

Determinants of uterine scarring

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ABSTRACT

Despite current recommendations to encourage vaginal birth, the rate of cesarean sections has increased significantly in recent years, leading to an increase in the rate of uterine scar defects. The association between these defects and multiple maternal comorbidities motivates their study for prevention. Using various online library search engines such as PubMed, Medscape, UpToDate, Cochrane, we selected studies on the factors that cause deficient uterine scarring. In literature, it has various names, such as: isthmocele, niche, uterine scar dehiscence or uterine diverticulum. For this paper, 11 scientific articles were selected, choosing only the factors for which a positive statistical link was observed, meaning the increase of the risk of uterine scar defect. Currently, there is no unanimity on the factors that influence the quality of uterine scarring, for many of the factors analyzed there are also other contradictory studies.

Keywords: uterine scar defect, cesarean section, uterine tranche defect, niche, pelvic pain

INTRODUCTION

In recent years, the number of cesarean sections has increased significantly, being reported as having a frequency of 1 in 3 women in the US to 4 in 5 women in some parts of the world (80-90% in private hospitals in Brazil) [1], which led to an increase in the incidence of uterine scar defects after cesarean section. According to the WHO statement in 2015 [2], rates of more than 10% of cesarean sections are not associated with a reduction in maternal and infant mortality, which is why they should be performed only when medically necessary. The prevalence of scar defects in a randomized population of women who have had a cesarean section is 84% [3].

As a result of this increase in the rate of cesarean section, there has been an increasing interest in the

long-term morbidity of uterine scar defects [4-6]. In many studies, a very important element is the identification of the etiopathogenesis and the factors that prevent a correct cure. A vital step in the management of any disease is prevention, and in order to be possible, the causative factors must be known. Thus, the purpose of this article is to highlight the determinants identified so far in literature in order to be eliminated and finally succeed in reducing the incidence of uterine scar defects (USD) [7].

The explanation for the appearance of USD is that, unlike the epithelial and peritoneal layers that heal by regenerating and recolonizing the area, the myometrium does not heal like this, but by forming different tissue compounds, such as collagen, edema, inflammation, and elastosis that appear in the healing process. The tissue resulting from these

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processes is less elastic and more prone to injury or rupture in subsequent pregnancies [8].

USDs may have a higher impact on patients' quality of life in terms of symptoms and associated complications: ectopic pregnancy on uterine scarring, spotting and postmenstrual bleeding, dehiscence or uterine rupture in subsequent pregnancies, chronic pelvic pain, dysmenorrhea, dyspareunia, and impaired fertility [3,9,10].

MATERIALS AND METHODS

Using various online library search engines, such as PubMed, Medscape, UpToDate, Cochrane, we selected studies on the factors that could influence the appearance of uterine scar defects after a cesarean section. The variables sought included the various names under which the uterine scar defect appears in literature: "uterine scar defect", "isthmocele", "niche", "uterine scar dehiscence" or "uterine diverticulum", as well as general terms such as "cesarean section", "uterine scar". The articles used in this paper were impact studies published in the last 19 years. The information was centralized and correlations were formulated between the data currently existing in literature.

RESULTS

For this paper, 11 scientific articles were selected considering both original articles and meta-analyses (Table 1). The articles were included in the table according to the factor or the determining factors of uterine scarring studied, appearing several times if they analyzed several different factors. In the table, we mentioned only the factors for which an associational relationship with statistical significance was obtained, i.e., those that increase the risk of a uterine scar defect.

DISCUSSIONS

Many factors that affect uterine scarring after cesarean section have been studied over time. There is still no unanimity on considers all these, especially given that there are conflicting results. Regarding gestational age, for example, Yazicioglu et al. [22] found no connection between gestational age when performing cesarean section and the risk of uterine scarring, unlike the study by Hayakawa et al. [21].

Although they do not find any difference on the risk of scar defect in terms of suture type, in single or double layer, Di Spiezio Sardo et al. [11] identifies a lower residual myometrial thickness in the case of the single layer suture.

Following an extensive review of literature and analyzing the results of the included studies, Ian-

none et al. [17] assumed that there must be an individual predisposing factor to explain the occurrence of defects in certain patients.

Currently, there is no clear set of criteria to determine which is a physiological, normal aspect of a uterine scar and which is a pathological aspect. In addition, there is no universal definition of USD, imaging criteria for framing and describing this entity being formulated in most studies. Ofili-Yebovi et al. [18] define USD as a "thin, noticeable myometrial scar on the scar of a caesarean section". According to them, a severe deficiency is when the myometrial thickness at the level of the scar is less than half of the thickness of the adjacent myometrium. According to Bij de Vaate et al. [23], the isthmocele can be defined on ultrasound as an anechoic area with a depth of at least 1 mm located at the level of the cesarean section scar. In a review [24], it was proposed to define a hypoechoic triangular defect located in the myometrium where a hysterotomy has been performed in the past. By correlating the objective measurements with the examiners' subjective observations, Vikhareva Osser and Valentin [20] stated that a major defect appears when the residual myometrial thickness is less than or equal to 2.2 mm on transvaginal ultrasound and less than or equal to 2.5 mm on hystero-graphy.

It is important to note that endometrial thickness could hypothetically influence the appearance of the uterine scar and alter the results, being variable with the period of the menstrual cycle. The evaluation of myometrium thickness is devoid of this disadvantage, which is why it is the one used in literature.

From a clinical point of view, a patient with isthmocele may present with pelvic pain, dysmenorrhea, infertility and metrorrhagia (abnormal uterine bleeding) [25].

It is important to determine whether imaging findings need to be correlated with these clinical aspects for diagnosis. Tower et al. [24] propose that USD is diagnosed in the absence of symptoms.

The methods used in the literature to quantify these defects are: transvaginal ultrasound (TVU) and saline infusion sonohysterography (SIS). Older studies of uterine scar defects used transvaginal ultrasound, but later studies have shown that SIS is superior, with better sensitivity [16]. Specifically, a prospective cohort observational study [15] concluded that half of the cases identified by SIS were not found by TVU, which means that SIS is a more sensitive method of diagnosis, therefore it should be the method of choice.

Residual myometrial thickness (RMT) is an ultrasound parameter that is determined by calculating the distance between the apex of the hypoechoic triangle and the anterior uterine wall. The clinical significance of the RMT is debatable. Roberge et al. [26] evaluated this thickness by transvaginal ultrasound and considered it to be a method of quantifying the

TABLE 1. Uterine scarring determinants

Authors	No. of patients	Determining factor	Conclusions
Di Spiezio Sardo et al. [11]	3,969	Suture type: Single layer versus double layer	Similar results in all aspects studied, except for the residual myometrial thickness, which is significantly higher in the case of the double layer suture.
Ceci et al. [12]	30	Simple interrupted sutures or continuous sutures (single layer)	The interrupted suture has a much smaller area of healing defect compared to the continuous one.
Vikhareva Osser et al. [13]	125	The position of the incision	The lower location of the incision is associated with a higher frequency of uterine scar defects.
Park et al. [14]	404	Duration of surgery	A short duration of surgery is significantly associated with the isthmocele.
Park et al. [14]	404	History of cesarean section	The risk of isthmocele is higher if a cesarean section is repeated.
Antila-Långsjö et al. [15]	371	Medical history of cesarean section	A medical history of cesarean section increases the risk of isthmocele.
Antila-Långsjö et al. [15]	371	Body mass index	For each unit of body mass index, the risk of uterine scar defect increases by 6%.
Antila-Långsjö et al. [15]	371	Diabetes mellitus	Gestational diabetes is an independent risk factor for isthmocele.
Osser et al. [13]	125	Maternal age	Variation of maternal age, parity, oxytocin administration and location of the scar with the degree of cervical dilation.
Pan et al. [16]	514	Hypertension disease	There is no increased risk in these patients, but the risk factor is the postpartum antihypertensive medication.
Iannone et al. [17]	N.A.	Genetic predisposition	The theory of the existence of a genetic predisposition, to explain why some patients develop isthmocele and others do not, remains valid.
Ofili-Yebovi et al. [18]	324	The position of the uterus	A retroflexed uterus is more commonly associated with uterine scar defects.
Armstrong et al. [19]	31	Triggering labor before cesarean section	Only those whose labor was triggered before the cesarean section later had uterine scar defects.
Vikhareva Osser et al. [20]	108	Duration of labor (greater than 5 hours) and cervical dilation (greater than 5 cm)	The risk of developing uterine scar defects increases with the duration of labor, with a dramatic increase if it exceeds 5 hours and if the cervical dilation is greater than 5 cm.
Park et al. [14]	404	Premature rupture of membranes	Premature rupture of membranes is associated with an increased risk of niche formation.
Pan et al. [16]	514	Infections	It has been shown that perioperative administration of multiple doses of antibiotics decreases the prevalence of USD.
Pan et al. [16]	514	Postoperative body temperature	Increased risk of uterine scar defect in patients with postoperative fever (>/ = 38) or subfebrile (37.5-38).
Pan et al. [16]	514	Serum fibrinogen	A serum fibrinogen level greater than 4.5 g/ L is associated with a higher risk of USD than a fibrinogen level below this value.
Hayakawa et al. [21]	137	Gestational age	Older gestational age is associated with an increased risk of niche formation.
Hayakawa et al. [21]	137	Preeclampsia	There is a connection between preeclampsia and the presence of a niche.

severity of the uterine scar defect. RMT is used by Vitale et al. [27] as a criterion for choosing the technique of approaching the symptomatic isthmocele (hysteroscopy versus laparoendoscopy). The meta-analysis of Kok et al. [28] supports the use of this parameter to predict the chances of a uterine rupture in the scar of a previous cesarean section during a subsequent labor.

CONCLUSIONS

Numerous determining factors of USD have been identified, but the mechanism of formation has not

been identified in all cases. It is also important to determine the impact of each factor on the scar in order to recognize the clinical importance of its avoidance or management.

The factors identified can be classified into 2 categories: surgical, which, in turn, are factors related to the surgical technique and factors related to surgery, and those related to the patient and her medical history.

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