 3D machine are more consistent with the location of the lesions and the percent of cavity obstructed which ultimately correlates more closely with prognosis. This study was conducted to assess the value of 3D ultrasound in the management of patients with suspected Asherman's syndrome.

Materials and Methods:

In this case series, from 1998 to 2004, fifty four women were identified during the evaluation for secondary infertility as suffering from Asherman's Syndrome. All patients were seen at an academic reproductive medicine practice by the same reproductive endocrinologist (ABC) and were routinely evaluated with a 3D ultrasound, HSG and hysteroscopy. Extent of cavity damage and severity of disease was defined by the March et al grading system (3). In this system, adhesions are judged to be severe if more than $\frac{3}{4}$ of the uterine cavity is obliterated, agglutination of the uterine walls or thick bands were

present, or the ostial areas and upper cavity were occluded. Adhesions were considered moderate if $\frac{1}{4}$ to $\frac{3}{4}$ was involved, no agglutination of the uterine walls was present, or ostial areas and the upper fundus were only partially involved. Adhesions were considered minimal if less than $\frac{1}{4}$ of the uterus was scarred, adhesions were thin or filmy, or ostial areas and the upper fundus were minimally involved or clear (3).

In addition to the 3D ultrasound, patients underwent a thorough infertility investigation, composed of documentation of ovulation, analysis of semen, baseline ovarian reserve testing, and HSG. Pre-operative sonographic evaluation included traditional 2D sagittal endometrial thickness, 3D routine acquisition (collection of anatomy as 3D volume data), multiplanar display (the simultaneous visualization of 3 orthogonal scan planes; longitudinal, transverse and a unique "horizontal" plane which often provides views of anatomy often not attainable using 2d ultrasound imaging), and volume rendering (use of computer rendering to create a 3D ultrasound image). For the purpose of standardization, all patients were evaluated, imaged, and operated on by the same physician. HSG was performed in standard fashion by placing a catheter tip within the external cervical os and injecting radiopaque oil-contrast material into the uterine lumen. All films were reviewed and interpreted by one physician. For patients who cycled, the HSG was scheduled in the proliferative phase of the menstrual cycle. Following the pre-operative HSG and 3D ultrasound, appropriate candidates () were scheduled for operative hysteroscopy. At time of hysteroscopy, percent of cavity obstructed, presence of outflow obstruction and severity of Asherman's syndrome were evaluated. Laparoscopy was performed in 18/54 (33%) of patients at the discretion of the treating physician. Indications included suspicion of concomitant intra-peritoneal pathology and high risk of uterine perforation

Intra-operative technique included careful dilatation of the cervix and insertion of a 10mm resectoscope. Precise targeted resection of intrauterine adhesions was performed. In cases where there were isolated islands of endometrium, attempts were made to connect them. In all cases, attempts were made to restore normal uterine anatomy with a minimum of cautery and trauma. No curettage was performed. Postoperatively, a number eight pediatric Foley catheter was transcervically inserted into the uterus, and the balloon was expanded with 2cc of saline. In addition, conjugated estrogen (2mg po bid), and doxycycline (100mg po bid) were administered for at least 10 days to all patients. In all cases, the Foley catheter either spontaneously fell out or was removed within 14 days (all remained in place at least 48hrs). Postoperative 3D sonograms were performed on all patients at their post-operative check. The percent cavity obstructed and endometrial thickness (following two weeks of post-operative estrogen therapy) were evaluated at the time of this procedure. The results of the hysteroscopy were compared to the results of both the 3D sonogram and the HSG to evaluate each procedure's diagnostic accuracy.

Four patients required repeat hysteroscopic procedures to lyse persistent or de-novo adhesions. For statistical analysis, the sensitivity of HSG and 3D ultrasound for identifying the presence and severity of IUA as well as outflow obstruction were calculated using hysteroscopy as the gold standard. Pregnancy rates and live birth data were also collected for all patients. Informed consent was obtained for all surgical procedures.

Results:

The patients ranged in age from 26-49 with a mean age of 35.8 years. Fifty three (98.15%) of these women suffered from secondary infertility (one presented with amenorrhea only), and presented with a medical history and clinical symptoms suggestive of Asherman's syndrome/IUA as the etiology for their reproductive complications. 7/54 (12.96%) of patients presented with hypomenorrhea and 12/54 (22.22%) presented with amenorrhea. All patients had a history of antecedent intra-uterine trauma preceding presentation (Table I).

On pre-operative HSG, 22/54 (40.74 %) patients presented with cavities that were less than or equal to 30% obstructed (mild), 10/54 (18.52%) patients had cavities that were greater than 30% but less than or equal to 60% obstructed (moderate), and 22/54 (40.74%) patients had cavities that were greater than 60% obstructed (severe). On 3D ultrasound, 30/54 (55.56%) patients had cavities that were less than or equal to 30% obstructed (mild), 18/54 (33.33%) patients had cavities that were greater than 30% but less than or equal to 60% obstructed (moderate), and 6/54 (11.11%) patients had cavities that were greater than 60% obstructed (severe) (see Figure II).

Laparoscopy was performed in 18/54 (33.33%) patients and perforations occurred in 2/18 (3.70%) of cases (both perforations occurred in patients who underwent concomitant laparoscopy with hysteroscopy).

In 54/54 (100%) of patients the extent of cavity obstruction and location of lesions found during hysteroscopy was consistent (defined in this study as less than a 20% discrepancy in detection of percent cavity obstructed) with their pre-operative 3D ultrasound findings, while the pre-operative results of the HSG were consistent in 36/54 (66.67%) of patients. In the 18/54 (33.33%) cases where the hysteroscopy was consistent with the 3D ultrasound but not the HSG, 11/18 (61.11%) had evidence of lower uterine segment outflow obstruction (in total, 13 patients demonstrated lower uterine segment obstruction on hysteroscopy). In these 11 patients, the pre-operative 3D ultrasound correctly differentiated between complete cavity obliteration and lower segment outflow obstruction. In the 7/18 (38.89%) patients that did not have evidence of outflow obstruction but had pre-operative HSG's that were inconsistent with the hysteroscopy, 7/7 (100%) of the HSG's incorrectly over-graded the severity of intra-cavitary adhesive disease.

Post-operatively, balloon catheter remained in place for at least 10 days in 46/54 (85.19%) patients. In 48/54 (88.89%) of patients, the post-operative cavity was designated adequate to attempt conception (adequacy was defined as less than 20% of obstruction remaining as seen on 3D ultrasound) following one operative procedure. The remaining 6/54 (11.11%) required additional lysis of adhesions prior to attaining a cavity adequate to attempt conception

A pregnancy rate of 45/50 (90%) was achieved in patients who desired fertility; 3/54 (5.56%) did not desire fertility and 1/54 (1.85%) left our academic office and no follow up data could be obtained. Of those pregnancies, 19/45 (42.22%) were spontaneous, 8/45 (17.78%) were achieved with injectable gonadotropins and IUI and 18/45 (40%) were achieved with IVF/Ovum Donation. The live birth rate was 35/50 (70%). Neither etiology of Asherman's Syndrome nor number of prior D&C's predicted outcome.

Discussions:

There are numerous modalities employed to diagnose and classify Asherman's Syndrome. Common protocols include use of HSG (4, 5, 6, 8, 9, 13, 14), MRI (15, 16, 17), sonohysterography (6, 10, 11, 12), and transvaginal ultrasound (both 2D (6, 9, 10, 11, 12, 18) and 3D (11, 18, 19, 20)). The most widely studied and utilized in current practice is HSG. Its high sensitivity, which has been reproduced in numerous large scale studies, has traditionally made it the preferred mechanism for screening patients with suspected IUA. However, many studies have shown that HSG produces a large number of false positive results; specifically in those whose cavities contain lesions other than IUA, such as cervical stenosis, endometrial polyps and myomas (4, 11). Furthermore, as the image produced by HSG is determined by contrast perfusion, the ability to evaluate the entire cavity and accurately assess the grade of disease is limited, notably in patients with adhesions in the lower uterine segment. Even in cases without lower tract obstruction, HSG over-graded the severity of adhesions in this study due to decreased clarity in comparison to 3D ultrasound. Additional imaging could assist the surgeon by pre-operatively presenting a more precise map of the intrauterine pathology.

Sonohysterography (SHG) has been studied for its utility in identifying intrauterine adhesions, however, despite a few small studies and case reports (6, 10, 21,) that demonstrated a diagnostic accuracy superior to HSG, a larger study has concluded that both 2D-SHG and HSG have similar sensitivity with high false positive rates(11). It has been proposed that adding 3D imaging to SHG may improve these results (11). Conventional 2D transvaginal ultrasound has also been utilized, but because conflicting data has been produced, its efficacy in diagnosing and prognosticating Asherman's remains questionable (6, 9, 7). While Fedele et al and Shalev et al demonstrated in a small series the ability to achieve useful information with 2D TVS, these results have been difficult to reproduce (7, 9). In fact, in a series published by Soares et al, two dimensional TVS failed to detect IUA in any of the four cases studied, and gave three false positive diagnoses (6). Sylvestre et al also looked at the efficacy of 2D ultrasound (in a series of 209 patients) and showed a sensitivity of 97% and a specificity of 11%, suggesting that while the 2D ultrasound can be an effective screening test, there are a large number of false positive IUA results, most commonly with respect to polyps, myomas, cervical stenosis, and mullerian abnormalities (11). Therefore, 2D ultrasound does not appear to offer a more accurate diagnostic modality than HSG (4).

There are limited studies in the English literature comparing the diagnostic and prognostic capabilities of 3D ultrasound to other modalities. In one study, Sylvestre et al demonstrated an increase in specificity for 3D ultrasound (45%) versus 2D ultrasound (11%) in the demonstration of intrauterine lesions (11). They concluded that the addition of the coronal plane was responsible for the gain in accuracy (11). The only comparable modality, MRI, has shown promise in some case reports, but at tremendous increase in imaging time and cost (15, 16, 17).

In this study, we not only evaluated the ability of 3D ultrasound to identify the presence of adhesions but also to correctly classify the severity of disease, most notably with respect to percent cavity obstructed and lower tract obstruction. We demonstrated that 3D ultrasound had a higher sensitivity than HSG in correctly assessing the grade of cavity adhesion and differentiating lower tract obstruction from severe cavity disease. Therefore, as prognosis in Asherman's patients is based on severity of disease, it appears

from our data that 3D ultrasound, more accurately assesses prognosis. Furthermore, we suggest that because data obtained from 3D ultrasound correlates more closely with the character and extent of disease, it could be a helpful tool in predicting fertility outcome post-operatively. We attribute a great deal of our high pregnancy rates to the pre-operative information obtained by the 3D ultrasound because its visual images allowed us to perform a more thorough procedure which ultimately resulted more optimal treatment and higher success rates. Therefore, we propose that a clearer pre-operative visual picture, such as that provided by the 3D ultrasound, assists in intra-operative visual capabilities and this, combined with good surgical technique and post-operative care, leads to successful reproductive outcome.

However, as a case series with a single, non-blinded operator and interpreter our study is limited. The operator was cognizant of the participant's pre-operative HSG and 3D ultrasound results prior to performing hysteroscopy. This knowledge could have biased his intra-operative assessment. Therefore, the sensitivity values, which favor 3D ultrasound as being more consistent with hysteroscopic findings, could be flawed due to operator bias. In addition, because the same operator performed all surgical procedures, it is likely that his surgical skills improved greatly, possibly making him more adept at correlating the imaging findings with the surgical findings.

In summary, our study is the first to demonstrate the benefit of 3D ultrasound over HSG in the management of Asherman's Syndrome. 3D ultrasound provides a more accurate depiction of adhesions and extent of cavity damage than HSG in patients with suspected Asherman's syndrome, particularly when differentiating severe IUA from lower uterine segment outflow obstruction. Therefore, grading systems utilizing HSG to classify severity of disease should be revised to include 3D ultrasound findings

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