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Original Article

Long-term effects of hysteroscopic adhesiolysis on postoperative pregnancy rates and fertility outcomes in patients with intrauterine adhesions

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Abstract: Objective: To investigate the long-term effects of hysteroscopic adhesiolysis on postoperative pregnancy rates and fertility outcomes in patients with intrauterine adhesions (IUA). Methods: A retrospective analysis was conducted on 105 patients with IUA treated at Baoji Maternal and Child Health Hospital from June 2022 to December 2023. All patients underwent hysteroscopic adhesiolysis. Based on the adjunctive treatment, patients were divided into two groups: the observation group (n=55), which received adhesiolysis plus balloon uterine stent placement, and the control group (n=50), which received adhesiolysis alone. We compared clinical efficacy, changes in endometrial thickness, menstrual volume, and serum estrogen levels, including estrogen receptor (ER) and progesterone receptor (PR) levels, between the two groups. Additionally, we recorded and compared the 3-month postoperative recurrence rate of IUA, pregnancy rates and outcomes, and complications. The predictive value of ER and PR levels for postoperative pregnancy was also analyzed. We then compared the general data of patients who became pregnant after surgery with those who did not, and used multivariate logistic regression to analyze the factors influencing postoperative non-pregnancy. Results: The overall treatment efficacy was significantly higher in the observation group than in the control group (P<0.05). The observation group showed significantly greater improvements in endometrial thickness, menstrual volume, and serum estrogen levels compared to the control group (all P<0.05). The recurrence rate of adhesions during follow-up was significantly lower in the observation group than in the control group (P<0.05). The postoperative pregnancy rates and fertility outcomes were also significantly better in the observation group (both P<0.05). The sensitivity and specificity of ER levels in predicting postoperative pregnancy were 78.05% and 70.31%, respectively, with an AUC of 0.788. For PR levels, the sensitivity was 75.61%, specificity was 71.88%, and AUC was 0.834. Multivariate regression analysis indicated that age, adhesion severity, adhesion recurrence, and the use of a balloon uterine stent were independent risk factors affecting postoperative pregnancy in patients with IUA (P<0.05). Conclusion: The combination of adhesiolysis and intrauterine balloon stent placement in patients with moderate to severe intrauterine adhesions significantly IUA increases endometrial thickness and volume, promotes menstrual recovery, prevents re-adhesion, and improves pregnancy outcomes. This approach is recommended for clinical application.

Keywords: Hysteroscopy, adhesiolysis, postoperative pregnancy rate, fertility outcomes

Introduction

Intrauterine adhesions (IUA), a prevalent gynecological disorder stemming from uterine basal layer damage or infection, manifest as menstrual irregularities and abdominal pain, significantly impacting patients' daily lives and well-being [1, 2]. The escalating rate of induced abortions in recent times has contributed to an increase in IUA cases [3]. Notably, patients undergoing hysteroscopic adhesiolysis for IUA often face suboptimal pregnancy and live birth rates, hovering around 50-60% [4], unders coring the urgency to enhance postoperative pregnancy outcomes and mitigate adverse effects.

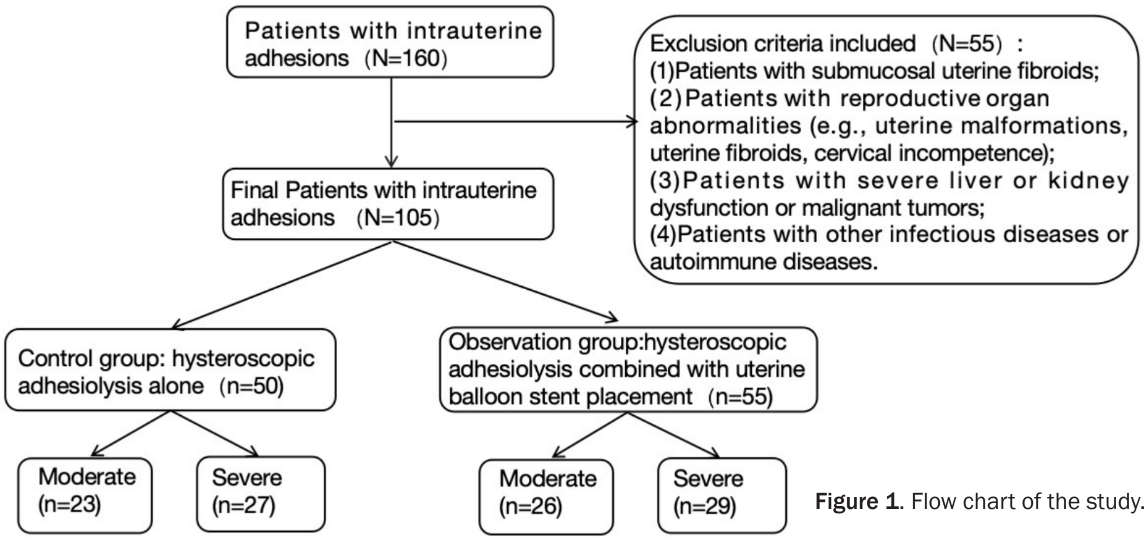

Figure 1. Flow chart of the study.

The gold standard treatment for IUA, hysteroscopic adhesiolysis, improves uterine cavity morphology, alleviates symptoms, and fosters endometrial regeneration [5]. However, a substantial risk of postoperative re-adhesion persists, reaching as high as 62.5% in moderate to severe cases, compromising surgical success and prognosis [6, 7]. Thus, preventing recurrent adhesions remains a pivotal challenge. Intrauterine devices, traditionally used post-surgery, have shown limited efficacy in this regard [8]. Alternatively, uterine balloon stents, widely employed for postpartum hemorrhage control, exhibit advantages including user-friendliness, rapid hemostasis, and proven safety and effectiveness [9].

Despite this, there is a notable lack of comprehensive research exploring the impact of combining hysteroscopic adhesiolysis with uterine balloon stent placement on postoperative pregnancy rates, fertility outcomes, and re-adhesion prevention in IUA patients. This study endeavors to evaluate the long-term benefits of this combined approach in enhancing postoperative pregnancy and fertility rates, while assessing its efficacy in preventing recurrent adhesions.

Materials and methods

Clinical data

A retrospective analysis was conducted on 105 patients with IUA treated at Baoji Maternal and Child Health Hospital from June 2022 to December 2023. All patients underwent hysteroscopic adhesiolysis. Based on the adjuvant treatment method, patients were divided into two groups: the observation group (55 cases, hysteroscopic adhesiolysis combined with uterine balloon stent placement) and the control group (50 cases, hysteroscopic adhesiolysis alone).

Inclusion Criteria: (1) Patients diagnosed with IUA based on comprehensive examinations [10]; (2) Patients without contraindications for intrauterine devices and uterine balloon stent placement; (3) Patients with complete clinical data.

Exclusion Criteria: (1) Patients with submucosal uterine fibroids; (2) Patients with reproductive organ abnormalities (e.g., uterine malformations, uterine fibroids, cervical incompetence); (3) Patients with severe liver or kidney dysfunction or malignant tumors; (4) Patients with other infectious diseases or autoimmune diseases.

This study was approved by the ethics committee of Baoji Maternal and Child Health Hospital, adhering to the principles of the Declaration of Helsinki. See **Figure 1** for the flow chart.

Treatment methods

All patients underwent thorough preoperative evaluations, including lower abdominal ultrasound, coagulation profile, hepatitis B surface antigen testing, and electrocardiography, to ensure the absence of contraindications and to finalize the treatment plan. The patients' preoperative status was meticulously assessed, and they were fully informed about the precautions related to transcervical resection of adhesions. Preoperative preparations were carried out, with the surgery scheduled for 5-7 days after the end of menstruation (or any time for amenorrheic patients).

Both groups underwent hysteroscopic adhesiolysis. After bladder evacuation, patients were placed in the lithotomy position and received either general intravenous anesthesia or combined spinal-epidural anesthesia. A speculum was used to expose the cervix, followed by the gradual dilation of the cervix and uterine cavity using a uterine probe and dilators. A hysteroscope was then introduced through the cervical canal to inspect the uterine cavity, allowing for the visualization and assessment of adhesion tissue, including its location and extent. Bipolar needle electrodes were used to excise the adhesion scar tissue. In the observation group, a disposable uterine balloon stent (JBUS-404000, USA) was placed in the uterine cavity postoperatively. The uterine balloon was initially inflated with 2-3 ml of saline. Daily, 8-10 ml of saline was rapidly injected and immediately withdrawn, leaving 2-3 ml in the balloon to prevent adhesions and dislodgement. The stent was removed after 5-7 days. Starting from the first postoperative day, patients were administered oral estradiol valerate tablets at a dosage of 2-4 mg twice daily for 21 days, followed by dydrogesterone at 10 mg twice daily for the next 10 days, resulting in a total treatment duration of 3 months. Hysteroscopy was performed after the first and third withdrawal bleeds to monitor the condition.

Outcome measures

(1) Overall Treatment Effectiveness at 3 Months Postoperatively: The effectiveness of treatment in both groups was evaluated and compared at 3 months post-surgery, categorized as follows:

Markedly Effective: Menstruation nearly returned to normal, ultrasound showed significant endometrial thickening and normalcy, and no recurrence of IUA.

Effective: Significant improvement in menstruation compared to before, ultrasound showed endometrial thickening, and no recurrence of IUA.

Ineffective: Menstruation remained irregular, ultrasound showed no endometrial thickening, or recurrence of IUA was observed.

(2) Endometrial Thickness and Menstrual Volume Changes: The changes in endometrial thickness and menstrual volume before and after treatment in both groups were recorded and compared.

(3) Serum Estrogen Levels: Immunohistochemistry was used to detect and compare the serum estrogen levels of the two groups of patients before and after treatment, including estrogen receptor (ER) and progesterone receptor (PR) levels [11].

(4) Recurrent IUA: The incidence of recurrent IUA at 3 months post-surgery was recorded and compared between the two groups.

(5) Pregnancy Rates and Outcomes: The pregnancy rates and fertility outcomes after surgery for IUA were recorded and compared between the two groups through telephone or outpatient follow-up.

(6) Incidence of Complications: Over a follow-up period of 3 months, the incidence of complications such as organ damage, infection, and hyponatremia was recorded and compared between the two groups.

(7) Analysis of General Data in Pregnant vs. Non-Pregnant Patients Post-Surgery: A comparative analysis of general data between patients who became pregnant and those who did not post-surgery was conducted. Multivariate logistic regression was used to analyze factors influencing non-pregnancy after surgery.

Statistical analysis

SPSS 20.0 statistical software was used for data analysis. The sample size was calculated using the formula $N=Z^2 \times (P \times (1-P))/E$, where Z is the confidence interval, P is the prevalence rate, E is the sampling error range, and σ is the standard deviation, typically assumed to be 0.5. Quantitative data were expressed as mean ± standard deviation ($\overline{x} \pm sd$), and the t-test was used for comparisons between the two groups. The paired t-test was used for comparisons before and after treatment within the same group. The chi-square (X^2) test was employed for count data. Multivariate logistic regression

Table 1. Comparison of general information

Variable	Observation Group (n=55)	Control Group (n=50)	t/X^2	P
Age (years)			0.003	0.955
≤30	30 (54.55)	27 (54.00)		
>30	25 (45.45)	23 (46.00)		
BMI (kg/m^2)			0.001	0.970
≤23	31 (56.36)	28 (56.00)		
>23	24 (43.64)	22 (44.00)		
Degree of adhesion			0.017	0.896
Moderate	26 (47.27)	23 (46.00)		
Severe	29 (52.73)	27 (54.00)		
Disease duration (months)			0.012	0.911
≤6	28 (50.91)	26 (52.00)		
>6	27 (49.09)	24 (48.00)		
Number of miscarriages			0.036	0.850
≤1	32 (58.18)	30 (60.00)		
>2	23 (41.82)	20 (40.00)		

BMI: Body Mass Index.

Table 2. Comparison of treatment efficacy

Treatment effective	Observation Group (n=55)	Control Group (n=50)	T	P
Markedly effective	30 (54.55)	22 (44.00)	-	-
Effective	23 (41.82)	18 (36.00)	-	-
Ineffective	2 (3.64)	10 (20.00)	-	-
Overall treatment efficacy rate	53 (96.36)	40 (80.00)	6.928	0.009

was used to analyze the risk factors for postoperative non-pregnancy. A *P*-value of less than 0.05 was considered statistically significant.

Results

Comparison of general data

There was no significant difference in age, BMI, or disease duration between the two groups (all P>0.05), indicating that the groups were comparable (**Table 1**).

Comparison of treatment efficacy

Post-treatment evaluation revealed that in the observation group, 30 patients showed markedly effective results, 23 effective results, and 2 ineffective results, resulting in an overall treatment efficacy rate of 96.36%. In the control group, 22 patients had markedly effective results, 18 effective results, and 10 ineffective results, yielding an overall treatment efficacy rate of 80.00%. The treatment efficacy rate in the observation group was significantly higher than in the control group, with a statistically significant difference (P<0.05) (**Table 2**).

Changes in endometrial thickness and menstrual volume before and after treatment

Both groups successfully completed their respective treatment protocols. No statistically significant differences were observed in endometrial thickness and menstrual volume between the two groups prior to treatment (both P>0.05). Post-treatment, both groups exhibited increased endometrial thickness and menstrual volume compared to pre-treatment levels (both P<0.05). The observation group demonstrated significantly greater improvements in these parameters compared to the control group, with the differences being statistically significant (both P<0.05) (**Figure 2**).

Comparison of serum estrogen levels

Before treatment, there were no significant differences in ER and PR levels between the two groups (both P>0.05). After treatment, ER and

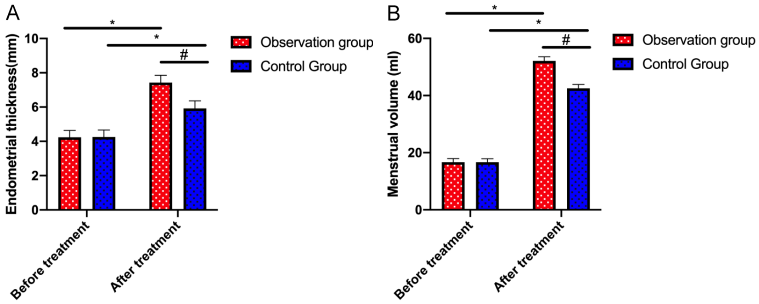

Figure 2. Changes in endometrial thickness and menstrual volume before and after treatment in both groups. A: Changes in endometrial thickness before and after treatment in both groups. B: Changes in menstrual volume before and after treatment. Note: * indicates a significant difference within the group before and after treatment (P<0.05); # indicates a significant difference between the groups after treatment (P<0.05).

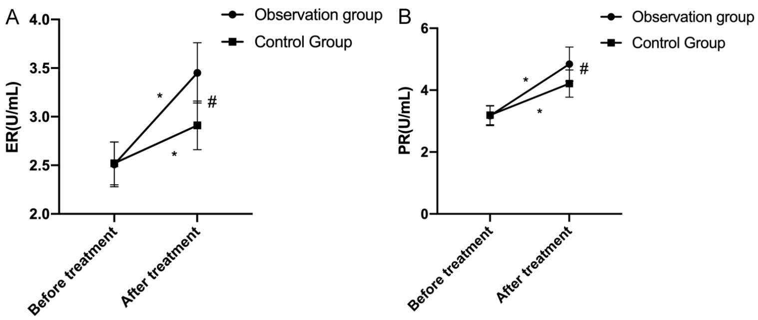

Figure 3. Comparison of serum estrogen levels. A: Comparison of serum ER between the two groups before and after treatment. B: Comparison of serum PR between the two groups before and after treatment. Note: * indicates P<0.05 for comparison before and after treatment within the group; # indicates P<0.05 for comparison between groups after treatment. ER: Estrogen receptor; PR: progesterone receptor.

PR levels significantly improved in both groups compared to pre-treatment levels, with the improvement in the observation group being more pronounced than in the control group (both P<0.05) (**Figure 3**).

Comparison of the incidence of intrauterine re-adhesion

The incidence of re-adhesion in the observation group was 12.73%, significantly lower than the 36.00% incidence in the control group, with a statistically significant difference (P<0.05) (**Table 3**).

Postoperative pregnancy rates and fertility outcomes

All 105 patients completed follow-up. Among them, 65 became pregnant postoperatively, resulting in an overall pregnancy rate of 61.90%. Specifically, in the observation group, 42 patients conceived, boasting a pregnancy rate of 76.36%. Among these pregnancies, 35 resulted in successful deliveries, whereas 7 ended in miscarriages, yielding a miscarriage rate of 16.67%. Conversely, in the control group, only 23 patients became pregnant, with a pregnancy rate of 46%. Out of these pregnancies, 14 were successful deliveries, and 9 were miscarriages, resulting in a notably higher miscarriage rate of 39.13%. Statistical analysis revealed that the postoperative pregnancy rate in the observation group was significantly elevated compared to the control group (P=0.001), while the miscarriage rate was significantly reduced (P=0.044) (**Table 4**).

Analysis of the predictive value of ER and PR levels for postoperative pregnancy

ROC analysis of postoperative ER and PR levels revealed that these levels are valuable predictors of postoperative pregnancy. The sensitivity and specificity of ER for predicting postoperative pregnancy were 78.05% and 70.31%, respectively, with an AUC of 0.788. For PR, the sensitivity was 75.61%, the specificity was 71.88%, and the AUC was 0.834 (**Figure 4**).

Comparison of complication rates

After treatment, the incidence of organ damage, infection, and hyponatremia in the observation group was 1, 1, and 0, respectively, with an overall adverse reaction rate of 3.64%. In contrast, the control group exhibited 3 cases of organ damage, 3 of infection, and 2 of hyponatremia, with an overall adverse reaction rate of 18.00%. The adverse reaction rate in the observation group was significantly lower than in the control group (P<0.05) (**Table 5**).

Table 3. Comparison of the incidence of intrauterine re-adhesion

Re-adhesion	Observation Group (n=55)	Control Group (n=50)	T	P
Mild	5 (9.09)	10 (20.00)	-	-
Moderate	2 (3.64)	5 (10.00)		
Severe	0	3 (6.00)	-	-
Incidence of re-adhesion	7 (12.73)	18 (36.00)	7.820	0.005

Table 4. Postoperative pregnancy rates and fertility outcomes

Pregnancy	Observation Group (n=55)	Control Group (n=50)	T	P
Postoperative pregnancy rate	42 (76.36)	23 (46.00)	10.242	0.001
Successful delivery rate	35 (83.33)	14 (60.87)	4.041	0.044
Miscarriage rate	7 (16.67)	9 (39.13)	4.041	0.044

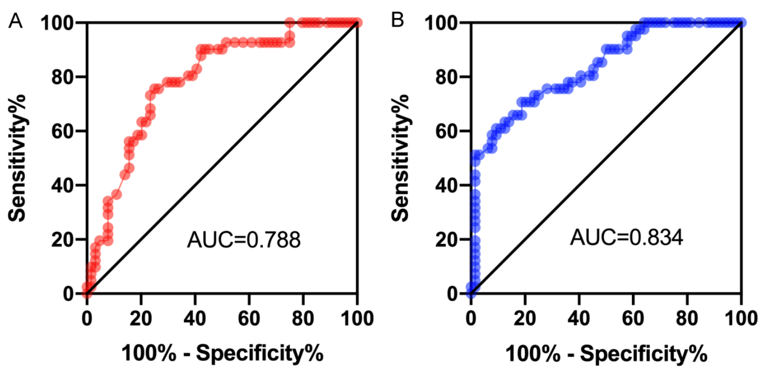

Figure 4. Analysis of the predictive value of ER and PR levels for postoperative pregnancy. A: ROC of ER level for predicting postoperative pregnancy. B: ROC of PR level for predicting postoperative pregnancy. Note: ER: Estrogen receptor; PR: progesterone receptor.

Logistic regression analysis of factors influencing postoperative non-pregnancy

Compared to non-pregnant patients, pregnant patients were younger, had milder adhesion severity, no recurrence, and had undergone balloon stent insertion; all these differences were statistically significant (P<0.05), as shown in **Table 6**. The five variables with statistically significant differences were included in the multivariate logistic regression analysis. It indicated that age, adhesion severity, adhesion recurrence, and the use of balloon stent insertion were independent risk factors affecting pregnancy after intrauterine adhesion surgery (**Table 7**).

Discussion

IUA, a prevalent gynecological issue primarily triggered by repeated abortions or curettage, have emerged as a significant contributor to infertility, with severe cases leading to reduced pregnancy rates, accounting for 4.8% to 22.0% of infertility cases [12, 13]. Clinically, transcervical resection of adhesions forms a cornerstone in the management of IUA, yet the recurrence of adhesions remains a formidable challenge.

Our study investigated the long-term impact of combining hysteroscopic adhesiolysis with a balloon uterine stent on postoperative pregnancy rates, reproductive outcomes, and IUA recurrence in patients. The results underscored the superiority of this combined approach over hysteroscopic adhesiolysis alone. Patients in the observation group, who received the combined treatment, exhibited significantly improved endometrial thickness, menstrual volume, lower re-adhesion rates, and fewer complications compared to the control group. The effectiveness of the balloon uterine stent can be attributed to its ability to create a supportive environment within the uterine cavity, facilitating new tissue growth and mitigating the risk of re-adhesion [14-16]. By conforming to the uterine cavity's morphology and minimizing local tissue irritation, the silicone stent promotes optimal healing and reduces inflammatory responses [17, 18]. This is consistent with previous research [19], reinforcing the safety, reliability, and efficacy of the balloon stent in reducing re-adhesion rates.

Table 5. Comparison of adverse reaction rates [n, (%)]

Adverse reactions	Observation Group (n=55)	Control Group (n=50)	X^2	P
Organ damage	1 (1.82)	3 (6.00)	-	-
Infection	1 (1.82)	3 (6.00)	-	-
Hyponatremia	0	3 (6.00)	-	-
Incidence of adverse reactions	2 (3.64)	9 (18.00)	5.761	0.016

Table 6. Univariate analysis

Factor	Pregnant group (n=65)	Non-pregnant group (n=40)	X^2	P
Age (years)			5.36	<0.001
≤30 (n=57)	45 (69.23)	12 (30.00)		
>30 (n=48)	20 (30.77)	28 (70.00)		
Disease duration (months)			0.399	0.528
≤6 (n=54)	35 (53.85)	19 (47.50)		
>6 (n=51)	30 (46.15)	21 (52.50)		
Degree of adhesion			7.212	0.007
Moderate (n=49)	37 (56.92)	12 (30.00)		
Severe (n=56)	28 (43.08)	28 (70.00)		
Relapse			29.43	<0.001
Yes (n=25)	5 (7.69)	20 (50.00)		
No (n=80)	60 (92.31)	20 (50.00)		
Surgical options			9.823	0.002
Single hysteroscopic adhesiolysis (n=50)	23 (35.94)	27 (67.50)		
Hysteroscopic adhesiolysis combined with balloon uterine stent (n=55)	42 (64.06)	13 (32.50)		
Number of miscarriages			0.438	0.508
≤1 (n=62)	40 (61.54)	22 (55.00)		
>2 (n=43)	25 (38.46)	18 (45.00)		

Table 7. Multivariate logistic regression analysis

Factor	B	S.E.	Wals	P	OR	95% C.I.	
						Lower limit	Upper limit
Age (years)	0.241	0.912	3.557	0.021	1.134	1.143	6.855
Relapse	0.218	0.681	2.529	0.004	1.672	1.231	8.295
Surgical options	0.311	0.862	4.923	0.011	1.313	1.282	7.196
Degree of adhesion	0.355	0.764	2.791	0.013	1.552	1.155	7.721

Endometrial regeneration and restoration are crucial for fertility, often compromised by IUA and inflammation, further exacerbated by hysteroscopic procedures [20]. While earlier studies [21] reported modest increases in pregnancy and live birth rates post-hysteroscopy. Based on our findings, we further investigated the influence of incorporating a balloon uterine stent during hysteroscopic adhesiolysis on pregnancy rates and outcomes between the two groups. Results indicated a significantly higher postoperative pregnancy rate of 76.36% in the observation group compared to 46% in the control group. This is likely attributed to the balloon's larger surface area, effectively isolating the uterine wound from the myometrium. By maintaining the balloon for a week postoperatively, it acts as a mechanical barrier, separating the uterine lateral walls, facilitating endometrial repair and proliferation along its surface. This enhances fluid drainage, improves IUA conditions, and promotes menstrual normalization, ultimately leading to earlier return to normalcy and increased pregnancy rates [22, 23]. Consistent with previous studies [24], we observed that adhesion separation combined with uterine balloon stent placement significantly outperforms adhesion separation with an intrauterine contraceptive device in terms of pregnancy rates.

To gain insights into factors influencing postoperative pregnancy, we conducted a detailed analysis. Univariate analysis revealed significant associations between age, adhesion severity, recurrence, postoperative menstruation, and balloon stent use with pregnancy outcomes. Multivariate logistic regression further identified age, adhesion severity, postoperative menstruation, and balloon stent use as independent risk factors. These findings align with prior research that also recognizes age, adhesion severity, and postoperative menstruation as crucial determinants of post-IUA surgery pregnancy outcomes [25-27]. Notably, younger patients exhibited superior recovery, self-healing abilities, and ovarian function, contributing to higher pregnancy rates. Conversely, severe adhesions correlated inversely with pregnancy rates. Overall, our study has a few areas for improvement. The small sample size may compromise the stability of our conclusions, necessitating larger, multi-center studies for further validation. Moreover, long-term prognosis and post-pregnancy recurrence rates were not analyzed, which should be addressed in future research.

In conclusion, the combined approach of adhesion separation and uterine balloon stent placement for moderate to severe IUA patients undergoing hysteroscopic adhesiolysis effectively enhances endometrial thickness and volume, promotes menstrual recovery, prevents adhesion recurrence, and improves pregnancy outcomes. This strategy merits clinical promotion.

Disclosure of conflict of interest

None.

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