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The cesarean delivery rate has been raising nonstop for over three decades [1]. In the United States, in the year 2011, one-third of women who gave birth had a cesarean delivery [2]. This trend has been verified not only in the United States but also worldwide. The steady increase number of cesarean deliveries is due to multiple factors including the relative perceived safety of cesarean delivery operation in modern medicine [3]. Other important factors that resulted in a higher cesarean section rate are that there has been a constant decrease rate of operative vaginal deliveries, vaginal delivery of twin with cephalic presentation, vaginal breech deliveries, vaginal birth after cesarean section (VBAC), and medicolegal concerns for possible complications as a result of bad outcomes in patients attempting VBAC [3]. Unfortunately, this rapid

increase of cesarean births has not resulted in decreased neonatal morbidity or mortality, which raises significant attention on the possible overuse of cesarean birth [4]. A concern about the uncontrolled raise of cesarean sections was recognized in the early 1970s [5]. An epidemiologic study revealed that “severe” maternal complications such as hemorrhage that required hysterectomy or massive blood transfusion, uterine rupture, anesthetic complications, shock, venous thromboembolism, cardiac arrest, acute renal failure, assisted ventilation, major infection, and wound disruption were threefold increased for cesarean delivery as compared with vaginal delivery [6]. Also, well-known long-term effects of cesarean deliveries such as infertility, pelvic adhesions, and pelvic pain have been described in many textbooks [1]. Subsequent pregnancies have a documented higher rate of perinatal complications not only maternal but also neonatal complications such as prematurity, low Apgar scores, neonatal intensive care unit (NICU) admissions, and higher perinatal death.

There are maternal and fetal long-term deleterious consequences of a previous cesarean section scar. Maternal consequences could be divided in obstetrical complications (in subsequent pregnancies) and non-obstetrical complications (not related to future pregnancies).

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19.1 Niche in the Scar

The healing process of the cesarean section scar can in occasions be incomplete. In that situation, there is a disruption of the myometrium at the site of the uterine scar. This “gap” in the anterior lower uterine segment receives different names, being the terms “niche” [7] or isthmocele [8] the most commonly used (Fig. 19.1). This defect and its relation with some clinical symptoms such as menorrhagia, abdominal pain, dyspareunia, and dysmenorrhea were first described by Morris [9] using the term “cesarean scar syndrome.”

The estimated incidence of cesarean scar defect (CSD) ranges between 24 and 56 % [10]. This incidence varies considerably depending on the reports. This is due to variation

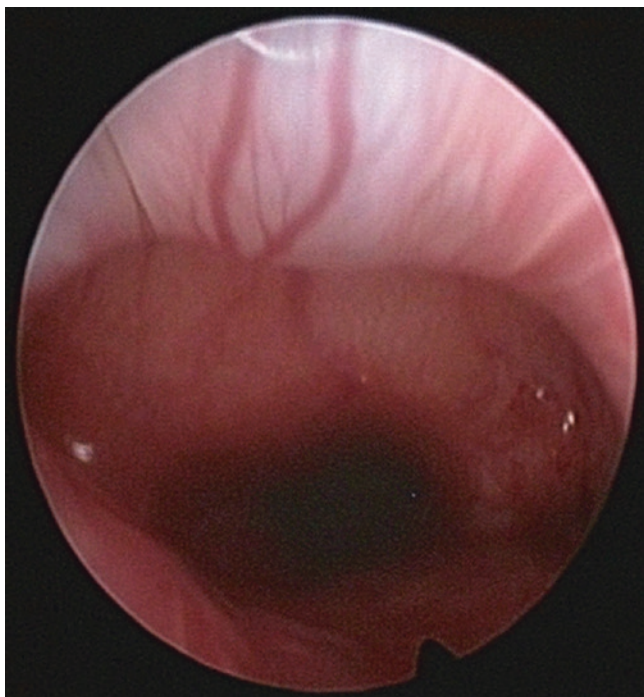


Fig. 19.1 Hysteroscopic appearance of cesarean scar defect

on definitions and the differences in the methods used for the diagnosis of the defect.

There is a clear relationship between the anatomic defect and the presence of different degrees of postmenstrual bleeding and other gynecological symptoms such as dysmenorrhea, chronic pelvic pain, and infertility.

The diagnosis of this condition is based on the clinical symptoms, ultrasound evaluation, and hysteroscopy. There is a high correlation between transvaginal ultrasound and hysteroscopy in the diagnosis of CSD.

Different treatments have been proposed: medical therapy with the use of oral contraceptives to reduce menstrual blood, hysteroscopy surgery to facilitate the drainage of blood and to reduce the local production, and laparoscopic or vaginal surgery to correct the defect.

19.2 Etiopathogenesis

The reason why the defect does not appear in all women undergoing cesarean section is unknown, and the pathogenesis of the scar defect remains unknown. Different factors have been described as a possible cause of a cesarean scar defect (CSD). One possible factor related with the CSD is the difference in myometrial contraction between the thicker superior edge of the incision and the inferior one. This difference in thickness is usually more evident as the number of cesarean increases. The approximation of incision edges with different thickness can contribute to the development of the CSD [11].



Fig. 19.2 View of the cesarean scar defect in a retroverted uterus

Another possible factor suggested is the surgical technique used to close the hysterotomy; it is argued that the presence of a CSD can be in relation with the suture material used, with the suture technique, or both. Furthermore the combination of an ischemic suturing technique and a slow absorbable suture material can produce an abnormal healing [12]. Regarding the technique, Yazicioglu found that the frequency of incomplete healing was significantly lower in the group treated by full-thickness suturing [13]. A recently published meta-analysis found no significant difference in the risk of uterine scar defect with single-layer closure compared to double-layer closure [14].

Oflili-Yebovi found a relationship between multiple previous cesarean section and CSD and also noted that uterine retroflexion was another variable that was clearly associated (Fig. 19.2). In a retroflexed uterus, the lower segment is under a degree of tension, which may affect to the healing of the cesarean section scar [15].

There is an association between the degree of cervical dilatation and the duration of labor with an increase in the risk of CSD if the duration of labor is ≥ 5 h or the cervical dilatation is ≥ 5 cm [16]. In late labor, the modified cervix becomes part of the lower uterine segment. Low incisions are more common if cesarean section is performed late in labor and cervical tissue may be included in the closing sutures, interfering with the healing of the scar.

19.3 Clinical Manifestation

It is well documented that some late complications are present after a previous cesarean section. As well as the obstetrical complications, some gynecological disturbances have been described in patients who have a CSD. Postmenstrual abnormal bleeding, chronic pelvic pain, and secondary infertility are linked to this pathology.



Fig. 19.3 Debris accumulated in the cesarean scar defect and in the cervical canal

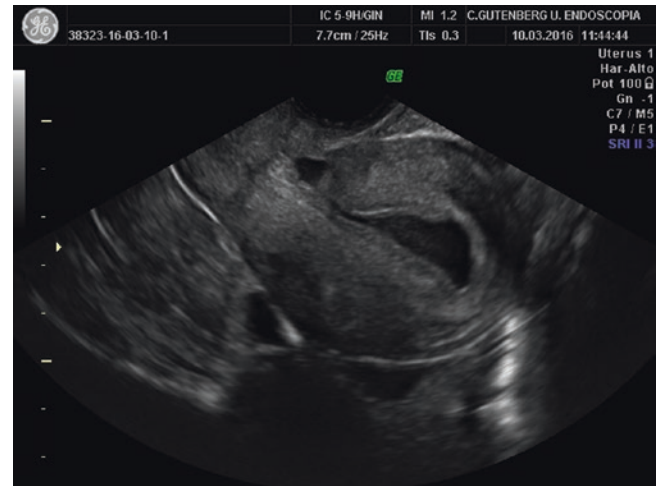


Fig. 19.5 Hematometra due to retrograde passage of blood

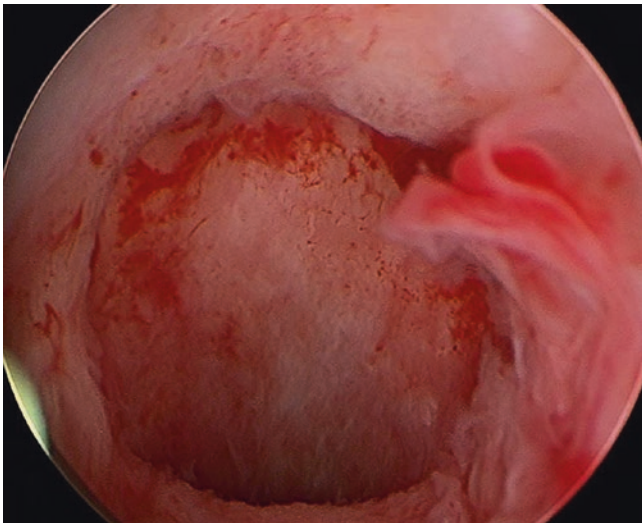


Fig. 19.4 Congested endometrium above the scar

The classic symptom in those patients is the presence of postmenstrual abnormal bleeding, of about 2–12 days of duration, usually scarce and dark in color. Morris [9] was the first to describe a relation between this postmenstrual bleeding and the presence of anatomic and histologic changes at the site of the cesarean scar.

Postmenstrual bleeding (PB) is estimated to occur in one in three (33.6 %) of women with a niche in the scar. There is a direct relation between the size of the defect and the quantity and duration of the bleeding, mainly in retroverted uteri. Probably a triple mechanism is involved in this postmenstrual bleeding. On the one hand, the disruption in the continuity of the endometrium acts as a reservoir pouch, in which some menstrual blood and debris are accumulated (Fig. 19.3); the slow outflow of this retained blood is linked to the PB. Another related mechanism is poor contractility of

the uterine muscle around the scar, due to the existence of fibrotic tissue, which prevents normal myometrial contractions [10]. Last but not least, there is minimal production in situ due to local changes that take place in the niche as congested endometrium above the scar, lymphocytic infiltration, and the presence of small polyps [9] (Fig. 19.4).

The presence of a disruption in the myometrium at the site of the cesarean scar is associated with different clinical symptoms as dysmenorrhea, chronic pelvic pain, and dyspareunia. Among these symptoms, dysmenorrhea is the most common with an incidence of 53 %, followed by chronic pelvic pain in 39.6 % and dyspareunia in 18.3 % [17].

All those symptoms are probably caused by chronic inflammation and the lymphocytic infiltration present in the scar.

Secondary infertility has also been related to CSD. The accumulation of blood in the niche can affect the normal characteristics of the mucus and interfere with sperm transportation through this mucus. There is also minimal retrograde passage of blood, to the uterine cavity, especially in retroverted uteri, that can affect the quality of the endometrium with consequences during embryo implantation (Fig. 19.5).

19.4 Diagnosis

The diagnosis of cesarean scar defect is based on a previous history of cesarean section, clinical symptoms, and diagnostic tools as ultrasound and hysteroscopy.

Currently, there is lack of consensus on the definition of cesarean scar defect. Ultrasound is usually the first diagnostic modality used in women with postmenstrual bleeding. The ultrasound study can be performed with conventional 2D ultrasound, 3D or saline infusion sonohysterogram (SIS),

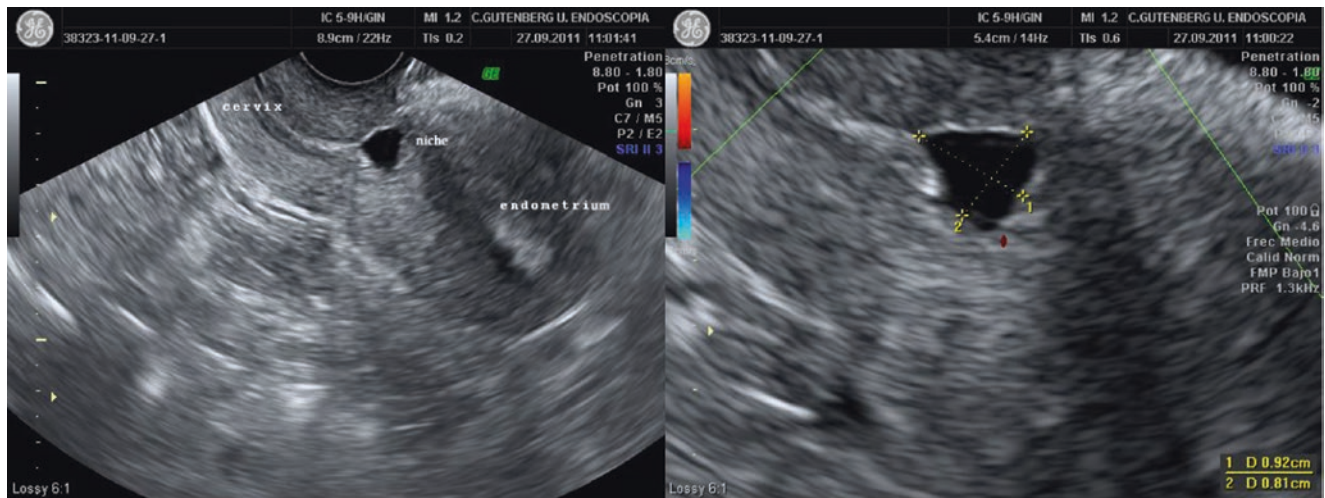
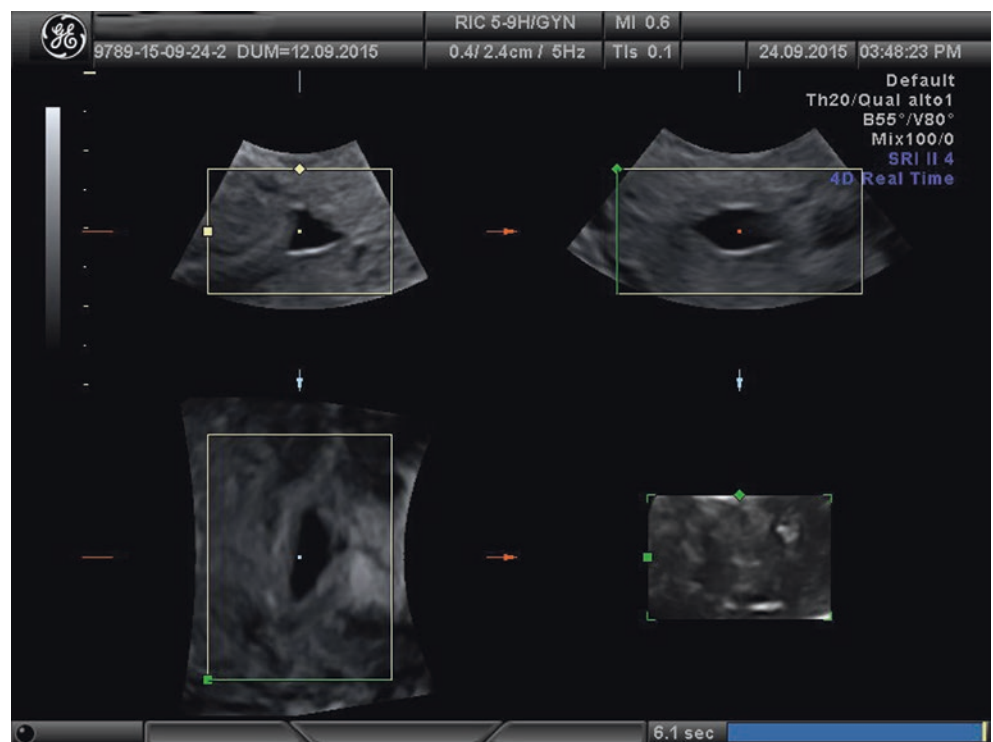


Fig. 19.6 Anechoic area at the site of a previous cesarean section. This niche is usually *triangular-shaped*

Fig. 19.7 3D view of the niche



or gel (GIS) to fill the niche and to create a better image. Hysterosalpingography, hysteroscopy, and RMN can be also used to diagnose this defect.

19.5 Ultrasound

Transvaginal ultrasound is accurate in detecting cesarean scar defects. The niche is defined by the presence of an anechoic area at the site of a previous cesarean section

(Fig. 19.6). This niche is usually triangular in shape with the vertex toward the isthmus. Another proposed diagnostic criterion is the presence of fluid within the incision site [18]. The prevalence of a niche on evaluation with conventional 2D ultrasound is 24 % [16]. The best time to perform ultrasonography diagnosis of CSD is during the late proliferative phase in which the cervical mucus can fill the niche. The use of 3D ultrasound facilitates the study of the defect in multiple planes and offers more information than conventional ultrasonography (Fig. 19.7).

19.6 Hysterosalpingography

Cesarean scar defects can also be diagnosed by hysterosalpingography, usually as an incidental finding. The presence of anatomic defect as a diverticulum or thin linear defects at the lower uterine cavity is a common finding in patients with a previous cesarean section, and these defects can be found at around 60 % of patients [19].

19.7 Sonohysterography

The use of SIS or GIS provides a clear visualization of the CSD due to the filling of the niche with liquid, facilitating the diagnosis. Moreover, more defects are detected using sonohysterography and more defects are classified as large than with the use of conventional 2D ultrasound [20]. The instillation of liquid inside this defect allows us to find different shapes and sizes. The prevalence of a niche on evaluation with gel is around 56 % [16]. The main advantage of the use of gel is that remains longer time filling the disruption; this allows performing a better evaluation of the defect.

19.8 Hysteroscopy

Hysteroscopy allows a direct visualization of the scar defect. During hysteroscopy, a pseudo-cavity is visualized in the anterior wall of the low uterine segment or in the upper third of the cervical canal. Hysteroscopically, a *double arch* of fibrous tissue is identified and a dome between those arches (Fig. 19.8). The dome of the isthmocele is covered by a congestive endometrium with different grades of inflammation. In the early proliferative phase, blood and some clots are usually visualized filling the anatomical defect and the cervical canal.

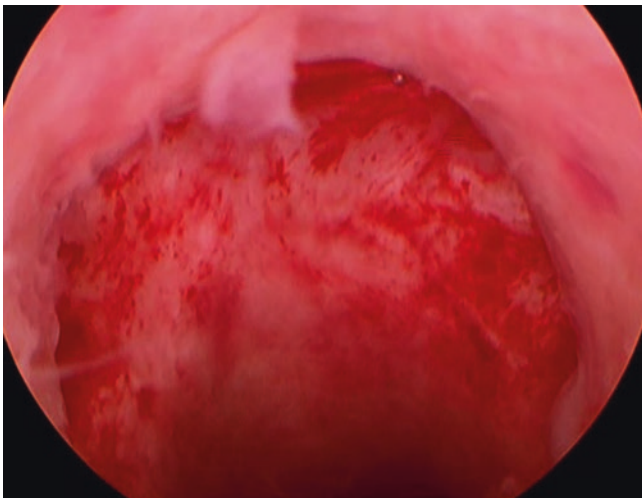


Fig. 19.8 A pseudo-cavity is visualized in the anterior wall of the low uterine segment

19.9 MRI

Magnetic resonance imaging (MRI) can also detect myometrial defect located at the lower uterine segment. The MRI displays a linear low signal niche, sometimes filled with fluid (Fig. 19.9). The use of MRI can be useful to planning the corrective surgery and to rule out other conditions.

19.10 Classification of CSDs

There are two main classifications used for the CSD. The one proposed by Gubbini [21] in which the depth and the base of the isthmocele are measured and the surface of the isthmocele is calculated. According to the result of the surface, the isthmocele is classified into three grades: grade 1 with less than 15 mm³, grade 2 with a surface between 16 and 25 mm³, and grade 3 with more than 26 mm³. In his review, he found that more than 55 % of cases were grade 1.

Yebovi focused the other classification of the CSD on the measurement of the endometrial thinning at the cesarean defect; he defined the degree of thickness by the ratio between the myometrial thickness at the level of the defect and the thickness of the adjacent myometrium and defined a severe defect a ratio >50 % [14] and dehiscence a ratio equal or superior to 80 %.

Other authors have defined CSD as severe when the remaining myometrium at the level of the niche is less than 2.2 mm visualized with ultrasound examination or 2.5 mm in women who underwent hydrosoneography for the diagnosis of the CSD [22] (Fig. 19.10).

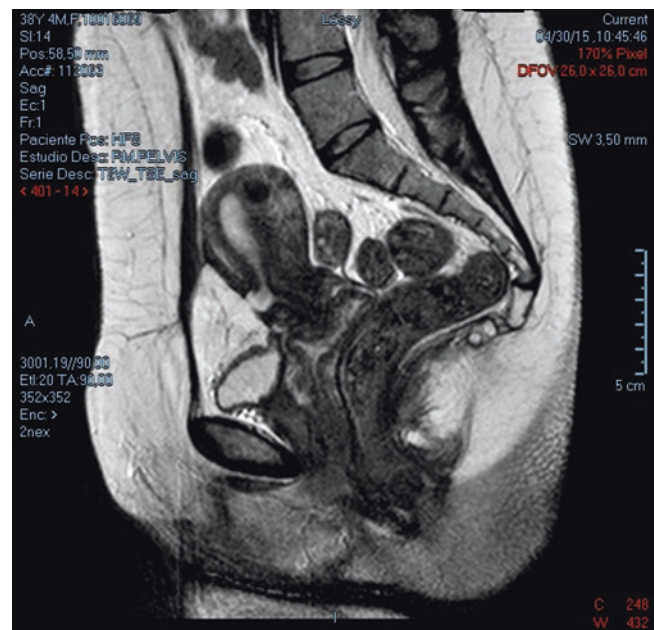


Fig. 19.9 Visualization of the defect with MRI

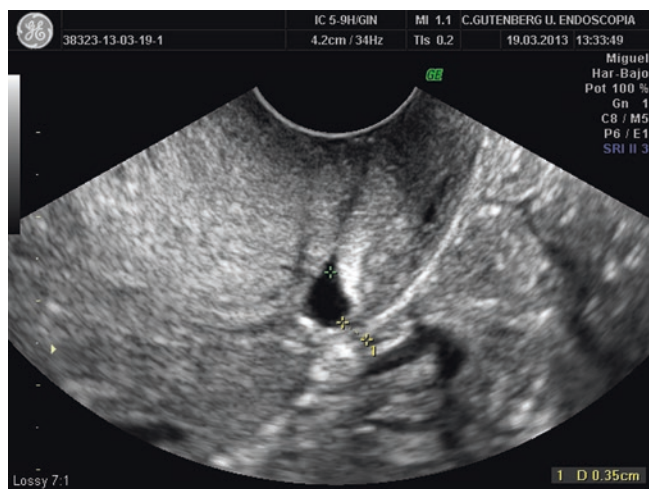


Fig. 19.10 Measurement of the endometrial remaining myometrium

19.11 Treatment

Various surgical options have been proposed to treat the CSD: on one hand, a reparative treatment with laparoscopic repair of the dehiscence and, on the other, the resectoscopy correction in order to improve the symptoms. Other alternatives are the vaginal repair of the CSD and the use of oral contraceptives to reduce menstrual blood. The surgical treatment should only be reserved for symptomatic patients with postmenstrual bleeding, chronic pelvic pain, or secondary infertility. The first two options are the commonly used, and the election of any of them is usually related with anatomical conditions of the CSD.

19.12 Resectoscopic Surgery

The first reference about the use of the resectoscope in the treatment of a CSD was made by Fernandez [23] who performed the resection of the fibrotic tissue of the inferior part of the scar to facilitate the drainage of the menstrual blood collected in the scar, improving the postmenstrual bleeding. Since then, multiple articles have been published, and the resectoscopy has become the most reported approach for the treatment of symptomatic CSD. Fabres in addition to the resection of the fibrotic tissue underneath the pouch defect used the local fulguration of the dilated blood vessels and endometrial glands in the CSD, responsible of the in situ production [24] (Fig. 19.11). The main risk associated with the resectoscopy surgery is the possibility of uterine perforation and secondary bladder injury; in order to prevent this complication, some authors recommend to avoid the resecto-

sopic surgery if the remaining myometrium at the level of the niche is less than 2 mm [25].

19.13 Laparoscopic Surgery

The purpose of the laparoscopic management is to restore the myometrial continuity at the site of the CSD which leads to a reduction of the niche and consequently to an improvement of the related symptoms. The main advantage of the laparoscopic approach is that we can consider this as a reparative surgery which leads to an increase in the thickness of the uterine wall, something that can't be done with the hysteroscopic approach [26]. Klemm firstly used a combined laparoscopic-vaginal approach to repair the defect [27]. Donnez described a totally laparoscopic approach with excision of the fibrotic tissue around the scar and laparoscopic suture to approximate the healthy myometrium of each side of the opened scar [28]. The laparoscopy surgery offers a clear visualization of the surgical area after the dissection of the bladder with low risk of damage (Fig. 19.12).

19.14 Vaginal Surgery

The vaginal approach of the cesarean section defect is also considered a reparative surgery, which corrects the defect and increases the thickness of the uterine wall. As we referred before, this was firstly used in combination with laparoscopy approach. A new vaginal repair technique has been recently proposed in which after the opening of the cervico-vesical space and the dissection of the bladder, the scar is opened and the fibrotic tissue removed. The opened scar is secondary closed with two layers of suture [29]. The approach that uses the vaginal route is a minimally invasive way of repairing the myometrial continuity.

19.15 Medical Treatment

The use of oral contraceptives can be a conservative alternative for the management of the postmenstrual bleeding. The published results on effectiveness are conflicting. While different studies have concluded that the medical therapy fails to eliminate the bleeding [10], others support the use of oral contraceptives for treating intermenstrual bleeding in patients with defects at the previous cesarean uterine to reduce the menstrual blood [30]. There are no consistent studies about the use of the hormonal intrauterine device.

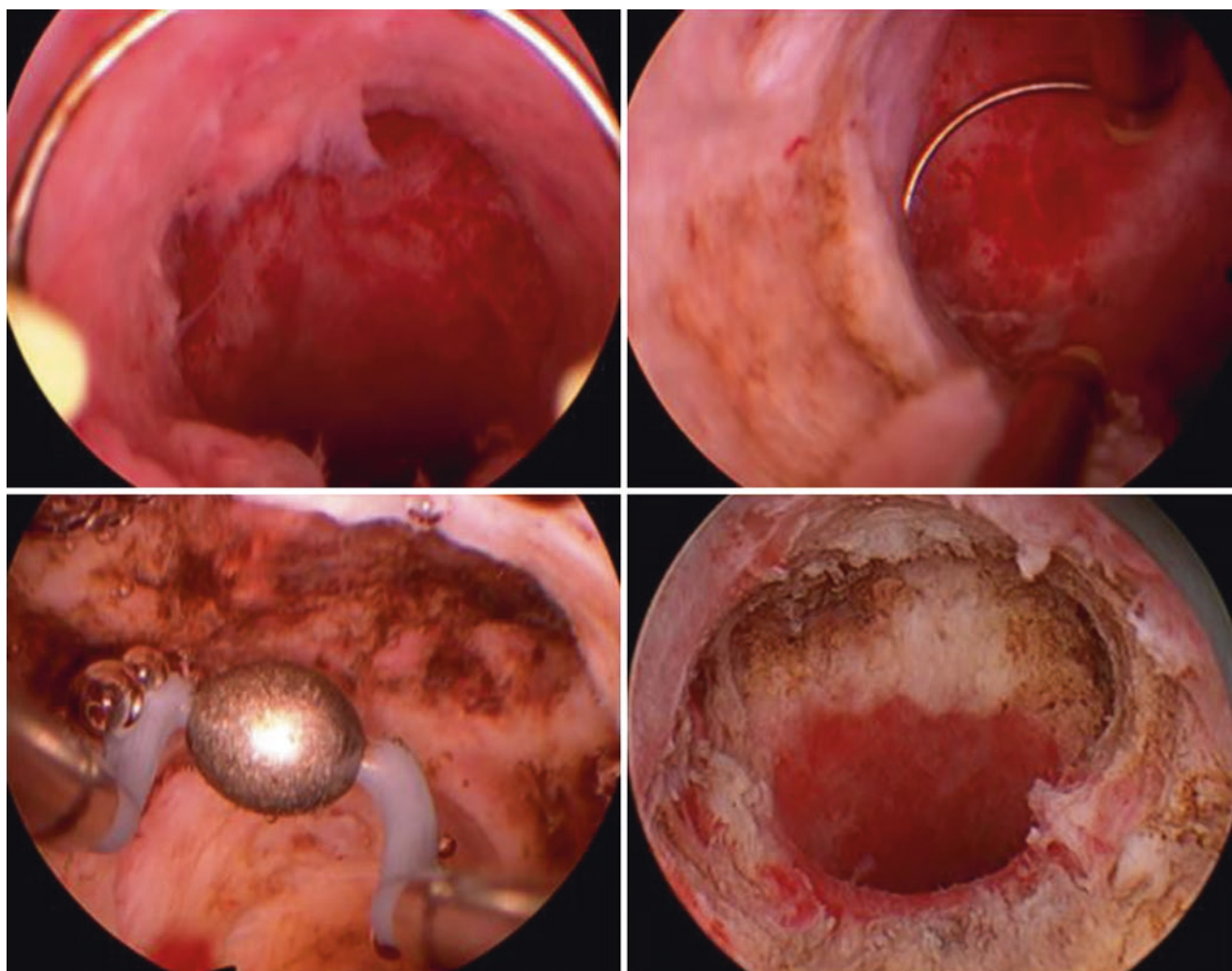


Fig. 19.11 Hysteroscopy surgery: (1) view of the cesarean scar defect; (2) resection of the fibrotic tissue of the inferior part of the scar; (3) local fulguration of the dilated blood vessels and endometrial glands; (4) final view

19.16 Surgical Outcomes

The surgical outcomes are different depending on the surgical procedure. After hysteroscopy surgery, between 59.6 [8] and 64 % [25] of patients reported a postoperative improvement of postmenstrual bleeding. This improvement was more evident in patients with anteflexed uterus.

19.16.1 Cesarean Scar Pregnancy

A cesarean scar (ectopic) pregnancy occurs when a pregnancy implants on a cesarean delivery scar (Fig. 19.13). Although it has also been referred to as a cesarean delivery scar ectopic pregnancy in the literature, a more appropriate

term may be cesarean delivery scar pregnancy or cesarean scar pregnancy.

The first case of a cesarean scar ectopic pregnancy was reported in English medical literature in 1978 [31]. Since then, there are only 19 cases published until 2001 [32]. But over the past 5 years, there has been a substantial increase in the number of cesarean scar pregnancy (CSP) published in the English language literature.

Cesarean scar pregnancy is a rare entity, incidence being reported between 1:800 and 1:2,216 and a rate of only 6.1 % in women with ectopic pregnancy and at least one previous cesarean section [33, 34–38]. It is the least common form of ectopic pregnancy.

However, the incidence is rising with the increased incidence of cesarean deliveries (Table 19.1), and the diagnosis

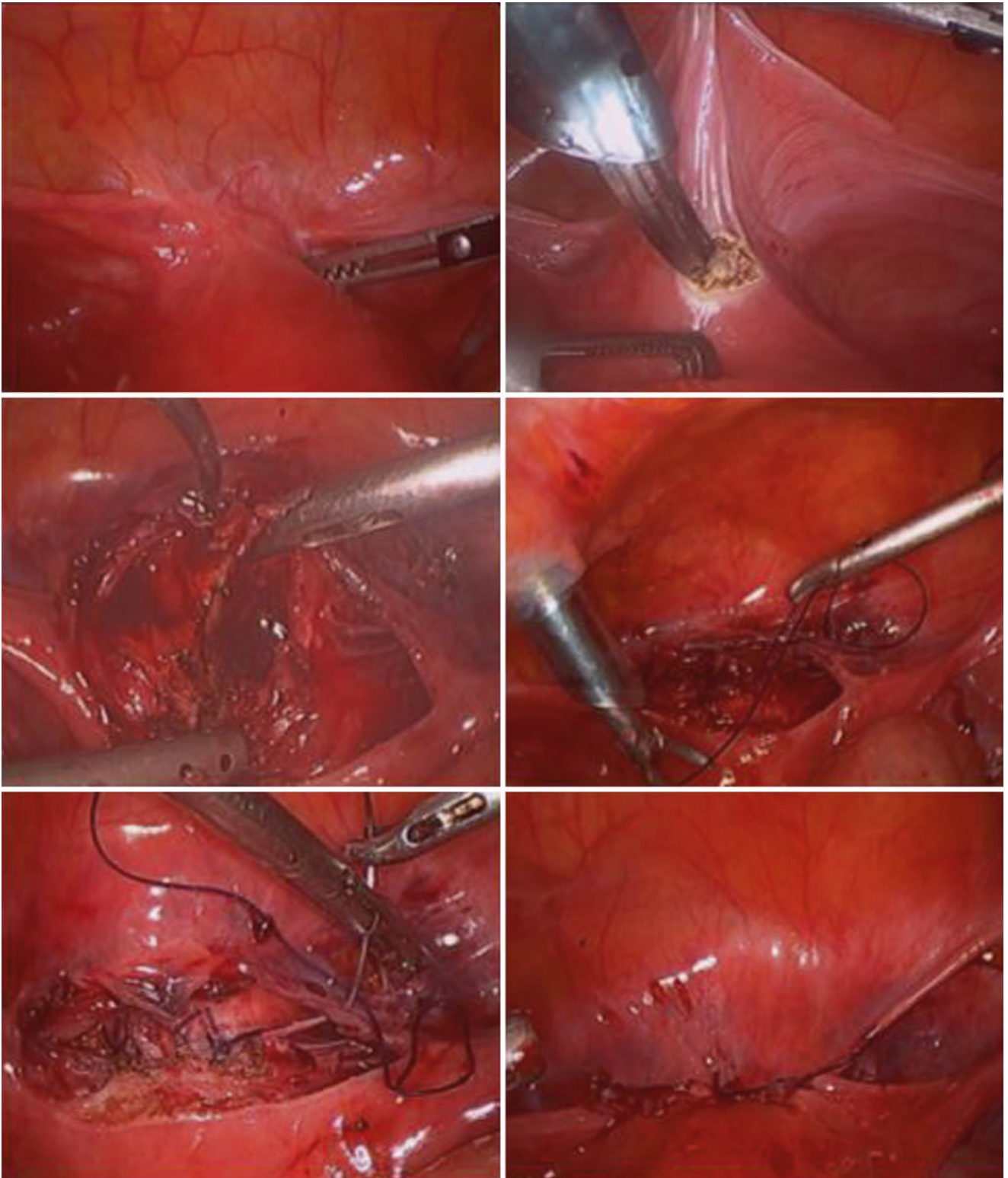


Fig. 19.12 Laparoscopic repair of cesarean scar defect: (1) identification of the affected area; (2) bladder dissection; (3) opening of the scar; (4) first-layer suture; (5) second-layer suture; (6) final view

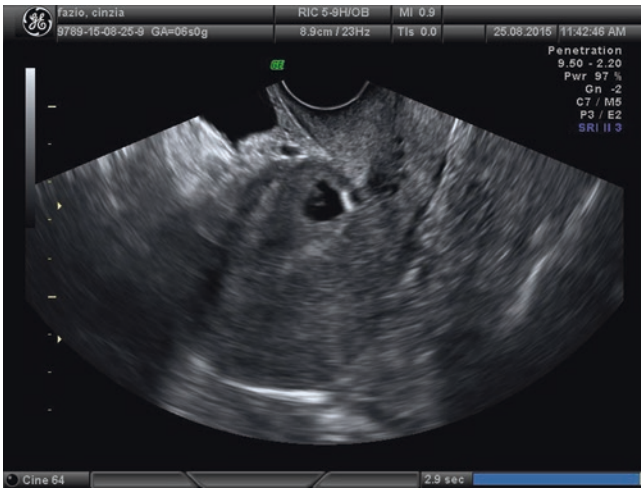


Fig. 19.13 Presence of the gestation sac in the anterior part of the uterine isthmus

is being made earlier because of the increased use of transvaginal sonography [34, 35, 37, 32, 39].

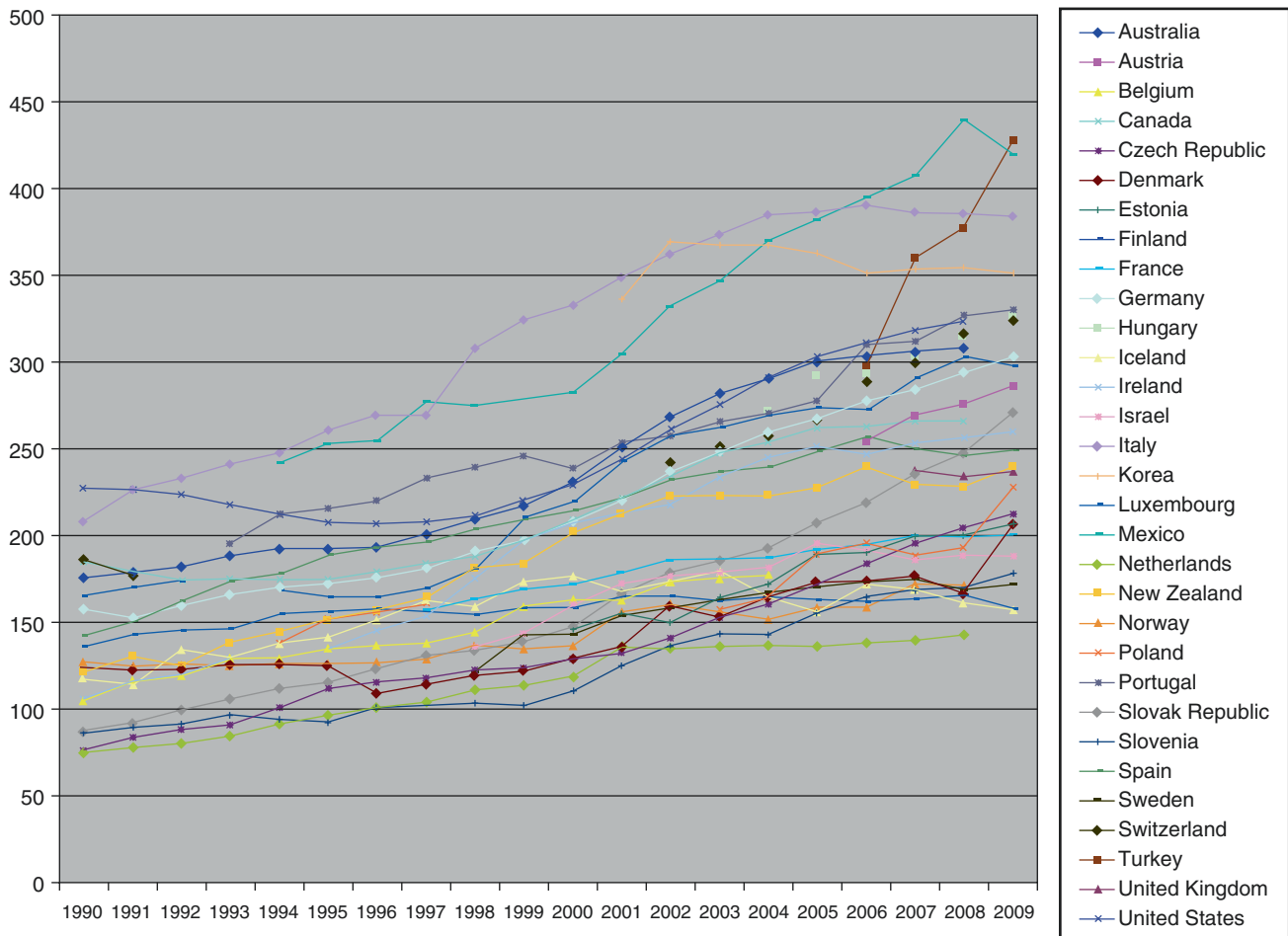
Up to 72 % of cesarean scar pregnancies occur in women who have had two or more cesarean deliveries [33, 34, 36].

The exact cause and mechanism are not well understood, but it is generally thought that a cesarean scar pregnancy occurs when a blastocyst implants on fibrous scar tissue within a wedge-shaped myometrial defect in the anterior lower uterine segment at the site of a prior cesarean scar. The possible etiology could be a trophoblastic invasion of the myometrium through a microscopic tract.

The myometrial defect most commonly develops after cesarean deliveries, but scar pregnancies have also been reported after other uterine surgeries such as dilatation and curettage, myomectomy, metroplasty, hysteroscopy, and manual removal of the placenta [32, 33, 35, 39]. The dehiscent myometrial defect may be related to incomplete healing or increased fibrosis along the uterine scar.

Table 19.1 Cesarean rate 1990–2009 (Source OECD Health Data 2011)

OCED Countries, Cesarean section, procedures per 1000 live births, 1990 – 2009



Fibrosis occurring after multiple cesarean deliveries leads to poor vascularity, which impairs healing. Multiple cesarean deliveries also increase the risk of implantation on the scar, likely due to an increased scar surface area [34, 36, 37, 39, 40].

19.17 Natural History

Very few of these pregnancies reported in the literature progressed beyond the first trimester [36, 41] as almost all are terminated during this period. It is likely that if a developing pregnancy in a cesarean section scar were to continue to the second or third trimesters, there would be a substantial risk of uterine rupture with catastrophic hemorrhage, with a high risk of hysterectomy causing serious maternal morbidity and loss of future fertility. There is also a danger of invasion of the bladder by the growing placenta. A pregnancy that protrudes through the scar, if viable, can implant on other abdominal organs and continue to grow as a secondary abdominal pregnancy [32, 42].

However, if the pregnancy continues within the uterus, the risk of placenta accreta is significantly increased, up to three- to fivefold [43, 44]. CSP progressing to 35 weeks of gestation has been described, but this case was complicated by massive hemorrhage and disseminated intravascular coagulopathy at CS, requiring a lifesaving hysterectomy [41]. There are very few cases reported in the literature of ectopic pregnancy within a cesarean scar resulting in live birth [45].

CSP may present from as early as 5–6 weeks [40] to as late as 16 weeks [46]. A light, painless vaginal bleeding is usually the early presenting symptom in 39%. Approximately 16% of women complain of accompanying mild to moderate pain and 9% complain of only abdominal pain [46]. It can be an incidental finding in an asymptomatic woman (37%). Severe acute pain with profuse bleeding implies an impending rupture.

Collapse or hemodynamic instability strongly indicates a ruptured CSP. Clinical examination in stable women is usually unremarkable. The uterus may be tender if the CSP is in the process of rupture.

19.18 Diagnosis of CSP

Transvaginal ultrasound (TVUS): TVUS on its own has a diagnostic sensitivity of 86.4% (95% CI 0.763–0.9050) [48]. TVUS is the first line to diagnosis or to confirm CSP (Fig. 19.14). The criteria are:

- No fetal parts in the uterine cavity or cervix
- Thin or absence of myometrial layer between the bladder and gestational sac

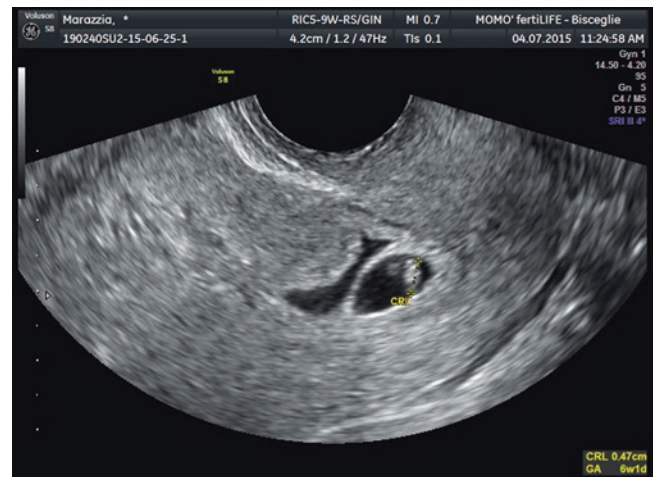


Fig. 19.14 TVUS is the first line to diagnosis or to confirm CSP

- Presence of the gestation sac with or without a fetal pole with or without fetal cardiac activity (depending on the gestation age) in the anterior part of the uterine isthmus with a triangular-“shaped gestational sac” image

The thickness of the intervening myometrium between the gestation sac and the bladder has been shown to be less than 5 mm in two-thirds of the cases [47].

In order to reduce the risk of a false diagnosis, a combined approach is recommended: a TVUS to obtain the fine details of the gestation sac and its relation to the scar followed by a meticulous abdominal scan with a full bladder [34, 48]. The abdominal scan provides a *panoramic view* of the uterus and an accurate measurement of the distance between the gestation sac and the bladder.

19.19 Doppler

The color flow Doppler shows a circular peritrophoblastic perfusion surrounding the gestational sac that helps to reach a diagnosis [49] and to delineate the CSP sac location of the placenta in relation to the scar and the bladder [36] (Fig. 19.15).

19.20 3D Ultrasound

3D US has been used to enhance the diagnostic accuracy of a CSP [23, 24, 50, 51] (Fig. 19.16).

Combination of the multiplanar views and surface-rendered images helps identify subtle anatomical details of a well-developed trophoblastic shell around the gestational sac [50]. The thin myometrium between the gestational sac and the bladder wall can be recognized with confidence.



Fig. 19.15 Detailed 3D vision of a cesarean scar pregnancy

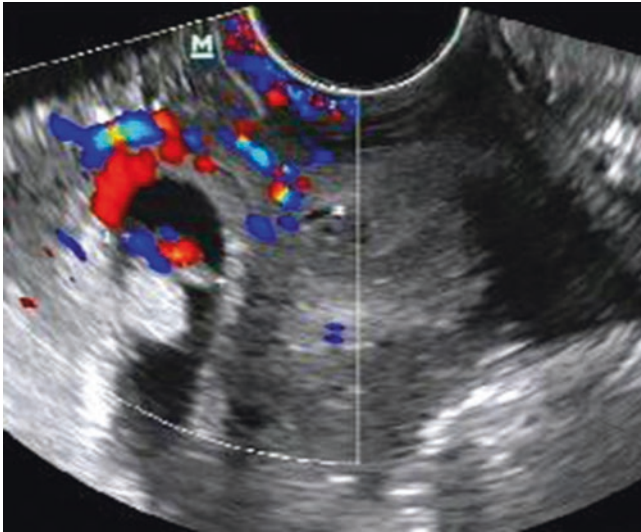


Fig. 19.16 Gestational sac surrounded by rich blood flow signal

Furthermore, peritrophoblastic flow surrounding the CSP may be illustrated by 3D power Doppler.

19.21 MRI

The superior soft tissue characterization and anatomical information provided by MRI allows patients and clinicians to consider conservative management as initial therapy, especially with the increasing availability of minimally invasive uterine artery embolization [52]. MRI can accurately detect the exact location of pregnancy, thus confirming the diagnosis [53, 54].

Huang et al. [55] performed a study regarding the use of intravenous contrast in MRI done for patients with CSP; this study concluded that contrast-enhanced MRI could be used

as a reliable adjunct and initial imaging modality for diagnosing CSP in selected cases. The imaging features of contrast-enhanced MRI may result in a more accurate diagnosis before specific treatment for CSP.

19.22 Diagnostic Hysteroscopy

Diagnostic hysteroscopy only helps to confirm the finding of a normal and empty uterine cavity together with the pregnancy tissues at the lower corpus [56].

Hysteroscopic removal of conceptive tissues implanted in a cesarean section scar seems to be a feasible and safe procedure that might be considered as a treatment option [57].

19.23 Diagnostic Laparoscopy

Another diagnostic option for CSP is laparoscopy [58–60]. The uterus size is usually seen normal or bulky (depending on the gestation age) with the CSP arising as a hillock with a “salmon red” ecchymotic aspect, bulging the uterine serosa from the previous cesarean section scar behind the bladder [61].

The fallopian tubes and the ovaries are seen normal.

19.24 Management of CSP

Generally, termination of pregnancy in the first trimester is strongly recommended, as there a high risk of subsequent uterine rupture, massive bleeding, and life-threatening complications as with any ectopic pregnancy.

Treatment objectives should be to perform feticide prior to rupture, to remove the gestational sac, and to retain patient’s future fertility.

Treatment can be divided to medical or surgical approach or an association between both.

19.25 Medical Treatment

The administration of methotrexate (MTX) is a standard treatment for tubal ectopic pregnancy, and it is also effective with CSP. The administration can be systemic or local.

19.26 Systemic MTX

CSPs have been shown to respond well to it (dose of 50 mg/m²), especially in those with b-hCG levels <5,000 mIU/ml [62]. Conservative medical treatment is appropriate for a woman who is pain-free and hemodynamically stable with an unruptured CSP of <8 weeks of gestation and a myometrial

thickness <2 mm between the CSP and the bladder. All women considered suitable for MTX treatment should have prior baseline full blood count and liver and renal function tests performed. They must be agreeable to surgery if medical treatment fails or if the CSP ruptures.

Systemic treatment alone is not the best treatment option due to 62 % complication rate. IM MTX injection has a slow action and the pregnancy continues to grow. It is recommended to use more than one injection and to associate it with other treatments.

19.27 Local MTX

MTX can be injected locally with ultrasound guidance, to the gestational sac via transabdominal or via transvaginal route. Transabdominal route requires a longer needle, used with caution not to penetrate the bladder wall, and does not require any anesthesia. The transvaginal approach allows for a shorter distance to the gestational sac with minimal risk of bladder injury.

19.28 Surgical Treatment

19.28.1 Uterine Artery Embolization

It has been described as a treatment option alone or in combination with dilatation and curettage [63]. It has a complication rate of about 47 %.

19.29 Dilatation and Curettage (D&C)

A review of the literature by Arslan et al. [64] shows that uterine curettage was either unsuccessful or caused complications in eight out of nine women, requiring surgical

treatment, and in a case series of eight CSPs, Wang et al. [59] had four secondary referrals after failed curettage, thus indicating a failure rate of 70 % [12, 17].

The gestation sac of a CSP is not actually within the uterine cavity and the chorionic villi implant into the cesarean section scar of the lower segment. Therefore, not only the trophoblastic tissue is unreachable by the curette but also such attempts can potentially rupture the uterine scar leading to severe hemorrhage and cause more harm. Profuse bleeding during the procedure and absence of chorionic villi in the specimen obtained by curettage must prompt immediate laparoscopy/laparotomy.

19.30 Laparoscopic Removal

Operative laparoscopy should be performed only after a prior TVS confirms the diagnosis (Fig. 19.17). The CSP mass is incised and the pregnancy tissue removed in an endobag. Bleeding can be minimized by local injection of vasopressin (1 unit/ml, 5–10 ml), hemostasis achieved by bipolar diathermy and the uterine defect closed with endoscopic suturing (Fig. 19.18).

19.31 Open Laparotomy Removal

Laparotomy followed by wedge resection of the lesion (hysterotomy) should be considered in women who do not respond to conservative medical and/or surgical treatments, present too late or if facilities and expertise for operative endoscopy are not available. Laparotomy is mandatory when uterine rupture is confirmed or strongly suspected (Fig. 19.19).

This conventional low-tech surgery, which is available in all hospitals, has the advantage of complete removal of the CSP and simultaneous repair of the scar (Fig. 19.20).

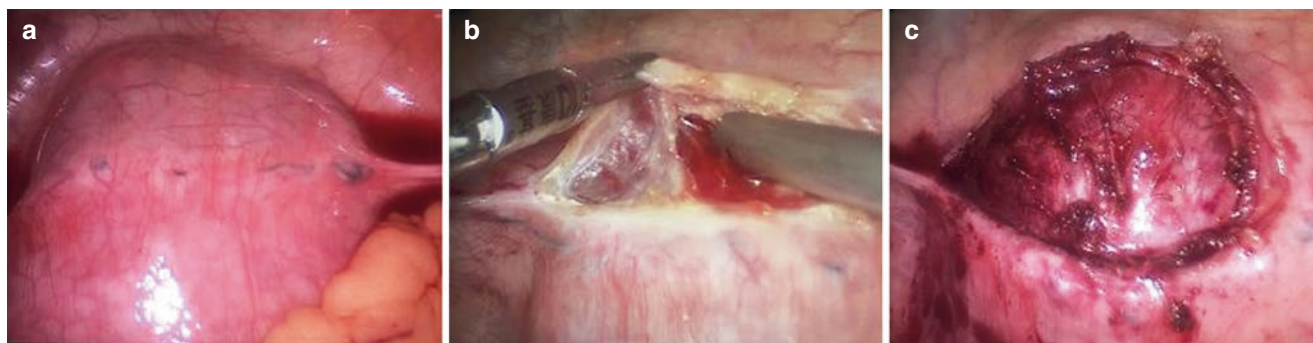


Fig. 19.17 In laparoscopy, we found (a) the violet lesion in the lower segment of the uterus. (b) Partial bladder reflex of the uterus peritoneum was detached. (c) The bladder reflex of the uterus peritoneum was completely detached (Pictures are courtesy of Dr. Xin Luo.

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This approach, however, inflicts a larger surgical wound, longer hospital stay, and longer recovery time, with a possible higher risk of a future placenta previa/accreta.

19.32 Hysteroscopic Evacuation

In 2005, Wang et al. [65] have described a successful treatment of CSP by operative hysteroscopy and suction curettage. At a 4-week follow-up, serum b-hCG level became normal, with restoration of normal echotexture of the uterus on ultrasound scan. Clinical follow-up at 3 months did not reveal any complication. The authors have since reported

hysteroscopic management of six more cases with success in all of them, with no complication and no blood transfusion [58]. They conclude that this procedure offers an important alternative treatment for CSP, with a short operative time (mean 36.7 ± 20.8 min), less blood loss (mean 50.0 ± 0.0 ml), short postoperative stay (mean 1.1 ± 0.9 days), and a rapid return of the pregnancy test to negative (<4 weeks, mean 22 days). Most importantly, the fertility is conserved after the surgery. The procedure requires general anesthesia, operative skill, and facilities. Direct visualization of the CSP with meticulous coagulation of the blood vessels at the implantation site is crucial to prevent severe intraoperative hemorrhage.

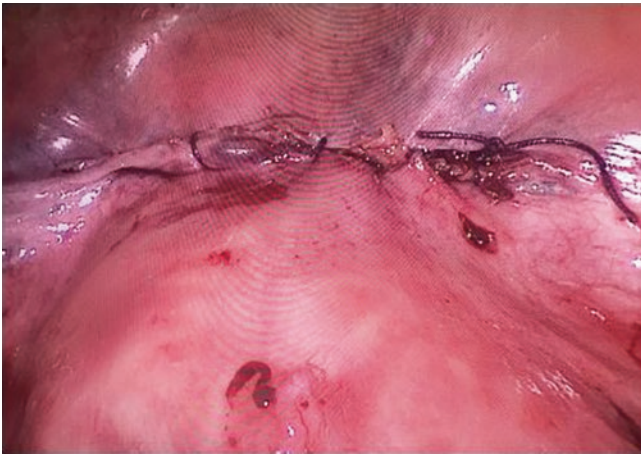


Fig. 19.18 Final view (Pictures are courtesy of Dr. Xin Luo, Department of Obstetrics and Gynecology, The First Affiliated Hospital of Jinan University, HuangPu Road West, Guangzhou, People's Republic of China)

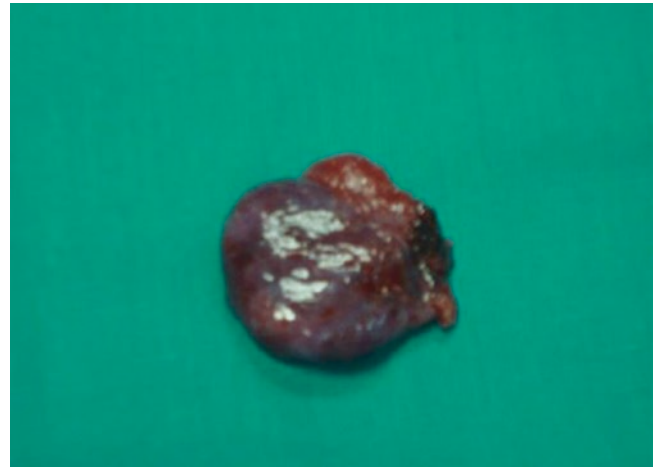


Fig. 19.20 Detailed view of the complete removal of the CSP (Pictures are courtesy of Dr. Gabriel Fiol Ruiz, Servicio de Ginecología y Obstetricia, Hospital Torrecárdenas, Almería, Spain)

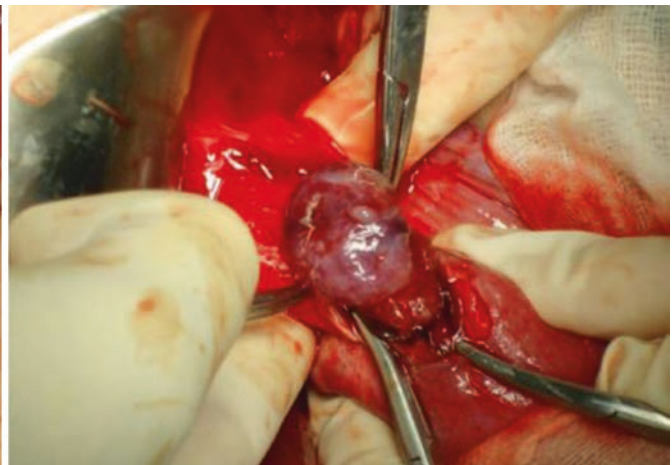
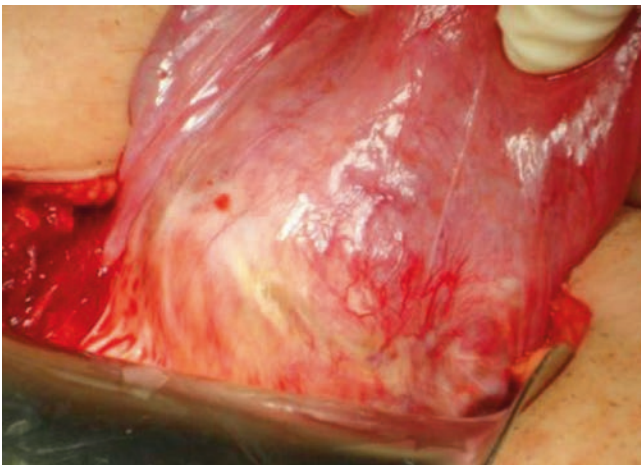


Fig. 19.19 Laparotomy followed by wedge resection of the lesion (Pictures are courtesy of Dr. Gabriel Fiol Ruiz, Servicio de Ginecología y Obstetricia, Hospital Torrecárdenas, Almería, España)

19.33 Which Is the Best Treatment Option?

Timor-Tritsch et al. [1] published a review where all the first-line treatment choices for CSP were analyzed. The results of the review expressed as the rate of complications based on the different first-line treatment options are shown in Table 19.2: alone or in any combination, D&C, dilatation and curettage; MTX, methotrexate; TAUS, transabdominal; TVUS, transvaginal; and UAE, uterine artery embolization.

The review concluded that transvaginal- or transabdominal-guided local and ultrasound-directed methotrexate injection with or without additional intramuscular methotrexate administration as well as surgical excision by hysteroscopic guidance carried the lowest complication rate.

There is no universal agreement on the best or most preferred treatment modality. It is therefore difficult to decide on the optimal management. Patient counseling and briefing, although vital, may be limited by this lack of reliable data.

19.34 Uterine Rupture

Uterine rupture during pregnancy is a catastrophic life-threatening complication; fortunately, the incidence is low, but when it occurs, it could lead to devastating consequences for both the mother and the fetus. Uterine rupture refers to a complete disruption of all uterine layers, including the serosa. It often leads to maternal hemorrhage and adverse fetal outcomes. By comparison, uterine dehiscence generally refers to an incomplete, and frequently clinically occult, uterine scar separation where the serosa remains intact and is not usually associated with adverse outcomes.

Accurate prediction of uterine rupture is important to better counsel patient regarding route of delivery. A large number of studies have been conducted looking at predictive factors of uterine rupture [66]. It is not clear how to define uterine scar defect. Some authors have described scar defects as concavities with a depth of more than 1–6 mm [67]. Osser et al. [20] proposed the evaluation of the uterine scar defect according to the ratio between the remaining myometrium over the defect and myometrium thickness at the cesarean

scar site. With the aim to accurately predict the patient at risk of uterine rupture, different imaging modalities have been proposed.

19.35 Ultrasound

Ultrasound with both transabdominal (TAS) and vaginal (TVS) approach is widely used to visualize the cervix and low uterine segment (LUS) during pregnancy (Fig. 19.21). A well-designed prospective observational study of lower uterine segment measurement in women who have had one prior cesarean revealed that by utilizing 3.5 mm of uterine thickness as the cut off, they were able to distinguish the patient who have a 99.3 % negative predictive value for uterine rupture or dehiscence. Although it has a high sensitivity (88 %) and specificity (73.2 %), the positive predictive value was low (11.8 %), suggesting that not all uterine segment thinner than 3.5 mm were clinically abnormal [68]. In an effort to compare the accuracy of transabdominal and transvaginal ultrasound to measure the thickness of the lower uterine segment, Prasanga et al. [69] measured the low uterine segment using both transvaginal and transabdominal ultrasound of 83 pregnant women with a prior cesarean delivery admitted for

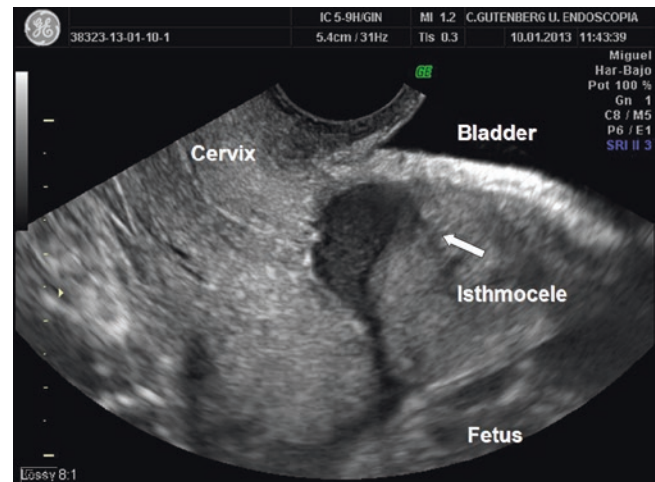


Fig. 19.21 Ultrasound view of the cervix and low uterine segment

Table 19.2 The table resuming the Timor-Tritsch et al. [1] review, with the first-line treatment choices for CSP

First-line treatment choices for cesarean scar pregnancy with the most and the least complication rates			
Treatment	Cases	Complications	%
MTX alone	87	54	62.1
D&C	305	189	61.9
UA embolization	64	30	40.9
Hysteroscopy	119	22	18.4
Local intragestational injection of MTX/KCL	81	8	9.6



Fig. 19.22 TVS is a more accurate method of assessing the thickness of the lower uterine segment

an elective repeat cesarean delivery at term. The actual low uterine thickness was measured during the cesarean delivery using a sterile ruler after the neonate had been delivered. They concluded that TVS is a more accurate method of assessing the thickness of the LUS compared with TAS (Fig. 19.22).

19.36 3D Ultrasound

A comparison between 2D and 3D transabdominal and transvaginal ultrasound measurement of the lower uterine segment in late pregnant women with a history of one cesarean delivery reported that 3D ultrasound had lower interobserver and intra-observer variability, noting that vaginal ultrasound measurements were more reproducible than using transabdominal approach [70].

Unfortunately, the absence of solid evidence using 3D ultrasound resulting in meaningful clinical outcomes precludes the use 3D ultrasound outside of a research setting.

19.37 Magnetic Resonance Imaging (MRI)

The use of MRI for visualization of previous cesarean hysterotomy incision site in the nonpregnant state has been reported for over 20 years [71].

This technology is currently used more often in attempts to diagnose placenta accreta.

The incidence of uterine rupture in women with history of cesarean delivery is estimated between 0.3 and 1 %, being 0.78 % in patients attempting VBAC and 0.22 % with elective repeat cesarean delivery [72].

The most important predictive factor of uterine rupture is the location of the prior uterine incision. After a previous classical cesarean delivery, the risk of uterine rupture escalates exponentially to up to 12 % [73]. Other described known factors are the use of prostaglandins and oxytocin for labor induction or augmentation, labor dystocia, advanced maternal age, short inter-pregnancy interval, and single-layer uterine closure [74]. On the other hand, a prior successful vaginal delivery significantly reduces the likelihood of uterine rupture [72, 75].

19.38 Clinical Course in Patients with Uterine Rupture

Different clinical signs should alert the clinician of uterine rupture including non-reassuring fetal heart rate (FHR) abnormalities, abdominal pain, uterine contraction abnormalities, loss of the presenting part, and vaginal bleeding. FHR patterns associated with uterine rupture are consistently reported to be non-reassuring, but there is no FHR pattern pathognomonic of rupture. The diagnosis is often suspected clinically, and confirmation occurs at the time of emergency cesarean section with the finding of hemoperitoneum and fetus partially or totally located outside the uterus.

19.39 Management

Suspected uterine rupture represents a life-threatening obstetrical emergency. The entire staff should be notified and an emergency protocol should be activated. The patient should be stabilized and taken for emergency cesarean section. An expedite intervention could prevent devastating consequences for both the mother and the fetus.

In the presence of uterine rupture, the uterine defect should be closed assuring adequate hemostasis. In cases where the uterine rupture is too large or irregular that prevents a safe hemostatic closure, hysterectomy should be strongly considered as a lifesaving measure. Attention should be placed to surrounding organs to identify possible damage. The use of uterotonics is recommended.

Maternal morbidity was assessed in a literature review of 880 cases of uterine rupture during 142,075 trials of labor after cesarean delivery (TOLACs, 6.2 ruptures per 1,000 trials of labor) [76]. For every 1,000 trials of labor, the rate of uterine rupture-related complications was 1.8 for packed red blood cell transfusion, 1.5 for pathologic fetal acidosis (cord pH<7.00), 0.9 for hysterectomy, 0.8 for genitourinary injury, 0.4 for perinatal death, and 0.02 for maternal death.

In a large review of over 140,000 patients undergoing VBAC, the most common serious maternal complication

was the need to undergo hysterectomy, which was reported in 14 to 33 % of women with uterine rupture. Other complications included urinary tract or bowel lacerations, need for blood transfusion, and postoperative infection [76].

It is unclear how to counsel a patient who had uterine rupture regarding future fertility. The risk of recurrence is high and difficult to predict and can occur at any time including the second trimester [77]. There is no consensus on the optimum timing of delivery. It is a common practice to deliver by elective cesarean section at 37 weeks to decrease the risk of recurrence.

A less morbid variant of uterine rupture is dehiscence of the low uterine segment, also known as “uterine window” which refers to an incomplete uterine scar separation in which the uterine serosa is intact. Most uterine dehiscence are subclinical and only diagnosed as an incidental finding at the time of cesarean section. There is insufficient data on management of “uterine windows” to make evidence-based management recommendations. If diagnosed during the antepartum period, the patient should be thoroughly counseled about potential risks and recommended to alert the physician if symptoms of possible uterine rupture are present.

19.40 Pathological Findings of Cesarean Scar Pregnancy

The morphological appearance of ultrasound in the diagnosis of cesarean scar pregnancy is a consideration in the pathological examination of the scar.

The more frequent aspects are shown in the following figures (Figs. 19.23, 19.24, 19.25, 19.26, 19.27, 19.28, and 19.29).

19.41 Other Long-Term Complications

19.41.1 Chronic Pain

An unfortunate complication of any surgical intervention is chronic pain on surgical site. It has been described after thoracic, breast, and abdominal surgery [78]. The persistence of pain on the incision site is not an uncommon complication after cesarean delivery. Nikolajsen et al. [79] surveyed via questionnaire 244 consecutive patients who were delivered by cesarean section. The response rate was 92 % and the mean follow-up time was 10.2 months. Forty-one patients (18.6 %) reported pain 3 months after the cesarean, and 27 (12.3 %) had unresolved persistent pain at the time of the survey, with 13 patients (5.9 %) characterized their pain as present daily or almost daily. Factors associated with persistent pain after cesarean include pain in other locations, severe

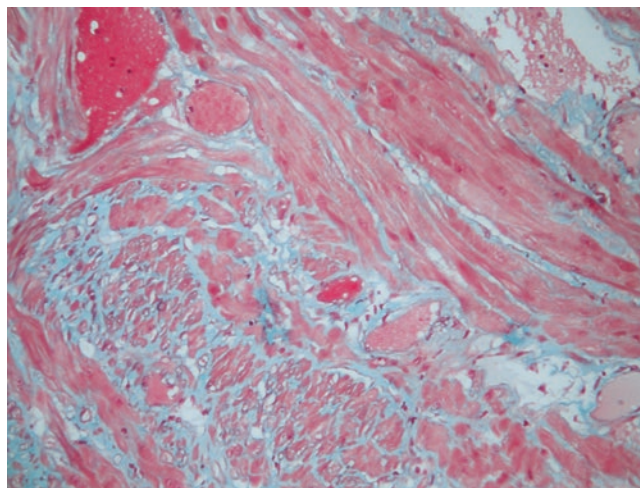


Fig. 19.23 Histological slide of a scar of cesarean section, stained with the Masson' trichromic stain. The muscular fibers, in red, are arranged on orthogonal planes. Single fibers or thin bundles are circumscribed by a small amount of collagen (in green). This kind of scar is present in 44 % of cases in our series

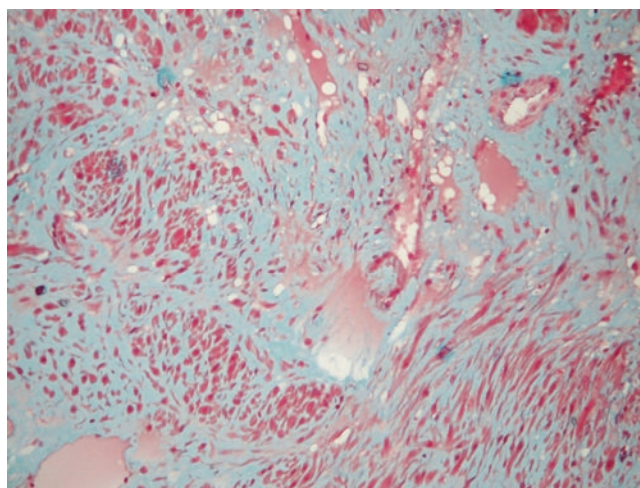


Fig. 19.24 A case of irregular distribution of the muscular fibers in a scar of cesarean section. The fibers missed a dynamic architectural disposition; they are mainly single and surrounded by a rich collagen stroma. This picture is present in the 17 % of our cases

postoperative acute pain, and the type of skin incision performed [79]. The Pfannenstiel incision, commonly used in the United States for cesarean deliveries, has numerous benefits including a low incidence of incisional hernia and accepted cosmesis. However, a possible complication of this incision is iliohypogastric or ilioinguinal nerve entrapment [80–82]. Branches of the ilioinguinal nerve and the iliohypogastric nerve are commonly severed when performing transverse abdominal incisions. This often results in persistent numbness around the scar. Less commonly, patients have persistent, radiating pain due to nerve entrapment. The diagnostic triad of nerve entrapment after surgery includes burning or

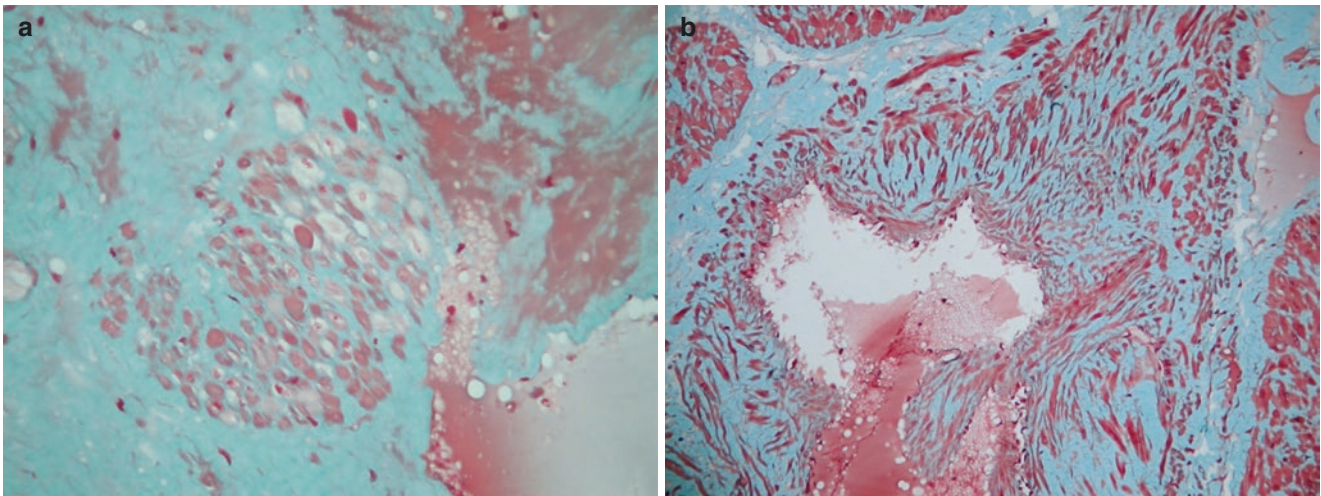


Fig. 19.25 Different histological features in the residual muscular fibers. In (a) the fibers are different in size, with homogeneous cytoplasm and scanty nuclei (predominance of regressive phenomena). In

(b) the regenerative muscular fibers seem to originate from the muscular wall of a vein (predominance of proliferative phenomena)

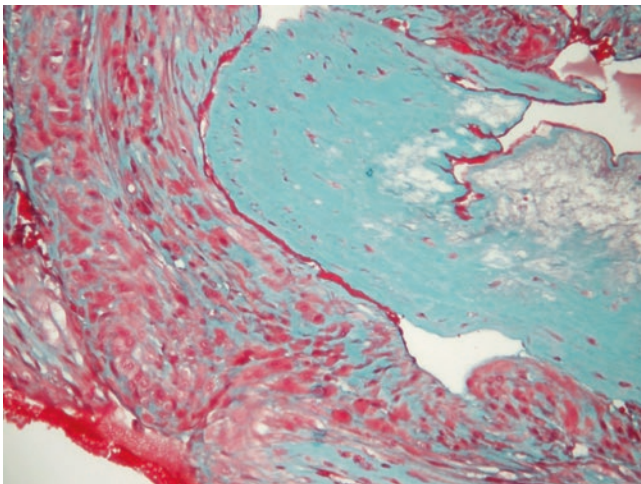


Fig. 19.26 Evident thick fibrous scar immediately under the mesothelium. The pattern of the collagen fibers, of longitudinal type in the figure, is crossed with the prevalent arrangement of the muscular fibers (in red, in the bottom left). This kind of cesarean section scar is a clear mechanical obstacle in an attempt of vaginal delivery in a subsequent pregnancy

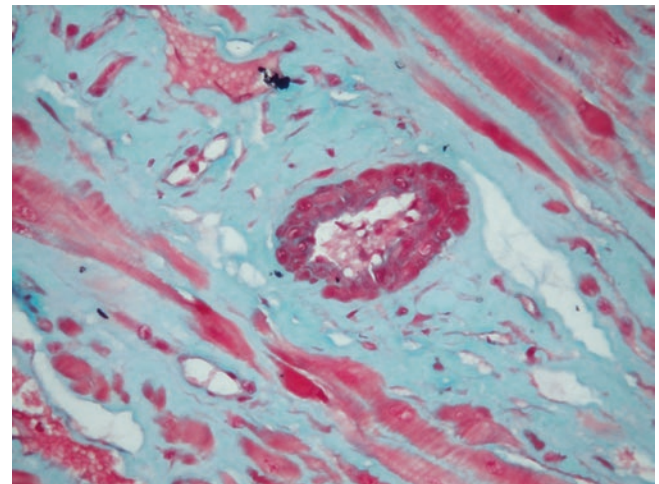


Fig. 19.27 A small artery in a scar of cesarean section shows a proliferation of the myocytes of the median layer. The latter have a polygonal epithelioid shape, a scanty cytoplasm, and a large nucleus with evident nucleolus. This aspect may be the sign of a different hemodynamic stress on the arterial flow or the effect of a hormonal stimulation

lancinating pain near the incision that radiates to the area supplied by the nerve, evidence of impaired sensory perception of the nerve, and pain relieved by local infiltration with an anesthetic [83]. Treatment involves surgical repair of the scar with resection of the compromised nerve or nerve block.

Surgical technique and number of previous skin incisions with increased fibrosis as a result of multiple surgeries on the same surgical site may also increase the risk of developing nerve entrapment and chronic incisional pain. Other factors also associated with increased risk of chronic pain are length of the incision, closure of the peritoneum, and emergency cesarean section [80].

An infrequent cause of chronic cyclic pain reported in 0.1 % of patients delivered by cesarean section is the presence of incisional scar endometriosis [84]. It presents as a tender palpable mass that increases in size during menstruation.

Another potential source of pain and abnormal vaginal bleeding most commonly postmenstrual spotting is the presence of a uterine “niche” (a defect on the endometrial side of the uterine wall). There has been an association between the number of previous cesarean and the size of the defect, with several reports of resolution of symptoms after laparoscopic or hysteroscopic repair of the defect [85].

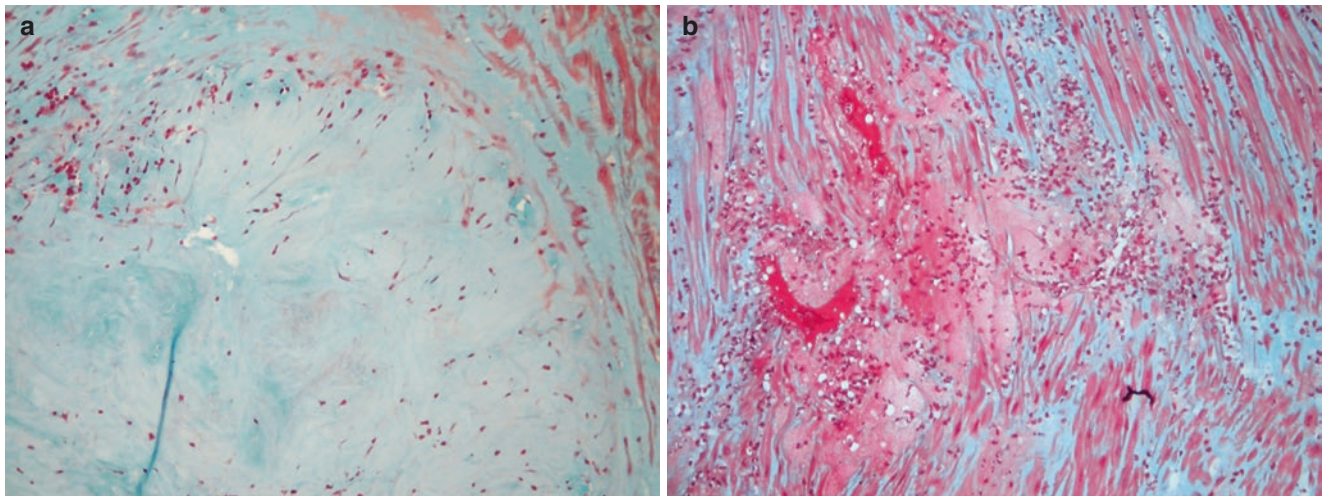


Fig. 19.28 Residual signs of inflammation are also present after several years since the cesarean delivery. The inflammatory cells may be scanty present in sclerotic scary areas (a) or in areas with regression of the muscular fibers, with initial fibrotic substitution (b). These aspects,

a long time after the surgery, may suggest that the scar of the cesarean section is a dynamic situation and the contraction of the myometrium should produce a continuous stimulus able to modify the nature and the function of the scar

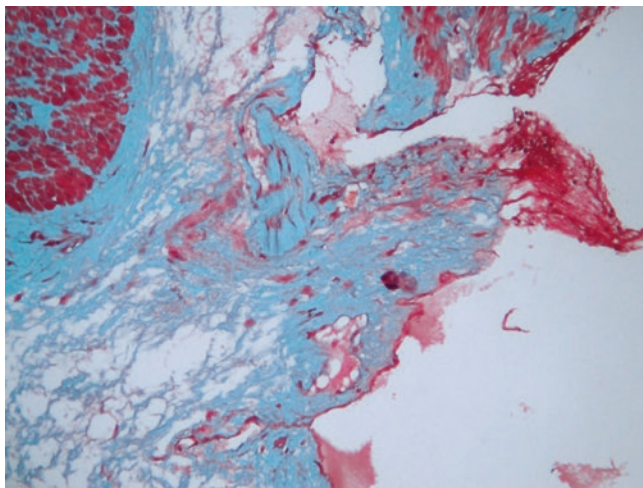


Fig. 19.29 In a scar of cesarean section, the overlying mesothelium (arrow) shows proliferative phenomena in a patient in which a surgical suture has been performed during the intervention

presence of pelvic adhesions has been associated with peri-operative complications such as increased operative and delivery time, increased blood loss, and increased risk of bladder injury [88].

19.42 Fertility

There is evidence indicating subsequent subfertility after cesarean delivery. A recent systematic review reported that women who delivered by cesarean section had 10 % fewer subsequent pregnancies than women who delivered vaginally [89]. It is suggested that surgery involving the uterus may compromise local vasculature or produce intrauterine scarring resulting in subsequent decreased fertility. Moreover, the presence of adhesions could decrease fertility by obstructing the tubal patency.

19.41.2 Pelvic Adhesions

Abdominal surgery is a well-accepted risk factor for development of adhesions. The most common location is between the uterus and surrounding organs. The incidence and severity of adhesions increase with increasing number of cesarean. Tulandi et al. [86] reviewed more than 1,200 charts of patient who underwent cesarean section and found no adhesions in primary cesarean, 24.4 % in patient undergoing their second cesarean and 42.8 % on their third cesarean delivery. It has been speculated that the risk of adhesion formation may also be determined by surgical technique [87]. The

19.42.1 Fetal/Neonatal Complications

19.42.1.1 Unexplained Stillbirth

The effect of cesarean delivery on future stillbirth is controversial. Studies of the risk of stillbirth following prior cesarean delivery have reported mixed results. Large epidemiologic studies demonstrated that cesarean delivery is associated with an increased risk of stillbirth in subsequent pregnancies [90, 91].

Others have reported no association [92, 93].

Although the exact cause is unknown, the association may be due to scar tissue from prior cesarean that may lead to placenta malfunction in the following pregnancy leading to stillbirth. The conflicting results may be due to several

factors such as different study populations, variable definitions of unexplained stillbirth, and different adjustments for potential confounders.

19.43 Small for Gestational Age

Another long-term reported complication of cesarean delivery is an increased risk of small for gestational age fetuses (less than fifth percentile). This could be due to placenta dysfunction as a result of intrauterine scarring produced during the first cesarean.

19.44 Preterm Birth

A South Australian cohort study [94] demonstrated that previous cesarean section is associated with an increased risk of preterm birth (OR 1.17; 95 % CI 1.04–1.31). These findings were also confirmed by Smith et al. [95] who reported the adjusted OR of 1.45 (95 % CI 1.21–1.74) for preterm birth between 24 and 32 weeks of gestation.

19.45 Summary

As the rate of cesarean delivery continues to increase, the resulting negative consequences are a growing concern. Although it is often difficult to establish causality, it is well known that the morbidity increases with the number of cesarean deliveries. The spectrum of complication could be from as severe as massive maternal hemorrhage with both maternal and fetal demise up to only cosmetic concerns as a result of the abdominal scar. Pregnancies following a previous cesarean delivery are at increased risk of complications. These risks are higher with a higher number of previous pregnancies. Cesarean delivery may also increase the risk of adverse reproductive outcomes, including decreased future fertility and increased rate of spontaneous abortion and ectopic pregnancies. It is important for both clinicians and patients to be aware of this increased risk of complications associated with cesarean deliveries. Both short- and long-term complications as a result of having a cesarean should be considered when discussing mode of delivery.

References

- Timor-Tritsch IE, Monteagudo A (2012) Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. *Am J Obstet Gynecol* 207(1):14–29
- Hamilton BE, Hoyert DL, Martin JA, Strobino DM, Guyer B (2013) Annual summary of vital statistics: 2010–2011. *Pediatrics* 131(3):548–558
- Sachs BP, Kobelin C, Castro MA, Frigoletto F (1999) The risks of lowering the cesarean-delivery rate. *N Engl J Med* 340(1):54–57
- Gregory KD, Jackson S, Korst L, Fridman M (2012) Cesarean versus vaginal delivery: whose risks? Whose benefits? *Am J Perinatol* 29(1):7–18
- Hibbard LT (1976) Changing trends in cesarean section. *Am J Obstet Gynecol* 125(6):798–804
- Liu S, Liston RM, Joseph KS, Heaman M, Sauve R, Kramer MS et al (2007) Maternal mortality and severe morbidity associated with low-risk planned cesarean delivery versus planned vaginal delivery at term. *CMAJ* 176(4):455–460
- Monteagudo A, Carreno C, Timor-Tritsch IE (2001) Saline infusion sonohysterography in nonpregnant women with previous cesarean delivery: the ‘niche’ in the scar. *J Ultrasound Med* 20:1105–1115
- Gubbini G, Casadio P, Marra E (2008) Resectoscopic correction of the “isthmocele” in women with postmenstrual abnormal uterine bleeding and secondary infertility. *J Minim Invasive Gynecol* 15(2):172–175
- Morris H (1995) Surgical pathology of the lower uterine segment cesarean section scar: is the scar a source of clinical symptoms? *Int J Gynecol Pathol* 14(1):16–20
- Bij de Vaate AJ, Brolmann HA, van der Voet LF, van der Slikke JW, Veersema S, Huirne JA (2011) Ultrasound evaluation of the cesarean scar: relation between a niche and postmenstrual spotting. *Ultrasound Obstet Gynecol* 37:93–99
- Thurmond AS, Harvey WJ, Smith SA (1999) Cesarean section scar as a cause of abnormal vaginal bleeding: diagnosis by sonohysterography. *J Ultrasound Med* 18:13–16
- Fabres C, Aviles G, De La Jara C et al (2003) The cesarean delivery scar pouch: clinical implications and diagnostic correlation between transvaginal sonography and hysteroscopy. *J Ultrasound Med* 22:695–700
- Yazicioglu F, Go˘kdogan A, Kelekci S, Aygu˘n M, Savan K (2006) Incomplete healing of the uterine incision after caesarean section: is it preventable? *Eur J Obstet Gynecol Reprod Biol* 124:32–36
- Roberge S, Demers S, Berghella V, Chaillet N, Moore L, Bujold E (2014) Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis. *Am J Obstet Gynecol* 211(5):453–460
- Ofili-Yebovi D, Ben-Nagi J, Sawyer E, Yazbek J, Lee C, Gonzalez J, Jurkovic D (2008) Deficient lower-segment cesarean section scars: prevalence and risk factors. *Ultrasound Obstet Gynecol* 31:72–77
- Vikhareva Osser O, Valentin L (2010) Risk factors for incomplete healing of the uterine incision after caesarean section. *BJOG* 117(9):1119–1126
- Wang CB, Chiu WW, Lee CY, Sun YL, Lin YH, Tseng CJ (2009) Cesarean scar defect: correlation between cesarean section number, defect size, clinical symptoms and uterine position. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol* 34(1):85–89
- Tower AM, Frishman GN (2013) Cesarean scar defects: an under-recognized cause of abnormal uterine bleeding and other gynecologic complications. *J Minim Invasive Gynecol* 20(5):562–572
- Surapaneni K, Silberzweig JE (2008) Cesarean section scar diverticulum: appearance on hysterosalpingography. *AJR Am J Roentgenol* 190(4):870–874
- Osser OV, Jokubkiene L, Valentin L (2010) Cesarean section scar defects: agreement between transvaginal sonographic findings with and without saline contrast enhancement. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol* 35(1):75–83
- Gubbini G, Centini G, Nascetti D, Marra E, Moncini I, Bruni L et al (2011) Surgical hysteroscopic treatment of cesarean-induced isthmocele in restoring fertility: prospective study. *J Minim Invasive Gynecol* 18(2):234–237
- Vikhareva Osser O, Valentin L (2010) Risk factors for incomplete healing of the uterine incision after caesarean section. *BJOG Int J Obstet Gynaecol* 117(9):1119–1126

23. Fernandez E, Fernandez C, Fabres C, Alam VV (1996) Hysteroscopic correction of cesarean section scars in women with abnormal uterine bleeding. *J Am Assoc Gynecol Laparosc* 3(4, Supplement):S13
24. Fabres C, Arriagada P, Fernandez C, Mackenna A, Zegers F, Fernandez E (2005) Surgical treatment and follow-up of women with intermenstrual bleeding due to cesarean section scar defect. *J Minim Invasive Gynecol* 12(1):25–28
25. Chang Y, Tsai EM, Long CY, Lee CL, Kay N (2009) Resectoscopic treatment combined with sonohysterographic evaluation of women with postmenstrual bleeding as a result of previous cesarean delivery scar defects. *Am J Obstet Gynecol* 200(4):370 e1–370 e4
26. Api M, Boza A, Gorgen H, Api O (2015) Should cesarean scar defect be treated laparoscopically? A case report and review of the literature. *J Minim Invasive Gynecol* 22(7):1145–1152
27. Klemm P, Koehler C, Mangler M, Schneider U, Schneider A (2005) Laparoscopic and vaginal repair of uterine scar dehiscence following cesarean section as detected by ultrasound. *J Perinat Med* 33(4):324–331
28. Donnez O, Jadoul P, Squifflet J, Donnez J (2008) Laparoscopic repair of wide and deep uterine scar dehiscence after cesarean section. *Fertil Steril* 89(4):974–980
29. Luo L, Niu G, Wang Q, Xie HZ, Yao SZ (2012) Vaginal repair of cesarean section scar diverticula. *J Minim Invasive Gynecol* 19(4):454–458
30. Tahara M, Shimizu T, Shimoura H (2006) Preliminary report of treatment with oral contraceptive pills for intermenstrual vaginal bleeding secondary to a cesarean section scar. *Fertil Steril* 86(2):477–479
31. Larsen JV, Solomon MH (1978) Pregnancy in a uterine scar sacculus: an unusual cause of postabortal haemorrhage. *S Afr Med J* 53:142–143
32. Fylstra DL (2002) Ectopic pregnancy within a cesarean scar: a review. *Obstet Gynecol Surv* 57:537–543
33. Ash A, Smith A, Maxwell D (2007) Cesarean scar pregnancy. *BJOG* 114(3):253–263
34. Maymon R, Halperin R, Mendlovic S, Schneider D, Herman A (2004) Ectopic pregnancies in a caesarean scar review of the medical approach to an iatrogenic complication. *Hum Reprod Update* 10:515–523
35. Wang CB, Tseng CJ (2006) Primary evacuation therapy for cesarean scar pregnancy: three new cases and review. *Ultrasound Obstet Gynecol* 27:222–226
36. Jurkovic D, Hillaby K, Woelfer B, Lawrence A, Salim R, Elson CJ (2003) First trimester diagnosis and management of pregnancies implanted into the lower uterine segment cesarean section scar. *Ultrasound Obstet Gynecol* 21:220–227
37. Rosen T (2008) Placenta accreta and cesarean scar pregnancy: overlooked costs of the rising cesarean section rate. *Clin Perinatol* 35:519–529
38. McKenna DA, Poder L, Goldman M, Goldstein RB (2008) Role of sonography in the recognition, assessment, and treatment of cesarean scar ectopic pregnancies. *J Ultrasound Med* 27:779–783
39. Gurel S (2008) Ectopic pregnancy. *Ultrasound Clin* 3:331–343
40. Seow KM, Huang LW, Lin YH, Lin MY, Tsai YL, Hwang JL (2004) Cesarean scar pregnancy: issues in management. *Ultrasound Obstet Gynecol* 23:247–253
41. Herman A, Weinraub Z, Avrech O, Maymon R, Ron-El R, Bukovsky Y (1995) Follow up and outcome of isthmic pregnancy located in a previous caesarean section scar. *Br J Obstet Gynaecol* 102:839–841
42. Marcus S, Cheng E, Goff B (1999) Extrauterine pregnancy resulting from early uterine rupture. *Obstet Gynecol* 94:804–805
43. Clark SL, Koonings PP, Phelan JP (1985) Placenta previa/accreta and prior cesarean section. *Obstet Gynecol* 66:89–92
44. Miller DA, Chollet JA, Goodwin TM (1997) Clinical risk factors for placenta previa-placenta accreta. *Am J Obstet Gynecol* 177:210–214
45. Ahmadi F, Moinian D, Pooransari P, Rashidi Z, Haghghi H (2013) Ectopic pregnancy within a cesarean scar resulting in live birth: a case report. *Arch Iran Med* 16(11):679–682
46. Smith A, Maxwell D, Ash A (2007 May) Sonographic diagnosis of caesarean scar pregnancy at 16 weeks. *J Clin Ultrasound* 35(4):212–215
47. Weimin W, Wenqing L (2002) Effect of early pregnancy on a previous lower segment cesarean section scar. *Int J Gynecol Obstet* 77:201–207
48. Chuang J, Seow KM, Cheng WC, Tsai YL, Hwang JL (2003) Conservative treatment of ectopic pregnancy in a caesarean section scar. *BJOG* 110:869–870
49. Vial Y, Petignat P, Hohlfeld P (2000) Pregnancy in a cesarean scar. *Ultrasound Obstet Gynecol* 16:592–593
50. Shih JC (2004) Cesarean scar pregnancy: diagnosis with three-dimensional (3D) ultrasound and 3D power Doppler. *Ultrasound Obstet Gynecol* 23:306–307
51. Wang CJ, Yuen LT, Yen CF, Lee CL, Soong YK (2004) Three-dimensional power Doppler ultrasound diagnosis and laparoscopic management of a pregnancy in a previous cesarean scar. *J Laparoendosc Adv Surg Tech* 14:399–402
52. Wu R, Klein MA, Mahboob S, Gupta M, Katz DS (2013) Magnetic resonance imaging as an adjunct to ultrasound in evaluating cesarean scar ectopic pregnancy. *J Clin Imaging Sci* 3:16
53. Koroglu M, Kayhan A, Soyulu FN, Erol B, Schmid-Tannwald C et al (2013) MR imaging of ectopic pregnancy with an emphasis on unusual implantation sites. *Jpn J Radiol* 31:75–80
54. Osborn DA, Williams TR, Craig BM (2012) Cesarean scar pregnancy: sonographic and magnetic resonance imaging findings, complications, and treatment. *J Ultrasound Med* 31:1449–1456
55. Huang Q, Zhang M, Zhai RY (2014) The use of contrast-enhanced magnetic resonance imaging to diagnose cesarean scar pregnancies. *Int J Gynaecol Obstet* 127:144–146
56. Hwu Y-M, Hsu C-Y, Yang H-Y (2005) Conservative treatment of caesarean scar pregnancy with transvaginal needle aspiration of the embryo. *BJOG* 112:841–842
57. Yang Q, Piao S, Wang G, Wang Y, Liu C (2009) Hysteroscopic surgery of ectopic pregnancy in the cesarean section scar. *J Minim Invasive Gynecol* 16:432–436
58. Wang C-J, Chao A-S, Yuen L-T, Wang C-W, Soong Y-K, Lee C-L (2006) Endoscopic management of cesarean scar pregnancy. *Fertil Steril* 85:494–497
59. Wang YL, Su TH, Chen HS (2006) Operative laparoscopy for unruptured ectopic pregnancy in a caesarean scar. *BJOG* 113:1035–1038
60. Wang Y-L, Su T-H, Chen H-S (2005) Laparoscopic management of an ectopic pregnancy in a lower segment cesarean section scar: a review and case report. *J Minim Invasive Gynecol* 12:73–79
61. Roberts H, Kohlenber C, Lanzarone V, Murray H (1998) Ectopic pregnancy in lower segment uterine scar. *Aust N Z J Obstet Gynaecol* 38:114–116
62. Ravhon A, Ben-Chetrit A, Rabinowitz R, Neuman M, Beller U (1997) Successful methotrexate treatment of a viable pregnancy within a thin uterine scar. *Br J Obstet Gynaecol* 104:628–629
63. Gao L, Huang Z, Gao J, Mai H, Zhang Y, Wang X (2014) Uterine artery embolization followed by dilatation and curettage within 24 hours compared with systemic methotrexate for cesarean scar pregnancy. *Int J Gynaecol Obstet* 127:147–151
64. Arslan M, Pata O, Dilek TU, Aktas A, Aban M, Dilek S (2005) Treatment of viable cesarean scar ectopic pregnancy with suction curettage. *Int J Gynecol Obstet* 89:163–166
65. Wang C-J, Yuen L-T, Chao A-S, Lee C-L, Yen C-F, Soong Y-K (2005) Cesarean scar pregnancy successfully treated by operative hysteroscopy and suction curettage. *BJOG* 112:839–840

66. Bujold E, Jastrow N, Simoneau J, Brunet S, Gauthier RJ (2009) Prediction of complete uterine rupture by sonographic evaluation of the lower uterine segment. *Am J Obstet Gynecol* 201(3):320.e1–320.e6
67. Roberge S, Boutin A, Chaillet N, Moore L, Jastrow N, Demers S et al (2012) Systematic review of cesarean scar assessment in the nonpregnant state: imaging techniques and uterine scar defect. *Am J Perinatol* 29(6):465–471
68. Rozenberg P, Goffinet F, Phillippe HJ, Nisand I (1996) Ultrasonographic measurement of lower uterine segment to assess risk of defects of scarred uterus. *Lancet* 347(8997):281–284
69. Marasinghe JP, Senanayake H, Randeniya C, Seneviratne HR, Arambepola C, Devlieger R (2009) Comparison of transabdominal versus transvaginal ultrasound to measure thickness of the lower uterine segment at term. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet* 107(2):140–142
70. Martins WP, Barra DA, Gallarreta FM, Natri CO, Filho FM (2009) Lower uterine segment thickness measurement in pregnant women with previous cesarean section: reliability analysis using two- and three-dimensional transabdominal and transvaginal ultrasound. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol* 33(3):301–306
71. Hebisch G, Kirkinen P, Haldemann R, Paakkoo E, Huch A, Huch R (1994) Comparative study of the lower uterine segment after cesarean section using ultrasound and magnetic resonance tomography. *Ultraschall Med (Stuttgart, Germany)* 15(3):112–116
72. National Institutes of Health Consensus Development conference statement: vaginal birth after cesarean: new insights March 8–10, 2010 (2010) *Obstet Gynecol* 115(6):1279–1295
73. Landon MB, Lynch CD (2011) Optimal timing and mode of delivery after cesarean with previous classical incision or myomectomy: a review of the data. *Semin Perinatol* 35(5):257–261
74. Landon MB (2010) Predicting uterine rupture in women undergoing trial of labor after prior cesarean delivery. *Semin Perinatol* 34(4):267–271
75. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW et al (2004) Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. *N Engl J Med* 351(25):2581–2589
76. Chauhan SP, Martin JN Jr, Henrichs CE, Morrison JC, Magann EF (2003) Maternal and perinatal complications with uterine rupture in 142,075 patients who attempted vaginal birth after cesarean delivery: a review of the literature. *Am J Obstet Gynecol* 189(2):408–417
77. Chibber R, El-Saleh E, Al Fadhli R, Al Jassar W, Al HJ (2010) Uterine rupture and subsequent pregnancy outcome – how safe is it? A 25-year study. *J Matern Fetal Neonatal Med Off J Eur Assoc Perinatal Med Fed Asia Ocean Perinatal Soc Int Soc Perinatal Obstet* 23(5):421–424
78. Macrae WA (2001) Chronic pain after surgery. *Br J Anaesth* 87(1):88–98
79. Nikolajsen L, Sorensen HC, Jensen TS, Kehlet H (2004) Chronic pain following caesarean section. *Acta Anaesthesiol Scand* 48(1):111–116
80. Silver RM (2010) Delivery after previous cesarean: long-term maternal outcomes. *Semin Perinatol* 34(4):258–266
81. Sippo WC, Burghardt A, Gomez AC (1987) Nerve entrapment after Pfannenstiel incision. *Am J Obstet Gynecol* 157(2):420–421
82. Tosun K, Schafer G, Leonhartsberger N, Herwig R, Pinggera GM, Bartsch G et al (2006) Treatment of severe bilateral nerve pain after Pfannenstiel incision. *Urology* 67(3):623 e5–623 e6
83. Stulz P, Pfeiffer KM (1982) Peripheral nerve injuries resulting from common surgical procedures in the lower portion of the abdomen. *Arch Surg (Chicago, Ill: 1960)* 117(3):324–327
84. Andolf E, Thorsell M, Kallen K (2013) Caesarean section and risk for endometriosis: a prospective cohort study of Swedish registries. *BJOG* 120(9):1061–1065
85. Bij de Vaate AJ, van der Voet LF, Naji O, Witmer M, Veersema S, Brolmann HA et al (2014) Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following cesarean section: systematic review. *Ultrasound Obstet Gynecol* 43:372–382
86. Tulandi T, Agdi M, Zarei A, Miner L, Sikirica V (2009) Adhesion development and morbidity after repeat cesarean delivery. *Am J Obstet Gynecol* 201(1):56.e1–56.e6
87. Lyell DJ, Caughey AB, Hu E, Daniels K (2005) Peritoneal closure at primary cesarean delivery and adhesions. *Obstet Gynecol* 106(2):275–280
88. Clark EA, Silver RM (2011) Long-term maternal morbidity associated with repeat cesarean delivery. *Am J Obstet Gynecol* 205(6 Suppl):S2–10
89. Gurol-Urganci I, Bou-Antoun S, Lim CP, Cromwell DA, Mahmood TA, Templeton A et al (2013) Impact of caesarean section on subsequent fertility: a systematic review and meta-analysis. *Hum Reprod* 28(7):1943–1952
90. Murphy DJ, Stirrat GM, Heron J (2002) The relationship between caesarean section and subfertility in a population-based sample of 14 541 pregnancies. *Hum Reprod* 17(7):1914–1917
91. Smith GC, Wood AM, Pell JP, Dobbie R (2006) First cesarean birth and subsequent fertility. *Fertil Steril* 85(1):90–95
92. Taylor LK, Simpson JM, Roberts CL, Olive EC, Henderson-Smart DJ (2005) Risk of complications in a second pregnancy following caesarean section in the first pregnancy: a population-based study. *Med J Aust* 183(10):515–519
93. Wood SL, Chen S, Ross S, Sauve R (2008) The risk of unexplained antepartum stillbirth in second pregnancies following caesarean section in the first pregnancy. *BJOG* 115(6):726–731
94. Kennare R, Tucker G, Heard A, Chan A (2007) Risks of adverse outcomes in the next birth after a first cesarean delivery. *Obstet Gynecol* 109(2 Pt 1):270–276
95. Smith GC, Pell JP, Dobbie R (2003) Caesarean section and risk of unexplained stillbirth in subsequent pregnancy. *Lancet* 362(9398):1779–1784