

Study on influencing factors and related clinical issues in cesarean scar pregnancy

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Objective: This study aims to investigate the etiological and bleeding risk factors of cesarean scar pregnancy (CSP) and attempts to determine the clinical value of uterine artery embolization (UAE) combined with curettage, methotrexate (MTX) chemotherapy combined with curettage, and uterine curettage alone in terminating CSP. **Materials and methods:** A total of 154 patients with CSP and 155 patients with cicatricial uterus termination of pregnancy in the same period who were hospitalized in the Department of Obstetrics and Gynecology, Second Affiliated Hospital of Nanchang University from January 2013 to March 2020 were enrolled in this study. The clinical characteristics of the two groups were statistically analyzed, and CSP patients were divided into the UAE + uterine curettage group (n = 49), MTX + uterine curettage group (n = 33) and uterine curettage alone group (n = 72) according to different treatment methods. The scar thickness, intraoperative blood loss, time to resumption of menstruation and other indicators were compared and analyzed among the three groups. **Results:** The proportion of CSP patients with cesarean section time < 24 months and ≥ 60 months was significantly higher than that of pregnant women with scar uterus. In the MTX + curettage group, 2 cases had intraoperative blood loss of more than 200 mL where the gestational age was more than 10 weeks, in which they were given Foley's catheter balloon compression hemostasis. In patients with simple uterine curettage, 6 cases had intraoperative blood loss of more than 200 mL with a gestational age of more than 8 weeks. Two cases were given emergency interventional treatment, while four underwent Foley catheter balloon compression hemostasis. The recovery time of β -hCG in the UAE + curettage group was shortest, which was found to be statistically significant. Furthermore, menopause time, blood β -hCG level and gestational sac diameter were found to be positively correlated with the amount of bleeding, while the thickness of the uterine scar was negatively correlated with the amount of bleeding. **Conclusions:** Gestational age, blood β -hCG level before treatment, gestational sac diameter and scar thickness were early warning indicators to evaluate the amount of bleeding in the treatment of CSP. UAE OR MTX pretreatment before cesarean section in CSP patients can significantly reduce intraoperative blood loss, and MTX + curettage is safe and effective for patients with abundant blood flow around the gestational sac with a gestational age of 8--10 weeks. However, in regard to CSP patients with a gestational age greater than 10 weeks and rich blood flow around the gestational sac, UAE pretreatment followed by termination of pregnancy is preferred. In case of hemorrhage during uterine curettage,

the emergency intrauterine balloon compression can achieve adequate hemostasis.

Keywords

Cesarean scar pregnancy (CSP); Uterine artery embolization (UAE); Methotrexate (MTX); Uterine curettage

1. Introduction

Cesarean scar pregnancy (CSP), defined as embryo implantation in the previous lower uterine segment anterior wall cesarean scar, is a serious long-term potential complication of cesarean section and is categorized as a special type of ectopic pregnancy [1]. If not managed properly, it can cause fatal massive hemorrhage or uterine rupture, therefore, once the diagnosis is confirmed, timely termination of pregnancy is recommended. However, no uniform treatment plan yet exists. Hence, this study retrospectively analyzed the clinical data of CSP patients who underwent uterine artery embolization (UAE) + uterine curettage, methotrexate (MTX) chemotherapy + uterine curettage and simple uterine curettage alone to terminate their pregnancies during a span of 7 years in the Second Affiliated Hospital of Nanchang University, to investigate the influencing factors regarding the incidence of CSP, bleeding risk factors and the feasibility and effectiveness in clinical application of the three treatment modalities

2. Materials and methods

2.1 Source of data

From January 2013 to March 2020, 154 patients with CSP and 155 pregnant patients with scarred uterus termination of pregnancy in the same period at the Second Affiliated Hospital of Nanchang University were enrolled in the study. The pregnant patients with scarred uterus terminated pregnancy were their own personal requirements and get husband's understanding. Subjects were aged 22–47 years, and the number of previous pregnancies was 2–13, number of cesarean sections was 1–3. Of the 154 patients with CSP, 73 had no obvious symptoms while 81 had vaginal bleeding, of which 3 had spontaneous massive vaginal bleeding and the others had persistent slight bleeding. Twenty-five of the 81 patients with CSP vaginal bleeding had lower abdominal pain and dis-

comfort. Of the 155 pregnant patients with scarred uterus, 12 had a little vaginal bleeding with lower abdominal distension discomfort.

2.2 Diagnosis and classification

(1) Diagnosis: Excluding 3 cases of bleeding were diagnosed by trans-abdominal gynecological color Doppler ultrasound, 151 patients with CSP were diagnosed by vaginal ultrasonography. Pelvic MRI was performed in 96 patients without emergency treatment or with vascular filling and rich blood flow around the gestational sac as indicated by color Doppler ultrasound.

(2) Classification: The latest Expert Consensus on the Diagnosis and Treatment of Uterine Scar Pregnancy after Cesarean Section (2016) proposes that all patients with CSP (including patients with CSP diagnosed before 2016) should be divided into three types according to the growth direction of the gestational sac at the scar as well as the thickness of the uterine scar. Type I (26 patients): a small part of the fetal sac implants at the scar, and the thickness of the scar is > 0.3 cm; Type II (118 patients): the fetal sac partially implants at the scar but does not protrude to the bladder, and the thickness of the scar is > 0.3 cm; Type III (10 patients): the fetal sac completely implants at the scar and protrudes to the bladder, and the thickness of the scar is ≤ 0.3 cm or discontinuous [2].

2.3 Treatment

All pregnant patients with scarred uterus were treated with surgical abortion, and CSP patients voluntarily chose treatment options according to their general conditions and economic conditions. Accordingly, 154 CSP patients underwent UAE followed by uterine curettage (49 cases, including 2 cases of type I, 40 cases of type II and 7 cases of type III), MTX followed by uterine curettage (33 cases, including 6 cases of type I, 26 cases of type II and 1 case of type III) and uterine curettage alone (72 cases, including 18 cases of type I, 52 cases of type II and 2 cases of type III). Patients who received UAE treatment completed uterine curettage surgery within 72 hours following intervention. For patients with blood HCG $\geq 20,000$ U/L, if they have previously undergone MTX treatment, uterine curettage surgery was performed after the HCG decreased to less than 20,000 U/L.

2.4 Outcome measures

(1) Preoperative conditions: age, number of pregnancies, number of cesarean sections, gestational age, time from this pregnancy to the previous cesarean section, size of gestational sac, serum β -hCG and progesterone levels before treatment in CSP patients, and scar thickness in CSP patients;

(2) Intraoperative conditions in CSP patients: duration of surgery, intraoperative blood loss;

(3) Therapeutic effect indicators in CSP patients: time for serum β -hCG to decrease to normal, hospital day, treatment costs, and time to resumption of menstruation.

2.5 Statistical analysis

All data were statistically processed using SPSS 16.0. The test values of the measured data among the CSP groups were

expressed as mean \pm SD ($\bar{x} \pm s$). One-way analysis of variance (One-Way ANOVA) was used for the comparison of equal variance, and the rank sum test was used for uneven variance. Spearman correlation analysis was used for the analysis of bleeding risk factors. χ^2 test was used for the comparison of pregnancy with scarred uterus and CSP group rate. The difference was considered to be statistically significant if $P < 0.05$.

3. Results

3.1 Etiological factors of CSP

The age, number of miscarriages, number of cesarean sections, time to previous cesarean section and other indicators of the 154 CSP patients were compared to 155 pregnant women with scarred uterus termination of pregnancy in the same period, in which a significant difference in the distribution of "Time to previous cesarean section" was found ($P < 0.05$), of which the "Time to previous cesarean section" of the 29 cases (18.83%) were < 24 months, higher than the pregnant with scarred uterus group, $\chi^2 = 8.757$, $P = 0.003$. Moreover, 54 cases (35.06%) were ≥ 60 months, higher than the pregnant with scarred uterus group, $\chi^2 = 12.201$, $P = 0.000$. After regression analysis, it was found that there was no correlation between "Time to previous cesarean section" and the incidence of CSP (Table 1).

3.2 Comparison of general data among three groups of CSP patients

No significant difference in age, times of pregnancy, times of cesarean section, gestational age, time from this pregnancy to previous cesarean section, blood β -hCG and progesterone levels before treatment, and the diameter of the gestational sac among the three groups of CSP was present. Additionally, the thickness of scar was thinnest in the UAE + uterine curettage group, which was statistically significant ($P < 0.05$). The thickness of scar was similar between the MTX + uterine curettage group and the uterine curettage alone group, which was not statistically significant (Table 2).

3.3 Comparison of therapeutic effects among the three groups of CSP patients

The operation time among the three groups of patients with CSP was shortest in the MTX + uterine curettage group and longest in the uterine curettage alone group, which was observed to be statistically significant ($P < 0.05$). The hospital day was shortest in the group that underwent uterine curettage alone. As certain patients in the MTX + uterine curettage group required repeated multiple drug treatments, their hospital day was longest, which was statistically significant ($P < 0.05$). Hospitalization costs were highest in the UAE + uterine curettage group and lowest in the uterine curettage alone group, which was observed to be statistically significant ($P < 0.05$).

Two patients with MTX + uterine curettage more than 10 weeks were present; both were type II, had intraoperative blood loss of more than 200 mL, and underwent emergency Foley catheter balloon compression hemostasis. Six patients

Table 1. Comparison of clinical data of CSP pregnant with scarred uterus group n (%).

Variable	CSP Group, n = 154, (100%)	Pregnant with scarred uterus Group, n = 155, (100%)	χ^2	P value
Age				
< 30	64 (41.56)	63 (40.65)	0.027	0.870
≥ 30	90 (58.44)	92 (59.35)		
Number of miscarriages				
0	1 (0.65)	3 (1.94)	1.307	0.860
1	30 (19.48)	28 (18.06)		
2	36 (23.38)	35 (22.58)		
3	42 (27.27)	46 (29.68)		
≥ 3	45 (29.22)	43 (27.74)		
Number of cesarean sections				
1	89 (57.79)	90 (58.06)	0.002	0.961
≥ 2	65 (42.21)	65 (41.94)		
Interval (month)				
< 24	29 (18.83)	16 (10.32)	16.661	0.000
24–60	71 (46.10)	107 (69.03)		
≥ 60	54 (35.06)	32 (20.65)		

had intraoperative blood loss of more than 200 mL (2 cases of type III, 4 cases of type II) and were more than 8 weeks of gestational age, of which 2 cases (all type III) were given emergency interventional therapy and 4 cases (type II) were given Foley catheter balloon compression hemostasis. None of the patients who underwent UAE + uterine curettage had blood loss greater than 200 mL. The bleeding volume of the three groups was least in the UAE + uterine curettage group and most in the uterine curettage alone group, which was found to be statistically significant.

The most direct indicators in evaluating the success of treatment were found to be the presence or absence of residual uterine cavity, whether blood β -hCG returns to normal, and whether menstruation resumes. Among the 154 patients treated, 4 patients had residual uterine cavity, including 3 patients in the simple uterine curettage group and 1 patient in the MTX + uterine curettage group. The diameter of residual tissue was less than 1.5 cm. Four patients with residual uterine cavity were given MTX systemic chemotherapy while inducing uterine contractions, in which their serum β -hCG eventually returned to normal. The recovery time of serum β -hCG in the UAE + uterine curettage group was significantly different, where the MTX + uterine curettage group was similar to the uterine curettage alone group. Due to timely treatment, no significant difference in the time of resumption of menstruation existed among the three groups (Table 3).

3.4 Secondary complications among the three groups of CSP

In the UAE + uterine curettage group, 36 patients (73.47% in UAE group) had different degrees of lower abdominal pain following intervention, of which seven patients required analgesic drugs. Twenty patients in the UAE + uterine curettage group had irregular vaginal bleeding following interventional surgery, and all patients in the MTX + uterine curettage group had irregular small amount of vaginal bleeding

during chemotherapy, with no special treatment. Furthermore, 12 patients that underwent MTX + uterine curettage had different degrees of liver function impairment and were given liver protection treatment, which did not cause irreversible damage. No complications such as uterine perforation occurred during uterine curettage among the three groups.

3.5 Correlation analysis of risk factors for bleeding in patients with CSP

A correlation analysis was performed between pretreatment indicators (age, number of pregnancies, number of cesarean sections, gestational age, time from previous cesarean section) and bleeding volume among the 72 patients in the simple uterine curettage group. After analysis, it was found that the gestational age, blood β -hCG level and gestational sac diameter had statistical significance ($P < 0.05$), in which the correlation coefficient was > 0 , which was positively correlated with the amount of bleeding. The uterine scar thickness was also statistically significant ($P < 0.05$), where the correlation coefficient was < 0 , which was negatively correlated with the amount of bleeding (Table 4).

4. Discussion

Due to the adjustment of China's "second child policy", drawbacks in the history of high cesarean section rate began to appear, and the incidence of CSP began to increase annually. In the present study, 154 cases of CSP were evaluated, of which 108 patients accounted for 70.13% of the total in the past four years. Since CSP may lead to uterine rupture, uncontrollable bleeding and even loss of fertility [3, 4], it is particularly important to determine its etiological factors and early diagnosis as well as provide active and effective treatment.

Table 2. Comparison of general data among three groups of CSP patients ($\bar{x} \pm s$).

Category	UAE + uterine curettage Group (n = 49)	MTX + uterine curettage Group (n = 33)	The uterine curettage alone Group (n = 72)	P value
Age (year)	32.33 ± 5.23	31.85 ± 5.93	32.11 ± 5.77	0.931
Number of pregnancies	4.27 ± 1.29	4.94 ± 2.28	4.64 ± 1.83	0.410
Number of CS	1.49 ± 0.65	1.48 ± 0.62	1.50 ± 0.63	0.968
Gestational age (days)	52.96 ± 12.24	50.21 ± 12.86	50.79 ± 11.62	0.520
Time since last cesarean section (months)	57.47 ± 48.65	46.27 ± 55.51	54.99 ± 51.42	0.610
Pre-treatment serum β -hCG level (U/L)	64081.54 ± 48197.99	43285.09 ± 52274.54	47289.57 ± 52000.04	0.117
Progesterone level (ng/mL)	52.96 ± 12.24	50.21 ± 12.86	50.79 ± 11.62	0.520
Diameter of gestational sac (mm)	29.35 ± 10.87	28.42 ± 17.58	27.58 ± 14.34	0.798
Uterine scar thickness (mm)	2.27 ± 0.71	2.98 ± 1.14	2.78 ± 0.97	0.002

Table 3. Comparison of therapeutic effect among three groups of CSP patients ($\bar{x} \pm s$).

Groups	Operation time (min)	Hospital day (days)	Hospital costs (RMB)	Intraoperative blood loss (mL)	Time for serum β -hCG to return to normal (days)	Time to resumption of menses (days)
UAE + uterine curettage Group (n = 49)	16.94 ± 3.20**	8.24 ± 2.16**	18581.78 ± 2294.50**	17.76 ± 6.93**	12.53 ± 3.27**	40.80 ± 5.12
MTX + uterine curettage Group (n = 33)	14.42 ± 2.17#	15.12 ± 1.92#	9929.80 ± 1988.75#	57.85 ± 50.74#	20.85 ± 3.13	43.73 ± 5.60
uterine curettage alone Group (n = 72)	19.26 ± 3.29	6.28 ± 2.18	5233.14 ± 2144.31	113.18 ± 83.86	20.25 ± 4.46	42.58 ± 7.14

Note: * $P < 0.05$ compared with MTX + uterine curettage group; # $P < 0.05$ compared with uterine curettage alone group.

Table 4. Multivariate correlation analysis of risk factors for bleeding in patients with CSP.

Variable	P value	Correlation coefficient
Gestational age	0.031	0.254
Blood β -hCG level	0.044	0.238
Gestational sac diameter	0.043	0.239
Thickness of uterine scar	0.026	-0.263

4.1 Etiological factors of CSP

At present, the pathogenesis of CSP is not clear. Various scholars hold the opinion that multiple cesarean sections increase the damage done to the endometrium as well as the scar area, thereby increasing the probability of gestational sac implantation in the endometrium [5, 6]. The findings of this study demonstrate that undergoing multiple cesarean sections does not significantly increase the occurrence of CSP, which is in contrast to the above assertion. However, the incidence of CSP significantly increased when the time from previous cesarean section was < 24 months or ≥ 60 months. Reasons for this may be that the time from previous cesarean section is too short, the uterine scar site is not completely healed, multiple scar fissures may exist, and endometrial preparation is not sufficient, which is not conducive to embryo implantation. Additionally, the abnormal operation of fertilized eggs and missing of optimal implantation time cause trophoblasts to invade the extracellular matrix of cesarean scars and trigger CSP [7–10]. C-kit and PI3K play a role in scar formation and healing process, and C-kit and PI3K mRNA expression levels as well as positive expres-

sion in scar tissue are significantly increased 5 years after operation, resulting in excessive proliferation of collagen fibers [11]. However, regression analysis shows that the interval time of previous cesarean section is not the risk factor for CSP, which might be related to the insufficient sample size.

4.2 Early diagnosis of CSP

The diagnosis of CSP mainly relies on medical history, clinical manifestations and auxiliary examinations. There may be no clear history of menopause at the onset of CSP, and most patients present with painless vaginal bleeding [12]. In this study, serum β -hCG was not found to be specific for the diagnosis of CSP, which may be related to the large range of serum β -hCG fluctuations at the site of gestational sac implantation in CSP patients as well as in normal early pregnancies. Therefore, serum β -hCG cannot be used as the main diagnostic investigation for CSP, however, it is very important in evaluating the therapeutic effect during the follow-up. Simple, effective and economical transvaginal ultrasound serves as the main auxiliary examination for the early diagnosis of CSP [13, 14]. The ultrasonographic characteristics of CSP are as follows: (1) No gestational sac is apparent in the uterine cavity and cervical canal; (2) Trophoblast is mainly located between the bladder and anterior wall of the uterus; (3) The uterus between the gestational sac and bladder is thin or even disappears; (4) The sagittal plane of the anterior wall of the uterus between the gestational sac and cervical canal is discontinuous [7, 15]. MRI allows for multi-slice and multi-directional imaging with higher resolution for soft tissue than ultrasonography, which is more sensitive in demonstrating blood flow. Therefore, MRI is another imaging modality

for cases in which ultrasonography is difficult and may not provide a definitive diagnosis [12]. As patients in this study group refused laparoscopic and open surgery, in view of medical safety, MRI was performed in 96 patients who did not require emergency treatment or had rich blood flow around the gestational sac as indicated by color Doppler ultrasound, providing reference in selecting termination of pregnancy.

4.3 The therapy selection of CSP

Principles of treatment of CSP is removal of the lesion, reduction of bleeding and preservation of reproductive function [3]. Moreover, treatment methods include interventional therapy, drug therapy, surgical treatment and combined therapy. Uterine artery embolization (UAE) blocks the blood supply of the gestational sac by selectively embolizing the uterine artery, resulting in ischemic necrosis of the embryo and significantly reducing bleeding during embryo dissection and abortion [3, 16, 17]. This study found that the bleeding volume of patients in the UAE + uterine curettage group was significantly less than that of patients in the other two groups, and no patients in the UAE + uterine curettage group underwent hysterectomy due to massive hemorrhage. However, Cao *et al.* [16] reported that two patients with CSP had uncontrollable bleeding following UAE treatment. Therefore, the following points must be considered prior to commencing UAE: (1) Definite diagnosis: CSP is not only often misdiagnosed as a cervical pregnancy, but it is also confused with normal intrauterine pregnancy. If uterine artery embolization is performed in a normal pregnancy, wastage of medical resources as well as an increase in economic burden for patients occurs, and complications following embolization may be encountered, leading to ischemic injury of non-target tissues. Therefore, a definitive diagnosis is a prerequisite for the successful treatment of UAE; (2) Timing of surgery: In this study, all patients who underwent UAE underwent uterine curettage within 72 hours after embolization to avoid failure of surgery due to the establishment of collateral circulation. In regard to patients with special circumstances requiring subsequent uterine curettage, it was necessary to perform a second embolization in order to avoid massive hemorrhage; (3) Check: In patients with CSP more than 10 weeks pregnant, the placenta has already been formed. Considering that the blood supply of uterus is partly from the communication branches of ovarian vessels and internal pudendal artery, simple embolization of the uterine artery still risks massive hemorrhage, hence, planning for laparotomy or balloon tamponade hemostasis should be done for such patients; (4) Fully inform the relevant risks of interventional therapy such as premature ovarian failure, abdominal pain, uterine ischemic necrosis, and uncontrollable bleeding following interventional therapy. Premature ovarian failure is mainly caused by embolic agents that block blood vessels supplying the ovary with blood circulation. Whether menstruation resumes after surgery is an important evaluation index. No significant difference in the onset time of menstruation between patients treated with UAE and the other two

groups were present, however, 36 patients (73.47% in UAE group) had different degrees of abdominal pain after UAE, which may be related to transient uterine ischemia, hypoxia, edema, hyperkalemia and histamine stimulation of pain sensation in muscle fiber cells.

MTX is currently the first-line drug for conservative treatment, which inhibits trophoblastic cell division in order to kill embryos and may be administered locally and systemically. Jin li *et al.* found that no significant difference in the treatment success rate between the two routes of administration [18]. In this group of data, 33 patients were treated with MTX + uterine curettage, and the MTX dosing regimen was calculated as 50 mg/m² intramuscular injection, in which the number of doses was determined according to the level of blood HCG decline, where the cumulative dose was not more than 200 mg. Previous studies [19] have shown that blood HCG ≥ 20000 U/L is a factor of massive hemorrhage. Combined with experiences in treating CSP at our hospital, uterine curettage was given when HCG decreased to less than 20000 U/L. Here, intraoperative blood loss was significantly reduced compared to patients who underwent uterine curettage alone. However, there were still 2 patients (type II) having a blood loss greater than 200 mL. Foley's catheter balloon compression was urgently given for hemostasis, and the gestational age of both patients were greater than 10 weeks. Kanat-Pektas *et al.* [20] reported that 3.6%, 1.1%, and 7.3% of CSP patients who underwent MTX alone, UAE, and uterine curettage, respectively, had hysterectomies done due to excessive bleeding. Thus, the risk of hysterectomy by uterine curettage alone was twice that of MTX-treated patients and seven times that of UAE-treated patients. In this study, color Doppler ultrasound and MRI suggested that CSP patients with rich blood flow around the gestational sac (RI: 0.44 ± 0.13) required initial MTX or UAE pretreatment, hence, no patients who underwent uterine curettage alone had hysterectomies due to massive hemorrhage. Two patients with type III uterine curettage alone had a blood loss of more than 200 mL. Considering that the gestational sac protruded into the bladder and the uterine scar was ≤ 0.3 cm in patients with type III uterine curettage, balloon compression may cause an uncertain hemostatic effect or risk uterine rupture, hence, 2 patients with type III uterine curettage were given emergency interventional therapy. In addition, 4 patients with type II uterine curettage who had a blood loss of more than 200 mL underwent Foley's catheter balloon compression for hemostasis. The gestational age of these 6 patients were more than 8 weeks.

Patients with a bleeding volume greater than 200 mL in simple uterine curettage and MTX + uterine curettage were more than 8 weeks or even more than 10 weeks of gestational age. Reasons for this may be that after 8 weeks of pregnancy, the placental villi's development flourishes and are firmly connected to the decidua basalis, having branches of umbilical artery and umbilical vein in each villous trunk. The increase in maternal uterine spiral blood into the inter-

villous space while the cesarean scar was relatively poor, resulted in the stimulation of villous trophoblasts that invade the scar and its surrounding deep uterus, causing a significant increase in bleeding volume after 8 weeks of pregnancy. After 10 weeks of pregnancy, the placenta was preliminarily formed, the dissection area following uterine curettage was large, and the scar did not contract. Even after MTX treatment, a risk of massive hemorrhage was still present.

In order to explore which factors were related to the severity of bleeding during CSP treatment, this study conducted a dedicated analysis and found that the three indicators of menopause time, serum β -hCG level before treatment, and gestational sac diameter were significantly positively correlated to the amount of bleeding, while uterine scar thickness was negatively correlated to the amount of bleeding. Therefore, the above four indicators may be used as early warning markers in order to assess the amount of bleeding in the treatment of CSP.

4.4 Remedies following treatment failure

Regardless of the method used to treat CSP, a preemptive plan for massive hemorrhage and persistent ectopic pregnancy should be made. According to the data of this study, in order to minimize the risk of residual uterine cavity and avoid massive hemorrhage caused by repeated scratching and scarring, the operation was performed by experienced senior surgeons under the guidance of color Doppler ultrasound. Accordingly, 154 patients had only 4 cases of residual uterine cavity (3 in the simple uterine curettage group and 1 in the MTX + uterine curettage group), where the diameter of residues was less than 1.5 cm. For the 4 patients with residual uterine cavity, MTX treatment was given while inducing uterine contractions, which were all successful. UAE and uterine cavity balloon compression hemostasis were remedial measures in controlling intraoperative bleeding. Since the materials required for balloon compression hemostasis are available at all hospitals, are easy to operate and have good hemostatic effect, they could be popularized in primary hospitals, saving valuable time in the transfer treatment of such patients.

In summary, gestational age, pretreatment serum β -hCG levels, gestational sac diameter and scar thickness were early warning indicators in assessing the amount of bleeding in the treatment of CSP. Moreover, UAE or MTX treatment done prior to termination of pregnancy in patients with CSP could significantly reduce the amount of bleeding during uterine curettage. Patients pretreated with UAE were found to have less bleeding, and it was not appropriate to choose uterine curettage alone to terminate the pregnancy for type III patients. Factors such as blood flow around the gestational sac have important reference value in the selection of CSP treatment options. In regard to patients with rich blood flow around the gestational sac of more than 10 weeks of gestation, UAE pretreatment is preferred prior to termination of pregnancy. For patients with rich blood flow around the gestational sac between 8 and 10 weeks of gestational age, after

acquiring informed consent from patients and their families, preparation for blood transfusion, UAE or balloon compression hemostasis, MTX systemic chemotherapy should be performed until HCG is less than 20,000 IU/L, color Doppler ultrasound-guided uterine curettage is a good choice.

This study attempted to compare the surgical effect and safety of the three treatment schemes and further clarified that pretreatment is recommended for patients with more than 8 weeks of gestation and rich blood flow around the gestational sac. MTX pretreatment may be considered for patients between 8 and 10 weeks of gestation, whereas UAE pretreatment is recommended for patients who are over 10 weeks of gestation. Emergency uterine cavity balloon compression is beneficial for hemostasis during operation if much bleeding is present. The limitations of this study are that the sample size was relatively small. Moreover, CSP termination of pregnancy also includes other methods such as hysteroscopic surgery and laparoscopic surgery, which were not included in the scope of this study. Therefore, treatment choice still requires further elucidation.

Author contributions

JX and XJH conceived and designed the experiments; JL and YYX analyzed the data; JX and XJH wrote the paper. FF, WZ and LLL critically revised the manuscript.

Ethics approval and consent to participate

The study protocols were approved by the Ethical Committee of the Second Affiliated Hospital of Nanchang University. Written consent to participate was obtained from the patient in this study.

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Conflict of interest

The authors declare no conflict of interest.

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