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Original Article

A comparative study on the value of 2D-TVS combined with 3D-TVS and hysteroscopy in the diagnosis of intrauterine adhesion

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Abstract: Objective: To analyze the value of 2D-TVS combined with 3D-TVS in the diagnosis of intrauterine adhesion. Methods: 89 patients with suspected but unconfirmed intrauterine adhesion in our hospital were selected as the research subject taking 2D-TVS examination, 3D-TVS examination and hysteroscopy examination. The diagnostic value was analyzed with reference to the results of hysteroscopy examination. Results: The diagnostic accuracy, specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV) of 2D-TVS for intrauterine adhesion was 86.52%, 75.00%, 92.98%, 85.71% and 86.89%, respectively and that of 3D-TVS was 85.39%, 66.67%, 93.55%, 81.82%, and 86.57%, respectively. The results of 2D-TVS combined with 3D-TVS diagnosis were 95.51%, 72.73%, 98.72%, 88.89%, and 96.25%, respectively. Conclusion: The combination of 2D-TVS and 3D-TVS for intrauterine adhesion can achieve higher diagnostic efficiency, so it can be regarded as an effective method for the diagnosis of intrauterine adhesion.

Keywords: Intrauterine adhesion, transvaginal two-dimensional ultrasound (2D-TVS), transvaginal three-dimensional ultrasound (3D-TVS), hysteroscopy, diagnosis

Introduction

Intrauterine adhesion is more frequent in patients who have undergone dilation and curettage, spontaneous abortion and artificial abortion. In recent years, a higher incidence of intrauterine adhesion is associated with the rising cesarean section rate [1]. It has been clinically confirmed that as long as one factor damages the endometrium, there is a risk of causing intrauterine adhesion, and the inducing factors include infection, intrauterine operation, and radiotherapy [2].

At present, the pathogenesis of intrauterine adhesion is not fully clarified, but it is considered to be closely related to endometrial fibrosis caused by different factors. The major clinical manifestations of patients are secondary amenorrhea, hypomenorrhea, periodic abdominalgia, and inoculation fade [3]. The diagnosis of intrauterine adhesion was often conducted by hystero-salpingography and the comprehensive physical manifestations of patients, but there has been a high rate of misdiagnosis or missed diagnosis since some patients do not manifest typical symptoms, or some patients are unwilling to endure the pain of invasive examination [4, 5]. A study on large samples found that 1.7% of patients with secondary amenorrhea manifest varying severity of intrauterine adhesion, and as many as 40% of infertile patients manifest intrauterine adhesion [6]. Therefore, it is essential to make accurate diagnosis of intrauterine adhesion.

With the advancement of medical technology, ultrasound has witnessed significant development for the advantages of simple operation, non-invasive detection, reusing and affordability. Transvaginal ultrasound (TVS), including transvaginal two-dimensional ultrasound (2D-TVS) and transvaginal three-dimensional ultrasound (3D-TVS) has become a common meth-

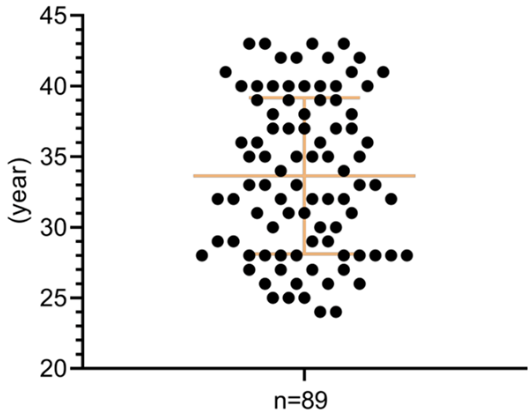

Figure 1. Age scatter plot of 89 patients with ages ranging from 24 years to 43 years.

od for the diagnosis and treatment of gynaecopathia [7]. In previous studies on ultrasound diagnosis of intrauterine adhesion, most of them were designed to study the single application of 2D-TVS or 3D-TVS [8, 9], while there were few studies on the joint application of the two methods. In this study, 89 patients with suspected intrauterine adhesions were selected as the study subjects to analyze the advantages of the combined application of 2D-TVS and 3D-TVS in the diagnosis.

Materials and methods

Materials

There were 89 patients with suspected but unconfirmed intrauterine adhesion in our hospital, all of whom were married, aged from 24 to 43 years (**Figure 1**), with an average age of 33.16 ± 8.97 years. Among these people, 11 patients had amenorrhoea, 45 patients had hypomenorrhea and 16 patients were infertile, and all of them had undergone uterine cavity operation. (1) Inclusion criteria: patients with unconfirmed intrauterine adhesion; patients who were initially judged as suspected cases for showing typical manifestations of intrauterine adhesion after undergoing gynecological examination; patients without contraindications for examination; patients signing consent form and the study was approved by the hospital ethics committee. (2) Exclusion criteria: patients with confirmed intrauterine adhesion; patients with amenorrhea or hypomenorrhea caused by vaginal factors; patients with amenorrhea or hypomenorrhea caused by vaginal foreign bodies; patients with the medical history of other confirmed gynecological diseases.

Methods

The instruments include Olympas hysteroscope (Japan) and Philips color Doppler ultrasound diagnostic apparatus (two-dimensional and three-dimensional examinations can be performed simultaneously). Before receiving the examination, the patients needed to empty urinary bladder. The bladder lithotomy position was selected for examination, and 2D-TVS examination was performed first. The probe was fitted with condom and inserted into the vaginal posterior fornix to scan the uterine appendages from longitudinal views and transverse views, recording endometrium, continuity, echo as well as intrauterine effusion and uterine size. After obtaining the optimizing contour of the sagittal section of the uterine and the endometrial image through the two-dimensional examination, we turned on the 3D-TVS and set the database angle and sampling frame to collect the three-dimensional data, and chose the highest quality image to complete the three-dimensional reconstruction in multiplane imaging mode. Patients were advised to hold their breath as necessary throughout the examination to prevent displacement artifacts. After obtaining the A, B, and C planes, we rotated the three axes to conduct the three-dimensional reconstruction and observed them from all side.

In addition, all patients needed to receive spectroscopy, and the effectiveness of ultrasound diagnosis was analyzed based on the results of spectroscopy.

Observation index

The results of spectroscopy are used as the gold standard to analyze the diagnostic efficacy and ultrasonographic manifestation of 2D-TVS and 3D-TVS, to analyze the diagnostic efficacy of 2D-TVS combined with 3D-TVS.

Statistical methods

Statistical analysis is carried out with SPSS23.0, and enumeration data is represented by [n (%)]. The results are compared by X^2 test and $P<0.05$ indicates statistically significant difference.

Table 1. Comparison of 2D-TVS examination and hysteroscopy diagnosis (case)

2D-TVS	Hysteroscope		Total
	Positive	Negative	
Positive	53	8	61
Negative	4	24	28
Total	57	32	89

Results

2D-TVS examination results

Of 80 cases diagnosed by hysteroscopy, 9 cases were confirmed to have no intrauterine adhesion. 61 cases were confirmed to have intrauterine adhesion by 2D-TVS examination, among which 57 cases were reconfirmed by hysteroscopy. The diagnostic efficacy analysis of the 2D-TVS examination compared with hysteroscopy is as follows (**Table 1**). The diagnostic accuracy, specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV) of 2D-TVS for intrauterine adhesion were 86.52% (77/89), 75.00% (24/32), 92.98% (53/57), 85.71% (24/28) and 86.89% (53/61), respectively. 4 cases were misdiagnosed by 2D-TVS, including 2 cases with intrauterine adhesion and 2 cases with incomplete septate uterus malformation. In addition, 8 cases of missed diagnosis occurred in the diagnosis of 2D-TVS, among which 5 cases manifested inhomogeneous endometrium thickness. The ultrasonographic manifestation of 2D-TVS showed as follows: the discontinuity, banded hypoechoic and hyperechoic occurred in the endometrium of 37 cases (**Figure 2**). 11 cases manifested uterine line separation (**Figure 3**), thin endometrium with low resolution. 7 cases had multiple inhomogeneous hypoechoic zone. 1 case manifested a mesh-like echoless zone near the lower uterine cavity and the cervical ostium, and 1 case manifested endometrial lining.

3D-TVS examination results

67 cases were confirmed to have intrauterine adhesion by 3D-TVS examination, among which 62 cases were reconfirmed by hysteroscopy. The diagnostic efficacy of 3D-TVS examination was as follows (**Table 2**). The diagnostic accuracy, specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV) of 3D-TVS for intrauterine adhesion were 85.39% (76/89), 66.67% (18/27), 93.55% (58/62), 81.82% (18/22) and 86.57% (58/67), respectively. 4 cases with normal uterine were misdiagnosed by 3D-TVS. 9 cases were missed by 3D-TVS examination, of which 2 cases of uterine cavity contour were not found. 3D-TVS examination showed that the coronal section of the uterus showed varying degrees of damage to the endometrium, and the discontinuity occurred in endometrium and there were no clear boundary, no regular edge between the endometrium and the muscular layer. Some area manifested serrated margin (**Figure 4**). The 3D-TVS showed that the normal uterine cavity is an inverted triangle with a homogeneous and continuous endometrium (**Figure 5**).

The examination results of 2D-TVS combined with 3D-TVS

80 cases were confirmed to have intrauterine adhesion by 2D-TVS combined with 3D-TVS, among which 78 cases were reconfirmed. The diagnostic efficacy of 2D-TVS combined with 3D-TVS was as follows (**Table 3**). The diagnostic accuracy, specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) of 2D-TVS combined with 3D-TVS for intrauterine adhesion were 95.51% (85/89), 72.73% (8/11), 98.72% (77/78), 88.89% (8/9) and 96.25% (77/80), respectively (**Figures 6** and **7**). 1 case with normal uterine was misdiagnosed by 2D-TVS combined with 3D-TVS. 3 cases were missed by 2D-TVS combined with 3D-TVS examination, including 1 case of membranous adhesion zone near the bottom of the uterine cavity, 1 case of adhesion at the cornual of the uterus and 1 case of adhesion at central column of the IUD.

Discussion

Intrauterine adhesion can occur in the cervix, uterine cavity, or in both parts. The configuration of uterine cavity of patients with adhesion is irregular. The irregular adhesion zone and local effusion or local blood stasis will also occur in these two parts [10]. The specific degree of endometrial damage directly affects the components of the adhesion zone, which basically include fibrous tissues without vascular, endometrial tissue, uterine smooth muscle tissue and connective tissue. Some patients also manifest varying degrees of leukocyte infiltration [11, 12].

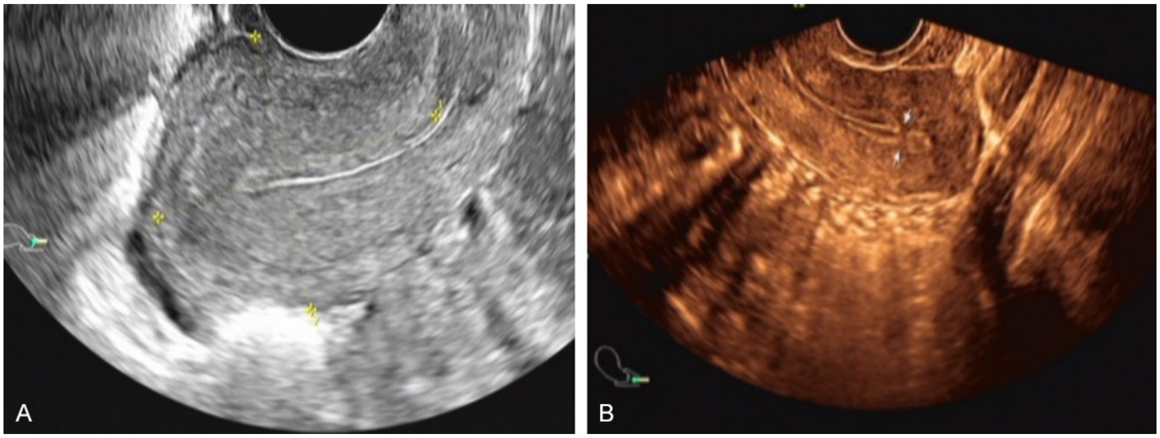

Figure 2. Manifestation of 2D-TVS examination. 2D-TVS of normal uterus shows continuity of endometrium in longitudinal section of uterus (A). 2D-TVS of intrauterine adhesion shows the discontinuity of the endometrium of the longitudinal section of the uterus, with the double arrow indicating the hypoechoic zone connected to the front and back walls (B).

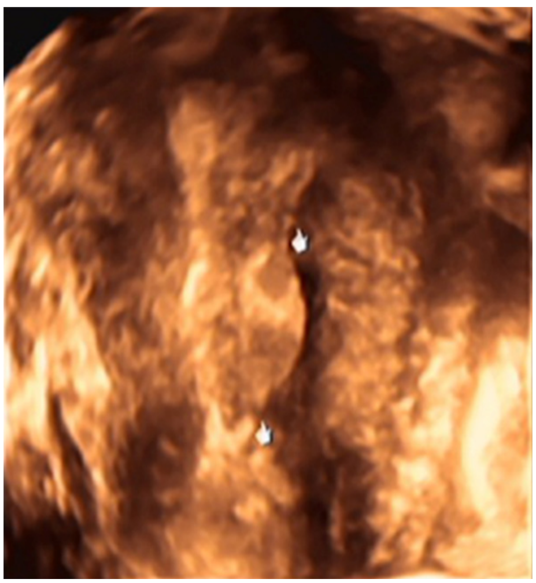

Figure 3. Multiple sections of two-dimensional ultrasound can show the discontinuity of the endometrium, hypoechoic in the uterus, and uterine cavity separation.

Table 2. Comparison of 3D-TVS examination and hysteroscopy diagnosis (cases)

3D-TVS	Hysteroscope		Total
	Positive	Negative	
Positive	58	9	67
Negative	4	18	22
Total	62	27	89

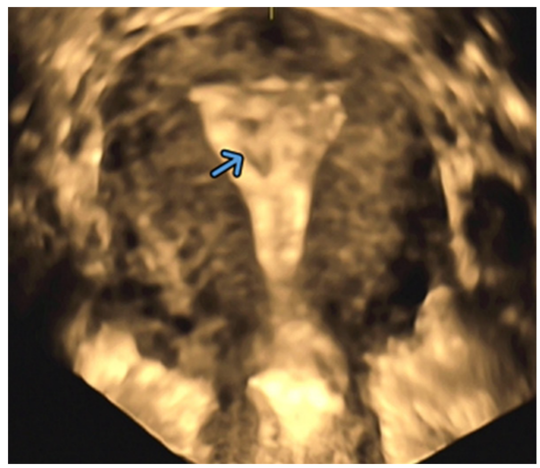

Figure 4. The 3D imaging of infertility shows the discontinuity and impairment of endometrium.

Hysteroscopy has always been regarded as a gold standard for the diagnosis of intrauterine adhesion. However, this examination is invasive and easily affected by the menstrual cycle. At the same time, the operation is complicated and the expense is high, so the patients need to carry a heavy medical burden. In addition, the primary medical centers cannot carry out this examination for its high technical requirements, which may cause delay in patients' condition and prevent them from receiving effective treatment in time [5, 13]. Studies have suggested that the intrauterine adhesion would be worsen if it cannot be treated in time [14]. Therefore, it is very important to choose an examination that is non-invasive, affordable, rapid and operation-friendly. As a commonly used diagnostic method, ultrasound is characterized by its non-invasiveness and simple

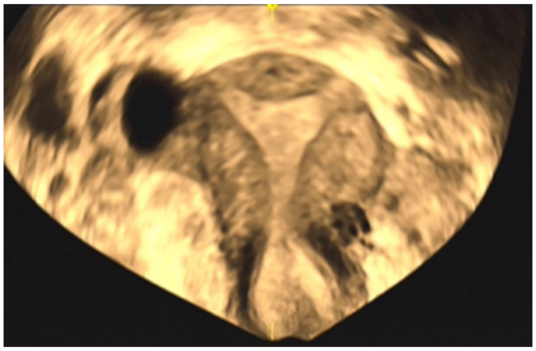

Figure 5. Three-dimensional imaging of normal uterus shows the continuous and homogeneous echo.

Table 3. Comparison of 2D-TVS combined with 3D-TVS examination and hysteroscopy diagnosis (cases)

2D-TVS combined with 3D-TVS	Hysteroscope		Total
	Positive	Negative	
Positive	77	3	80
Negative	1	8	9
Total	78	11	89

operation advantages. And the vaginal ultrasound applied to the current clinical practice has further played the value of ultrasound diagnosis [15]. Inserting the vaginal probe into the vagina for examination can show the image of uterine cavity directly and clearly. This examination is greatly suitable for the diagnosis of intrauterine adhesion because it is close to the pelvic organs, and intestinal gas and abdominal wall fat will not affect the test results [16, 17]. In this study, The diagnostic accuracy, specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) of 2D-TVS for intrauterine adhesion were 86.52%, 75.00%, 92.98%, 85.71% and 86.89%, respectively. The sonogram echogram shows that the thickness and echo of endometrium are inhomogeneous; the discontinuity occurs in the endometrium. There is a hypoechoic zone in the uterine cavity, and the uterine line, seemingly, endometrial lining is separated. The study suggests that it may be the suspected intrauterine adhesion if the echo clumps and inhomogeneous thickness of the endometrium are found in the transverse section of the uterine cavity by the transvaginal ultrasound [18]. Three-dimensional ultrasound appears after the use of two-dimensional ultrasound. Compared with two-dimensional ultrasound, it can provide more detailed lesion information, which can clearly display the coronal section of the uterus, making the doctor's interpretation of diagnosis tests more direct and clear [19]. In this study, two-dimensional and three-dimensional ultrasound were used to detect suspected intrauterine adhesion, and it found that the accuracy and positive predictive value (PPV) of two-dimensional ultrasound diagnosis were 75.50% and 78.08%, respectively, and those of three-dimensional ultrasound were 94.11% and 94.87% ($P<0.05$) [20]. It is suggested that 3D ultrasound has higher diagnostic value than 2D ultrasound. In this study, the accuracy and sensitivity of three-dimensional ultrasound for gynecological examination were 97.00% and 97.00%, respectively, suggesting that three-dimensional ultrasound can be used as a useful diagnostic method for gynecological diseases. In this study, the diagnostic sensitivity of 3D-TVS to intrauterine adhesion was 93.55%, and the specificity, accuracy, positive and negative predictive values were 66.67%, 85.39%, 86.57%, and 81.82%, respectively, which were close to two-dimensional ultrasound. The differences in analysis of the research results were attributed to the different characteristics of the included objects, the different inspection instruments, and the different technical levels of the inspectors.

It is clinically found that although 2D ultrasound is highly accurate for diagnosing uterine lesions, it is difficult to determine the types of uterine dysplasia. In contrast, 3D ultrasound can ensure that the configuration of the uterine fundus, and the configuration of endometrial cavity can be displayed more accurately and intuitively [21]. Studies have shown that the diagnostic value of three-dimensional ultrasound used in the bicornuate uterus or uterine septum is better than that of two-dimensional ultrasound. The former can observe the clear shape of the uterine fundus and uterine cavity, which will ensure that doctors can choose the correct treatment scheme more quickly according to the accurate identification of uterine malformation [22, 23]. However, the accuracy of 3D ultrasound imaging technology is also affected by different factors, including the instruments and the technical level of the inspectors. It found that the image quality of 3D and 2D ultrasound is similar [24]. Therefore, this study analyzed the value of 2D-TVS

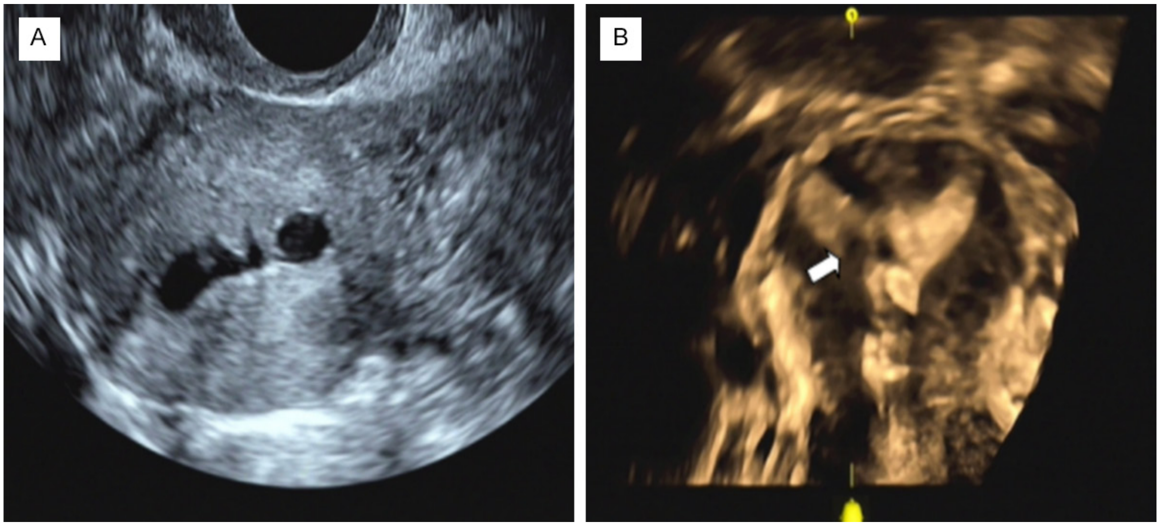

Figure 6. Two-dimensional ultrasound shows the discontinuity of endometrial cross-section, uterine cavity separation, uterine effusion, and intrauterine adhesion (A). Three-dimensional imaging shows filling defects of the endometrium (B).

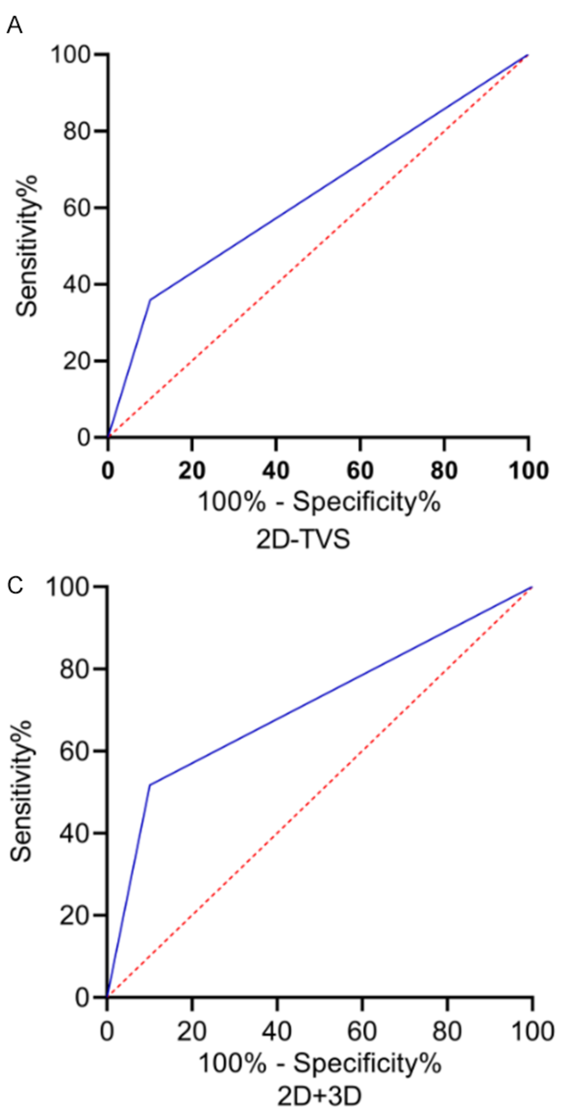

Figure 7. ROC curve of uterine cavity adhesion diagnosed by 2D-TVS, 3D-TVS and combination. According to hysteroscopy results, the ROC of 2D-TVS in diagnosing uterine cavity adhesion was 0.6292, 95% CI=0.5470-0.7114, P=0.0029. The ROC of 3D-TVS in diagnosing uterine cavity adhesion was 0.6461, 95% CI=0.5647-0.7274, P=0.0008. The ROC of 2D+3D diagnosis of uterine cavity adhesion was 0.7079, 95% CI=0.6305-0.7852, P<0.0001.

combined with 3D-TVS in diagnosing intrauterine adhesion, and found that the combination of the two methods is of higher diagnostic values. The suspected adhesion can be determined on the basis of the clear display of the two-dimensional section, and the diagnostic accuracy could be improved based on three-dimensional reconstruction under the appropriate sampling frame [25]. It is suggested that 2D-TVS and 3D-TVS examinations can be used in the clinical examination at the same time when conditions permit, so as to ensure a higher diagnostic accuracy.

In summary, both 2D-TVS and 3D-TVS are feasible for the diagnosis of intrauterine adhesion and can be selected flexibly in clinical practice. Based on this finding, it is suggested to combine the above two methods to ensure higher diagnostic efficacy. It can be the first choice when conditions permit. Although this paper confirmed the value of 2D-TVS combined with 3D-TVS method, the analysis of the sonogram echogram of each examination is far from comprehensive and the analysis of missed diagnosis and misdiagnosis is not thorough enough due to the small number of subjects in this study, making the research results less scientific. We should focus on more comprehensive and in-depth analysis in the future and provide more useful information for the diagnosis of intrauterine adhesion.

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Disclosure of conflict of interest

None.

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