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Isthmocele: When Surgery Is Both the Problem and the Solution

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Isthmocele is defined as a pouch-like defect of the anterior uterine wall, at the level of the uterine isthmus, connected to the uterine cavity. One of the most important characteristics of the isthmocele is that it is usually an "iatrogenic" disease, being a possible consequence of cesarean section: the uterine isthmus heals without a proper *restitutio ad integrum* of the myometrial layers after hysterotomy of the anterior wall, and a fibrotic reaction leads to a *locus of minor resistentiae*. Consistently, the prevalence of isthmocele, defined for this reason also cesarean scar defect, increases with the number of previous cesarean sections. According to recent data [1], an isthmocele is present in approximately 60% of patients after a primary cesarean section and in 100% after 3 cesarean sections. Considering these elements, the worldwide reduction of cesarean deliveries recommended by the World Health Organization [2] may play a role to decrease the incidence of post-cesarean isthmocele.

In addition to the number of hysterotomies, several other cesarean section-related variables may play a role in the development of this condition [3]. On the one hand, the intraoperative single-layer suture of the myometrium during cesarean section may cause a higher risk of isthmocele development; on the other hand, synthetic absorbable monofilament sutures for uterine closure was associated with increased residual myometrial thickness compared to synthetic absorbable multifilament sutures, and may potentially decrease the incidence of isthmocele.

Although isthmocele can be asymptomatic, it may cause adverse reproductive outcomes, pelvic pain, and abnormal uterine bleeding. In most cases, a small amount of blood collects within the pouch-like defect during the menstrual phase of the cycle, inducing an inflammatory reaction. This collection and reaction can be considered, at least in part, the underlying cause of the irregular vaginal bleeding (especially as post-menstrual spotting), pelvic pain (for the action of inflammatory cytokines of perilesional nerve fibers), and secondary infertility/subfertility due to disturbed embryo implantation triggered by an immune switch toward

inflammation at the maternal-embryonal interface [4]. Also, isthmocele may increase the rate of cesarean scar pregnancy, a potentially life-threatening condition that deserves accurate management to avoid massive uterine bleeding [5].

On that basis, when a woman complains post-menstrual spotting, pelvic pain, or secondary infertility/subfertility arise after a cesarean section, an isthmocele should be suspected and investigated, being the treatment possible and effective. Diagnosis of this condition relies upon several tools, including 2D and 3D transvaginal ultrasound, and magnetic resonance imaging in selected cases (due to the high costs). However, the diagnostic confirmation is performed by diagnostic hysteroscopy, which allows direct visualization of the pouch-like defect within the anterior uterine wall [6]. After diagnosis, the ultrasound evaluation of myometrial residual thickness may have paramount importance for the management of cesarean scar defect, because this measure is directly associated with the risk of uterine scar dehiscence in a subsequent pregnancy (thicker is the residual myometrium at the level of hysterotomy, less likely is the risk of uterine rupture). Despite available data do not allow to draw a firm conclusion about the best surgical technique for the management of isthmocele, accumulating evidence suggests that hysteroscopic approach, using a miniresectoscope for channel-like 360° endocervical ablation, is a safe and feasible method [7]. Considering these pieces of evidence altogether, the recent work published in *Journal of Investigative Surgery* may shed new light on the isthmocele repair by laparoscopic approach, which was recently investigated in a systematic review [8]. Although these data need to be confirmed in a large setting with an appropriate sample size, the laparoscopic "muscle flap filling suture method" and "folding suture method" combined with hysteroscopic incision may offer a new perspective for the management of the disease [9]. Nevertheless, we remark once again that each surgical technique for the management of isthmocele, especially when aimed to restore fertility, should be carefully considered taking into account how the surgical outcomes will

potentially affect the ones of subsequent pregnancy and delivery [10].

Disclosure statement

The authors have no proprietary, financial, professional or other personal interest of any nature in any product, service or company. The authors alone are responsible for the content and writing of the paper.

Authors' contribution

All the authors conform the Journal and the International Committee of Medical Journal Editors (ICMJE) criteria for authorship, contributed to the intellectual content of the study and gave approval for the final version of the article.

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