Ultrasound Obstet Gynecol 2023; **62**: 336–344
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.26171.

State-of-the-Art Review

Diagnosis and management of isthmocele (Cesarean scar defect): a SWOT analysis

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ABSTRACT

The purpose of this State-of-the-Art Review was to provide a strategic analysis, in terms of strengths, weaknesses, opportunities and threats (SWOT analysis), of the current evidence regarding the management of uterine isthmocele (Cesarean scar defect). Strengths include the fact that isthmocele can be diagnosed on two-dimensional transvaginal ultrasound, and that surgical repair may restore natural fertility potential and prevent secondary infertility, as well as reduce the risk of miscarriage and other obstetric complications. However, there is a lack of high-quality evidence regarding the best diagnostic method and criteria, as well as the potential benefits of surgical repair with respect to fertility. There is a need for experienced surgeons skilled in the various isthmocele repair techniques. Isthmocele repair does not prevent the need for Cesarean delivery in subsequent pregnancies. There is increasing awareness regarding the accuracy of transvaginal ultrasound in diagnosing isthmocele. This may lead to surgical correction and prevention of obstetric and perinatal complications in subsequent pregnancies, including Cesarean scar pregnancy. Regarding threats, the existence of different surgical techniques means that there is a risk of selecting an inadequate approach if the type of isthmocele and the patient's characteristics are not considered. There is a risk of overtreatment when asymptomatic defects are repaired surgically. Finally, there is an absence of cost-effectiveness analyses to justify routine repair. Thus, while there are many data suggesting that isthmocele has an adverse effect on both natural fertility and the outcome of assisted reproduction techniques, high-quality evidence to support surgical isthmocele repair in all asymptomatic patients desiring future fertility are lacking. There is increasing agreement to recommend hysteroscopic repair of isthmocele as a first-line approach as long as the residual myometrial thickness is at least 2.5–3.0 mm. © *2023 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

In recent decades, the rate of Cesarean section has increased worldwide, leading to the emergence of problems both obstetric (risk of developing placenta previa, placenta accreta, pregnancy implantation at the level of the scar and uterine rupture in subsequent pregnancies) and gynecological (abnormal uterine bleeding, typically postmenstrual, dyspareunia and abdominal/pelvic pain). Most such problems are due to the presence of an isthmocele, also known as a 'niche' or 'Cesarean scar defect', which arises due to a defect in the healing of a Cesarean section scar at the isthmic level[1]. In addition, many studies have linked the presence of the most pronounced isthmoceles with secondary subfertility[2,3].

A meta-analysis published in 2013 estimated that undergoing a Cesarean section could reduce the probability of subsequent pregnancy by an average of 10% compared with vaginal delivery[4]. Similar results have been described in patients treated by assisted reproductive technology (ART): Vissers *et al.*[5] analyzed 1317 patients with previous vaginal or Cesarean delivery undergoing *in-vitro* fertilization (IVF) with intracytoplasmic sperm injection. While the number and quality of transferred embryos were similar, the live-birth rate was lower in the group with a previous Cesarean section, compared with that of the patients who had delivered the previous pregnancy vaginally (15.9% *vs* 23.3%; odds ratio, 0.63 (95% CI, 0.45–0.87)). Specifically, isthmocele has been associated with decreased clinical pregnancy and increased miscarriage rates[6–8].

Three main hypotheses have been proposed to explain the pathogenic implications of isthmocele in fertility disorders[5]: that it affects adversely the environment for sperm transport and embryo implantation; that it acts as a physical barrier to embryo transfer in patients undergoing IVF with embryo transfer; and that it leads to psychological problems in the woman that ultimately reduce the likelihood of pregnancy.

The most common method to diagnose isthmocele is two-dimensional (2D) transvaginal ultrasonography (TVS), with or without injection of contrast agents, mainly saline, although some studies have used three-dimensional

(3D) TVS, hysterosalpingography, hysteroscopy or magnetic resonance imaging. Although there is no diagnostic method universally considered as the gold standard[9], the modified Delphi consensus by Jordans *et al.*[10] in 2019 found that gel or saline sonography is a useful adjunct to conventional ultrasound for diagnosis of this lesion. They defined isthmocele as an anechoic defect within the myometrium of the lower uterine segment at least 2.0 mm in depth[10], although previous studies have used a cut-off of 1 mm in depth[11]. Their consensus has since been complemented with an additional statement on the diagnostic criteria for isthmocele in the first trimester[12].

Traditionally, when indicated, surgical treatment of isthmocele has been performed using a hysteroscopic approach, although, in some circumstances, when the residual myometrial thickness (RMT) is $< 2–3$ mm, a laparoscopic, laparotomic or vaginal route seems to be the best option to avoid potential surgical complications[13]. However, there is conflicting evidence regarding the recommended route of repair[14].

In this Review, we aimed to evaluate, in terms of strengths, weaknesses, opportunities and threats (SWOT analysis), the current evidence regarding management of uterine isthmocele.

METHODOLOGY

A standard SWOT analysis was performed, according to previously published and widely accepted recommendations on critical evaluation of external (opportunities, threats) and internal (strengths, weaknesses) components of a given condition or diagnostic technique[15,16]. Following Delphi-like methodology[17], hierarchical selection of arguments and definitions concerning internal and external factors were achieved by consensus of all authors, who are expert gynecologists, including clinicians, sonologists and surgeons, within the field of reproductive medicine.

STRENGTHS

Isthmocele can be diagnosed by transvaginal sonography

TVS is used to detect and characterize isthmocele in patients with abnormal uterine bleeding, infertility or reproductive failure after ART. In fact, 2D-TVS is the first-line imaging approach in the diagnosis of isthmocele[10] (Figure 1). On sonography, an isthmocele appears typically as a triangular defect in the isthmic portion of the anterior wall of the uterine corpus, with its base oriented towards the uterine cavity. The shape and morphology may vary, with the anterior isthmus appearing as a round, square or wedge-shaped cavity, or even a cribriform area[11].

Several proposals regarding diagnostic criteria have been published, as were two recent Delphi consensuses regarding standard criteria and methodology for ultrasonographic definition and measurements of isthmoceles in both the non-pregnant uterus[10] and early pregnancy[12]. The currently recognized TVS diagnostic criteria are based on high-level consensus (reaching over 70–90%) regarding both ultrasonographic features and measurement technique, achieved in the Delphi analysis of Jordans *et al.*[10].

Since acquisition of the simple sagittal plane and contrast sonohysterography are straightforward to learn, the examiner requires no more than medium-level diagnostic skills to perform this assessment, and mid-range ultrasound equipment will be sufficient, so this diagnostic approach should be readily available. Current research suggests that the diagnostic performance of 3D-TVS is not significantly better than that of 2D-TVS[10]; thus, the use of 3D technology does not seem necessary (Figure 2). Although there is a lack of cost-effectiveness analyses comparing TVS and magnetic resonance imaging (Figure 3) in the diagnosis of isthmocele, it is reasonable to hypothesize that ultrasonographic assessment would be a cheaper and acceptable approach.

TVS can be complemented by contrast-enhanced sonohysterography, based on intrauterine instillation of saline solution or gel (Figure 4). Some studies have concluded that this technique increases the sensitivity and specificity compared with TVS alone in the diagnosis of isthmocele[18,19].

Isthmocele repair restores natural fertility potential and prevents secondary infertility

Isthmocele is associated with postmenstrual vaginal bleeding, which may decrease the frequency of sexual intercourse and increase the use of contraceptives, decreasing the chances of spontaneous pregnancy[20]. Stegwee *et al.*[21] interviewed symptomatic patients and concluded that unpredictable bleeding made women feel insecure and affected their sexual response and behavior.

The surgical hysteroscopic correction of isthmocele in patients affected by secondary infertility and abnormal uterine bleeding was effective in restoring fertility in seven of nine women in the first 6–12 months after surgery[1,22]. A prospective cohort study in 2011[23] reported achievement of spontaneous pregnancy within

Figure 1 Two-dimensional transvaginal ultrasound image of isthmocele.

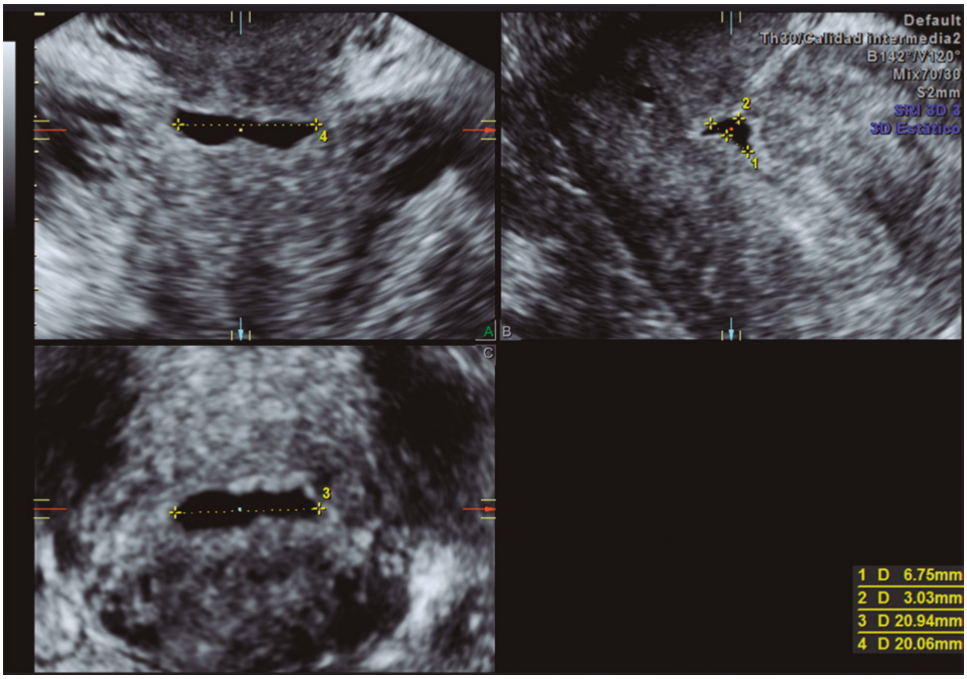

Figure 2 Three-dimensional transvaginal ultrasound image of isthmocele.

12–24 months in all 41 patients with secondary infertility who underwent hysteroscopic isthmoplasty. Four of these women had a miscarriage and the remaining 37 delivered at full-term, delivering by elective Cesarean section.

Isthmocele repair could reduce risk of miscarriage and other obstetric complications

Women who develop isthmocele have an increased risk of complications in the next pregnancy, including miscarriage[24], Cesarean scar pregnancy (CSP) with life-threatening bleeding[25], placenta previa and placenta accreta[26–28] and uterine dehiscence or rupture in the third trimester[28,29]. Risk factors for massive hemorrhage due to CSP include multiple gestation, late diagnosis with large gestational sac, high serum β-human chorionic gonadotropin level and thin RMT[30].

It seems reasonable to assume that the risk of uterine rupture depends on myometrial resistance, which depends mainly on wall thickness. Laparoscopic repair of isthmocele was associated with a significant increase in myometrial thickness measured 3–6 months after surgery (from 1.77 mm preoperatively to 6.67 mm afterwards)[31]. In contrast, hysteroscopic repair does not always lead to a significant increase in postoperative myometrial wall thickness[32].

Several studies have attempted to correlate RMT with the risk of uterine rupture. Rozenberg *et al.*[33] estimated prospectively the risk of uterine rupture/dehiscence in patients with prior Cesarean section according to the myometrial thickness measured by abdominal ultrasound in 642 patients with full bladder at 36–38 weeks of gestation. They reported a 4% rupture/dehiscence rate (15 ruptures, 10 dehiscences); moreover, the frequency increased as the myometrial thickness decreased. There

Figure 3 Isthmocele (arrow) as depicted by magnetic resonance imaging.

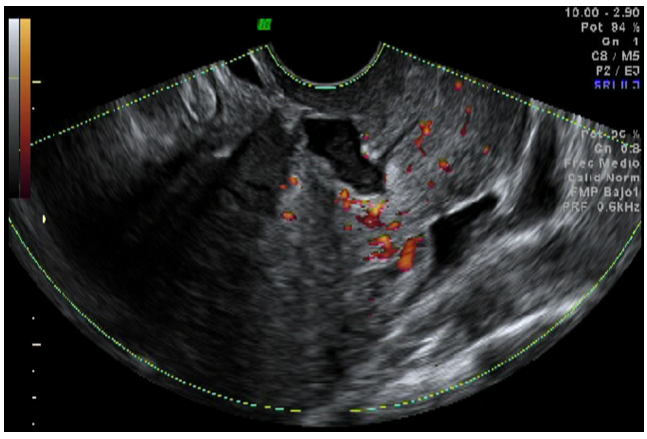

Figure 4 Transvaginal saline-contrast sonohysterography showing isthmocele.

was no case of uterine rupture when myometrial thickness was > 4.5 mm and most ruptures occurred when myometrial thickness was ≤ 2.5 mm. Using a cut-off of 3.5 mm, the ultrasonographic measurement of myometrial thickness provided a sensitivity of 88.0%, a specificity of 73.2%, a positive predictive value of 11.8% and a negative predictive value of 99.3% in estimating the risk of uterine rupture or dehiscence. Uharček *et al.*[34] also found that a myometrial thickness < 2.5 mm is the best parameter to predict the risk of rupture, although another study[35] considered 1.8 mm to be the optimal cut-off point. These results can be very useful in deciding the delivery route in patients with a prior Cesarean section, both with and without a diagnosis of isthmocele. Other factors, such as the presence of intracavitary fluid and the size of the isthmocele, could be variables to consider for deciding trial of labor, although there is no evidence regarding the value of these variables.

From a reproductive point of view, estimation of the risk of uterine rupture might be useful in the pregestational evaluation of non-pregnant women with isthmocele, to offer preventive reparative surgery before attempting to conceive, even in patients whose only symptom is secondary infertility. Pomorski *et al.*[36] estimated that a D/RMT ratio > 1.3, where D is depth of the isthmocele, is associated with a likelihood of dehiscence of > 50% and that D/RMT > 0.7 has a sensitivity of 71% and a specificity of 94% for the prediction of uterine dehiscence/rupture.

There are only a few, low-quality studies evaluating the best surgical approach for correction of isthmocele. Tanos *et al.*[37] carried out a review including four prospective studies, two case series and one retrospective cohort study, with various RMT cut-offs. They concluded that RMT < 3 mm should be considered the criterion for electing a laparoscopic approach for isthmocele repair rather than hysteroscopic resection.

Regarding the recommended interval before conceiving again and the delivery route after repair of an isthmocele, the consensus statement from the Global Congress on Hysteroscopy Scientific Committee recommends that patients wait at least 3 months after the procedure, using contraception during this period, and suggests that a 3-month follow-up diagnostic hysteroscopic study is carried out to visualize surgical outcome[38]. Finally, as a precautionary measure, they recommend delivery by Cesarean section at no later than 38 weeks of gestation because of a hypothetical increased risk of uterine rupture[38]. Despite the lack of consensus in cases of laparoscopic repair, it seems reasonable to apply these same recommendations regarding conception and delivery following isthmocele repair.

Isthmocele repair may be best treatment for secondary infertility

A retrospective study of 310 patients undergoing IVF found a lower clinical pregnancy rate in women with previous Cesarean section compared to those with previous vaginal delivery (40.3% *vs* 54.8%; $P < 0.05$), and the clinical pregnancy rate was even lower in patients with isthmocele (12.5%)[39]. It is thought that the presence of intracavitary fluid causes a hostile environment for embryonic implantation, probably due to the embryotoxic effect of high concentrations of iron secondary to hemoglobin degradation[40].

Vitale *et al.*[41], in their meta-analysis in 2020, evaluated fertility after surgical repair of isthmocele. They included five studies of repair by hysteroscopic resection and seven of repair using a laparoscopic approach and found pregnancy rates after surgery of 88.7% and 45.1%, respectively[41]. Despite the higher pregnancy rates after hysteroscopic isthmoplasty, no conclusions should be drawn regarding the superiority of one technique over the other due to the observational nature and small size of the included studies. However, clearly, isthmocele repair had considerable impact in these patients.

The systematic review and meta-analysis of Harjee *et al.*[42], in 2021, concluded that the surgical correction of isthmocele may be effective for treating infertility, with a very low complication rate. Again, this conclusion is based on only observational studies with a small sample size. Although the paucity of scientific evidence available prevents determination of the surgical indication and optimal approach for isthmocele repair in these patients, surgery should be considered in cases with fluid visible inside the endometrial cavity, after careful consideration of the risk–benefit balance.

Isthmocele repair can improve other symptoms

Although not all patients are symptomatic, abnormal bleeding and pain have a negative impact on physical and psychological quality of life and social relationships[43,44]. Therefore, it is generally agreed that isthmocele management should be decided based on the patient's symptoms and plans for future childbearing[31]. Several studies have demonstrated that surgical resection of isthmoceles reduces postmenstrual spotting, with high satisfaction rates[45,46]. Moreover, Stegwee *et al.*[21] found that postmenstrual spotting and pain had considerable impact on sexual behavior, work activity and even self-esteem, with patients reporting significant improvement in their quality of life after surgical repair.

WEAKNESSES

Heterogeneity of diagnostic criteria

The diagnostic gold standard for isthmocele has not been determined. Studies analyzing the association with adverse pregnancy outcome have applied different diagnostic criteria and technical approaches to define and classify isthmocele, including TVS, saline contrast and gel instillation sonohysterography and magnetic resonance imaging[47]. This clinical heterogeneity should be considered a weakness of the reported results.

In an attempt to homogenize image definition and characterization of isthmocele, the aforementioned Delphi

consensus for the non-pregnant uterus provides recommendations and statements concerning the ultrasonographic appearance and assessment of this lesion, and methodological issues and tips useful to improve the consistency and accuracy of TVS diagnosis[10]. However, some of these recommendations are based on a limited number of studies, which, in most cases, had a retrospective or non-analytical design. Besides, some of these recommendations have been defined as 'good practice points', derived from experts' opinions. In some cases, measurements of isthmocele dimensions are difficult, for example in the case of branched or complex-shaped lesions, in which the distance between the deepest part of the isthmocele and the vesicovaginal fold can be difficult to determine. Another weakness of current knowledge is the absence of a consistent relationship between lesion features and reproductive and obstetric outcomes.

Absence of high-quality evidence of benefit for fertility outcome after surgical correction of isthmocele

There have been only a few studies addressing the efficacy of surgical correction of isthmocele in restoring fertility in women with a Cesarean section scar defect and secondary infertility, and most of them were observational and lacked a control group. Two recent systematic reviews synthesized the existing evidence. The first, published by Vitale *et al.*[41] in 2020, included 33 studies analyzing both relief of symptoms and fertility outcomes after surgery for isthmocele correction. They included one randomized controlled trial (RCT)[46] and one prospective study with a control group[48]. The rest were case series and case reports. Surgical repair results were analyzed depending on the technique employed (laparoscopic, laparotomic, hysteroscopic or vaginal approach). They did not find any improvement in fertility outcomes after surgical correction of the scar defect. The second systematic review, published by Harjee *et al.*[42] in 2021, focused on fertility outcomes after surgical repair in patients with secondary infertility due to the presence of an isthmocele. This review included 13 studies, one RCT and 12 case series. These investigators suggested that surgical treatment might be effective in patients with secondary infertility. The only available RCT addressing the impact of hysteroscopic correction of isthmocele on fertility outcomes[49], including 56 patients with secondary infertility (28 who underwent hysteroscopic surgery and 28 who had expectant management), found significantly higher pregnancy rates after hysteroscopic correction (75.0% *vs* 32.1%, $P = 0.001$).

Two recent studies not included in the aforementioned systematic reviews did not find a negative impact of the presence of isthmocele on pregnancy rates after embryonic transfer in the absence of accumulation of intracavitary fluid[24,50]. Lawrence *et al.*[50], in a prospective, observational study, found that patients with secondary infertility who underwent IVF and had an existing isthmocele after previous Cesarean section had a risk of approximately 40% of developing fluid visible on ultrasound in the endometrial cavity during the course of ovarian stimulation. In those cases, the transfer was cancelled. No significant differences were found in reproductive outcome (pregnancy, biochemical pregnancy, ectopic pregnancy, miscarriage and ongoing pregnancy/delivery rates) after frozen embryo transfer between patients with and those without an isthmocele, when women with intracavitary fluid were excluded prior to the embryo transfer procedure[50]. Asoglu *et al.*[24], in a retrospective study, compared 75 women with isthmocele with 75 controls. Isthmocele was defined in the midsagittal plane as an anechoic indentation, with a depth > 1 mm, on a previous Cesarean scar. The clinical pregnancy rates were 49.3% and 50.7%, respectively. The miscarriage rate was greater in the isthmocele group (8%) than in the control group (4%); however, the difference did not reach statistical significance. They concluded that isthmocele does not seem to have a significant impact on the chance of pregnancy in women undergoing ART. However, the embryo transfer procedure may be more difficult in the presence of an isthmocele[24].

Need for surgeons with skill and experience in different techniques

The first surgical approach in the treatment of isthmocele was reported in 1996 by Fernandez *et al.*[51], who described its hysteroscopic resection. Nowadays, surgical treatment can be performed by two additional approaches: intra-abdominal surgery by laparotomy or laparoscopy, and vaginal surgery. The decision regarding which route is best in each case is based on factors related to the defect, the desire for future fertility and the ability of the surgeon to use one or other approach.

The laparoscopic route is a more complex and technically demanding technique, and there are only a limited number of surgeons who are able to perform this technique. On the other hand, not all gynecological surgeons are trained to perform hysteroscopic resection of isthmoceles. This could result in many surgeons performing one technique rather another depending on their individual skills, rather than selecting the best technique indicated for the particular scar defect.

Isthmocele repair does not prevent need for Cesarean delivery in subsequent pregnancies

Although vaginal delivery has been proposed as an option in patients with mild or moderate isthmocele after Cesarean section, following no observed increase in incidence of uterine rupture or postpartum blood loss[52], the current recommendation for delivery in patients with previous hysteroscopic, laparoscopic or vaginal isthmoplasty is that they undergo a scheduled Cesarean section at no later than 38 weeks of gestation in order to avoid the hypothetical increased risk of uterine rupture[38].

OPPORTUNITIES

Awareness of isthmocele ultrasound diagnosis

The frequency of occurrence of isthmocele is likely increasing because of progressive increase in the number of

Cesarean deliveries. In recent years, studies have addressed the adverse effects of isthmocele on the reproductive prognosis of patients with a previous Cesarean section. The reliability and accessibility of ultrasonographic diagnosis of isthmocele has contributed to a rise in awareness of this entity, reinforcing concerns about its consequences. Thus was performed the recent Delphi consensus on the evaluation of isthmocele in early pregnancy, which complements the previously defined statement on isthmocele in the non-pregnant uterus[10].

Prevention of obstetric and perinatal complications in subsequent pregnancies

Several obstetric, perinatal and delivery complications have been described in women achieving pregnancy after a previous Cesarean section[42,47]. The risk of scar dehiscence and uterine rupture constitutes the most dangerous complication. Additionally, the risks of placenta previa and placenta accreta spectrum disorder are increased, and are associated with isthmoceles[53]. During a normal pregnancy, the trophoblast penetrates the myometrium as far as the Nitabuch fibrinoid layer. Scarred areas in the lower uterine segment after a Cesarean section have thin or absent decidua basalis, which may cause an unopposed invasion of the trophoblast that is thought to create placenta accreta spectrum disorders[54]. It has been proposed that placenta increta and percreta may arise secondary to uterine scar defects, giving the trophoblast greater access to deeper layers of the myometrium[55]. There are no studies documenting the reduction in risk of this complication after surgical repair of the scar defect, but it might be hypothesized that, with an appropriate technique, adequate myometrial healing should be achieved, thus avoiding unbalanced trophoblast penetration right through the uterine wall.

Prevention of Cesarean scar pregnancy (CSP)

The true incidence of CSP is unknown. Most publications estimate this to occur in around 1:1800 to 1:2500 previous Cesarean section scars[56–58]. This constitutes a potentially dangerous consequence of a previous Cesarean delivery and usually presents with abnormal uterine bleeding during the first trimester. It has been proposed that CSP can either progress to the uterine cavity (Type 1, endogenic type) or invade deeply into the scar, especially in the presence of a scar defect progressing towards the bladder and the abdominal cavity (Type 2 or exogenic type), with a high risk of uterine rupture and heavy bleeding during the first trimester[59,60]. The endogenic type could potentially lead to a viable pregnancy but with a high risk of abnormal placentation and bleeding complications[61]. In the first case, there is a measurable layer of myometrium between the gestational sac and the anterior uterine surface, while, in the second, the gestational sac is closer to the uterine surface or the bladder[54]. There also seems to be a difference between these in terms of prognosis if the pregnancy continues. In a retrospective study of 17 patients with a CSP diagnosed between 5 and 9 weeks of gestation, the gestational age at delivery was significantly lower and the rate of placenta accreta spectrum disorder and Cesarean hysterectomy was significantly higher in cases with implantation inside the isthmocele compared with pregnancies implanted on the properly healed scar[62]. There is ongoing debate regarding whether CSP facilitates excessive trophoblastic invasion. In a case series of 10 patients who decided to continue the pregnancy following a diagnosis of first-trimester CSP, all 10 cases developed placenta percreta[63]. However, other studies have failed to confirm this association[64].

To the best of our knowledge, there is no clinical evidence that surgical correction of an isthmocele would prevent or reduce the incidence of CSP, although it might be hypothesized that surgical restoration of the myometrium should help to prevent CSP.

THREATS

Risk of overdiagnosis and overtreatment

Defining a disease or a risk factor is not easy, since clinical data do not always show discrete boundaries. Thus, there is a need for consensus statements and definitions of normality. It is well documented that a change in a threshold value for a medical condition can lead to patient overtreatment[65]. Medical overuse has been defined as the provision of health services for which the potential harm exceeds the potential benefit. The negative consequences to patients that result from overtreatment can be psychological, physical, social or financial, and the treatment burden can cause distress and dissatisfaction with healthcare services[65,66].

Since there is little evidence of an association between an ultrasound diagnosis of isthmocele and infertility in a patient who is asymptomatic, there is a risk that offering surgical intervention under these circumstances may constitute unnecessary intervention i.e. overtreatment.

Three different conservative surgical techniques without clearly defined indications

Lesion features such as shape, RMT and presence of fluid may play a key part in the decision regarding surgical treatment, and can be helpful in the choice between hysteroscopic resection or abdominal or vaginal approach.

Hysteroscopic treatment

Hysteroscopic management should be considered as a ‘resection’ and not as a ‘repair’ (Figure 5). In most studies, hysteroscopic resections were complication-free. Most researchers recognize that reduced RMT may be a limitation for hysteroscopic resection, leading to failure or complications, but there is no consensus regarding the specific isthmocele features or myometrial thickness necessary to enable a hysteroscopic approach to be used.

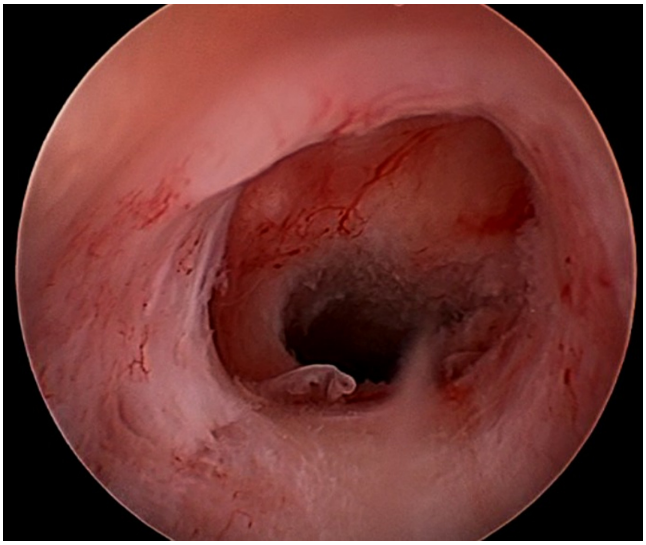

Figure 5 Isthmocele observed by hysteroscopy.

Chang *et al.*[67] considered that RMT should be 2 mm or greater to avoid uterine rupture, whereas Li *et al.*[68] considered a cut-off of > 3.5 mm in patients who desired future fertility and > 2.5 mm for those without a desire for future fertility, due to the risk of bladder injury during the hysteroscopic procedure.

Only three studies have reported on RMT after hysteroscopic resection[68–70]. In all cases, there was a significant increase in RMT after surgical repair, although it was always less than the increase obtained after laparoscopic correction. Pregnancy rates after hysteroscopic resection of the isthmocele ranged from 6.6% to 100%. This high variability among results might be due to the observational nature and small size of these studies.

In patients whose symptoms persisted after hysteroscopic resection, Cohen *et al.*[71] carried out a second procedure, without complications and with improvement of symptoms in six of eight women.

Laparoscopic treatment

Laparoscopy allows complete exploration of the pelvis and direct access to the isthmocele, allowing adhesiolysis to be performed if adhesions are present. After dissection of the bladder, complete resection of all fibrotic tissue can be performed, followed by defect closure with a single or double layer depending on the surgeon's preference. Laparoscopic surgery under hysteroscopic control allows precise localization and verification of the defect followed by its complete resection. The recommended RMT for performance of laparoscopic repair is usually < 3 mm, based on the findings of Bujold *et al.*[72], who estimated that a lower uterine segment with RMT < 2.3 mm is an independent factor associated with an increased risk of uterine rupture.

No complications were reported in most series, except incidental cystotomy in 2% of cases and one case of profuse intraoperative bleeding that required blood transfusion, and the recurrence rate ranged from 0 to 33%[73,74]. Between 64% and 100% of patients remained asymptomatic after surgery. RMT was increased in all cases after surgery, allowing hysteroscopic resection in patients whose symptoms persisted. The take-home baby rate for patients who conceived after isthmocele repair ranged from 21.8% to 75% across studies[48,74–76].

Vaginal approach

When using a vaginal approach, isthmocele excision is performed, followed by a double-layer uterine closure of the defect, and an increase in RMT following the procedure has been reported in several studies[48,77–79]. In two studies, persistence of isthmocele was observed in 13%[48] and 31.37%[77] of cases, respectively. Only one study reported pregnancy rate after vaginal repair (39.2%)[78]. Complications reported when using this technique include hematoma (2.5%), pelvic infection (2.4%) and bladder injury (2%)[79].

Absence of cost-effectiveness analyses

An important limitation regarding the generalization of surgery for isthmocele in infertile asymptomatic patients is the lack of cost-effectiveness studies. It is difficult to assess the cost-effectiveness of a procedure that can be performed with several different surgical techniques. Office hysteroscopy offers several advantages in terms of cost over the other approaches, as it is mainly an outpatient procedure that does not require general anesthesia, leading to faster recovery[80]. Though the other techniques might be advantageous in terms of RMT and obstetric outcomes, it is likely that they do not have the same cost-effectiveness benefits.

Nabothian inclusion cysts as potential cause of misdiagnosis

Although few studies have focused on this issue, Vissers *et al.*[5] warned against the possibility of false-positive diagnosis of isthmocele in the presence of Nabothian inclusion cysts that are located high in the cervix.

CONCLUSIONS

This SWOT analysis is summarized in Figure 6. There is currently no agreement regarding the diagnostic criteria or surgical technique for isthmocele. It seems clear that symptomatic patients should be offered treatment. This can be medical in patients without a desire for future fertility, but is necessarily surgical in patients with secondary infertility.

Although much has been written about the association between the presence of isthmocele and secondary subfertility or impairment of ART, there is no high-quality evidence of such an association. There is insufficient high-quality evidence to support surgical isthmocele repair in asymptomatic patients who desire future fertility.

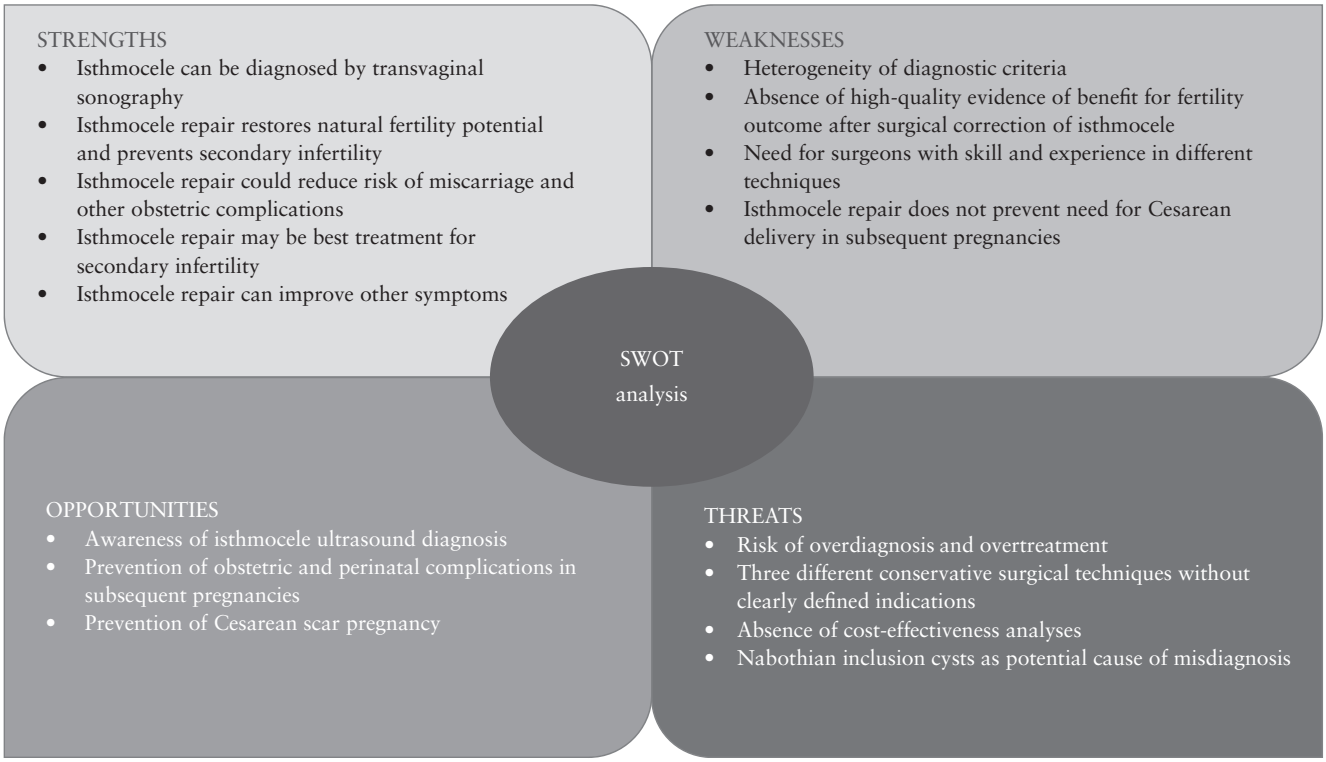

Figure 6 SWOT chart for isthmocele.

Regarding the risk of peripartum uterine rupture in patients with isthmocele or history of isthmocele repair, the current recommendation is to offer elective Cesarean section at 38 weeks of gestation age, to minimize the risk of uterine rupture. The location, depth and shape of isthmoceles and presence of fluid inside the uterine cavity should be taken into account when considering surgical repair of the defect.

There seems to be general agreement that the surgical technique of choice should be hysteroscopy as long as the RMT is at least 2.5–3.0 mm. If it is not, the technique of choice is laparoscopic/robotic, laparotomy or vaginal. Well-designed studies are needed to increase understanding of this common pathology and improve awareness of the potential consequences in patients diagnosed with isthmocele.

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