Italian Journal of
Gynæcology & Obstetrics
March 2023 - Vol. 35 - N. 1 - Quarterly - ISSN 2385 - 0868

# Presentation of isthmocele and its management options: a review

Rahul **Manchanda**, Sesha Sindhura **Singhu** *, Apoorva **Dave**

Department of Gynaecology Endoscopy, PSRI, New Delhi, India.

**ARTICLE INFO**

**History**
**Received:** 15 September 2022
**Received in revised form:** 13 October 2022
**Accepted:** 25 October 2022
**Available online:** 21 March 2023

**DOI:** 10.36129/jog.2022.78

**Key words**
*Isthmocele; caesarean scar defect; myometrial defect, niche.*

***Corresponding author**: Sesha Sindhura **Singhu**, DNB. Department of Gynaecology Endoscopy, PSRI, Press Enclave Marg, J Pocket, Phase II, Sheikh Sarai, 110017, New Delhi, India.
Email: sindhura1387@gmail.com.
ORCID: 0000-0001-5108-9613.

**ABSTRACT**

**Objective.** Rapidly increasing trend of caesarean sections in day-to-day obstetric practice has increased the incidence of isthmocele. The present study aims to perform a literature review to give a comprehensive knowledge of isthmocele – a defect in the uterine wall due to previous caesarean section. Isthmocele is defined as an iatrogenic myometrial defect of the isthmocervical anterior uterine wall at the site of previous caesarean scar due to defective tissue healing.
**Materials and Methods.** A non-systematic review of various articles on isthmocele and its management techniques was undertaken by searching in the databases like PubMed, Scopus, EMBASE, web of science, science direct, etc. The studies describing about isthmocele and its different management techniques were included in present study.
**Results.** Isthmocele has been studied in various aspects such as: risk factors, clinical symptoms, classification, diagnosis and different management options have been reported according to the actual literature data.
**Conclusions.** Cost effective diagnostic tool for isthmocele are transvaginal ultrasound and saline infusion sonography which are highly specific as well as sensitive. Treatment plan should be individualized depending upon the presenting symptoms like secondary infertility, size of the defect, and future conception plans. The small defects can be repaired minimal invasively with sparing techniques by hysteroscopy, and larger defects are managed by laparoscopy, vaginal approach and combined hysteroscopy and laparoscopy.

## INTRODUCTION

There has been a rising trend in overall caesarean delivery rates worldwide over the past three decades [1-3]. Uterine incisions given during caesarean sections usually heal without consequences, but there are chances of various complications in association with caesarean sections (CSs). Although rate of CS has been decreased lastly, but even if we try to decrease and keep the rate low (under 30%), still the number of performed CS is increasing [4], and it has increased the concern regarding the short and long-term morbidity associated with caesarean scar defect, which is a new entity being described in literature [5]. Poidevin in 1961 first described caesarean scar defect, also called isthmocele, niche, diverticulum or pouch as a wedge-shaped myometrial defect in the anterior uterine wall due to defective tissue healing [6]. The radiological definition of Isthmocele is stated as a hypoechoic or anechoic, triangular area at caesarean scar site

with atleast 2 mm depth of indentations in the myometrium [7-9].

Various risk factors have been linked with the development of the isthmocele, but only few risk factors are proven till date which includes multiple caesarean sections, retroflexed uterus and other factors like a lower position of caesarean section, incomplete closure of the hysterotomy, early adhesions of the uterine wall and a genetic predisposition may also result in development of a niche [10, 11]. When caesarean section conducted in active labour, or when cervical dilation of more than 5 cm there are high chances of developing isthmocele. The single-layer myometrial closure as compared to double-layer closure appears to increase the risk of isthmocele development and is associated with smaller defects [7-12].

Majority of isthmoceles are asymptomatic and are incidentally diagnosed [13]. Symptoms such as abnormal uterine bleeding, postmenstrual spotting, dysmenorrhea, pelvic pain, and infertility have now been linked to isthmocele [7, 9, 14]. Various obstetric complications like placenta accrete, placenta praevia, uterine rupture, scar dehiscence and ectopic pregnancy in caesarean scar defects have been linked with isthmocele in the literature [15, 16]. In the literature there are no definitive criteria for the diagnosis of isthmocele [12, 15, 17]. Several imaging techniques such as sonohysterography, ultrasonography, hysterography, hysteroscopy, and magnetic resonance imaging can be used to assess the anterior uterine wall and diagnose isthmocele [18].

Management of isthmocele depends on its size, associated symptoms, infertility issues and pregnancy plans. Various management options include expectant or pharmacological treatment, surgical treatment that includes uterus sparing techniques such as hysteroscopic, laparoscopic, laparotomic, or transvaginal procedures limited to the defect site and even hysterectomy if needed [19].

## AIMS AND OBJECTIVES

First, to review literature available on isthmocele and its symptomatology, second to assess current place of different management options for isthmocele.

## MATERIALS AND METHODS

A non-systematic review of various articles on isthmocele and its management techniques was undertaken by searching in the databases like PubMed, Scopus, EMBASE, web of science, science direct etc. The studies describing about isthmocele and its different management techniques were included in present study. We searched studies from 2015 to 2022. The keywords used were isthmocele, niche, caesarean section defect, caesarean section scar, caesarean section diverticulum.

## RESULTS AND DISCUSSION

Since the beginning, there have been several theories on aetiology of isthmocele. The most widely accepted one is due to the inadequate healing of myometrium at caesarean scar site [20].

The other risk factors are as follows:

1. Hysterotomy closure technique: a double layer closure of uterine cavity decreases the incidence of isthmocele formation but this remains a debatable topic and no significant difference for niche formation is found with both single layer and double layer hysterotomy closure in a recent metanalysis [21].

   Locking sutures, no peritoneum closure leads to adhesion formation which leads to pull on the scar, endometrium sparing repairs not approaching the myometrium in its entire width and interrupted suturing techniques are various factors linked with isthmocele development [10]. Abnormal healing may result from the use of a delayed absorbable suture along with ischemic technique of suturing [22].
2. Site of incision: when caesarean section is done in second stage of labour, the uterine incision is placed at a lower level than usual and increases the chances of inadequate healing due to entrapment of cervical mucous glands in stitch line [23, 24].
3. Anatomy of uterus: in patients with retroflexed uterus, the caesarean scar remains at higher traction causing Isthmocele [23].
4. Number of caesarean sections: repeated caesarean sections associated with decreased perfusion of scar tissue, altered scar healing and progressive thinning of the area leading to isthmocele formation [24].

   According to the literature, isthmocele formation increases with repeated caesarean sections, after one, two and three caesarean sections chances of niche are 62%, 68.2% and 77.8% respectively [24].

Presence of an individual/genetic predisposition may influence isthmocele development via poor haemostasis, impaired wound healing, inflammation and adhesion formation [10].

### *Clinical features*

Majority of isthmoceles are asymptomatic which are incidentally diagnosed on ultrasound [13].

1. Gynaecological presenting symptoms: around 28.9% to 82% of patients with isthmocele will present with abnormal uterine bleeding (AUB) as the main symptom [7, 9, 22, 25]. Isthmocele defect appears as diverticulum or pouch which act as a reservoir for menstrual blood and also due to fibrotic tissue which is responsible for reduced contractility of the uterus culminates in delaying the drainage of the menstrual blood flow causing AUB [7, 26, 27]. Size of isthmocele is associated with postmenstrual bleeding or postmenstrual spotting which is more in patients with larger defects [14, 28]. Isthmocele is associated with dysmenorrhea and pelvic pain. Size of the isthmocele is correlated with dysmenorrhea, pelvic pain. Pelvic pain is due to inflammatory infiltration, fibrosis, anatomic disruption of lower uterine segment [14, 29].
2. Infertility: caesarean scar defects are also responsible for Infertility. The lower fertility rate might be due to the menstrual blood in that scar site diverticula, which affects the cervical mucus, sperm motility and implantation [30, 31]. In isthmocele, residual menstrual blood responsible for chronic inflammation, which affects fertility [15]. In 20% women who were undergoing IVF with isthmocele clinicians are facing difficult embryo transfer due to a distorted anatomy, especially in a retroflexed uterus. In women with isthmocele there are higher chances of unsuccessful IVF [32].
3. Obstetric complications: isthmocele is associated with placenta previa, adherent placenta, scar dehiscence, caesarean scar ectopic pregnancy and uterine rupture [16]. Overall rate of uterine rupture during pregnancy is less than 2%, but in larger defects, this risk may reach up to 5% [16]. Practically ultrasound assessment of scar thickness in of no use as a prognostic marker of uterine rupture [16, 33]. Caesarean scar ectopic pregnancy occurs when implantation of embryo in the myometrium of the scar defect which is rarest obstetric complication.

### *Classification of isthmocele*

Depending on size of defect, authors classified large defect as a myometrial reduction of > 50% of the wall thickness or even > 80% by some authors [12, 28]. Residual myometrium (RM) < 2.2 mm by TVUS and < 2.5 mm by SHG comes under large defect [18].

Marotta *et al*. took the cut-off of residual myometrium < 3 mm as a large defect and RM ≥ 3 mm as a small defect for management of isthmocele [18].

Radiological diagnosis may be incidental or it can be associated with clinical symptoms. So, it can be classified as asymptomatic or symptomatic when presenting with symptoms such as AUB, infertility and pelvic pain [15]. Isthmocele was classified using ultrasound as follows: grade 1 ≤ 15 $mm^2$; grade 2 16-25 $mm^2$; and grade 3 > 25 mm [34, 35].

### *Diagnosis of isthmocele*

Diagnosis is done with the help of presenting symptoms along with a previous history of caesarean section which is confirmed by radiological and hysteroscopic findings. As of now there are no specific guidelines for diagnostic techniques [12, 15, 17].

1. Ultrasonography: to evaluate the uterine wall integrity in nonpregnant patients, first and most commonly used method is transvaginal ultrasound (TVUS) [14, 18]. Transvaginal ultrasound is best done in early proliferative phase of menstrual cycle to diagnose isthmocele, as it best shows the collection of menstrual blood within the isthmocele, which helps in easy identification even without the need of saline or gel infusion and there is minimal chance of pregnancy [12, 13, 36].

   On transvaginal ultrasound, defect appears as an anechoic defect in the myometrium with the base communicating to the uterine cavity, or it appears as a deformity (wedge, shape, concavity or sacculation) on the anterior isthmus [22, 37].

   Most common finding on transvaginal ultrasound is either "U" or "V" shaped notch. These defects may appear in different shapes such as a thin linear defect, focal saccular outpouching, unilateral or bilateral diverticula and fistula, and they can present in various sites such as the body of the uterus, lower uterine segment, upper endocervical canal and the isthmus [25].

Naji used a method to evaluate isthmocele scar, which is most commonly used recently [38]. On ultrasound in both sagittal and transverse planes, evaluate the scar size, depth and residual myometrium thickness and measures the width of myometrium above and below the defect and also calculated the ratio of residual myometrium and myometrium overlying the defect [18].

2. Hysterosalpingogram (HSG): in 60 percent patients who underwent HSG, isthmocele is identified as an incidental finding as diverticula or thin linear defects at the lower uterine cavity but its limitation is it cannot measure the myometrial thickness [39]. HSG may not clearly identify the defect especially if blood or mucus gets accumulated in the isthmocele [13].
3. Sonohysterography: in this method, gel or saline is used as ultrasound contrast media to delineate defect. A study was done to compare transvaginal ultrasound and sonohysterography showed that higher prevalence of isthmocele diagnosis with sonohysterography [56-84%] than transvaginal ultrasound [24-70%] which requires in detail evaluation to find out whether it was an incidental finding or due to higher sensitivity of sonohysterography for isthmocele diagnosis [39].

   Similar to saline instillation sonohysterography, gel instillation sonography (GIS) also showed higher prevalence (64.5%) than TVUS (49.6%) for isthmocele diagnosis [9]. Isthmocele defect appears larger and residual myometrium was smaller in both GIS and SIS when compared to TVUS [9]. Prevalence of isthmocele and defect size is more with SHG due to increased pressure inside uterus during gel or saline instillation which increase the defect size [12].
4. Magnetic resonance imaging (MRI): on sagittal T2 weighed images, MRI is useful to delineate defect size, residual myometrium thickness, contents of pouch and surrounding pelvic area and it is a good modality to measure isthmocele, but limits its usage due to high cost and low availability. Nevertheless, residual myometrium thickness was almost same as assessed by TVS according to Marotta *et al*. [18].
5. Diagnostic hysteroscopy: hysteroscopy is useful for direct visualization of isthmocele and its confirmation [17, 22]. On hysteroscopy isthmocele appears as pouch or discontinuity of anterior uterine wall, but it is not useful to assess residual myometrium thickness (RMT) [40].

   On hysteroscopy defect usually appears as a cavity with occasional double arch of fibrous tissue in the anterior wall of uterine isthmus or in the upper third of the cervical canal and base of defect is usually congested with inflammatory signs, neovascularisation which is prone for contact bleeding. Thus, hysteroscopy is helpful in excluding differential diagnosis of abnormal uterine bleeding such as polyps and submucosal fibroids [20]. The big disadvantage of hysteroscopy is that we cannot measure RMT with this method [40].
6. Diagnostic laparoscopy: diagnostic laparoscopy is useful to assess the defect on outer surface which can be done along with hysteroscopy. To delineate defect accurately two light sources can be used, one full illumination light source from inside uterine cavity via hysteroscopy and one partially dimmed light source inside abdomen via laparoscopy [20].
7. Intraoperative diagnosis: laparoscopic identification of uterine niche is challenging especially if bladder is densely adherent to anterior uterine wall. In such cases, authors used different techniques by combining both hysteroscopic and laparoscopic approach to detect the uterine niche [41]. When laparoscopy light source is put off along with simultaneous hysteroscopy light, source on so that light shines through the defect is known as Halloween sign or positive diaphanoscopy or transillumination sign [42].

   One of the techniques is using two independent optical systems. Another new technique in uterine niche identification is by using fluorescence-guided surgery with indigo cyanine green (ICG) application in which diluted indigo cyanine green solution is applied to the uterine cavity and this fluorescence can be detected easily by laparoscopic fluorescence guided vision without second optical system which is useful to do targeted resection [43].

***Management options***

Only done for symptomatic women coming with infertility issues post caesarean section, recurrent miscarriages, history of caesarean scar ectopic, AUB and post-menstrual spotting affecting quality of life. However, efficacy of treatment is yet to be ascertained. Routine repair of incidentally diagnosed asymptomatic niche is not recommended [13, 18].

There are various treatment options ranging from clinical treatment with expectant or pharmacological management, surgical management, and hysterectomy to sparing techniques such as hysteroscopic, laparoscopic, laparotomic, or transvaginal procedures limited to the defect site [19].

Expectant treatment is an option for women with small isthmoceles (Residual Myometrium (RM) ≥ 3 mm). However, in a randomized study done by Vervoort *et al.* [44] showed that as compared to expectant management, the hysteroscopic niche resection was found to be efficacious in reducing the symptoms in women coming with complaints of postmenstrual spotting and past history of caesarean having small defects with residual myometrium of ≥ 3 mm thickness.

1. Medical treatment: hormonal treatment helps in AUB for symptomatic relief. If pregnancy is not desired, oral contraceptives are suitable. LNGIUS was not found to be useful in decreasing menstrual length [45].

   Thurmond *et al.* observed that clinical management could not reduce symptoms in most of the subjects treated with oral contraceptives [26]. However, Tahara *et al*. stated that after three cycles of oral contraceptives at a relatively higher doses gave positive results in treating intermenstrual bleeding [46]. Despite the contrasting results, currently the first choice of management for symptomatic niche is the resection of the defect because of its minimally invasive approach and good therapeutic results [17, 30, 47, 48].
2. Uterine sparing surgical treatment: consider conservative surgical options after excluding other causes of presenting complaints. It includes either hysteroscopic resection or transabdominal excision plus repair by laparotomy or laparoscopic or robotic or vaginal route [49].
3. Hysteroscopic niche resection or isthmoplasty: hysteroscopic niche resection is the least invasive which can be used for both diagnosis and treatment and it can be done even as office procedure [49, 50].

   Hysteroscopic niche resection is useful when residual myometrium thickness is good enough to withstand resection and it should be sufficient enough to prevent complications such as perforation, bladder damage during surgery, uterine tear during future pregnancy. There is no universal cut-off for the optimal residual myometrium thickness to proceed with hysteroscopic resection. Residual myometrium thickness more than 2 mm suggested, as has a measurement above 2.5 mm, but most of them accepted cut-off of more than 3 mm [19, 51, 52].

   Theoretically, the minimal RMT thickness necessary can be calculated using two variables: the minimum thickness required to prevent bladder damage due to surgery, and the minimum thickness needed to prevent future uterine tear [34].

   Operative hysteroscopy done under anaesthesia by using 9 mm resectoscope. After instilling bladder with methylene blue, diagnostic hysteroscopy was done to prevent risk of injury during cervical dilatation using hegar dilators up to size 10. By using pure cutting current, resect inferior and superior edges of the defect and scar tissue was completely removed using a resectoscopic loop until the muscular tissue below was evident [34]. If defect is high (isthmic part, superior and middle thirds of the cervical canal), an inverted ablation was done in the cervical canal underneath the isthmic endometrium. Main aim was to replace the treated area by noninflamed monostratified cuboidal epithelium, avoiding formation of adhesion formation (Asherman syndrome) [34]. In cases of low cervical defect (inferior third of the cervical canal), endocervical tissue was treated as a part of electrosurgical conization limited to the area of the diverticulum. In this procedure removal of diverticulum edges was done so that wall of diverticulum is in continuous with cervical canal [34]. Bottom of the pouch was treated with pure cutting 3 mm roller ball electro cautery as the residual myometrium is thin to induce scar retraction. All these procedures were done under direct vision while modulating technique according to the muscle tissue below [34].

   Histology of resected specimen in the caesarean section scar showed inflammatory infiltration of the endocervix, fibrosis and necrotic tissue, endometriosis which after removal was replaced by endocervical mucosa with monostratified cubic-cell-type epithelium [34, 47, 53].

   For those patients who are presenting with secondary infertility due to isthmocele, surgical intervention is a good option and majority will become pregnant spontaneously with in a period of 12 to 24 months and delivered at term by elective caesarean section [54]. Whether or not the surgical correction of isthmocele increases the risk for uterine rupture is certainly subject

to debate, and more studies are required to confirm the absence of such a risk [54]. But it is not possible to conclude hysteroscopic correction of isthmocele is associated with restoration of fertility, so we need to have more detailed information to identify prevalence of isthmocele in infertility patients and its general effects [34].
Hysteroscopy can also be performed vaginoscopically without general anaesthesia, so office procedure may be performed using Channel-like 360° Isthmocele Treatment with a 16F mini-resectoscope [55].
Hysteroscopic resection of niche is associated with improved quality of life by reducing symptoms [56]. Moreover, operative hysteroscopy could have a positive effect on niche-related subfertility, but further research is needed [56].

4. Niche repair: in cases with residual myometrium thickness less than 3 mm, repair is done by transabdominal (laparotomy, laparoscopic, robotic) or vaginal route which involves defect identification, fibrotic tissue excision and approximation of excised area in 2 layers with absorbable sutures [32].
Vervoorts *et al.* in 2018 concluded that in retroflexed uterus repair done laparoscopically along with hysteroscopy with round ligament plication, using hyaluronic acid as adhesion barrier is effective in reducing symptoms [32].
In Nirgianakis' "Rendez-vous technique", Halloween sign or positive diaphanoscopy or transillumination was elicited in which laparoscopy light source is put off with simultaneous hysteroscopy light source on so that light shines through the defect [42].
In "slip and hook" technique, to identify defect via laparoscopically, hegar dilator is placed with in cervical canal and blindly slipped to bulge out anteriorly and perforate the defect [57].
In "Donnez technique", in patients with retroflexed uterus, large isthmoceles are excised laparoscopically using $CO_2$ laser, with round ligaments shortening [58].
Vaginal repair of niche is done when isthmocele is at lower level, in which after separation of bladder from cervix, niche is identified, excised and closed in 2 layers with absorbable sutures.
In nutshell, smaller niches of < 2.5-3 mm with RMT > 3 mm can be treated hysteroscopically. Vaginal route is preferred when niche is at the lower level. Transabdominal approach is preferred for large defects, especially if the residual myometrium is < 3 mm as bladder can be mobilized out of surgical field offering better niche visualization with lesser bladder injury. It is a better approach for women desiring future pregnancy since uterine wall thickness and strength increase. Among transabdominal routes, laparoscopy and robotic surgery offer advantages of being minimally invasive with lesser morbidity. Incidental endometriosis is reported in 21% women; hence, consent for correction of any associated pathology should also be taken if transabdominal route is planned [58].
5. Hysterectomy: hysterectomy offers definitive treatment for niche-related gynaecological symptoms.
In reproductive age group women isthmocele should always be treated surgically irrespective of the modality in order to prevent chances of having caesarean scar pregnancy in future [59].

***Outcome***

Post menstrual spotting is reduced by a median of 3.8 days, symptomatic relief in cases of AUB is 72.4% with hysteroscopic niche resection and pain relief in 97% [18, 23]. AUB gets resolved within first month in 87.5% patients and in the second month after surgery 96.8% patients feel better [60]. Recurrence is seen in up to 5% patients [10].
Donnez *et al*. reported 93% symptom-free patients with laparoscopic repair and at 3-month follow-up mean myometrial thickness increased from 1.4 mm to 9.6 mm, 44% infertile women conceived and confined at full term by elective caesarean section [58].
Enderle *et al*. conducted a study on retrospective series of 18 surgically treated women and showed poor obstetric outcomes with miscarriages in 55% women [61]. Only one patient delivered vaginally, who was treated with transvaginal repair; others underwent caesarean [61].

***Prevention of niche formation***

Efforts should be made to minimize caesarean rates and that will prevent the formation of uterine niche primarily choosing the correct surgical method by ensuring thicker residual myometrium and strong scar are the basis of secondary prevention of niche formation [62]. A recent study performed on 138 women in reducing isthmocele formation and ensuring sufficient residual myometrium by using

far-far-near-near double-layer unlocked technique for uterine closure may be preventive [62].
It has been shown that careful selection is needed for the patients who need surgical management, long learning curve and also efficacy of these treatments yet need to be proven. For bleeding symptoms, hormonal treatment is preferable, whereas subfertility may require surgical correction [46]. Hysteroscopic resection is preferred for smaller niches with RMT > 3 mm, niche located lower down can be treated transvaginally, and transabdominal approach is preferred for large defects and in women desiring future pregnancy [32, 45, 49]. Laparoscopy and robotic surgery offer advantages of being minimally invasive with lesser morbidity [57].

## CONCLUSIONS

Rapidly increasing trend of caesarean sections in day-to-day obstetric practice has increased the incidence of isthmocele. So, it is the need of the hour to study about this newer clinical entity due to its rising trends in such cases and its diagnosis requires high index of suspicion by the clinicians. Possibility of Isthmocele should always be kept in mind as a differential diagnosis in women having symptoms such as post menstrual spotting, secondary infertility, pelvic pain and abnormal uterine bleeding in women with previous CS deliveries. A single systemic classification of isthmocele is required to provide an effective tool for the gynaecologists to make its diagnosis and provide management. Future studies may further delineate risk factors influencing this pathology and also to choose various treatment modalities effectively according to clinical symptoms.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors contribution*

R.M.: Supervision. S.S.S.: Conceptualization, writing – original draft. A.D.: Writing – review & editing.

### *Funding*

None.

### *Study registration*

N/A.

### *Disclosure of interests*

N/A.

### *Ethical approval*

N/A.

### *Informed consent*

N/A.

### *Data sharing*

N/A.

## REFERENCES

1. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. PLoS One. 2016;11(2):e0148343. doi: 10.1371/JOURNAL.PONE.0148343.
2. Cavallaro FL, Cresswell JA, França GVA, Victora CG, Barros AJD, Ronsmans C. Trends in caesarean delivery by country and wealth quintile: cross-sectional surveys in southern Asia and sub-Saharan Africa. Bull World Health Organ. 2013;91(12):914-22. doi: 10.2471/BLT.13.117598.
3. Stanton CK, Holtz SA. Levels and trends in cesarean birth in the developing world. Stud Fam Plann. 2006;37(1):41-8. doi: 10.1111/J.1728-4465.2006.00082.
4. Dellino M, Crupano FM, Rossi AC, Xuemin H, Tinelli R, Cicinelli E, et al. Relationship between prelabour uterine rupture and previous placenta previa diagnosis: case reports and review of literature. Ital J Gynaecol Obstet. 2022;34(1):48-53. doi: 10.36129/jog.34.01.08.
5. di Spiezio Sardo A, Saccone G, McCurdy R, Bujold E, Bifulco G, Berghella V. Risk of Cesarean scar defect following single- vs double-layer uterine closure: systematic review and meta-analysis of randomized controlled trials. Ultrasound Obstet Gynecol. 2017;50(5):578-83. doi: 10.1002/UOG.17401.
6. Poidevin Lo. The value of hysterography in the prediction of cesarean section wound defects. Am J Obstet Gynecol. 1961;81(1):67-71. doi: 10.1016/S0002-9378(16)36308-6.

7. Bij de Vaate AJ, Brölmann HA, van der Voet LF, van der Slikke JW, Veersema S, Huirne JA. Ultrasound evaluation of the Cesarean scar: relation between a niche and postmenstrual spotting. Ultrasound Obstet Gynecol. 2011;37(1):93-9. doi: 10.1002/uog.8864.
8. Naji O, Abdallah Y, Bij De Vaate AJ, Smith A, Pexsters A, Stalder C, et al. Standardized approach for imaging and measuring Cesarean section scars using ultrasonography. Ultrasound Obstet Gynecol. 2012;39(3):252-9. doi: 10.1002/UOG.10077.
9. van der Voet LF, Bij De Vaate AM, Veersema S, Brölmann HAM, Huirne JAF. Long-term complications of caesarean section. The niche in the scar: a prospective cohort study on niche prevalence and its relation to abnormal uterine bleeding. BJOG. 2014;121(2):236-44. doi: 10.1111/1471-0528.12542.
10. Vervoort AJMW, Uittenbogaard LB, Hehenkamp WJK, Brölmann HAM, Mol BWJ, Huirne JAF. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. Hum Reprod. 2015;30(12):2695-702. doi: 10.1093/HUMREP/DEV240.
11. Kremer TG, Ghiorzi IB, Dibi RP. Isthmocele: an overview of diagnosis and treatment. Rev Assoc Med Bras (1992). 2019;65(5):714-21. doi: 10.1590/1806-9282.65.5.714.
12. Tulandi T, Cohen A. Emerging Manifestations of Cesarean Scar Defect in Reproductive-aged Women. J Minim Invasive Gynecol. 2016;23(6):893-902. doi: 10.1016/j.jmig.2016.06.020.
13. Sipahi S, Sasaki K, Miller CE. The minimally invasive approach to the symptomatic isthmocele - what does the literature say? A step-by-step primer on laparoscopic isthmocele - excision and repair. Curr Opin Obstet Gynecol. 2017;29(4):257-65. doi: 10.1097/GCO.0000000000000380.
14. Wang CB, Chiu WWC, Lee CY, Sun YL, Lin YH, Tseng CJ. Cesarean scar defect: correlation between Cesarean section number, defect size, clinical symptoms and uterine position. Ultrasound Obstet Gynecol. 2009;34(1):85-9. doi: 10.1002/UOG.6405.
15. Tower AM, Frishman GN. Cesarean scar defects: an underrecognized cause of abnormal uterine bleeding and other gynecologic complications. J Minim Invasive Gynecol. 2013;20(5):562-72. doi: 10.1016/J.JMIG.2013.03.008.
16. Futyma K, Gałczyński K, Romanek K, Filipczak A, Rechberger T. When and how should we treat cesarean scar defect - isthmocoele? Ginekol Pol. 2016;87(9):664-8. doi: 10.5603/GP.2016.0063.
17. Raimondo G, Grifone G, Raimondo D, Seracchioli R, Scambia G, Masciullo V. Hysteroscopic treatment of symptomatic cesarean-induced isthmocele: a prospective study. J Minim Invasive Gynecol. 2015;22(2):297-301. doi: 10.1016/J.JMIG.2014.09.011.
18. Marotta ML, Donnez J, Squifflet J, Jadoul P, Darii N, Donnez O. Laparoscopic repair of post-cesarean section uterine scar defects diagnosed in nonpregnant women. J Minim Invasive Gynecol. 2013;20(3):386-91. doi: 10.1016/J.JMIG.2012.12.006.
19. Abacjew-Chmylko A, Wydra DG, Olszewska H. Hysteroscopy in the treatment of uterine cesarean section scar diverticulum: A systematic review. Adv Med Sci. 2017;62(2):230-9. doi: 10.1016/J.ADVMS.2017.01.004.
20. Kaur A AA. Isthmocele: a review of management options for this novel entity. Int J Human Heal Sci. 2019;3(3):127-33. doi: 10.31344/ijhhs.v3i3.90.
21. Roberge S, Demers S, Berghella V, Chaillet N, Moore L, Bujold E. Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis. Am J Obstet Gynecol. 2014;211(5):453-60. doi: 10.1016/J.AJOG.2014.06.014.
22. Fabres C, Aviles G, de la Jara C, Escalona J, Muñoz JF, Mackenna A, et al. The cesarean delivery scar pouch: clinical implications and diagnostic correlation between transvaginal sonography and hysteroscopy. J Ultrasound Med. 2003;22(7):695-700. doi: 10.7863/JUM.2003.22.7.695.
23. Pomorski M, Fuchs T, Rosner-Tenerowicz A, Zimmer M. Standardized ultrasonographic approach for the assessment of risk factors of incomplete healing of the cesarean section scar in the uterus. Eur J Obstet Gynecol Reprod Biol. 2016;205:141-45. doi: 10.1016/J.EJOGRB.2016.08.032.
24. Van der Voet LF, Vervoort AJ, Veersema S, Bijdevaate AJ, Brölmann HAM, Huirne JAF. Minimally invasive therapy for gynaecological symptoms related to a niche in the caesarean scar: a systematic review. BJOG. 2014;121(2):145-56. doi: 10.1111/1471-0528.12537.
25. Monteagudo A, Carreno C, Timor-Tritsch IE. Saline infusion sonohysterography in

nonpregnant women with previous cesarean delivery: the "niche" in the scar. J Ultrasound Med. 2001;20(10):1105-15. doi: 10.7863/JUM.2001.20.10.1105.
26. Thurmond AS, Harvey WJ, Smith SA. Cesarean section scar as a cause of abnormal vaginal bleeding: diagnosis by sonohysterography. J Ultrasound Med. 1999;18(1):13-6. doi: 10.7863/JUM.1999.18.1.13.
27. Laganà AS, Garzon S, Alkatout I, Hortu İ, Gitas G, Vitale SG, et al. Isthmocele: When Surgery Is Both the Problem and the Solution. J Invest Surg. 2022;35(1):231-2. doi: 10.1080/08941939.2020.1836692.
28. Regnard C, Nosbusch M, Fellemans C, Benali N, van Rysselberghe M, Barlow P, et al. Cesarean section scar evaluation by saline contrast sonohysterography. Ultrasound Obstet Gynecol. 2004;23(3):289-92. doi: 10.1002/UOG.999.
29. Morris H. Surgical pathology of the lower uterine segment caesarean section scar: is the scar a source of clinical symptoms? Int J Gynecol Pathol. 1995;14(1):16-20. doi: 10.1097/00004347-199501000-00004.
30. Bij De Vaate AJM, van der Voet LF, Naji O, Witmer M, Veersema S, Brölmann HAM, et al. Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review. Ultrasound Obstet Gynecol. 2014;43(4):372-82. doi: 10.1002/UOG.13199.
31. Setubal A, Alves J, Osório F, Guerra A, Fernandes R, Albornoz J, et al. Treatment for Uterine Isthmocele, A Pouchlike Defect at the Site of a Cesarean Section Scar. J Minim Invasive Gynecol. 2018;25(1):38-46. doi: 10.1016/J.JMIG.2017.09.022.
32. Vervoort AJMW, Vissers J, Hehenkamp WJK, Brölmann HAM, Huirne JAF. The effect of laparoscopic resection of large niches in the uterine caesarean scar on symptoms, ultrasound findings and quality of life: a prospective cohort study. BJOG. 2018;125(3):317-25. doi: 10.1111/1471-0528.14822.
33. Ofili-Yebovi D, Ben-Nagi J, Sawyer E, Yazbek J, Lee C, Gonzalez J, et al. Deficient lower-segment Cesarean section scars: prevalence and risk factors. Ultrasound Obstet Gynecol. 2008;31(1):72-7. doi: 10.1002/UOG.5200.
34. Gubbini G, Centini G, Nascetti D, Marra E, Moncini I, Bruni L, et al. Surgical hysteroscopic treatment of cesarean-induced isthmocele in restoring fertility: prospective study. J Minim Invasive Gynecol. 2011;18(2):234-7. doi: 10.1016/J.JMIG.2010.10.011.
35. Vikhareva Osser O, Valentin L. Risk factors for incomplete healing of the uterine incision after caesarean section. BJOG. 2010;117(9):1119-26. doi: 10.1111/J.1471-0528.2010.02631.
36. Liu SJ, Lv W, Li W. Laparoscopic repair with hysteroscopy of cesarean scar diverticulum. J Obstet Gynaecol Res. 2016;42(12):1719-23. doi: 10.1111/JOG.13146.
37. Roberge S, Boutin A, Chaillet N, Moore L, Jastrow N, Demers S, et al. Systematic review of cesarean scar assessment in the nonpregnant state: imaging techniques and uterine scar defect. Am J Perinatol. 2012;29(6):465-72. doi: 10.1055/S-0032-1304829.
38. Ahmadi F, Torbati L, Akhbari F, Shahrzad G. Appearance of uterine scar due to previous cesarean section on hysterosalpingography: various shapes, locations and sizes. Iran J Radiol. 2013;10(2):103-10. doi: 10.5812/IRANJRADIOL.5143.
39. Fonda J. Ultrasound diagnosis of caesarean scar defects. Australas J Ultrasound Med. 2011;14(3):22-30. doi: 10.1002/J.2205-0140.2011.TB00120.
40. Florio P, Filippeschi M, Moncini I, Marra E, Franchini M, Gubbini G. Hysteroscopic treatment of the cesarean-induced isthmocele in restoring infertility. Curr Opin Obstet Gynecol. 2012;24(3):180-6. doi: 10.1097/GCO.0B013E3283521202.
41. Mashiach R, Burke YZ. Optimal Isthmocele Management: Hysteroscopic, Laparoscopic, or Combination. J Minim Invasive Gynecol. 2021;28(3):565-74. doi: 10.1016/J.JMIG.2020.10.026.
42. Nirgianakis K, Oehler R, Mueller M. The Rendez-vous technique for treatment of caesarean scar defects: a novel combined endoscopic approach. Surg Endosc. 2016;30(2):770-1. doi: 10.1007/S00464-015-4226-6.
43. Krentel H, Lauterbach LK, Mavrogiannis G, de Wilde RL. Laparoscopic Fluorescence Guided Detection of Uterine Niche-The Next Step in Surgical Diagnosis and Treatment. J Clin Med. 2022;11(9):2657. doi: 10.3390/JCM11092657.
44. Vervoort AJMW, van der Voet LF, Hehenkamp WJK, Thurkow AL, van Kesteren PJM, Quartero H, et al. Hysteroscopic resection of a uterine caesarean scar defect (niche) in women with postmenstrual spotting: a randomised controlled trial. BJOG. 2018;125(3):326-34. doi: 10.1111/1471-0528.14733.

45. Zhang X, Yang M, Wang Q, Chen J, Ding J, Hua K. Prospective evaluation of five methods used to treat cesarean scar defects. Int J Gynaecol Obstet. 2016;134(3):336-9. doi: 10.1016/J.IJGO.2016.04.011.
46. Tahara M, Shimizu T, Shimoura H. Preliminary report of treatment with oral contraceptive pills for intermenstrual vaginal bleeding secondary to a cesarean section scar. Fertil Steril. 2006;86(2):477-9. doi: 10.1016/J.FERTNSTERT.2006.01.020.
47. Gubbini G, Casadio P, Marra E. Resectoscopic correction of the "isthmocele" in women with postmenstrual abnormal uterine bleeding and secondary infertility. J Minim Invasive Gynecol. 2008;15(2):172-5. doi: 10.1016/J.JMIG.2007.10.004.
48. Florio P, Gubbini G, Marra E, Dores D, Nascetti D, Bruni L, et al. A retrospective case-control study comparing hysteroscopic resection versus hormonal modulation in treating menstrual disorders due to isthmocele. Gynecol Endocrinol. 2011;27(6):434-8. doi: 10.3109/09513590.2010.495431.
49. Tantini C, Viana GA, Gubbini G. Cesarean scar defects: Hysteroscopic treatment of isthmocele in menstrual disorders and infertility. Minimally Invasive Gynecology. Springer, Cham. 2018:181-91. doi: 10.1007/978-3-319-72592-5_16.
50. Jha S, Surabhi K. Hysteroscopy "As one stop approach" in the management of intrauterine pathology. Focus on patient's satisfaction. Ital J Gynaecol Obstet. 2021;33(2):102-9. doi: 10.36129/jog.33.02.04
51. Chang Y, Tsai EM, Long CY, Lee CL, Kay N. Resectoscopic treatment combined with sonohysterographic evaluation of women with postmenstrual bleeding as a result of previous cesarean delivery scar defects. Am J Obstet Gynecol. 2009;200(4):370.e1-370.e4. doi: 10.1016/J.AJOG.2008.11.038.
52. Li C, Guo Y, Liu Y, Cheng J, Zhang W. Hysteroscopic and laparoscopic management of uterine defects on previous cesarean delivery scars. J Perinat Med. 2014;42(3):363-70. doi: 10.1515/JPM-2013-0081.
53. Fabres C, Arriagada P, Fernández C, MacKenna A, Zegers F, Fernández E. Surgical treatment and follow-up of women with intermenstrual bleeding due to cesarean section scar defect. J Minim Invasive Gynecol. 2005;12(1):25-8. doi: 10.1016/J.JMIG.2004.12.023.
54. Harper LM, Macones GA. Predicting success and reducing the risks when attempting vaginal birth after cesarean. Obstet Gynecol Surv. 2008;63(8):538-45. doi: 10.1097/OGX.0B013E31817F1505.
55. Casadio P, Gubbini G, Morra C, Franchini M, Paradisi R, Seracchioli R. Channel-like 360° Isthmocele Treatment with a 16F Mini-Resectoscope: A Step-by-step Technique. J Minim Invasive Gynecol. 2019;26(7):1229-30. doi: 10.1016/j.jmig.2019.04.024.
56. Szafarowska M, Biela M, Wichowska J, Sobociński K, Segiet-święcicka A, Doniec J, et al. Symptoms and Quality of Life Changes after Hysteroscopic Treatment in Patients with Symptomatic Isthmocele-Preliminary Results. J Clin Med. 2021;10(13):2928. doi: 10.3390/JCM10132928.
57. Api M, Boza A, Gorgen H, Api O. Should Cesarean Scar Defect Be Treated Laparoscopically? A Case Report and Review of the Literature. J Minim Invasive Gynecol. 2015;22(7):1145-52. doi: 10.1016/J.JMIG.2015.06.013.
58. Donnez O, Donnez J, Orellana R, Dolmans MM. Gynecological and obstetrical outcomes after laparoscopic repair of a cesarean scar defect in a series of 38 women. Fertil Steril. 2017;107(1):289-96.e2. doi: 10.1016/J.FERTNSTERT.2016.09.033.
59. Laganà AS, Pacheco LA, Tinelli A, Haimovich S, Carugno J, Ghezzi F, et al. Optimal Timing and Recommended Route of Delivery after Hysteroscopic Management of Isthmocele? A Consensus Statement From the Global Congress on Hysteroscopy Scientific Committee. J Minim Invasive Gynecol. 2018;25(4):558. doi: 10.1016/j.jmig.2018.01.018.
60. de Albornoz AVC, Carrasco IL, Pastor NM, Blanco CM, Matos MM, Pacheco LA, et al. Outcomes after Hysteroscopic Treatment of Symptomatic Isthmoceles in Patients with Abnormal Uterine Bleeding and Pelvic Pain: A Prospective Case Series. Int J Fertil Steril. 2019;13(2):108-12. doi: 10.22074/IJFS.2019.5704.
61. Enderle I, Dion L, Bauville E, Moquet PY, Leveque J, Lavoue V, et al. Surgical management of isthmocele symptom relief and fertility. Eur J Obstet Gynecol Reprod Biol. 2020;247:232-7. doi: 10.1016/J.EJOGRB.2020.01.028.
62. Kalem Z, Kaya AE, Bakırarar B, Basbug A, Kalem MN. An Optimal Uterine Closure Technique for Better Scar Healing and Avoiding Isthmocele in Cesarean Section: A Randomized Controlled Study. J Invest Surg. 2021;34(2):148-56. doi: 10.1080/08941939.2019.1610530.