Ectopic pregnancies: Diagnosis, Management and impact on female fertility – Review article

WOMEN'S HEALTH

Women's Health
Volume 21: 1–9

DOI: 10.1177/17455057251387428
journals.sagepub.com/home/whe
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Exclusive hysteroscopic approach for the treatment of cesarean scar pregnancy: Systematic review of the literature

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Abstract

Background: The increase in cesarean section rates in developed countries over the past decades have led to several direct postoperative complications or long-term effects for subsequent pregnancies like cesarean scar pregnancy (CSP).
Objective: Many therapies have been proposed for CSP treatment; however, there is no consensus on the best practice to adopt. Exclusive hysteroscopic treatment has been reported rarely but with good results. To understand the role, the safety, and effectiveness of this approach, we performed a systematic review of the literature.
Design: This study is a systematic review. The literature review was performed according to the Preferred Reporting Items for Systematic Reviews.
Data Sources and Methods: We searched in PubMed, Scopus, and Google Scholar databases until December 2024, with a combination of keywords: ectopic pregnancy, scar pregnancy, hysteroscopy, and treatment. Case reports of randomized controlled trials, prospective controlled studies, prospective cohort studies, retrospective studies, case series, and case reports were considered eligible.
Results: We identified 265 manuscripts, but at the end of the screening process, we included a total of 8 manuscripts and 158 patients. We have analyzed for each study the age of the patients, pregnancy history, gestational age, presenting symptoms, Transvaginal ultrasound findings, basal beta human chorionic gonadotropin (beta-hCG), the type of hysteroscope used, complications and their management, and time of beta-hCG negativization.
Conclusion: The hysteroscopic method represents a feasible and safe approach to the CSP treatment with good outcomes and reproducible even with high levels of beta-hCG and a gestational sac over the 3 cm. An initial gestational sac visualization with a diagnostic hysteroscope and the successive use of the resectoscope seems to be the most effective and safe method. Further multicentric studies and randomized clinical trials are needed to improve and standardize the technique.

Plain Language Summary

Cesarean scar pregnancy treated with the use of Hysteroscopy

The increase in cesarean section rates in developed countries over the past decades have led to several direct postoperative complications or long-term effects for subsequent pregnancies like cesarean scar pregnancy Many therapies

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have been proposed for cesarean scar pregnancy treatment; however, there is no consensus on the best practice to adopt. Exclusive hysteroscopic treatment has been reported rarely but with good results. To understand the role, the safety and effectiveness of this approach, we performed a systematic review of the literature. We searched in PubMed, Scopus, and Google Scholar databases until December 2024, with a combination of keywords: ectopic pregnancy, scar pregnancy, hysteroscopy, and treatment. Case reports of randomized controlled trials, prospective controlled studies, prospective cohort studies, retrospective studies, case series, and case reports were considered eligible for our research. We identified a total of eight manuscripts and 158 patients. We have analyzed for each study the age of the patients, pregnancy history, gestational age, presenting symptoms, TVUS findings, basal beta human chorionic gonadotropin, the type of hysteroscope used, complications and their management, and the time of beta-hCG negativization. The hysteroscopic method represents a feasible and safe approach to the cesarean scar pregnancy treatment with good outcomes and reproducible even with high levels of beta-hCG and a gestational sac over 3 cm. Further multicentric studies and randomized clinical trials are needed to improve and standardize the technique.

Keywords
cesarean scar pregnancy, hysteroscopy, treatment, surgical approach, management

Received: 7 March 2025; revised: 10 August 2025; accepted: 19 September 2025

Introduction

Ectopic pregnancy is the implantation of the gestational sac outside the uterine cavity and is the most common cause of mortality during the first trimester of pregnancy. Patients with a history of previous cesarean deliveries may present with scar tissue formation on the muscular wall of the uterine isthmus, eventually resulting in a cesarean scar defect (CSD). Abnormal wound healing may be due to inadequate closure of the uterine incision, postoperative infection, maternal diabetes, reduced blood flow to the affected tissue, and the short interval between cesarean delivery and subsequent pregnancy. It is unclear whether hysterotomy suture technique, prolongation of the second stage of labor, multiple cesarean deliveries, and retroverted uterus influence scar defect formation too.[1]

In the context of the sustained increase in cesarean section (CS) rates in developed countries over the past decades, several direct postoperative complications or long-term effects for subsequent pregnancies have been revealed, such as cesarean scar pregnancy (CSP).[2,3]

Furthermore, CSP is a precursor to placenta accreta spectrum (PAS) disorders due to the risk of trophoblast penetration through the myometrium up to the uterine vessels.[4] The frequency of CSP has a rate of 6.1% in women who had $\geqslant$1 prior CS and ectopic pregnancy, in the range of 0.04%–0.05% (1/1800–1/2216) of all pregnancies and 0.15% in women who had previous CSs.[5,6] According Vial et al., two types of CSP exist[7]: type I or endogenous type, when the CSP implants on the scar of a preceding cesarean delivery and advances inward to the cervicohistomal space or uterine cavity. In this case, a myometrial thickness between the gestational sac/placenta and the uterine serosa or bladder may be measured with abdominal and transvaginal ultrasound.

Type II, when CSP is implanted inside the flaw of an incompletely healed scar, results in deep invasion and progression to the bladder and abdominal cavity.

An alternative classification, proposed by the Chinese Expert Consensus in 2016,[8] classifies CSP into three types: Types I and II involve gestational sac growth into the cervico-isthmic space (as in Vial's Type I), with myometrial thickness $>$3 mm and $\leqslant$3 mm, respectively. Type III is characterized by deep implantation into the scar defect, with outward growth beyond the serosa (as in Vial's type II) and a residual myometrial thickness (RMT) $<$3 mm or absent. However, the most widely used classification remains that of Vial et al., which we adopt in our study.

Unrecognized or mismanaged CSP has the potential to result in serious both fetal and maternal morbidity and mortality (e.g., hemorrhage, dehiscence or rupture of the uterus in the second or third trimester of pregnancy, preterm delivery, and PAS).

Clinical outcomes appear to be better for type I CSP than for type II. The endogenous type of CSP has the potential to result in viable pregnancy, but with an elevated risk of hemorrhage at the placental site.[9,10]

Nearly one-third are asymptomatic at the moment of ultrasound diagnosis. Among patients with symptomatology, the most common manifestation is a vaginal bleeding and usually shows up at the end of the first or beginning of the second trimester.

Transvaginal ultrasound combined with color Doppler evaluation is generally considered the gold standard for the diagnosis of CSP. In patients with previous uterine scarring, early ultrasound findings suggestive of CSP include[11]: (1) empty uterine cavity and closed and empty endocervical canal (differential diagnosis with ongoing abortion or cervical pregnancy); (2) anterior location of gestational sac covering the visible or presumed site of previous cesarean

scar; (3) evidence of functional trophoblastic/placental circulation on Doppler scanning and increased vascularity at the bladder/placental interphase; and (4) presence of trophoblast between the bladder and anterior uterine wall as a sign of deep implantation. Irregularities or interruptions of the bladder line or an anterior swelling of the sac in the bladder may be observed.

After the diagnosis of CSP, counseling should be given to the patient.

Hemodynamically unstable patients require immediate surgery, performing hysterectomy and/or uterine artery embolization (UAE) if possible.[12]

In hemodynamically stable patients, several conservative treatment modalities have been reported, including local or systemic administration of methotrexate (MTX), mifepristone, potassium chloride, uterine dilatation and curettage, hysterotomy via transvaginal or laparoscopic approach of the uterine scar, high-intensity focused ultrasound, and angiographic UAE or a combination of these.[13,14] Exclusive hysteroscopic treatment has been reported rarely but with good results. For this reason, we have performed a systematic review of the literature to understand the role, the safety, and effectiveness of this minimally invasive surgical approach,

Materials and methods

Our research was exempt from the approval by the Institutional Review Board. We reviewed the English literature present in MEDLINE (PubMed), Scopus, Web of Science, Cochrane Library, and Google Scholar regarding the CSP's hysteroscopic management. Two authors, GS and LV, independently performed the research articles' analysis. The systematic review was performed according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for Systematic Review.[15] The document was submitted to International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42025638875), defining methods for literature search, article examination and inclusion criteria, data extraction, and analysis. All previously mentioned databases were systematically searched up to December 2024, except for Web of Science and the Cochrane Library, which were consulted up to August 5, 2025. All the articles were analyzed, evaluating the references contained therein. For the articles' selection, we included articles that focused on hysteroscopic therapy for the management of CSP, without other combinations of therapies (e.g., UAE, vasopressin, and MTX). Only original articles in English were evaluated. Case reports, randomized controlled trials, prospective controlled studies, prospective cohort studies, retrospective studies, and case series were considered eligible. Reviews, Letters to the Editor, and abstracts accepted at conferences were ruled out, but the review was analyzed to find additional cases. Articles not relevant to the topic, Non-English articles and patients treated with combination treatments were also excluded. Two authors (GS and LV) evaluated the study starting from the title and the abstract and then considered the entire work's reading. They found that the entire reference list omitted no sources and excluded duplicates; indeed, they rejected revisions that did not report the original data to avoid duplications. The results were compared, and any disagreement was discussed and resolved by consensus. Studies with ambiguous or insufficient data, low-quality data, or non-quantifiable outcomes were also excluded. We have analyzed for each study the age of the patients, pregnancy history, gestational age, presenting symptoms, TVUS findings, basal beta human chorionic gonadotropin (beta-hCG), the type of hysteroscope used, complications and their management, and time of beta-hCG negativization. The methodological quality of the included studies was assessed using the JBI Critical Appraisal Checklist for case reports (Supplemental Table 1). Where possible, continuous variables were reported as means, while discrete and dichotomous variables were presented as percentages. Due to the low number of patients treated exclusively with hysteroscopy, some data are presented descriptively.

Results

We identified 3842 manuscripts, of these 151 records were identified on PubMed, 25 were identified on Web of Science, 94 on Scopus, 3570 on Google Scholar, and 2 on the Cochrane Library. Records excluded for selection criteria and duplicates were $n=2889$. We included in our review a total of eight manuscripts at the end of the screening process and 158 patients (Table 1). The PRISMA flow diagram of the selection process is provided in Figure 1. In our analysis, the patients' median age was 31.8 years. About 100% had one previous CS (this information is not available for 23.4% of the patients). The mean gestational age was 57.7 days. The presenting symptoms are mentioned in only two case reports and a case series: 3.2% of the patients had abdominal pain, 4.6% had vaginal bleeding and 20% were asymptomatic. The beta-hCG preoperative mean value was 27972.2 mUI/ml. Only the heterotopic pregnancy, obviously, did not report the beta-hCG value. The mean of the largest diameter of the gestational sac was mentioned in four studies and was 30 mm. Only one study reported the embryonic pole length (2.5 mm) and one the presence of cardiac activity. In four studies, the RMT was precisely indicated, and the mean thickness was 3.8 mm. Two studies indicated an RMT cut off: in one study, only patients with an RMT of >2 mm received such treatment; in the other study, it was indicated how many patients had an RMT $>$ or <3 mm. Despite being an extremely important finding, only three studies report the CSP type. One study reports the Chinese's medical society classification, which divides CSP into three types. Type I and II CSPs in

Table 1. Manuscript included in the review.

Author	Patients (*n*)	Age, year (mean)	No. of cesarean (mean)	Clinical symptoms (% presence)	Gestation age, days (mean)	Preoperative beta-hCG mIU/ml (mean)	Largest diameter of the gestational sac, mm (mean)	Cesarean scar pregnancy type[a]	Residual myometrial thickness, mm (mean)	Hysteroscopic approach	Complication rate (%)	Success rate (%)	Time for beta-hCG normalization (days)
Mollo et al.[16]	1	40	1	Asymptomatic	42	10,074	8	NA	NA	Diagnostic hysteroscopy (1.8-mm hysteroscope) + 9 mm (30°–4 mm telescope) bipolar resectoscope	0	100	9
Shao et al.[17]	87	31.4	1.01	NA	56.3	39,989	NA	Type I (100%)	⩾2	NA	Total (3.4) Severe: Estimated blood loss >1000 ml (0.05) Vaginal bleeding 2 weeks after hysteroscopy and emergency laparoscopy (0.025)	93.1	29.8
Li et al.[18]	37	31	NA	NA	66	1227	29	NA	4	Diagnostic hysteroscopy (outer diameter 4.5 mm); treatment hysteroscopy (outer diameter 6.5 mm or resectoscope outer diameter, 8 mm)	Total: NA Excessive bleeding and subtotal hysterectomy (0.03)	64.9	NA
Liu et al.[19]	1 (heterotopic pregnancy)	30	2	NA	51	NA	17	NA	2	Intrauterine 6 mm Bigatti shaver to excise most of the products of conception before following with the bipolar 9 mm resectoscope	0	100	NA
Carlucci et al.[20]	1	38	1	Abdominal pain	35	98,000	NA Embryonic pole 2.5 mm	NA	2.30	9 mm bipolar resectoscope with a 4 mm loop	0	100	NA
Deans and Abbott[21]	4	38	1	NA	44	40,483	NA Cardiac activity 50%	NA	NA	Operative hysteroscope with a 10-mm external diameter. 4-mm loop as working element	25 (one patient required a Foley catheter for clinical hemorrhage and 250 mg ergometrine to control active bleeding at the site of implantation)	100	26
Giampaolino et al.[22]	5	32.6	1.4	NA	49	9756	NA	Type I (100%)	3.36	9 mm bipolar resectoscope with a 4-mm loop	0	100	NA
Lin et al.[23]	22	32.5	1	Abdominal pain (20%) vaginal bleeding (36%) Asymptomatic (57%)	56	24,891	34.5	Type I and II (Chinese Medical Society of Obstetrics and Gynecology Expert Consensus); type I (Vial et al.[7]) (100%)	>3 (36%) ⩽3 (63.6%)	After cervical dilatation hysteroscopic surgery was performed under ultrasonographic monitoring	Blood transfusion (4.5) Procedure failure and need for MTX (4.5)	95.5	NA

MTX: methotrexate; beta-hCG: beta human chorionic gonadotropin.
[a]Vial et al. classification.[7]

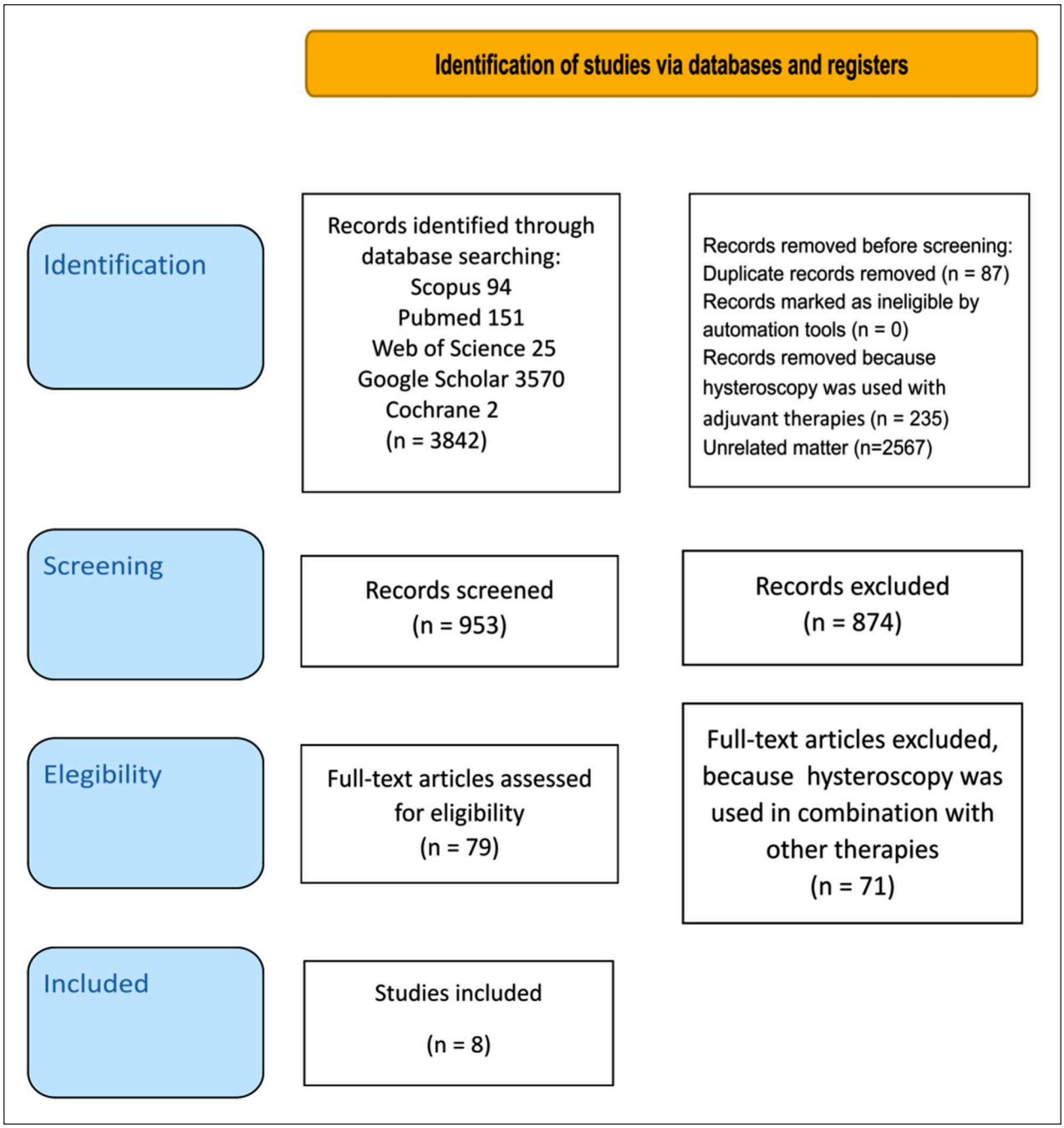

Figure 1. PRISMA flow diagram.
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses.

this classification correspond to type I CSP in the Vial classification that we used in this review. Therefore, we considered that the patients in this study have type I CSP. Thus, all cases for which the CSP type is available (72% of the total) had a type I CSP. The hysteroscope type used was mentioned in six studies and the most frequent approach used was a two-step protocol: a resectoscopic treatment follows a diagnostic hysteroscopy in 55% of the patients. In one study, a intrauterine Bigatti shaver was used to excise most of the products of conception before following with the bipolar resectoscope. One study does not mention the hysteroscope type, but only the need for cervical dilatation. The total complication rate is mentioned in seven studies with a mean of 4.1%. The rate of severe complication is reported: estimated blood loss >1000 ml in 0.03% of the patients, vaginal bleeding 2 weeks after hysteroscopy and emergency laparoscopy (0.02%), and excessive bleeding and subtotal hysterectomy (0.01%). The general

success rate is 87.4%. The median beta-hCG normalization was mentioned in only three studies (58% of the patients included in our review) and was 29.3 days.

Discussion

Optimal scar pregnancy management is unclear. Both diagnosis and counseling are supported by various non sonographic (clinical and anamnestic) and ultrasound markers.[24]

Today, the goal of treating a CSP is to terminate pregnancy, reduce bleeding, and preserve the patient's fertility. Furthermore, considering the increasingly advanced age for the first pregnancy and the need to resort to medically assisted procreation techniques, the resolution time of the ectopic pregnancy is also an important factor. In contrast to other types of ectopic pregnancies, for CSP, there is insufficient evidence to recommend any one specific intervention over another, but the current literature supports a surgical treatment rather than medical approach as the most effective.[25]

Moreover, it is difficult to predict when embryonic remnants will be completely eliminated after conservative treatment; indeed, the main disadvantage of medical therapy is the slow resolution of the pregnancy: medical treatment may terminate the pregnancy, but symptoms may continue with bleeding, sometimes severe.[26] One possible explanation is that poor venous flow within the fibrous scar tissue makes resorption of residual trophoblastic tissue difficult.[27] MTX is the most widely used chemotherapeutic agent well established as a reasonable non-surgical treatment for ectopic pregnancies. Fu et al. in CSP has demonstrated its effectiveness in 65.1% of CSPs; indeed, in our review, hysteroscopic approach alone had a success rate of 87.4%.[5] In Salari et al.'s systematic review and meta-analysis, the normalization time for serum-hCG after MTX administration is 41.6 days, whereas our results report the mean normalization time of 29.3 days after hysteroscopic treatment. Moreover, the surgical approach seems to have a higher rate of pregnancy termination than medical therapy.[28–30] Furthermore, it seems that medical treatment is more effective with lower beta-hCG levels ($<$5000 mIU/ml) compared to hysteroscopic treatment.[13]

Another aspect that is important to keep in mind is that medical therapy with MTX requires a wait of 6 months before conceiving. Therefore, the slower decline of beta-hCG, along with the side effects and the required waiting time before attempting pregnancy after MTX use, should assist clinicians in therapeutic decision-making; this may represent an additional argument against medical treatment, especially in women over 40 years of age.

Unlike dilatation and curettage, operative hysteroscopy is an endoscopic procedure that allows direct visualization of the uterine cavity and offers direct visualization of the pregnancy ensuring a complete removal of chorionic villi, which can sometimes infiltrate deep into the concavity of the CSD.[31]

To remove the gestational mass, the use of an electrical loop under direct vision is planned. Gently brushing the basal decidua from the myometrium with the loop resectoscope is sufficient to separate the chorionic villi and placental tissues from the myometrium. If the villi are highly vascularized, careful electrocoagulation of the blood vessels under direct vision is useful to prevent massive hemorrhage.[20]

However, some precautions should be taken when treating a CSP via hysteroscopy. According to Chen et al., the likelihood of a successful hysteroscopic approach is driven by several factors and appears to be more favorable for patients with type 1 rather than type 2 CSP, especially with a gestational sac diameter $\leqslant$30 mm and a gestational age $<$7 weeks.[24] The RMT should also be considered because if the thickness of the scar is too thin, as in cases of type II CSP, the hysteroscope may lead to uterine perforation and bladder injury.[32]

In our review, the mean gestational age was $<$8 weeks, and the mean gestational sac diameter 30 mm, and in studies in which data on the type of CSP are available, it is always CSP type I. The mean RMT value is 3.8 mm, but some studies reported only a cut off value. In fact, in literature, the cut offs most commonly assumed for considering RMT as thin are $<$2 or $<$3 mm; however, there is no universally accepted threshold for RMT.[32] Since in our review the hysteroscopic approach is used in selected cases, the number of complications appears to be very low.

The 55% of patients underwent diagnostic hysteroscopy first, and then, an operative resectoscopy was performed. Therefore, the gestational sac was first visualized with a minimally invasive approach and then removed with a 10-mm resectoscope with 4-mm lens. With the patient under general anesthesia, a Hegar dilatator (up to no. 10) is required to dilatate the cervix, and this could expose to an increased risk of perforation of the isthmocele and hemorrhage. However, in our review, the total complication rate is 4.1% and the rate of severe complication as estimated blood loss $>$1000 ml is 0.03%, vaginal bleeding 2 weeks after hysteroscopy and emergency laparoscopy is 0.02%, and excessive bleeding and subtotal hysterectomy is 0.01%. There are not enough data in our review to determine whether initial symptomatology impacts the success of the treatment. According to the studies considered, it seems that a beta-hCG value of less than 30,000 mUI/ml can be considered as a cut off for treatment being successful. However, in some cases, the treatment failed even with a lower beta-hCG value. Diakosavvas et al.[33] summarized the available evidence and demonstrated the effectiveness and safety of the hysteroscopic approach alone or in combination with other treatment techniques (High-intensity focused ultrasound and UAE). According to their results, the overall success rate in CSP cases was 91%, ranging

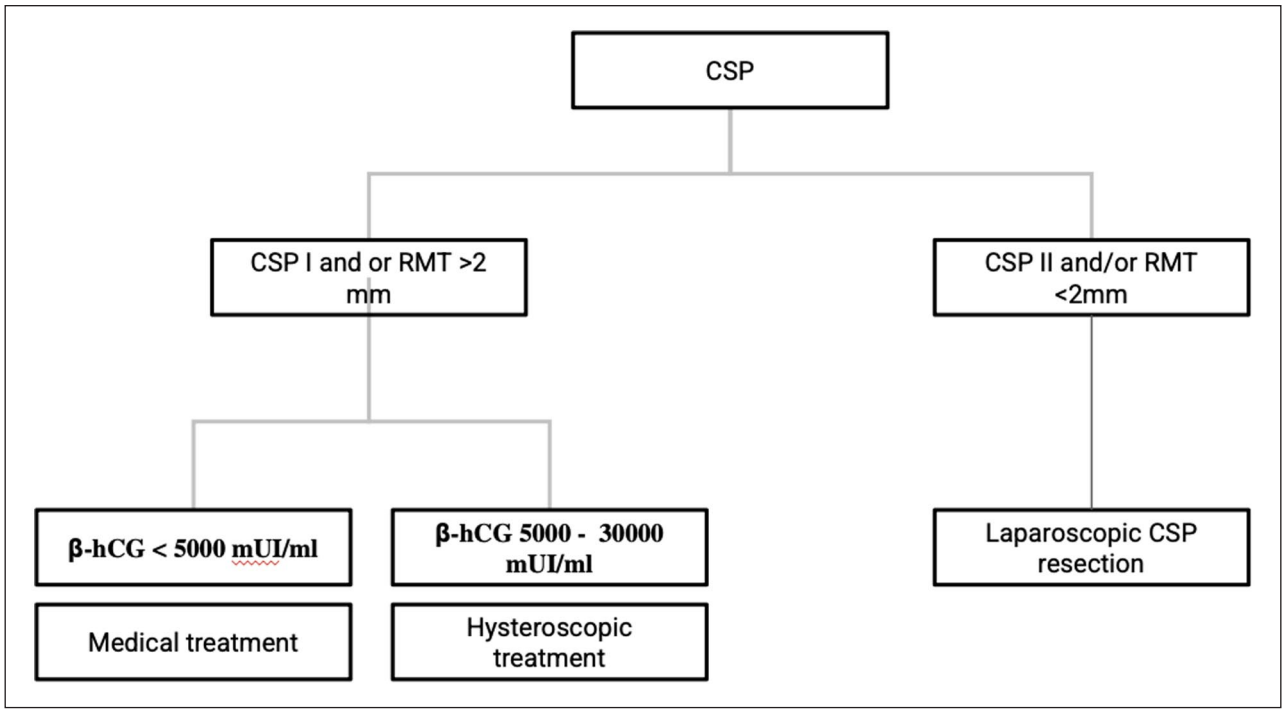

Figure 2. Clinical decision-making flowchart.

from 64.9% to 100%, with low rates of serious complications, such as hemorrhage (1.66%) and hysterectomy (0.28%). His results are similar to ours but it should be noted that although success and complication rates were comparable between the three treatment methods, HIFU and UAE were used preoperatively in more advanced CSP cases with a higher preoperative beta-hCG. However, in this review, some of the patients in the hysteroscopic only treatment group received adjuvant therapy. Other studies and reviews have demonstrated the effectiveness of hysteroscopy when used in combination with medical therapy or other techniques.[34,35]

In our review, studies involving combined approaches were excluded in order to highlight the actual success rate of a purely hysteroscopic approach, particularly when applied to carefully selected patients. Among these patients, the hysteroscopic approach has shown high efficacy and a low rate of adverse effects. It is important to consider that every adjuvant treatment carries its own potential risks; therefore, when feasible, a single-treatment strategy should be preferred. As emerged from our results the two-step technique with the initial use of the 5-mm diagnostic hysteroscope and the successive use of the resectoscope seems to be the most used and the most effective technique. Generally, in the first step, the diagnostic hysteroscope is used only for the visualization of the pregnancy and eventually for the rupture of the gestational sac. However, another similar interesting technique has been described in the literature to treat cervical pregnancies, even for advanced gestational ages, and this could be applied also to scar pregnancy in the future: during the first step, a 5-mm Bettocchi hysteroscope (Karl Storz, Tuttlingen, Germany) with a 5F bipolar electrode was used to identify and open the gestational sac; then, the pregnancy was terminated by cord section under an embryoscopic view. Finally, a partial vessel coagulation was performed. Afterward, the cervix was dilated, and a 10-mm resectoscope with the bipolar electrode was used to completely remove the gestational sac, the embryo, and the chorial villi.[36] To improve mini-invasiveness in the treatment of scar pregnancy and reduce the risk of perforation due to the use of the Hegar dilator, the 5-mm miniresector could be used, but only one case has been described and hysterosuction was delivered as adjuvant therapy.[33,37,38] According to our review, at the end of the procedure, monitoring serum hCG levels weekly until undetectable is reasonable to confirm resolution.

A limitation of the hysteroscopic approach is the inability to correct the CSD, which may lead to recurrence of CSP or even uterine rupture in subsequent pregnancies. This issue is particularly relevant in patients desiring fertility preservation. A laparoscopic approach enables both removal of the ectopic pregnancy and simultaneous myometrial repair, which may improve long-term reproductive outcomes.[39] However, it should be noted that laparoscopy is a more invasive approach and, from our perspective, should be reserved for more complex cases—such as those with severely thinned myometrial thickness or in type II CSP—where conservative or less invasive methods may not be sufficient (see Figure 2).

The strength of our study is the long period of time overviewed in the literature. Furthermore, we have analyzed many aspects of the case reported in literature and that could influence the management, like number of previous CS, the clinical symptoms, the scar pregnancy type, or the RMT.

Limitations

The limitations of our review are related to the lack of some information in the manuscripts retrieved. Especially, in the two manuscripts with more cases, some information is missing (type of CSP, gestational sac diameter, symptoms, and follow-up after therapy), and this limits the results of our systematic review. Another limitation is represented by the inclusion of case reports and case series among the manuscripts reviewed, which inherently carry a lower level of evidence compared to randomized controlled trials or large cohort studies.

Conclusion

CSP is a rare and dangerous condition that can lead to dire consequences such as placenta accreta, hysterectomy, and maternal death. In recent years, a conservative approach employing hysteroscopic treatment has been used with success. As described in our review, this approach seems to be safe, with good outcomes and reproducible even with high levels of beta-hCG and a gestational sac of more than 30 mm in CSP of type 1. The two-step technique with an initial visualization with the 5-mm hysteroscope and the successive use of the resectoscope seems to be the most effective and safe method. The total complication rate is of 4.1% and the general success rate is 87.4%. This technique also seems to give a rapid normalization of beta-hCG, which is 29.3 days. Other aspects such as the effectiveness of hysteroscopy in other types of CSP and the possible initial use of the diagnostic hysteroscope to terminate the pregnancy will need to be analyzed, and it will be necessary to acquire further data with further multicentric studies and randomized clinical trials in the future to improve and standardize the technique and necessary instrumentation.

Acknowledgements

None.

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Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki, and exempt from approval by the Institutional Review Board of Azienda Ospedaliero-Universitaria Riuniti di Foggia.

Consent for publication

Not applicable.

Author contributions

Guglielmo Stabile: Conceptualization; Writing – review & editing; Writing – original draft; Methodology; Project administration.
Laura Vona: Writing – original draft; Writing – review & editing; Software; Data curation; Investigation.
Felice Sorrentino: Investigation; Formal analysis.
Andrea Etrusco: Software; Data curation; Investigation.
Antonio Simone Laganà: Validation; Supervision; Visualization.
Stefania Carlucci: Writing – review & editing; Validation; Formal analysis.
Stefano Restaino: Writing – review & editing; Investigation; Validation.
Giuseppe Vizzielli: Supervision; Validation; Visualization.
Luigi Nappi: Project administration; Validation; Supervision; Resources.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

Supplemental material

Supplemental material for this article is available online.

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