

Role of Hysteroscopic Resection and Laparoscopic Repair in Treatment of Women with Cesarean Scar Defect

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Abstract:

Cesarean Scar Defect is a reservoir-like pouch defect on the anterior wall of the uterine isthmus located at the site of a previous cesarean delivery scar. The flow of menstrual blood through the cervix may be slowed by the presence of Cesarean Scar Defect, as the blood may accumulate in the niche because of the presence of fibrotic tissue, causing pelvic pain in the suprapubic area. Moreover, persistence of the menstrual blood after menstruation in the cervix may negatively influence the mucus quality and sperm quality, obstruct sperm transport through the cervical canal, interfere with embryo implantation, leading to secondary infertility. The removal of the local inflamed tissue may be performed by laparoscopic, combined laparoscopic-vaginal, or vaginal surgery, and operative hysteroscopy, a minimally invasive approach to improve symptoms and restore fertility.

Keywords: Hysteroscopic, Laparoscopic, Cesarean Scar Defect.

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Introduction:

The management should be guided by the severity and type of symptoms. Both medical and surgical methods have been described for the management of niche. The definitive management remains surgical with excision and repair of the uterine defect by laparotomy, laparoscopy, hysteroscopy or by a vaginal approach (1).

Medical treatment is the best for women with niche who do not desire to get pregnant seems to be oral contraception. (2), have published a survey on the role of oral contraceptives with estrogen and progesterone in 18 patients and have found it to be effective regarding the duration of flow (reducing from 10 days to 5 days). Other authors have also described oral contraceptives to be efficacious in reducing bleeding disorders. (3), have described less bleeding and less pain after the use of oral contraceptives or hysteroscopic resection with better results in women undergoing hysteroscopic correction compared with oral contraceptives. The usage of an intrauterine device with levonorgestrel has not shown a benefit in these women (4).

❖ **Surgical Management**

Vaginal Reconstruction:

Transvaginal repair surgery was performed under general anesthesia. Patients were placed in a dorsal lithotomy position and the bladder emptied before the surgery. For hydro-dissection and hemostasis, adrenaline (1:200,000) was injected into the vesicocervical space. A transverse incision was made at the anterior cervicovaginal junction. The bladder was then dissected away from the uterus and retracted upward by the anterior drawing hook. The location of the uterine defect was determined under the guidance of a probe in the uterus (5).

A transverse incision was then made at the most prominent area of the defect, and the defect was removed. Subsequently, an interrupted horizontal transverse figure-8-pattern suture was used for the first layer of closure with 0 absorbable sutures (6). The mattress suture was used in the second layer, and the vaginal epithelium was then continuously sutured using 0 absorbable sutures. Finally, the vagina was packed with 2 pieces of iodoform gauze, which were removed after 24 to 48 hours. Zhang et al. reported no complications (14 patients). This technique requires surgical expertise to avoid damaging the surrounding organs. It also necessitates that the niche is not too high or vaginal correction would be difficult (7). Outcomes show that menstruation duration diminishes after treatment and myometrial thickness increases. Most patients experience symptom relief. Zhang et al and Xie et al have noted a resulting 22% pregnancy rate (8).

Laparoscopic management of the niche:

The first laparoscopic niche repair was carried out Jacobson et al in 2003 (8). Women with a residual myometrial length less than 3mm, and desirous of future pregnancy are ideal candidates for laparoscopic management. Its great advantage over hysteroscopic resection remains that this is reparative surgery, where the myometrial thickness was restored. A major difficulty in performing the procedure laparoscopically is that the defect may not be very evident when seen laparoscopically and hysteroscopic guidance may be required many times to localize the defect. Therefore, first, the defect is recognized hysteroscopically, marked with the help of Hegar dilator or by translucency of a 5 mm hysteroscope and then the surgery is proceeded laparoscopically (9).

The bladder is then dissected from the uterus and the niche is opened and excised. Next, all fibrotic tissue in the uterine scar is excised in order to enable proper wound healing. Then, the myometrium is sutured in one or two layers. The use of an adhesion barrier can be applied in order to reduce reformation of adhesions. The effect on the niche is evaluated after surgery by hysteroscopy. A urinary Foley's catheter is generally removed after approximately 6-12 hours (10).



Figure 1: Laparoscopic tissue removal, a view of the vesicouterine pouch with scar tissue being pulled and resected (11).

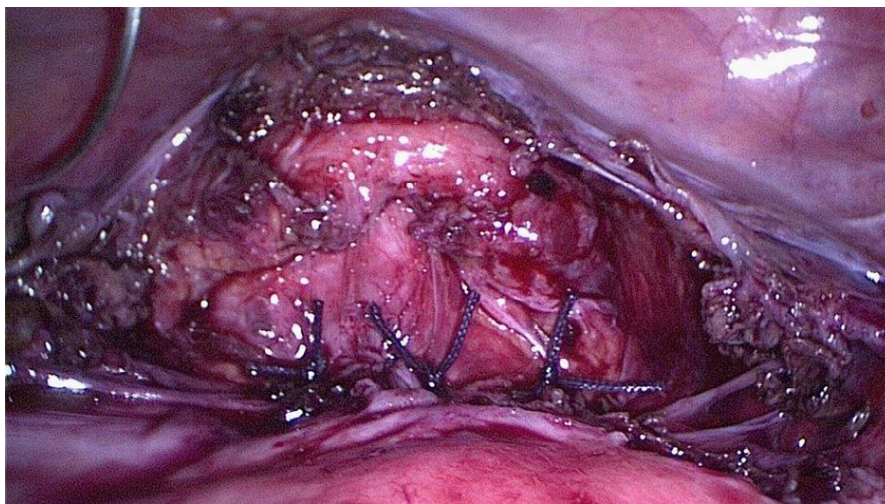


Figure 2: Laparoscopic suturing of the defect after Cesarean Scar Defect resection (12).

Operative Hysteroscopy:

Hysteroscopic resection was first introduced in 1996 by Fernandez et al. As known Hysteroscopy is the gold standard procedure for uterine cavity and cervical canal exploration and is the investigation of choice for AUB (13).

During the hysteroscopy, the Cesarean Scar Defect appears as a doming on the anterior wall of the cervical canal, easy to be localized on the isthmus site. Once diagnosed, an operative hysteroscopy can be performed to treat the defect, with a technique called isthmoplasty (14). According to the literature, the essential parameter to perform hysteroscopy is the residual myometrial thickness; indeed, with the hysteroscopic approach, there is a risk of bladder injury and uterine perforation if the myometrium thickness at the site of the defect is < 3 mm. (15).

Some authors suggest hysteroscopy to women with a residual myometrial thickness > 2 to 2.5 mm or with a scar defect size to myometrial thickness ratio $< 50\%$ and with no desire to get pregnant (16).

There is no homogeneous method to perform isthmoplasty, but almost every author uses a 9 mm resectoscope and unipolar electrical current. Gubbini et al. (17) performed a resection of

the defect by removing the Cesarean Scar Defect edges and by putting its wall in continuity with the cervical canal wall.

Fabres et al. (18) resected one edge of the scar and coagulated the thinnest part of the defect, allowing menstrual flow drainage to the cervix. Xie et al. (6) who published one of the largest studies on isthmoplasty, performed it by simply removing the fibrotic tissue under the defect. As reported by Abacjew-Chmylko et al. (15), some authors prefer to perform resectoscopy under ultrasonographic guidance, but this approach is not related to a lower morbidity rate. (15)

the mean time for resectoscopic treatment varies from 8 to 25 minutes. Li C et al. (19). Gubbini et al. (20) and Florio et al. (3) found an association between the duration of the isthmoplasty and the size of the niche.

The total amount of successful outcomes of isthmoplasty is 85.5% (59.6–100%). An evident attenuation of the symptoms was associated not only with the removal of the scar diverticulum, in which the menstrual blood tends to be retained, but also with the fulguration of dilated vessels that constitute a potential additional source of non-menstrual bleeding (15).

Good outcomes were also found regarding infertility: the majority of patients who desired to get pregnant conceived spontaneously between 12 and 24 months after the isthmoplasty (17).

According to Zhang et al. (21) the comparison between hysteroscopy and medical treatment, intrauterine device (IUD), laparoscopy, and vaginal repair showed that hysteroscopic surgery offered the advantages of shorter operation time, reduced blood loss, decreased length of hospital stay, and lower hospital fees. However, one of the limitations of the resectoscopic treatment is the impossibility of the performance of sutures (22).

This is why the scar defect could enlarge further, and the myometrial thickness at the level of the uterine isthmus could further decrease, increasing the risk of uterine rupture during future pregnancies (23).

In 2015, a Dutch, high-quality, multicentre, randomised control trial of hysteroscopic niche resection (HysNiche trial: Dutch Trial Register NTR3269) was established. The primary aim was to assess the impact of hysteroscopic resection on persistence of postmenstrual spotting (24).

Participants were randomly assigned to hysteroscopic niche resection or expectant management. In all cases, patients underwent baseline evaluation by sonohysterography with re-evaluation at 6 months. Inclusion criteria were a sonohysterographically confirmed defect of at least 2 mm in depth associated with at least a residual myometrium of 3 mm or more. (24). Significant improvements were reported in number of days of postmenstrual spotting (4 versus 7 days; $P = 0.04$) and in postmenstrual spotting-associated pain ($P = 0.02$). (24).

Proximal and Distal Correction vs Distal Correction Alone

Most surgeons carry out the procedure of a triangular resection with a resectoscope. This approach could theoretically eliminate symptoms more effectively than only distal correction but could potentially harm the internal os, which is usually difficult to locate.

In 2009, **Chang et al**(25) showed that resection of the cervical edge of the Cesarean Scar Defect is just as effective as resecting both edges without the risk of perforation or bladder injury. Following this technique, **Feng et al. (16)** and **Raimondo et al. (26)** obtained similar results.

Casadio et al. (27) published a case report on a new technique for hysteroscopic repair include channel like 360 degree ablation of the lower edge of the niche together with the opposite posterior endocervix using miniaturized hysteroscopy in 3 steps:

- **Step1:** resection of the posterior endocervix (allow paraphysiological creeping of the endocervical mucosa to cover the denuded surface)
- **Step 2:** resection of the lower edge of the niche
- **Step 3:** ball electrode coagulation of any remaining fibrosis and hemostasis

This technique is based on the rational that anterior inflamed niche will cause posterior wall inflammation.

Cohen et al. (28) studied repeated hysteroscopic resection of niche and found 8 patients underwent a second hysteroscopy after failure of the first hysteroscopy. Abnormal uterine bleeding (AUB) was the most common symptom, occurring in all patients. The average number of days of bleeding per cycle were significantly reduced following the second surgery [14.50 (range 8-21days) vs 11.75 (range 8-20days), respectively =0.009].

The second surgery improved symptoms in 6 out of the 8 patients with AUB and 1 of 2 patients with pain. There were no significant differences in fertility and obstetric outcomes between the first and the second surgery and no complications were reported during any of the surgeries (28).

There is no doubt that laparoscopic repair increases the residual myometrial thickness, but there were lots of debate about the effect of hysteroscopy on RMT. **Tsuji et al. (29)** studied 18 patient. RMT was thicker after hysteroscopic surgery (median: 2.1 mm and 4.2 mm, before and after surgery, respectively; $P = 0.0001$). Cesarean Scar Defect volume was significantly reduced after hysteroscopic surgery.

Regarding pregnancy outcome, **Tsuji et al. (30)** studied 38 women with secondary infertility due to Cesarean scar niche who underwent hysteroscopic surgery. Patients were followed up for 3 to 40 months after surgery. Surgery was successful in all cases and no complications were observed. Twenty-seven patients (71%) became pregnant (pregnant group), while 11 (29%) did not (non-pregnant group).

Baseline characteristics of age, body mass index, gravidity, parity, previous cesarean section, presence of endometriosis, retroflex uterus, and preoperative residual myometrial thickness were not significantly different between the groups. However, the median residual myometrium thickness was significantly higher after surgery than before surgery in the pregnant group (1.9 [1.1-

3.6] vs 4.9 [3.4-6.6] mm, $P < 0.0001$), whereas this difference was not significant in the non-pregnant group (30).

Of those who became pregnant, 85% conceived within 2 years of surgery. Although three pregnancies resulted in abortion 23 pregnancies resulted in healthy babies at 35-38 gestational weeks by scheduled cesarean sections with no obstetrical complications due to hysteroscopic surgery (30).

Most authors treated symptomatic Cesarean Scar Defects with hysteroscopy. Niche resection by hysteroscope is the least invasive of these techniques, but requires a sufficient thick residual myometrium between the niche and the bladder is sufficiently thick to prevent bladder injury. Early detection of impending bladder perforation can be done by instillation of methylene blue dye in the bladder before the procedure. Likewise, simultaneous ultrasonography can be performed to detect bladder injury (31).



Figure 3: The location of the niche by hysteroscopy. With bipolar resectoscopy, endometrial and scar tissue surrounding the niche is removed (32).

The cut-off value of the residual myometrium in various studies varies between 2.5 and 4.0 mm, as measured using sonohysterography. Cervical dilation was performed using Hegar dilators. A hysteroscopic niche resection can be performed in different ways; the distal rim can be resected to facilitate menstrual outflow, both distal and proximal part of the niche can be resected and it can be combined with coagulation of the vessels in the niche or the entire niche surface to prevent bleeding from the fragile vessels. The entire fibrotic part of the scar should be removed and the muscular part has been reached. The niche surface will be superficially coagulated (33).

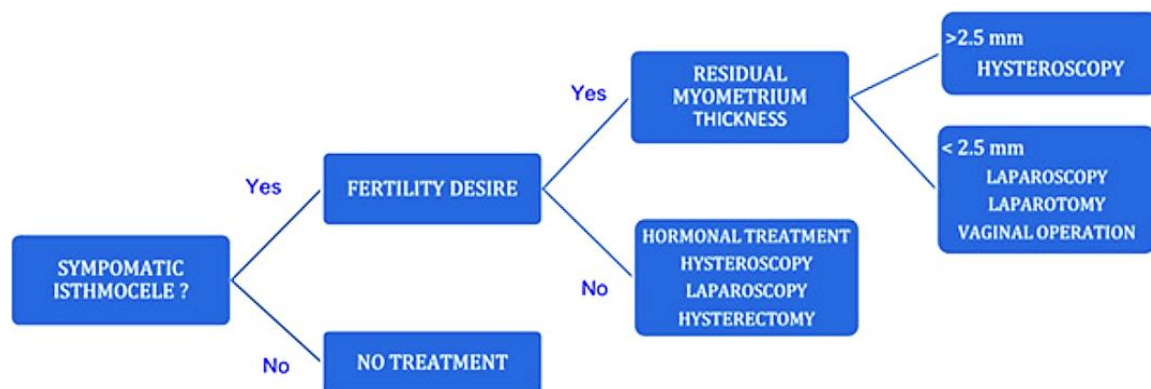


Figure 4: Clinical classification and treatment of Cesarean Scar Defect in according to flow chart for the treatment of Cesarean Scar Defect in women with AUB and infertility (34).

Laparotomic Reconstruction:

The principles followed are similar to laparoscopic reconstruction but the disadvantage is that patient has to undergo repeated laparotomies and the associated complications (35).

Hysterectomy:

For some women, it may be the treatment of choice especially if future fertility is not desired and other associated conditions are present for which hysterectomy might be indicated (35).

❖ Postoperative Advice:

It is advisable for a woman to use contraception during the first 6 months. After six months women are allowed to conceive. There is no solid evidence of the minimal required period for healing of the uterine wound to host a subsequent pregnancy (10).

❖ Outcomes of Surgical Management of Post-Cesarean Niche:

Hysteroscopic niche resection reduces post-menstrual spotting by a median of 3.8 days, with complete resolution of AUB in 72.4% cases and pain improvement in 97%. AUB gets cured in 87.5% patients within first month and 96.8% patients in the second month after surgery. Up to 5% patients may have recurrence (36).

After laparoscopic repair, **Donnez et al. (37)** reported 93% symptom-free patients, increase in mean myometrial thickness from 1.4 to 9.6 mm at 3-month follow-up, 44% pregnancy rate in infertile women, all delivered at full term by elective Cesarean. Pregnancy rate varied from 22–71% in various studies. **Calzolari et al. (38)**, in a retrospective study (n=35), noted niche as the primary cause of infertility in 45.7% (16/35) patients; all 16 women were relieved of AUB and pain, and 9/16(56.3%) conceived after hysteroscopic isthmoplasty.

In (39) study of 101 women with large niche and <3 mm RMT treated laparoscopically, 79% had symptom relief, post-menstrual spotting reduced by 7 days at 6 months, dysmenorrhea reduced, myometrial thickness increased, and overall, 83.3% women felt very satisfied.

Women who failed to conceive had higher BMI, higher niche grade, higher number of prior Cesareans and advanced age. **Enderle** reported poor obstetric outcomes in his retrospective

series of 18 surgically treated women, with approximately 55% miscarriages; hysteroscopy had poorer results as miscarriage occurred in 3/4 patients. One patient who underwent transvaginal repair delivered vaginally; others underwent Cesarean (40). Another study reported pregnancy rate of 71% as 10/14 infertile women conceived including six spontaneous pregnancies after laparotomy, laparoscopy or vaginal approach; eight had Cesarean; one had vaginal delivery, and one aborted, with no case of placenta accreta or rupture (41).

➤ **Niche and Impaired Fertility**

In addition to the gynecological symptoms, in theory, niches may impair subsequent fertility. It has been reported that a niche can reduce the chances of embryo implantation and may lead to spontaneous miscarriages if the implantation is close to or in the niche (42). A meta-analysis reported that a Cesarean Section reduces the probability of subsequent pregnancy by 10% [relative risk (RR) 0.91; 95% 0.87–0.95] on average, compared with a previous vaginal delivery (43).

So far, the most intriguing questions are: does a niche impair fertility and what underlying mechanism has been studied insufficiently? Based on the limited available evidence in the recent literature reviewed, combined with **Visser, Hehenkamp, et al.** observations during sonographic hysteroscopic evaluation and laparoscopic niche repair, they postulate further hypotheses to explain the association between subfertility and the presence of a niche, and to define the knowledge gaps for future research perspectives (44).

❖ **Hypothesis 1: niche-related accumulation of intrauterine fluid impairing implantation**

The accumulation of intracavitary fluid related to the niche may impair embryo implantation, which is in line with the known negative effect of intrauterine fluid in women with hydrosalpinx. Implantation within the normal endometrium is a precisely timed and complex process that could be affected by interference of intrauterine fluid film covering the endometrium. This fluid may play an important role in luminal closure to ‘lock’ the embryos in the right locations (45).

Accumulation of fluid is seen in approximately 42% of patients with a large niche. This may impair pregnancy outcomes due to reduced implantation yet may also be embryotoxic “degradation of hemoglobin in the uterine cavity, resulting in a higher iron exposure, which is known to be embryotoxic”. Future studies are needed to assess the effect on implantation of intrauterine fluid related to a niche and the additional value of surgical interventions on fertility outcomes. Whether removal of the fluid immediately before embryo transfer in women with a niche affects pregnancy outcomes is not known either (46).

Table 1: Overview of hypotheses on the intermediate role of the niche on fertility outcomes (44)

Hypothesis
Detrimental environment for sperm penetration and implantation
1. Niche-related accumulation of intrauterine fluid impairing implantation
2. Altered immunobiology and/or increased inflammation when a niche is present
3. Distorted contractility of the uterus caused by fibrosis or interruption of the myometrial layer at the site of the niche
4. Accumulation of mucus and old blood in the niche, which may impair sperm penetration
Physical barrier for embryo transfer and implantation
5. A large niche in combination with a strongly retroflexed uterus impairs accessibility for an eventual embryo transfer due to a distorted anatomy
Psychogenic causes that reduce the likelihood of pregnancy
6. Niche-related gynecological symptoms may interfere with sexual intercourse, and focused therapies for niche complaints may interfere with opportunities to conceive during the convalescence period

❖ **Hypothesis 2: altered immunobiology and/or increased inflammation when a niche is present**

In Naji et al. (47) cohort study evaluating the site of implantation using Transvaginal Ultrasound during early pregnancy in 380 women after a Cesarean Section concluded that the site of implantation is affected by the presence of a niche. The distance between implantation site and scar was related to the risk of spontaneous miscarriage. Implantation very close to or in the niche resulted in miscarriage in seven out of eight pregnancies. Implantation was also seen more frequently in the posterior part of the uterus. It appears that a niche is not a favorable site for implantation. Alternatively, differences in angiogenesis or inflammatory response of the endometrium influenced by regeneration of the uterine wound may play a role (48).

❖ **Hypothesis 3: distorted contractility of the uterus caused by fibrosis or interruption of the myometrial layer at the site of the niche**

The non-pregnant uterus shows myometrial contractile activity throughout the menstrual cycle. These contractions originate in the subendometrial myometrium and are controlled by steroids. It has been previously reported that throughout the menstrual cycle endometrial wavelike

activity patterns of the uterus with adequate wave patterns appear to be related to successful reproduction in natural cycles and assisted reproduction (45). Contractile waves from fundus to cervix are predominantly seen in the follicular phase and they disappear after ovulation or hCG administration. The pattern is essentially reversed in the luteal phase. It recurs in a similar fashion from cycle to cycle (49).

A niche involves a discontinuity at the site of a previous Cesarean scar. The uterine incision during a Cesarean Section is generally made transversely in the lower uterine segment and could lead to poor contractility of the uterine muscle around the scar and the accumulation of fluid in the defect. This is in line with the reduced thickness of the residual myometrium that is observed in the majority of patients after a Cesarean Section (50). An observational prospective study reported a significant decrease in muscular density in the myometrium covering the defect compared with the adjacent myometrium on histological exams after laparoscopic repair (51).

It is possible that in women with a niche, normal wave patterns are disturbed by uncoordinated or impaired uterine contractions during the menstrual cycle, which could lead to a lower implantation rate (44).

❖ **Hypothesis 4: accumulation of mucus and old blood in the niche, which may impair sperm penetration**

The mucus and fluid accumulation in these large niches and uterus may impair penetration of sperm cells and thus embryo implantation. The presence of blood in the cervix may cause impaired sperm-mucus interaction for immunological reasons. This cervical hostility was defined in terms of an abnormal or negative postcoital test due to absence of forward-progressing spermatozoa (48). The composition of the fluid and mucus accumulation has not yet been studied.

This factor may be less relevant in case of IUI or IVF if the barrier has already been overcome by the intrauterine catheter. Even in these situations, pregnancy outcomes remain lower, indicating the impairment of implantation to be an independent factor (49).

❖ **Hypothesis 5: a large niche in combination with a strongly retroflexed uterus impairs accessibility for an eventual embryo transfer due to a distorted anatomy**

Assisted reproductive techniques are widely used for the treatment of subfertility. A few women have been referred to OB-GYN department due to the inability to achieve an embryo transfer because of a large niche and a distorted anatomy. Sometimes a niche in combination with a strongly retroflexed uterus and/or a complex niche may hamper the insertion of an insemination or embryo transfer catheter. In rare cases, even under ultrasound guidance, it is impossible to enter the uterine cavity. In such cases, a laparoscopic niche resection to restore the anatomy for embryo transfer could be considered (52).

Embryo transfer can become problematic due to a distorted anatomy resulting from a large niche. Even under ultrasound guidance, the catheter may be placed into the niche more easily than into the uterine cavity. Two studies reported that embryo transfer in women with a history of a prior Cesarean Section, compared to women with a prior vaginal delivery, took longer and was more likely to have blood or mucus in the catheter (53, 54).

- ❖ **Hypothesis 6: niche-related gynecological symptoms may interfere with sexual intercourse, and focused therapies for niche complaints may interfere with opportunities to conceive during the convalescence period**

Approximately 60% of women have a niche after Cesarean Section, and approximately 30% of them experience postmenstrual spotting. The spotting can occur unpredictably during the menstrual cycle. According to Interviews and Focus Group Discussions among symptomatic women with a niche, the most commonly reported factor is that the lack of predictability of bleeding/spotting after normal menstruation makes these women feel insecure and gives them a sense of uncleanliness, frequently associated with shame and failure, which affects their sexual behaviour and arousal (55).

Some studies report a negative association between abnormal uterine bleeding or spotting and the sexual behaviour of both men and women. The presence of vaginal bleeding or spotting is associated with a decrease in genital sexual behaviours. The majority of men and women ($n = 287$) (60% of the men and 54% of the women) avoid sexual relations during vaginal spotting, reducing the chances of conception. In this group, 20% considered therapy because of the impact on their wellbeing (18%) or sexual functioning (21%) (56).

Various other conservative and surgical therapies are applied in order to treat niche-related gynecological symptoms, such as abnormal bleeding patterns, dysmenorrhea, chronic pelvic pain and dyspareunia. A very recent large prospective cohort study ($n = 146$) showed that laparoscopic niche resection improved most subdomains of a quality-of-life questionnaire, including the physical, mental and pain domains, all of which may impact sexual functioning (55).

Still, most treatments aiming to reduce symptoms, such as hormonal therapies, endometrial ablation or hysterectomies, interfere with future reproductive potential. In addition, with a laparoscopic niche repair both the waiting time for surgery and the time needed for uterine scar healing (generally 6 months after repair is advised) cause a delay in the resumption of reproductive activities (48).

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