Identifying risk factors for recurrent cesarean scar pregnancy: a case-control study

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Objective: To investigate risk factors for recurrent cesarean scar pregnancies.
Design: Case-control study.
Setting: University hospital.
Patient(s): Twenty-one women with recurrent cesarean scar pregnancies and 42 women with single cesarean scar pregnancies.
Intervention(s): None.
Main Outcome Measure(s): Risk factors and historical factors that might be predisposing factors in recurrent cesarean scar pregnancy.
Result(s): The risk factors of recurrent cesarean scar pregnancy were cesarean delivery history in rural community hospitals (odds ratio [OR] 4.75), thinner lower uterine segment ($\leq$5 mm; OR 7.10), gestational sac bulging into the uterovesical fold (OR 6.25), history of irregular vaginal bleeding or lower abdominal pain in an earlier cesarean scar pregnancy (OR 3.52), and early termination ($\leq$56 days) of the first cesarean scar pregnancy (OR 5.85).
Conclusion(s): These findings provide evidence for the prevention of recurrent cesarean scar pregnancy and early diagnosis of the disease. Early recognition and diagnosis of this disease might be feasible because of the identifiable risk factors. Clinicians should be aware of the possible existence of recurrence. An accurate and prompt diagnosis is crucial to avoid catastrophic complications such as uterine rupture, massive vaginal bleeding and placenta previa/accreta, which might lead to hysterectomy. (Fertil Steril® 2014;102:129–34. ©2014 by American Society for Reproductive Medicine.)
Key Words: Cesarean scar pregnancy, recurrent, risk factors

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A cesarean scar pregnancy (CSP) is a gestational sac located in the scar of an earlier cesarean delivery; CSP is a late serious complication of cesarean section (CS). The incidence of CSP is 1:2,216, and its rate is 6.1% in women with an ectopic pregnancy and at least one previous CS (1). The incidence of CSP is extremely low. Over the past ten years, there has been an increase in the incidence of CSP worldwide, especially in China. The increased prevalence of CSP might reflect the increase in cesarean delivery rates and the wide adoption of transvaginal color Doppler sonography–aided diagnosis (2). CSP is considered to be a life-threatening condition because of the high risk of uterine rupture and uncontrolled hemorrhage, which might lead to a hysterectomy, with dramatic consequences for the patient's reproductive future (3).

Treatment is partially dependent on the timing of the diagnosis, and a prompt and accurate diagnosis is crucial. Clinically stable patients have more conservative treatment options, including uterine artery embolization (UAE) coupled with methotrexate (MTX) arterial injection, curettage and packing, systemic MTX, local excision by operative laparoscopy, and hysteroscopy. After a CSP, women with preserved fertility could attempt an intrauterine pregnancy or have another CSP. There is currently no consensus on the optimal management of CSP, and little is known about the outcome of subsequent pregnancies (4, 5). A repeated CSP might occur after conservative therapy.

Although the majority of cases involve patients with CSP for the first time, a few recurrences have been diagnosed in recent years (5–9). In the literature, there are no clear statements regarding the risk factors related to recurrent CSP. The only known risk is the presence of a

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cesarean scar. No in-depth comparison of the risk factors of patients with recurrent CSP and those with a single CSP has been conducted. We hypothesized that such a study could help doctors to counsel patients before a recurrence and evaluate patients when the diagnosis is in question.

We initiated a case-control study to investigate the role of multiple historical factors in predisposing women to a repeated CSP, with the objective of finding the risk factors for recurrent CSP.

MATERIALS AND METHODS

Subjects

The cases of diagnosed CSP in the Department of Obstetrics and Gynecology, Women's Hospital, School of Medicine, Zhejiang University, People's Republic of China, from January 2007 to January 2013 were identified, and the clinical data of the cases were retrospectively reviewed. Written informed consent was obtained from each patient, and the study was approved by the Institutional Review Board. Our hospital is the largest obstetrics and gynecology medical treatment unit in Zhejiang province; many patients with high complexity (including CSP) are transferred to this hospital. There were 619 women diagnosed as having a single CSP in our hospital during the study period, and 42 of those women were randomly assigned to the control group (primary CSP) in a 2:1 ratio with the use of computerized randomization. A total of 21 women definitively diagnosed as having a recurrent CSP during the study period were assigned to the case group (recurrent CSP); one of those patients was diagnosed with CSP for the third time. All of the recurrent CSP patients had their first CSP in our hospital.

Women with a CSP confirmed by ultrasonography and a blood level of β-hCG indicating 5–12 weeks of gestation were recruited. The diagnostic ultrasonography standard was the presence of the following criteria (10): 1) an empty uterine cavity and cervical canal; 2) development of the gestational sac in the anterior portion of the lower uterine segment; and 3) absence of healthy myometrium between the bladder and the gestational sac. In the cases in which the diagnosis remains unclear after transvaginal ultrasound examinations combined with pulsed Doppler ultrasonography, three-dimensional ultrasound, and magnetic resonance imaging might be useful (Supplemental Fig. 1, available online at www.fertstert.org). The reproductive function of all 63 patients had been preserved successfully using conservative treatment, including UAE coupled with MTX arterial injection, and dilatation and curettage.

Investigation Content

The clinical characteristics of the first-time CSP of the 63 women were investigated; continuous variables included maternal age, gravidity, number of miscarriages, number of ectopic pregnancies, number of CSs, gestational age, interval between CS and CSP, gestational sac diameter, thickness of the lower uterine segment, treatment technique used for the first-time CSP, and amount of bleeding during the first-time CSP operation. Other variables of the first-time CSP were studied, such as timing of earlier CSs (during or before labor), hospital grade of the earlier CSs (university hospital or rural community hospital), presence of vaginal bleeding or lower abdominal pain, ultrasound heartbeat, and direction of gestational sac growth. All of the variables in this study were collected from the 63 study patients for their first CSP.

Statistical Analysis

This trial was performed as a case-control study. All of the data analyses were conducted with the use of SPSS 17.0 software. Statistical significance was set at $P<.05$, and the P values from all of the tests are reported. Descriptive statistics were used to summarize the entire population and to compare the patients in the two groups. The statistical significance of the experimental differences in the two groups was first assessed by a normal distribution test. If the data were normally distributed, we used an independent-sample t test for the continuous variables analysis; if the data were not normally distributed, we used a nonparametric test (Mann-Whitney test). The bivariate associations were evaluated with chi-square (χ^2) tests of the associations of the categoric data. Stratified analyses were used to assess for the confounding and affecting factors. An odds radio (OR) of >1 describes a risk factor or parameter that was more prevalent in the case group compared with the control group. A logistic regression model construction was completed with the use of the significant variables.

RESULTS

Risk Factors Comparison

A total of 63 women were enrolled in the study: 42 women with a single CSP and 21 women with recurrent CSP. The factors for repeated CSP that were examined by stratified analysis and calculated ORs are listed in Table 1. The patients with recurrent CSP were more likely to have had an earlier CS in a rural community hospital than those with a single CSP (OR 4.75; $P=.04$). There were more patients with a thinner lower uterine segment (≤ 5 mm) revealed by ultrasonography in the case group than in the control group (OR 7.10; $P=.04$). Some patients with recurrent CSP had particularly large defects on the ultrasound scan (Fig. 1). A difference in the growth direction of the gestational sac appeared on the ultrasound scans. The amniotic sacs in the recurrent CSP group were more likely to bulge under the cesarean scar (OR 6.25; $P=.02$). The women in the recurrent CSP group were more likely to have experienced an early termination of an earlier CSP (≤ 56 days) than those with a single CSP (OR 5.85; $P=.02$). The patients with recurrent CSP were more likely to have had a history of irregular vaginal bleeding or lower abdominal pain than those in the control group (OR 3.52; $P=.03$).

There was no significant difference between the case group and the control group regarding number of abortions, number of ectopic pregnancies, number of CSs, interval between CS and CSP, ultrasonic heart beat, treatment technique used for the first-time CSP, or amount of bleeding during the first-time CSP operation. Maternal age was not a risk factor for recurrent CSP (OR 2.40; $P=.31$). There was no significant