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Original Research

Treatment outcomes of uterine lesion resection versus hysterectomy for cesarean scar pregnancy

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Summary

Objective: To compare the effects of uterine lesion resection (ULR) and hysterectomy on cesarean scar pregnancy (CSP). *Materials and Methods:* A total of 147 patients admitted from January 2009 to January 2019 and diagnosed as CSP by pathological examination were selected, of whom 105 underwent ULR and 42 received hysterectomy. The gestational age, size of gestational mass, serum β-hCG level, previous treatments and clinical outcomes of the two groups were compared. *Results:* Compared with the hysterectomy group, the ULR group had significantly lower gestational age, size of gestational mass and proportion of persistent CSP ($p < 0.05$), and significantly higher serum β-hCG level ($p = 0.011$). The median gestational ages of ULR and hysterectomy groups at termination of pregnancy were 67 d and 83 d, respectively, and their median bleeding volumes were 400 mL and 650 mL, respectively ($p < 0.05$). In the ULR group, the median bleeding volumes of patients with gestational age of $\geq$ 10 weeks (n = 48) and $<$ 10 weeks (n = 57) were 500 mL and 300 mL, respectively ($p < 0.05$). Twenty-one cases (20%, 21/105) were switched to hysterectomy due to emergency CSP during curettage, of whom 6 had uterine perforation and 15 had massive bleeding (200-800 mL). The hysterectomy group all received emergency hysterectomy owing to massive bleeding. The proportions of blood transfusion and emergency CSP in the ULR group were significantly lower than those of the hysterectomy group ($p < 0.01$). Twenty-one patients (14.29%, 21/147) in the two groups suffered from serious complications. Neither group had bladder injury. *Conclusion:* ULR was mainly suitable for CSP patients with the gestational age of 9-10 weeks at termination of pregnancy, gestational mass size of 60-90 mm, failed initial treatment but stable hemodynamics. Hysterectomy instead of ULR was safer for patients in critical conditions with the gestational age of $>$ 12 weeks.

Key words: Uterine lesion resection; Hysterectomy; Cesarean scar pregnancy.

Introduction

Cesarean scar pregnancy (CSP), as a long-term complication of cesarean section, usually refers that fertilized egg implants and develops in the scar after surgery [1, 2]. In recent years, the incidence rate of CSP cases has soared [3]. In the early stage, CSP is easy to be confused with threatened abortion, inevitable abortion and cervical pregnancy, and the final diagnosis needs to be confirmed by the combination with serum human chorionic gonadotropin (hCG) level and related imaging data [4]. If CSP can be early diagnosed and effectively treated, the occurrence and progression of subsequent complications can be suppressed, and the uterine and fertility functions of patients can be well preserved [5, 6]. Missed diagnosis or improper treatment of CSP leads to hemorrhagic shock, uterine rupture and other serious consequences, even endangering patients' life [7]. At present, CSP is mainly treated by drugs, interventional therapy and surgery in clinical practice. Among them, surgery works best in repairing scar defects to fundamentally prevent relapse, so it is usually given first priority [8, 9]. Nowadays, the commonly used surgeries include transvaginal removal of intrauterine pregnancy residues or uterine artery embolization (UAE) alone, or in combination with perfusion of methotrexate at the local uterine wall or uterine artery, but a few cases still require uterine lesion resection (ULR) or hysterectomy to terminate pregnancy [10, 11]. Recently, Di Spiezio Sardo *et al*. successfully treated ectopic pregnancy by combining systemic and hysteroscopic intra-amniotic injections of methotrexate (MTX) with hysteroscopic resection [12]. Based on successful direct bipolar resection of sixth week CSP, Mollo *et al*. concluded that direct hysteroscopic approach was valuable for the first stage of CSP [13]. Besides, a case of hysteroscopic removal of twin CSP after failure of systemic MTX administration has been reported, without intra- or postoperative complications [14]. In addition, Laganà *et al*. found that absorbable monofilament sutures for uterine promoted the wound healing of scar, without increasing surgical cost, time or incidence rate of intraoperative complications [15]. Herein, we compared the effects of ULR and hysterectomy on CSP, aiming to determine the application conditions of these two methods and to provide clinical evidence for selecting a suitable strategy for treating CSP.

Materials and Methods

Baseline clinical data

Sample size was estimated according to $n = 2 \times [(t_\alpha + t_\beta)S/d]^2$, where n is the minimum case number of each

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group, S is the estimated overall standard deviation, d is the difference between two means, t_α is the t value at the significance level of α and t_β is the t value at the significance level of β. Pre-experiment showed that d was 5.4, and S was calculated as 7.58. Two-tailed α was 0.05, and β was 0.1, so t_α and t_β were 1.96 and 1.282, respectively. According to the equation, each group should include at least 41 cases.

A total of 147 patients admitted to our hospital for surgery from January 2009 to January 2019 and diagnosed as CSP by pathological examination were selected, of whom 105 underwent ULR and 42 received hysterectomy.

Inclusion criteria: 1) Patients with history of cesarean section and in accordance with the diagnostic criteria for CSP in "New Practical Obstetrics and Gynecology" [16]; 2) intact examination and follow-up data. Exclusion criteria: 1) Patients who recently received relevant drugs or surgery influencing the results of this study; 2) coagulation dysfunction; 3) uterine rupture or massive bleeding in the abdominal cavity.

Surgical methods

Surgical indications were recorded. ULR was performed as follows. The adhesion between the anterior isthmus of the uterus and the bladder was separated, and the bladder was pushed down to the level of external cervical orifice. Then the myometrium was cut horizontally along the boundary of gestational mass for removal. Finally, the uterine incision was intermittently sutured. Hysterectomy was indicated for patients in critical conditions. Total or subtotal hysterectomy was selected depending on patients' willingness and their conditions. The details of uterine artery occlusion were recorded, including UAE 3 days before surgery and temporary uterine artery ligation during surgery.

Procedure of UAE: Catheters were inserted into bilateral uterine arteries through puncture of the right femoral artery with the Seldinger technique, and the arteries were occluded by gelatin sponges with the diameter of 1,400-2,000 μm. Procedure of uterine artery ligation: Before incision of the myometrium, the main trunks of bilateral uterine arteries were separated and subjected to loop ligature of using rubber rings. When the uterine wall was cut through, the rubber rings were tightened, and the blood flow was occluded. After gestational mass was quickly removed, the rings were intermittently loosened.

Criteria for related indices

Determination of gestational age: Gestational age was recalculated according to the last menstrual period, diameter of gestational mass during the first ultrasonic examination and medical history. Determination of bleeding volume: The bleeding volumes before and 72 h after ULR and hysterectomy were recorded.

Emergency CSP: Emergency referred to hemorrhagic shock, disseminated intravascular coagulation, severe pelvic infection, uterine perforation or other serious conditions. Persistent CSP: Persistent CSP (PCSP) was determined according to whether patients had received initial treatment before surgery. PCSP referred to the situation when initial treatment was performed but failed, and non-persistent CSP (NPCSP) meant no initial treatment was conducted. The patients undergoing ULR or hysterectomy within 24 h after other treatments were also determined as NPCSP.

Statistical analysis

All data were statistically analyzed by SPSS16.0 software. The quantitative data conforming to normal distribution were represented as mean $\pm$ standard deviation (X $\pm$ SD) and compared by the t test. The non-normally distributed quantitative data were expressed as median (M) and compared with the Mann-Whitney rank sum test. The numerical data were represented as ratio and compared by using the χ^2 test. $p < 0.05$ was considered statistically significant.

Results

Treatment descriptions

Of the 105 patients in the ULR group, 72 did not receive UAE, 18 underwent UAE 3 days before hysterectomy, and 15 received uterine artery ligation during hysterectomy. Fifty-one patients (48.57%, 51/105) had PCSP and received curettage before, 3 of whom were treated with MTX initially, 3 were misdiagnosed as early pregnancy and had taken mifepristone, and 15 received hysteroscopic surgery after failed curettage, but still with pregnancy residues. Ninety-six cases (91.43%, 96/105) received hysterectomy in the past 6 years, and 18 cases were subjected to laparoscopic hysterectomy in the past 2 years.

Of the 42 patients in the hysterectomy group, 36 (85.71%, 36/42) had PCSP, among whom 33 had received curettage and 3 failed MTX treatment. The hysterectomy group all underwent abdominal surgery, of whom 24 patients received total hysterectomy and 18 underwent subtotal hysterectomy, with 24 cases (57.14%, 24/42) in the past 6 years.

Baseline clinical data

The two groups had similar age, number of pregnancy, number of parity, number of cesarean sections, proportion of cases with fetal heartbeat and uterine scar thickness ($p > 0.05$). The gestational age, size of gestational mass and proportion of persistent CSP of the ULR group were significantly lower than those of the hysterectomy group ($p < 0.05$). The serum β-hCG level of the ULR group was significantly higher than that of the hysterectomy group ($p = 0.011$) (Table 1).

Clinical outcomes

The median gestational ages of ULR and hysterectomy groups at termination of pregnancy were 67 d and 83 d, respectively, and their median bleeding volumes were 400 mL and 650 mL, respectively ($p < 0.05$). In the ULR group,

Table 1. — *Baseline clinical data.*

	ULR group (n = 105)	Hysterectomy group (n = 42)	*p*
Age (year)	33.46 ± 5.09	34.18 ± 5.12	0.096
Number of pregnancy (M)	3.0	4.0	0.387
Number of parity (M)	1.0	1.5	0.526
Number of cesarean sections (M)	1.0	1.0	0.704
Gestational age upon diagnosis (M)	64	79	0.001
Size of gestational mass (mm)	66.28 ± 13.29	92.18 ± 14.28	0.012
With fetal heartbeat (case)	42	9.0	0.196
Uterine scar thickness (mm, M)	2.0	2.1	0.117
Preoperative serum β-hCG level (U/L, M)	22789	814	0.011
PCSP (case)	51	36	0.013

Table 2. — *Clinical outcomes.*

	ULR group (n = 105)	Hysterectomy group (n = 42)	*p*
Gestational age at pregnancy termination (d, M)	67 (35-146)	83 (46-166)	0.096
Bleeding volume (mL, M)	400 (50-2300)	650 (300-2700)	0.387
Blood transfusion (case, %)	12 (11.43)	39 (92.86)	0.526
Emergency CSP (case, %)	21 (20.00)	42 (100.00)	0.704

the median bleeding volumes of patients with gestational age of $\geq$ 10 weeks (n = 48) and $<$ 10 weeks (n = 57) were 500 mL and 300 mL, respectively ($p < 0.05$).

Twenty-one cases (20%, 21/105) were switched to hysterectomy due to emergency CSP during curettage, of whom 6 had uterine perforation and 15 had massive bleeding (200-800 mL). All patients in the hysterectomy group received emergency hysterectomy owing to massive bleeding. The proportions of blood transfusion and emergency CSP in the ULR group were significantly lower than those of the hysterectomy group ($p < 0.01$) (Table 2).

Secondary complications

Twenty-one patients (14.29%, 21/147) in the two groups suffered from serious complications. In the ULR group, there were 3 cases of severe pelvic infection after surgery and 3 cases of huge hematoma in the anterior isthmus with the diameter of 6 cm, for whom conservative treatment was successful. In the hysterectomy group, 6 patients had severe pelvic infection and 9 had hemorrhagic shock complicated with disseminated intravascular coagulation before surgery. Neither group had bladder injury.

Discussion

Cheng *et al*. successfully removed pregnancy tissues in most cases of CSP with the gestational age of 5-8 weeks through transvaginal surgery [17]. In this study, the gestational age of the ULR group was about 9-10 weeks which was lower than that of the hysterectomy group ($>$ 12 weeks). For patients undergoing ULR, bleeding volume increased in those with the gestational age of $\geq$ 10 weeks, suggesting that it was safer and more effective to terminate pregnancy by abdominal surgery for the CSP cases with higher gestational age. CSP may be an early manifestation of pathological placenta, which elevates the risks of placenta adhesion, placenta implantation and even placental penetration with increasing gestational age, so pregnancy should be terminated as early as possible. A gestational age of over 8 weeks is one of the risk factors for hemorrhage [18, 19]. We herein analyzed CSP patients who suffered from hemorrhage after UAE combined with uterine curettage, and found that the average gestational age of patients with hemorrhage was 9.3 weeks and that gestational age was still one of the risk factors for uterine curettage even in combination with UAE. Therefore, gestational age affected the clinical outcome of CSP, and pregnancy should be terminated as early as possible before the gestational age of 10 weeks.

According to the latest released Expert Consensus on the Diagnosis and Treatment for Cesarean Scar Pregnancy (2016) by Obstetrics and Gynecology Branch of Chinese Medical Association [20], uterine curettage is suitable for CSP patients with the gestational age of $<$ 8 weeks. For patients with the gestational age of $\geq$ 8 weeks, uterine curettage needs to be combined with treatment method which can prevent hemorrhage. CSP is most commonly treated by transvaginal surgery, only limited to lower gestational age though. Generally, CSP is treated by MTX or UAE combined with curettage and ULR, with ULR being most effective. A few patients even have to receive hysterectomy. Currently available literatures are case reports. In contrast, this study enrolled a relatively large number of patients, and found that ULR was mainly applicable to CSP patients with the gestational age of 9-10 weeks while hysterectomy was

generally suitable for the patients with the gestational age of $>$ 12 weeks and uncontrollable hemorrhage, based on the treatment experience of our hospital in the past 10 years. Thus, gestational age is one of the important factors influencing the choice of treatment strategies, and selecting appropriate therapies based on gestational age can help to reduce the risk of hemorrhage. It is well-documented that curettage or hysteroscopic surgery was suitable for CSP patients with the gestational mass size of smaller than 30 mm, and hysteroscopic surgery can effectively terminate CSP with the size of about 25 mm [21]. However, Shi *et al*. reported that transvaginal surgery did not work well for patients with the gestational mass size of 30-50 mm, easily leading to the formation of retained products of conception (RPOC) [22]. In this study, the gestational mass size of the ULR group reached 65 mm and about 50% of the patients had RPOC. The size of the hysterectomy group was $>$ 90 mm which was significantly larger than that of the ULR group. Collectively, a larger gestational mass indicated more complex treatment and higher risk of hysterectomy. Likewise, Wang *et al*. found that for patients terminating pregnancy by UAE combined with curettage, the incidence rate of hemorrhage in the cases with the gestational mass size of $\geq$ 6 cm was 86.7%, and hysterectomy was required for some cases. For patients with large CSP masses, the termination of pregnancy by abdominal surgery not only benefits the thorough elimination of gestational mass, but also effectively controls the risk of hemorrhage. Wang *et al*. found that a serum β-hCG level of $\geq$ 20,000 U/L was a high-risk factor for hemorrhage, and transvaginal surgery should be cautiously selected to remove gestational mass [18]. Herein, the preoperative serum β-hCG level of the hysterectomy group was about 800 U/L which was significantly lower than that of the ULR group ($>$ 20,000 U/L), but the incidence rates of hemorrhage and critical state of CSP in the hysterectomy group exceeded those of the ULR group, suggesting that low serum β-hCG level did not represent the severity of CSP. Accordingly, the value of low serum β-hCG level for the selection of treatment is uncertain, which should be considered in combination with gestational age, size of gestational mass and blood flow sufficiency. Factors such as gestational age, size of gestational mass, special anatomical structure of implantation site of CSP and improper treatment methods can lead to the failure of complete removal of pregnancy tissues and subsequent PCSP. Cheung reported that 25% ~ 30% of patients underwent PCSP after curettage or MTX [23]. There were 87 cases of PCSP in this study. The primary treatment was curettage, and other methods included drug therapy, hysteroscopic surgery and UAE. Nevertheless, some patients received combined treatment, but still failed. Meanwhile, most PCSP patients suffered from hemorrhage during remedial curettage, thereby requiring emergency transabdominal ULR or hysterectomy. Hence, PCSP is a high-risk type of CSP, and its treatment is difficult and complex. Currently, there is limited experience of salvage therapy for PCSP, mostly involving MTX, curettage, hysteroscopic surgery, ULR and even hysterectomy. ULR has been recommended to terminate CSP which implanted in the scar layer of the uterus in order to reduce the risks of RPOC and hemorrhage. We herein did not identify the types of CSP, but transabdominal ULR may be the first choice for patients with PCSP and the risk of hemorrhage. The PCSP patients whose gestational age exceeded 12 weeks were prone to serious complications such as disseminated intravascular coagulation, so hysterectomy should be performed promptly if necessary to avoid fatal complications. ULR is the most accurate and effective method for terminating CSP by quickly controlling bleeding, repairing the scar defect of the uterus, and significantly shortening the follow-up time. Our study showed that most cases of refractory CSP were successfully treated by ULR. Compared with uterine curettage, ULR requires longer surgical time and more proficient skills, accompanied by considerable bleeding [21]. In our study, the median bleeding volume of the ULR group was 400 mL, and 15 patients lost more than 800 mL of blood. The blood transfusion rate was 11%, and 6 patients were switched to hysterectomy due to uncontrollable hemorrhage. Therefore, there was still risk of hemorrhage for ULR. Until now, whether uterine artery occlusion should be combined with ULR to reduce the risk of hemorrhage remains controversial. He *et al*. reported that 11 CSP patients who underwent ULR combined with uterine artery occlusion had no hemorrhage [24]. We did not find that uterine artery occlusion reduced the bleeding volume during ULR, which needs further studies. Considering the results of this study and previous literatures, for patients whose gestational age exceeds 10 weeks and who need to undergo ULR, uterine artery occlusion is recommended if ultrasonic examination shows abundant local blood flow signals in the lower uterine segment. Apart from the risk of hemorrhage, ULR may also lead to bladder injury and secondary infection. Therefore, it is still a risky operation and requires cautious selection and application.

In summary, gestational age, gestational mass size and failed initial treatment are of great significance to the selection of methods for treating CSP. ULR should be given first priority for CSP patients with the gestational age of 9-10 weeks at termination of pregnancy, gestational mass size of 60~90 mm, failed initial treatment but stable hemodynamics. Instead, hysterectomy is safer for patients in critical conditions with the gestational age of $>$ 12 weeks and unstable hemodynamics. When necessary, hysterectomy should be performed timely to prevent fatal complications. Regardless, this study still has limitations. It is a single-center retrospective study with a small sample size. Multi-center prospective studies are ongoing in our group to further compare the clinical effects of ULR and hysterectomy on CSP.

Ethics Approval and Consent to Participate

This study has been approved by the ethics committee of our hospital, and written informed consents have been obtained from all patients.

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Conflict of Interest

The authors declare no conflict of interest.

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