

# Postoperative reproductive results of infertile patients with intrauterine adhesions: A retrospective analysis

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#### Abstract

**Objective:** To explore the reproductive outcomes after hysteroscopic separation of intrauterine adhesions (IUA) in infertile patients due to IUA.

**Methods:** This retrospective study enrolled patients with fertility requirements and infertility due to IUA. Data were collected from the hospital medical records and by follow-up by telephone. The impact on pregnancy and pregnancy outcome of preoperative adhesion, menstrual conditions before and after surgery and postoperative re-adhesion was analysed.

**Results:** A total of 106 patients (median age, 28 years) were enrolled in the study. There was a significant correlation between preoperative menstrual patterns and pregnancy rate. There were 56 pregnancies (pregnancy rate 52.83%) after the operation. Patients with improved menstruation after the operation had a significantly higher pregnancy rate (pregnancy rate 56.25%; 45 of 80 patients) compared with the patients that did not experience any improvement in their postoperative menstrual status (pregnancy rate 21.43%; three of 14 patients). Of the 56 pregnancies, 40 (71.43%) resulted in live births and six (10.71%) patients had miscarriages. A total of 54 of 56 patients (96.43%) became pregnant within 2 years.

**Conclusion:** Pregnancy after intrauterine adhesion separation has a high rate of miscarriage and obstetric complications, so close monitoring of the patient is required.

#### **Keywords**

Intrauterine adhesions (IUA), infertility, pregnancy outcomes

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## Introduction

Intrauterine adhesion (IUA) refers to a series of clinical symptoms caused by the destruction and adhesion of the endometrium due to various reasons. The main clinical manifestations are amenorrhea, menstrual flow changes and abnormal pregnancy. It is one of the main causes of uterine cavity factors in infertility and miscarriage.<sup>1</sup> With the advent of hysteroscopy, IUA treatment has undergone great changes. Transcervical resection of uterine adhesions (TCRA) has become the first choice for the treatment of IUA.<sup>2</sup> Hysteroscopy is the main method for diagnosis, treatment and follow-up of patients with IUA.<sup>3</sup> In recent years, there have been many articles on the analysis of the reproductive results after the treatment of IUA.4-7This current study analysed the clinical data from patients with infertility caused by IUA and their reproductive outcomes were determined by telephone interviews in order to determine the relevance of menstrual factors, pregnancy rates and pregnancy outcomes.

### **Patients and methods**

#### Study population

This retrospective study enrolled consecutive patients with fertility requirements and infertility due to IUA that were admitted to Department of Gynaecology, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics, Gynaecology and Paediatrics, Fuiian Medical University, Fuzhou, Fuiian Province, China between January 2017 and June 2021. The inclusion criteria were as follows: (i) IUA was diagnosed under hysteroscopy; (ii) comprehensive infertility examinations had been completed, including fallopian tube patency examination, gynaecological B-ultrasound examination, husband semen examination and female hormone levels (luteinizing hormone, follicle stimulating hormone, oestradiol, prolactin, progesterone, testosterone) on days 2–3 of the menstrual cycle or in patients with amenorrhea at any time). The exclusion criteria were as follows: (i) any participants in whom abnormal results in the fertility work-up were recorded except for the presence of IUA.

The participants were informed of the purpose and procedures of the study. All participants provided written informed consent. The study protocol was checked by the Institutional Review Board of Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian Province, China and received their exemption. All patient information was de-identified. The reporting of this study conforms to STROBE guidelines.<sup>8</sup>

#### Surgical treatment

*Instruments.* A German Storz 0° hysteroscope (KARL STORZ Endoskope Berlin GmbH, Berlin, Germany) was used and it included the following: sheath diameter 8.5 mm cut mirror; needle; spherical and 90 degree ring electrodes; continuous perfusion uterine dilation instrument; German Storz TV laparoscope and camera system (KARL STORZ Endoskope Berlin GmbH). The type of ring used in this study was a round intrauterine device (Wuxi Tianyi Medical Equipment, Wuxi, China). The type of tube used in this study was a disposable hysterography water tube (Zhanjiang Shi da Industrial, Zhanjiang, China).

**Preoperative** preparation. Non-amenorrhea patients were operated on 3–7 days after menstruation and for those with amenorrhea surgery was performed at any time. None of the patients were pregnant. At the same time, a laparoscopic exploration was performed. There were no contraindications to surgery for blood tests, vaginal preparations and cardiopulmonary function tests before surgery. Cefmetazole was given 30 min before the operation to prevent infection and general anaesthesia was performed during the operation with tracheal intubation.

Surgical operations. The TCRA operators were trained in hysteroscopy. In general, during the operation, the patients with moderate adhesions would have circular rings placed in the uterine cavity according to the depth of the patient's uterine cavity. Patients with severe adhesions would have a double-lumen ring placed in uterine cavity. In addition, patients with mild adhesions would have nothing placed. Intrauterine adhesions were graded according to the American Fertility Society classification of intrauterine adhesions (Table 1).<sup>9</sup>

Postoperative adjuvant treatment. Postoperative adjuvant treatment was undertaken to prevent infection for 48 h after surgery. The double-lumen tube was taken out 1 week later. Patients that did not need a second hysteroscopy were instructed to take combined oestradiol tablets/oestradiol and dydrogesterone for one cycle as follows: for a total of one menstrual cycle, starting on the third day of menstruation, 2 mg/day oestrogen orally for 28 days and during the last 14 days of the cycle 10 mg dydrogesterone once daily orally. Then these patients attempted to get pregnant in the next month. Patients that needed a second hysteroscopy were instructed to take combined oestradiol tablets/oestradiol and dydrogesterone for three cycles as follows: for a total of three menstrual cycles, each cycle starting on the third day of menstruation, 2 mg/ day oestrogen orally for 28 days and during the last 14 days of the cycle 10 mg dydrogesterone once daily orally. These patients then underwent a second hysteroscopy and ring removal on days 3-7 of the third menstrual cycle after the first surgery. Wellrecovered patients attempted to get pregnant in the next month.

**Postoperative follow-up.** Patients with mild and severe adhesions returned to the hospital for hysteroscopy 1 month after surgery. Most patients with mild adhesions can prepare for pregnancy in the next month after re-examination. Some patients with severe adhesions underwent intrauterine adhesion separation surgery again and the use of postoperative medication and pregnancy preparation were guided according to the adhesion situation. Patients with moderate adhesions returned to the hospital for a review of the hysteroscopy and a ring was taken off in the 3rd month after surgery. Patients were followed up for 2–36

Characteristic	Scoring system			
Affected area	<1/3	1/3 to 2/3	>2/3	
	I	2	4	
Adhesions	Filmy	Filmy and dense	Dense	
	Í Í	2	4	
Menstrual pattern	Normal	Hypomenorrhoea	Amenorrhoea	
·	0	2	4	
Stage of adhesion				
Stage I (mild)	1-4			
Stage II (moderate)	5–8			
Stage III (severe)	9–12			

Table 1. The American Fertility Society classification of intrauterine adhesions.<sup>9</sup>

months after the separation of intrauterine adhesions so that menstrual changes before and after the operation, pregnancy status and pregnancy outcome could be monitored. Postoperative follow-up was undertaken by members of the healthcare team via telephone and social media contacts.

#### Statistical analyses

All statistical analyses were performed using the SPSS<sup>®</sup> statistical package, version 17.0 (SPSS Inc., Chicago, IL, USA) for Windows<sup>®</sup>. Continuous data are presented as mean  $\pm$  SD and compared between groups using Student's *t*-test. Categorical data are presented as *n* of patients (%) and compared using  $\chi^2$ -test. A *P*-value < 0.05 was considered statistically significant.

#### Results

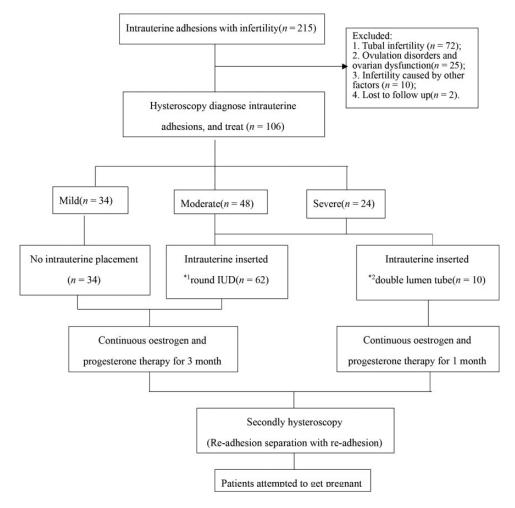
This retrospective study enrolled 106 IUA patients aged 18-42 years (median age, 28 years) (Figure 1). Of these, 23 patients had primary infertility and 83 patients had secondary infertility. There were 34 patients (32.08%) with mild adhesions, 48 (45.28%) with moderate adhesions and 24 (22.64%) with severe adhesions (Table 2; Figure 2). There were 30 patients (28.30%) with preoperative amenorrhoea, 64 (60.38%) with decreased menstruation and 12 (11.32%) had normal menstruation. The mean  $\pm$  SD operation time for patients with mild, moderate and severe intrauterine adhesions was  $20 \pm 5 \min$ .  $28 \pm 6 \min$  and  $31 \pm 3 \min$ . respectively; and the difference was not statistically significant. There was no significant difference in age among the three groups. None of the patients experienced complications during or after the operation.

A total of 80 of 94 patients (85.11%) with preoperative amenorrhea and decreased menstruation had improved menstruation after the operation. Table 3 shows that there was a significant correlation between preoperative menstrual patterns and pregnancy rate (P < 0.05). Patients with preoperative amenorrhea and decreased menstruation that had improved menstruation after the operation had a significantly higher pregnancy rate (pregnancy rate 56.25%; 45 of 80 patients) compared with the 14 patients that did not experience any improvement in their postoperative menstrual status (pregnancy rate 21.43%; three of 14 patients) (P < 0.05).

Postoperative re-adhesion was found in 15 of 106 patients (Table 4). There were 56 pregnancies in total (pregnancy rate 52.83%) after the operation; 52 of 91 patients (pregnancy rate 57.14%) without re-adhesions; and four in 15 patients (pregnancy rate 26.67%) after re-adhesion separation (P=0.048). Patients with mild adhesions had a significantly higher pregnancy rate than patients with moderate or severe adhesions (P = 0.026). Of the 56 pregnancies, 40 (71.43%) resulted in completed live births, six (10.71%) patients had miscarriages, four (7.14%) patients had ectopic pregnancies and six (10.71%) patients were still pregnant. Among the 40 live births, seven (17.50%) were premature, two (5.00%) had placenta previa, six (15.00%) had placental accrete and seven (17.50%) had postpartum haemorrhage. Of the 40 live births, 24 patients underwent caesarean section (caesarean section rate 60.00%). As for the cumulative pregnancy rate after surgery, 40 of 56 patients (71.43%) had a pregnancy within 1 year, 54 of 56 patients (96.43%) had a pregnancy within 2 years and two patients with moderate adhesions had a pregnancy > 2 years after surgery.

#### Discussion

In China, the abortion rate is as high as 0.29%.<sup>10</sup> This rate is close to the rate in Estonia, which has the highest abortion rate (0.30%) in the world.<sup>11</sup>As a consequence of the high abortion rate, IUA is



**Figure 1.** Flow chart showing the enrolment, inclusion and exclusion of patients with intrauterine adhesion (IUA) and infertility that were enrolled in a retrospective analysis of reproductive outcomes after transcervical resection of uterine adhesions. <sup>\*1</sup>Copper material: uterine cavity depth < 6 cm use trumpet, 6–8 cm use medium intrauterine device and > 8 cm use large intrauterine device; <sup>\*2</sup>Double lumen urinary catheter used to inject 5 ml of normal saline into the balloon. A knot was then tied and the end was removed and hidden in the vagina.

common in China.<sup>10</sup> The health of the uterine cavity is closely related to the reproductive success of women. Adhesions in the uterine cavity changes the normal uterine cavity shape, destroys the integrity of the endometrium, affects the intrauterine environment and other aspects, which cause the patient's fertility function to decline.<sup>12</sup> This current retrospective study analysed the reproductive status of 106 patients with

infertility caused by IUA and evaluated their prognosis according to menstrual and pregnancy status.

There are many ways to classify IUA and no one method is universally accepted.<sup>13</sup> All of the patients in this current study were diagnosed and classified using the gold standard of hysteroscopy. The clinical classification was based on the IUA scoring standard of the American Fertility

Characteristic	Patients with IUA and infertility $n = 106$				
Age, years	28 (18–42)				
Degree of adhesions					
Mild	34 (32.08%)				
Moderate	48 (45.28%)				
Severe	24 (22.64%)				
Preoperative menstruation status					
Amenorrhoea	30 (28.30%)				
Decreased menstruation	64 (60.38%)				
Normal menstruation	12 (11.32%)				

Data presented as median (range) or n of patients (%).

Society classification of intrauterine adhesions because it can clearly reflected the severity of the IUA.9 The extent of IUA reflects the degree of endometrial damage and to a certain extent determines the reproduction prognosis.<sup>1</sup> This current study demonstrated that patients with mild adhesions had a significantly higher pregnancy rate than patients with moderate or severe adhesions, which was consistent with a previous study.<sup>1</sup> Abnormal menstruation is the main manifestation of IUA<sup>14</sup> and dysfunctional preoperative menstruation has a negative impact on postoperative pregnancy.<sup>15</sup> This current study demonstrated a significant correlation between preoperative menstrual patterns and pregnancy rate. The postoperative menstrual



**Figure 2.** Representative images showing different degrees of intrauterine adhesion (IUA) in patients with IUA and infertility that were enrolled in a retrospective analysis of reproductive outcomes after transcervical resection of uterine adhesions: (a) mild fascicular adhesions; (b) moderate adhesions such as halfmoon adhesions and (c) severe adhesions in which the uterine cavity demonstrated cylindrical narrowing and lost the normal shape. The colour version of this figure is available at: http://imr.sagepub.com.

**Table 3.** The relationship between preoperative and postoperative menstruation and pregnancy of patients (n = 106) with intrauterine adhesion (IUA) and infertility that were enrolled in this retrospective analysis of reproductive outcomes after transcervical resection of uterine adhesions.

	Postoperative menstruation status <sup>a</sup>				
Preoperative menstruation status, $n = 106$	Amenorrhoea	Reduced menstruation	Normal menstruation	Pregnancy rate, %	Statistical analysis <sup>b</sup>
Amenorrhoea, $n = 30$	0/9	4/10	6/11	10/30 (33.33)	P = 0.036
Reduced menstruation, $n = 64$	0/0	3/5	35/59	38/64 (59.38)	
Normal menstruation, $n = 12$	0/0	0/0	8/12	8/12 (66.67)	
Pregnancy rate, %	0/9	7/15 (46.67%)	49/82 (59.76%)	56/106 (52.83)	P = 0.001

<sup>a</sup>Data presented as the number of pregnancies/number of patients in that postoperative menstruation status category. <sup>b</sup>Between-group comparisons undertaken using  $\chi^2$ -test.

Degree of adhesion		Pregnancy after surgery, <i>n</i>	Pregnancy rate, %	Statistical analysis <sup>a</sup>		
Preoperative	Mild adhesions, $n = 34$	24	70.59	0.026		
	Moderate adhesion, $n = 48$	22	45.83			
	Severe adhesions, $n = 24$	10	41.67			
Postoperative	Re-adhesion, $n = 15$	4	26.67	P = 0.048		
	No longer adhesion, $n = 91$	52	57.14			

**Table 4.** Postoperative re-adhesion and pregnancy rate in patients (n = 106) with intrauterine adhesion and infertility that were enrolled in this retrospective analysis of reproductive outcomes after transcervical resection of uterine adhesions.

Data presented as the number of pregnancies.

<sup>a</sup>Between-group comparisons undertaken using  $\chi^2$ -test.

volume reflects the repair of the endometrium,<sup>16</sup> so there is a predictability for the pregnancy outcome after IUA separation.<sup>17</sup> Postoperative menstrual recovery is related to pregnancy.<sup>6</sup>In this current study, 80 of 94 patients (85.11%) with preoperative amenorrhea and decreased menstruation had improved menstruation after the operation and they had a significantly higher pregnancy rate (pregnancy rate 56.25%; 45 of 80 patients) compared with the 14 patients that did not experience any improvement in their postoperative menstrual status (pregnancy rate 21.43%; three of 14 patients).

Transcervical resection of uterine adhesions is used as the standard procedure for the treatment of IUA, but the postoperative reproductive prognosis is poor.<sup>18</sup> It is reported in the literature that the overall pregnancy rate after TCRA is 40.4-64.7% and the live birth rate is 38.9–86.1%. 5,7,18,19 Among the previous studies, the pregnancy rates after surgery for mild, moderate and severe intrauterine adhesions were 58.0-64.7%, 30.0-33. 3% and 14.0-33.0%, respectively;<sup>5,7,18,19</sup> and the rates of miscarriage and premature delivery were relatively high.<sup>20</sup> Placental abnormalities such as placenta previa, placental adhesions, placenta accreta and the risk of ectopic pregnancy are greatly increased after TCRA, which seriously threatens the patient's reproductive health.<sup>20</sup>In this current study, the postoperative pregnancy rate for 106 patients was 52.83% (n = 56) and the live birth rate was 71.43% (40 of 56 pregnancies). This current study found that obstetric complications in pregnant women after TCRA were higher than those in the general population.<sup>4</sup> Among the 40 live births, seven (17.50%) were premature, two (5.00%) had placenta previa, six (15.00%)had placental accrete and seven (17.50%) had postpartum haemorrhage. These findings confirm that women that become pregnant after an IUA separation should be regarded as having a high-risk pregnancy and monitored extensively during their pregnancy and delivery to prevent complications.

It has been reported that IUA patients have the highest probability of pregnancy between 3 and 9 months after fitting an intrauterine device.<sup>21</sup> In this current study, 40 of 56 patients (71.43%) had a pregnancy within 1 year, 54 of 56 patients (96.43%) had pregnancy within 2 years and two patients with moderate adhesions had a pregnancy > 2 years after surgery. With the extension of the postoperative time, the cumulative pregnancy rate stabilized. The regenerated endometrium after surgery acts as a natural barrier to prevent the formation of re-adhesions.<sup>22</sup> After the end of the artificial menstrual cycle and other endometrial 8

repair treatments, the risk of re-adhesion in the exposed uterine cavity without endometrium is greatly increased over time.23 Therefore, patients with IUA should become pregnant as soon as possible after treatment when they meet the conditions for pregnancy and assisted reproductive methods can be adopted when necessary. However, research has suggested that due to the destruction of the endometrium, premature pregnancy may cause abnormal embryo or placental development.<sup>24</sup> This current study did not specifically analyse the correlation between pregnancy time and pregnancy outcome after separation of intrauterine adhesions, so in order to better guide the patient's pregnancy, further research is required.

Age is a direct influencing factor on female fertility and has an influence on postoperative pregnancy.<sup>25</sup> Ovarian function gradually declines after the age of 35 years old and the fertility gradually declines,<sup>26</sup> so age as a negative factor cannot be ignored.

The current study had several limitations. First, the sample size was small. For a more accurate evaluation, increasing the sample size may be necessary in future studies. Secondly, there were cotreatments including operative laparoscopic procedures with possible unequal distribution among the compared groups. Laparoscopic guidance is reported to aid hysteroscopically-directed division of severe IUAs and enable concurrent inspection of the pelvic organs.<sup>27</sup> The Advancing Minimally Invasive Gynecology Worldwide practice guidelines suggest that there is no evidence that hysteroscopic adhesiolysis guided by laparoscopy prevents uterine perforation or improves clinical outcome.<sup>28</sup> However, such an approach used in appropriately selected patients may minimize the consequences if perforation occurs.<sup>28</sup> Therefore, our institution does not routinely perform laparoscopic treatment at the same time, unless there are indications for operative laparoscopic procedures. However, all groups in the current study were similar with respect to the types and frequencies of concomitant factors; therefore, it is reasonable to make comparisons between the groups. In addition, all women were evaluated and managed by the same clinician (X.X.).

In summary, this current study has demonstrated that postoperative menstrual changes and uterine cavity re-adhesion are the main indicators that affect pregnancy after uterine adhesion separation. Age and the degree of uterine cavity adhesion also affect the likelihood of postoperative pregnancy. Therefore, combining the above indicators may roughly assess the reproductive prognosis of patients after intrauterine adhesion separation. TCRA is an effective method for the treatment of intrauterine adhesions, which may effectively improve menstruation and pregnancy rate. However, patients after separation of intrauterine adhesions have a higher rate of miscarriage and obstetric complications when pregnant. Therefore, once such patients become pregnant, they should be regarded as having a high-risk pregnancy and their monitoring should be strengthened to prevent obstetric complications and reduce the occurrence of adverse pregnancy outcomes.

#### Author contributions

Xi Xie, Xiu-Lan Weng: study conceptualization; Xiu-Lan Weng: methodology; Xiu-Lan Weng, Jing-Song Yi: software; Xi Xie, Chao-Bin Liu: formal analysis; Xiu-Lan Weng, Chao-Bin Liu: investigation; Xiu-Lan Weng, Jing-Song Yi: data curation; Xiu-Lan Weng: writing the original draft; Xi Xie: review and editing.

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#### **Declaration of conflicting interest**

The authors declare that there are no conflicts of interest.

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