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Original Article

Accuracy of three dimensional ultrasound and treatment outcomes of intrauterine adhesion in infertile women

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ABSTRACT

Objective: To determine the accuracy and usefulness of three-dimensional transvaginal ultrasound (3D-TVUS) in diagnosing intrauterine adhesion (IUA) and to evaluate treatment outcomes associated with fertility.

Materials and Methods: IUA patients (110) underwent hysteroscopy to definitively diagnose and treat adhesiolysis. Morphologic characteristics of endometrium suggesting IUA, such as marginal irregularity, thinning, defects, obliteration, fibrosis, and calcification, were identified and recorded by 3D-TVUS. The sensitivity of 3D-TVUS findings and the attainment of postoperative fertility were evaluated prospectively. The clinical records were followed up for 2 years for obstetrical outcomes and analyzed.

Results: On comparing the findings of 3D-TVUS with those of hysteroscopy in 110 patients, 45 (88.23%) patients were confirmed as IUA by hysteroscopy among 51 (46.36%) patients, with one finding in 3D-TVUS; 42 (97.67%) patients were confirmed among 43 (39.09%) patients with two findings; and 16 (100%) patients were confirmed among 16 (14.55%) patients with over three findings. A pregnancy rate of eight out of 47 (17.02%) was achieved in patients who desired fertility.

Conclusion: 3D-TVUS assessment of the uterus provides an accurate depiction of adhesion and extent of cavity damage in patients with suspected IUA.

Introduction

Intrauterine adhesion (IUA), also known as Asherman's syndrome, is the replacement of the entire or partial uterine cavity with fibrous scar tissue. Menstrual disturbance, cyclic pelvic pain, recurrent pregnancy losses, and subfertility follow when the fibrous adhesion is formed in the intrauterine cavity. Most IUA occurs by iatrogenic manipulation, such as diagnostic curettage (1.6%), abdominal myomectomy (1.3%), cervical biopsy or polypectomy (0.5%), and insertion of intrauterine device (0.2%) [1]. Gravid uterus is especially vulnerable to an injury by manipulation, and IUA is followed by spontaneous or artificial abortion at rates of 7% to 30% [2]. IUA often results in recurrent miscarriage (range, 5% to 39%) [3–6]. Another cause of IUA is endometrial tuberculosis with an incidence is 4%, which induces the obliteration of the uterine cavity in > 50% of cases. In endometrial tuberculosis, the performance of surgery is generally low and is often recurrent, making future fertility unlikely [1,3].

The imaging modalities used to diagnose IUA are hysterosalpingography (HSG), ultrasound, sonohysterography, and magnetic resonance imaging (MRI). Hysteroscopy is capable of both IUA diagnosis and treatment, and HSG is most widely utilized for diagnosis when IUA is suspected. However, it also has shortcomings, such as invasiveness and radiation exposure [7–9]. IUA can be

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diagnosed by ultrasound, with the characteristic appearance of hyperechoic areas within the endometrium. Two-dimensional transvaginal ultrasound (2D-TVUS) is noninvasive, relatively economical, and readily available. However, the sensitivity and specificity of 2D-TVUS for IUA are not high enough for clinical use (52% and 11%, respectively) [4].

3D-TVUS has recently been adopted in the gynecological sciences. By enabling multiplanar displays, which simultaneously visualizes three orthogonal scan planes, 3D-TVUS boasts an additional advantage of obtaining anatomical views that are often unattainable by 2D-TVUS.

The American Fertility Society proposed an IUA classification in 1988 [5]. It classifies IUAs into mild, moderate, and severe forms by scoring the extent of endometrial cavity obliteration, appearance of adhesions, and menstrual characteristics, based on hysteroscopic or HSG assessment. However, it is not without the disadvantage of invasiveness.

This study was conducted to assess the value of 3D-TVUS for diagnosing IUA through comparisons with hysteroscopic findings. Furthermore, we assessed the treatment outcomes of IUA using hysteroscopic adhesiolysis, specifically associated with pregnancy.

Materials and methods

Patient characteristics

This study was carried out at the Fertility Center of Kosin University Hospital, Busan, South Korea, and following Institutional Review Board approval (KUCMIRB 12-024).

There were 110 cases of IUA primarily diagnosed by 3D-TVUS among a total of 4577 first-visits between November 2008 and October 2010. Hysteroscopy was performed for the final diagnosis and treatment. The hysteroscopic findings were compared with 3D-TVUS imaging. The operative outcomes were also analyzed and their hospital course was carefully observed for comparison with 3D-TVUS results.

The cause for IUA was analyzed in the 110 women as follows: history of endometrial curettage, hysteroscopic surgery, and genital tuberculosis.

Ultrasound evaluation

The patients were examined by 3D-TVUS (Accuvix XQ, Medison, Seoul, Korea) using a 7.5 MHz transvaginal probe. Every examination was initiated with a 2D-TVUS evaluation of the endometrial cavity and, after switching to 3D-TVUS, the region of interest was selected with the volume box and the volume acquired. When possible, information regarding the scan was stored on a 540-MB removable hard disk for further evaluation and calculations. For the purpose of standardization, all patients were evaluated, imaged, and operated on by the same physician.

In 3D-TVUS, the morphological characteristics of the endometrium suggesting IUA were classified into six categories: marginal irregularity (in coronal plane), thinning (< 2 mm), defect (interrupted endometrial line), obliteration (undetectable endometrium suggesting extensive adhesion), fibrosis (hyperechoic lesion without posterior shadowing), or calcification (hyperechoic lesion with posterior shadowing; Figure 1). The participants were divided

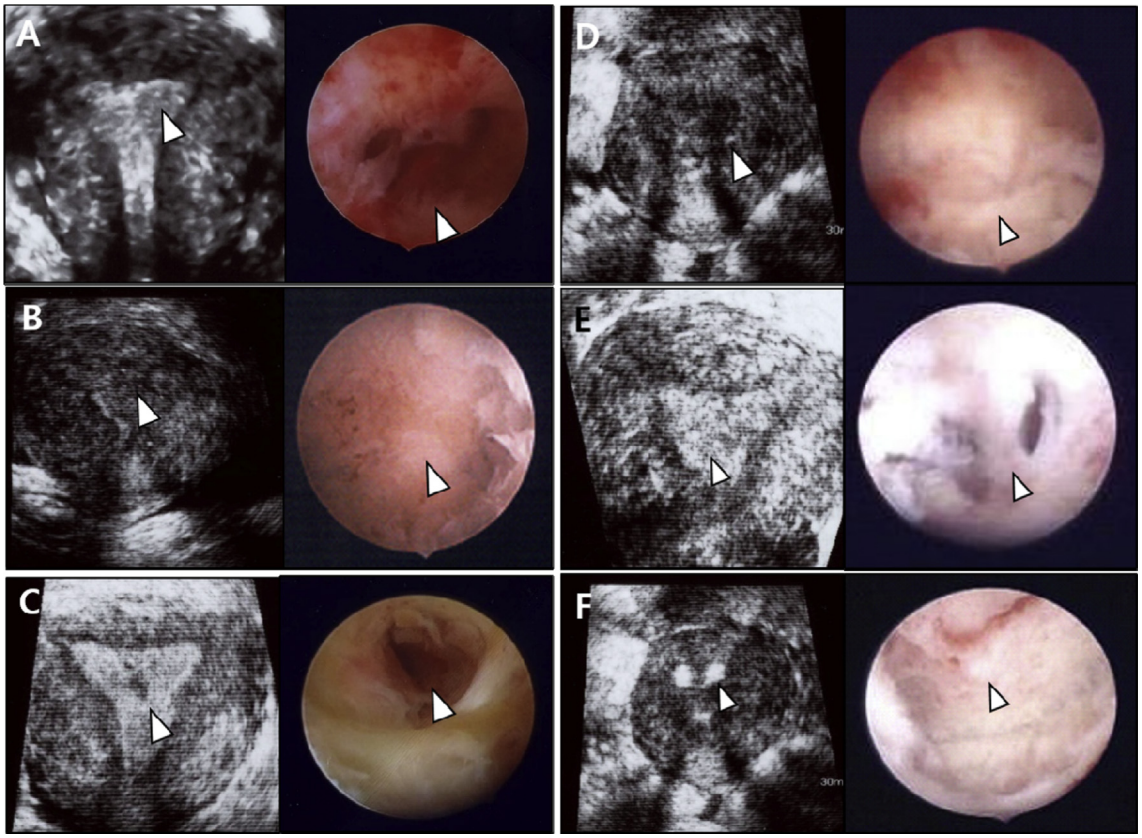

Figure 1. The classification of endometrial findings using three-dimensional ultrasound and suggesting intrauterine adhesion matched hysteroscopic findings: (A) marginal irregularity in sagittal plane, (B) thinning, (C) defect, (D) obliteration, (E) fibrosis, and (F) calcification.

Table 1
Clinical characteristics of patients ($n = 110$) enrolled in the study.

Characteristics ($n = 110$)	Median	Interquartile range
Age (y)	34	31.7–38.0
Years of infertility	2	1.0–4.25
Gravity	1.5	1.0–4.0
Parity	0	0–1.0
No. of curettage	1.0	0–3.0

into Group 1 with one 3D-TVUS finding, Group 2 with two findings, and Group 3 with three findings or more.

Adhesions were also reclassified by the extent of the cavity involved according to the American Fertility Society classification: mild (cavities that were ≤ 30% obstructed), moderate (cavities that were > 30%, but ≤ 60% obstructed), and severe (cavities that were > 60% obstructed) [5].

Hysteroscopy

Hysteroscopy was performed to confirm IUA. Simultaneous hysteroscopic adhesiolysis of IUA under general anesthesia was continued with hysteroscopy scissors using a controlled flow pump with saline or lactated Ringer's solution for distention by an experienced surgeon. The surgeon described and drew the IUA findings on paper charts.

The results of hysteroscopy were compared to the findings of the 3D-TVUS in order to evaluate the diagnostic accuracy of each 3D-TVUS.

Pregnancy follow-up

The clinical records were followed up for 2 years for the obstetrical outcome and analyzed. The time interval to conceive and the reproductive outcome were recorded.

Statistical analysis

The sensitivity of 3D-TVUS for identifying the presence and severity of IUA were calculated. Kappa correlation was applied to analyze the consistency of the 3D-TVUS findings and hysteroscopy in terms of IUA. A p value < 0.05 was considered a statistically significant difference for each analysis. Pregnancy and live-birth data were also collected for all patients.

Results

Patient characteristics

The mean age of 110 patients included in the final analysis was 32.51 ± 5.25 years. All had a history of infertility for > 1 year (3.24 ± 1.95 years) and parity was 0.46 ± 0.24 (Table 1). The number of curettage was 2.87 ± 1.73, and 78 patients (70.9%) had a history of endometrial curettage (curettage for miscarriage, vaginal bleeding, or curettage on postpartum uterus). Twelve patients (10.9%) had a history of hysteroscopic surgery and five patients (4.5%) had a history of genital tuberculosis.

3D-TVUS findings and correlation with hysteroscopy

3D-TVUS was performed at 11.21 ± 1.73 days after the last menstruation day. The thinnest endometrial depth was 2.77 ± 2.13 mm, and the thickest endometrial depth was 5.25 ± 1.46 mm.

Irregularity of endometrial margin was noted in 26 (23.64%) patients, thinning in 18 (16.36%) patients, defect in 48 (43.64%) patients, obliteration in 25 (22.73%) patients, fibrosis in 27 (24.55%) patients, and calcification in 19 (17.27%) patients (Table 2).

The consistency between 3D-TVUS and hysteroscopy findings was high; endometrial marginal irregularity (26/26,100%), endometrial thinning (18/18, 100%), endometrial defect (45/48, 93.8%), endometrial obliteration (25/25, 100%), endometrial fibrosis (26/27, 96.3%), and endometrial calcification (17/19, 89.5%).

Among 51 patients (46.36%) who showed one finding on 3D-TVUS (Group 1), 45 patients (88.23%) were confirmed to have the same finding by hysteroscopy. Forty-three patients (39.09%) comprised Group 2, which showed two findings on 3D-TVUS (Group 2), with those findings confirmed in 42 patients (97.67%) by hysteroscopy. The number who showed more than two findings by 3D-TVUS (Group 3), with all confirmed by hysteroscopy, was 16 patients (14.55%). Six cases from group 1 and only one from Group 2 turned out to lack the hysteroscopy findings (Table 3).

On 3D-TVUS, 75 (68.18%) patients had a uterine cavity with a total obstruction area of < 30% (mild obstruction), 26 (23.64%) patients showed the cavity obstruction area > 30%, but < 60% (moderate obstruction), and nine (8.18%) patients showed cavities with obstruction area > 60% (severe obstruction). On hysteroscopy, 69/75 (92%) patients confirmed mild adhesion (≤ 30% obstruction), 25/26 (96.15%) patients confirmed moderate adhesion (> 30%, but ≤ 60% obstruction), and 9/9 (100%) patients confirmed severe adhesion of > 60% obstruction (Table 4).

Seven false-positive findings were observed in our study with 3D-TVUS, as compared to hysteroscopy findings. The positive predictive value of 3D-TVUS was 93.64% according to classification of endometrial obliteration (mild, moderate, and severe). Examination of the relationship in classification of endometrial obliteration between the 3D-TVUS and HSC showed a Kappa value of 0.111, indicating a slight agreement in performance.

Conception and reproductive outcome

During the 2-year period, a total of 47 patients were observed without the follow-up loss. Among these, a pregnancy rate of eight of 47 (17.02%) patients was achieved in patients who desired fertility among 110 women diagnosed with IUA after hysteroscopic adhesiolysis. Of those pregnancies, one in 27 (3.70%) patients were

Table 2
Morphologic characteristics of endometrium using 3D-TVUS.

Morphologic characteristics	Ultrasonographic findings of endometrium	No. of IUA patients by 3D-TVUS	No. of IUA patients by hysteroscopy (%)
Marginal irregularity	Irregularity of margin in coronal plane	26	26 (100)
Thinning	Partial thin area < 2 mm	18	18 (100)
Defect	Interrupted endometrial line & isoechoic lesion	48	45 (93.8)
Obliteration	Extensively dense adhesion with undetectable endometrium	25	25 (100)
Fibrosis	Hyperechoic lesion without posterior shadowing	27	26 (96.3)
Calcification	Hyperechoic lesion with posterior shadowing	19	17 (89.5)

3D-TVUS = three-dimensional transvaginal ultrasound; IUA = intrauterine adhesion.

Table 3
Diagnostic accuracy of IUA according to morphologic characteristics of 3D-TVUS.

Group [a]	No. of IUA patients by 3D-TVUS	No. of IUA patients confirmed by hysteroscopy (%)	PPR (%)	NPR (%)
1	51	45 (88.2)	93.6	0
2	43	42 (97.6)	98.3	11.8
3	16	16 (100)	100	7.4

3D-TVUS = three-dimensional transvaginal ultrasound; IUA = intrauterine adhesion.
[a] Group 1 = one finding of 3D-TVUS; Group 2 = two findings; Group 3 = three findings or more.

Table 4
Classification of severity of IUA according to the altered area of endometrium seen by 3D-TVUS.

Classification	Involvement	No. of IUA patients by 3D-TVUS	No. of IUA patients confirmed by hysteroscopy (%)[a]
Mild	≤ 30% obstructed	75	69 (92.0)
Moderate	> 30%, but ≤ 60% obstructed	26	25 (96.1)
Severe	> 60% obstructed	9	9 (100)

3D-TVUS = three-dimensional transvaginal ultrasound; IUA = intrauterine adhesion.
Note. From "The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies, and intrauterine adhesions." by American Fertility Society, 1988, *Fertil Steril*, *49*, p. 944–55. Copyright© 1988, The American Fertility Society. Adapted with permission.
[a] Kappa value = 0.111.

spontaneous, two in seven (28.57%) patients were achieved with injectable gonadotropins and intrauterine insemination, and five in 13 (38.46%) were achieved with *in vitro* fertilization. Of eight pregnancies, four (50%) achieved a live birth and four (50%) experienced spontaneous miscarriage.

Discussion

IUA provokes diverse menstruation problems in women of childbearing age, and often causes sub-fertility or infertility. More effective diagnostic modalities have been searched for in this context. HSG is the conventional method for diagnosing IUA, with a reported sensitivity and specificity of 75% and 80%, respectively [6,7]. However, HSG has shortcomings, including invasiveness and possible radiation exposure. When the adhesion occurs in the lower segment of the uterus, careful examination is necessary due to contrast enhancement potentially being inadequate. Knopman et al [8] reported that HSG misclassified complete cavity obstructions in 61% cases when adhesion was limited to the lower uterine segment only [8].

MRI is a competent tool for diagnosing adnexal anomalies and IUAs [9,10]. However, it is expensive and the diagnostic performance for IUA remains unclear, making its clinical use limited to purposes other than investigation.

2D-TVUS is widely adopted over gynecology because it is safe and easy to use. However, its capability in diagnosing IUA is limited, although space-occupying lesions in uterine cavity may be identified. 3D-TVUS allows assessment that is more accurate by interactive visualization and multiplanar reformatting. The range and location of IUA are expected to be more consistently determined using 3D-TVUS, ultimately correlating more closely with prognosis [11]. Assessment by 3D-TVUS occurs in real time and is radiation free. Knopman et al [8] successfully reported the ability of 3D-TVUS in classifying IUA severity, showing percentages of cavity and lower-tract obstructions. The sensitivity of identifying IUA by 3D-TVUS was 100%, while sensitivity by HSG was only 66.7% [8].

This study attempted to systematically classify findings of IUA in 3D-TVUS and validated in hysteroscopy. The findings were classified according to endometrial marginal irregularity, endometrial thinning, endometrial defect, endometrial obliteration, endometrial fibrosis, and endometrial calcification. Those with two findings and three findings out of six using 3D-TVUS were predicted to have IUA in 97.6% and 100%, respectively. Those showing only one finding were diagnosed as IUA in 88.8% by hysteroscopy, with a false-positive rate of 13.7%.

We also classified the 3D-TVUS findings into mild, moderate, and severe forms in an attempt to compare to the American Fertility Society classifications for IUA. This three-step classification showed slight agreement (Kappa value = 0.111) with hysteroscopic findings. The findings of 3D-TVUS accurately diagnosed IUA confirmed by hysteroscopy in over 90% of cases, regardless of the severity of adhesion in the current study. These results showed that 3D-TVUS is a useful and accurate tool for predicting severe IUA.

After diagnosis of IUAs, treatment is considered when there are symptoms of pain or menstrual dysfunction, or more commonly when there is a history of infertility or recurrent pregnancy loss and the patient wishes to conceive [12]. It is difficult to obtain accurate data on fertility and pregnancy outcomes from recent studies because of small sample sizes, the variable duration of follow-up, and the retrospective nature of most studies in this area. The pregnancy rate after hysteroscopy was reported to be between 43% and 84%, and the miscarriage rate was from 4% to 36% among women who conceived [13]. In the current study, 47 women who wanted conception and were treated with hysteroscopy for IUA were followed-up for 2 years, with results indicating pregnancy rates of only 17.0%. However, 27 women (57.4%) attempted a natural pregnancy and did not receive any form of infertility treatment. The pregnancy rate was 35.0% (7/20), with four (57.1%) women achieving a live birth after receiving treatments, including as gonadotropins with IUI or IVF. Therefore, active and preemptive treatment is warranted in women who are diagnosed with IUA.

The prognosis of IUA counts in the extent of the disease and good surgical capabilities and postoperative care are enumerated as important factors for predicting reproductive outcomes associated with IUA [8]. 3D-TVUS, which provides vivid 3D perspective of the endometrial cavity, is a prompt and noninvasive modality for diagnosing IUA, and is expected to contribute to the improvement in fertility outcomes. However, the prognosis of fertility outcomes according to the extent of IUA was not readily estimated in the current study because the number of patients was relatively small and pregnancy was actively pursued in less than half of those who were diagnosed with IUA.

There were some limitations to our study. There was an inherent selection bias, given that this was a retrospective observational study undertaken in a single institution. Additionally, physicians who performed the hysteroscopy were not blinded to the results of 3D-TVUS examinations. Therefore, it is likely that we would try to "confirm" the diagnosis of IUA, thus leading to the high sensitivity associated with 3D-TVUS in IUA diagnoses.

To date, there have been no universally applied classification systems for IUA. This study is the first to classify the extent of IUA using 3D-TVUS, and the findings of IUA were compared to those of hysteroscopy. 3D-TVUS provided an accurate illustration of adhesion and the extent of cavity damage in patients with suspected IUA. In this context, a revision of the grading system to classify the severity of IUA is warranted.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

References

[1] Schenker JG, Margalioth EJ. Intrauterine adhesions: an updated appraisal. Fertil Steril 1982;37:593–610.
[2] Tam WH, Lau WC, Cheung LP, Yuen PM, Chunnmg TK. Intrauterine adhesions after conservative and surgical management of spontaneous abortion. J Am Assoc Gynecol Laparosc 2002;9:182–5.
[3] Bukulmez O, Yarali H, Gurgan T. Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic synechialysis. Hum Reprod 1999;14:1960–1.
[4] Salle B, Gaucherand P, Hilaire PD, Rudigos RC. Transvaginal sonohysterographic evaluation of intrauterine adhesions. J Clin Ultrasound 1999;27:131–4.
[5] American Fertility Society. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies, and intrauterine adhesions. Fertil Steril 1988;49:944–55.
[6] Soares SR, Dos Reis MMBB, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 2000;73:406–11.
[7] Dalfó AR, Úbeda B, Úbeda A, Monzon M, Rotger R, Ramos R, et al. Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: a comparison with hysteroscopy. Am J Roentgenol 2004;183:1405–9.
[8] Knopman J, Copperman AB. Value of 3D ultrasound in the management of suspected Asherman's syndrome. J Reprod Med 2007;52:1016–22.
[9] Dykes TA, Isler RJ, McLean AC. MR imaging of Asherman syndrome: total endometrial obliteration. J Comput Assist Tomogr 1991;15:858–60.
[10] Letterie GS, Haggerty MF. Magnetic resonance imaging of intrauterine synechiae. Gynecol Obstet Invest 1994;37:66–8.
[11] Bermejo C, Martínez Ten P, Cantarero R, Diaz D, Perez Pedregosa J, Barron E, et al. Three-dimensional ultrasound in the diagnosis of Müllerian duct anomalies and concordance with magnetic resonance imaging. Ultrasound Obstet Gynecol 2010;35:593–601.
[12] Magos A. Hysteroscopic treatment of Asherman's syndrome. Reprod Biomed Online 2002;4:46–51.
[13] Deans R, Abbott J. Review of Intrauterine Adhesions. J Minim Invasive Gynecol 2010;17:555–69.