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REVIEW

Surgical Treatment of Adenomyosis

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Abstract

Purpose of Review Adenomyosis is defined as the presence of endometrial tissue within the myometrium. The aim of the review is to describe contemporary surgical approaches for adenomyosis.

Recent Findings Hysterectomy has been standard practice for the treatment of adenomyosis for many years. However, uterine-sparing interventions have emerged recently allowing patients to retain or even enhance their fertility. If there is no wish for further fertility and no desire for uterine preservation, hysterectomy with bilateral salpingectomy is the gold standard treatment for symptomatic adenomyosis. Otherwise, the objectives of surgery are (a) to remove most (ideally the whole) of the adenomyotic tissue, (b) to preserve the integrity of the endometrial cavity, (c) to reconstruct the uterus, and (d) to preserve the functionality of the ovaries and the tubes. The following surgical methods have been proposed for uterus-sparing treatment of adenomyosis: classical excision of adenomyotic tissue after a single incision of the uterus, wedge resection, double- or triple-flap method, transverse H incision, and the PUSH technique. Post-operative clinical outcomes are in favor of fertility-sparing surgery of adenomyosis. The reduction of dysmenorrhea after uterus-sparing surgery for adenomyosis ranges from 54.6 to 84.6%. The reduction of menorrhagia ranges from 50.0 to 73.7%. The total delivery rate in patients who have undergone any uterus-sparing surgery for adenomyosis is 46.9%.

Summary In conclusion, hysterectomy has traditionally been the primary treatment for adenomyosis in women. However, contemporary medicine offers several excisional and non-excisional techniques for patients who wish to preserve their fertility.

Keywords Adenomyosis · Adenomyoma · Fertility-sparing treatment · Uterine-sparing surgery · Reproductive outcome

Introduction

Uterine adenomyosis is the condition in which endometrial epithelial and stromal cells are located inside the myometrium [1]. Women suffering from adenomyosis present with a variety of symptoms, most commonly dysmenorrhea, abnormal uterine bleeding (AUB-A according to FIGO), chronic pelvic pain, and infertility [2–4]. In some cases, adenomyosis is asymptomatic and is incidentally suspected with transvaginal sonography during a routine examination. Adenomyosis is often diagnosed while investigating patients for causes of infertility; it is associated with lower pregnancy rates, higher rates of miscarriage as well as pregnancy complications such as preeclampsia, fetal growth restriction (FGR), and low birth weight [5].

Etiology and Pathophysiology

Recently, with the advances in radiology and magnetic resonance imaging in particular, it has been revealed that there is a layer of cells called the inner myometrium (IM) or junctional zone (JZ) that separates the two layers of tissue. During the development of the embryo, the endometrium and the IM arise from the Mullerian ducts, while the outer myometrium (OM) is of mesenchymal origin [6]. Differences in imaging (MRI or ultrasound) of the JZ are used in the diagnosis of adenomyosis. In the past, adenomyosis was a histologic diagnosis in specimens of hysterectomy. Nowadays, histologic diagnosis remains the gold standard; however, uterine-sparing surgical techniques allow us to preserve the fertility of the patient and even improve the reproductive outcome.

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The pathogenesis of adenomyosis is not perfectly understood; however, several mechanisms have been proposed although none of these have been definitively established. There is the theory of the invasion of endometrial basalis into the myometrium, crossing an abnormal JZ due to tissue injury/repair and establishing adenomyotic lesions inside the myometrial wall [7]. Another theory suggests that adenomyosis forms where there is a trauma between the endometrial-myometrial interface [8]. This theory is supported by the fact that adenomyosis is more common in women who have sustained uterine trauma from curettage, uterine surgery, or cesarean section, but it does not explain adenomyosis in nulliparous women with no history of uterine trauma. The third theory suggests that the ectopic endometrium derives from the metaplasia of embryonic epithelial remnants [9]. Finally, like endometriosis, there is the theory that retrograde menstruation may also result in the deposition of adult stem cells into the myometrium and result in outside-to-inside invasion [10].

Epidemiology

The prevalence of adenomyosis is difficult to pinpoint because there is a large variation in the clinical manifestations of the disease with patients ranging from asymptomatic to having severe symptoms. In the past, the histological examination of the specimens after hysterectomy was the only way to diagnose the disease. As a result, the estimates are restricted to women undergoing hysterectomy, so their symptoms were likely more severe, and they were probably of older age and had no interest in preserving fertility. Even so, the estimated prevalence ranged from 8.8 to 61.5% [11••]. This wide range is the result of the lack of standardized criteria for diagnosis in histopathologic specimens as well as in imaging techniques [12]. A study of 1252 hysterectomy histological reports in Maryland showed uterine adenomyosis ranging from 12 to 58% and varied between pathologists from 10 to 88% [13]. These data show that adenomyosis is either under or overdiagnosed. With the advances in imaging techniques in recent years, it is now possible to diagnose adenomyosis in women prior to surgery. A study of 985 women who attended a general gynecological clinic in a university teaching hospital in London showed that 206 of them had sonographic findings consistent with adenomyosis (29.9%) using transvaginal ultrasound [14]. This percentage however is likely to be a bit higher than in the general population as these were symptomatic women who entered the clinic.

Surgical Treatment of Adenomyosis

Therapeutic Options

The standard treatment for adenomyosis has been hysterectomy, but, given the desire of many affected women to conceive, further medical and surgical approaches have slowly started to emerge.

Classification of Surgical Techniques

After diagnosis, there are two crucial issues that need to be addressed during the management of women with adenomyosis: (a) the wish to conceive, (b) the wish to preserve the uterus. Time has proven that adenomyosis is a non-malignant condition; therefore, this needs to be explicitly communicated with the patient and then to proceed to inform decision-making [15].

If there is no wish for further fertility and no wish for uterine preservation, hysterectomy with bilateral salpingectomy is the gold standard treatment for symptomatic adenomyosis (Fig. 1). The surgeon and patient will elect the method of choice (laparoscopic, robotic, open laparotomy, or vaginal), and the treatment will be definitive [16].

If the patient suffers from subfertility or wishes to preserve the uterus, the objective of the surgery is (a) to remove most (ideally tall) of the adenomyotic tissue, (b) to preserve the integrity of the endometrial cavity, (c) to reconstruct the uterus aiming to an anatomic result, and (d) to preserve the functionality of the ovaries and, if possible, the tubes. The control of symptoms is mainly achieved by the removal of the bulk of adenomyosis. The feasibility of a spontaneous pregnancy is achieved by keeping the endometrial cavity without permanent post-operative lesions. Therefore, the role of the technique is very important and the choice of it should depend on the pre-operative sonographic and MRI evaluation, as well as on the intra-operative findings [15].

In the majority of adenomyosis cases, the lesion typically exhibits some level of myometrial infiltration, ranging from minor to significant. During the excision of the lesion in these cases, the removal of healthy myometrial tissue is an inevitable consequence. It appears reasonable to propose that any categorization of the existing surgical techniques for excising adenomyosis should primarily consider the extent to which adjacent healthy myometrium is removed and the preservation of the structural integrity and, consequently, the functionality of the uterine wall. Surgical techniques can be classified into three main groups: complete excision of the adenomyotic tissue, partial excision, and non-excisional techniques.

Complete excision is typically possible in cases of focal adenomyosis, often in the form of adenomyomas. The preferred surgical method is adenomyomectomy, similar to leiomyomectomy, maintaining the integrity of the uterine wall as much as possible. Adenomyomectomy, a surgical procedure first introduced by Hyams in 1952, has seen

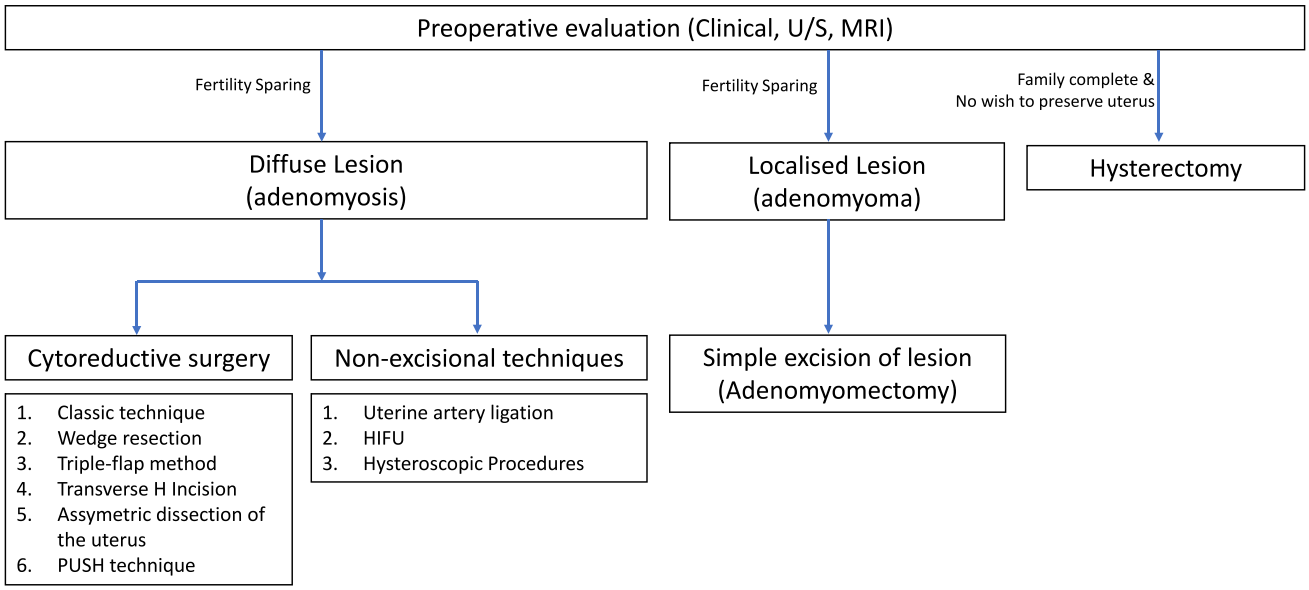

Fig. 1 Surgical classification of adenomyosis

the development of various surgical approaches in order to reduce its complications. Unlike leiomyomectomy, the surgical plane is not distinct between the adenomyoma and normal myometrium. Adenomyomectomy can be performed via laparotomy or laparoscopy, similar to leiomyomectomy [15].

Complete excision of lesions in cases of diffuse adenomyosis is generally not feasible due to the risk of removing a significant portion of healthy myometrium. This can result in a weakened uterine wall and, consequently, lead to poor pregnancy outcomes.

The following surgical methods have been proposed for uterus-sparing treatment of adenomyosis (Fig. 1).

- Classical excision of adenomyotic tissue after a single incision of the uterus (longitudinal or else)
- Wedge resection
- Double- or triple-flap method
- Transverse H incision
- PUSH technique

The *classic technique* (open, laparoscopic, or robotic) involves the recognition of the lesion's location and borders by inspection, palpation, or intraoperative ultrasound when possible. A longitudinal incision at the uterine wall along the adenomyotic region is performed, and the surgeon applies sharp and blunt dissection of the lesion with scissors, graspers, or diathermy in a fashion similar to the removal of a leiomyoma. The seromuscular uterine wall is sutured in two or three layers with absorbable sutures. The endometrial cavity is similarly closed with sutures. Alternatively, during laparoscopy mainly, the uterine wall can be reconstructed either with U-shape suturing, with the use of overlapping flaps, or using the triple-flap method [17–19].

The *wedge resection* of the uterine wall is applied in diffuse lesions located mainly in a localized area of the uterus (i.e., adenomyosis restricted only in the anterior or only in the posterior uterine wall). A typical cone-like resection involving the seromuscular uterine layer and the endouterine adenomyotic lesion as far as adenomyosis reaches is performed. The operation is completed with an anatomical approximation of the uterine wounds as described in the classic technique of partial adenomyomectomy [17].

The *triple-flap method* has been described mainly for an open approach and involves the midline bisection of the uterus until the endometrial cavity is opened. The surgeon uses palpation with the index finger into the cavity to facilitate maximum excision of adenomyotic tissue and grasping of adenomytic tissues with a Martin clamp to excise them from the surrounding myometrium leaving a myometrical thickness of 1 cm from serosa an endometrium. Then, the endometrium is initially closed, and the flaps of the uterine wall are approximated from one side of the bisected uterus to the anteroposterior plane of the other side while the contralateral side of the uterine wall is brought over the already reconstructed part of the uterus in such a way as to cover it [19].

The *transverse H incision technique* is another laparotomic modification for diffuse adenomyosis, mainly described for adenomyosis of the anterior uterine wall. A vertical incision perpendicularly to the midline is initially made on the uterine wall, and two transverse secondary incisions are applied perpendicularly to the first incision along the upper

and the lower parts of the uterus. The adenomyotic tissue underneath the two flaps is removed with the use of scissors or diathermy until a healthy myometrium, preserving the integrity of the endometrial cavity assessed with chromopertubation during surgery. The closure of the uterine wall is performed in multiple layers [20].

The *asymmetric dissection* of the uterus is a laparotomy technique, where the uterus is dissected longitudinally with a surgical electric knife in an asymmetrical fashion to divide the inside from the outside, preserving both the uterine cavity and bilateral uterine arteries. The myometrium should be dissected diagonally, as if hollowing out the uterine cavity, and with a transverse incision, the uterine cavity is opened, the index finger is inserted into the cavity, and adenomyotic lesions are removed using a loop electrode to a thickness of 5 mm of the inner myometrium. Similarly, adenomyosis is excised to a thickness of 5 mm of the serosal myometrium. The endometrial cavity is then closed, and the uterine flaps are reconstructed in layers (muscle and serosa) [21].

The *protection of uterine structure for healing* (PUSH) operation involves a full-layer mattress-type vertically penetrating suture aiming to assist the surgical overlapping of residual uterine muscle flaps [22]. An initial midline incision along the uterus is performed reaching the uterine cavity. Full excision of adnomyotic tissues is performed, and the uterus (left–right/anterior–posterior walls) is left with 2 submucosal inner-muscle flaps (left–right) and 2 subserosal outer-muscle flaps (left–right). The reconstruction of the uterus takes place anatomically by overlapping the flaps on each side and fixing them with vertical mattress-type penetrative sutures paying care not to remove any part of the outer flaps disregarding the size and their condition.

Optimal Surgical Technique

Complications after surgery are mostly associated with the type of approach (laparoscopy or laparotomy) and are anticipated. There is not enough evidence to support that one technique is superior to another and there does not seem to be a difference between the flap methods. It is however important to note that these operations are generally performed in centers of excellence and by highly qualified surgeons for the time being at least as they are beyond the scope of the average gynecologist. There is still a lack of large, well-designed, randomized studies designed to directly compare these methods. The treatment needs to be individualized according to the patient's needs. In general, single, well-defined lesions should be removed with single incisions, like myomas. Diffuse adenomyosis appears to be more challenging for the surgeon, and optimal restoration of the uterine wall is the most important factor. Optimal pre-operative imaging is of vast importance, as is communication with the patient and her needs. Treatment should be individualized according to the patient's needs and most importantly considering her wish to conceive or not. The wall thickness of the excised uterus should optimally range from 9 to 15 mm if the patient wishes to conceive which might reduce the risk of uterine rupture, as suggested in the recent study of Otsubo et al. [23].

Discussion

Clinical Outcome After Fertility Sparing Surgery

The reduction of dysmenorrhea after uterus-sparing surgery for adenomyosis ranges from 54.6 to 84.6%. The reduction of menorrhagia ranges from 50.0 to 73.7%. In prospective, well conducted prospective studies, uterus-sparing surgery the uterine volume appears to be decreased as much as 86%, the post-operative dysmenorrhea is reduced as much as 83%, and the post-operative menorrhagia is reduced as much as 71.3% (Table 1). Any systematic comparison between types of surgery is not possible because of the differences in the study methodology (different instruments of pain and bleeding measurement), the small number of participants, and the overall poor quality of the available studies (retrospective nature, non-selected patients) [19, 24–28].

Reproductive Outcome After Fertility Sparing Surgery

Prospective, high-quality studies show a total delivery rate of 46.9% (84/179) in patients who have undergone any uterus-sparing surgery for adenomyosis (Table 2). The total conception rate, the miscarriage rate, and the preterm delivery rate are 58.1% (104/179), 8.9% (16/179), and 9.6% (10/104). Moreover, in these studies, no case of uterine rupture has been reported. As previously mentioned, the retrospective nature of most of the studies, the non-uniform methodology of approaching the conception and pregnancy rates, and the non-randomization of the included patients make any comparison between surgical techniques inappropriate [19, 24–28].

Surgery for Adenomyosis and Infertility

The management of infertility in women with adenomyosis is a topic of ongoing debate, and there is no definitive answer whether uterus-sparing surgery, with or without medical interventions, improves the reproductive outcome. Systematic reviews and meta-analyses so far have clearly shown elevated risk of miscarriages and less favorable outcomes in general in women suffering from adenomyosis, so finding the ideal therapy for these women is of utmost importance [29•]. The symptoms of adenomyosis, both in

Table 1 Pre-operative and post-operative uterine size, abnormal uterine bleeding, and pelvic pain/dysmenorrhea rates (only prospectively performed studies included)

Author, year	n	Follow-up (months)	Age	Pre-op uterine volume (cm^3)	Post-op uterine volume (cm^3)	Pre-op pain score	Post-op pain score	Pre-op bleeding score	Post-op bleeding score
Yoon et al. (2023)	50	-	35.6 ± 3.3	-	-	7.28 ± 2.30	1.56 ± 1.30	Pictogram: 140 ± 91	Pictogram: 66 ± 65
Tskhay et al. (2019)	26	18	38.6 ± 8.2	455	63	-	-	-	-
Kitade et al. (2018)	76	36	36 (28–39)	-	-	9.3 (9–10)	3.5 (1–6)	-	-
Yang et al. (2017) (with plexus ablation)	50	36	40.4 ± 3.7	200.4 ± 55.3	134.0 ± 28.6	8.3 ± 1.2	2.6 ± 0.9	PABC score: 122.6 ± 34.2	PABC score: 62.2 ± 13.4
Yang et al. (2017) (without plexus ablation)	52	36	39.6 ± 4.0	202.3 ± 54.5	133.0 ± 35.1	8.3 ± 1.1	5.0 ± 1.4	132.6 ± 36.8	61.8 ± 13.5
Osada et al. (2011)	104	123	37.6 ± 6.9	-	-	10	1.67	10	2.87
Wang et al. (2009) (surgery only)	51	24	37.0 ± 4.8	-	-	3.86 ± 0.51	1.14 ± 0.87	3.08 ± 1.44	0.91 ± 0.77
Wang et al. (2009) (surgery + GnRH)	114	24	38.9 ± 3.8	-	-	3.94 ± 0.43	0.78 ± 0.84	3.68 ± 1.03	0.91 ± 0.77

terms of gynecological symptoms and in the reproductive outcome, seem to be due to the abnormal structure of the myometrium both in terms of cell structure as well as molecular factors that disrupt its normal function compared to that of the normal uterus. Increased myometrial thickness in particular may negatively affect the outcome of ART methods, although other studies have reported no association between adenomyosis and ART outcomes [30]. Most of the studies so far have shown that removal of the adenomyotic lesions and the subsequent reduction in myometrium thickness results in higher pregnancy rates as well as a reduction in the rate of miscarriage and pregnancy-related hypertensive disorders like preeclampsia. Additionally, it is believed that complete excision of the disease (adenomyomectomy) in cases of focal adenomyosis shows the best pregnancy outcomes with the least complications [31]. There is a large variance between the current studies in terms of methodology, and thus, there is an inherent bias in trying to find reliable data; however, the improved reproductive outcome after surgery seems to be consistent among studies. It is observed that the rates of conception are satisfactory, both natural as well as with ART methods, and the rates of miscarriage are better. Furthermore, there is a reduction in hypertensive-related complications, and the rates of full-term deliveries are also considered acceptable. The incidence of uterine rupture also appears to be increased, and as a result, cesarean section is the preferred method of delivery. There is a small number of studies reporting patients with placenta previa and placenta accreta spectrum after surgical treatment of adenomyosis in the literature [32, 33]. A recent registry-based Japanese study, comparing 1204 pregnancies with a history of adenomyosis with 151,105 no adenomyotic women, described a risk of 2.0% vs 0.5% for placenta accrete, respectively. Possibly, surgery for adenomyosis may increase the frequency and risk of perinatal complications, as is in cases of myomectomy [34].

Adenomyosis and ART

It is well established that adenomyosis alone is a cause of subfertility. Although ASRM suggests that there remains insufficient evidence that fibroids reduce fertility rates with or without ART, adenomyosis is often accompanied with leiomyomata and/or endometriosis, drastically influencing the reproductive potential of these patients [35–37]. Most of the studies noted the presence of endometriosis to some extent Moreover, surgery on the uterine body and the consequent disruption of the myometrium in women who underwent surgical treatments for adenomyosis further complicates the situation, compared to women without uterine pathology. All the above make these patients potential candidates for ART. Not all the studies mention the method of conception

Table 2 Pregnancy rates after fertility-sparing surgery for adenomyosis (only prospectively performed studies included)

Author, year	n	Follow-up (months)	Age (y)	Patients wishing to conceive (*n*, %)	Total conceptions (*n*, %)	Miscarriages (*n*, %)	Preterm (*n*, %)	Full-term (*n*, %)	Total deliveries (*n*, %)	Uterine rupture in pregnancy
Yoon et al. (2023)	50		35.6 ± 3.3	33/50 (66.0%)	18/33 (54.5%)	5/33 (15.1%)	3/33 (9.1%)	8/33 (24.2%)	10/33 (30/3%)	0/33
Tskhay et al. (2019)	26	18	38.6 ± 8.2	18/26 (69.2%)	3/18 (17%)	-	-	2/18 (11.0%)	2/18 (11.0%)	0/18
Kitade et al. (2018)	76	36	36	31/76 (40.7%)	12/31 (38.8%)	3/31 (9.7%)	-	-	9/31 (29.0%)	0/31
Osada et al. (2011)	104	123	37.6 ± 6.9	26/104 (25.0%)	16/26 (61.5%)	2/26 (7.6%)	-	-	14/26 (53.8%)	0/26
Wang et al. (2009) (surgery only)	51	24	37.0 ± 4.8	27/51 (52.9%)	20/27 (74.1%)	3/27 (11.1%)	2/27 (7.4%)	15/27 (55.6%)	17/27 (74.1%)	0/27
Wang et al. (2009) (surgery + GnRH)	114	24	38.9 ± 3.8	44/114 (38.6%)	35/44 (79.5%)	3/44 (6.8%)	5/44 (11.4%)	27/44 (61.4%)	32/44 (79.5%)	0/44
Total	507	18–123	35–38	181	104/179 (58.1%)	16/179 (8.9%)	10/104 (9.6%)	52/122 (42.6%)	84/179 (46.9%)	0/179 (0.0%)

and even fewer mention how many IVF cycles were needed for clinical pregnancy to be achieved. In a meta-analysis of published data by Vercellini et al., women with adenomyosis had a 28% reduction in the likelihood of clinical pregnancy at IVF/ICSI compared with women without adenomyosis [38]. Also, adenomyosis is more likely to be diagnosed in a woman undergoing IVF as thorough examinations and imaging are performed more often than in healthy women. It is fair to say however that since ART methods in general help women achieve pregnancy quicker than through natural conception, IVF might be preferable to natural conception, especially if other infertility factors co-exist. In addition, single embryo transfers are recommended to minimize the risk of uterine rupture.

Risk of Uterine Rupture

There are several reports of uterine rupture in patients with adenomyosis, even those without previous surgical operations [32]. In addition, the risk of rupture during pregnancy, especially under labor, is inherent with every uterine surgery. This might be of particular importance after surgery for adenomyosis, as there are cases of uterine rupture that occur prior to the onset of labor [33]. Even after a single cesarian section, there is a reported 0.2 to 1% risk of rupture in vaginal birth, and the risk is even higher after myomectomy. In some studies, the risk of uterine rupture is as high as 1 in 18 (almost 6%) after surgical treatment for adenomyosis. So, although vaginal delivery is possible, birth via elective cesarian section appears to be the safest option.

Optimal Time Between Surgery and Conception

Most studies fail to report the time between surgery and conception, and there is not enough data to exclude useful information. The follow-up period in most studies is rarely adequate and is often not stated at all. However, a minimum of 3 months between the operation and the attempts to conceive is suggested based on the limited data that is available as well as our experience with myomectomies, due to wound healing and other factors.

Conclusion

Hysterectomy has traditionally been the primary treatment for adenomyosis in women. However, contemporary medicine offers several excisional and non-excisional techniques for patients who wish to preserve their fertility. Currently, no single surgical technique has been proven superior, and the limited data and patient numbers restrict definitive conclusions. Patients must be informed about the risk of uterine rupture in subsequent pregnancies and should be considered

high-risk for complications, necessitating regular monitoring. Moreover, further research is required to establish the safety and effectiveness of these procedures. Non-excisional techniques, like radiofrequency ablation, hold promise in enhancing patients' quality of life and improving pregnancy outcomes [39].

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Data Availability No datasets were generated or analyzed during the current study.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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