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Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy

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The American College of Obstetricians and Gynecologists (ACOG), the American Institute of Ultrasound in Medicine (AIUM), and the Society of Family Planning (SFP) endorse this document.

Cesarean scar pregnancy is a complication in which an early pregnancy implants in the scar from a prior cesarean delivery. This condition presents a substantial risk for severe maternal morbidity because of challenges in securing a prompt diagnosis, as well as uncertainty regarding optimal treatment once identified. Ultrasound is the primary imaging modality for cesarean scar pregnancy diagnosis, although a correct and timely determination can be difficult. Surgical, medical, and minimally invasive therapies have been described for cesarean scar pregnancy management, but the optimal treatment is not known. Women who decline treatment of a cesarean scar pregnancy should be counseled regarding the risk for severe morbidity. The following are Society for Maternal-Fetal Medicine recommendations: We recommend against expectant management of cesarean scar pregnancy (GRADE 1B); we suggest operative resection (with transvaginal or laparoscopic approaches when possible) or ultrasound-guided vacuum aspiration be considered for surgical management of cesarean scar pregnancy and that sharp curettage alone be avoided (GRADE 2C); we suggest intragestational methotrexate for medical treatment of cesarean scar pregnancy, with or without other treatment modalities (GRADE 2C); we recommend that systemic methotrexate alone not be used to treat cesarean scar pregnancy (GRADE 1C); in women who choose expectant management and continuation of a cesarean scar pregnancy, we recommend repeat cesarean delivery between 34 0/7 and 35 6/7 weeks of gestation (GRADE 1C); we recommend that women with a cesarean scar pregnancy be advised of the risks of another pregnancy and counseled regarding effective contraceptive methods, including long-acting reversible contraception and permanent contraception (GRADE 1C).

Key words: cesarean scar ectopic, cesarean scar pregnancy, placenta accreta spectrum

Cesarean scar pregnancy (CSP) is a complication in which an early pregnancy implants in the scar from a prior cesarean delivery. Perhaps because of high worldwide cesarean delivery rates, there appears to be increased incidence and recognition of this condition over the past 2 decades. The clinical presentation is variable, and many women are asymptomatic at presentation. Patients may present to a variety of obstetric and gynecologic care providers, but maternal-fetal medicine subspecialists often are involved in the diagnosis and subsequent management of these pregnancies. CSP can be difficult to diagnose in a timely fashion. Ultrasound imaging is the primary imaging modality for CSP diagnosis. Expectantly managed CSP is associated with high rates of severe maternal morbidity, such as hemorrhage, placenta accreta spectrum (PAS), and uterine rupture. Given these substantial risks, pregnancy termination is recommended after CSP diagnosis. Several surgical and medical treatments have been described for this disorder; however at this time, optimal management remains uncertain. For this reason, an international registry has been created for providers to submit data on diagnosis, natural history, and management (https://csp-registry.com).

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What is cesarean scar pregnancy, and what is its incidence?

CSP occurs when an embryo implants in the fibrous scar tissue of a prior cesarean hysterotomy.[1] Although at times referred to as a cesarean scar ectopic pregnancy, these gestations are, in fact, within the uterine cavity and, unlike true ectopic pregnancies, may result in a liveborn infant. However, this condition presents a substantial risk for severe maternal morbidity that is complicated by challenges in securing a timely diagnosis and uncertainty regarding optimal treatment once identified.

Although relatively uncommon, reported international experience with CSP appears to be increasing, likely as a result of high contemporary cesarean delivery volume.[1]

High cesarean delivery rates are observed in many of the world's most populous developed nations, with an estimated 18.5 million women undergoing this procedure each year.[2] As such, there is mounting collective awareness of rare cesarean delivery-associated complications such as CSP.

The true incidence of CSP is unknown, because the condition is likely underdiagnosed and underreported. Reported single-center estimates of incidence range from 1:1800 to 1:2656 of overall pregnancies.[3,4] Although CSP incidence is believed to have increased over time, other factors, which include improved imaging with ultrasound and magnetic resonance imaging (MRI), increased use of transvaginal ultrasonography, and possibly increased physician awareness, may contribute to a perceived increase in incidence.

What is the pathogenesis of CSP?

Although the pathogenesis of CSP is incompletely understood, the mechanism has been postulated to involve blastocyst implantation within a microscopic dehiscence tract in the scar from a prior cesarean delivery.[5–8] Because of the fibrous nature of scar tissue, these inherently deficient implantation sites are at risk for dehiscence, PAS, and hemorrhage as the CSP enlarges.

CSP and placenta accreta appear to have similar disease pathways and may exist along a common disease continuum.[9] In 1 series in which pregnancies complicated by either CSP or early PAS underwent histopathologic analysis by blinded pathologists, findings were indistinguishable between groups, with a high interobserver correlation.[10] Histopathologic analyses for both groups were characterized by myometrial or scar tissue villous invasion with little or no intervening decidua.

The implantation patterns of CSP can be categorized as either endogenic (also referred to as "on the scar") or exogenic ("in-the-niche").[11,12] Endogenic is defined as growing within the uterine cavity and exogenic as arising from a deeply implanted gestational sac into the scar that may grow toward the bladder or abdominal cavity. These ultrasonographic appearances may influence obstetric prognosis.[11,12] It has been suggested recently that early first-trimester determination of whether a CSP is growing "on the scar" or "in the niche" of the prior cesarean hysterotomy may be used to predict subsequent pregnancy outcome[12,13] (Figure 1). In 1 small retrospective experience, patients with pregnancies growing "on the scar" had variable obstetric outcomes, whereas those with pregnancies growing "in the niche" all underwent hysterectomy with PAS at delivery.[13]

How does CSP present clinically, and are there known risk factors?

Although second-trimester diagnoses have been reported, CSP usually presents in the first trimester. In 1 review of published CSP case series, the average gestational age at diagnosis was 7.5 ± 2.5 weeks.[11] The clinical presentation is variable, ranging from asymptomatic ultrasonographic detection to a presentation with uterine rupture and hemoperitoneum, typically in the absence of a timely diagnosis. In the review mentioned earlier, approximately one-third of cases were asymptomatic, and approximately one-third presented with painless vaginal bleeding.[11] Nearly one-quarter of presentations involved pain, with or without bleeding. Women with ruptured CSP may also present with hemodynamic collapse.

Although by definition prior cesarean delivery is a prerequisite for CSP development and placenta previa may modify this risk, it is not clear if the number of prior cesarean deliveries further increases the risk. Although some reports and anecdotal observations suggest an over-representation of women with multiple prior cesarean deliveries in CSP cohorts, a review of the literature reveals that 52% of CSP cases occur in women with a single prior cesarean delivery.[1,3,14] Interestingly, the indication for prior cesarean delivery may be a risk factor for CSP, with previous delivery for breech presentation appearing to be a more common indication in women who later experience CSP.[6,11,15,16] It is hypothesized that the lower uterine segment is often less well developed in pregnancies the are delivered for malpresentation and that a thicker hysterotomy presents a greater risk for poor healing and resultant microscopic dehiscence. No published data exist regarding an association between hysterotomy closure technique and CSP.

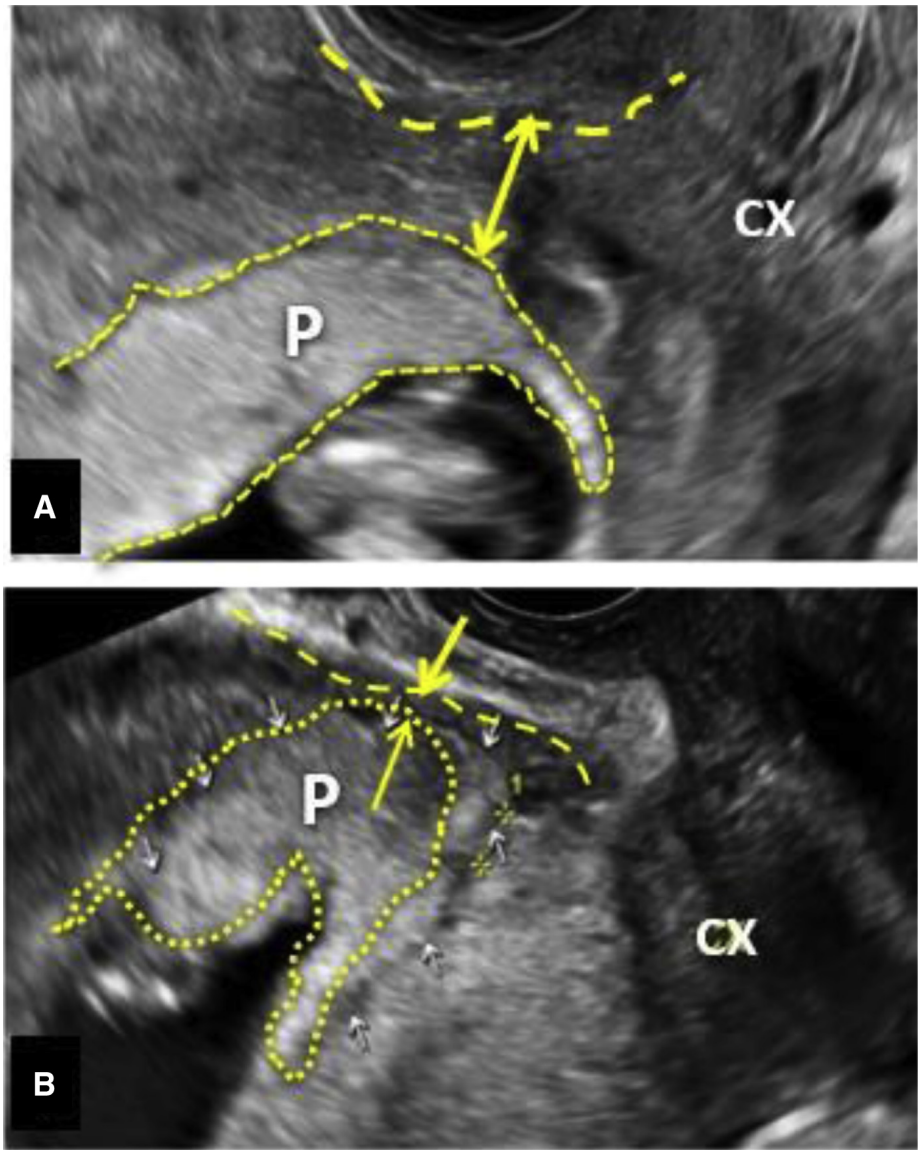
How is CSP diagnosed?

Ultrasound imaging is the primary imaging modality for CSP diagnosis, although a correct and timely determination can be difficult. The initial finding of a low, anteriorly located gestational sac should raise concern for a possible CSP and warrants further investigation.[17] When women with suspected CSP are being evaluated, a high degree of clinical suspicion is needed because a missed or delayed diagnosis can result in uterine dehiscence, hemorrhage, loss of fertility, or maternal death.

Transvaginal ultrasound imaging is the optimal modality for the evaluation of suspected CSP because it provides the highest image resolution[18] (Figures 2 and 3). Grayscale combined with color Doppler ultrasound imaging are recommended for CSP diagnosis. One group suggests combining transvaginal ultrasound imaging with a transabdominal ultrasonogram with a full maternal bladder to provide a "panoramic view" of the uterus and the relationship between the gestational sac and bladder.[6] Although test performance characteristics are unknown and likely influenced by examiner experience and skill, in 1 review, 94 of 111 CSP cases (84.6%) were detected by transvaginal ultrasound imaging, with the remaining 17 pregnancies (15.4%) incorrectly diagnosed as incomplete abortions or cervical pregnancies.[11]

Since diagnostic criteria were first proposed by Vial et al[16] in 2000, other authors have suggested modifications to enhance the ultrasonographic detection of CSP.[3,18] One

FIGURE 1
Implantation patterns of cesarean scar pregnancy



A, "On-the-scar," or endogenic, form has a considerable myometrial layer (*clear space*) between the placenta and anterior uterine surface (*solid arrow*). **B,** "In-the-niche," or exogenic, form has a thin myometrial interphase below the placenta (*between the 2 arrows*).

Cx, cervix; *P,* placenta.

(Used with permission from 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.e1-6; Figures 1, B, and 2, B.)

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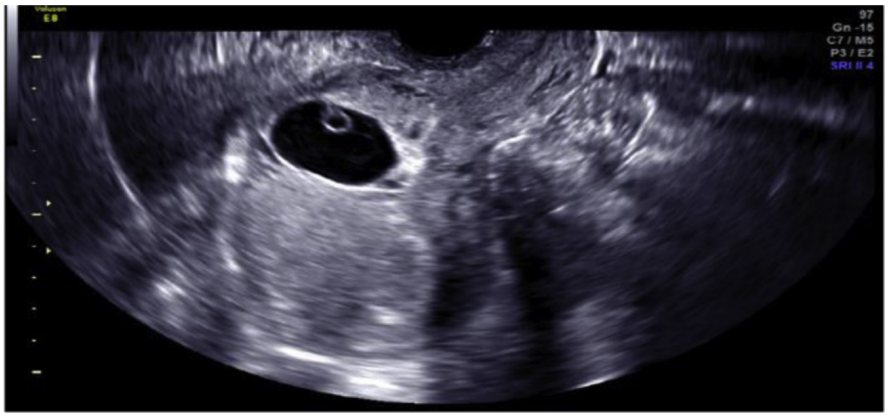
approach proposes the following ultrasonographic criteria to diagnose CSP: (1) an empty uterine cavity and endocervix; (2) placenta, gestational sac, or both embedded in the hysterotomy scar; (3) a triangular (at 8 weeks of gestation and earlier) or rounded or oval (after 8 weeks of gestation) gestational sac that fills the scar "niche" (the shallow area representing a healed hysterotomy site); (4) a thin (1–3 mm) or absent myometrial layer between the gestational sac and bladder; (5) a prominent or rich vascular pattern at or in the area of a cesarean scar; and (6) an embryonic or fetal pole, yolk sac, or both with or without fetal cardiac activity (Figure 4). All of these criteria may not be observed. Especially with very early diagnosis and before fetal cardiac activity, the woman must have confirmation of pregnancy (for example, a positive pregnancy test result).[18] Bulging or ballooning of the lower uterine segment in the midline sagittal transabdominal view has also been considered to be supportive of CSP diagnosis.[19,20]

FIGURE 2
Transvaginal 2-dimensional ultrasound image of a cesarean scar pregnancy



A gestational sac can be seen clearly embedded within a hysterotomy scar.

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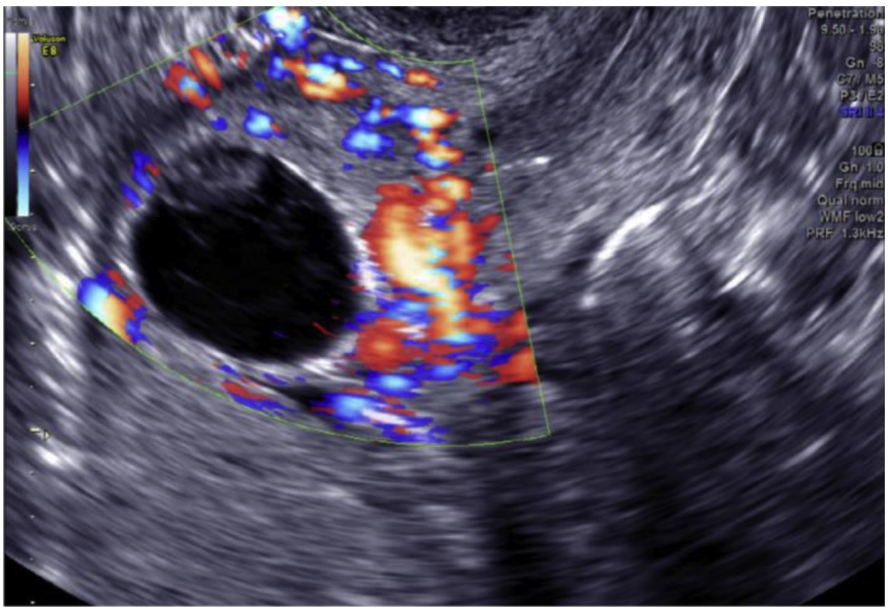
A challenge in the diagnosis of CSP is distinguishing it from other clinical entities with a similar ultrasonographic appearance. In a literature review that collected 751 cases of CSP, 107 cases (13.6%) were originally misdiagnosed as cervical ectopic pregnancies, spontaneous abortions in transit, or low implantation of an intrauterine pregnancy.[21] Given the importance of prompt diagnosis, referral to an experienced center for a second opinion may be preferable to ongoing follow-up examinations that are likely to lead to a delay in diagnosis.

Are other modalities useful for the diagnosis of CSP?

Transvaginal 3-dimensional ultrasound and 3-dimensional power ultrasound imaging have been used in an attempt to enhance the accuracy of CSP diagnosis, with case reports supporting the utility of these techniques.[22–24] However, because of limited published experience with these approaches, there are insufficient data to support a benefit of routine use of 3-dimensional ultrasound imaging for the diagnosis or management of CSP.

FIGURE 3
Doppler image of a cesarean scar pregnancy



The image shows a prominent vascular pattern in the area of a hysterostomy scar.

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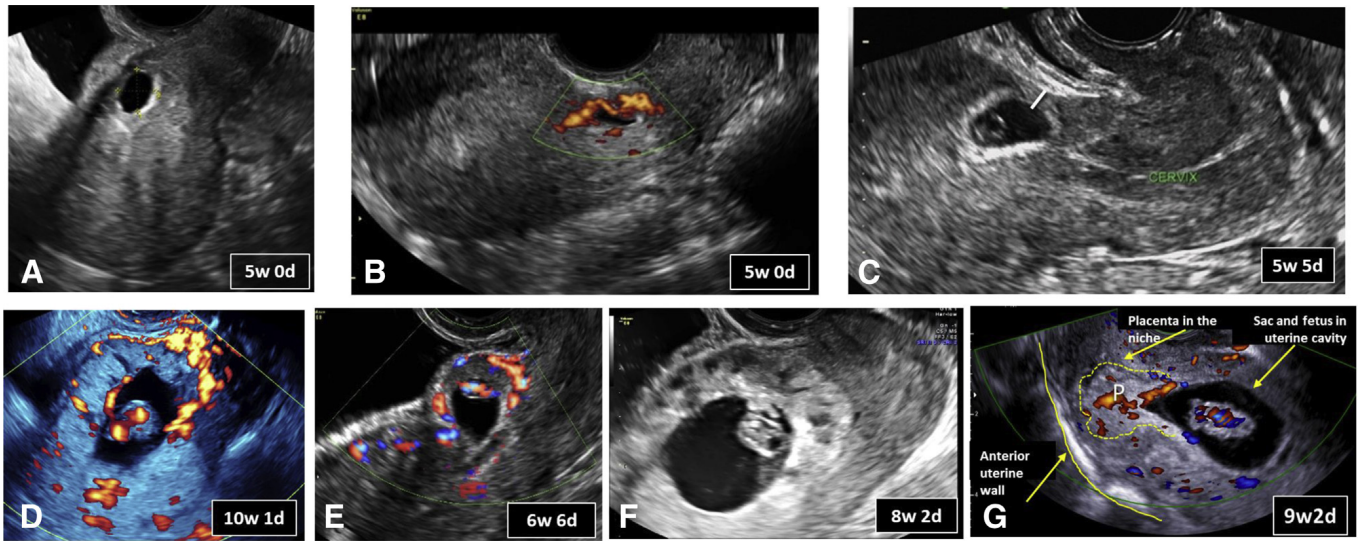
FIGURE 4
Ultrasonographic features of cesarean scar pregnancy in the first trimester



A, Two-dimensional ultrasound image shows an empty uterine cavity and closed, empty endocervical canal. **B,** Low implantation with blood flow around the gestational sac. **C,** Implantation "in the niche" with thin myometrial layer between gestational sac and bladder (*line*). **D,** Doppler imaging shows blood flow around the chorionic/gestational sac at the site of placental implantation. **E,** Altered bladder line with bulge of gestational sac into bladder. **F,** Placental lacunae in a cesarean scar pregnancy at 8 weeks of gestation. **G,** After 7 weeks of gestation, the gestational sac extends towards the uterine cavity, elongates, and eventually assumes an intracavitary position. The placenta stays anchored in the area of the scar/niche in its initial site of implantation.

P, placenta.

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MRI has been used as an adjunct to ultrasound imaging for the diagnosis of CSP, although its incremental benefit over ultrasound imaging alone is unknown.[1,6,7,25–27] Both T1- and T2-weighted images can demonstrate a gestational sac embedded within the lower uterine segment at the level of a prior cesarean scar niche and an empty endometrial cavity and endocervix. In 1 MRI series, most CSPs presented as a thin-walled diverticulum at the cesarean scar niche.[27] MRI may also provide useful information regarding the degree of invasion and whether there is evidence of PAS.[1] Most authors do not recommend MRI as a routine component of CSP evaluation, because transvaginal ultrasound imaging with color Doppler interrogation is believed to be reliable in securing a correct diagnosis. However, in cases in which ultrasound imaging is inconclusive, MRI could be considered as an adjunct study. Given the risks associated with delayed diagnosis, the use of multiple ultrasound imaging approaches and modalities, such as MRI, are likely preferable to serial ultrasound examinations.

CSP diagnosis has been reported with the use of hysteroscopy and laparoscopy.[7,11,28,29] Although these methods are not recommended solely for diagnostic purposes, they can be used to confirm a diagnosis at the time of planned operative intervention. With laparoscopic examination, CSP has been described as an ecchymotic bulge with a "salmon-red" appearance beneath the bladder at the level of the prior cesarean scar with an otherwise normal-appearing uterus.[7,29]

What is the natural history of CSP?

Limited information exists regarding the natural history of CSP, because few recognized CSPs continue to a viable gestational age. Those that do are believed to be at high risk for severe complications in the second and third trimesters, although the rates of these complications are unknown. CSPs have resulted in live births, often associated with PAS, cesarean hysterectomy, and massive hemorrhage at delivery.[11,15,30] Series describing outcomes of expectantly managed CSPs all involve small case numbers and high hysterectomy rates that range from 50–100% and usually are associated with PAS.[10,31–34] In case series of women who were treated expectantly, most required additional treatment, and more than 50% had severe complications.[30] In 1 series that prospectively followed 10 women with a first-trimester ultrasonographic diagnosis of a pregnancy implanted in or on a prior cesarean scar, all the women had PAS diagnosed at the time of repeat cesarean delivery.[32]

Because of the high risk of severe maternal morbidity, expectant management is not recommended for a recognized CSP, and pregnancy termination generally is advised

as soon as the diagnosis is confirmed.[1,11,13] For cases in which a CSP is suspected but the diagnosis is not certain, short-interval follow-up, a second opinion, or additional imaging with MRI should be considered to make a timely diagnosis without undue delay. **We recommend against expectant management of CSP (GRADE 1B).**

An exception to the recommendation against expectant management involves early CSP that is characterized by fetal death or other evidence of early pregnancy failure. In the case of an early CSP that is definitively diagnosed as nonviable, expectant management may be pursued with serial ultrasound surveillance, quantitative beta-human chorionic gonadotropin (beta-hCG) measurements, and monitoring for maternal symptoms such as bleeding or pelvic pain. However, it should be recognized that it can take several months for a nonviable CSP to resolve spontaneously, and expectant management of nonviable CSP has been associated with the development of a uterine arteriovenous malformation (AVM).[20] Uterine AVM in this clinical context has been associated with persistent, severe vaginal bleeding and may require umbilical artery embolization or even hysterectomy. In a series by Timor-Tritsch et al,[20] 20% (2/10 women) of expectantly treated women experienced an AVM.

What CSP treatment modalities have been reported?

Although many different options for the management of CSP have been reported, the optimal treatment is not known (Table 1). Surgical, medical, and minimally invasive therapies and various combinations of such treatments have been described. However, the medical literature consists predominantly of case series, with a limited number of randomized controlled trials comparing treatment approaches. These series are influenced by variable levels of clinical experience, institutional capability, provider skill, and case complexity, which hinders comparisons between studies. Conclusions regarding optimal CSP therapy are further limited by a lack of head-to-head comparisons between medical and surgical approaches.

The modalities that have been described for CSP treatment include hysteroscopy, laparoscopy, laparotomy, open surgery, transvaginal surgery, curettage (including both sharp and vacuum aspiration techniques), uterine artery embolization (UAE), methotrexate (both local guided injection and systemic administration), direct potassium chloride (KCl) injection, needle-guided sac decompression, high-intensity focused ultrasound imaging, the use of balloon catheters, and combinations of these methods.[35] In

TABLE 1
Treatment options for cesarean scar pregnancy[a]

Method	Studies, n		Patients, n	Efficacy, %[b]	Complications, %[c]
	Case series	Randomized controlled trials			
Expectant management	5	0	41	41.5	53.7
Systemic methotrexate	18	3	339	75	13
Needle aspiration+systemic methotrexate	6	0	148	84.5	15.5
Curettage	21	0	243	48	21
Hysteroscopy[d]	7	0	95	83	3.2
Transvaginal resection[e]	6	0	118	>99	0.9
Uterine artery embolization+curettage	5	2	295	93.6	3.4
Uterine artery embolization+curettage+hysteroscopy	1	1	87	95.4	1.2
Uterine artery embolization+curettage+systemic methotrexate	13	1	427	68.6	2.8
Local and systemic methotrexate	2	0	34	75	2.3
Laparoscopy	7	0	69	97.1	0
Local methotrexate	2	1	74	64.9	4.1
High-intensity focused ultrasound imaging	1	0	16	100	0
High-intensity focused ultrasound imaging+hysteroscopic suction curettage	1	0	52	100	0
Double cervical ripening balloon catheter[f]	2	0	48	97.7[g,h]	4.2[g,h]

[a] Unless otherwise noted, data from Birch Petersen K et al,[36] 2016; [b] Women who did not need additional treatment; [c] Severe complications such as hemorrhage, hysterectomy; [d] 11 women also had systemic methotrexate and hysteroscopy; [e] 12 women also had systemic methotrexate and transvaginal resection; [f] 34 women also had systemic methotrexate; [g] Reference 37; [h] Reference 38.

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1 review, the authors reported that treatment selection was influenced by physician specialty, with gynecologic surgeons favoring curettage, laparoscopy, and hysteroscopy and obstetricians more readily pursuing needle-based injections and interventional radiology involvement.[21] Publication bias likely also limits conclusions that can be drawn from the available literature.

CSP treatment decisions are guided by a principal goal of preserving maternal health, followed by a secondary goal of preserving fertility when possible. Management decisions should be determined after considering pregnancy viability, gestational age, maternal health, future family planning wishes, physician skill and experience, and institutional resources. Preferred management may differ between institutions based on resources, personnel, and clinical experience. Even with efforts to tailor treatment strategies to individual patients and clinical presentations, there remains a substantial risk for complications with any management approach.

Systematic reviews have been inconsistent with regard to the identification of a single optimal CSP treatment modality that best balances procedural success and risks. In a review by Timor-Tritsch and Monteagudo[21] that included 751 reported cases of CSP and 31 different treatment approaches, a 44.1% complication rate was reported overall. Complications included unplanned emergency operations that included hysterectomy (4.8%), laparotomy (5.3%), and UAE (2.9%). Among procedures described by the authors as first line, the highest complication rates were observed with intramuscular methotrexate alone (54/87 cases; 62.1%), curettage alone or in combination with other modalities (189/305 cases; 61.9%), and UAE alone or in combination with other modalities (30/64 cases; 46.9%). The lowest complication rates among first-line therapies were reported with hysteroscopy alone or in combination (22/119 cases; 18.4%) and local intragestational injection of methotrexate or KCl (8/81 cases; 9.6%). Based on observed complication rates, this review supported the use of local methotrexate and hysteroscopy-based approaches to CSP treatment and discouraged the stand-alone use of systemic methotrexate, curettage, and UAE. Of note, most of the available literature does not distinguish between sharp and suction curettage, although the complication rates appear to be lower with suction curettage.

Different conclusions were reached in a systematic review by Birch Petersen et al[36] that compiled 2037 CSP cases, some of which overlapped with the Timor-Tritsch report, and included data from 4 randomized trials and 48 case series. Among CSP cases with available gestational age data, most were detected in the first trimester. Treatment modalities were condensed into 14 main approaches. Success was defined as the efficacy of a first-line treatment modality to resolve a CSP. Major complications were defined as hysterectomy, estimated blood loss >1000 mL, or a need for blood transfusion. The lowest success rates were observed with expectant management (41.5% success, 53.7% complications), curettage (n=243; 48.1% success, 21% complications), UAE and methotrexate (n=427; 68.6% success, 2.8% complications), systemic methotrexate (n=339; 75.2% success, 13% complications), and combined local and systemic methotrexate (n=34; 76.5% success, 2.3% complications). Among reported therapies, the highest success rates were observed with transvaginal CSP resection (n=118; 99.2% success, 0.9% complications), laparoscopy (n=69; 97.1% success, 0% complications), UAE with curettage, hysteroscopy, or both (n=85; 95.4% success, 1.2% complications), and UAE alone (n=295; 93.6% success, 3.4% complications). Based on this review of the literature, the authors concluded that interventional approaches appeared superior to medical approaches.[36]

Since publication of these reviews, treatment with a cervical double-balloon catheter that can terminate the pregnancy while compressing the blood supply to the gestational sac has been reported. A few series have reported a low rate of complications (4.2%) and a high success rate (97.7%) with this technique.[37,38]

It should be emphasized that, although transvaginal CSP resection, UAE, and laparoscopy alone or in combination appeared to be superior to medical and minimally invasive treatments in the Birch Petersen et al[36] review, these interventions require resources such as specially equipped procedural suites or operating rooms, advanced equipment, anesthesia availability, and trained staff. As a result, some of these interventions are not widely available, and they may be costly. Furthermore, little high-quality evidence exists that compares these methods head-to-head with less resource-intensive modalities, such as local intragestational injections of methotrexate or KCl.

What are the recommended treatment approaches for CSP?

Surgical treatment

Both medical and interventional treatment options have been described for the management of CSP. Among surgical management options, transvaginal and laparoscopic CSP resection appear to have low complication rates, although published data regarding these techniques are limited.[39–41] A potential advantage of these approaches is that the scar tissue can be excised and the surrounding myometrium reapproximated at the time of CSP removal. It is unknown if this practice decreases the risk of CSP reoccurrence.

Curettage alone, without adjuvant treatments, has been associated with high complication rates, which include hemorrhage and perforation, because of an inability to completely access and remove trophoblastic tissue outside of the endometrial cavity and because scar tissue contracts poorly after curettage. As with PAS, sharp curettage may sever deeply invading blood vessels and expose the patient to ongoing bleeding. In addition to a high complication rate, additional treatment is reported to be required after 52% of

curettage cases.[36] Again, it should be noted that the published literature incompletely distinguishes between sharp curettage and vacuum aspiration, which may provide different success and complication rates with CSP management. **We suggest operative resection (with transvaginal or laparoscopic approaches when possible) or ultrasound-guided vacuum aspiration be considered for surgical management of CSP and that sharp curettage alone be avoided (GRADE 2C).**

Although sharp curettage alone is not recommended as a primary CSP treatment, higher efficacy and lower complication rates have been reported with ultrasound-guided vacuum aspiration.[42] In a series that involved 191 women with CSP who underwent suction curettage, there was a 4.7% rate of blood transfusion and a single case of hysterectomy because of hemorrhage. Among women who returned for follow-up, there was a 6% rate of repeat surgery because of retained products of conception. Shirodkar placement as an adjunct to curettage has also been described, in which the cerclage suture is placed before curettage and only secured in the setting of hemorrhage to minimize bleeding.[43]

Gravid hysterectomy is an alternative surgical option that may be considered for the definitive management of CSP. This approach may be particularly appropriate for early second-trimester CSP presentations or for women who do not desire future fertility.

Medical treatment

When pursuing medical treatment of CSP, local or intragestational injection of methotrexate is a preferred approach, with or without accompanying systemic methotrexate. Stand-alone systemic methotrexate is not recommended because of a higher reported risk of complications.[16,30] Although a small randomized trial of systemic vs local methotrexate demonstrated no difference in overall cure rates,[44] reviews suggest a high risk of complications with intramuscular methotrexate alone,[21,45] and local methotrexate appears to be a more effective approach. In a literature review by Cheung[45] of 96 cases of intragestational methotrexate for CSP, success was achieved in 73.9% after a single local methotrexate injection and increased to 88.5% after an additional local or intramuscular methotrexate injection. No baseline clinical characteristics were found to influence the outcome other than serum beta-hCG >100,000 IU/L, which was associated with treatment failure. Intragestational injection is performed typically with a 20-gauge needle under ultrasound guidance using a transvaginal approach. Sac aspiration may be performed before injection to verify appropriate needle placement. There are limited data regarding optimal dosing for local methotrexate injection, with doses of 1 mg/kg of maternal weight and up to 50 mg being described.[18,36,45,46] Varying dosages of systemic methotrexate have been reported in the management of CSP; in general, these dosages are comparable with those used for ectopic pregnancy.[7,47] **We suggest intragestational methotrexate for medical treatment of CSP, with or without other treatment modalities (GRADE 2C). We recommend that systemic methotrexate alone not be used to treat CSP (GRADE 1C).**

When women with CSP who have been treated medically are observed, the gestational mass can take weeks to months to resolve. A transient increase in beta-hCG levels and CSP mass size can be observed after methotrexate therapy. After local conservative CSP treatment that involved 22 women, 1 study reported a mean time to resolution of 88 days (range, 26–177).[18] An understanding of this anticipated posttherapy course may help to minimize unnecessary additional treatments. During the posttreatment observation period, patients should be monitored for concerning symptoms such as hemorrhage or uterine AVM development. Interval ultrasonographic surveillance may be helpful to observe for CSP resolution.

Intragestational KCl has also been described for the treatment of CSP in a small number of cases.[33] This approach may be particularly appropriate for the management of CSP heterotopic pregnancies with a coexisting intrauterine pregnancy, because methotrexate exposure may have embryocidal or teratogenic consequences for the intrauterine cotwin. As with methotrexate, ultrasound-guided KCl injection can be accompanied by sac aspiration. In a case report and review of the literature, 5 cases of CSP heterotopic pregnancies treated with local KCl were described.[48] All resulted in healthy live births of the cotwin, although 2 cases were complicated by postpartum hemorrhage, with 1 case resulting in hysterectomy because of placenta accreta. Hysteroscopic and laparoscopic approaches for treating CSP heterotopic pregnancies have also been described.[49,50]

Adjunct treatment options

UAE is a minimally invasive procedure that has been used in various combinations to treat CSP. UAE has been reported as a stand-alone procedure and in combination with curettage, methotrexate, and hysteroscopy, which complicates comparisons between studies. One review indicated high success and low complication rates when UAE was performed without methotrexate or with and without curettage.[36] When methotrexate was added to a UAE strategy, there was a higher risk (31.4%) that additional treatments would be needed. In a small randomized trial that compared UAE followed by vacuum aspiration (n=37) with systemic methotrexate followed by vacuum aspiration (n=35), UAE was associated with a significant reduction in blood loss.[51] Two women in the methotrexate group required hysterectomy vs none in the UAE group. UAE may be a uterine- and fertility-preserving procedure, although reported outcomes in the setting of CSP vary significantly, and its role as an adjunct to other management approaches requires further study.

As previously mentioned, Timor-Tritsch et al[37,38,52] have also reported ultrasound-guided placement and inflation of balloon and Foley catheters to tamponade a CSP

gestational sac that is complicated by bleeding or as a prophylactic measure. Their experience suggests that this technique may be well tolerated and efficacious, which supports a potential option that warrants further study.

How should CSP be managed in women who decline treatment?

Women who decline treatment of a CSP should be counseled about the risk for significant obstetric complications, which include PAS, massive hemorrhage, uterine rupture, severe maternal morbidity, and potentially maternal death. Management of such cases should include a very high index of suspicion for PAS with appropriate antepartum management and delivery planning. Women should be counseled regarding signs and symptoms of preterm labor or any symptoms that suggest uterine rupture. Repeat cesarean delivery is recommended between 34 0/7 and 35 6/7 weeks of gestation. As with other medically indicated late preterm births, betamethasone administration is recommended before delivery.[53] **In women who choose expectant management and continuation of a CSP, we recommend repeat cesarean delivery between 34 0/7 and 35 6/7 weeks of gestation (GRADE 1C).**

As with PAS, delivery should occur at level III or level IV facilities with appropriate expertise and resources, which includes the capability to manage massive hemorrhage.[54] A multidisciplinary team approach to delivery is recommended, and the team should be prepared for the potential need for cesarean hysterectomy and massive transfusion.

How does a history of a CSP impact future pregnancies?

Women can become pregnant after uterine-preserving management of a CSP, although there appears to be an increased risk for recurrent CSP and other severe maternal morbidities. Ben Nagi et al[55] reported a 5% rate of recurrent CSP among 21 pregnancies achieved after prior conservative CSP management. However, other series have reported high rates of complications. Seow et al[56] reported 7 pregnancies among 14 women with prior CSP who were treated conservatively. The mean interval between CSP and subsequent pregnancy was 13 months (range, 0–34 months). Four pregnancies were intrauterine, with 1 twin pregnancy; all were delivered by uncomplicated cesarean delivery between 35 and 36 weeks of gestation. Two pregnancies were complicated by placenta accreta: 1 was a triplet pregnancy (involving intrauterine twins and a recurrent CSP) that resulted in a cesarean hysterectomy and massive hemorrhage at 32 weeks of gestation, although the other involved accreta noted at the time of cesarean delivery that did not require hysterectomy at 37 weeks of gestation. The final pregnancy involved a woman who became pregnant 3 months after curettage and cervical balloon treatment for a CSP. In the subsequent pregnancy, she experienced spontaneous uterine rupture and died of hypovolemic shock, with a stillborn fetus.

Summary of recommendations

No.	Recommendations	GRADE[a]
1	We recommend against expectant management of cesarean scar pregnancy.	1B: Strong recommendation, moderate-quality evidence
2	We suggest operative resection (with transvaginal or laparoscopic approaches when possible) or ultrasound-guided vacuum aspiration be considered for surgical management of cesarean scar pregnancy and that sharp curettage alone be avoided.	2C: Weak recommendation, low-quality evidence
3	We suggest intragestational methotrexate for medical treatment of cesarean scar pregnancy, with or without other treatment modalities.	2C: Weak recommendation, low-quality evidence
4	We recommend that systemic methotrexate alone not be used to treat cesarean scar pregnancy.	1C: Strong recommendation, low-quality evidence
5	In women who choose expectant treatment and continuation of a cesarean scar pregnancy, we recommend repeat cesarean delivery between 34 0/7 and 35 6/7 weeks of gestation.	1C: Strong recommendation, low-quality evidence
6	We recommend that women with a cesarean scar pregnancy be advised of the risks of another pregnancy and counseled regarding effective contraceptive methods, which would include long-acting reversible contraception and permanent contraception.	1C: Strong recommendation, low-quality evidence

[a] Grading of recommendations, assessment, development, and evaluation.

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In a review of the literature, which included the series mentioned earlier, Sadeghi et al[57] reported 59 subsequent pregnancies (81%) among 73 women with a CSP who retained their uterus. Of these, 15 cases (25%) were complicated by recurrent CSP. The largest single-center experience to describe pregnancy after CSP included 32 pregnancies with a 15.6% recurrent CSP rate.[58] A more recent single-center series included 10 spontaneous pregnancies in 8 women with a history of CSP; 4 (40%) were repeat CSP.[59] Women who consider pregnancy after a CSP should be informed that there is a significant risk of recurrence and severe maternal morbidity. **We recommend that women with a CSP be advised of the risks of another pregnancy and counseled regarding effective contraceptive methods, including long-acting reversible contraception and permanent contraception (GRADE 1C).**

Society for Maternal-Fetal Medicine Grading System: Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)[67,a]

Grade of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A: Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens or vice versa.	Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Strong recommendation that can apply to most patients in most circumstances without reservation: Clinicians should follow a strong recommendation, unless a clear and compelling rationale for an alternative approach is present.
1B: Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens or vice versa.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation that applies to most patients: Clinicians should follow a strong recommendation, unless a clear and compelling rationale for an alternative approach is present.
1C: Strong recommendation, low-quality evidence	Benefits appear to outweigh risks and burdens or vice versa.	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.	Strong recommendation that applies to most patients: Some of the evidence base supporting the recommendation is, however, of low quality.
2A: Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Weak recommendation: Best action may differ depending on circumstances or patient or societal values.
2B: Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation: Alternative approaches are likely to be better for some patients under some circumstances.
2C: Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation: Other alternatives may be equally reasonable.
Best practice	Recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging and inefficient use of time and resources, to bring together and carefully summarize) or (2) recommendation to the contrary would be unethical.		

[a] Adapted from Guyatt GH, et al,[68] 2008.

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Although a short interval between successful conservative CSP management and subsequent pregnancy may increase the risk for recurrent CSP or PAS, there is no consensus about how long to wait before attempting another pregnancy for women who desire another pregnancy after counseling regarding the risks.[14,30] Some experts have recommended waiting 12–24 months before attempting to become pregnant again, although there is limited supporting evidence.[4,60]

Given the increased risk for CSP recurrence, some advocate evaluation of the uterus and cesarean scar by saline infusion sonohysterography before a subsequent pregnancy. However, it is not clear whether the detection of a defect is associated with higher risks and should influence counseling regarding the advisability of another pregnancy. Interpregnancy repair or revision of a cesarean scar has been reported with the use of a variety of surgical modalities. However, there are insufficient data to support a benefit to this practice.[21,61–66]

Should a woman with a history of a CSP become pregnant, close ultrasonographic monitoring is recommended to confirm the presence of an intrauterine pregnancy and to exclude recurrent CSP or PAS. An initial ultrasound examination is recommended on presentation to prenatal care, ideally at less than 8 weeks of gestation, to confirm a normal intrauterine location. Repeat cesarean delivery is recommended between 34 0/7 to 35 6/7 weeks of gestation, before the onset of labor. Betamethasone administration is recommended before anticipated late preterm delivery.[53] The delivery team should be prepared for obstetric hemorrhage and the potential need for cesarean hysterectomy.

Conclusion

Because of high worldwide cesarean delivery rates, an increased incidence of CSP has been recognized. CSP can be difficult to diagnose in a timely fashion; this diagnosis should be considered in women with a prior cesarean delivery who undergo early first-trimester ultrasonography. Several surgical and medical treatments have been described for this disorder; however, at this time, optimal management remains uncertain. For this reason, an international registry has been created for providers to submit data on diagnosis, natural history, and management (https://csp-registry.com). ■

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