Clinical Efficacy of Combined Hysteroscopic and Laparoscopic Surgery and Reversible Ligation of the Uterine Artery for Excision and Repair of Uterine Scar in Patients with Type II and III Cesarean Scar Pregnancy

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Background: With the changes in China's family planning policy, the incidence of cesarean scar pregnancy (CSP) significantly increased in recent years. The present study aimed to investigate the clinical efficacy of combined hysteroscopic and laparoscopic surgery and reversible ligation of the uterine artery for cesarean scar excision and repair in patients with type II and III CSP.

Material/Methods: This was a retrospective study of 173 patients with type II and III CSP. They were assigned to the hysteroscopy and laparoscopy group (group A), hysteroscopy group (group B), and curettage group (group C) according to the surgery they underwent. The surgical indicators (intraoperative bleeding volume and hospital stay), postoperative recovery (time of serum β-hCG returning to the normal, postoperative residual lesion, the thickness of the uterine scar, and recovery time of menstruation), and the postoperative complications were compared among the 3 groups.

Results: In patients with type II and III CSP, significant differences ($P<0.05$) were observed between group A vs. groups B and C in terms of the time of serum β-HCG returning to normal, postoperative residual lesions, the thickness of the uterine scar, and recovery time of menstruation, while there were no significant differences in intraoperative bleeding volume and postoperative hospital stay ($P>0.05$).

Conclusions: For patients with type II and III CSP, hysteroscopy and laparoscopy surgery and reversible ligation of the uterine artery achieved better clinical outcomes than hysteroscopy or curettage with respect to postoperative recovery. This could be suitable for patients with CSP and desire for fertility.

MeSH Keywords: Hysteroscopy • Laparoscopy • Postoperative Complications • Uterine Artery Embolization

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Background

A cesarean scar pregnancy (CSP) is a type of ectopic pregnancy in which the fertilized egg implants itself in the uterine incision scar left by a previous cesarean section, and this is a time-limited definition limited to early pregnancy only (≤12 weeks) [1]. The incidence of CSP is 1: 1800 to 1: 2216 and accounts for 6.1% of all ectopic pregnancies or in 0.15% of women with a history of cesarean section [2,3].

Recently, the family planning policy of China was adjusted, and many women with a history of cesarean section are allowed the possibility of becoming pregnant again, and the incidence of CSP has been increasing. CSP can cause uncontrollable severe bleeding, uterine rupture, and damage to the surrounding organs such as the bladder, seriously threatening the women's reproductive health and even their lives. Therefore, the definitive diagnosis should be made available as early as possible for reasonable treatments [4,5].

Ultrasound is the preferred diagnostic choice for CSP, but MRI is an effective method when a definitive diagnosis cannot be obtained by ultrasound [6–8]. In 2016, the *Chinese Journal of Obstetrics and Gynecology* published the *Expert Opinion of Diagnosis and Treatment of Cesarean Scar Pregnancy*, in which the CSP is classified as types I, II, and III based on the relationship between the gestational sac and uterine incision scar by ultrasound [1,9]. The muscular thickness at the scar in the anterior uterine wall of types II and III CSP is ≤3 mm in both cases, with a rich blood supply at the scar, and the risks of major bleeding and residual pregnancy tissues are high.

Presently, there is no consensus on the management of CSP. Individualized therapeutic strategies are planned based on the location of the gestational sac, the thickness of the uterine scar, and blood supply [4,10,11]. Surgical methods for CSP mainly include curettage, removal of pregnancy tissues, and repair of the uterine scar. In critical situations such as major bleeding, hysterectomy can be performed to save the life of patients [5,12]. Curettage involves ultrasound-guided curettage and hysteroscopic removal of pregnancy tissues. The removal of the pregnancy products and repair of the uterine scar can be performed by laparotomy and laparoscopy (or combined with hysteroscopy), which can be performed transvaginally [13]. To reduce the risk of intraoperative bleeding in patients with type II and III CSP, uterine arterial embolization (UAE) or temporary occlusion of the uterine artery is often used as a pretreatment, followed by curettage or removal of the pregnancy tissues.

Hence, the present study aimed to investigate the clinical efficacy of combined hysteroscopic and laparoscopic surgery and reversible ligation of the uterine artery for cesarean scar excision and repair in patients with type II and III CSP. The patients were grouped according to the surgery they underwent: hysteroscopy and laparoscopy *vs.* hysteroscopy *vs.* curettage.

Material and Methods

General data

Patients with type II and III CSP who were hospitalized at the Gynecology Department of Ningbo Women and Children's Hospital between May 2015 and April 2019 were retrospectively analyzed; 173 patients with complete follow-up data were included in this study. All patients were confirmed with type II and III CSP by three-dimensional B-mode ultrasound and/or pelvic enhanced MRI before surgery and met the diagnostic criteria for CSP [1]. Of the 173 patients, there were 109 with type II CSP. They were grouped based on the surgical strategy used: hysteroscopy and laparoscopy (group A1), hysteroscopy (group B1), and curettage (group C1). The surgical strategy for patients in group A1 included laparoscopic reversible ligation of the bilateral uterine arteries, removal of the pregnancy tissues of the uterine scar, repair of the uterine scar, and hysteroscopic exploration. In group B1, UAE and hysteroscopic removal of pregnancy tissues were used. For group C1, UAE and ultrasound-guided curettage were used. There were 64 patients with type III CSP. They were grouped according to the surgery they underwent: hysteroscopy and laparoscopy (group A2), hysteroscopy (group B2), and curettage (group C2). The surgical methods were the same as above. The selection of the surgical strategy was made after a comprehensive discussion between the patient and the surgeon about the surgical options and their pros and cons. The patient would then determine the surgical method they preferred and signed the surgery informed consent before the surgery, as per routine clinical practice. The study was approved by the Ethics Committee of Ningbo Women and Children's Hospital. The informed consent was waived off due to the retrospective nature of the study. All patient data were kept confidential.

Surgical methods

1) The patients in the hysteroscopy and laparoscopy group (groups A1 and A2) underwent laparoscopic reversible ligation of bilateral uterine arteries, removal of pregnancy tissues of the uterine scar, repair of the uterine scar, and hysteroscopic exploration. After general anesthesia induction, the posterior lobe of the broad ligament was opened by laparoscopy. The ureter was separated and pushed away to expose the internal iliac artery. After finding the uterine artery, it was dissociated and ligated with a slipknot. Intrauterine injection of 2 U of pituitrin diluent was performed, followed by separating the peritoneal reflection. The bladder was

pushed down to expose the lower uterine scar, the scar tissues were cut, and the pregnancy tissues were removed. The weak tissues of the uterine scar were removed. Then, a 1-0 absorbable suture was used for continuous suturing of the uterine incision, and mattress suture was used for the uterine seromuscular layer for reinforcement. Hysteroscopic exploration was performed to remove any residual pregnancy tissues. After completing the surgery, the ligatures of the bilateral uterine arteries were removed.

2) The patients in the hysteroscopy group (groups B1 and B2) underwent UAE and hysteroscopic removal of the pregnancy tissues. During surgery, methotrexate (MTX) 50 mg/m^2 was given. Under local anesthesia, a 4F Cobra catheter was inserted into the left internal iliac artery by a percutaneous puncture (Seldinger technique). After superselection, it was inserted into the left uterine artery. Next, the half-dose of MTX was injected into the left uterine artery after arteriography. The left uterine artery was embolized with a gelatin sponge strip to occlude the end. Superselection was performed to the right uterine artery using the looping technique. After completing the arteriography, the remaining half-dose of MTX was injected into the right uterine artery, and the right uterine artery was embolized with a gelatin sponge strip to occlude the end. Routine extubation and hemostasis by pressure bandage were performed. At 24-48 h after embolization, routine hysteroscopic removal of the pregnancy tissues was performed [14,15].

3) The patients in C1 and C2 groups underwent UAE and ultrasound-guided curettage. At 24–48 h after UAE (performed as above), ultrasound-guided curettage was performed. The intraoperative vacuum aspiration and curettage of the pregnancy tissues were performed [16].

Outcome measures and follow-up

The surgical indicators and postoperative recovery among the 3 groups of patients with type II and III CSP were compared. The surgical indicators included intraoperative bleeding volume, hospital stay, and surgical complications. The intraoperative bleeding volume was calculated by using the volumetric method after the blood was collected by the aspirator. The conditions of postoperative recovery included the time of serum β-HCG returning to the normal, postoperative residual lesion, the thickness of the uterine scar, and the recovery time of menstruation. The serum β-HCG levels were detected every 2 days during hospitalization and, after discharge, at the outpatient clinic once a week until it returned to normal. Ultrasound was performed 1 week after discharge. If there were any residual lesions, reexamination was performed every week until it returned to normal. Ultrasound was performed 3 months after surgery to measure the thickness of the uterine scar.

Statistical analysis

SPSS 25.0 software (IBM, USA) was used for data analysis. The continuous data with a normal distribution were presented as means±standard deviations and compared using the independent-samples analysis of variance and the Bonferroni post hoc test. For continuous data that did not conform to the normal distribution were presented as median (P$_{25}$–P$_{75}$), and compared using the Kruskal-Wallis test. The categorical data were presented as n (%) and compared using the chi-square test. The significant level (α) was 0.05.

Results

Comparison of the general data of the patients

There were no significant differences among the 3 groups in age, time from last menstruation, the average diameter of the gestational sac, and the number of cesarean sections (all $P > 0.05$, Tables 1, 2).

There were no significant differences in age, time from last menstruation, the average diameter of the gestational sac, and number of cesarean sections among groups A1, B1, and C1 (H and chi-square value was 3.056, 1.882, 1.723, and 0.156, respectively, all P>0.05)

Comparison of different surgical indicators of type II CSP patients

The surgery was successfully completed in all patients with type II CSP without any surgical complications. Postoperative ultrasound in group A1 showed no significant residual lesions in the uterine isthmus. Eight patients with residual lesions in group B1 and 11 in group C1 were conservatively treated with success. Among patients with type II CSP, comparison between group A1 *vs.* groups B1 and C1 showed statistically significant differences ($P < 0.05$) in terms of the postoperative time of serum β-HCG returning to the normal, residual lesion, thickness of the uterine scar, and recovery time of menstruation. There were no significant differences in intraoperative bleeding volume and postoperative hospital stay ($P > 0.05$), as shown in Table 3. Compared with groups B1 and C1, and for group A1, the postoperative time of serum β-HCG returning to normal remained shorter, the residual lesions were reduced, the thickness of the scars was increased, and the recovery time of menstruation was shorter.

Table 1. Comparison of general data of patients with type II CSP.

Groups		A1	B1	C1	P
Number of cases (n)		23	35	51	–
Age (years)		27 (25–31)	28 (25–32)	29 (26–34)	0.217
Time from last menstruation (days)		48 (46–52)	49 (47–53)	49 (47–52)	0.390
Average diameter of the gestational sac (mm)		19 (18–22)	20 (19–22)	19 (18–22)	0.423
Number of cesarean sections	1	22	33	49	0.925
	2	1	2	2	

The continuous data were not normally distributed and the H test was used.

Table 2. Comparison of general data of patients with type III CSP.

Groups		A2	B3	C2	P
Number of cases (n)		16	21	27	–
Age (years)		30.38±4.29	31.24±5.53	30.3±4.3	0.769
Time from last menstruation (days)		51 (48.25–53.75)	51 (48.5–52.5)	51 (48–53)	0.946
Average diameter of the gestational sac (mm)		21 (20–24)	21 (20–23)	21 (19–23)	0.749
Number of cesarean sections	1	13	18	23	0.923
	2	3	3	4	

Age met the normal distribution; the H test was used for continuous data that were not normally distributed.

Comparison of the outcome measures with different surgical methods in patients with type III CSP

The surgery in all groups for type III CSP patients was completed successfully. Color Doppler ultrasound in group A2 showed no significant residual lesions in the uterine isthmus. There were 8 patients with residual lesions in group B2, among whom one patient underwent hysteroscopy and laparoscopy combined with the removal of pregnancy tissues of the uterine scar on day 14 after surgery due to the presence of residual lesions in the uterine scar, as revealed by postoperative color Doppler ultrasound and increased bleeding; the remaining 7 patients were successfully treated conservatively. There were 10 patients with residual lesions in group C2, among whom 2 underwent hysteroscopy and laparoscopy combined with the removal of the pregnancy tissues of uterine the scar on days 23 and 35 after surgery, respectively, due to the presence of residual lesions in the uterine scar, as revealed by postoperative color Doppler ultrasound and increased bleeding; the remaining 8 patients were successfully treated conservatively.

Among patients with type III CSP, comparison between group A2 *vs.* groups B2 and C2 showed statistically significant differences ($P<0.05$) in terms of the postoperative time of serum β-HCG returning to the normal, residual lesion, thickness of the uterine scar, and recovery time of menstruation. No significant differences were observed in intraoperative bleeding volume and postoperative hospital stay ($P>0.05$), as shown in Table 4. Compared with groups B2 and C2, the postoperative time of serum β-HCG returning to normal was shorter, the residual lesions were reduced, the thickness of the scars was increased, and the recovery time of menstruation was shorter in group A2.

Discussion

CSP is a special type of ectopic pregnancy that poses a great reproductive harm to women of childbearing age with a history of cesarean section. Although there is no consensus on the treatment of CSP, the basic therapeutic principles include early diagnosis, timely treatment, and bleeding reduction to preserve the fertility of the patients [10,12,17]. Currently, the pathogenesis of CSP remains unclear, but some studies suggested that CSP is related to uterine scar defects and the formation of microfissures due to the destruction of the endometrial basal layer after cesarean section [18–20]. The muscle layer in the CSP remains weak, and the thickness of the scar is <3 mm. The risk of CSP, massive hemorrhage, dangerous placenta previa, and uterine rupture can be increased during

Table 3. Comparison of different surgical indicators for type II CSP patients.

Groups		A1	B1	C1	P
n		23	35	51	–
Intraoperative bleeding volume (ml)		100 (80–120)	80 (50–100)	80 (50–100)	0.551
Postoperative hospital stay (days)		4 (4–4)	4 (3–5)	4 (3–4)	0.192
Time of serum β-HCG returning to normal (days)		18 (15–21)	33 (27–45)*	33 (24–42)*	<0.001
Postoperative residual lesion (n)	Yes	0	8	11	0.046
Number of cases (n)	No	23	27	40	
Absorption time of residual lesion (days)		0 (0–0)	0 (0–0)	0 (0–0)	0.049
Postoperative thickness of uterine scar (mm)		4 (3.6–5)	2 (1.8–2.2)	2 (1.8–2.3)	<0.001
Recovery time of menstruation (days)		42.96±6.79	50.51±12.4*	51.02±15.98*	0.047

The recovery time of menstruation met the normal distribution; the H test was used for the variables that did not meet the normal distribution. * P<0.05 *vs.* the A1 group.

Table 4. Comparison of outcome measures with different surgical methods in patients with type III CSP.

Groups		A1	B1	C1	P
n		16	21	27	–
Intraoperative bleeding volume (ml)		110 (100–157.5)	180 (100–200)	150 (100–200)	0.146
Postoperative hospital stay (days)		5 (5–5.75)	5 (4.5–5.5)	5 (4–6)	0.916
Time of serum β-HCG returning to normal (days)		24 (18.75–24.75)	35 (22.5–42)*	35 (27–39)*	<0.001
Postoperative residual lesion (n)	Yes	0	8	10	0.015
Number of cases (n)	No	16	13	17	
Absorption time of residual lesion (days)		0 (0–0)	0 (0–50.0)*	0 (0–54.0)*	0.014
Postoperative thickness of uterine scar (mm)		3.8 (3.5–4.375)	2 (1.8–2)*	2 (1.6–2.2)*	<0.001
Recovery time of menstruation (days)		43.5 (36–47.75)	52 (39–66)*	49 (40–60)*	0.012

The continuous data did not meet the normal distribution, and the H test was used. * P<0.05 *vs.* the A2 group.

pregnancy, and laparoscopic surgery is a recommended treatment strategy to repair these uterine defects [21–23]. The muscular thickness of the scar in the anterior uterine wall of type II and III CSP is ≤3 mm in both types. In type II CSP, the gestational sac is partially implanted in the muscle layer of the uterine scar, and the local muscle layer is damaged. In type III CSP, the gestational sac is completely implanted into the muscle layer of the uterine scar and protrudes towards the bladder, and the damage it causes to the muscle layer is more serious. According to previous reports, patients with exogenous CSP a uterine scar thickness <3 mm and who undergo hysteroscopic surgery or curettage often suffer from uncontrollable bleeding, uterine perforation, and bladder injury during surgery, and the rate of secondary treatment after surgery is high, and the uterine scars might not be repaired [21,23,24]. The first-intention cure rate of exogenous CSP with hysteroscopic surgery alone

is approximately 75% [15,25]. The main causes for treatment failure include increased intraoperative bleeding, conversion to transabdominal or laparoscopic surgery, postoperative residual lesions, a slow decrease in β-HCG levels, and slow absorption of local masses, among others. The present study suggests that for treating patients with type II and III CSP, hysteroscopy combined with laparoscopy were superior over hysteroscopy and curettage with respect to postoperative time of serum β-HCG returning to the normal, residual lesion, thickness of the uterine scar, and recovery time of menstruation.

For types II and III CSP, the muscular layer at the scar of the anterior uterine wall is thin, but the blood supply is rich, and they are at high risk of massive hemorrhage. Thus, pretreatment is often recommended before the curettage or removal of any pregnancy tissues in patients with type II and III CSP.

UAE is often used as a pretreatment. The intraoperative local injection of methotrexate directly acts on the gestational sac, destroys the villous tissues, and prevents the development of the embryo. This is conducive to the subsequent curettage, thus lowering the risk of bleeding [14,16,26]. Nevertheless, postembolization syndrome, pelvic infection, damage to the ovarian function, or endometrial atrophy leading to amenorrhea, intrauterine adhesions, and infertility might occur, affecting the reproductive function of patients [27–29]. In addition, rare complications such as ureteral injury, bladder necrosis, lower limb necrosis, pulmonary embolism, and nerve injury have been reported [30]. In this study, the patients in group A (A1 and A2) underwent pretreatment with reversible ligation of the bilateral uterine arteries and showed no significant difference in intraoperative bleeding volume compared with the UAE groups. Therefore, ligation could avoid the UAE-related complications, with little effect on the uterine and ovarian blood supply.

Conclusions

This study strongly suggests that combined hysteroscopic and laparoscopic surgery and reversible ligation of the uterine artery can completely remove the pregnancy tissues, reduce or avoid the use of methotrexate, and repair the weak uterine scars. This is considered suitable for patients with CSP and subsequent fertility desire. Nevertheless, due to the limited sample size and unavailability of long-term follow-up data, further research with large sample size and long-term follow-up is warranted to explore the long-term clinical efficacy and reproductive outcomes of patients with treated type II and III CSP. In addition, hysteroscopic surgery combined with laparoscopic surgery requires high operation skills of surgeons, and increases the costs, limiting its clinical use. As a treatment option for CSP, hysteroscopic surgery combined with laparoscopic surgery and reversible ligation of the uterine artery will benefit patients with CSP by improving surgeons' skills.

Conflict of interests

None.

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