Review Article

Cesarean Scar Pregnancy: Current Understanding and Treatment Including Role of Minimally Invasive Surgical Techniques

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Abstract

The incidence of cesarean scar pregnancy (CSP) is increasing reflecting the global increase in cesarean section (CS) rate which has almost doubled since 2000. CSP differs from other types of ectopic pregnancy in its ability to progress while still carrying a significant risk of maternal morbidity. Little is known about precise etiology or natural history although current interest in the pathology of placenta accretes spectrum disorders might be enlightening. Early detection and treatment of CSP are challenging. Once diagnosed, the recommendation is to offer early termination of pregnancy because of the potential risks of continuing the pregnancy. However, as the likelihood of future pregnancy complications for any CSP varies depending on its individual characteristics, this might not always be necessary nor might it be the patient's preferred choice if she is asymptomatic, hemodynamically stable, and wants a baby. The literature supports an interventional rather than a medical approach but the safest and most efficient clinical approach to CSP in terms of treatment modality and service delivery has yet to be determined. This review aims to provide an overview of CSP etiology, natural history, and clinical implications. Treatment options and methods of CSP repair are discussed. We describe our experience in a large tertiary center in Singapore with around 16 cases/year where most treatment modalities are available as well as an "accreta service" for continuing pregnancies. We present a simple algorithm for approach to management including a method of triaging for those CSPs suitable for minimally invasive surgery.

Keywords: Cesarean scar defect, cesarean scar pregnancy, high-intensity focus ultrasound, hysteroscopy, laparoscopy, methotrexate

Introduction

Cesarean scar pregnancy (CSP) occurs when an early pregnancy implants on the cesarean scar defect (CSD), myometrial tissue previously disrupted by cesarean delivery. The first case of CSP was reported in 1978 in a patient with a previous cesarean section (CS) who had heavy bleeding and abdominal pain after uterine curettage for a suspected miscarriage at 6 weeks. Eventual laparotomy revealed erosion of a major vessel in the scar sacculus by the products of conception which was successfully obliterated with subsequent revision of the previous surgical site.[1] The incidence of CSP is increasing due to the rising number of primary CSs and decline in vaginal deliveries after previous CS and now accounts for 6.1% of all "ectopic" pregnancies.[2] Unlike a tubal ectopic pregnancy, a CSP may progress, and successful deliveries have been reported but there are risks associated with this noninterventional approach with emerging evidence that CSP is an entity in the continuum leading to placenta accrete spectrum disorder (PASD).[3] Many treatment options have been suggested but no single best therapy has been identified due to its rarity. Most treatment regimens focus on the pregnancy

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itself and although some options do incorporate myometrial repair there are no clear guidelines on the management of the CSD. Currently, first-trimester termination is recommended to minimize complications.[4]

Pathogenesis: Cesarean Scar Defect

The scar defect is typically located at the lower anterior uterine wall in the case of previous lower segment CS. This is where incomplete healing of tissue cut at operation results in thinning or even dehiscence of the remaining myometrium.[5] The CSD can be defined in terms of depth, residual myometrial thickness (RMT), and adjacent myometrial thickness (AMT).[6] When the depth is more than 2 mm or RMT is <5 mm the defect is known as a niche.[5-7] A large CSD is a defect with a 50%–80% reduction in wall thickness compared to the AMT or if the RMT is <2.2 mm by transvaginal ultrasound (TVUS) or <2.5 mm by hysterosalpingogram.[5,6,8]

CSD formation has been associated with several perioperative factors. Including the level of uterine incision, indication for CS, duration of labor and cervical dilatation before CS, closure technique, adhesions, and a retroverted uterus,[8] A study comparing RMT after vaginal delivery and CS showed that women who delivered vaginally had an isthmus myometrial thickness of 11.6 mm compared to 8.3 mm, 6.7 mm, and 4.7 mm, respectively, in women after 1, 2 and 3 or more CSs ($P < 0.001$).[9] This agrees with another study showing progressive myometrial thinning of the CSD with increasing number of CS.[10] Scar defects were seen in 61%, 81%, and 100% in women after one, two, or three or more CS, respectively ($P = 0.004$).[8] An RMT of <3 mm is associated with increased risk of uterine dehiscence and rupture and future gynecological symptoms.[11,12]

Cesarean Scar Pregnancy

Lower uterine pregnancy implantation may be on, in, or near the scar or may occupy the cervico isthmus space and not involve the scar at all. When the pregnancy implants in or on the CSD it is called CSP.[13,14]

The precise etiology of CSP is not well understood. Pathology is complex and related to disrupted myometrium and surrounding vasculature.[15] It has been postulated that the blastocyst implants into microtubular tracts, produced by the healing process although the relationship between CSP incidence and number and time between previous CSs has not been established.[16]

Natural History of Cesarean Scar Pregnancy

Information on the natural history of CSP is limited as few have continued to a viable gestational age. Series describing expectant management of diagnosed CSPs all involve small case numbers and hysterectomy rates between 50% and 100%, usually associated with PASD.[17-19] In one series which prospectively followed women with a first-trimester scar-related pregnancy all had PASD diagnosed at the time of the repeat cesarean delivery.[3]

Classification of Cesarean Scar Pregnancy

Several classification systems exist. Classification is linked to the direction of the growth of the CSP and RMT which guide management options. When stratifying patients for ongoing pregnancy risks, proximity to adjacent uterine vascularity and trophoblastic blood flow also need to be determined.

Cesarean Scar Pregnancy-Type I, II, and III

This system describes the relationship of gestation sac with CSD and direction of pregnancy development. The Chinese Journal of Obstetrics and Gynecology published an Expert Opinion of Diagnosis and Treatment of Cesarean Scar Pregnancy in which the CSP was classified into three types (I, II, and III) based on the relationship between the gestation sac and previous CS scar site as determined by ultrasound[20,21] A type I (or endogenic) CSP implants on the scar and grows inwards while types II or III (exogenic) CSPs implant deep in a well vascularised CSD with an overlying RMT <3 mm and grow out towards the abdominal cavity.

Type I CSPs have the potential to reach and develop into the endometrial cavity and can progress to the second and third trimesters whereas Types II and III are more likely to result in early uterine rupture or PASD.

Cesarean Scar Pregnancy-in the Niche and on the Scar

This classification is based on the relationship between CSP and RMT and indicates a CSP either "in the niche" or "on the scar." "On the scar" implantations have a measurable myometrial thickness between the conceptus and anterior uterine surface and bladder and generally better outcomes than "in the niche" implantations which are intimately related to the anterior uterine surface close to the bladder with minimal if any, intervening myometrium.[22] An RMT <2 mm in the first-trimester ultrasound examination is associated with PASD at delivery.

Clinical Presentation

Many patients are asymptomatic and diagnosed incidentally during a routine first-trimester ultrasound. The most frequent symptom is light, painless vaginal bleeding. Clinical examination is often unremarkable. Some patients have

mild lower abdominal pain and tenderness. The differential diagnosis of any pregnant patient with first-trimester pain and bleeding and a previous CS should include CSP. Severe pain with or without hemodynamic instability may indicate rupture the gestational age at diagnosis ranges from 5 to 16 weeks, with an average of 7.5 ± 2.5 weeks.[23,24]

Diagnosis of Cesarean Scar Pregnancy

TVUS usually provides a reliable diagnosis without the need for additional imaging. Magnetic resonance imaging can aid preoperative planning for surgical intervention by indicating the depth of myometrial invasion and any bladder involvement.

A CSP is differentiated from an intra-uterine pregnancy as it is below the mid-sagittal line on TVUS.[16]

Further sonographic differentiating features for CSP include:

1. Gestational sac or solid mass of trophoblast located anteriorly at the level of the internal os embedded at the site of the previous lower uterine segment CS scar
2. An empty uterine cavity
3. A thin or absent layer of myometrium between the gestational sac and the bladder
4. Abundant peritrophoblastic blood flow in the area of the gestational sac as demonstrated by low pulse repetition Doppler study
5. An empty endocervical canal.

Differential Diagnoses

The mot common differential diagnoses are spontaneous miscarriage and cervical ectopic pregnancy. The latter differs from a CSP by myometrial presence between it and the bladder and the hourglass shape of the ballooned cervical canal. An inevitable miscarriage is seen low in the uterine cavity but without the abundant blood flow seen with a CSP indicating detachment from its implantation site.[15,25]

Prediction of Placenta Accrete Spectrum Disorders

Following diagnosis, PASD risk in any ongoing CSP needs to be determined. This can be done by looking at the cross-over sign (COS) during US imaging.[26-28]

The COS looks at the pregnancy site in relation to the scar and where the superior-inferior (S-I) diameter of the gestational sac lies perpendicular to the "endometrial line" which connects the internal os and uterine fundus on sagittal view. It can be used to predict the natural progression of CSP. There are four groups:

1. Normal-gestation sac away from the cesarean scar and close to the fundus
2. COS-1 –sac in the scar with at least two-thirds of the S-I sac diameter above the endometrial line.
3. COS-2+ –sac in the scar with less than two-thirds of the S-I diameter above the endometrial line.

COS-2 –sac in the scar with less than two-thirds of the S-I diameter above the endometrial line, but no intersection between the S-I diameter and the endometrial line.

First-trimester features of COS-1, pregnancy implantation in the niche, and gestational sac below the uterine midline have all been independently associated with PAS disorder and adverse surgical outcomes.[26-28] Diagnosis before 9 weeks is preferable. After this soft markers to predict, PASD are not reliable and there is increased morbidity from surgical intervention.[29]

Management of Cesarean Scar Pregnancy

Objective

Continuing a CSP carries intrinsic risks of uterine rupture and PASD as well as the high likelihood of life-threatening hemorrhage and visceral damage at the time of delivery.[28] Decisions on management should be based on the likelihood of these consequences which depend on the characteristics of the CSP.

Factors governing optimal treatment choice include CSP type, RMT, gestational age, serum beta-human chorionic gonadotrophin level, presence or absence of fetal cardiac activity, hemodynamic stability, availability of expertise including access to endoscopic surgical facilities and interventional radiology and patient's wish for future fertility and preparedness to run the risks involved. The decision, especially when the patient conceived after fertility treatment, should involve a multidisciplinary team consensus including the parents and their wishes to continue the pregnancy.[30]

The two main approaches are termination of the pregnancy (TOP), either medically or surgically, with the removal of the CSP, with or without revision of the scar, and continuation of the pregnancy. TOP potentially allows preservation of fertility and may reduce future gynecological symptoms if the niche is repaired but does mean loss of the current pregnancy and risk of recurrence at the next pregnancy. Continuation of the pregnancy involves accepting the associated risks. Should the patient opt to continue the pregnancy formal myometrial repair at the time of the CS may allow uterine preservation and potentially future fertility.[31] Management options can be divided into expectant, surgical, and medical approaches to treatment.

Expectant management

Expectant management of a CSP has been described but carries a high risk of major complications especially if a fetal cardiac activity is present. Live births were achieved at 73% but the

hysterectomy rate was 70%.[32] Imaging features may indicate pregnancies more suitable for this approach for women with a viable CSP who wish to continue. Findings favoring a better outcome include an endogenic type CSP, COS-2 on ultrasound and an RMT >3 mm.[26] It is noteworthy that currently the society of fetal and maternal medicine currently recommends against expectant management. It might be considered for a CSP without fetal cardiac activity particularly if there is evidence of spontaneous resolution.[4]

Termination of cesarean scar pregnancy

This can be achieved either medically (nonsurgically) or surgically. Nonsurgical options include methotrexate (MTX), direct local embryocidal injection into the sac with concomitant sac aspiration, uterine artery embolization (UAE) and high-intensity focused ultrasound therapy (HIFU). Surgical treatment options include laparoscopy, laparotomy, hysteroscopy and curettage, and gestational sac suction evacuation. Although treatment may be described in terms of single or multiple modality practically speaking, most cases of CSP are managed with a combination of options.

Medical management-cesarean scar pregnancy

There have been numerous reviews on the use of both local and systemic MTX to treat a CSP. MTX provides a noninvasive, relatively low-cost treatment for patients who wish to preserve fertility but has been associated with a 57% failure rate and a complication rate of 62.1%. As with its use in tubal ectopic pregnancy, MTX is appropriate for women who are pain-free and hemodynamically stable with an unruptured nonviable pregnancy <8 weeks' gestation with a human chorionic gonadotropin (HCG) <5000 iu/ml for whom a single intramuscular dose of 50 mg/m^2 may be adequate. Multiple doses might be required for more advanced, viable gestations. High-dose intravenous MTX infusion with folinic acid rescue, has been reported to have a success rate of 85.7%. Some authors have questioned the ability of MTX to penetrate poorly vascularised fibrous tissue and advocated local administration directly into the gestation sac, especially in cases of viable CSP. This is thought to produce a high local concentration and interrupt the pregnancy more rapidly than systemic administration.[33-35]

High-intensity focused ultrasound therapy-cesarean scar pregnancy

Over the past 10 years, ultrasound-guided HIFU (USgHIFU) has been used to treat solid tumors. Since Wang *et al*. reported their preliminary results in 2002 many studies have shown that USgHIFU is safe and effective in treating fibroids and has also been used for treating adenomyosis.

Recently, CSPs have been treated successfully with HIFU and authors claim that HIFU combined with suction curettage under hysteroscopic guidance is a safe and effective method for treating patients with CSP at early gestational ages.[36-38]

Uterine artery embolization-cesarean scar pregnancy

UAE in combination with other treatment modalities such as MTX, dilatation, and curettage (D and C) or hysteroscopic resection has been successfully used to treat CSP. In a systematic review, UAE combined with D and C was highly effective for CSP management with only 6.4% of cases needing additional treatment and severe complications, namely hemorrhage and hysterectomy, only occurring in 3.4% of cases. A combination of UAE, D and C and hysteroscopy has also been found to be efficacious with a success rate of 95.4% and a complication rate of only 1.2%.[39-43]

Surgical treatment–cesarean scar pregnancy

Surgical treatment is indicated for patients who are hemodynamically unstable or in cases of failed medical management. It may be used in combination with pharmacological therapy to increase the success of treatment and limit risk of complications. Minimally invasive surgical techniques are generally the first-line treatment options but do require surgical expertise. They carry the advantage of potentially allowing contemporaneous scar repair at the time of CSP management. Surgery is ideally performed before 9 weeks to reduce the risk of visceral injury aspiration and/or resection of gestational sac contents can be performed either through operative hysteroscopy or laparoscopy, the choice depending on the CSP type. Hysteroscopy is more suitable for the endogenic CSP type while laparoscopy is indicated for exogenic types. The two modalities may be used together in some circumstances.

UAE, bilateral uterine artery ligation, local vasopressin injection, and intrauterine balloon tamponade have all been used successfully as adjuncts to surgical treatments for the prevention and control of heavy bleeding. Studies have shown that hysteroscopy and laparoscopy surgery and reversible ligation of the uterine artery achieve better clinical outcomes than hysteroscopy or curettage with respect to postoperative recovery making it more suitable for patients with CSP and desire for fertility.

Hysteroscopy-cesarean scar pregnancy

An operative hysteroscopy is a good option when the RMT is more than 3 mm. It allows direct visualization for detachment of the CSP from the CSD and may be used in combination with laparoscopy if the RMT is 3 mm to reduce the complication risk. Electrocoagulation should be used with caution to avoid bladder trauma and subsequent dehiscence. In general, hysteroscopic treatment of scars in the nonpregnant state is not recommended when the myometrium thickness is <3 mm.

One study quoted a 91% success rate of hysteroscopic treatment for CSP, with rates of hemorrhage <500 mL and hysterectomy of 1.66% and 0.28%, respectively.[43] In another study of 439 patients who had a hysteroscopy with dilatation and curettage alone or in association with systemic MTX, UAE or laparoscopic bilateral uterine artery ligation the success and complication rates were 93.6%, and 8.2%, respectively. Thirty-seven women conceived again and 22 completed a term pregnancy without uterine rupture. The recurrence rate of CSP was 10.8%.[44-47]

Laparoscopy-cesarean scar pregnancy

Laparoscopic management is probably the most effective method with the lowest complication rates and allows simultaneous scar repair hysteroscopy can help identify the CSD and assess the adequacy of any repair. Multilayer repair has a lower risk of wedge defect formation and uterine rupture improving the success rate with minimal impact on subsequent fertility. Blood loss during laparoscopic repair can also be reduced with dilute vasopressin or electrosurgical energy avoiding more invasive techniques which might injure normal myometrium. The bladder is dissected free from the uterus, and CSD is excised along with pregnancy followed by repair of the defect. Bilateral uterine artery ligation may reduce peri-operative blood loss. In a seven-case series of 69 women laparoscopy had a 97.1% success rate with no reported severe complications.[43]

Vaginal repair-cesarean scar pregnancy

A transvaginal hysterotomy is an effective treatment for CSP but requires surgical expertise. The bladder is dissected away through an incision in the anterior cervicovaginal junction, and the CSP is identified in the anterior part of the lower uterine segment. The pregnancy tissue is removed through a transverse incision. The myometrial and vaginal defects are repaired. Several authors have described vaginal approaches to cesarean scar pregnancies. The success rate of treatment was 99.5%, complication rate was 1.4%, and hysterectomy rate was 0.5%.[48]

Approaches in our Institution and Management Algorithm–Cesarean Scar Pregnancy

Our unit is a tertiary specialist center in Singapore with a delivery rate of 12,000/year and a commensurate number of gynecology episodes. The CS rate is just over 30%. Most operating modalities are available. Patients with a confirmed diagnosis of CSP are referred to the multidisciplinary cesarean scar clinic. Management options are discussed depending on hemodynamic stability age, fertility wishes, fetal viability, and RMT. We follow the algorithm shown below [Figure 1] to triage CSPs suitable for a minimally invasive surgical technique. Stable patients with an unruptured CSP and an RMT more than 3 mm, are offered hysteroscopic guided suction evacuation (HSE), with added laparoscopy with or without repair if the RMT is 3 mm or <3 mm if patient seeking fertility preservation [Figure 2].

Thirty-seven patients were diagnosed with a CSP between May 2020 and June 2022. After the exclusion of three patients, who opted to continue the pregnancy despite counseling on the intrinsic risks and who were subsequently monitored in the high-risk antenatal clinic and delivered by the obstetric "accrete team," the treatment outcomes of 34 patients were available for the final analysis. Of the 34 patients initially diagnosed with a CSP and entered into the study 12 (35.3%) were more than 39 years old and 24 (70.5%) had had 2 CS s or more. The majority[28] were diagnosed under 9 weeks gestation

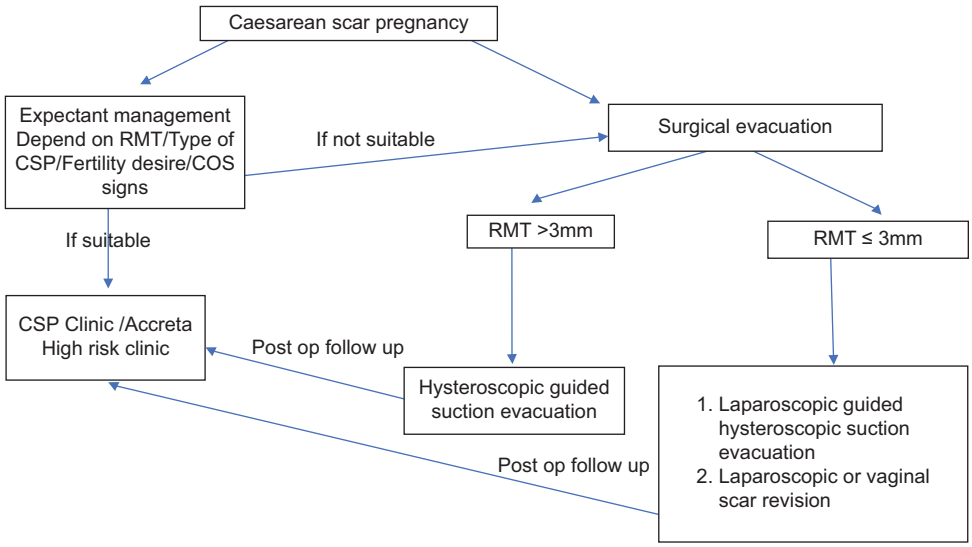

Figure 1: Algorithm for surgical management of cesarean scar pregnancy. CSP: Cesarean scar pregnancy, RMT: Residual myometrial thickness, COS: Cross-over sign

with more than half having a beta HCG level >10,000iu at presentation despite 52.9% having a negative FH at diagnosis. Only 13 (38.2%) of the women had an RMT of more than 3 mm [Table 1]. Women with an RMT 3 mm or <3 mm were still eligible for inclusion but with added laparoscopy. In total, 22 women had HSE with 9 having it performed under laparoscopic guidance because the RMT was 3 mm or <3 mm. The remainder of patients having laparoscopy had either laparoscopic repair in 5 patients and one repair being done vaginally under laparoscopic guidance. The median blood loss in HSE cohort alone was 50 ml. Among the remaining 6 women, 2 had MTX, 3 had a laparotomy and 1 was finally diagnosed with miscarriage [Table 2].

This small retrospective study showed that, in well-selected cases, HSE is a safe and efficacious method of treating CSP which can be offered in a single setting. There are several in-built features to reduce the blood loss including the administration of tranexamic acid at induction,[49] cervical infiltration with pitressin before inserting the hysteroscope, hydrodissection during gestational sac dislodgement and the option of inserting a Foley catheter postoperatively.[50] It has advantages over simple dilatation and evacuation in that it allows localization of the pregnancy and visualization to ensure completeness especially if a grasper or scissors are required. However, it does have the drawback that, by avoiding the resection often involved in the minimally invasive approach, it does not allow contemporaneous myometrial defect repair which leaves the risk of recurrence and other niche-related problems in the future. HSE is an efficacious treatment for CSP <9 weeks with added laparoscopy if RMT 3 mm or <3 mm.

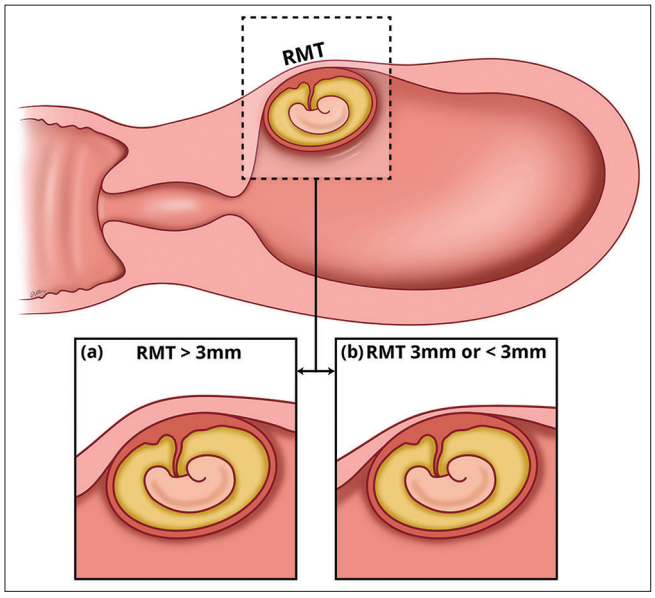

Figure 2: Cesarean scar pregnancy according to the RMT. RMT: Residual myometrial thickness

Conclusion

CSP is rare and differs from other types of ectopic pregnancy in its ability to progress while still carrying a significant risk of severe, potentially life-threatening, maternal morbidity. It is an iatrogenic condition and incidence is increasing due to the global rise in CS rate. Little is known about precise etiology or natural history although current interest in PASD might be contributory. Early detection is key and requires a high index of suspicion, strict diagnostic criteria, and properly trained experienced sonographers. Management of CSP should be discussed in a multidisciplinary team including minimal invasive surgeons, the accreta team, and interventional radiologists.

Treatment of CSP is challenging. Currently, the recommendation is to offer early termination of pregnancy because of the potential risks of continuing the pregnancy. However, as the

Table 1: Description of cesarean scar pregnancy

	n (%)	Mean±SD, median
Age (years)		38±3, 38
≤39	22/34 (64.7)	36±2, 36
>39	12/34 (35.3)	41±2, 41
Previous LSCS		
1	10/34 (29.4)	
2	15/34 (45.5)	
3	6/34 (17.6)	
4	3/34 (8.8)	
GA (weeks)		6.2±1.2, 5.9
<9	28/29 (96.6)	6.0±1.0, 5.9
>9	1/29 (3.4)	9.7, NA
Cardiac activity		
Present	16/34 (47.1)	
Absent	18/34 (52.9)	
RMT (mm)		
≤3	21/34 (61.8)	
>3	13/34 (38.2)	
BHCG level (iu)		
<10,000	14/34 (41.2)	
>10,000	20/34 (58.8)	

SD: Standard deviation, LSCS: Lower segment cesarean section, GA: Gastational age, RMT: Residual myometrial thickness, BHCG: Beta-human chorionic gonadotrophin, NA: Not available

Table 2: Mode of treatment and estimated blood loss

	n	Blood loss (mL), median
Hysteroscopic-guided suction evacuation	13/34	50
Laparoscopic-guided suction evacuation	9/34	100
Laparoscopic-guided vaginal repair	1/34	150
Laparoscopic repair	5/34	200
Miscarriage	1/34	-
Methotrexate medical treatment	2/34	-
Laparotomy	3/34	150

likelihood of future pregnancy complications for individual CSPs varies depending on several factors this might not always be the only option especially if the patient desires fertility when it should be discussed in the high-risk clinic with a maternal-fetal medicine specialist with a special interest in PASD. RMT, type of cesarean scar pregnancy, and fertility concerns are all important considerations when deciding on the optimal surgical management.

The literature supports an interventional rather than medical approach but the safest and most efficient clinical approach to CSP in terms of treatment modality and service delivery is yet to be determined. There is an urgent need for further research on this topic with adequate reporting on possible prognostic markers, as well as ways to conserve fertility during delivery. Ideally, this would be based on well-designed, high-quality, prospective multi-center randomized controlled trials with the objectives of improving the quality of care for women and allowing an expert consensus on definitive treatment to be reached.

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Conflicts of interest

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