Original Research

Is preprocessing helpful for suction and curettage in treating cesarean scar pregnancy?

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Summary

Objective: To evaluate the efficacy of suction and curettage (SC), with and without preprocessing, as a therapeutic strategy for cesarean scar pregnancy (CSP). *Materials and methods*: This retrospective study included 257 patients with CSP who received ultrasound-guided SC. Patients were grouped into the direct SC group (122 cases) and the preprocessing SC group (135 cases). The preprocessing SC group was further divided into four subgroups based on the different preprocessing methods (methotrexate injection, oral mifepristone, methotrexate with mifepristone, and uterine artery embolization/chemoembolization). *Results*: There was no significant difference in success rates between the preprocessing SC group and the direct SC group (94.07% *vs*. 97.54%, $p > 0.05$). The preprocessing SC group had increased intraoperative bleeding, longer operation times, prolonged hospital stays, and increased in-hospital costs (all p values < 0.05, compared with the direct SC group). Among the preprocessing SC group, the in-hospital cost for the uterine artery embolization/chemoembolization subgroup was significantly higher than that for the other subgroups. *Conclusions*: Preprocessing steps may do not increase the success rate of SC for CSP under certain conditions. Optimization of the preprocessing step requires further research. *Content*: The effectiveness of suction and curettage and other methods in treating cesarean scar pregnancy has been evaluated.

Key words: Cesarean section; Ectopic pregnancy; Cesarean scar pregnancy; Termination of pregnancy.

Introduction

Cesarean scar pregnancy (CSP) is a particular form of ectopic pregnancy caused by the embryo's implanting into a cesarean scar [1]. In the general obstetric population, CSP is related to the number of cesarean sections, and the incidence is estimated at about 1/3000 [2]. To distinguish CSP from intrauterine pregnancy in the early first trimester, ultrasound is the most commonly used and most important visual assessment [3]. The main risk in CSP is abnormal bleeding, and worse, catastrophic hemorrhage during the first trimester. Recent systemic reviews demonstrated that the success rates of various treatment modalities were about 60%-95% [4-7]. For patients choosing to continue with a CSP pregnancy, the risks of placenta accreta, uterine rupture, massive hemorrhage, and even hysterectomy must be considered [2]. To reduce the risks of these complications, termination of pregnancy is usually considered at the time of CSP diagnosis.

Currently, there is no ideal CSP treatment. As a noninvasive procedure, suction and curettage (SC) is sometimes used as one of the treatment options [8-12]. SC with ultrasonic monitoring is an effective treatment for some types of CSP [13, 14]. When considering the treatment plan, it is important that the thickness of postoperative incisions and several other clinical features be considered [15].

To reduce the risk of bleeding, several preprocessing steps before SC have been suggested, such as injection of methotrexate (MTX) [16] and uterine artery embolization

(UAE) [17]. These preprocessing steps may reduce the bleeding risk of SC to a certain extent [13]. However, contrary to their intended purpose, preprocessing steps may also increase the risk of bleeding because of the prolonged treatment time [13]. In addition, preprocessing steps increase medical costs. As there is no consensus, it is necessary to evaluate the risks and benefits of preprocessing steps before SC to enable evidence-based recommendations. We retrospectively collected the data of patients who had undergone SC for the treatment of CSP in our hospital, and evaluated the efficacy and safety of SC with and without preprocessing steps.

Materials and Methods

Clinical data of patients who were diagnosed with CSP and treated with SC between 1 July 2010 and 1 August 2016 in the Second Xiangya Hospital of Central South University were collected and analyzed. This study included only patients treated by SC for the first time and in the first trimester. Patients only treated with conservative methods such as UAE and other non-SC treatments such as surgical resection, hysteroscopic excision, and hysterectomy were excluded.

The authors had no access to information that could identify individual participants during and after data collection.

CSP was diagnosed by a history of previous cesarean delivery, elevated serum β-human chorionic gonadotrophin β-hCG), and ultrasound characteristics, which included an

empty uterine cavity and cervical canal, a myometrial defect between the sac and the bladder wall, and a gestational sac located at the anterior part of the uterine isthmus.

SC was performed in this study when the thickness of the previous scar was more than 3 mm during the first trimester, according to our classification and therapeutic strategy for CSP [13]. Our SC procedures were performed with suprapubic ultrasonic monitoring to reduce the bleeding risk. Also, before operating on the SC group, we had blood transfusion products available on standby and prepared for excision of the mass, UAE, or laparotomy in case of massive hemorrhage. During the procedure, we first addressed the gestational tissue under ultrasonographic monitoring, aspirated it quickly (Nos. 6-8 aspirating cannula; usually No. 7), and then cleaned other areas of the uterine cavity. Next, pressure was applied to the cesarean scar surface, and 30-50 mL of saline solution was injected using a Foley catheter to prevent bleeding.

To assess the differences between SC with preprocessing and SC without preprocessing, the patients were divided into two groups (Figure 1), the direct SC group (treated directly with SC) and the preprocessing SC group (preprocessing techniques applied before SC). Several alternative preprocessing methods have been used, including MTX injection (locally or systemically, 50 mg), oral mifepristone (10-25 mg), MTX with mifepristone, and UAE/uterine artery chemoembolization (UACE). The preprocessing SC group was further divided into four subgroups termed the MTX, mifepristone, MTX and mifepristone, and UAE/UACE groups, respectively. In the UAE/UACE method, the right femoral artery was accessed, and a 5F uterine arterial catheter was inserted into the left and right internal iliac arteries in sequence for angiography. After confirmation of placement, the catheter was extended into both uterine arteries (with or without an injection of MTX, 100 mg), and the two uterine arteries were embolized with gelatin sponge particles.

To better compare the success rates and perioperative outcomes between groups, we only collected data from patients who were treated for the first time with SC. Thus, patients who had a previous failed SC or other treatments were excluded from the analysis. Serum β-hCG was measured before and one day after surgery. If this value did not fall below 50% of the previous value, treatment was considered a failure.

Treatment success was confirmed by the following criteria: successful removal of the focus (intraoperative ultrasound monitoring), subsequent negative β-hCG, and confirmed chorionic villi by pathological examination. Other outcome variables included operation time, volume of blood loss, length of hospital stay, and in-hospital cost. The in-hospital cost included all hospital costs from admission to discharge, including examination, drug, and SC costs.

Statistical analysis was performed using IBM SPSS 20.0 (IBM Corp., Armonk, NY). Continuous variables are presented as the mean $\pm$ standard deviation or quartiles and were tested using the Mann-Whitney U test, or Kurakal-Wallis H test. Categorical variables are presented as percentages and were tested using the Chi-square or Fisher exact test. All tests of hypotheses were two tailed with the type 1 error rate fixed at 5%.

Results

This study included 257 women who were diagnosed with CSP and received SC treatment during the time of hospitalization. The average age was 32.34 $\pm$ 4.81 years (22 to 44), gravida 4.25 $\pm$ 1.71 (2 to 11) and para 1.39 $\pm$ 0.54 (1 to 3). The average gestational age was 50.87 $\pm$ 10.66 days (30 to 83), and average β-hCG was 40939.58 $\pm$ 62873.15 mIU/mL. Of this group, 122 patients (122/257, 47.47%) received SC without preprocessing steps (the direct SC group), and the other 135 patients (135/257, 52.53%) received SC after a preprocessing step (the preprocessing SC group).

Table 1 shows the general characteristics of the 257 patients. There were no significant differences in the variables examined between the preprocessing SC and the direct SC groups ($p > 0.05$).

The overall success rate of the 257 patients was 95.72% (246/257). The success rate was 94.07% (127/135) for the preprocessing SC group and 97.54% (119/122) for the direct SC group. Although the direct SC group showed a higher success rate (97.54% *vs.* 94.07%), the difference was non-significant ($p > 0.05$) (Table 1).

Table 2 shows the perioperative outcomes in patients with successful SC. Compared with the direct SC group, the preprocessing SC group had longer operation times, greater blood loss, longer hospital stays, and higher in-hospital costs (all p-values < 0.05).

In the preprocessing SC group, patients were given one of four preprocessing methods: MTX injection (9/127, 7.09%), oral mifepristone (48/127, 37.80%), MTX with mifepristone (60/127, 47.24%), or UAE/UACE (10/127, 7.87%). Perioperative outcomes in the four subgroups were presented in Table 3. There was no significant difference in the volume of intraoperative blood loss among the four preprocessing subgroups, although between-group differences were observed in operation time, hospital stay, and in-hospital cost. The MTX and mifepristone group showed the longest operation times and hospital stays. The hospital stay for the mifepristone group was significantly shorter than those for the MTX and mifepristone and the UAE/UACE groups (Kruskal-Wallis H test, $p < 0.05$), and the in-hospital cost was significantly higher for the UAE/UACE group than for the other three groups (Kruskal-Wallis H test, $p < 0.05$).

Discussion

Sel *et al.* reported that vacuum extraction could be a useful and practical method for treating CSP; validation studies with larger sample sizes are needed [8]. Our research focused on comparing the effectiveness of prepro-
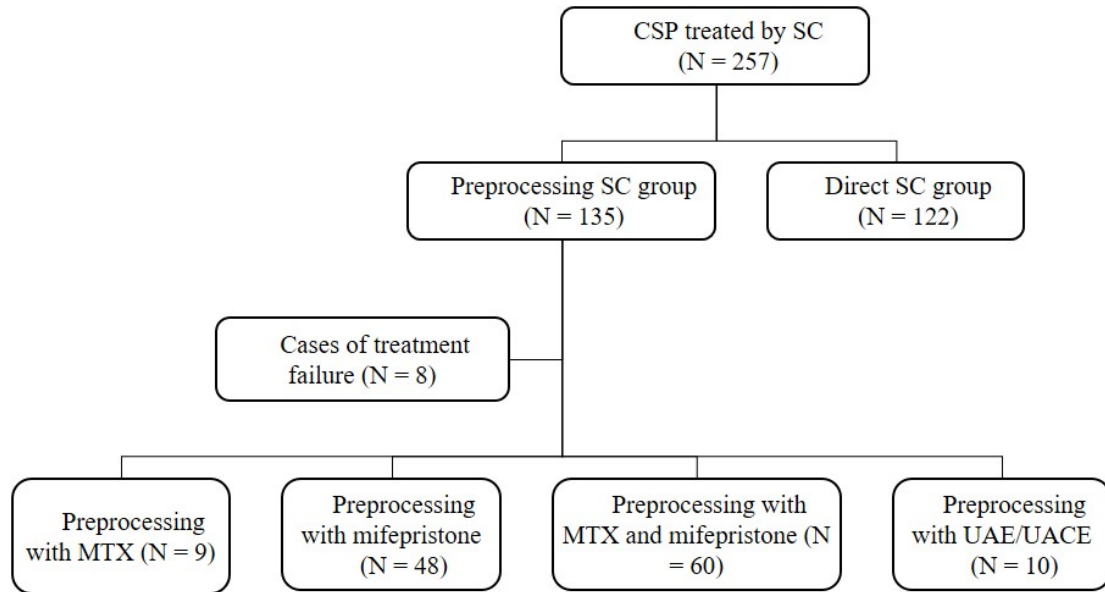
Figure 1. — Flow-chart of the cesarean scar pregnancy cases. CSP: cesarean scar pregnancy; SC: suction and curettage; MTX: methotrexate; UAE: uterine artery embolization; UACE: uterine artery chemoembolization.

Table 1. — *General characteristics and SC success rates by study groups.*

Characteristic	Preprocessing SC Group (N = 135) Mean ± SD, Median (Q1, Q3)	Direct SC Group (N = 122) Mean ± SD, Median (Q1, Q3)	p [1]
Age (years)	32.72 ± 4.76 33.00 (29.00, 36.00)	31.93 ± 4.85 31.50 (28.00, 35.00)	0.20
Gravidity (N)	4.24 ± 1.63 4.00 (3.00, 5.00)	4.26 ± 1.80 4.00 (3.00, 5.00)	0.98
Parity (N)	1.41 ± 0.55 1.00 (1.00, 2.00)	1.37 ± 0.53 1.00 (1.00, 2.00)	0.57
Previous cesarean delivery (N)	1.30 ± 0.47 1.00 (1.00, 2.00)	1.33 ± 0.51 1.00 (1.00, 2.00)	0.66
Gestational age (days)	51.67 ± 11.00 49.00 (44.00, 57.00)	49.98 ± 10.25 47.00 (43.00, 54.00)	0.16
Preoperative β-hCG (mIU/mL)	41422.58 ± 43239.59 25505.00 (10258.50, 55544.00)	40348.25 ± 80899.71 23596.00 (9168.00, 50340.85)	0.36
Minimum thickness of myometrial wall (mm)	4.19 ± 2.11 4.00 (3.00, 5.00)	4.24 ± 2.33 4.00 (3.00, 5.00)	0.98
Time between previous cesarean delivery and index pregnancy (years)	6.86 ± 4.27 6.00 (3.00,10.00)	6.90 ± 3.74 6.50 (4.00, 9.00)	0.74
Maximum diameter of sac (mm)	29.73 ± 12.47 30.00 (21.00, 37.00)	26.51 ± 13.76 23.00 (16.25, 31.75)	< 0.01
Success suction and curettage	127 (94.07%)	119 (97.54%)	0.17
Massive bleeding [2]	3 (2.22%)	2 (1.64%)	1.00
Reoperation [3]	6 (4.44%)	2 (1.64%)	0.35

Data are presented as mean ± standard deviation, median (quartile 1, quartile 3) or n (%). Abbreviations: SC, suction and curettage; β-hCG, β-human chorionic gonadotrophin. [1] Mann-Whitney U test or Chi-square test. [2] Intraoperative blood loss more than 500mL. [3]After the failure of SC, different methods including laparotomy, laparoscopic surgery, or hysteroscopy were used for reoperation.

cessing methods before CS. Under certain circumstances, CSP can be treated by SC with ultrasound or hysteroscopic guidance [10]. Data from Jurkovic *et al.* demonstrated that ultrasound-guided suction curettage is an effective method for treating pregnancies implanted into a lower uterine segment cesarean section scar [12]. We used ultrasound mon-

Table 2. — *Perioperative outcomes in patients with successful SC by study groups.*

Outcome	Preprocessing SC Group (N = 127)	Direct SC Group (N = 119)	p [1]
Operation time (minutes)	26.85 ± 15.55 20.00 (15.00, 30.00)	21.18 ± 11.30 20.00 (14.00, 30.00)	< 0.01
Blood loss (ml)	93.73 ± 140.19 50.00 (20.00, 100.00)	56.84 ± 96.03 30.00 (20.00, 50.00)	0.01
Hospital stay (days)	9.33 ± 4.67 8.00 (6.00,12.00)	4.11 ± 1.75 4.00 (3.00, 5.00)	< 0.01
In-hospital cost (yuan)	9652.47 ± 5071.58 8218.61 (6370.04, 11394.20)	6566.11 ± 1948.45 6395.00 (5317.66, 7739.03)	< 0.01

Data are presented as mean ± standard deviation, median (quartile 1, quartile 3). Abbreviations: SC, suction and curettage.
[1] Mann-Whitney *U* test.

Table 3. — *Perioperative outcomes in four subgroups of preprocessing suction and curettage.*

Outcome	MTX group (N = 9)	Mifepristone group (N = 48)	MTX & mifepristone group (N = 60)	UAE/UACE group (N = 10)	p [1]
Operation time (minutes)	25.56 ± 9.82 20.00 (17.50, 35.00)	23.52 ± 16.63 20.00 (15.00, 30.00)	30.37 ± 15.58 29.50 (20.00, 40.00)	22.20 ± 10.39 22.50 (12.25, 30.00)	0.02
Blood loss (mL)	53.33 ± 61.44 20.00 (20.00, 75.00)	88.77 ± 88.62 50.00 (30.00, 100.00)	110.21 ± 182.00 50.00 (20.00, 100.00)	53.50 ± 65.91 15.00 (10.00, 105.00)	0.17
Hospital stay (days)	8.33 ± 4.44 7.00 (5.00, 12.50)	6.56 ± 2.50 6.00 (5.00, 8.00)	11.47 ± 4.83 10.50 (8.00, 14.00)	10.70 ± 5.23 9.50 (7.75, 12.00)	< 0.01
In-hospital cost (yuan)	8193.50 ± 3733.30 6826.40 (5445.60, 11914.82)	7401.18 ± 2109.24 7157.66 (5951.17, 8371.82)	10079.18 ± 3547.04 9866.49 (7254.05, 12274.25)	21853.20 ± 8589.75 23856.68 (17548.23, 27017.50)	< 0.01

Data are presented as mean ± standard deviatsion, median (quartile 1, quartile 3). Abbreviations: MTX, methotrexate. UAE, uterine artery embolization. UACE, uterine artery chemoembolization. [1] Kruskal-Wallis H test.

itoring in our treatment methods. Not all CSPs are suitable for SC treatment [13]; our study focused on comparing different SC processing methods for cases that could receive SC after assessment. According to Polat *et al*., with early diagnosis, CSP with a β-hCG level < 17,000 mIU/mL and a myometrial thickness > 2 mm can be treated with SC [11]. Therefore, for each patient, the choice of CSP treatment should be based on the patient's condition and severity. The average myometrial thickness of our SC cases was about 4 mm. In this regard, we have been somewhat conservative in choosing SC treatment methods.

The success rates for the preprocessed SC group and the direct SC group were 94.07% and 97.54%, respectively; the between-group difference was not significant. This suggested that the preprocessing steps did not significantly increase the success rate of the operation. However, significant differences were found in other outcomes. The operation time in the preprocessing group was significantly longer than that in the direct SC group, although the two groups had the same median operation time of 20 min, suggesting that direct SC may not have an obvious disadvantage over preprocessing SC in operation time.

Similarly, the difference in the volumes of blood loss between the two groups was statistically significant, but the

difference in the median blood loss (20 mL) was clinically negligible. Therefore, the preprocessing steps did not seem better in terms of controlling blood loss in SC. When MTX and mifepristone are used, atrophy or bleeding may occur in the lesion, and the invasiveness of trophoblasts is reduced. These changes may cause adhesions to surrounding tissues, which makes SC more difficult and requires a longer operation time. In addition, blood clots from bleeding lesions may block the tube at the beginning of SC, which also increases the operation time and bleeding. Notably, in the preprocessing SC group, one patient suffered a massive hemorrhage (1,000 mL). However, there was also one case of massive hemorrhage in the direct SC group, with an 800 mL blood loss. Therefore, for SC both with and without preprocessing steps, attention should be paid to the risk of massive hemorrhage. We speculate that there were two reasons for the low average bleeding volume in our study population. First, patients with a high risk of bleeding did not receive SC treatment in our study; in those cases, other treatments such as laparotomy were performed [13]. Therefore, our data may only show treatment results for low-risk CSP patients (suitable for SC). Second, the representativeness of the average volume of blood loss may be limited by the small sample size, as there were only nine cases in

the MTX group. With respect to hospital stay, when pre-processing was performed, sufficient monitoring time was required to observe a decline in serum β-hCG, which reflected the therapeutic effect. For the mifepristone group (oral mifepristone therapy before SC), SC was performed after 3 days of hospitalized observation following the medication due to the potential risk of hemorrhage and for monitoring the level of β-hCG.

Shu *et al.* reported a CSP patient who previously received MTX and mifepristone and was treated by laparoscopy-guided curettage and aspiration [18]. Ozyuncu *et al.* reported that CSP could be successfully treated by MTX as a potential treatment option for ectopic pregnancies under certain conditions. These experiences suggest the effectiveness of MTX for treating CSP [19]. Mifepristone can reduce the risk of bleeding by reducing progesterone and villous activity, although it is no longer commonly used for CSP. In conservative treatment of CSP, MTX is used both locally and systemically. The toxicity of MTX depends on its concentration and duration of activity. Therefore, the use of MTX should be fully assessed. In the preprocessing method using MTX, ultrasound-guided local injection of MTX is considered a safe and recommended procedure compared to systemic use of MTX [16, 20]. UAE is effective in controlling uterine bleeding [17, 21, 22], as the embolization agents block the blood vessels, which directly decreases bleeding. Considering the time for absorption, SC is generally performed after 24-72 h of UAE [23], which may result in higher medical costs, as our results have shown. As another option, the combination of UAE, local MTX injection, and SC for the treatment of CSP has been evaluated by Liu [9]. This treatment was not included in our study. Our success rate was higher, possibly because we were more conservative in evaluating cases for suitability of SC treatment (such as a thicker myometrium). UAE is a useful method for patients with uncontrollable (preoperative or intraoperative) bleeding. In the process of SC, we also needed to evaluate the possibility of UAE in case of massive hemorrhage. Therefore, it is necessary to carefully assess the patient's condition and adopt a suitable treatment plan. In our data, UAE accounted for relatively few patients, and it is difficult to draw any conclusions based on small amounts of data. This is one of the study limitations. Another limitation is that we had insufficient data to evaluate the incidence of MTX side effects and blood product use. These indicators are important for clinical treatment. Ultimately, the choice of CSP treatment should be based on the patient's condition and severity.

Our data could provide valuable information for obstetricians, gynecologists, and patients who are dealing with this situation. We evaluated two treatment strategies, direct SC and preprocessing treatment with SC. Our treatments and results could provide evidence-based information for the selection of treatment methods. However, as a retrospective study, bias was unavoidable when some of the relevant data were not documented as required. To better understand and evaluate SC for CSP, larger sample sizes in other populations are still needed.

Conclusions

Preprocessing steps may do not increase the success rate of SC for CSP under certain conditions. Optimization of the preprocessing step requires further research.

Ethics Approval and Consent to Participate

The study protocol was approved by the Medical Ethics Committee of the Second Xiangya Hospital of Central South University (approval number: 2017018). All procedures were performed in accordance with the ethical standards of the Institutional Research Committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All subjects gave their informed consent for inclusion before they participated in the study.

Acknowledgments

Conflict of Interest

The authors declare no conflict of interest.

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