Analysis of factors affecting the prognosis of patients with intrauterine adhesions after transcervical resection of adhesions

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Objectives: To study the factors affecting the prognosis of patients with intrauterine adhesions (IUAs) after transcervical resection of adhesions (TCRA), analyze the reproductive outcome, and guide prognostic improvements.
Design: Prospective study.
Patients: Our study included 292 patients diagnosed with IUAs who underwent follow-up office hysteroscopy at Shenyang Women's and Children's Hospital between June 2018 and June 2022.
Interventions: Patients were divided into case (52 patients whose hysteroscopy results indicated the presence of IUAs) and nocase (240 patients whose uterine cavity had returned to normal shape without obvious adhesion) groups on the basis of the results of a 2-month follow-up hysteroscopy following TCRA. Clinical data were collected and compared with various influencing factors, and the combined effect of these factors was assessed using multifactorial logistic regression analysis. A nomogram prediction model was constructed and internally validated on the basis of multifactorial analysis.
Main Outcome Measures: Intrauterine re-adhesion was observed at a 2-month follow-up after TCRA.
Results: Postoperative re-adhesion occurred in 52 of 292 patients with IUAs. Multifactorial binary logistic regression analysis showed that IUA barrier gel reapplication 5 days after TCRA was a protective factor. In contrast, the preoperative American Fertility Society scores demonstrated that severe IUAs and chronic endometritis were risk factors. The results of the multifactorial analysis were used to build a nomogram model, and the area under the curve value of the nomogram model for predicting postoperative recurrence was 0.914 (95% confidence interval: 0.864–0.956). The bootstrap method was subsequently used to resample 1,000 times for internal validation. The results showed that the internal validation C-index was 0.9135, and the calibration and ideal curves were well-matched.
Conclusion: The prognosis of patients with IUAs after TCRA is related to the severity of preoperative IUAs, presence of chronic endometritis, and IUA barrier gel reapplication 5 days after TCRA. Therefore, clinicians should monitor patients using targeted data to reduce recurrence risk after TCRA and improve the prognosis of patients with IUAs. (Fertil Steril® 2024;■:■–■. ©2024 by American Society for Reproductive Medicine.)
Key Words: Intrauterine adhesion, re-adhesion, transcervical resection of adhesions, influence factors, alignment diagram prediction model

Intrauterine adhesions (IUAs) obstruct the uterine cavity because of endometrial damage, endometrial fibrosis, and scarring. They often lead to severe clinical complications such as menstrual disorders (amenorrhea), infertility, and recurrent miscarriage, affecting reproductive capacity (1). Intrauterine adhesions comprise 36.6% of infertility cases (24.6% of secondary infertility and 12.0% of primary infertility cases) and are a prevalent cause of secondary infertility; this trend is increasing annually (2). Transcervical resection of adhesions (TCRA) is the standard treatment strategy for IUA in patients with fertility needs (3). However, the high recurrence rate after TCRA remains a major challenge in IUA treatment (re-adhesion rate up to 62.5%) (4). Therefore, adjuvant therapeutic measures are available to improve IUA prognosis after TCRA, such as simultaneous intrauterine device (IUD) placement, intrauterine balloon, or gel application during TCRA to serve as a barrier to the anterior and

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posterior uterine walls and prevent re-adhesion (5–7). Nonetheless, IUA recurrence is high, with an estimated 14%–48% of patients experiencing re-adhesion formation after adjuvant therapies (8–12). This study aimed to explore the factors influencing IUA prognosis after TCRA, analyze reproductive outcomes and provide guidelines for improving outcomes.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Shenyang Women's and Children's Hospital (approval number: 202325). There are no conflicts of interest to declare.

Study population

Patients with IUAs who underwent hysteroscopy due to reproductive needs in the outpatient department of Shenyang Women's and Children's Hospital from June 2018 to June 2022 were selected, and subsequent treatments and follow-up were performed. The inclusion criteria were as follows: moderate and severe IUAs confirmed by office hysteroscopy in our hospital, age $\leq$45 years, fertility requirements, complete outpatient review data, and complete clinical and imaging data. The exclusion criteria were as follows: previous TCRA with recurrent IUA, infertility due to uterine factors other than IUA (including congenital uterine anomalies and severe uterine adenomyosis), contraindications to the use of estrogen and progesterone (coronary heart disease, venous thromboembolism, stroke, transient ischemic attack, active liver disease, breast cancer, high-risk endometrial cancer, or unexplained vaginal bleeding), allergy to intrauterine adhesion barrier gel, and presence of severe intercurrent illness (e.g., coagulative disorders, systemic disease, severe cardiopathy). Ultimately, 292 patients were included. On the basis of hysteroscopy results from approximately 2 months postoperatively, the patients were divided into case group (whose hysteroscopy results suggested that uterine adhesions remained) and nocase group (whose uterine cavity returned to its normal shape without obvious adhesions).

Data collection

The following clinical data were collected: age, body mass index, age at menarche, menstrual cycle (regular or irregular), number of pregnancies, number of deliveries, history of missed abortion dilation and curettage (D&C), abortion D&C, and diagnostic curettage, severity at first presentation of IUA, presence of other common gynecological conditions (including the combination of endometriosis, fibroids, and ovarian cysts), presence of chronic endometritis (CE), preoperative endometrial thickness, preoperative endometrial volume, preoperative endometrial receptivity, preoperative uterine arteries, preoperative estrogen treatment, intrauterine adhesion barrier gel reapplication 5 days after TCRA, preoperative and postoperative American Fertility Society (AFS) scores, and preoperative and postoperative menstrual volume visual analogue scale (VAS) scores; and reproductive outcomes.

Hysteroscopy procedure

The patients underwent office hysteroscopy 3–7 days after menstruation at our hospital. The timing of office hysteroscopy for women with secondary amenorrhea was not limited. All examinations were conducted by the same team of experienced outpatient gynecologists using the same equipment. Specialist physicians graded IUA severity using the 1988 AFS (13) scoring criteria, which included adhesion extent, nature, and menstrual status and classified IUA into mild, moderate, and severe. Patients with moderate and severe IUAs confirmed by office hysteroscopy were admitted to the hospital for TCRA.

Surgical methods and postoperative treatment procedures

Women with IUA underwent TCRA 3–7 days after menstruation; secondary amenorrhea did not affect the time of the procedure. Preoperatively, endometrial thickness, endometrial volume, and uterine artery blood flow were determined by transvaginal ultrasound. A hysteroscopic surgery system (Karl Storz, Tuttlingen, Germany) was used to perform TCRA. The same team of gynecologists performed each procedure while the patients were under combination spinal anesthesia or general anesthesia. Under ultrasound guidance, the adherent tissue was carefully separated intraoperatively to restore the shape of the uterine cavity; the operative video and/or image data were retained during the operation. Endometrial samples were collected intraoperatively for CD138 immunostaining for CE diagnosis. CD138-positive cells $\geq$5 per 10 high-power fields are diagnostic of CE. Oral doxycycline was administered as regular postoperative treatment in cases in which the patient had CE. Intraoperatively, 3 mL of intrauterine adhesion barrier gel (Bairuiji Biomedical Co., Ltd., National Machinery Registration, No. 20153141542) was injected for the first time; an intrauterine balloon tube with 3–5 mL volume (depending on the size of the uterine cavity and degree of adhesion) was placed in the uterine cavity and removed 5 days later. In some patients, 3 mL of intrauterine adhesion barrier gel was reinjected when the balloon tube was removed. The first intrauterine balloon dilatation with a 16-Fr Foley catheter (Wellead, Guangzhou, China) was performed 10 days after TCRA, and office hysteroscopy was performed 20 days after TCRA (hysteroscopy was delayed until the end of menstruation in cases where patients were menstruating); patients were treated for 2–3 cycles in the described order. When membranous adhesions in any part of the uterine cavity or muscular adhesions that were $<$1/3 of the uterine cavity were detected during office hysteroscopy, the adhesions were immediately separated using a scope or micro-scissors. All patients were administered sequential estrogen-progesterone treatment immediately after TCRA to promote endometrial repair.

Criteria for judging intrauterine re-adhesion

Currently, there is no uniform standard for the duration of postoperative follow-up. The Chinese Expert Consensus on Clinical Diagnosis and Treatment of Uterine Adhesions (14) recommends that postoperative follow-up be conducted once a month for 3 months and subsequently once every 6 months

until 1 year for TCRA. The American Association of Gynecological Laparoscopists (AAGL) (1) recommends re-evaluation of uterine morphology 2–3 months postoperatively. Meanwhile, we have shown previously (15) that early second-look hysteroscopy combined with intrauterine balloon dilatation after hysteroscopic TCRA might improve the prognosis and postoperative pregnancy rate in women with IUA. By comparing intraoperative imaging data of TCRA and postoperative follow-up hysteroscopy, the following were used as the criteria for intrauterine re-adhesion: both uterine horns were visible at TCRA, but 1 or both horns were not visible at follow-up, and membranous, fibrous, or muscular adhesions were found to have reappeared in any part of the uterine cavity at follow-up.

Statistical methods

SPSS version 26.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Normally distributed data were expressed as mean±SD, and non-normally distributed data as M (P25, P75). The t-test was used to compare groups of normally distributed data; a nonparametric test (rank-sum test for paired samples and 2 independent samples) was used to compare non-normally distributed data. Categorical data were tested using the Chi-square ($\chi 2$) (for paired data) or Fisher's test. Risk factors were analyzed using multifactorial logistic regression analysis with backward regression (likelihood ratio). R software (R Foundation for Statistical Computing, Vienna, Austria) was used to construct the column-line graph model. The predictive value of the model was analyzed using the receiver operating characteristic (ROC) curve; internal validation was performed using the bootstrap method with computer simulation of adequate sampling. Statistical significance was set at $P<.05$.

RESULTS

Occurrence of postoperative re-adhesion

Approximately 2 months after hysteroscopic adhesion separation, 52/292 (17.81%) patients with IUA had postoperative re-adhesion formation.

Recovery of patients with IUA after TCRA

Comparison of preoperative and postoperative AFS scores. Among the 292 patients, the pre- and postoperative AFS scores 2 months postoperatively were 8 (7, 8) and 2 (2, 2), respectively, with significant difference ($P<.05$) (Table 1).

Comparison of mean pre- and postoperative menstrual volume VAS scores. Among the 292 patients, the mean pre- and postoperative menstrual volume VAS scores were 4 (3, 5) and 5 (4, 6), respectively, with significant difference ($P<.05$) (Table 2).

Reproductive outcomes

By April 2023, 220 patients had been followed up for 11 to 44 months. Notably, 114 (51.8%) patients became pregnant, with 85 (74.6%) live births; 15 (13.2%) reported missed abortion, spontaneous abortion, inevitable abortion, or unplanned pregnancy with a request for abortion; 2 (1.7%) reported induced abortions; and 12 (10.5%) were in gestational states. Of the patients who became pregnant, 45 (39.5%) had spontaneous pregnancies, and 69 (60.5%) had assisted reproductive technology pregnancies (17 ovulation induction and 52 in vitro fertilization–embryo transfer pregnancies). Of the 85 live births, 16 (14.0%) were preterm, and 69 (60.5%) were full-term. Of the patients who had live births, 14 (16.5%) had vaginal deliveries, and 71 (83.5%) had cesarean births. Of the 85 deliveries, 41 (48.2%) patients experienced obstetric complications, including 25 (29.4%) placenta accreta, 2 (2.4%) placenta increta, 1 (1.2%) low-lying placenta, 10 (11.8%) postpartum hemorrhage, 3 (3.5%) placental abruptions, and no uterine ruptures.

TABLE 1

Comparison of preoperative and postoperative AFS scores.

	Value	*P* value
AFS scores		
Preoperative	8 (7, 8)	0
Postoperative	2 (2, 2)	

AFS, American Fertility Society.

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Analysis of factors influencing postoperative re-adhesion in patients with IUA

A comparison of gravidity, number of prior uterine surgeries, preoperative endometrial thickness, preoperative endometrial volume, preoperative AFS classification, IUA and CE co-occurrence, intrauterine adhesion barrier gel reapplication 5 days after TCRA, and preoperative estrogen treatment in patients with and without postoperative re-adhesion formation showed significant differences ($P<.05$) (Table 3).

Logistic regression analysis of factors influencing postoperative re-adhesion in patients with IUA

Using variables that were found to differ in univariate analyses as independent variables, multifactorial logistic regression analyses using backward regression showed that preoperative AFS classification, patients with IUA and CE, and intrauterine adhesion barrier gel reapplication 5 days after TCRA were all factors influencing the occurrence of postoperative re-adhesion in patients with IUA. The risk of re-adhesion formation in patients with severe AFS was 11.8

TABLE 2

Comparison of preoperative and postoperative menstrual volume VAS scores.

	Value	*P* value
Menstrual volume VAS scores		
Preoperative	4 (3, 5)	0
Postoperative	5 (4, 6)	

VAS, visual analogue score.

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TABLE 3

Analysis of factors affecting postoperative re-adhesion in patients with IUA.

		Case group (52)	Nocase group (240)	*P* value
Age (y)		32.23 ± 5.25	32.47 ± 4.94	.754
Height (cm)		162.00 (158.0, 166.8)	161.00 (159.0, 165.0)	.385
Weight (kg)		61.500 (55.0, 66.8)	60.000 (53.0, 69.8)	.707
BMI (kg/m^2)		23.315 (20.2, 25.5)	23.000 (20.2, 26.0)	.892
Age at menarche (y)		14.000 (13.0, 14.0)	14.000 (13.0, 14.0)	.632
Menstrual cycle	Irregular	24 (46.15)	78 (32.50)	.061
	Regular	28 (53.85)	162 (67.50)	
Number of pregnancies		2.000 (1.0, 3.8)	2.000 (1.0, 2.8)	.002[b]
Number of deliveries		0.000 (0.0, 0.0)	0.000 (0.0, 0.0)	.348
Infertility	Yes	24 (46.15)	118 (49.17)	.694
Number of prior uterine surgery		2.000 (1.0, 3.0)	1.000 (1.0, 2.0)	.009[b]
Combined endometrial polyps	Yes	1 (1.92)	21 (8.75)	.161
Combined uterine Fibroids	Yes	10 (19.23)	24 (10.00)	.06
Combined ovarian cysts	Yes	1 (1.92)	12 (5.00)	.546
History of hysteroscopic endometrial Polypectomy	Yes	2 (3.85)	13 (5.42)	.906
History of hysteroscopic Submucosal myomectomy	Yes	1 (1.92)	2 (0.83)	.446
History of missed abortion D & C	Yes	15 (28.85)	91 (37.92)	.218
History of abortion D & C	Yes	33 (63.46)	118 (49.17)	.061
History of spontaneous abortion D & C	Yes	1 (1.92)	11 (4.58)	.624
Diagnostic curettage	Yes	1 (1.92)	8 (3.33)	.928
History of induced labor D & C	Yes	3 (5.77)	7 (2.92)	.545
History of residue placenta D & C	Yes	1 (1.92)	0 (0.00)	.178
History of hydatidiform mole D & C	Yes	2 (3.85)	3 (1.25)	.218
Preoperative endometrial receptivity typing	A-type	6 (11.54)	53 (22.08)	.099
	B-type	26 (50.00)	124 (51.67)	
	C-type	20 (38.46)	63 (26.25)	
Preoperative endometrial thickness (cm)		0.400 (0.3, 0.5)	0.500 (0.4, 0.6)	.017[a]
Preoperative endometrial volume (mL)		1.295 (0.8, 2.0)	1.600 (1.0, 2.1)	.047[a]
Preoperative uterine artery resistance index RI (right side)		0.830 (0.8, 0.9)	0.840 (0.8, 0.9)	.138
Preoperative uterine artery resistance index RI (left side)		0.840 (0.8, 0.9)	0.840 (0.8, 0.9)	.99
Preoperative uterine artery pulsatility index PI (right side)		2.23 ± 0.52	2.33 ± 0.58	.244
Preoperative uterine artery pulsatility index PI (left side)		2.38 ± 0.51	2.37 ± 0.57	.91
AMH (ng/mL)		2.710 (1.9, 5.6)	3.210 (1.9, 5.8)	.729
Preoperative AFS classification	Moderate	16 (30.77)	211 (87.92)	0[b]
	Severe	36 (69.23)	29 (12.08)	
Presence of CE	Yes	41 (78.85)	31 (12.92)	0[b]
Reapplication of intrauterine adhesion barrier gel 5 days after TCRA	Yes	2 (3.85)	37 (15.42)	.026[a]
Preoperative estrogen treatment	Yes	15 (28.85)	34 (14.17)	.010[a]

AFS, American Fertility Society, AMH, anti-müllerian hormone; BMI, body mass index; CE, chronic endometritis; D & C, dilation and curettage, IUA, intrauterine adhesions; PI, pulsatility index; RI, resistance index; TCRA, transcervical resection of adhesions.
[a] $P < .05$.
[b] $P < .01$.

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times higher than in those with moderate IUA. The risk of re-adhesion formation in IUA patients with CE was 26.5 times higher than in those without CE. The risk of re-adhesion formation with intrauterine adhesion barrier gel reapplication 5 days after TCRA was 0.2 times higher than in those without gel reapplication (Table 4).

Establishment and validation of an alignment diagram prediction model for postoperative re-adhesion in patients with IUA

The independent variables identified in the multifactorial analysis were incorporated into the prediction model constructed using R software. The model included 3 variables: preoperative AFS classification, IUA and CE co-occurrence, and intrauterine adhesion barrier gel reapplication 5 days after TCRA, the values of which were entered to obtain the corresponding scores in the first row. The corresponding probability of re-adhesion after TCRA was obtained by calculating the total score. The C-indices of the 3 variables that individually predicted postoperative re-adhesion in patients with IUA and CE, intrauterine adhesion barrier gel reapplication 5 days after TCRA, and preoperative AFS classification were 0.830, 0.558, and 0.78, respectively. This result showed that the generated nomogram model significantly improved prediction accuracy (Supplemental Fig. 1A, available online).

According to the ROC analysis results, the area under the curve of the alignment diagram for predicting re-adhesion in a patient after TCRA was 0.914 (95% confidence interval [CI]: 0.864–0.956), indicating better predictive ability of the model (Supplemental Fig. 1B). The bootstrap method was subsequently used to resample the scoring system 1,000 times for internal validation. The results showed that the C-index of the internal validation was 0.9135, and the calibration curve fitted well with the ideal curve, indicating that the scoring system was stable (Supplemental Fig. 1C).

DISCUSSION

Since Asherman's first systematic report on IUA in 1948, there has been a gradually increasing interest in the importance of IUA. The detection rate of IUA has increased with the introduction of noninvasive examination methods such as uterine ultrasonography and the widespread use of hysteroscopy (16). Schenker et al. (17) demonstrated that abortion curettage, missed abortion D&C, diagnostic curettage, uterine artery embolism, endometrial tuberculosis infection, and IUD placement were closely associated with IUA development in 1,856 IUA cases, among which abortion curettage was the most prevalent cause of IUA. The traditional method of separating IUAs using instruments, such as dilation rods, probes, and biopsy forceps, increases the risk of uterine perforation, myometrial wall damage, and uterine cavity "false channel formation" due to the blind surgical procedure. Hysteroscopy allows the visualization of the entire uterine cavity and clarifies the location, extent, and nature of adhesions, uterine horns, and tubal ostiums, avoiding blind procedures and improving the treatment effect and surgical safety (4). Therefore, TCRA is the first-line treatment for IUA; however, the incidence of re-adhesion formation after TCRA remains high (3.1%–23.5%), especially severe adhesions (20%–62.5%) (4). Meanwhile, the results of this study showed that approximately 2 months after TCRA, 52 (17.81%) of 292 patients with IUA had postoperative re-adhesion, indicating that the incidence of postoperative re-adhesion requires reduction. Moreover, there is no expert consensus on a systematic treatment plan to prevent intrauterine re-adhesion. Therefore, the factors causing postoperative re-adhesion in patients with IUA should be investigated, and a systematic treatment plan should be developed. Two hundred ninety-two patients with moderate to severe IUA were enrolled between June 2018 and June 2022 and underwent TCRA with concomitant endometrial biopsy, first-time injection of intrauterine adhesion barrier gel, and indwelling intrauterine balloon tube during the procedure. Postoperatively, the patients were administered secondary intrauterine adhesion barrier gel, intrauterine balloon dilatation, early second-look hysteroscopy, and sequential estrogen-progesterone treatment. This systematic and comprehensive management improved treatment and reproductive outcomes.

The formation time of postoperative re-adhesion is 5 to 7 days (18). The AAGL (1) recommends IUA barrier gel for IUA treatment. Therefore, we initially employed the barrier gel intraoperatively to prevent adhesions. However, current studies rarely mention the timing of IUA barrier gel application. Since IUA barrier gel starts to degrade after 7 days and is completely degraded and absorbed after 14 days, we reapplied this gel treatment while removing the intraoperative indwelling intrauterine balloon tube 5 days postoperatively, aiming to reduce the risk of re-adhesion formation. Our results also confirmed that the risk of re-adhesion formation with IUA barrier gel reapplication 5 days after TCRA was 0.2 times higher compared with not reapplication. The reapplication of IUA barrier gel 5 days after surgery was negatively correlated with intrauterine re-adhesion formation. However, in the current study, we reapplied IUA barrier gel at only one time point. We consider this a limitation, and further in-depth research on reapplication time points is warranted in the future.

The safety and efficacy of intrauterine balloon dilatation are crucial in preventing recurrent IUAs after TCRA to reduce the area, probability, and duration of traumatic contact, controlling factors that promote adhesion occurrence. Meanwhile, given the time it takes for postoperative re-adhesion formation, our patients underwent intrauterine balloon dilatation on postoperative day 10 to bluntly separate fresh loose adhesions in the cavity and lower segments of the uterus and prevent the formation of dense and muscular adhesions. The intervention area expansion achieved at this stage extends the time for endometrial repair, improving postoperative adhesion control, uterine cavity recovery, endometrial repair, and menstrual cycle (8).

Although intrauterine balloon dilatation can prevent the wound from adhering to each other through the barrier effect, the uterine cavity cannot be visualized. In addition, owing to the shape of the Foley catheter, adhesion recurrence at the uterine horns could not be prevented. Therefore, we conducted early office hysteroscopy 20 days postoperatively. Patients were treated for 2–3 cycles in the described order. Patients were administered sequential estrogen-progesterone treatment immediately after TCRA to promote endometrial repair.

The AFS classification score demonstrates IUA prognosis and has been shown to directly influence conception and lead to different pregnancy outcomes (19, 20). The study found a significant decrease in postoperative AFS scores and improvement in menstrual flow in 188 of 292 patients, consistent with previous reports (14, 19, 20). The study also reported a significant increase in postoperative menstrual

TABLE 4

Logistic regression analysis of factors influencing postoperative re-adhesion in patients with IUA.

	P	OR	(95% CI)
Preoperative AFS classification	0	11.8	4.68–29.73
Presence of CE	0	26.5	10.51–66.73
Reapplication of autocrosslinked hyaluronic acid gel 5 days after TCRA	.035	0.2	0.04–0.89

AFS, American Fertility Society; IUA, intrauterine adhesions; TCRA, transcervical resection of adhesions; CE, chronic endometritis; OR, odds ratio, CI, confidence interval.

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volume VAS scores, indicating that the proposed systemic treatment regimen enhances IUA prognosis.

We successfully followed up on 220 patients with IUA and assessed their reproductive outcomes; the postoperative clinical pregnancy rate was 51.8%. The live birth rate was 74.6%, with a full-term live birth rate of 60.5% and a preterm birth rate of 14.0%. However, clinicians should pay more attention to the fact that damage to the basal layer of the endometrium, inadequate endometrial blood supply, and deformation or volume reduction of the uterine cavity caused by IUAs present a risk for postpregnancy comorbidities in patients with IUA, such as placental implantation abnormalities, postpartum hemorrhage, and other serious obstetric complications. The results of this study showed that the incidence rates of placenta adherence and postpartum hemorrhage were 29.4% and 11.8%, respectively. These values were higher than the 10.1% and 11.4% incidence rates reported previously (21). The high preoperative AFS scores 8 (7,8) of the participants in this study suggest that adhesions were more severe, which may be the reason for a higher incidence of obstetric complications.

The multifactorial logistic regression analysis results of the present study showed that a major risk factor influencing re-adhesion after TCRA was IUA severity at first detection. Valle and Sciarra (22) reported that the recurrence rate after TCRA was 62.5%, whereas the present study demonstrated that the risk of re-adhesion formation was 11.8 times higher in patients with severe IUA than in those with moderate IUA. Patients with severe IUA initially have significantly scarred endometrium. The TCRA removes existing scar tissue; however, it does not affect the fibrosis-promoting mechanism that sets off after endometrial damage. Therefore, patients with severe IUA at initial examination are at a higher risk of postoperative re-adhesion (23, 24).

Furthermore, this study revealed that the combination of CE in patients with IUA was a risk factor for re-adhesion (odds ratio 26.481, $P<.05$). There was a positive correlation between CE and IUA in patients with IUA. Liu et al. (25) found that the expression of uterine transforming growth factor $\beta 1$ (which promotes fibrosis and inhibits extracellular matrix degradation) was elevated in the endometrium of patients with IUA and CE, whereas the expression of matrix metalloproteinase 9, which stabilizes fibrosis, was reduced. The risk of re-adhesion may be higher in patients with IUA. Routine endometrial biopsy during TCRA is recommended to diagnose CE as early as possible to standardize the treatment of patients with IUA and CE.

Despite extensive research, the nomogram model is rarely utilized in clinical practice. This model visualizes the results of multifactorial logistic regression and displays the relative significance of each factor in the form of scores that are convenient to calculate and easy to understand. We constructed an alignment diagram prediction model for postoperative re-adhesion in patients with IUA on the basis of multifactorial analysis and validated the results of the nomogram model with ROC analysis and bootstrap method. This approach confirmed the high predictive accuracy and discriminability of the column chart model. Presenting the nomogram to the patients, helps them to visualize the risk factors for re-adhesion and their degree of significance, thus improving their understanding of the disease and the importance of treatment adherence.

CONCLUSION

The IUA prognosis after TCRA is related to severe preoperative IUA, presence of CE, and IUA barrier gel reapplication 5 days after TCRA. Patients with moderate to severe IUA should undergo precise surgery and long-term management, including IUA barrier gel reapplication 5 days after TCRA, intrauterine balloon dilatation, early second-look hysteroscopy, and sequential estrogen-progesterone treatment. In addition, this study notes that in nonexperimental studies, the decision to use IUA barrier gel may be influenced by a variety of factors. Although the model in this study considered several key factors, there may still be unmeasured confounding factors (such as the hospital's geographical location and the patients' demographic characteristics). Therefore, although the predictive model in this study performed well in assessing the risk of patient re-adhesion, it is not directly useful for causal reasoning. The inference of causality requires caution, and the influence of confounding factors should be fully controlled. Moreover, this study has certain limitations, being a single center study. Multicenter prospective studies conducted in future would allow in-depth analysis of the multiple factors that affect the prognosis of IUA patients after TCRA.

CRediT Authorship Contribution Statement

Jiantong Zhang: Writing – original draft, Writing – review & editing, Investigation, Sata curation. **Cong Shi:** Conceptualization, Methodology. **Jianhua Sun:** Supervision, Conceptualization. **Jumin Niu:** Conceptualization, Methodology, Writing – review & editing, Supervision.

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Declaration of Interests

J.Z. has nothing to disclose. C.S. has nothing to disclose. J.S. has nothing to disclose. J.N. has nothing to disclose.

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