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## Isthmocele: A Frequently Overlooked Consequence of a Cesarean Section Scar

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### Introduction

The number of deliveries performed by cesarean section has been increasing steadily over the last 3 decades [1,2]. This trend is not limited to the United States but also worldwide. Among factors that resulted in a higher cesarean section rate is that there has been a constant decrease rate of operative vaginal deliveries, vaginal delivery of twin gestation, breech deliveries, and, vaginal birth after cesarean section (VBAC) [3]. However, this increase of cesarean births has not resulted in decreased neonatal morbidity or mortality, which raises significant concern on the possible overuse of cesarean birth [4]. A epidemiologic study revealed that “severe” maternal complications such as hemorrhage that required hysterectomy or massive blood transfusion, uterine rupture, cardiac arrest, acute renal failure, major infection, wound disruption was threefold increased for cesarean delivery as compared with vaginal delivery [5]. Also, well known long term effects of cesarean deliveries such as infertility, pelvic adhesions, and pelvic pain has been previously described [5].

There are maternal and fetal long-term deleterious consequences of a previous cesarean section scar. Maternal consequences could be divided in obstetrical complications, those encountered in subsequent pregnancies, and non-obstetrical complications.

The following review focuses on non-obstetrical complications which should also be considered as a deleterious effect of the current high cesarean section rate.

### Isthmocele

The healing process of the cesarean section scar can be defective. In that situation there is disruption of the myometrium at the site of the uterine scar. This “gap” in the anterior lower uterine segment is commonly known as isthmocele. This defect was first described by Morris H. using the term “cesarean scar syndrome” [6].

The incidence of cesarean scar defects (CSD) or isthmocele ranges between 24% and 56% [7].

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

The diagnosis of this condition is based in the clinical symptoms, the ultrasound and hysteroscopy.

### Etiopathogenesis

The pathogenesis of the uterine scar defect remains unknown. Several factors have been associated with the develop of a cesarean scar defect (CSD).

### Uneven thickness of the incision edges

One hypothetical factor related to the formation of CSD is the difference in myometrial contraction between the thicker superior edge of the hysterotomy incision and the inferior edge. The uneven approximation of incision edges with different thickness can contribute to the development of the CSD.

### Surgical hysterotomy closing technique

Other 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 a ischemic technique and a slow absorbable suture can produce an abnormal healing [2]. Regarding to the technique, Yazicioglu F et al, [8] reported that the frequency of incomplete healing was significantly lower in the group treated by full

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thickness hysterostomy repair. A recently published meta-analysis found no significant difference in the risk of uterine scar defect with single-layer compared to double-layer hysterotomy closure [9].

### Number of prior cesarean section

Oflin-Yebovi D et al. [10] found a relationship between multiple previous cesarean section and CSD. They report by evaluating 354 women with previous cesarean section that the odds of a scar becoming deficient with the consequent isthmocele formation increase with the number of previous cesarean sections. It is speculated that a second scar on a highly vascular granulation tissue from the prior cesarean section is replaced by a vascular scar tissue. Thus, further injury to the scar tissue will compromise future healing.

### Uterus in retroflexion

Uterine retroflexion was another variable that was clearly associated to an increased risk of isthmocele formation. In a retroflexed uterus the lower segment is under a degree of tension, which may affect to the healing of the Cesarean section scar.

### Indication for the cesarean section

There is an association between the degree of cervical dilatation and the duration of labor with an increase in the risk of develops CSD. If the patient was on active labor for more than 5 hours or cervical dilatation is  $\geq 5$ cm there is an increase odd of subsequent Isthmocele [11]. In late labor, the modified cervix becomes part of the lower uterine segment. Low incisions are more common if caesarean section is performed late in labor and cervical tissue may be included in the closing sutures, affecting to the healing of the scar.

## Clinical Manifestations

It is well documented that some late complications are present after a previous cesarean section. Some gynecological consequences such as postmenstrual spotting, chronic pelvic pain, and secondary infertility have been described in patients who are diagnosed with a CSD.

The most common symptom in patients with CSD is postmenstrual abnormal uterine bleeding (AUB) that is frequently described as dark. Morris H et al, [6] were the first to describe a correlation between postmenstrual bleeding and the presence of anatomic and histologic changes at the cesarean scar. Postmenstrual bleeding is estimated to present in 33,6% of women with a niche in the scar. There is a direct relation between the size of the defect and the amount and duration of the vaginal bleeding. It is believed that the reason for the postmenstrual AUB is caused by the disruption in the continuity of the endometrium acts as a reservoir pouch, in which some menstrual blood and debris are accumulated, and subsequently comes out slowly creating the spotting. Another possible mechanism is the poor contractility of the uterine muscle around the scar, due to the presence of fibrotic tissue that affect to the normal muscular contractions [7].

The presence of a disruption in the myometrium at the site of the cesarean scar is also associated with other symptoms as dysmenorrhea with an incidence of 53%, followed by chronic pelvic pain 39.6% and dyspareunia 18.3% [12]. All these symptoms are probably caused by chronic inflammation, the presence of small polyps and/or lymphocytic infiltration present in the scar.

Secondary infertility has also been associated with the presence of CSD. The presence of accumulated blood in the niche, can affect to

the normal characteristics of the mucus which interferes with sperm transportation. There is also minimal retrograde flow of blood, to the uterine cavity, especially in retroverted uteri, that can affect the quality of the endometrium with consequences on embryo implantation.

## Diagnosis

The diagnosis of the cesarean scar defect is based in previous history of cesarean section, clinical symptoms and ultrasound and/or hysteroscopy.

Currently, there is lack of consensus on the definition of cesarean scar defect. Ultrasound, in its conventional 2D or 3D modality, is usually the first diagnostic modality used in women with postmenstrual bleeding. Moreover, sonohysterography with saline (SIS) or gel (GIS) to fill the niche could be helpful in the diagnosis. Hysterosalpingography, Hysteroscopy and RMN can be also used to diagnose this defect.

### Ultrasound

The niche is defined by the presence of an anechoic area at the site of a previous cesarean section. This niche is usually triangular-shape with the vertex toward the isthmus. Another criterion for the diagnosis is the presence of fluid within the incision site [13]. The prevalence of a niche on evaluation with conventional 2D ultrasound is 24% [11]. The best time to perform the ultrasound study is late proliferative phase in which the cervical mucus can fill the niche. The use of 3D ultrasound facilitates the evaluation of the defect in multiple planes and offer more information than the conventional 2D ultrasonography.

### Hysterosalpingogram

Cesarean scar defects can also be diagnosed by hysterosalpingogram, usually as an incidental finding. The presence of anatomic defects as diverticula or thin linear defects at the lower uterine cavity is a common finding in patients with a previous cesarean section, and this defect can be found in around a 60% of patients with the use of hysterosalpingography [14].

### Sonohysterography

The use of saline (SIS) or gel (GIS), provides a clearly visualization of the CSD due to the filling of the niche with liquid, facilitating in this way the diagnosis. Moreover, more defects are detected using sonohysterography and more defects are classified as large than with the use of conventional ultrasound [15]. The instillation of liquid inside the defect allows to find different shapes and size of defects. The prevalence of a niche on evaluation with gel is around 56%. (8)

### Hysteroscopy

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

### MRI

Magnetic Resonance Imaging (MRI) can also detect the myometrial defect located at the lower uterine segment. The MRI display a linear low signal niche, sometimes filled with some fluid collection. The use of MRI can be useful to planning the surgery and

to rule out other conditions.

## Classification of CSDs

There are two recognized main classifications used to classify CSD. One proposed by Gubbini G. et al [16] in which the depth and the base of the isthmocele are measured and the surface of the isthmocele is calculated. According to the size of the surface, the isthmocele are classified into three grades: grade 1 when less or equal to 15mm<sup>3</sup>, grade 2 with a surface between 16 and 25mm<sup>3</sup> and grade 3 when larger than 25mm<sup>3</sup>. In their initial report, they found that more than 55% of cases were grade 1.

Oflili-Yebovi D et al, [10] based their classification of the CSD on the measurement of the endometrial thinning at the cesarean defect, they 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% and dehiscence a ratio equal or superior to 80%.

Other authors have defined CSD as severe when the remaining myometrium is less than 2,2mm visualized by vaginal ultrasound or 2,5mm in women who undergo sonohysterogram [11].

## Treatment

Various medical and surgical options have been proposed to treat the CSD. On one hand, a laparoscopic repair of the dehiscence is recommended; however, other experts recommend hysteroscopy with a resectoscopic approach. Another alternative also described is the vaginal repair of the CSD. Regardless of the surgical modality used to repair the defect, all patients will benefit from the use of oral contraceptives after the procedure to reduce menstrual blood. It is important to note that surgical treatment should only be reserved for symptomatic patients.

### Medical treatment

The use of oral contraceptives can be a conservative alternative for the management of postmenstrual bleeding. The published data on effectiveness of the medical treatment of CSD are conflicting. While different studies have concluded that the medical therapy fails to eliminate the bleeding [7], 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 [17]. Unfortunately, there is no consistent study about the use of hormonal intrauterine device to treat this condition.

### Surgical treatment

**Resectoscopic hysteroscopy surgery:** The first report about the use of the hysteroscopic resectoscope in the treatment of CSD was published by Fernandez E et al [18] 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 symptoms of postmenstrual bleeding. Since then, multiple articles have been published and the resectoscopy have become the most common approach for the treatment of symptomatic CSD. Fabres C, et al in addition to the resection of the fibrotic tissue underneath the pouch perform local fulguration of the dilated blood vessels and endometrial glands in the CSD, responsible of the "in situ" production of blood [19]. The main risk associated to the resectoscopy surgery is the possibility of uterine perforation and bladder injury. To prevent this complication, some authors recommend to avoid the resectoscopic surgery if the remaining myometrium at the level of the niche is less than 2mm [20].

**Laparoscopic surgery:** The purpose of the laparoscopic management is to restore the myometrial integrity 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 it is 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 [21]. Klemm P et al. initially used a combined laparoscopic-vaginal approach to repair the defect [22]. Donnez O et al, [23] subsequently described a complete 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 avoiding the vaginal approach. The laparoscopic approach offers a clear visualization of the surgical area after the dissection of the bladder with low risk of complications.

**Vaginal surgery:** The vaginal approach of the cesarean section defect is also considered a reparative surgery which repairs the defect and increases the thickness of the uterine wall. As stated before, this was firstly used in combination with laparoscopy approach. A new vaginal repair technique was 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 is excised. The opened scar is then closed with 2 layers of suture [24]. This approach is an alternative minimally invasive way to repair the myometrial continuity.

## Summary

As the rate of cesarean delivery continues to increase, the resulting negative consequences are a growing concern. Although often difficult to establish causality, it is well known that the morbidity increases with the number of cesarean deliveries. Pregnancies following a previous cesarean delivery are at increased risk of complications. These risks are higher as the number of previous pregnancies increases. Cesarean delivery may also increase the risk of adverse reproductive outcomes, including decreased future fertility, 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.

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