Early first-trimester transvaginal ultrasound screening for cesarean scar pregnancy in patients with previous cesarean delivery: analysis of the evidence

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Obstetric hemorrhage is a leading cause of maternal morbidity and mortality. An important etiology of obstetric hemorrhage is placenta accreta spectrum. In the last 2 decades, there has been increased clinical experience of the devastating effect of undiagnosed, as well as late diagnosed, cases of cesarean scar pregnancy. There is a growing body of evidence suggesting that cesarean scar pregnancy is an early precursor of second- and third-trimester placenta accreta spectrum. As such, cesarean scar pregnancy should be diagnosed in the early first trimester. This early diagnosis could be achieved by introducing regimented sonographic screening in pregnancies of patients with previous cesarean delivery. This opinion article evaluates the scientific and clinical basis of whether cesarean scar pregnancy, with special focus on its early first-trimester discovery, complies with the accepted requirements of a screening test. Each of the 10 classical screening criteria of Wilson and Jungner were systematically applied to evaluate if the criteria were met by cesarean scar pregnancy, to analyze if it is possible and realistic to carry out screening in a population-wide fashion.

Key words: cesarean scar pregnancy, first trimester, placenta accreta spectrum, pregnancy, screening

Introduction

Obstetric hemorrhage is a leading cause of maternal morbidity and mortality,[1] even in high-resource settings such as the USA, where hemorrhage accounts for more than 10% of all maternal deaths.[2] Patients with a previous cesarean delivery (CD) and a low-lying placenta are at increased risk of having a life-threatening condition,[3] namely placenta accreta spectrum (PAS), which is an important etiology of obstetric hemorrhage,[4] as is cesarean scar pregnancy (CSP).[5] Deaths due to morbidly adherent placenta, including PAS, have increased.[6] Furthermore, PAS may lead to long-lasting postpartum maternal morbidity in the form of a recently described list of pathologies under the collective term 'Cesarean scar disorder.'[7]

Over time, 2 conclusions regarding CSP and PAS have become evident. The first is that, terminating a CSP at a later stage is more complex and associated with more complications than when it is recognized and treated earlier.[8] The second, that some expectantly managed CSPs develop dangerous second- and third-trimester PAS requiring more experienced management. Earlier detection and referral to a tertiary center allows for a multidisciplinary approach and the potential for better maternal and neonatal outcomes.[9,10] We believe that all pregnancies with previous CD should undergo transvaginal ultrasound (TVS) screening for CSP early in the first trimester to locate the gestational sac in the uterus.[11] Implementing such screening for CSP would enable timely identification of this high-risk condition during its initial stages.[12–14]

The 3 major principles of screening are: the disease should be recognizable in its latent or early symptomatic stage; there should be a suitable test or examination for it; and there should be an agreeable policy of whom to treat as patients. Whilst all 3 would seem to apply to screening for CSP and justify early implementation at 5 to 7 weeks, it is simplistic to rely on only these 3 requirements and think that they carry the necessary weight when medical practice, protocols, and economic factors have to be satisfied. Aware of the literature regarding the concept of clinical implementation of screening, we sought to apply the 10 'classical' principles of screening outlined in the seminal work of Wilson and Jungner published in 1968, entitled: 'Principles and practice of screening for disease.'[15] These criteria are still highly regarded by public health workers.

Application of the 'Wilson and Jungner' principles for screening to CSP

Wilson and Jungner's principles[15] constitute the fundamentals of what should be known about the specific importance of a health problem, its

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natural progression, the characteristics of the available tests and follow-up treatments, and the cost-effectiveness of screening, before making a decision that such screening is appropriate. When considered in the context of CSP, we proffer the following:

The condition sought should be an important health problem

CSP manifests with different degrees of severity. Its 'benign' form, termed endogenous, type 1 or 'on-the-scar,' may pose a relatively small health problem but one that is sufficiently important to support an indication of system-wide screening.[16] Its second form, the exogenous, type 2 or 'in-the-niche' variety, if left to progress, can lead to clinical manifestations of PAS, with increased risks of prematurity, obstetric hemorrhage, and maternal morbidity and mortality, even under optimal medical management.[13,16,17] Thus, although relatively rare, CSP poses a significant clinical and economic burden on both individuals and the healthcare system, warranting implementation of screening measures.[18–20] Early detection in many cases would prevent the adverse consequences of CSP.[21]

The natural history of the condition, including development from latent-to-declared disease, should be adequately understood

The natural history of CSP is fully understood: CSP can be considered as the latent phase and first-trimester expression of PAS[17,22,23] and, if expectantly managed, can develop into a potentially dangerous form of PAS in the second or third trimester.[13,17,19,24–26] The prevalence and types of markers of CSP/PAS, such as abnormal placental positioning and vascular patterns, differ between the early first trimester (6–9 weeks of gestation) and later first trimester (11–14 weeks of gestation),[27] and diagnosis is significantly more accurate at the earlier stage. The most common sonographic markers for PAS include low, anterior placement of a gestational sac, coupled with a history of 1 or more cesarean deliveries.[28] Given that CSP is a first-trimester manifestation of PAS, these sonographic markers are equally relevant for CSP.

There should be a recognizable latent or early symptomatic stage

CSP itself is recognizable in its 'latent' and early first-trimester stage by testing of human serum chorionic gonadotropin (hCG) and by ultrasound examination. The preferred diagnostic test is TVS, which demonstrates the low, anteriorly positioned gestational sac, below the bladder and adjacent to the internal cervical os. Vaginal bleeding and pain may sometimes be the first sign of a CSP but patients may be asymptomatic and their practitioners may become aware of a CSP only when detected by ultrasound.[29]

There should be a suitable test or examination

Screening tests should be easy to administer and return a rapid result. Both measurement of hCG and TVS fulfill these criteria and, therefore, are suitable tests utilized in the early diagnosis or exclusion of CSP. hCG testing for pregnancy is well established[30] and, even though it is not specific for CSP, as an accessible and inexpensive diagnostic tool, it is likely to remain the staple for exclusion of an intrauterine pregnancy in this scenario. Screening tests should also be effective. Diagnosis of CSP by TVS was advocated in 2006 by Rotas et al[31] who, in a review of 112 cases of CSP, reported a sensitivity of 84.6% for TVS at a mean gestational age of 7.5 weeks. Using location of the center of the gestational sac as a marker of CSP at 5 to 10 weeks of gestation yielded a sensitivity of 93.0%.[32] More recently, Chew et al[33] evaluated retrospectively the respective diagnostic performances at 4.9 to 11.9 weeks of the Royal College of Obstetricians & Gynaecologists (RCOG) guideline,[34] the Timor-Tritsch et al[32] method and a combined method. The sensitivities of the RCOG, Timor-Tritsch and combined methods were 58.3%, 94.4%, and 100%, respectively.

There are several, simple methods to obtain correct diagnostic ultrasound images to satisfy screening for CSP in the first trimester. The criteria that should be met are as follows: (a) partially full bladder facilitates evaluation of the lower uterine segment; (b) a sagittal 2-dimensional image of the whole uterus, showing the uterine fundus and cervix (external and internal cervical ora), should be obtained; (c) on the sagittal image, an imaginary line dividing the uterus in half between the fundus and the external cervical os should be drawn (Figure 1). If the center of the gestational sac is above the line, it is most likely to be an intrauterine pregnancy. If it is below the line, the diagnosis is most likely CSP or, in very rare cases, a cervical pregnancy (in the latter, the lack of a history of CD will be evident).[32] A CSP can also be diagnosed when there is a gestational sac and/or early placenta within the post CD niche, with very thin ($\leq$2 mm) or nonmeasurable myometrial thickness between the urinary bladder and the sac.[32,35] Importantly, ultrasound is most useful up to 6 to 7 weeks, as later in the first trimester the sac with the embryo will slowly populate the uterine cavity and may be misdiagnosed as an intrauterine pregnancy. The earlier in the first trimester that ultrasound is performed, the more reliable is the diagnosis.

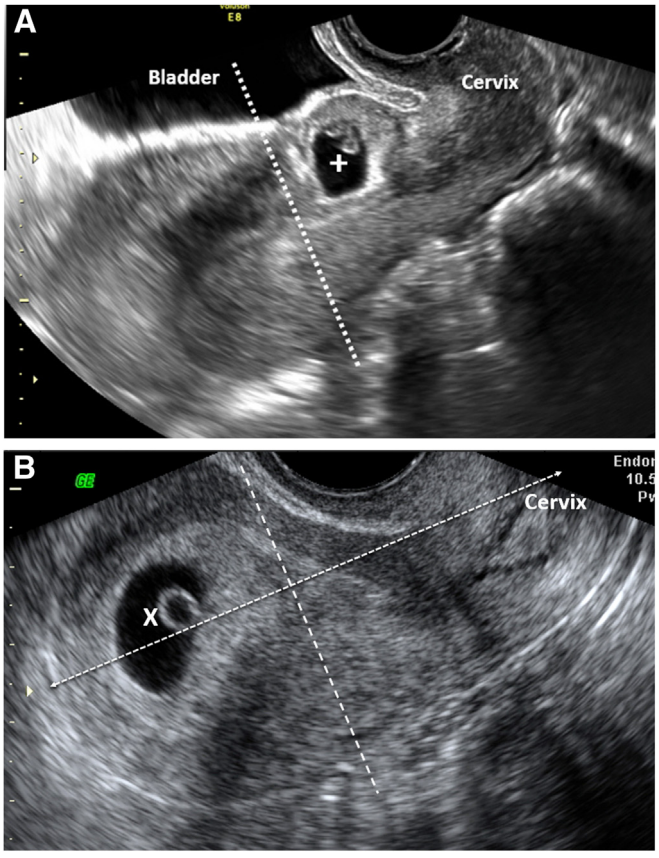
The test should be acceptable to the population

Some screening tests are instrumental to disease prevention but may be so uncomfortable or invasive that people find them difficult to accept or undergo. An example is colonoscopy to detect bowel disease. In the context of genetic testing, acceptability has a strong focus on social, legal, and ethical considerations, as pointed out by King et al.[36] However, these issues largely do not apply to CSP since both tests, serum hCG measurement and ultrasound, are routinely performed in the first trimester of pregnancy and are accepted and used worldwide.

There should be an agreed policy on whom to treat as patients

Pregnant patients diagnosed with CSP are the target population for treatment. Patients should make an informed choice between safe termination and expectant management based on the

FIGURE 1
Easy sonographic differential diagnosis of CSP and intrauterine pregnancy in the first part of the first trimester



Position of the gestational sac is diagnostic. **A,** Cesarean scar pregnancy at 6 weeks and 6 days. The center of the sac (+) is below the line dividing the uterus in halve closer to the cervix. **B,** Intrauterine pregnancy at 5 weeks and 3 days. The center of the sac (x) is above the line dividing the uterus in halve, closer to the uterine fundus.

CSP, cesarean scar pregnancy.

gestational age at diagnosis and the timing of when management can begin. The earlier the termination, the lower the rate of complications.[8] The criterion of whom to treat is extensively discussed by Wilson and Jungner.[15] They opine that, when a physician, during an office visit, screens the patient and identifies the need for treatment, the situation is straightforward. However, with a community-based health issue, care needs to be taken to ensure that the information obtained does not harm the patient. Care should be taken to avoid confusion about the screening process if the physician caring for the patient does not take part in the case-finding protocol. As long as a clear screening policy has been agreed upon, the potential for confrontation between the screening and the treating physicians can be avoided. Thus, there are a variety of methods of handling CSP depending on a number of factors but all are enhanced by earlier diagnosis.

There should be an accepted treatment for patients with recognized disease

Wilson and Jungner considered that the ability to treat the condition adequately is perhaps the most important and that abiding by the Hippocratic oath, that is, avoiding harm to the patient at all costs, should be the primary aim.[15] Furthermore, they say that an answer should be provided to 2 questions: does treatment at the presymptomatic stage of a disease (in our case, a small early first-trimester gestational sac) affect its course including the prognosis; and does treatment of the developed clinical condition (in our setting, PAS) at an earlier stage affect its course and prognosis? The answers to these questions are that terminating CSP or expectantly managing it are the 2 valid considerations to fulfill this requirement. Our view of the above 2 management choices affecting the clinical course of CSP is supported by others.[19,20,37–48]

Facilities for diagnosis and treatment should be available

To fulfill this requirement, the healthcare system should ensure that diagnostic and treatment services, as well as specialized care, are available regionally for patients identified with the condition (in our case CSP) by screening. We reason that the widespread availability of biochemistry laboratories and ultrasound facilities, staffed by competent sonologists, readily meets the first part of this requirement. Adequate treatment facilities, including specialized centers to care for CSP and PAS and reduce complications, seem to be accessible to patients without the need for reorganization of our healthcare delivery system.

The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to the possible expenditure on medical care as a whole

Health, economic and human emotional analyses are essential considerations in CSP screening programs. While economic analysis is beyond the scope of this Opinion, it is likely that there are hypothetical economic benefits, which have not yet been rigorously quantified, and that the implications of early CSP screening vary across different healthcare systems, making generalizations difficult.

In determining whether detection of disease by screening will be economical for a country's resources, there are 2 main considerations, the first is medical, the second economical. There is little question that screening has the potential

to reduce morbidity and mortality. What is unclear is whether the actual monetary cost of such screening would equal that associated with reduction in the presently reported morbidity and mortality. On the face of it, the cost of caring for a complicated case of PAS with prenatal care (mainly in specialized centers), delivery (operating room, personnel, medical equipment, blood bank, etc.) and postnatal care is likely to be considerable. However, despite the increasing cost of diagnostic technologies and treatment, population-based screening for CSP is likely to become cost-effective. Potential savings resulting from early diagnosis, lowering acute healthcare utilization, namely hospital and intensive care unit use as well as avoiding expensive treatments, are expected to affect the cost of screening for CSP. Formal health economic evaluations are required to assess the exact cost-benefit profile of screening for CSPs. There is extensive literature addressing healthcare economics in general. However, very few articles touch upon the cost-benefit of diagnosing and treating pregnant patients[49,50] and even fewer address this aspect in relation to CSP and PAS.[51,52] Nevertheless, we are confident that formal assessment of the cost-benefit aspects of screening for CSP in the early first trimester,[11] which would entail adding a transvaginal first-trimester scan, is likely to result in favor of proving the benefit of screening.

Case-finding should be a continuing process and not a 'once and for all' project

By way of an analogy, screening for diabetes in pregnancy is routinely performed in most healthcare settings. Indirectly, one could infer the findings of structured lifestyle intervention in the perinatal period and over a lifetime, due to reduction in adverse healthcare outcomes, as well as the demonstrated cost savings, when screening for diabetes, and apply most of the concept to CSP.[53] Other indirect inferences can be found in studies involving ultrasound evaluation of pregnancies before invasive prenatal screening for fetal aneuploidy[54] and of preeclampsia,[55] which are now routine in some jurisdictions. Recruiting patients for screening can be achieved by examination of patients in the physician's office as part of normal obstetrical services. In this context, with the help of health education, regular offers of examination are likely to be made. This has the possibility to gradually cover more pregnancies at risk using reexamination of those presenting with a new pregnancy after a previous CD. Early recognition of CSP and early PAS starts with patient education. Distribution of brochures explaining the importance of early diagnosis should be done by the nursing staff at hospital discharge following CD (Figure 2). Patients should be advised that, in a future pregnancy, an early visit to an obstetrician for TVS is important.[37]

The Wilson and Jungner criteria[15] set a foundational framework for screening. The criteria were groundbreaking when developed and have endured with time, emphasizing principles such as the disease being an important health problem and the existence of an acceptable treatment. However, newer guidelines such as those of Prorok[56] and Andermann,[57–59] which built upon Wilson and Jungner's work, refined the criteria based on further research and experience of advancements in technology and understanding of disease progression. They also emphasize considerations such as equity and patient preferences, which are increasingly recognized as important factors in screening decisions.

Other literature supporting screening for CSP

A review of PubMed was performed in November 2023, searching for the terms 'cesarean scar pregnancy' and 'cesarean scar ectopic pregnancy' in addition to 'diagnosis,' 'screening,' and 'review,' to find peer reviewed articles containing direct as well indirect reference to advocate screening for CSP. This resulted in 74 articles containing paragraphs discussing the need for early diagnosis. Of these, 22 explicitly suggested or called for screening for CSP in the first trimester,[8,16,27,35,41,49,60–75] and 52 indirectly implied the need for early diagnosis and supported it with data.[9,31,37,43,44,48,65,76–99,100–119]

Conclusion

In the USA, over 30% of pregnant patients give birth by CD. One of the complications for those who have a subsequent pregnancy is that implantation can occur at the site of the incision of the former CD, either on the scar itself or within a niche (scar defect). The resulting CSP is considered a precursor to placental pathology, that is, PAS, which poses a significant risk for the pregnancy in terms of morbidity and mortality in all 3 trimesters. Early first-trimester diagnosis is crucial for early intervention and timely referral of the patient to a high-risk facility providing multidisciplinary care. As such, a well-planned screening program, which could involve obstetricians, gynecologists, radiologists, sonographers, nurse practitioners as well as maternal fetal specialists, should be implemented. Professional societies should develop guidelines and train healthcare professionals to identify the target population and implement, manage and monitor the screening program. They should also identify and support specialized care centers for patients with CSP and PAS. Furthermore, a cost-benefit analysis of the economic viability of implementing such a screening program should be performed in order to determine the potential savings from preventing complications and optimizing resource allocation within the healthcare system. Overall, a comprehensive approach incorporating these tasks would ensure the success of a CSP screening program, benefiting both patients and the system, whilst meeting legal and ethical obligations by creating standards of patient autonomy and consent.

We have evaluated the validity of a screening program for CSP/PAS by applying the classic criteria developed by Wilson and Jungner in 1968. We identified quotations in the published literature explicitly calling for, as well as indirectly supporting, screening for CSP.

FIGURE 2
A sample of a patient information brochure about cesarean scar pregnancy to be handed to patients at discharge from the hospital or at the first postpartum visit in the office after a cesarean delivery

We have provided arguments that an early screening program for CSP is a realistic goal and can be implemented. Our appeal for first-trimester screening for CSP is supported by scores of caregiver opinions based upon their decades of personal clinical experience, as well as published peer reviewed scientific research. We urge healthcare providers, professional societies and policymakers to recognize the importance of early CSP screening and to take concrete steps toward its success. ■

REFERENCES

1. The American College of Obstetricians and Gynecologists. Safe Motherhood Initiative: Obstetric Hemorrhage. 2015. Available at: http://www.acog.org/community/districts-and-sections/district-ii/programs-and-resources/safe-motherhood-initiative/obstetric-hemorrhage. Accessed July 23, 2024.

2. CDC. Pregnancy mortality surveillance system. Available at: https://www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm#causes. Accessed May 28, 2024.

3. Bachmann C, Abele H, Hoopmann M. Placenta Previa et Percreta: a potentially life-threatening condition. Diagnostics (Basel) 2023;13:539.

4. Jauniaux E, Bunce C, Grønbeck L, Langhoff-Roos J. Prevalence and main outcomes of placenta accreta spectrum: a systematic review and meta-analysis. Am J Obstet Gynecol 2019;221:208–18.

5. De Braud LV, Knez J, Mavrelos D, Thanatsis N, Jauniaux E, Jurkovic D. Risk prediction of major haemorrhage with surgical treatment of live cesarean scar pregnancies. Eur J Obstet Gynecol Reprod Biol 2021;264:224–31.

6. Joseph KS, Lisonkova S, Boutin A, et al. Maternal mortality in the United States: are the high and rising rates due to changes in obstetrical factors, maternal medical conditions, or maternal mortality surveillance? Am J Obstet Gynecol 2024;230:440.e1–13.

7. Klein Meuleman SJM, Murji A, van den Bosch T, et al. Definition and criteria for diagnosing cesarean scar disorder. JAMA Netw Open 2023;6:e235321.

8. Timor-Tritsch I, Buca D, Di Mascio D, et al. Outcome of cesarean scar pregnancy according to gestational age at diagnosis: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2021;258:53–9.

9. Cal M, Nunes C, Clode N, Ayres-de-Campos D. Placenta accreta overlying a caesarean section scar: a 10-year experience in a tertiary-care centre in Portugal. Acta Med Port 2021;34:266–71.

10. Calì G, Timor-Tritsch IE, Palacios-Jaraquemada J, et al. Outcome of cesarean scar pregnancy managed expectantly: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2018;51:169–75.

11. Timor-Tritsch IE, D'Antonio F, Calí G, Palacios-Jaraquemada J, Meyer J, Monteagudo A. Early first-trimester transvaginal ultrasound is indicated in pregnancy after previous cesarean delivery: should it be mandatory? Ultrasound Obstet Gynecol 2019;54:156–63.

12. Panaiotova J, Tokunaka M, Krajewska K, Zosmer N, Nicolaides KH. Screening for morbidly adherent placenta in early pregnancy. Ultrasound Obstet Gynecol 2019;53:101–6.

13. Yang X, Zheng W, Zhang H, Wei X, Yan J, Yang H. Expectant management of cesarean

scar pregnancy in 13 patients. J Matern Fetal Neonatal Med 2022;35:8066–71.
14. Vial Y, Petignat P, Hohlfeld P. Pregnancy in a cesarean scar. Ultrasound Obstet Gynecol 2000;16:592–3.
15. Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: World Health Organization; 1968.
16. 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.
17. Timor-Tritsch IE, Monteagudo A, Cali G, et al. Cesarean scar pregnancy is a precursor of morbidly adherent placenta. Ultrasound Obstet Gynecol 2014;44:346–53.
18. Glenn TL, Bembry J, Findley AD, et al. Cesarean scar ectopic pregnancy: current management strategies. Obstet Gynecol Surv 2018;73:293–302.
19. Vieira de Mello P, Bruns RF, Fontoura Klas C, Raso Hammes L. Expectant management of viable cesarean scar pregnancies: a systematic review. Arch Gynecol Obstet 2023;308:701–7.
20. Spong CY, Yule CS, Fleming ET, Lafferty AK, McIntire DD, Twickler DM. The cesarean scar of pregnancy: ultrasound findings and expectant management outcomes. Am J Perinatol 2024;41:e1445–50.
21. Pekar-Zlotin M, Zur-Naaman H, Maymon R, Tsviban A, Melcer Y. Outcomes of cesarean scar pregnancies in early gestation according to the new Delphi Consensus criteria. J Ultrasound Med 2023;42:2039–44.
22. Timor-Tritsch IE, Monteagudo A, Cali G, et al. Cesarean scar pregnancy and early placenta accreta share common histology. Ultrasound Obstet Gynecol 2014;43:383–95.
23. Calì G, Forlani F, Minneci G, et al. First-trimester prediction of surgical outcome in abnormally invasive placenta using the cross-over sign. Ultrasound Obstet Gynecol 2018;51:184–8.
24. Cali G, Forlani F, Timor-Tritsch IE, Palacios-Jaraquemada J, Minneci G, D'Antonio F. Natural history of cesarean scar pregnancy on prenatal ultrasound: the crossover sign. Ultrasound Obstet Gynecol 2017;50:100–4.
25. Calí G, Timor-Tritsch IE, Forlani F, et al. Value of first-trimester ultrasound in prediction of third-trimester sonographic stage of placenta accreta spectrum disorder and surgical outcome. Ultrasound Obstet Gynecol 2020;55:450–9. Erratum in: Ultrasound Obstet Gynecol. 2020 Jun;55(6):892.
26. He F, Li JQ, Tang XL, Lin Y, Su CH, Chen DJ. [Expectant management of 11 cases of cesarean scar pregnancy]. Zhonghua Fu Chan Ke Za Zhi 2017;52:594–9. Chinese.
27. Calì G, Timor-Tritsch IE, Palacios-Jaraquemada J, et al. Changes in ultrasonography indicators of abnormally invasive placenta during pregnancy. Int J Gynaecol Obstet 2018;140:319–25.
28. Conturie CL, Lyell DJ. Prenatal diagnosis of placenta accreta spectrum. Curr Opin Obstet Gynecol 2022;34:90–9.
29. Timor-Tritsch IE, Monteagudo A, Calì G, D'Antonio F, Kaelin Agten A. Cesarean scar pregnancy: diagnosis and pathogenesis. Obstet Gynecol Clin North Am 2019;46:797–811.
30. Kadar N, DeVore G, Romero R. Discriminatory hCG zone: its use in the sonographic evaluation for ectopic pregnancy. Obstet Gynecol 1981;58:156–61.
31. Rotas MA, Haberman S, Levgur M. Cesarean scar ectopic pregnancies: etiology, diagnosis, and management. Obstet Gynecol 2006;107:1373–81.
32. Timor-Tritsch IE, Monteagudo A, Cali G, El Refaey H, Kaelin Agten A, Arslan AA. Easy sonographic differential diagnosis between intrauterine pregnancy and cesarean delivery scar pregnancy in the early first trimester. Am J Obstet Gynecol 2016;215:225.e1–7.
33. Chew LE, Chua C-PE, Lombardo P, Goodyear M, Teo SY. Accuracy of first trimester sonographic features in diagnosing caesarean scar pregnancy. Sonography 2023;10:155–65.
34. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ. Diagnosis and management of ectopic pregnancy: green-top guideline no. 21. BJOG 2016;123:e15–55.
35. Shainker SA, Coleman B, Timor-Tritsch IE, et al. Special Report of the Society for Maternal-Fetal Medicine Placenta Accreta Spectrum Ultrasound Marker Task Force: consensus on definition of markers and approach to the ultrasound examination in pregnancies at risk for placenta accreta spectrum. Am J Obstet Gynecol 2021;224:B2–14. Erratum in: Am J Obstet Gynecol. 2021 Jul;225(1):91.
36. King JR, Notarangelo LD, Hammarström L. An appraisal of the Wilson & Jungner criteria in the context of genomic-based newborn screening for inborn errors of immunity. J Allergy Clin Immunol 2021;147:428–38.
37. Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol 2012;207:14–29. Erratum in: Am J Obstet Gynecol. 2014 Apr;210(4):371-4.
38. Michaels AY, Washburn EE, Pocius KD, Benson CB, Doubilet PM, Carusi DA. Outcome of cesarean scar pregnancies diagnosed sonographically in the first trimester. J Ultrasound Med 2015;34:595–9.
39. Birch Petersen K, Hoffmann E, Rifbjerg Larsen C, Svarre Nielsen H. Cesarean scar pregnancy: a systematic review of treatment studies. Fertil Steril 2016;105:958–67.
40. Kanat-Pektas M, Bodur S, Dundar O, Bakır VL. Systematic review: what is the best first-line approach for cesarean section ectopic pregnancy? Taiwan J Obstet Gynecol 2016;55:263–9.
41. Maheux-Lacroix S, Li F, Bujold E, Nesbitt-Hawes E, Deans R, Abbott J. Cesarean scar pregnancies: a systematic review of treatment options. J Minim Invasive Gynecol 2017;24:915–25.
42. Timor-Tritsch IE, Monteagudo A, Bennett TA, Foley C, Ramos J, Kaelin Agten A. A new minimally invasive treatment for cesarean scar pregnancy and cervical pregnancy. Am J Obstet Gynecol 2016;215:351.e1–8. Erratum in: Am J Obstet Gynecol. 2020 Jun;222(6):618.
43. Timor-Tritsch IE, Monteagudo A, Calì G, D'Antonio F, Agten AK. Cesarean scar pregnancy: patient counseling and management. Obstet Gynecol Clin North Am 2019;46:813–28.
44. Naeh A, Shrim A, Shalom-Paz E, Amir M, Hallak M, Bruchim I. Cesarean scar pregnancy managed with local and systemic methotrexate: a single center case series. Eur J Obstet Gynecol Reprod Biol 2019;238:138–42.
45. Gulino FA, Ettore C, Ettore G. A review on management of caesarean scar pregnancy. Curr Opin Obstet Gynecol 2021;33:400–4.
46. Huo S, Shen L, Ju Y, Liu K, Liu W. Treatments for cesarean scar pregnancy: 11-year experience at a medical center. J Matern Fetal Neonatal Med 2023;36:2162818.
47. Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, Miller R, Timor-Tritsch IE, Gyamfi-Bannerman C. Society for maternal-fetal medicine (SMFM) consult series #49: cesarean scar pregnancy. Am J Obstet Gynecol 2020;222:B2–14. Erratum in: Am J Gynecol. 2020 Oct 6.
48. Drever N, Bertolone J, Shawki M, Janssens S. Caesarean scar ectopic pregnancy: experience from an Australian Tertiary Centre. Aust N Z J Obstet Gynaecol 2020;60:330–5.
49. Panaitescu AM, Ciobanu AM, Gică N, Peltecu G, Botezatu R. Diagnosis and management of cesarean scar pregnancy and placenta accreta spectrum: case series and review of the literature. J Ultrasound Med 2021;40:1975–86.
50. Fitzpatrick V, Erwin K, Rivelli A, et al. The potential impact of introducing a cost tool to facilitate cost-of-care conversations in routine OB care: lessons from the CONTINUE pilot study. PEC Innov 2023;2:100136.
51. Nehme L, Ye P, Huang JC, Kawakita T. Decision and economic analysis of hostile abortion laws compared with supportive abortion laws. Am J Obstet Gynecol MFM 2023;11:101019.
52. Hong T, Chai Z, Liu M, Zheng L, Qi F. The efficacy and health economics of different treatments for type 1 cesarean scar pregnancy. Front Pharmacol 2022;13:822319.
53. Lloyd M, Morton J, Teede H, et al. Long-term cost-effectiveness of implementing a lifestyle intervention during pregnancy to reduce the incidence of gestational diabetes and type 2 diabetes. Diabetologia 2023;66:1223–34.
54. Battarbee AN, Vora NL, Hardisty EE, Stamilio DM. Cost-effectiveness of ultrasound before non-invasive prenatal screening for fetal aneuploidy. Ultrasound Obstet Gynecol 2023;61:325–32.
55. Mewes JC, Lindenberg M, Vrijhoef HJM. Cost-effectiveness analysis of implementing

screening on preterm pre-eclampsia at first trimester of pregnancy in Germany and Switzerland. PLoS One 2022;17:e0270490.
56. Prorok PC, Chamberlain J, Day NE, Hakama M, Miller AB. UICC Workshop on the evaluation of screening programmes for cancer. Int J Cancer 1984;34:1–4.
57. Andermann A, Blancquaert I, Beauchamp S, Déry V. Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years. Bull World Health Organ 2008;86:317–9.
58. Andermann A, Blancquaert I, Déry V. Genetic screening: a conceptual framework for programmes and policy-making. J Health Serv Res Policy 2010;15:90–7.
59. Andermann A, Blancquaert I, Beauchamp S, Costea I. Guiding policy decisions for genetic screening: developing a systematic and transparent approach. Public Health Genomics 2011;14:9–16.
60. Einerson BD, Gilmer JB. Zuckerman LC placenta acreta spectrum. Obstet Gynecol 2023;142:31–50.
61. Rosen T. Placenta accreta and cesarean scar pregnancy: overlooked costs of the rising cesarean section rate. Clin Perinatol 2008;35:519–29. x.
62. Coutinho CM, Noel L, Giorgione V, Marçal LCA, Bhide A, Thilaganathan B. Placenta accreta spectrum disorders and cesarean scar pregnancy screening: are we asking the right questions? Rev Bras Ginecol Obstet 2021;43:347–50.
63. Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. Am J Obstet Gynecol 2018;218:75–87.
64. Bhatia A, Palacio M, Wright AM, Yeo GSH. Lower uterine segment scar assessment at 11-14 weeks' gestation to screen for placenta accreta spectrum in women with prior cesarean delivery. Ultrasound Obstet Gynecol 2022;59:40–8.
65. López-Girón MC, Nieto-Calvache AJ, Quintero JC, Benavides-Calvache JP, Victoria-Borrero A, López-Tenorio J. Cesarean scar pregnancy, the importance of immediate treatment. J Matern Fetal Neonatal Med 2022;35:1199–202.
66. Duncan CI, Reynolds-Wright JJ, Cameron ST. Utility of a routine ultrasound for detection of ectopic pregnancies among women requesting abortion: a retrospective review. BMJ Sex Reprod Health 2022;48:22–7.
67. Wan X, Liao Y, Hu T, et al. A systematic review and meta-analysis of risk factors in the conservative treatment of cesarean scar pregnancy. Ann Palliat Med 2021;10:10434–43.
68. Noël L, Thilaganathan B. Caesarean scar pregnancy: diagnosis, natural history and treatment. Curr Opin Obstet Gynecol 2022;34:279–86.
69. Buresch AM, Chavez MR, Kinzler W, Vintzileos AM. Use and value of ultrasound in diagnosing cesarean scar pregnancy: a report of three cases. J Reprod Med 2014;59:517–21.
70. Majangara R, Madziyire MG, Verenga C, Manase M. Cesarean section scar ectopic pregnancy - a management conundrum: a case report. J Med Case Rep 2019;13:137.
71. Gonzalez N, Tulandi T. Cesarean scar pregnancy: a systematic review. J Minim Invasive Gynecol 2017;24:731–8.
72. Abinader RR, Macdisi N, El Moudden I, Abuhamad A. First-trimester ultrasound diagnostic features of placenta accreta spectrum in low-implantation pregnancy. Ultrasound Obstet Gynecol 2022;59:457–64.
73. Sliutz G, Sanani R, Spängler-Wierrani B, Wierrani F. First trimester uterine rupture and scar pregnancy. Med Hypotheses 2009;73:326–7.
74. Takashima A, Takeshita N, Kinoshita T. A case of scarred uterine rupture at 11 weeks of gestation having a uterine scar places induced by in vitro fertilization-embryo transfer. Clin Pract 2018;8:1038.
75. Begam MA, Mirghani H, Al Omari W, et al. Caesarean scar pregnancy: time to explore indications of the caesarean sections? J Obstet Gynaecol 2019;39:365–71.
76. Guzmán López JA, Gutiérrez Sánchez LÁ, Pinilla-Monsalve GD, Timor-Tritsch IE. Placenta accreta spectrum disorders in the first trimester: a systematic review. J Obstet Gynaecol 2022;42:1703–10.
77. Collins K, Kothari A. Catastrophic consequences of a caesarean scar pregnancy missed on ultrasound. Australas J Ultrasound Med 2015;18:150–6.
78. Chen YJ, Wang PH, Liu WM, Lai CR, Shu LP, Hung JH. Placenta accreta diagnosed at 9 weeks' gestation. Ultrasound Obstet Gynecol 2002;19:620–2.
79. Gherman RB, McBrayer S, Tichenor J, Wing DA. Placenta increta complicating first-trimester D&C. Obstet Gynecol 1999;93(5 Pt 2):845.
80. Cali G, Forlani F, Foti F, et al. Diagnostic accuracy of first-trimester ultrasound in detecting abnormally invasive placenta in high-risk women with placenta previa. Ultrasound Obstet Gynecol 2018;52:258–64.
81. Purbadi S, Tjahjadi H, Purwoto G, et al. Early gestational age placenta accreta case report: can we avoid missed diagnosis? Am J Case Rep 2021;22:e934168.
82. Ballas J, Pretorius D, Hull AD, Resnik R, Ramos GA. Identifying sonographic markers for placenta accreta in the first trimester. J Ultrasound Med 2012;31:1835–41.
83. Rac MW, Moschos E, Wells CE, McIntire DD, Dashe JS, Twickler DM. Sonographic findings of morbidly adherent placenta in the first trimester. J Ultrasound Med 2016;35:263–9.
84. Zosmer N, Fuller J, Shaikh H, Johns J, Ross JA. Natural history of early first-trimester pregnancies implanted in cesarean scars. Ultrasound Obstet Gynecol 2015;46:367–75.
85. Ash A, Smith A, Maxwell D. Caesarean scar pregnancy. BJOG 2007;114:253–63.
86. Casikar I, Reid S, Condous G. Ectopic pregnancy: ultrasound diagnosis in modern management. Clin Obstet Gynecol 2012;55:402–9.
87. Fylstra DL. Ectopic pregnancy within a cesarean scar: a review. Obstet Gynecol Surv 2002;57:537–43.
88. Osborn DA, Williams TR, Craig BM. Cesarean scar pregnancy: sonographic and magnetic resonance imaging findings, complications, and treatment. J Ultrasound Med 2012;31:1449–56.
89. Patel MA. Scar ectopic pregnancy. J Obstet Gynaecol India 2015;65:372–5.
90. Parker VL, Srinivas M. Non-tubal ectopic pregnancy. Arch Gynecol Obstet 2016;294:19–27.
91. Giampaolino P, De Rosa N, Morra I, et al. Management of cesarean scar pregnancy: a single-institution retrospective review. Biomed Res Int 2018;2018:6486407.
92. Jabeen K, Karuppaswamy J. Non-surgical management of caesarean scar ectopic pregnancy - a five-year experience. J Obstet Gynaecol 2018;38:1121–7.
93. Grechukhina O, Deshmukh U, Fan L, et al. Cesarean scar pregnancy, incidence, and recurrence: five-year experience at a single tertiary care referral center. Obstet Gynecol 2018;132:1285–95.
94. Darwish HS, Habash YH, Habash MY. Ectopic pregnancies in caesarean section scars: 5 years experience. Clin Imaging 2020;66:26–34.
95. Al-Jaroudi D, Aboudi S, Baradwan S. Different treatment modalities for cesarean scar pregnancies: a single-center experience and literature review. Arch Gynecol Obstet 2021;303:1143–51.
96. Timor-Tritsch IE, Horwitz G, D'Antonio F, et al. Recurrent cesarean scar pregnancy: case series and literature review. Ultrasound Obstet Gynecol 2021;58:121–6.
97. Mai ZS, Chen YQ, Liao M, Ma C, Han YB. Early detection of a cesarean scar pregnancy with placenta increta by contrast-enhanced ultrasound in the first trimester: a case report and literature review. J Obstet Gynaecol Res 2022;48:251–5.
98. Iyibozkurt AC, Topuz S, Gungor F, Kalelioglu IH, Cigerli E, Akhan SE. Conservative treatment of an early ectopic pregnancy in a cesarean scar with systemic methotrexate–case report. Clin Exp Obstet Gynecol 2008;35:73–5.
99. Moschos E, Sreenarasimhaiah S, Twickler DM. First-trimester diagnosis of cesarean scar ectopic pregnancy. J Clin Ultrasound 2008;36:504–11.
100. McKenna DA, Poder L, Goldman M, Goldstein RB. Role of sonography in the recognition, assessment, and treatment of cesarean scar ectopic pregnancies. J Ultrasound Med 2008;27:779–83.
101. Jiao LZ, Zhao J, Wan XR, et al. Diagnosis and treatment of cesarean scar pregnancy. Chin Med Sci J 2008;23:10–5.

102. Sadeghi H, Rutherford T, Rackow BW, et al. Cesarean scar ectopic pregnancy: case series and review of the literature. Am J Perinatol 2010;27:111–20.
103. Hong SC, Lau MS, Yam PK. Ectopic pregnancy in previous caesarean section scar. Singapore Med J 2011;52:e115–7.
104. Litwicka K, Greco E. Caesarean scar pregnancy: a review of management options. Curr Opin Obstet Gynecol 2011;23:415–21.
105. Yu XL, Zhang N, Zuo WL. [Cesarean scar pregnancy: an analysis of 100 cases]. Zhonghua Yixue Zazhi 2011;91:3186–9. Chinese.
106. Singh D, Kaur L. When a cesarean section scar is more than an innocent bystander in a subsequent pregnancy: ultrasound to the rescue. J Clin Ultrasound 2017;45:319–27.
107. Li JJ, Liu XY. [Management options of caesarean scar pregnancy]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao 2014;36:209–13. Chinese.
108. Suzuki N, Kyozuka H, Fukuda T, et al. Late-diagnosed cesarean scar pregnancy resulting in unexpected placenta accreta spectrum necessitating hysterectomy. Fukushima J Med Sci 2020;66:156–9.
109. Kim SY, Yoon SR, Kim MJ, Chung JH, Kim MY, Lee SW. Cesarean scar pregnancy; diagnosis and management between 2003 and 2015 in a single center. Taiwan J Obstet Gynecol 2018;57:688–91.
110. Detti L, Gordon JC, Christiansen ME, et al. Diagnosis of placental position by early first-trimester ultrasound: a pilot study. Reprod Sci 2019;26:1512–8.
111. Li K, Dai Q. Differential diagnosis of cesarean scar pregnancies and other pregnancies implanted in the lower uterus by ultrasound parameters. Biomed Res Int 2020;2020:8904507.
112. Shah P, Manandhar R, Thapa M, Saha R. Ruptured cesarean scar pregnancy: a case report. JNMA J Nepal Med Assoc 2019;57:209–12.
113. Riaz RM, Williams TR, Craig BM, Myers DT. Cesarean scar ectopic pregnancy: imaging features, current treatment options, and clinical outcomes. Abdom Imaging 2015;40:2589–99.
114. Jiří H, Hynek H, Petr K, Lubomír H, Anna B, Ladislav K. Cesarean scar pregnancy. Ceska Gynekol 2022;87:193–7. English.
115. Lincenberg KR, Behrman ER, Bembry JS, Kovac CM. Uterine rupture with cesarean scar Heterotopic pregnancy with survival of the intrauterine twin. Case Rep Obstet Gynecol 2016;2016:6832094.
116. Rouzi AA, Almarzouki A, Tallab F, Ashkar L. Medical management of early pregnancy failure with misoprostol with rupture of the cesarean section scar pregnancy. Clin Exp Obstet Gynecol 2017;44:477–9.
117. Luo L, Ruan X, Li C, Chen S, Hu Q, Mueck AO. Early clinical features and risk factors for cesarean scar pregnancy: a retrospective case-control study. Gynecol Endocrinol 2019;35:337–41.
118. Morente LS, León AIG, Reina MPE, Herrero JRA, Mesa EG, López JSJ. Cesarean scar ectopic pregnancy-case series: treatment decision algorithm and success with medical treatment. Medicina (Kaunas) 2021;57:362.
119. Salsac N, Brichant G, Petit P, Chantraine F, Nisolle M. Cas clinique. Rupture utérine en début de grossesse sur cicatrice de césarienne [Uterine rupture in a patient with a cesarean scar pregnancy]. Rev Med Liege 2022;77:202–5. French.