

Therapeutic approach for the cesarean scar pregnancy

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Abstract

The aim of this study was to explore the pros and cons of different treatments of cesarean scar pregnancy (CSP).

We retrospectively studied 205 cases of CSP that were treated in our hospital from June 2013 to June 2014, 189 of which had surgical operation.

The average age of the patients was (32.98 ± 4.56) years. Data from those 189 cases were analyzed.

Two hundred five patients from Beijing Obstetrics and Gynecology Hospital.

One hundred eighty-nine cases who had operative treatment, 111 of which received curettage under hysteroscopy, 70 of which received curettage under ultrasonography, 8 of which received laparoscopic Cesarean scar resection.

Management of 189 ectopic Cesarean scar pregnancy cases discussed in this article was usage of methotrexate (MTX) via the utility of uterine arterial chemotherapy embolization (UACE).

All of 189 patients were cured without hysterectomy. Hysteroscopy provides a clear view for us, making it easy to identify the range of affected tissues, and clean the pregnancy tissue. Curettage under ultrasonography is relatively simple and inexpensive. Laparoscopic surgery is more suitable for exogenous CSP patients that can reduce the operation risk and prevent uterine perforation. However, laparoscopic surgery costs much more than those 2 and needs longer time of hospitalization.

Treatment options should be personalized according to different situations. Minimal invasion, thorough treatment, quick recovery, low risk of hysterectomy, preserved fertility function, and improved life quality are the principles we have been pursuing for.

Abbreviations: CDFI = Color Doppler flow imaging, CSP = cesarean scar pregnancy, MTX = methotrexate, UACE = uterine arterial chemotherapy embolization.

Keywords: cesarean scar pregnancy, cesarean section, operative treatment

1. Introduction

Cesarean scar pregnancy (CSP) is defined as gestational sac, villa, or placenta planting only at the scar of previous Cesareans. As the development of gestation, villa would implant into uterine myometrium, even worse resulting in uterine rupture.^[1,2] CSP is 1 rare type of ectopic pregnancy and late complications of Cesarean section.^[3] It has occurred more often than before with the increasing Cesarean surgeries and the improvement of ultrasound diagnosis.^[4] However, it is so difficult to get diagnosed that the misdiagnosis rate of CSP at first consultation is as high as 76%.^[5] CSP can be misdiagnosed as threatened abortion, incomplete abortion, cervical pregnancy, malignant trophoblastic tumor, and so forth in first trimester. It can cause uterine or

unmanageable bleeding if it is not treated in a time or in an improper way like curettage.^[6] Some of CSP patients would have to receive hysterectomy-losing fertility function and have severe life-threatening complications. In contrast, if the patients are diagnosed as early as possible and receive a proper treatment, the complications mentioned above and hysterectomy can be avoided, which means fertility function can be preserved. Consequently, we retrospectively studied 205 cases of CSP that were treated in our hospital from June 2013 to June 2014 to explore a proper approach to treat CSP.

2. Patients and methods

This study was approved by The Institutional Review Board of Ethics Committee of Beijing Obstetrics and Gynecology Hospital. We retrospectively studied Cesarean scar pregnancy cases that were diagnosed and treated in our hospital from June 2013 to June 2014 by searching through the institutional OB/GYN database by the term "Cesarean scar pregnancy." Medical records analyzed consist of the age, gestational age, number of previous Cesarean sections, time interval between last pregnancy and Cesarean scar pregnancy, and clinical management (See Table 1).

Our protocol for diagnosis had been previously published.^[7] Transabdominal or transvaginal ultrasonography-Color Doppler flow imaging (CDFI) was used to diagnose pregnancies and assess the thickness of the uterine lower segment underlying the Cesarean scar.

Management of 189 ectopic Cesarean scar pregnancy cases discussed in this article was usage of methotrexate (MTX) via the utility of uterine arterial chemotherapy embolization (UACE). Femoral artery puncture and sheath placing was done through

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Table 1
Summary of patients.

	n	Mean ± standard deviation
Age		32.98 ± 4.56
Time of amenorrhea		52.15 ± 13.7 d
Number of previous cesarean		1.22 ± 0.43 d
Time interval between last pregnancy and CSP		4.78 ± 3.15 y
Parameter of gestational sac		2.1 ± 1.14 cm
Thickness of cesarean incision scar		0.3 ± 0.16 cm
Surgery approach		
Curettage under hysteroscopy	111	
Curettage under ultrasonography	70	
Laparoscopic cesarean scar resection	8	

CSP = cesarean scar pregnancy.

Seldinger technique at a single inguinal region. Catheters were used for performing super-selective angiography in uterine artery and then infusing MTX 50 mg; finally, gelfoam particles were used to do embolization in uterine artery under X-ray until the stem of uterine artery was fully filled that was confirmed by DSA angiography later. Operations were taken 24 to 72 hours after the interventional therapy. All patients were followed for 3 to 6 months after the surgery, and gynecological examination, blood β -hCG level, and ultrasound were done in every consultation.

3. Results

There are totally 205 CSP cases collected from the database, the age of which range from 23 to 49 years with an average of 32.98 ± 4.56 years. Time of amenorrhea ranged from 32 to 120 days, with a mean of 52.15 ± 13.7 days. The number of previous Cesarean section ranged from 1 to 3 with an average of 1.22 ± 0.43 days. One hundred sixty-two of CSP patients had Cesarean section only once, 41 patients of twice Cesarean section, and 2 patients of 3 times. The time interval between last pregnancy and CSP ranged from 5 months to 18 years, with a mean of 4.78 ± 3.15 years. Of 205 CSP cases, 13 patients received drug induction and 3 patients failed in induced abortion in other hospital. So, we studied those 189 cases to explore the pros and cons of different approaches. The parameter of gestational sac ranged from 0.6 to 6.23 cm with an average of 2.1 ± 1.14 cm. Gestational sac of 5 cases grows toward out of the uterine that manifested as dark area or uneven mass. The thickness of Cesarean section incision scar ranged from 0.1 to 0.8 cm with a mean of 0.3 ± 0.16 cm. Blood β -hCG level ranged from 28 to 289,972 mIU/mL with a median of 31,004.6 mIU/mL.

Of 189 patients who had already received MTX perfusion and uterine artery embolization (UAE), 111 of whom received curettage under hysteroscopy (CUH), 70 of whom received curettage under ultrasonography (CUU), and 8 of whom received laparoscopic Cesarean scar resection (LCSR). All these 189 CSP patients have been cured and their blood β -hCG level, gynecological examination, and ultrasound test result were all normal. Figure 1 shows different aspects of 3 surgery approaches. Operation time varies significantly ($P < .0001$) among 3 surgery approaches. Operation time of CUH group ranged from 5 to 50 minutes with a median of 20 minutes. Operation time of CUU group ranged from 5 to 50 minutes with a median of 20 minutes. Operation time of LCSR group ranged from 56 to 120 minutes with a median of 75 minutes. Amount of bleeding during operation is not significantly different among 3 groups. Amount of bleeding during operation of CUH group ranged from 5 to 130 mL with a median of 50 mL. Amount of bleeding during

operation of CUU group ranged from 10 to 800 mL with a median of 20 mL. Amount of bleeding during operation of LCSR group ranged from 10 to 300 mL with a median of 30 mL. Length of stay are not significantly different among 3 groups. Length of stay of CUH group ranged from 3 to 14 days with a median of 6 days. Length of stay of CUU group ranged from 2 to 27 days with a median of 6 days. Length of stay of LCSR group ranged from 5 to 13 days with a median of 9 days. Hospitalization expenses are significantly different ($P < .0001$) among 3 groups. Expenses of CUH group ranged from ¥9175.79 to ¥21,096.46 with a median of ¥12,337.48. Expenses of CUU group ranged from ¥5514.29 to ¥20,765.85 with a median of ¥10,608.1. Expenses of LCSR group ranged from ¥5317.44 to ¥27,193.31 with a median of ¥17,513.6. See Table 2.

Of the patients who received curettage under hysteroscopy, 22 patients had a baldachin at the Cesarean scar, parameter of which ranged from 0.5 to 2.5 cm. One of the patients who received CUU had second embolization surgery in both anterior stem of internal iliac artery due to hemorrhage of 130 mL during operation. Uneven echo area ranging $3.3 \times 3.7 \times 1.4$ cm was found in 1 patient who had received CUU when routine check on first week after the surgery. She therefore had to receive a second CUU, followed by injection of MTX 30 mg through cervix. There was a 64-day triplet pregnancy in CUU group. Three patients in LCSR group had an ultrasound result of uneven echo. One of them had received induced abortion in other hospital, but her blood β -hCG level was not decreased apparently. She was then given intramuscular injection of MTX 50 mg for 2 days. Reexamination by ultrasonography showed a dark area inside the uterine and a baldachin ranging $4 \times 4 \times 3$ cm at cervix internal ora. Finally, she came to out hospital and received LCSR along with intramuscular injection of MTX 50 mg at lower uterine segment and curettage under hysteroscopy. One patient of LCSR group failed in drug induction and then was given CUU. Owing to a hemorrhage, she was then given embolization at both sides of uterine artery. However, after the surgery, an uneven echo ranging $4.6 \times 4.9 \times 4.2$ cm was found at lower segment of uterine by routine ultrasound test. So, she received LCSR and curettage.

4. Discussion

CSP is diagnosed by vaginal or abdominal ultrasound CDFI. Level of β -HCG has an important reference value before and after the treatment of CSP. It is difficult to give an early diagnosis of CSP, so it is easy to be misdiagnosed as threatened abortion, incomplete abortion, cervical pregnancy, malignant trophoblastic tumor, and so forth. Uncontrollable vaginal bleeding is often caused by inappropriate induced abortion or curettage, some-

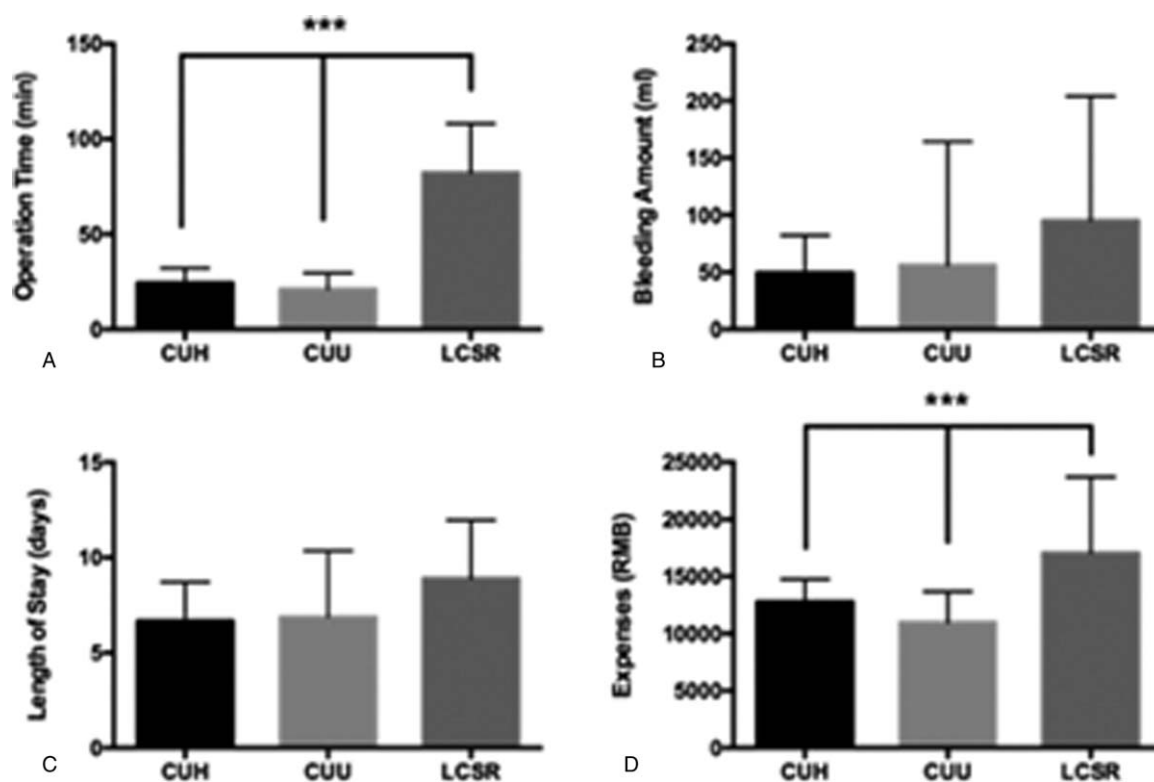


Figure 1. Aspects of 3 different surgery approaches. Operation time and expenses are significantly different among 3 surgery approaches, while bleeding amount and length of stay are not significantly different in 3 surgery approaches. CUH=curettage under hysteroscopy, CUU=curettage under ultrasonography, LCSR=laparoscopic cesarean scar resection. Data are shown as mean + standard deviation, $n_1=111$, $n_2=70$, $n_3=8$, $^*P < .0001$.

times making hysterectomy a must in control the hemorrhage. Even worse, patients will lose reproductive function and be life-threatening. Generally accepted mechanism of CSP is that minimal wholes at scar caused by inflammation, poor healing of Cesarean incision, or broad Cesarean scars makes moving too fast or maldeveloped fertilized eggs fall into it and implant into muscular layer.^[8]

Most CSP patients have a history of menolipsis and Cesarean section, and some of them also have vaginal bleeding to abdominal pain. Their uterine will be found larger and softer in gynecological examination and their blood β -hCG level will increase in different degrees. Ultrasonography is necessary and it is the simplest and most practical method with an accuracy of 84.6% in diagnosing CSP.^[4,6] The diagnostic criteria for CSP^[2,4,7] include confirmation by transvaginal ultrasound based on the following reasons: A gestational sac is located anteriorly at the uterine isthmus within a visible myometrial defect at the site of a previous lower-segment Cesarean section delivery scar; An empty uterine cavity and cervical canal are found; Evidence of a

functional trophoblastic/placental circulation on color Doppler examination.

The principles of treatment for CSP are to diagnose early, to manage early, and keep reproductive function as much as possible. Methods we use at present are conservative treatment and operative treatment.^[9-11] Conservative treatment consists of drug therapy and conservative operative treatment.^[10,12] Drug therapy means to use local or systemic MTX, which can inhibit dihydrofolate reductase as a folic acid antagonist.^[13] DNA synthesis in embryonic cells will therefore be interfered, resulting in inhibiting embryonic development. Conservative operative treatment means perfusion embolization of uterine artery and perfusion of MTX into uterine artery, making drugs enter into the embryo. It can directly kill trophoblasts, improving the curative effect by 2 to 22 times.^[14] However, the total treatment lasts for a long time and risks such as hemorrhage, infection, mass or uterine eruption, or even hysterectomy are likely to happen.

Uterine artery embolization, also known as UAE, has been the first choice taking the place of other surgical treatments in

Table 2

Different aspects of 3 surgery approaches.

Surgery approach	n	Operation time, min		Bleeding amount, mL		Length of stay, d		Expenses, Yuan	
		Median	P25-P75	Median	P25-P75	Median	P25-P75	Median	P25-P75
Curettage under hysteroscopy	111	20.0	20.0~30.0	50.0	20.0~80.0	6.0	6.0~7.0	12,337.48	11,622.97~13,233.50
Curettage under ultrasonography	70	20.0	20.0~20.0	20.0	20.0~57.5	6.0	5.0~7.0	10,608.10	8892.61~12,305.74
Laparoscopic cesarean scar resection	8	75.0	60.0~107.5	30.0	20.0~187.5	9.0	5.5~11.8	17,513.60	12,131.98~21,304.32
P		.000		.275		.113		.000	

controlling hemorrhage in gynecology, as UAE was used to treat postpartum hemorrhage in 1980s.^[15] Uterine artery chemotherapy embolization, UACE, followed by surgery is the first choice of treating CSP.^[3] The advantages of UACE are UACE can block the blood supply resulting in ischemic necrosis of the gestational sac as well as prevent or control the hemorrhage during curettage.^[16] Embolization is only in the stem of uterine artery, and peripheral arteries and capillaries can also give supply to the uterine. Gelfoam particles can be resolved in 2 to 3 weeks so the blood circulation can recover competitively at that time. The menstruation and reproductive function will be normal.^[17] Perfusion through uterine artery can keep a local high concentration of MTX improving the curative effect by 2 to 22 times. After the perfusion embolization, fever, infective endometritis, and retention caused by absorbing the necrotic tissue inside the uterine cavity would cause coagulation disorder or even delayed disseminated intravascular coagulation (DIC). So, curettage should be taken within 24 to 72 hours after the surgery.^[18–20]

Patients who received surgery had a shorter length of stay in hospital, less amount of bleeding, preserved fertility, and an improved life quality. In our study, 92% patients had operative treatments that are curettage under hysteroscopy, CUU, and LCSR. All 189 patients have been cured and none of them received hysterectomy. According to the statistical analysis, there is no significant difference among those 3 approaches in terms of amount of bleeding in operation and length of stay. The expense of CUU is the least among 3 approaches. Curettage under hysteroscopy can give an intuitive view of the lesion making it easy to know about the location, size, whether there is active bleeding, and so forth.^[21] It can avoid missing the lesion or extensive damage on endometrium caused by single curettage.^[22] Moreover, curettage under hysteroscopy has a shorter operation time than other 2 approaches. LCSR is suitable for cases that the lesion grows toward outside the uterine because resection of lesion and uterus repair can be done at the same time. But it has a high expense and a long operation time.

For those CSP patients whose ultrasound examination revealed that the embryo sac was small, the villi were shallow, and the local blood flow was not abundant, with low blood β -HCG levels or growth in the uterine cavity, could receive curettage guided by ultrasound. For those CSP patients whose ultrasound examination revealed a diverticulum or complicated grows toward the uterine cavity, hysteroscopic curettage is the best choice. It can directly help to observe the location, size, and active bleeding of the lesion and to solve the problems caused by a simple curettage such as missed suction and excessive damages. Above 2 methods can be selected according to patient's wishes and economic conditions. For those CSP patients whose ultrasound examination revealed that the lesion invading toward the convex, too deep lesion, and myometrium, local large masses, rich blood supply CSP, or any other complicated cases of failure by other surgical methods, at the meantime maintaining fertility requirements, laparoscopic surgery would be the best choice. It helps to remove the lesions locally and repair the uterus reducing the incidence of uterine perforation and a second surgery.

5. Conclusion

Etiology is essential in preventing CSP from happening. Indication for Cesarean section should be taken strictly to reduce Cesarean section rate. As the Cesarean section rate increased, the number of CSP patients has been rising gradually and great importance should be attached to early diagnosis and early

treatment.^[23] In this article, we get a conclusion that conservative treatment is not the main approach any more. Although conservative treatment has limited effect and needs a long time, it costs less than surgery and is still practical in grassroots hospitals. UACE has been universally used in clinical practice and become the first choice in treating CSP with the development of interference techniques. The reason why more and more doctors choose UACE is not only obvious effect and short length of stay but also that it can preserve the reproductive function. Curettage under hysteroscopy can give a clear view of the lesion, while CUU is much more convenient and costs less. Laparoscopic surgery is suitable for cases that the lesion grows toward outside the uterine and can prevent perforation of uterus.^[24,25] However, it costs much more and has a much longer length of stay than the other 2 approaches. Treatment plan should be decided according to the different situations individually. The final purpose is to reduce the risk of hysterectomy and improve the life quality of patients.

Author contributions

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