THE JOURNAL OF
Obstetrics and Gynaecology Research

doi:10.1111/jog.14771 J. Obstet. Gynaecol. Res. Vol. 47, No. 6: 2014–2020, June 2021

Management for delayed diagnosis in cesarean scar pregnancy with hemorrhage intra- or postuterine dilation and curettage

Xuetang Mo[1,2], Shiyan Tang[1,3] and Cuilan Li[1,4]

[1]*The Third Affiliated Hospital of Guangzhou Medical University and Key Laboratory for Major Obstetric Diseases, Guangzhou, China*
[2]*Gynaecological Laboratory, University of Hong Kong, Pok Fu Lam, Hong Kong*
[3]*Department of Women's and Reproductive Health, University of Oxford, Oxford, UK*
[4]*OB-GYN Associate of Advantia Health, Silver Spring, Maryland, USA*

Abstract

Aim: This study aimed to examine the characteristics, management, and outcomes of delayed diagnosis of cesarean scar pregnancy (CSP) with hemorrhage intra- or postuterine curettage for early pregnancy termination.

Methods: The retrospective study, cases were identified from the interrogation of the hospital database and clinical data including the success rate of different treatments, vaginal bleeding time, abnormal beta-human chorionic gonadotropin (β-hCG) time, and menstrual recovery time, preservation of uterus were analyzed.

Results: Medical records of 80 confirmed CSP cases with dilation and curettage (D&C) as primary treatment were analyzed; among them, 22 were treated with uterine arterial embolization (UAE) + methotrexate (MTX); 32 with UAE + surgery; 26 with only surgery or resection and repair. Treatment with UAE had less intraoperative blood loss ($p < 0.05$). UAE + surgery treatment had the highest success rate (96.8%, $p < 0.05$), the least vaginal bleeding duration after treatment (11.9 ± 9.6 days, $p < 0.05$), and least β-hCG normalization time (17.4 ± 7.8 days, $p < 0.05$).

Conclusion: UAE + surgery treatment is a favorable and effective option to control massive hemorrhage intra- or post-uterine curettage for early CSP termination.

Key words: cesarean scar pregnancy, hemorrhage, laparoscopic or hysteroscopic resection and repair, uterine arterial embolization.

Introduction

Cesarean scar pregnancy (CSP) is a type of ectopic pregnancy characterized by the implantation of the gestational sac at the site of previous cesarean scar (CS). It is a life-threatening condition [1] with a high risk of uterine rupture, massive vaginal bleeding, placenta previa, and placenta accrete.[2] Women with a history of multiple cesarean sections have a 10 times higher risk of placenta previa as compared with women who had vaginal deliveries. Placenta implanted over the uterine scar is abnormally adherent in up to 30%–40% of cases, often resulting in uncontrollable hemorrhage at the time of delivery.[3] Abnormally implanted placentae are responsible for 50%–65% of all obstetric hysterectomies; 66% of these

Received: September 7 2020.
Accepted: March 10 2021.
Correspondence: Cuilan Li, The Third Affiliated Hospital of Guangzhou Medical University and Key Laboratory for Major Obstetric Diseases, Guangzhou 510145, China.
Email: ninacuilanli@gmail.com
Xuetang Mo and Shiyan Tang contributed equally to this work and should be considered co-first authors.

patients have a history of previous cesarean section.[4, 5] The number of deliveries by cesarean section has been increasing steadily in recent decades with an accompanying increase in the incidence of CSP worldwide.[6, 7] According to a recent study, cesarean delivery rates in China increased from 28.8% in 2008 to 36.7% in 2018.[8]

The exact pathogenetic mechanism of CSP remains unclear; however, several studies have described the diagnosis and management of this condition.[1, 9, 10] CSP can potentially develop into placenta previa [11] or cause urinary rupture; thus, delayed diagnosis of CSP is dangerous. Among patients diagnosed as CSP, 12.9% had a history of severe vaginal bleeding during the first trimester of pregnancy.[12] Pregnancy needs be terminated in the first trimester once CSP has been confirmed, to avoid catastrophic complications, such as massive hemorrhage, uterine rupture, and even death.[13] Approximately 14% cases of CSP were misdiagnosed as intrauterine pregnancy or missed/incomplete/inevitable miscarriage, cervical pregnancy, or trophoblastic tumor.[14–18] These misdiagnoses may lead to dilation and curettage (D&C), a preferred technique for surgical abortion,[19] which can cause profuse bleeding and necessitate emergency surgical intervention.[18, 20] However, there are few researches on the management of suspected CSP with hemorrhage intra- or postuterine curettage for early pregnancy termination; in addition, the optimal approach in terms of patient safety and clinical effectiveness is yet to be explored.

In the present study, we retrospectively analyzed the efficacy of the currently available treatment of choice for the management of CSP associated with hemorrhage which occurred intra- or post-uterine D&C. Both the medical, UAE and surgical methods, their advantages, complications, and failure rates were discussed. The insights gained from this study may help guide clinical decision-making in these patients.

Materials and Methods

This is a retrospective study of CSP patients treated at the Third Affiliated Hospital of Guangzhou Medical University between January 2005 and December 2018. Patients who underwent D&C as primary treatment and were diagnosed as CSP because of hemorrhage occurring intra- or postuterine curettage were included in our study. All information about treatment methods was shared and the decision was discussed with the patient about this controversial issue.

The inclusion criteria were: (1) patients with a history of cesarean section delivery; (2) pregnant women who underwent D&C as their primary treatment for pregnancy termination; (3) hemorrhage occurring during or post primary treatment; (4) delayed diagnosis of CSP. As a tertiary referral hospital, patients with emergency or massive hemorrhage or suspected CSP are often admitted. Delayed diagnosis of CSP was defined as CSP not being the primary diagnosis or the major diagnosis that led to primary D&C treatment, which is typically made after review of ultrasound results by experienced radiologists with/without intraoperative confirmation. Patients with irregular vaginal bleeding in early pregnancy due to any reason such as cervical pregnancy, inevitable abortion, incomplete abortion, cesarean scar choriocarcinoma, or other blood system disease other than CSP were excluded from the study.

The CSP is diagnosed according to the following criteria: (1) history of low-transverse cesarean delivery in the lower uterine segment; (2) positive urine pregnancy test or serum beta-human chorionic gonadotropin (β-hCG) level; (3) confirmation of CSP by transvaginal ultrasound. Intraoperative blood loss was estimated based on the increase in weight (in mL/g) of blood-stained sponges, as described in previous reports.[6, 21, 22] Postpartum hemorrhage (PPH) is defined by World Health Organization (WHO) as blood loss of ≥500 mL within the first 24 h postpartum.[23] In our study, moderate hemorrhage was defined as blood loss ≥200 and < 500 mL during suction curettage or within 24 h after D&C.[24–26] Blood loss of ≥500 mL was considered as massive uterine hemorrhage. If the massive bleeding could still not be controlled, emergency hysterectomy was performed.

Successful treatment was defined as: (1) cessation of bleeding after treatments, bleeding less than 200 mL after treatments; (2) no more operations or medication therapy were needed; (3) resolution of the CSP mass; (4) normalization of serum β-hCG level; (5) preservation of intact uterus.

Data pertaining to the following variables were collected: age, gravidity, parity, β-hCG level, time elapsed since the last cesarean delivery. Ultrasonography was used to measure the thickness of the lower uterine segment, gestational sac size, and uterine diverticula. The study outcomes, follow-up data, and complications were analyzed. All patients agreed to the treatment and research.

Treatments

The patients were categorized into following groups: (1) uterine arterial embolization (UAE) + medical group: UAE combined with methotrexate (MTX); (2) UAE + surgery group: UAE combined with ultrasound-guided hysteroscopy and/or laparoscopy; (3) surgery group: ultrasound-guided hysteroscopy and/or laparoscopy.

UAE was performed under conscious sedation and local anesthesia if bleeding was not controlled after hemostatic therapy, in accordance with the procedure described elsewhere.[25, 27] Medical treatment is intralesional injection MTX. Surgical treatment included laparoscopy and/or hysteroscopy. Surgery was performed within 48 h after UAE. The serum β-hCG levels were determined on days 1, 4, 7, and weekly until they returned to normal levels (<5 mIU/mL). Patients who underwent surgery were monitored by transvaginal three-dimensional (3D) ultrasonography to confirm the absence of intrauterine pregnancy and recovery of the endometrium.

Statistical analysis

Statistical analyses were performed using SPSS software, version 17.0 (SPSS Inc.). Between-group differences were assessed using either chi-squared, Mann–Whitney test, or *t*-test. The *p*-values <0.05 were considered indicative of statistical significance.

Results

A total of 113 patients who underwent D&C as primary treatment and were diagnosed as CSP with hemorrhage that occurred intra- or post-uterine curettage were included in our study. Fifteen patients with less than 200 mL bleeding who did not receive any of the treatments mentioned were excluded. Five patients who were treated at other hospitals after their primary treatment were also excluded. Ten patients were excluded because of incomplete medical records or loss to follow-up. Three received preventive UAE combined with D&C as their primary treatment were also excluded. Therefore, 80 patients were registered in this study(Figure 1). All patients had hemorrhage during the operation or within 24 h of undergoing uterine curettage, with an estimated blood loss of 250–1700 mL in a single episode. This study included 56 referred CSP patients who had been misdiagnosed at other hospitals and clinics. These patients had experienced massive uterine bleeding during D&C and were referred to our hospital with subsequent treatment for CSP.

The average age of all patients was 32.0 ± 5.2 years (range 22–46). Among 80 women, 40 had a history of one cesarean section delivery, 33 had two cesarean section deliveries, and seven had three cesarean section deliveries. The mean period from present pregnancy to the most recent cesarean section of all

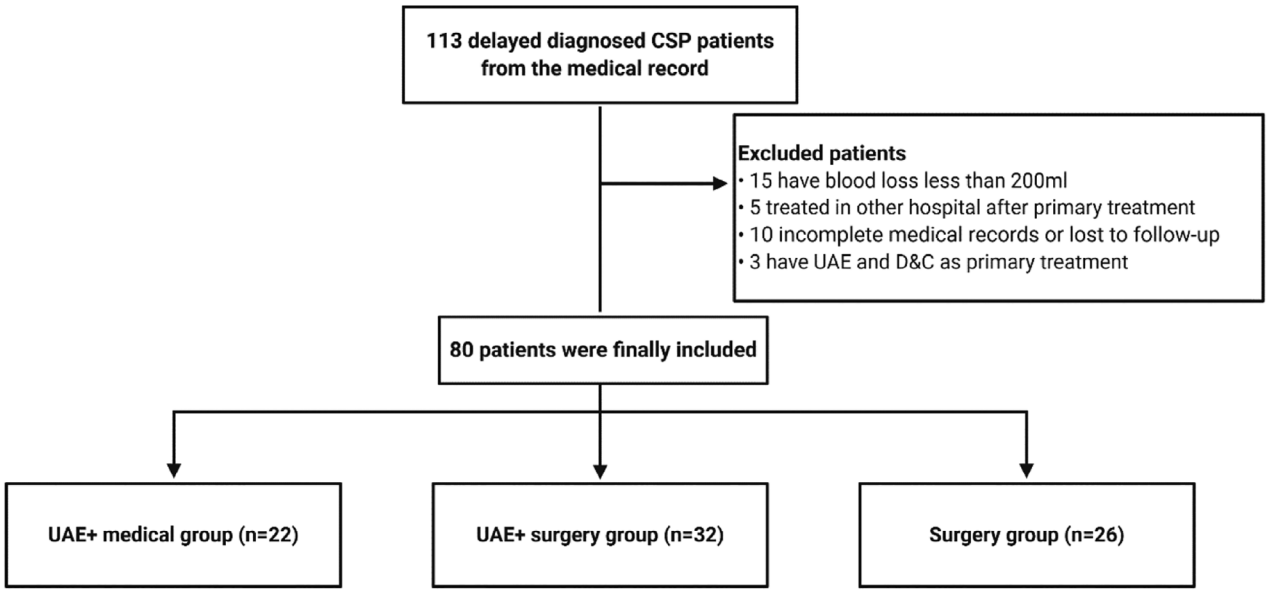

Figure 1 Schematic illustration of the study design and patient-selection criteria. CSP, cesarean scar pregnancy; D&C, dilation and curettage; UAE, uterine artery embolization

patients was 47.46 (5–120 months). Seventeen patients had irregular menstrual cycles in the intervening period between the current and the last pregnancy. The mean duration of amenorrhea of all patients was 46.03 ± 11.7 days. The patients' characteristics and demographics in the three groups are shown in Table 1. There were no significant between-group differences with respect to maternal age, gravidity, parity, prior abortion, interval between CS and CSP, prior CSs, thickness of the lower uterine, β-hCG at admission, symptoms at diagnosis, gestational age, gestational sac size, or estimated vaginal bleeding before further treatment ($p > 0.05$).

In the UAE + surgery group, 19 patients underwent hysteroscopic repair, 13 patients underwent combined hysteroscopy and laparoscopy. In surgery group, 10 patients underwent hysteroscopic repair, 13 underwent combined hysteroscopy and laparoscopy.

The success rate was 86.4% (19/22) in UAE medical group, 96.8% (31/32) in UAE + surgery group, 76.9% (20/26) in surgery group, with significant difference ($p < 0.05$) (Table 2). Three were unsuccessful in UAE + MTX group because of further surgery treatment needed. One case in UAE surgery group failed for unsatisfied ß-hCG level. Three patients in the surgery group had uncontrollable bleeding during cystoscopy of laparoscopy and emergency hysterectomy was required.

The average intraoperative blood loss was 5.1 ± 2.0, 20.3 ± 10.1, and 60.3 ± 43.2 mL in the three groups, with significant difference ($p < 0.05$). The duration of vaginal bleeding was longer in the UAE + medical treatment group (29.5 ± 15.7 days), followed by the surgery alone group (16.8 ± 6.4 days), then is the UAE + surgery group (11.9 ± 9.6 days) (Table 2).

All patients in the UAE + medical group and UAE + surgery group had intact uterus preserved after the treatment. However, in the surgery-only group, three patients underwent hysterectomy because of uncontrolled bleeding.

The time required for reduction in ß-hCG to the normal level was significantly shorter in the UAE + surgery group (17.4 ± 7.8 days), compared with the other two groups. Normal menstrual recovery time was similar in the three groups.

Table 1 Characteristics of patients disaggregated by study group

Characteristics	UAE + medical group (n = 22)	UAE + surgery group (n = 32)	Surgery group (n = 26)	p-value
Maternal age (years)	32.4 ± 5.1	32.3 ± 3.5	31.2 ± 2.6	0.292
Gravidity (times)	3.6 ± 1.2	4.0 ± 1.7	4.5 ± 1.4	0.340
Number of prior abortion	1.9 ± 0.5	1.6 ± 0.4	2.0 ± 0.6	0.316
Interval between CS and CSP (months)	42 (6–120)	48 (8–100)	49 (9–90)	0.194
Number of prior cesarean section delivery	1.3 ± 0.5	1.5 ± 0.6	1.6 ± 0.5	0.291
Thickness of the lower uterine segment (mm)	1.2 (0.5–8.0)	1.4 (0.3–7.8)	1.6 (0.5–9.0)	0.434
Symptoms at diagnosis				0.401
Abdominal pain	3 (13.6%)	5 (15.6%)	3 (11.5%)	
Vaginal bleeding	14 (63.6%)	22 (68.8%)	13 (50.0%)	
Both	2 (9.1%)	2 (6.3%)	5 (19.2%)	
None	3 (13.6%)	3 (9.4%)	5 (19.2%)	
Gestational age (days)	50.7 ± 10.9	57.4 ± 10.1	62.5 ± 10.0	0.057
Gestational sac size (mm)	24.2 ± 10.0	30.8 ± 9.3	34.54 ± 11.4	0.091
Presence of fetal heartbeat	10 (45.5%)	16 (50.0%)	16 (61.5%)	0.385
β-hCG at admission (milliunits/mL)				0.343
≤5000	2 (9.1%)	4 (12.5%)	3 (11.5%)	
>5000 and ≤ 10 000	5 (22.7%)	10 (31.3%)	7 (26.9%)	
>10 000	15 (68.2%)	18 (56.2%)	16 (61.5%)	
Estimated vaginal bleeding after primary treatment (mL)				0.083
≥200 and < 500	11 (50.0%)	8 (25.0%)	5 (19.2%)	
≥500, and < 1000	10 (45.5%)	17 (52.1%)	16 (61.5%)	
≥1000	1 (4.5%)	7 (21.9%)	5 (19.3%)	

Note: Data presented as mean ± SD, median (range), or n (%). and Abbreviations: CS, cesarean section; β-hCG, beta-human chorionic gonadotropin; UAE, uterine artery embolization.

Table 2 Treatment efficacy in 80 CSP subjects with hemorrhage, by study group

Outcomes	UAE + medical group (n = 22)	UAE + surgery group (n = 32)	Surgery group (n = 26)	p-value
Success (%)	19 (86.4%)	31 (96.8%)	20 (76.9%)	0.041
Intraoperative blood loss (mL)	5.1 ± 2.0	20.3 ± 10.1	60.3 ± 43.2	0.013
Duration of vaginal bleeding after treatment (days)	29.5 ± 15.7	11.9 ± 9.6	16.8 ± 6.4	0.041
Preservation of fertility				0.090
Uterus intact	22 (100%)	32 (100%)	23 (88.5%)	
Hysterectomy	0 (0%)	0 (0%)	3 (11.5%)	
Time for ß-hCG reduction to normal level (days)	29.5 ± 15.7	17.4 ± 7.8	20.8 ± 9.4	0.048
Normal menstrual recovery (days)	41.2 ± 13.4	42.3 ± 11.5	38.0 ± 11.6	0.092
Mean follow-up time (months)	10.5 ± 3.6	12.4 ± 4.5	11.5 ± 3.9	0.436

Note: Normally distributed continuous variables are presented as mean ± SD, while non-normally distributed variables are presented as median (range). and Abbreviations: CSP, cesarean scar pregnancy; β-hCG, beta-human chorionic gonadotropin; UAE, uterine artery embolization.

Discussion

In a woman with a history of cesarean section, improper healing of the incision site may be associated with uterine diverticulum, and placenta accreta at the cesarean scar of subsequent pregnancy.[28–30] CSP is currently classified into two types: type 1 CSP characterized by implantation occurring at the scar site and the growth of gestational sac towards the cervico-isthmic space or uterine cavity (type 1 endogenic type); and type 2 CSP with deep invasion of the scar and growth of the gestational sac towards the urinary bladder and abdominal cavity (type 2, exogenic CSP).[31, 32] Type 1 CSP may allow a viable birth but with a higher risk of massive hemorrhage from the site of implantation, while type 2 is more likely to cause rupture and bleeding during the first trimester.[31] Women with placenta implanted on top of a well-healed scar may have a substantially better outcome, compared to women with CSP implanted into the scar defect.[33]

The first CSP case reported by Larsen et al.[16] in 1978 was a delayed diagnosis CSP case with severe persistent hemorrhage caused by an unusual uterine scar sacculus. The authors pointed that CSP should be carefully explored in case of incomplete abortion, especially with heavy bleeding. Dhar et al.[34] reported two cases of missed diagnosis of CSP, in whom massive vaginal bleeding occurred after suction evacuation for missed abortion. Misdiagnosis of CSP is not uncommon; especially after 7 weeks of gestation, the gestational sac grows towards the uterine cavity and slowly changes its shape. If the sac assumes an intracavitary position, it is liable to be misdiagnosed as intrauterine pregnancy.[12] Therefore, early pregnancy termination with a history of section, routine transvaginal ultrasound is recommended.[20]

CSP with hemorrhage intra- or post-uterine curettage for early pregnancy termination should be treated in a timely manner using safe and effective individualized management. Due to the lack of direct visualization, curettage is associated with 28% risk of hemorrhage but 4% when combined with UAE.[35] Our results showed three further management for massive hemorrhage during or after D&C to treat CSP because of not getting diagnosed before the surgery. UAE + medical treatment is a less invasive management option for clinically-stable women. UAE combined with local or systemic methotrexate has been widely adopted as a treatment for CSP throughout the world.[22, 36, 37] However, this treatment might be associated with prolonged return time of β-hCG as well as impaired liver function and bone marrow suppression.[38, 39] UAE + surgery treatment, including laparoscopy, and hysteroscopy, can remove the residual gestational tissue and repair the uterine defect simultaneously with less blood loss, shorter vaginal bleeding days after treatments as well as rapid normalization of the β-hCG level. Hysterectomy is performed only in emergency situations such as heavy bleeding. When surgical treatment is performed to remove ectopic pregnancy without residual chorionic villi, β-hCG level should decrease to half of the pre-surgical level at 24 h after surgery operation.[40]

We found that the UAE + surgery group had the best outcomes in terms of recovery time to normal serum β-hCG level and resolution of abnormal pregnancy mass, and thus UAE + surgery treatment is recommended in treating hemorrhage after D&C. The purpose of UAE for intra- or post-uterine curettage

massive hemorrhage is to block the blood flow in uterine arteries, decreasing local vascularization, and inducing trophoblastic degeneration in early-stage pregnancy termination. A previous study showed that adjunctive UAE does not seem to be necessary for all patients with CSP[15] while some controversial opinion that preventive UAE should be used before D&C to prevent massive bleeding.[41] However, some patients still experience massive intro-operative bleeding during evacuation even after pre-treatment with UAE.

UAE has been widely used as a conservative treatment for massive hemorrhages, such as postpartum hemorrhage and hemorrhage caused by ectopic pregnancy.[42, 43] In the recent two decades, UAE combined with D&C has been proposed as an effective first-line conservative therapy for CSP to preserve the patient's fertility. In a retrospective study, UAE for treatment of CSP was associated with a success rate of 98%; moreover, it was associated with minimal blood loss and short hospitalization time.[37]

In conclusion, suspected CSP with hemorrhage intra- or post-uterine curettage requires prompt treatment as their safety and individual characteristics should be taken into consideration. UAE was found to be an effective treatment to prevent and control major hemorrhage with a higher success rate. UAE with surgery resection and repair treatment was associated with more favorable outcomes in terms of duration of vaginal bleeding, duration of abnormal serum β-hCG levels, and presence of abnormal pregnancy mass when compared with other treatment modalities.

Limitations

Long-term follow-up may be expected to evaluate the ovarian or reproductive function after different treatments. Multiple centers and large sample exploration may be a further benefit for the conclusion of this exploration.

Acknowledgments

We wish to thank the doctors, radiologists of the Third Affiliated Hospital of Guangzhou Medical University, China. We would like to thank all the patients who agreed to participate in our study. This work was supported by the Clinical research about Cesarean scar pregnancy from previous cesarean delivery of Science and Technology Innovation Project from Guangzhou Medical University (2014); The practice and Research of the implementation of Double Early Education, Early Clinical Training & Early Research Training, for medical undergraduates, Research on the teaching reform of clinical teaching base in Guangdong Province in 2014, key Funding in Teaching Research, Funding number 2014JDA028.

Author contributions

Xuetang Mo and Shiyan Tang performed data collection, analysis, and manuscript writing. Cuilan Li conceived the presented idea and design experiment and supervised the project.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Birch Petersen K, Hoffmann E, Rifbjerg Larsen C, Svarre Nielsen H. Cesarean scar pregnancy: a systematic review of treatment studies. *Fertil Steril*. 2016;**105**:958–67.
2. Jurkovic D, Hillaby K, Woelfer B, Lawrence A, Salim R, Elson CJ. First-trimester diagnosis and management of pregnancies implanted into the lower uterine segment Cesarean section scar. *Ultrasound Obstet Gynecol*. 2003;**21**:220–7.
3. Zaideh SM, Abu-Heija AT, El-Jallad MF. Placenta praevia and accreta: analysis of a two-year experience. *Gynecol Obstet Invest*. 1998;**46**:96–8.
4. Kastner ES, Figueroa R, Garry D, Maulik D. Emergency peripartum hysterectomy: experience at a community teaching hospital. *Obstet Gynecol*. 2002;**99**:971–5.
5. Zelop CM, Harlow BL, Frigoletto FD Jr, Safon LE, Saltzman DH. Emergency peripartum hysterectomy. *Am J Obstet Gynecol*. 1993;**168**:1443–8.
6. Wang JH, Xu KH, Lin J, Xu JY, Wu RJ. Methotrexate therapy for cesarean section scar pregnancy with and without suction curettage. *Fertil Steril*. 2009;**92**:1208–13.
7. Seow KM, Huang LW, Lin YH, Lin MY, Tsai YL, Hwang JL. Cesarean scar pregnancy: issues in management. *Ultrasound Obstet Gynecol*. 2004;**23**:247–53.
8. Li HT, Hellerstein S, Zhou YB, Liu JM, Blustein J. Trends in Cesarean Delivery Rates in China, 2008-2018. *JAMA*. 2020; **323**:89–91.
9. Armbrust R, Kratschell R, Henrich W, David M. Operative Therapy for Heterotopic Scar Pregnancy and Successful Birth of the Intrauterine Foetus - Case Report and Review of the Literature. *Geburtshilfe Frauenheilkd*. 2015;**75**:384–8.
10. Bodur S, Ozdamar O, Kilic S, Gun I. The efficacy of the systemic methotrexate treatment in caesarean scar ectopic

pregnancy: A quantitative review of English literature. *J Obstet Gynaecol*. 2015;**35**:290–6.
11. Ben Nagi J, Ofili-Yebovi D, Marsh M, Jurkovic D. First-trimester cesarean scar pregnancy evolving into placenta previa/accreta at term. *J Ultrasound Med*. 2005;**24**:1569–73.
12. Cali G, Timor-Tritsch IE, Palacios-Jaraquemada J, et al. Outcome of Cesarean scar pregnancy managed expectantly: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2018;**51**:169–75.
13. Liu S, Sun J, Cai B, Xi X, Yang L, Sun Y. Management of Cesarean Scar Pregnancy Using Ultrasound-Guided Dilation and Curettage. *J Minim Invasive Gynecol*. 2016;**23**:707–11.
14. Lai YM, Lee JD, Lee CL, Chen TC, Soong YK. An ectopic pregnancy embedded in the myometrium of a previous cesarean section scar. *Acta Obstet Gynecol Scand*. 1995;**74**:573–6.
15. Godin PA, Bassil S, Donnez J. An ectopic pregnancy developing in a previous caesarian section scar. *Fertil Steril*. 1997;**67**:398–400.
16. Larsen JVSM. Pregnancy in a uterine scar sacculus—an unusual cause of postabortal haemorrhage. A case report. *S Afr Med J*. 1978;**53**:142–3.
17. Gonzalez N, Tulandi T. Cesarean scar pregnancy: a systematic review. *J Minim Invasive Gynecol*. 2017;**24**:731–8.
18. Wang XR, Wang YF, Kang SW, Zhang Y. Treatment outcomes of uterine lesion resection versus hysterectomy for cesarean scar pregnancy. *Clin Exp Obstet Gynecol*. 2020;**47**:882–6.
19. Kulier R, Fekih A, Hofmeyr GJ, Campana A. Surgical methods for first trimester termination of pregnancy. *Coch Database Systematic Rev*. 2001;(4):Cd002900.
20. D'Antonio F, Palacios-Jaraquemada J, Lim PS, Forlani F, Lanzone A, Timor-Tritsch I, et al. Counseling in fetal medicine: evidence-based answers to clinical questions on morbidly adherent placenta. *Ultrasound Obstet Gynecol*. 2016;**47**:290–301.
21. Dahmani S, Orliaguet GA, Meyer PG, Blanot S, Renier D, Carli PA. Perioperative blood salvage during surgical correction of craniosynostosis in infants. *Br J Anaesth*. 2000;**85**:550–5.
22. Wang JH, Qian ZD, Zhuang YL, Du YJ, Zhu LH, Huang LL. Risk factors for intraoperative hemorrhage at evacuation of a cesarean scar pregnancy following uterine artery embolization. *Int J Gynaecol Obstet*. 2013;**123**:240–3.
23. WHO Guidelines for the Management of Postpartum Haemorrhage and Retained Placenta. Geneva 2009.
24. Ma Y, Shao M, Shao X. Analysis of risk factors for intraoperative hemorrhage of cesarean scar pregnancy. *Medicine*. 2017;**96**:e7327.
25. Wang Q, Ma H, Peng H, He L, Bian C, Zhao X. Risk factors for intra-operative haemorrhage and bleeding risk scoring system for caesarean scar pregnancy: a case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2015;**195**:141–5.
26. Wang Y, Tan G, Cheng X, Xu Y, Xu F, Qu P. Association of hemorrhage at termination in caesarean scar pregnancy using the crossover sign of ultrasound image. *J Obstet Gynaecol Res*. 2020;**46**:1378–83.
27. Lian F, Wang Y, Chen W, Li J, Zhan Z, Ye Y, et al. Uterine artery embolization combined with local methotrexate and systemic methotrexate for treatment of cesarean scar pregnancy with different ultrasonographic pattern. *Cardiovasc Intervent Radiol*. 2012;**35**:286–91.
28. Higgins MF, Monteith C, Foley M, O'Herlihy C. Real increasing incidence of hysterectomy for placenta accreta following previous caesarean section. *Eur J Obstet Gynecol Reprod Biol*. 2013;**171**:54–6.
29. Lapointe-Milot K, Rizcallah E, Takser L, Abdelouahab N, Duvareille C, Pasquier JC. Closure of the uterine incision with one or two layers after caesarean section: a randomized controlled study in sheep. *J Mat-Fetal Neonatal Med*. 2014;**27**:671–6.
30. Wang CB, Chiu WW, Lee CY, Sun YL, Lin YH, Tseng CJ. Cesarean scar defect: correlation between Cesarean section number, defect size, clinical symptoms and uterine position. *Ultrasound Obstet Gynecol*. 2009;**34**:85–9.
31. Vial Y, Petignat P, Hohlfeld P. Pregnancy in a cesarean scar. *Ultrasound Obstet Gynecol*. 2000;**16**:592–3.
32. Ghezzi F, Lagana D, Franchi M, Fugazzola C, Bolis P. Conservative treatment by chemotherapy and uterine arteries embolization of a cesarean scar pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2002;**103**:88–91.
33. Kaelin Agten A, Cali G, Monteagudo A, Oviedo J, Ramos J, Timor-Tritsch I. The clinical outcome of cesarean scar pregnancies implanted "on the scar" versus "in the niche". *Am J Obstet Gynecol*. 2017;**216**:510 e1-e6.
34. Dhar RS, Bhargava V. Missed Diagnosis of Cesarean Scar Pregnancy: A Growing Reality. *Nepal J Obstet Gynaecol*. 2010;**5**:49–52.
35. Maheux-Lacroix S, Li F, Bujold E, Nesbitt-Hawes E, Deans R, Abbott J. Cesarean scar pregnancies: a systematic review of treatment options. *J Minim Invasive Gynecol*. 2017;**24**:915–25.
36. Song Y, Shin JH, Yoon HK, Kim JW, Ko GY, Won HS. Bleeding after dilatation and curettage: the efficacy of transcatheter uterine artery embolisation. *Clin Radiol*. 2015;**70**:1388–92.
37. Cao S, Zhu L, Jin L, Gao J, Chen C. Uterine artery embolization in cesarean scar pregnancy: safe and effective intervention. *Chin Med J (Engl)*. 2014;**127**:2322–6.
38. Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. *Am J Obstet Gynecol*. 2012;**207**:14–29.
39. Sugawara J, Senoo M, Chisaka H, Yaegashi N, Okamura K. Successful conservative treatment of a cesarean scar pregnancy with uterine artery embolization. *Tohoku J Exp Med*. 2005;**206**:261–5.
40. Billieux MH, Petignat P, Anguenot JL, Campana A, Bischof P. Early and late half-life of human chorionic gonadotropin as a predictor of persistent trophoblast after laparoscopic conservative surgery for tubal pregnancy. *Acta Obstet Gynecol Scand*. 2003;**82**:550–5.
41. Qian ZD, Weng Y, Du YJ, Wang CF, Huang LL. Management of persistent caesarean scar pregnancy after curettage treatment failure. *BMC Pregnancy Childbirth*. 2017;**17**:208.
42. Wee L, Barron J, Toye R. Management of severe postpartum haemorrhage by uterine artery embolization. *Br J Anaesth*. 2004;**93**:591–4.
43. Zakaria MA, Abdallah ME, Shavell VI, Berman JM, Diamond MP, Kmak DC. Conservative management of cervical ectopic pregnancy: utility of uterine artery embolization. *Fertil Steril*. 2011;**95**:872–6.

