Clinical research protocol

A multicenter, prospective, randomized controlled clinical study on the outcome of IVF-ET in patients with non-recurrent miscarriage and infertility after hysteroscopic septum resection.

Sponsor: Xiangya Third Hospital, Central South University

Team Leader: Xiangya Third Hospital, Central South University

Funding source: Self-raised funds

Research Institution: Xiangya Third Hospital, Central South University

Principal Investigator: Xu Dabao

Version number: 1.1

Version Date: March 24, 2025

Head record

Research Proposal Summary

Research Title: A multicenter, prospective, randomized controlled clinical study on the IVF-ET outcome of hysteroscopic uterine septum resection in patients with non-recurrent miscarriage and infertility.

Research objective:

The evaluation of the impact of hysteroscopic uterine septum resection on fertility in infertile patients without recurrent miscarriage mainly focuses on assessing its effect on subsequent IVF-ET outcomes.

Research Design:

Multicenter, prospective, randomized, controlled, interventional study.

Research process:

This study was a multicenter randomized controlled trial. Patients with septate uterus and concurrent infertility who planned to undergo IVF-ET to achieve pregnancy were selected and randomly assigned in a 1:1 ratio to either the surgical group (hysteroscopic septate resection) or the control group (non-surgical treatment). Both groups underwent IVF-ET and were followed up for at least 12 months after the first embryo transfer. If pregnancy was achieved, follow-up continued until delivery. Intraoperative and postoperative hysteroscopic follow-up was recorded in the surgical group, followed by IVF-ET postoperatively. The non-surgical group underwent IVF-ET directly. The main comparisons were the pregnancy outcome of the first embryo transfer after grouping, and the cumulative pregnancy rate within 12 months after the first embryo transfer to evaluate

the clinical value of surgical treatment. Other comparisons included miscarriage rate, adverse pregnancy outcomes (such as preterm birth, uterine rupture, placental abnormalities, abnormal fetal position, cesarean section rate, cervical insufficiency, premature rupture of membranes, etc.), economic burden, and patients' reproductive quality of life scores.

Selection criteria:

(1) diagnostic criteria for septate uterus after a 3D color Doppler ultrasound examination .
(2) Age between 20 and 40 years old;
(3) Eligible for infertility diagnosis: Those who have had regular sexual intercourse for at least 12 months without achieving clinical pregnancy;
(4) Planned IVF/ICSI (non-PGD);
(5) Sign an informed consent form and be able to accept and adhere to treatment and follow-up.

Exclusion criteria:

(1) Recurrent miscarriage;
(2) Combined with untreated intramural fibroids larger than 3cm and intrauterine adhesions, with an AFS score ≥5;
(3) Uncontrolled endocrine disorders, such as thyroid dysfunction (FT3 and FT4 not normal), hyperprolactinemia (more than twice the upper limit of normal), atypical endometrial hyperplasia or malignant lesions, acute inflammation of the reproductive system, coagulation disorders, etc.; if there are endometrial polyps or submucosal fibroids, they can still be enrolled after removal.
(4) Combined with adenomyosis (uterine body > 50 days of pregnancy),

untreated chocolate cysts with a diameter > 4cm, or severe dysmenorrhea and a clearly palpable DIE lesion (diameter > 1cm) on gynecological tri-manual examination.

(5) Untreated severe hydrosalpinx (diameter > 3 cm) or hydrosalpinx with reflux confirmed by ultrasound;

(6) Other serious organ diseases or other diseases that are contraindications or relative contraindications for surgery; other situations where assisted reproductive technology is not suitable.

(7) Those who have already participated in other interventional clinical studies (within the last three months).

Statistical methods:

The primary analysis will be conducted according to the intention-to-treat (ITT) principle, meaning all randomized subjects will be statistically analyzed according to their original random assignments; sensitivity analysis will then be performed based on the actual treatment regimens received by patients. Categorical variables will be described as frequencies and percentages, with chi-square tests used for inter-group comparisons. Normality tests will be performed on continuous variables. Normally distributed continuous variables will be described as mean ± standard deviation, with t-tests used for inter-group comparisons; non-normally distributed continuous variables will be described by median (25th percentile - 75th percentile), with Wilcoxon rank-sum tests used for inter-group comparisons. For dichotomous outcome measures, relative risk (RR) and corresponding 95% confidence intervals (95% CI) will be calculated. SPSS software will be used for statistical analysis. P <

0.05 will be considered statistically significant. Finally, the clinical utility index (CUI) will be calculated using the live birth rate to evaluate the clinical value of TCRS.

List of research centers and researchers

Institutional Serial Number	principal investigators	Organization Name
01	Xu Dabao	Xiangya Third Hospital of Central South University
02	Cong Qing	Obstetrics and Gynecology Hospital Affiliated to Fudan University
03	Deng Shan	Peking Union Medical College Hospital
04	Du Xin	Hubei Provincial Maternal and Child Health Hospital
05	Feng Limin	Beijing Tiantan Hospital, Capital Medical University
06	Gao Ting	Anhui Provincial Hospital
07	Huang Xiaowu	Capital Medical University Affiliated Fuxing Hospital
08	Li Qiang	Tongji Hospital, affiliated with Tongji Medical College of Huazhong University of Science and Technology
09	Ma Rui	The First People's Hospital of Yunnan Province
10	Huang Xiufeng	Women's Hospital Affiliated to Zhejiang University School of Medicine
11	Tang Shuai	The First Affiliated Hospital of Army Medical University
12	Wang Lina	The First Hospital of Jilin University

13	Wang Yingmei	Tianjin Medical University General Hospital
14	Wei Li	Xijing Hospital of Air Force Medical University
15	Yan Lei	Shandong University Affiliated Reproductive Hospital
16	Zhang Hao	Guangzhou First People's Hospital
17	Zhu Tianyuan	Gansu Provincial Maternal and Child Health Hospital

Research Text

1. Research Background

Septate uterus is the most common type of congenital uterine anomaly (CUA) in women, accounting for 35% of such abnormalities [1]. Septate uterus is closely related to adverse pregnancy outcomes such as recurrent miscarriage, infertility, premature birth, and fetal malformations. 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-related outcomes, septate uterus has received much attention in clinical practice [2]. In 1988, the American Fertility Society (AFS) revised the classification system of female reproductive organ developmental abnormalities [3], which divided septate uterus into two subtypes: complete (a) and partial (b), and classified them as type V. In 2024, the American Society for Reproductive Medicine (ASRM) proposed two numerical indicators: a septum length greater than 1 cm and an endometrial indentation angle of less than 90° at the fundus septum can be diagnosed as incomplete septate uterus [4]. In particular, it pointed out that it is very important to distinguish between arcuate uterus and septate uterus. Arcuate uterus is a normal variation and is not related to adverse clinical outcomes. Only with a clear diagnosis can the beneficiaries of surgical intervention be accurately determined.

septate uterus. Although two-dimensional ultrasound can 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. It can clearly show the shape 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 terms of diagnostic accuracy. Its sensitivity and specificity are almost 100% [5][6]. In 2024, the American Society for Reproductive Medicine (ASRM) recommended the use of three-dimensional transvaginal ultrasound with or without saline irrigation as a first-line non-invasive diagnostic tool for uterine morphology assessment (Level B evidence). Hysterosalpingography (HSG) can more clearly show the internal structure of the uterine cavity by filling the uterine cavity with contrast agent. Its sensitivity and specificity for the diagnosis of uterine malformations are 78% and 90%, respectively [7]. In addition, HSG can be used to assess the patency of both fallopian tubes, thereby preliminarily screening for fallopian tube factors affecting infertility. However, this examination cannot assess the shape of the uterus, so it is difficult to differentiate between bicornuate uterus. The advantage of hysteroscopy is that it can accurately determine the type of septum (complete or incomplete septum), and perform pathological examinations to rule out other intrauterine lesions and provide reliable information on the vagina, cervical canal and other related sites. However, hysteroscopy cannot assess the external contour or thickness of the uterine wall, so it is also difficult to differentiate between septate uterus and bicornuate uterus. This deficiency can be compensated for by combining laparoscopy with hysteroscopy, while clarifying the specific condition of the fallopian tubes. Magnetic resonance imaging (MRI): MRI examination can well display the internal structure of the uterine cavity and the external morphology of the uterus, and has high accuracy in diagnosing septate uterus. Its advantages include non-invasiveness, high resolution of soft tissue, and assistance in the diagnosis of other types or complex

uterine malformations [8]. In summary, to clarify the diagnosis of septate uterus and clearly differentiate it from other uterine malformations, this study used three-dimensional transvaginal ultrasound as the diagnostic standard, adopting the ASRM 2024 diagnostic criteria for septate uterus . Specifically, when the septum length is greater than 1 cm and the angle of endometrial indentation at the fundus is less than 90° , an incomplete septate uterus can be diagnosed; if the lower edge of the septum reaches or exceeds the internal cervical os, a complete septate uterus is diagnosed. For controversial cases, a combined hysteroscopy and laparoscopy examination can be used for definitive diagnosis.

In recent years, hysteroscopic transcervical resection of septa (TCRS) has been increasingly widely used in clinical practice and has become the standard procedure for correcting septate uterus. To reduce the incidence of postoperative intrauterine adhesions, various interventions are adopted in clinical practice, including estrogen therapy, intrauterine balloon or IUD placement, and intrauterine injection of sodium hyaluronate gel. However, studies have shown that different postoperative interventions have no significant difference in their effectiveness in reducing the incidence of postoperative intrauterine adhesions [9]. In this study, we uniformly adopted the measures of placing a 12Fr Foley balloon and injecting cross-linked sodium hyaluronate gel to prevent adhesions after surgery to simplify some data collection and analysis processes. Disposable intrauterine stents were placed when necessary.

TCRS can be treated using various methods such as 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 a significant impact on postoperative prognosis. In the clinical treatment of uterine septum , clinicians need to comprehensively consider their own technical proficiency , hospital equipment conditions, and the patient's specific condition to choose 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 shape of the uterine cavity should be restored as much as possible in the first surgery. For cases where there is bilateral uterine wall cohesion, it is necessary to perform a full incision if necessary. Postoperative intervention measures should also be taken to reduce the occurrence of intrauterine adhesions, so as to achieve the best surgical effect in treating septate uterus [10].

existing observational and non- randomized controlled studies on the impact of hysteroscopic uterine septum resection on IVF/ICSI outcomes in patients with uterine septum infertility , there is still controversy regarding whether TCRS should be routinely performed before in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) in patients with uterine septum infertility. The 2024 American Society of Reproductive Medicine (ASRM) guidelines on uterine septum state that patients with infertility and/or undergoing fertility treatment should be informed that septum resection may not necessarily improve live birth rates. Given the limitations of existing literature and the low surgical risk, septum resection can be offered to patients under a collaborative decision-making model (Level B evidence). The guidelines also recommend hysteroscopic septum resection for patients with a history of recurrent miscarriage

under a collaborative decision-making model (Evidence strength: B; Recommendation strength: moderate) [11].

However, current randomized controlled trials suffer from several problems, including small sample sizes, unstable results, and low statistical power. Furthermore, these studies lack descriptions of randomization and concealed allocation schemes, and do not specify whether blinding was used to evaluate efficacy, potentially leading to selection bias . Additionally, the specific surgical techniques used in these studies — hysteroscopic septate resection of the uterus— are unclear, the surgical instruments and the surgeons' skill levels are uncertain, and inclusion criteria are inconsistent, resulting in lower levels of evidence . Therefore, there is an urgent need for high-quality, large-sample, prospective randomized controlled multicenter clinical trials with fully randomized designs , standardized inclusion and exclusion criteria, and treatment protocols to obtain stronger evidence. This evidence will guide the clinical treatment of infertile patients with septate uteruses planning IVF/ICSI , aiming to improve the uterine environment, enhance fertility, and improve pregnancy outcomes.

Therefore, our research group plans to conduct a multicenter, prospective, randomized controlled clinical trial, primarily enrolling patients with septate uterus infertility (non-recurrent miscarriage and non- PGD) planning IVF/ICSI . Participants will be divided into two groups: one group will undergo hysteroscopic septate resection (surgical group), and the other group will only receive preconception counseling, observation, and, when necessary, hysteroscopy and non- septate surgery (non-surgical treatment group, control group). This study aims to provide evidence-based medical support for the selection of treatment methods for patients with

septate uterus infertility planning IVF/ICSI , and to evaluate the impact and clinical application value of TCRS on IVF/ICSI outcomes (non-PGD) in patients with septate uterus infertility without recurrent miscarriage.

2. Research Objective

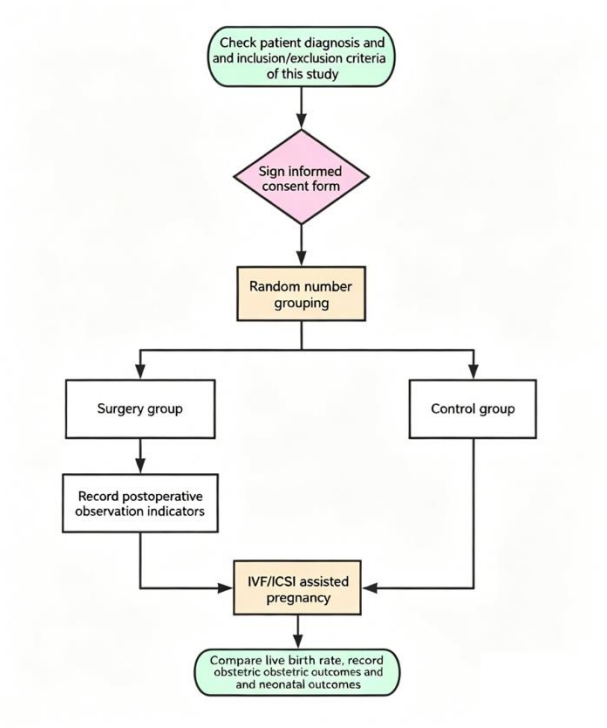
Evaluating the impact of hysteroscopic septum resection versus non-surgical (conservative observation) hysterosalpingography (PTD) on fertility in infertile patients with non-recurrent miscarriages and those without preimplantation genetic diagnosis (PGD) primarily assesses the impact on subsequent IVF/ICSI outcomes. This will contribute to providing evidence-based medicine, establishing standardized treatment procedures for this patient population, avoiding ineffective, duplicate, and overtreatment, shortening treatment time, and reducing medical costs.

3. Research Design

Sample size calculation

The primary outcome measure of this study was the live birth rate. Based on the retrospective clinical data analysis, the live birth rate for unoperated septate uterus was approximately 37%, and it was projected that the live birth rate would increase to 57% after surgery [12]. Using a two-sided test with an α error of 5% and a β error of 20%, the minimum total sample size was calculated to be 94 cases using the PASS sample size calculation software. Considering a dropout rate of approximately 20%, the sample size should be 236, and we included 118 patients in each group.

flow chart



4. Research Content

Study period

April 2025 to March 2027

Number of cases enrolled

Total cases: 236, 50 of which were from our center.

Selection criteria

(1) diagnostic criteria for septate uterus after a 3D color Doppler ultrasound examination .

(2) Age between 20 and 40 years old;

(3) Eligible for infertility diagnosis: Those who have had regular sexual intercourse for at least 12 months without achieving clinical pregnancy;

(4) Planned IVF/ICSI (non-PGD);

(5) Sign an informed consent form and be able to accept and adhere to treatment and follow-up.

Exclusion criteria

(1) Recurrent miscarriage;

(2) Combined with untreated intramural fibroids larger than 3cm and intrauterine adhesions, with an AFS score ≥5;

(3) Uncontrolled endocrine disorders, such as thyroid dysfunction (FT3 and FT4 not normal), hyperprolactinemia (more than twice the upper limit of normal), atypical endometrial hyperplasia or malignant lesions, acute inflammation of the reproductive system, coagulation disorders, etc.; if there are endometrial polyps or submucosal fibroids, they can still be enrolled after removal.

(4) Combined with adenomyosis (uterine body > 50 days of pregnancy), untreated chocolate cysts with a diameter > 4cm, or severe dysmenorrhea and obvious DIE lesions (diameter > 1cm) palpable on gynecological tri-manual examination.

(5) Untreated severe hydrosalpinx (diameter > 3 cm) or hydrosalpinx with reflux confirmed by ultrasound;

(6) Other serious organ diseases or other diseases that are contraindications or relative contraindications for surgery; other situations where assisted reproductive technology is not suitable.

(7) Those who have already participated in other interventional clinical studies (within the last three months).

Research Steps

(1) Patients with septate uterus who presented to the outpatient clinic and had infertility , and who planned to undergo IVF-ET to achieve pregnancy , and who met the diagnostic criteria for septate

uterus, were selected. The researchers conducted interviews with these patients, and if they agreed to participate in the study, they signed the relevant informed consent forms. Information such as the patients' past medical history, menstrual history, and pregnancy and reproductive history was collected, and a quality of life assessment scale was completed . All patients underwent three-dimensional ultrasound examination between days 16 and 24 of their menstrual cycle to further clarify the diagnosis and conduct an initial assessment of the length, extent, nature, and degree of the uterine septum (three-dimensional ultrasound structured report). After assessing the inclusion and exclusion criteria , patients were randomly assigned to groups using a random number table:

Surgical Group: Underwent uterine septum surgery, during which potential endometrial polyps, mild intrauterine adhesions, and submucosal fibroids can be addressed simultaneously. Anesthesia is not limited, and hysteroscopy follows a "no uterine probing, no cervical dilation" strategy. Hysteroscopic surgery is divided into two categories: one is plasma hysteroscopic resection (actually TCIS), using a 7mm outer diameter hysteroscopic resectoscope to reduce the difficulty of cervical dilation; the other is miniature (5 or 7Fr) hysteroscopic cold knife incision , equipped with a 5Fr bipolar electrocautery rod for hemostasis. When incising the septum , the principle of protecting the endometrium is followed. If there is significant bulging of the left and right lateral walls , correction can be performed simultaneously and recorded in detail. To prevent uterine fundus rupture in late pregnancy, it is necessary to ensure that at least 10mm of the myometrial layer is preserved (assessed using preoperative 3D color Doppler ultrasound and intraoperative monitoring ultrasound).

A 3D ultrasound should be performed 16-24 days after the first menstrual period following surgery. A hysteroscopy should be performed after the second menstrual period to observe the uterine cavity. If any residual septum is found, it should be treated and recorded. Once the hysteroscopy confirms there are no contraindications, the patient can undergo IVF/ICSI assisted reproductive treatment after the first menstrual period.

Control group: Received routine preconception counseling and observation without TCRS treatment, and underwent IVF/ICSI. If other indications for hysteroscopic surgery were present, hysteroscopy was performed 3-7 days after menstruation ended. During the procedure, any possible endometrial polyps, mild intrauterine adhesions, submucosal fibroids, etc., were treated simultaneously, but uterine septum was not treated .

Both groups of cervical septa were left untreated. Following TCRS, a 12Fr Foley balloon was placed (3ml of normal saline was injected into the balloon, and it was left in place for 5 days), and cross-linked sodium hyaluronate gel was simultaneously injected into the uterine cavity to prevent intrauterine adhesions. Disposable intrauterine stents were placed if necessary, such as when bilateral uterine walls were addressed during the procedure, there was mild intrauterine adhesion, or the uterine cavity was small (distance between the bilateral uterine horns less than 35mm). A 12 -month follow-up was conducted after the surgery or treatment course , recording IVF/ICSI reproductive outcomes within 12 months of initiating the embryo transfer cycle.

(2) Follow-up phase

Post-operative follow-up for both groups of patients was conducted

according to standard IVF protocols for 12 months. If pregnancy occurred, follow-up was changed to pregnancy follow-up until postpartum. Follow-up ended if a patient was lost to follow-up (defined as being unable to be contacted at two consecutive follow-up visits) or withdrew from the study .

Pregnancy follow-up

First pregnancy follow-up: 10-14 days after embryo transfer, serum hCG is measured .

Second pregnancy follow-up: Around 8 weeks of gestation, relevant indicators from early pregnancy ultrasound examinations are obtained.

Third pregnancy follow-up: around 28 weeks of gestation. Mainly to obtain information on fetal development, placental condition, pregnancy status, and the occurrence of complications during pregnancy.

Fourth pregnancy follow-up: 6 weeks postpartum. Through telephone interviews or in-person visits, combined with patient-provided prenatal check-up records, copies of obstetric medical records, or access to the postpartum information registration system and neonatal medical records, the following information was collected from the patient: ① Detailed information on pregnancy complications occurring in late pregnancy (e.g., gestational hypertension, gestational diabetes, placental abruption, placenta accreta, placenta previa, intrauterine growth restriction, cervical insufficiency, premature rupture of membranes, preterm birth, stillbirth, abnormal amniotic fluid, etc.); ② Delivery-related information (e.g., gestational age, delivery method, stillbirth, presence of placental, umbilical cord, or amniotic fluid abnormalities, fetal distress, presence of delivery complications, etc.); ③ Neonatal-related information (sex, birth weight, presence of 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); Concomitant medications and adverse events were inquired about and recorded.

Pregnancy follow-up should focus on obstetric interventions during pregnancy, such as tocolytic therapy, and detailed records of any concurrent medications used. If the pregnancy terminates, the reason for termination, gestational age, and other relevant information must be clearly recorded .

This study does not involve sample collection.

5. Evaluation indicators

Key evaluation indicators:

The primary outcome of the study was the live birth rate of pregnancies within 12 months of initiating embryo transfer.

Secondary evaluation indicators:

（1）Pregnancy rate and cumulative pregnancy rate, miscarriage rate and cumulative miscarriage rate, and preterm birth rate within 12 months of embryo transfer in both groups. Obstetric complications, neonatal outcomes, cost-effectiveness, and other adverse events.

（2）Preoperative and postoperative endometrial thickness, preoperative and postoperative fertility quality of life scores (optional), time from surgery to pregnancy, and incidence of surgical complications were included in the surgical group .

6. Security considerations

（1）Risks of adhesions after uterine septum surgery: Postoperative placement of a 12Fr Foley balloon (for 5 days) and injection of

cross-linked sodium hyaluronate gel to prevent intrauterine adhesions. Disposable intrauterine stents may be placed if necessary, especially if bilateral uterine walls are treated during surgery, there are mild intrauterine adhesions, or the uterine cavity is small (distance between the bilateral uterine horns less than 35mm). Close monitoring of menstrual flow is necessary postoperatively, and regular assessment using 3D ultrasound is required to determine if adhesions have formed. Surgical treatment of intrauterine adhesions may be necessary in such cases.

（2）Risks of postoperative bleeding and electrocautery injury after TCRS: Uterine contraction agents and hemostatic drugs are available during the procedure to reduce the risk of bleeding. Intraoperative distension pressure is reduced , and the presence of bleeding points is thoroughly assessed to ensure complete hemostasis. Simultaneously, the frequency of electrocautery use is minimized , and the electrocautery power is appropriately reduced to avoid electrocautery injury.

（3）Other risks of hysteroscopic surgery, such as water intoxication and infection: Strictly follow the operating procedures, control the operation time, minimize the distension pressure , and ensure thorough 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 (ITT) principle, meaning all randomized subjects will be statistically analyzed according to their original random assignments; sensitivity analysis will then be performed based on the actual

treatment regimens received by patients. Categorical variables will be described as frequencies and percentages, with chi-square tests used for inter-group comparisons. Normality tests will be performed on continuous variables. Normally distributed continuous variables will be described as mean ± standard deviation, with t-tests used for inter-group comparisons; non-normally distributed continuous variables will be described by median (25th percentile - 75th percentile), with Wilcoxon rank-sum tests used for inter-group comparisons. For dichotomous outcome measures, relative risk (RR) and corresponding 95% confidence intervals (95% CI) will be calculated. SPSS software will be used for statistical analysis. $P < 0.05$ will be considered statistically significant. Finally, the clinical utility index (CUI) will be calculated using the live birth rate to evaluate the clinical value of TCRS.

8. Quality Management

Researchers should ensure that data is authentic, accurate, complete, and traceable, and should ensure the integrity of basic clinical research documents during retention, avoiding intentional or unintentional alteration or loss.

9. Explanation of the format for publishing research findings

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

All original medical records and data (including but not limited to clinical medical records and follow-up data) and collected clinical data (including but not limited to data collection forms and biological

samples) involved in the study are jointly owned by the lead unit and the sub-center, but are only for use in this study and shall not be used for other extended studies or unauthorized purposes.

All new intellectual property rights arising from this collaboration shall be jointly owned by the lead institution and the sub-center, unless otherwise agreed upon in the agreement . As the initiator of this project, the researcher has the right to publish content related to this project for academic research purposes and promises not to use project data and information for commercial purposes or unauthorized uses.

10. Ethical Statement

The clinical research will adhere to the relevant regulations of the World Medical Association's Declaration of Helsinki, the Ethical Review Guidelines for Biomedical Research Involving Human Subjects, the Ethical Review Guidelines for Life Science and Medical Research Involving Human Subjects, and the Management Guidelines for Investigator-Initiated Clinical Research Conducted by Medical and Health Institutions. The research protocol will be approved by the ethics committee before the clinical research can commence. Throughout the research process, the personal privacy and data confidentiality of the participants will be fully protected. I solemnly promise to strictly abide by research norms and integrity-related regulations.

11. References

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