Clinical research plan

A multicenter, prospective, randomized, controlled clinical study on the effect of hysteroscopic uterine septum resection on the natural pregnancy outcomes in patients with non-recurrent spontaneous abortion

Sponsor: The Third Xiangya Hospital of Central South University

Lead unit: The Third Xiangya Hospital of Central South University

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Research unit: The Third Xiangya Hospital of Central South University

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Study Protocol Summary

Research title: A multicenter, prospective, randomized, controlled clinical study on the effects of hysteroscopic uterine septum resection on the natural pregnancy outcomes in patients with non-recurrent miscarriage

Purpose of the study:

To compare the effects of hysteroscopic septate resection versus expectant management on spontaneous pregnancy outcomes in women with septate uterus and non-recurrent miscarriage.

Study Design:

Multicenter, prospective, randomized, controlled, interventional clinical study.

Research process:

This study was a multicenter randomized controlled trial. Patients with uterine septate who planned to try to conceive naturally were randomly assigned to a group receiving hysteroscopic hysterectomy and a non-surgical treatment group (hysteroscopic endometrial polypectomy and other uterine intrauterine surgeries were allowed, but septum removal was not performed) in a 1:1 ratio. The patients were followed up for at least 12 months after the start of pregnancy attempts. The intraoperative and postoperative hysteroscopic review of the surgical group was recorded. The clinical pregnancy rate, ongoing pregnancy rate, and live birth rate (follow-up to delivery) within 12 months after the two groups were followed up to evaluate the clinical value of hysteroscopic hysterectomy. At the same time, the cumulative miscarriage rate and premature birth

rate, health economics indicators, and patient reproductive quality of life scores were compared to evaluate the long-term effect of surgical treatment.

Inclusion criteria:

(1) The patient meets the 2024 ASRM diagnostic criteria for uterine septate after 3D color Doppler ultrasonography;
(2) The patient may not have ever been pregnant, or may have a history of live birth, one biochemical pregnancy, or one fetal arrest. The patient may also be an infertile patient who wishes to conceive naturally, such as a patient with laparoscopic ostomy for hydrosalpinx, or a patient whose infertility factor can be treated.
(3) Aged between 20-40 years old;
(4) Plan to try to conceive naturally to achieve your wish of having a baby;
(5) Normal ovarian reserve function (AMH>1.1ng/ml, FSH<12U/L on the 2nd to 5th day of menstruation);
(6) The man's semen is generally normal;
(7) Sign the informed consent form and accept and adhere to treatment and follow-up. Patients in the control group can undergo hysteroscopy or hystero-laparoscopy to treat other problems, but no mediastinectomy.

Exclusion criteria:

(1) Recurrent miscarriage;
(2) Patients with uterine intramural fibroids larger than 3 cm and moderate to severe intrauterine adhesions;
(3) Uncontrolled endocrine disorders, such as abnormal thyroid

function (FT3, FT4 abnormal), hyperprolactinemia (greater than 2 times the upper limit of normal), combined with uncontrolled endometrial hyperplasia, combined with EIN or malignant lesions, acute inflammation of the reproductive system, coagulation dysfunction, etc.; if combined with endometrial polyps or submucosal myoma, they can still be included in the group after resection;

(4) Patients with combined adenomyosis (uterine body>50 days of pregnancy), chocolate cysts>4cm in diameter without treatment, or severe dysmenorrhea and clear DIE lesions (diameter>1cm) can be palpated in the gynecological triple examination;

(5) There is untreated bilateral hydrosalpinx or obstruction;

(6) Other major organ diseases and other surgical contraindications or relative contraindications. Other conditions that are not suitable for assisted reproductive treatment. Participated in other clinical research (within the past three months);

(7) Those who are assessed to need IVF (for example, those whose fallopian tubes cannot be cleared, or whose ovulation dysfunction cannot be treated with medication, etc.).

Statistical methods:

The primary analysis will be conducted according to the intention-to-treat principle (ITT), that is, all randomized subjects will be statistically analyzed according to the original randomly assigned groups; sensitivity analysis will be performed according to the actual treatment regimen received by the patients. Categorical variables will be described as frequencies and percentages, and the chi-square test will be used for inter-group comparisons. Continuous variables will be tested for normal distribution. Continuous

variables that conform to normal distribution are described as mean ± standard deviation, and the t test will be used for inter-group comparisons; continuous variables that do not conform to normal distribution are described by median (25th percentile-75th percentile), and the Wilcoxon rank sum test will be used for inter-group comparisons. For binary outcome indicators, relative risks (RR) and corresponding 95% confidence intervals (95% CI) will be calculated. SPSS software will be used for statistical analysis. $P < 0.05$ is considered statistically significant. Finally, the clinical utility index (CUI) was calculated using the live birth rate indicator to evaluate the clinical value of TCRS.

List of research centers and researchers

Institution No.	Principal Investigator	Institution Name
01	Xu Dabao	The Third Xiangya Hospital of Central South University
02	Congqing	Obstetrics and Gynecology Hospital Affiliated to Fudan University
03	Deng Shan	Peking Union Medical College Hospital
04	Du Xin	Hubei Maternal and Child Health Hospital
05	Feng Limin	Beijing Tiantan Hospital Affiliated to Capital Medical University
06	Gao Ting	Anhui Provincial Hospital
07	Huang Xiaowu	Fuxing Hospital Affiliated to Capital Medical University
08	Li Qiang	Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology
09	Ma Rui	Yunnan Provincial First People's Hospital
10	Huang Xiufeng	Department of Obstetrics and Gynecology, Zhejiang University School of Medicine
11	Tang Shuai	The First Affiliated Hospital of Army Medical University
12	Wang Lina	Jilin University First Hospital
13	Wang Yingmei	Tianjin Medical University General

		Hospital
14	Wei Li	Air Force Medical University Xijing Hospital
15	Yan Lei	Reproductive Hospital Affiliated to Shandong University
16	Zhang Hao	Guangzhou First People's Hospital
17	Zhu Tianyuan	Gansu Maternal and Child Health Hospital

Research text

1. Background

Septate uterus is the most common type of congenital uterine anomaly (CUA) in women , accounting for 35% of such abnormalities. Septate uterus is closely related to adverse pregnancy outcomes such as recurrent miscarriage, infertility, premature birth, and fetal malformation . The degree of impact on pregnancy is affected by factors such as the size, thickness, and vascularization level of the septum . As one of the malformations with the worst reproductive outcomes, uterine septum has attracted much attention in clinical practice [1]. In 1988, the American Fertility Society (AFS) revised the classification system for female reproductive organ anomalies [2], which divides septate uterus into two subtypes: complete (a) and partial (b), which are collectively classified as Class V. In 2024, the American Society for Reproductive Medicine (ASRM) proposed two numerical indicators: a septum length greater than 1 cm and an angle formed by the indented endometrium of the uterine fundus septum less than 90° can be diagnosed as an incomplete septate uterus [3]. It was particularly pointed out that it is very important to distinguish between an arcuate uterus and a septate uterus. The arcuate uterus is a normal variation and is not associated with adverse clinical outcomes. Only with a clear diagnosis can the population that will benefit from surgical intervention be accurately determined.

There are various diagnostic methods for septate uterus. Although two-dimensional ultrasound can only diagnose about 50% of uterine malformations, it is usually used as a preliminary screening method for uterine malformations due to its low false positive rate . With the continuous development of medical imaging technology, three-dimensional ultrasound has gradually replaced two-dimensional

ultrasound , which can clearly display the contour morphology of the uterine fundus and the characteristics of the endometrium, thereby achieving a more accurate diagnosis of the type of uterine malformation. This technology makes up for the shortcomings of two-dimensional ultrasound in diagnostic accuracy , and its sensitivity and specificity are almost close to 100% [4][5]. In 2024, the American Society for Reproductive Medicine (ASRM) recommended the use of three-dimensional transvaginal ultrasound with or without saline infusion as a first-line non-invasive diagnostic tool for uterine morphology assessment (level B evidence). Hysterosalpingography (HSG) can more clearly display the internal structure of the uterine cavity by filling the uterine cavity with contrast agent . Its diagnostic sensitivity and specificity for uterine malformations are 78% and 90%, respectively [6]. In addition, HSG can be used to evaluate the patency of both fallopian tubes, thereby preliminarily screening for tubal-related infertility factors. However, this examination cannot evaluate the appearance of the uterus, so there are certain difficulties in distinguishing a bicornuate uterus . The advantage of hysteroscopy is that it can accurately determine the type of septum (complete septum or incomplete septum), and simultaneously perform pathological examinations and other operations to exclude other intrauterine lesions and provide reliable information on related parts such as the vagina and cervical canal. However, hysteroscopy cannot evaluate the external contour or thickness of the uterine wall, so there are limitations in distinguishing between uterine septum and bicornuate uterus. This deficiency can be compensated by combined laparoscopy and clarify the specific situation of the fallopian tubes. Magnetic resonance imaging (MRI): MRI examination can well display the internal structure of the uterine cavity and the appearance of the uterus, and has a high accuracy

in diagnosing a septate uterus . Its advantages include non-invasiveness, high resolution of soft tissue, and help in the diagnosis of other types or complex uterine malformations [7]. In summary, in order to clarify the diagnosis of uterine septation and clearly distinguish it from other uterine malformations, this study used three-dimensional transvaginal ultrasound as the diagnostic standard and adopted the ASRM 2024 septum diagnostic criteria. Specifically, when the length of the septum is greater than 1 cm and the angle formed by the concave endometrium of the septum at the bottom of the uterus is less than 90°, it can be diagnosed as an incomplete uterine septate ; if the lower edge of the septum reaches or exceeds the internal cervical os, it is diagnosed as a complete uterine septate. For controversial cases, a combined hysteroscopy and laparoscopy can be used to confirm the diagnosis.

In recent years, hysteroscopic transcervical resection of septa (TCRS) has been increasingly used in clinical practice and has become the standard procedure for correcting uterine septum. In order to reduce the occurrence of postoperative intrauterine adhesions, a variety of intervention measures are often taken in clinical practice , including estrogen therapy, intrauterine balloon or contraceptive device placement, and intrauterine injection of sodium hyaluronate gel. However, studies have shown that there is no significant difference in the effect of different postoperative intervention measures in reducing the incidence of postoperative intrauterine adhesions [8]. This study uniformly adopted the postoperative placement of a 12Fr Foley balloon and the injection of cross-linked sodium hyaluronate gel to prevent adhesions in order to simplify some data collection and analysis processes, and a disposable intrauterine stent was placed when necessary.

using a variety of methods, including hysteroscopic cold knife incision, monopolar or bipolar electrode incision, and laser incision . The duration of hysteroscopic surgery , the thickness and distribution of residual endometrium after surgery , and the number of surgeries have an important impact on postoperative prognosis . In the clinical treatment of uterine septate, clinicians need to comprehensively consider their own technical proficiency , hospital equipment conditions, and the specific conditions of the patient to select the most appropriate surgical method. In the specific surgical operation, careful operation should be performed to avoid complications such as uterine perforation , and the endometrium should be protected as much as possible . The normal morphology of the uterine cavity should be restored as much as possible in the first operation . In the case of bilateral uterine wall cohesion, full incision should be performed if necessary. Intervention measures should also be taken after surgery to reduce the occurrence of intrauterine adhesions, so as to achieve the best surgical effect of treating uterine septate [9].

the existing observational studies and non- randomized controlled studies on the effect of hysteroscopic septate resection on the outcome of natural pregnancy attempts in patients with uterine septate , there is still controversy about whether TCRS should be routinely performed before natural pregnancy attempts . The 2024 American Society of Reproductive Medicine (ASRM) guidelines for uterine septate pointed out that patients with infertility and/or undergoing fertility treatment should be informed that septate resection may not necessarily increase the live birth rate. Given the limitations of the existing literature and the low risk of surgery, septate resection can be offered to patients under shared decision-making (level B evidence). At the same time, the guidelines recommend that hysteroscopic septate

resection be offered to patients with septate who have a history of recurrent miscarriage under a shared decision-making model (evidence strength: B; recommendation strength: moderate).

However, there are many problems with current randomized controlled studies , including small sample size, unstable indicators, and low test power. In addition, these studies did not describe the random allocation and concealed allocation scheme , nor did they clarify whether the blind method was used to evaluate the efficacy, so there may be a risk of selective bias. In addition, the specific surgical method of hysteroscopic hysterectomy used in the study is unclear, the surgical instruments and the proficiency of the operator are uncertain, and the inclusion criteria of the study are not unified, resulting in a low level of research evidence . Therefore, it is urgent to carry out high-quality, large-sample prospective randomized controlled multicenter clinical trials, using a fully randomized design , unified inclusion and exclusion criteria and treatment plans, in order to obtain more powerful evidence, so as to guide the clinical treatment of patients with uterine septate who plan to try to conceive naturally , improve the uterine cavity environment, improve their fertility and improve pregnancy outcomes.

To this end, this research group intends to conduct a multicenter, prospective, randomized controlled clinical study, mainly including patients with uterine septate who plan to try to conceive naturally . The study will divide the subjects into two groups: one group undergoes hysteroscopic hysterectomy (surgical group), and the other group only receives routine pre-pregnancy counseling and observation (non-TCRS group, control group). In addition, the study will also include infertile patients who use hysteroscopy and laparoscopy as a treatment method and aim to try to conceive naturally. By comparing the live

birth rate, pregnancy rate, and premature birth rate of the two groups , we will provide evidence-based medical evidence for the choice of treatment methods for patients with uterine septate who plan to try to conceive naturally , and evaluate the impact of TCRS on the outcome of postoperative natural pregnancy attempts and its clinical application value.

2. Purpose

Compare the effects of hysteroscopic uterine septate resection and non- surgical (conservative observation) on the natural pregnancy outcomes of patients with uterine septate and non-recurrent miscarriage, and also cover the treatment of other infertility factors for infertile patients with the purpose of natural conception (such as laparoscopic treatment of fallopian tube factors or hysteroscopic fallopian tube catheterization, etc.). This study will provide evidence-based medical evidence for the treatment of patients with uterine septate who want to have children, thereby guiding clinical decision-making.

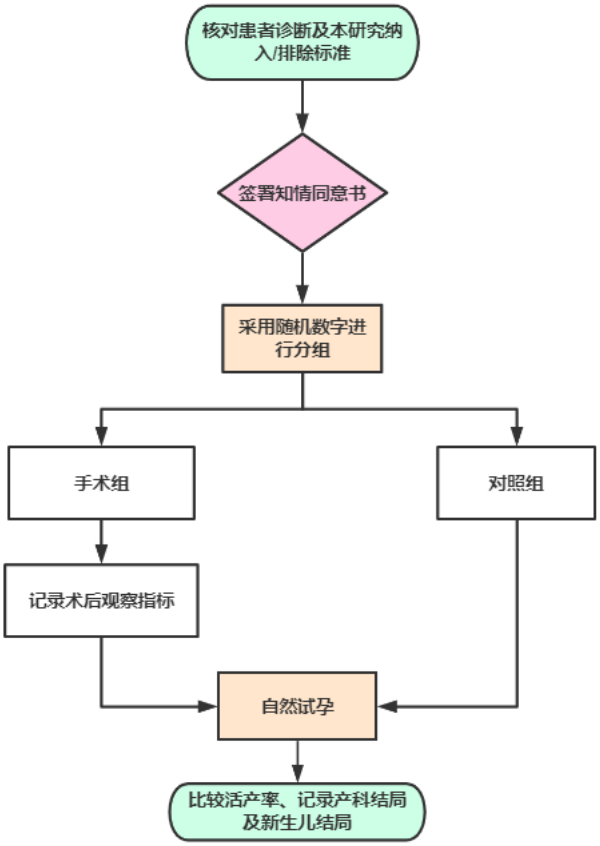
3. Study Design

3.1 Sample size calculation

The primary outcome measure of this study was live birth rate. According to the results of retrospective clinical data analysis, the clinical pregnancy rate in the surgical group was 50%, and the clinical pregnancy rate in women with uterine septate who did not undergo surgery was 35%. Using a two-sided test, the α error was set to 5%, the β error was set to 20%, and the total minimum sample size was calculated using the PASS sample size calculation software to be

167 cases. Considering the withdrawal rate of about 20%, the final sample size was adjusted to 418 , and 209 women were planned to be included in each group.

3.2 Flowchart



4. Research content

4.1 Research period

April 2025 to March 2028

4.2 Number of patients enrolled

Total number of cases: 418, 50 in our center

4.3 Selection criteria

(1) The patient meets the 2024 ASRM diagnostic criteria for uterine septate after 3D color Doppler ultrasonography;

(2) The patient may not have ever been pregnant, or may have a history of live birth, one biochemical pregnancy, or one fetal arrest. The patient may also be an infertile patient who wishes to conceive naturally, such as a patient with laparoscopic ostomy for hydrosalpinx, or a patient whose infertility factor can be treated.

(3) Aged between 20-40 years old;

(4) Plan to try to conceive naturally to achieve your wish of having a baby;

(5) Normal ovarian reserve function (AMH>1.1ng/ml, FSH<12U/L on the 2nd to 5th day of menstruation);

(6) The man's semen is generally normal;

(7) Sign the informed consent form and accept and adhere to treatment and follow-up. Patients in the control group can undergo hysteroscopy or hystero-laparoscopy to treat other problems, but no mediastinectomy.

4.4Exclusion criteria

(1) Recurrent miscarriage;

(2) Patients with uterine intramural fibroids larger than 3 cm and moderate to severe intrauterine adhesions;

(3) Uncontrolled endocrine disorders, such as abnormal thyroid function (FT3, FT4 abnormal), hyperprolactinemia (greater than 2 times the upper limit of normal), combined with uncontrolled endometrial hyperplasia, combined with EIN or malignant lesions, acute inflammation of the reproductive system, coagulation dysfunction, etc.; if combined with endometrial polyps or submucosal myoma, they

can still be included in the group after resection;

(4) Patients with combined adenomyosis (uterine body>50 days of pregnancy), chocolate cysts>4cm in diameter without treatment, or severe dysmenorrhea and clear DIE lesions (diameter>1cm) can be palpated in the gynecological triple examination;

(5) There is untreated bilateral hydrosalpinx or obstruction;

(6) Other major organ diseases and other surgical contraindications or relative contraindications. Other conditions that are not suitable for assisted reproductive treatment. Participated in other clinical research (within the past three months);

(7) Those who are assessed to need IVF (for example, those whose fallopian tubes cannot be cleared, or whose ovulation dysfunction cannot be treated with medication, etc.).

4.5 Research steps

（1）who visited the outpatient clinic , planned to achieve pregnancy through natural conception , and met the diagnostic criteria for uterine septate were selected. The researchers received the patients and had a detailed conversation with them. If the patients agreed to participate in the study, after signing the relevant informed consent form, the patients' medical history, menstrual history, pregnancy and childbearing history, and other information were collected, and the quality of life assessment scale was filled out . All patients underwent three-dimensional ultrasound examination on the 16th to 24th day of menstruation to further clarify the diagnosis and conduct an initial assessment of the length, range, nature, and degree of uterine septate (generating a three-dimensional ultrasound structured report). After completing the inclusion criteria assessment, the patients were randomly divided into two groups at a 1:1 ratio using

a random number table :

Surgical group: patients received surgical treatment for uterine septum, during which possible endometrial polyps, mild intrauterine adhesions, and submucosal myomas could be treated simultaneously. There was no limit on the anesthesia method, and hysteroscopy followed the hysteroscopic operation strategy of "no exploration of the uterus, no dilation of the uterus". Hysteroscopic surgery is divided into two categories: one is plasma hysteroscopic resection (actually TCIS), which uniformly uses a 7mm external diameter hysteroscopic resectoscope to reduce the difficulty of cervical dilation; the other is micro (5 or 7Fr) hysteroscopic cold knife incision, equipped with a 5Fr bipolar electrocoagulation stick for electrocoagulation and hemostasis. When cutting the septum, the principle of protecting the endometrium should be followed. If the left and right side walls are obviously convex, correction can be performed at the same time and detailed records should be recorded. In order to prevent rupture of the uterine fundus in late pregnancy, it is necessary to ensure that the uterine fundus muscle layer retains at least 10mm thickness (combined with preoperative three-dimensional color ultrasound and intraoperative monitoring ultrasound judgment).

16 to 24 days after the first menstruation after the operation, recheck with three-dimensional ultrasound, and recheck with hysteroscopy after the second menstruation to observe the uterine cavity. If there is any residual septum, it should be treated and recorded. After the hysteroscopy recheck confirms that there are no contraindications, you can actively try to get pregnant after the first menstruation.

Control group: routine pre-pregnancy counseling and observation without TCRS treatment, active pregnancy attempts . If combined with

other hysteroscopic indications, hysteroscopy was performed within 3-7 days after menstruation ended, and possible endometrial polyps, intrauterine adhesions (mild), submucosal myomas and other lesions were treated during the operation, and uterine septum was not treated.

The cervical septum was not treated in both groups. After TCRS, a 12Fr Foley balloon was uniformly placed (3 ml of saline was injected into the balloon and placed for 5 days) and cross-linked sodium hyaluronate gel was injected into the uterine cavity to prevent the formation of intrauterine adhesions. A disposable intrauterine stent was placed when necessary, such as when the bilateral uterine walls were treated during the operation, mild intrauterine adhesions were combined, and the uterine cavity was small (the distance between the bilateral uterine angles was less than 35 mm). A follow-up of 12 months was performed after the operation or treatment course, and the reproductive outcomes of pregnancy within 12 months after the pregnancy attempt were recorded .

(2) Follow-up phase

The two groups of patients were followed up for 12 months or more from the time they decided to try to conceive to track their reproductive outcomes. If the patient successfully became pregnant, they would enter the pregnancy follow-up stage and continue to be followed up until postpartum. If the patient was lost to follow-up (defined as lost to follow-up if they could not be contacted for two consecutive follow-ups) or voluntarily withdrew from the study, the follow-up would be terminated.

Pregnancy follow-up

First pregnancy follow-up: After menopause , measure blood hCG.

Second pregnancy follow-up: around 8 weeks of pregnancy, obtain relevant indicators of early pregnancy ultrasound examination.

The third pregnancy follow-up: around 28 weeks of pregnancy. Mainly to obtain information on fetal development, placental status and pregnancy complications during pregnancy.

Fourth pregnancy follow-up: 6 weeks after delivery, through telephone interviews or on-site visits, combined with the patient's prenatal examination records, photocopied obstetric medical records or login to the postpartum information registration system, and neonatal medical records, the following information was collected: ① Detailed information on pregnancy complications in the late pregnancy (e.g., hypertensive disorders complicating pregnancy, gestational diabetes, placental abruption, placenta accreta, placenta previa, intrauterine growth restriction, cervical insufficiency, premature rupture of membranes, premature birth, stillbirth, amniotic fluid abnormalities, etc.); ② Extracting delivery-related information (e.g., gestational age, mode of delivery, stillbirth, placental, umbilical cord or amniotic fluid abnormalities, fetal distress, delivery complications, etc.); ③ Neonatal-related information (gender, birth weight, Apgar score, birth defects, etc.); ④ Detailed information on postpartum complications (e.g., postpartum depression, puerperal infection and/or late postpartum hemorrhage) and neonatal complications (e.g., neonatal respiratory distress syndrome, neonatal jaundice, neonatal infection, neonatal death and/or neonatal hospitalization); inquire and record concomitant medications and adverse events.

Pregnancy follow-up should focus on obstetric intervention measures during pregnancy, such as pregnancy preservation treatment, and record the use of concomitant medications in detail. If the pregnancy is terminated, the cause of termination, gestational age and other related information should be clearly recorded .

This study does not involve sample collection.

5. Evaluation indicators

5.1 Main evaluation indicators

Live birth rate within 12 months after the start of pregnancy attempt in both groups .

5.2 Secondary evaluation indicators

（1）within 1 to 2 months of starting to try to conceive, the miscarriage rate, the premature birth rate , as well as the obstetric complications, neonatal outcomes, cost-effectiveness, and the occurrence of other adverse events .

The changes in endometrial thickness before and after mediastinectomy, the changes in quality of life scores of patients before and after surgery , the time interval from surgery to pregnancy, and the incidence of surgical complications were analyzed in the surgical group.

6. Security considerations

（1）Risk of wound adhesion after uterine septum surgery: Place a 12Fr Foley balloon (5 days) and inject cross-linked sodium hyaluronate gel after surgery to prevent the formation of intrauterine adhesions. If necessary, place a disposable intrauterine stent. If the bilateral walls of the uterine cavity are treated during surgery, mild intrauterine adhesions occur, and the uterine cavity is small (the distance between the bilateral uterine angles is less than 35mm). Closely observe changes in menstrual volume after surgery, regularly evaluate whether adhesions are formed through three-dimensional ultrasound, and take surgical treatment of intrauterine adhesions if necessary.

（2）Risk of bleeding after TCRS surgery and risk of electrothermal injury: Uterine contraction and hemostatic drugs are available during surgery to reduce the risk of bleeding, uterine distension pressure is reduced during surgery, the presence of bleeding points is fully assessed, and complete hemostasis is ensured. At the same time, the frequency of electrosurgery is reduced as much as possible during surgery, and the power of the electrosurgery is appropriately reduced to avoid electrothermal injury.

（3）Other risks of hysteroscopic surgery, such as water intoxication, infection, etc.: Strictly follow the operating specifications, control the operation time, minimize the uterine distension pressure, and ensure complete hemostasis to reduce the occurrence of surgery-related complications.

（4）Other unforeseen risks.

7. Statistical analysis

The primary analysis will be conducted according to the intention-to-treat principle (ITT), that is, all randomized subjects will be statistically analyzed according to the original randomly assigned groups; sensitivity analysis will be performed according to the actual treatment regimen received by the patients. Categorical variables will be described as frequencies and percentages, and the chi-square test will be used for inter-group comparisons. Continuous variables will be tested for normal distribution . Continuous variables that conform to normal distribution are described as mean ± standard deviation, and the t test will be used for inter-group comparisons; continuous variables that do not conform to normal distribution are described by median (25th percentile-75th percentile), and the Wilcoxon rank sum test will be used for inter-group comparisons. For binary outcome

indicators, relative risks (RR) and corresponding 95% confidence intervals (95% CI) will be calculated. SPSS software will be used for statistical analysis. $P < 0.05$ is considered statistically significant. Finally, the clinical utility index (CUI) was calculated using the live birth rate indicator to evaluate the clinical value of TCRS.

8. Quality Management

Researchers should ensure that the data are authentic, accurate, complete and traceable, and should ensure the integrity of basic clinical research documents during the retention period to avoid intentional or unintentional changes or losses.

9. Description of the publication format of research results

This project is a multi-center clinical study. The project will follow the principles of equality, mutual benefit, honesty and trustworthiness, and the sub-centers and the lead unit will jointly carry out the research.

The ownership of the original medical records and data involved in the research process (including but not limited to clinical medical records, follow-up materials) and the collected clinical data (including but not limited to data collection forms, biological samples) are jointly owned by the team leader unit and the sub-center, but are limited to use in this study and not for other extended studies.

The new intellectual property rights generated by this cooperation, unless otherwise agreed, shall be jointly owned by the group leader and the sub-center. As the initiator of this project, the researcher has the right to publish the relevant content of this project for the purpose of academic research and promises not to use the project data and information for commercial activities.

10. Ethical Statement

Clinical research will follow the World Medical Association's Declaration of Helsinki, Ethical Review Methods for Biomedical Research Involving Humans, Ethical Review Methods for Life Science and Medical Research Involving Humans, and Management Methods for Clinical Research Initiated by Investigators in Medical and Health Institutions. Before the start of the study, the clinical research will be implemented only after the research plan is approved by the ethics committee. The personal privacy and data confidentiality of the subjects will be protected during the research process. I promise to abide by the relevant regulations on scientific research norms and integrity.

11. References

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