

A Debate on Surgical Intervention for Adenomyosis Prior to In-Vitro Fertilization

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Abstract

Adenomyosis is a benign uterine disorder distinguished by the ectopic presence of endometrial glands and stroma within the myometrium. It affects around 20% of individuals of reproductive age. Adenomyosis commonly presents with abnormal uterine bleeding, dysmenorrhea, chronic pelvic pain, dyspareunia, and is associated with infertility. While the mechanisms linking adenomyosis to infertility remain unclear, several factors may contribute to impaired reproductive outcomes. Although hysterectomy is the standard surgical treatment for symptomatic adenomyosis, it is not a suitable option for patients desiring fertility preservation. Conservative surgical interventions for adenomyosis before in-vitro fertilization (IVF) aim to improve reproductive outcomes but carry inherent risks. The decision to pursue conservative surgery for adenomyosis remains a topic of debate, requiring careful consideration of potential benefits and surgical risks. Identifying optimal candidates for surgical intervention is crucial to maximizing benefits while minimizing complications. This article explores the debate surrounding conservative surgical intervention for adenomyosis prior to IVF.

Keywords: Adenomyosis; In-vitro fertilization; Conservative surgery; Adenomyomectomy; Reproductive outcomes.

Surgical Intervention for Adenomyosis Prior to In-Vitro Fertilization: Yes

Conservative surgery for adenomyosis prior to in-vitro fertilization (IVF) is a potential strategy for improving pregnancy outcomes in patients with adenomyosis. Conservative surgical procedures encompass adenomyomectomy for focal adenomyosis and conservative cytoreductive uterine-sparing surgery for diffuse adenomyosis.

Surgical Intervention for Adenomyosis Prior to In-Vitro Fertilization: No

Conservative surgery may offer an option for patients with adenomyosis seeking to preserve fertility; however, it carries inherent risks, including surgical complications, recurrence, potential impacts on uterine integrity, and fertility outcomes are not always guaranteed.

Evidence suggests that such surgical interventions may improve fertility through various mechanisms. Key contributing factors include restoring the uterine cavity to optimal conditions, alleviating symptoms, and providing a long-term treatment to improve pregnancy outcomes and enhance quality of life.

Yes: Improving reproductive outcomes

Adenomyosis has been found to negatively impact IVF outcomes, leading to significantly reduced implantation and live birth rates, as well as an increased early pregnancy loss risk (1, 2). Consequently, uterine-sparing surgical interventions may play a role in improving reproductive outcomes for patients with adenomyosis undergoing IVF, as evidenced by findings from numerous studies. A prospective study evaluating reproductive outcomes following adenomyomectomy in patients with severe uterine adenomyosis reported that 70 individuals sought fertility following surgery, with 49 undergoing assisted reproduction and 21 attempting natural conception (3). The live birth rate was 76.2% among those who pursued assisted reproduction (3). Additionally, Osada et al. evaluated radical resection with triple-flap uterine reconstruction in 104 patients with extensive adenomyosis (4).

Among 26 patients desiring pregnancy post-surgery, 16 conceived, including 12 through IVF (4). Two experienced pregnancy loss, while 14 (87.5%) had term deliveries without uterine complications (4). Furthermore, Wang et al. evaluated 65 subfertile individuals with pathology-confirmed extensive uterine adenomyosis (5). Of these, 28 underwent conservative surgery with or without GnRH agonist therapy, while 37 received 6 months of GnRH agonist therapy alone (5).

Over a 3-year follow-up, those undergoing conservative surgery had significantly higher cumulative clinical pregnancy and delivery rates compared to those treated with GnRH agonist therapy alone (46.4% [13/28] versus 10.8% [4/37], $P=0.002$; and 32.1% [9/28] versus 8.1% [3/37], $P=0.022$, respectively) (5). Likewise, a study of subfertile patients with adenomyosis included 18 treated with conservative surgery and GnRH agonist therapy and 22 with GnRH agonist alone, followed over three years (6).

The combined treatment group showed better reproductive outcomes, with six patients (33.3%) having term delivery compared to one (4.5%) in the GnRH-only group ($P=0.0328$) (6). A study evaluated 53 patients with adenomyoma who underwent conservative surgical treatment, divided into a

Also, due to the diffuse nature of adenomyosis, selecting the optimal uterus-sparing surgical approach could be challenging. Evidence suggests that adenomyosis itself does not inherently compromise IVF outcomes. A prospective study of 4,002 IVF cycles found no significant difference in live birth rates between those with and without sonographic features of adenomyosis (23). Similarly, a study of single frozen embryo transfer found no significant differences in clinical pregnancy, miscarriage, or live birth rates between patients with and without adenomyosis, as identified by three-dimensional ultrasound (24). These findings highlight the need to carefully weigh surgical risks against potential reproductive benefits, as surgery may not provide a clear advantage in improving IVF outcomes, given that adenomyosis may not adversely affect IVF success.

No: Risks of complications

Conservative surgery for adenomyosis presents potential complications that should be thoroughly discussed during patient counselling. The most significant of these complications is uterine rupture, particularly in subsequent pregnancies. The exact risk remains unclear, but several studies have reported instances of uterine rupture in subsequent pregnancies following conservative surgery (3, 25-31). Cases of uterine rupture following adenomyosis resection may be attributed not only to direct damage of the uterine wall but also to excessive energy use during the procedure (30). Applying high-power cutting current may impair tissue healing, potentially increasing the risk of rupture in subsequent pregnancies (32). Using vasopressin and cold scissors for adenomyotic tissue resection may promote improved tissue healing and potentially reduce uterine rupture risk (33).

Excessive bleeding is a major challenge in conservative surgical treatment of adenomyosis, sometimes necessitating blood transfusion and, in severe cases, may lead to incomplete excision or urgent hysterectomy (34). Intraoperative blood loss during conservative procedures can vary considerably, with values ranging between 30 and 80 mL in laparoscopic procedures, whether or not uterine artery occlusion is performed (35), to 370-400 mL in cases utilizing the double-flap or triple-flap techniques (4, 36).

Several techniques have been adopted to minimize intraoperative bleeding, including vasopressin infiltration at the site of uterine incision (37), transient occlusion of uterine arteries (34), controlled use of high-power energy sources (32), and using cold scissors (32). Furthermore, suturing of uterine defects

modified adenomyomectomy group and a wedge resection group (7). Among 24 patients with infertility in the modified adenomyomectomy group, 11 pursued natural conception, with a pregnancy rate of 23.1% (7). Another 11 patients opted for assisted reproductive technology (ART), which resulted in a higher pregnancy rate of 36.4% ($P=0.039$) (7). Overall, three patients (12.5%) in this group had live births (7).

In contrast, patients with infertility in the wedge resection group attempted natural conception exclusively, but none became pregnant (7). A retrospective study evaluated patients with infertility and severe dysmenorrhea diagnosed with adenomyosis who underwent uterus-sparing surgery through double-flap adenomyomectomy followed by 3–6 courses of GnRH agonist therapy (8). A total of 62 pregnancies were conceived among 56 individuals (56.5% through spontaneous pregnancies, 9.7% undergoing ART after failed spontaneous pregnancies, and 33.8% undergoing ART directly) (8). Of the 114 patients diagnosed with infertility prior to surgery, 47 (41.2%) became pregnant following the procedure (8). Of these pregnancies, 45 (72.6%) resulted in live births (8). A series of 28 individuals with histologically confirmed adenomyomas indicated that conservative surgery for adenomyomas is associated with a favourable reproductive prognosis (9). The cumulative pregnancy rate over a 36-month follow-up period was 74.7% (9). Notably, among these patients, only one underwent IVF (9).

Yes: Optimizing the uterine environment

Infertility and subfertility in patients with adenomyosis can result from various factors, including anatomical distortion of the uterine cavity (10), disruption of the junctional zone (11), abnormal uterine contractility (12), impaired endometrial receptivity (13), dysregulated hormonal signalling (14), and increased intrauterine oxidative stress, mediated by elevated levels of free radicals within the uterus (15). Conservative surgical interventions for adenomyosis aim to enhance fertility by optimizing the uterine environment through the excision of adenomyotic tissue that distorts the uterine cavity (4). Restoring the normal uterine cavity creates a more favourable environment for embryo implantation and development, thereby improving reproductive outcomes.

Additionally, these procedures decrease uterine volume, which, when enlarged due to adenomyosis, has been associated with lower live birth rates in IVF (13, 16). Surgical steps of adenomyomectomy is demonstrated in **Figure 1**. Since adenomyosis can

is performed in a multilayered fashion with barbed sutures (38), more experienced surgeons tend to achieve lower blood loss through refined surgical techniques (39).

Intrauterine and intra-abdominal adhesions are recognized complications of conservative surgical treatment for adenomyosis. Intrauterine adhesions may occur following wedge resection, with one study reporting a prevalence of 25.2% (36/143) (37), while another study found a lower incidence of 3.8% (4/103) (3). These adhesions can lead to Asherman syndrome, which is associated with menstrual irregularities, infertility, and a higher risk of pregnancy loss, preterm labour, and abnormal placentation in subsequent pregnancies (40). Also, abdominal adhesions were identified in five of eight patients who returned for delivery following adenomyomectomy. Among them, 25% (2/8) had mild adhesions, 25% (2/8) had moderate adhesions, and 12.5% (1/8) had severe adhesions (3). Several techniques can help reduce the risk of adhesion formation, although complete prevention cannot be guaranteed. A meticulous surgical approach, precise bleeding control, and minimally invasive techniques can reduce tissue trauma (41).

Adhesion prevention products may further reduce risk (42). The surgeon's skill and expertise remain critical in optimizing surgical outcomes (43, 44). Abnormal placentation, particularly placenta accreta spectrum (PAS), is a recognized risk in future pregnancies following conservative surgery for adenomyosis (34). Surgical resection of adenomyotic lesions can disrupt the uterine wall, potentially increasing the likelihood of abnormal placental attachment in subsequent pregnancies (34). One study has shown a marked rise in the incidence of PAS in women who undergo adenomyomectomy compared to those with adenomyosis who do not receive surgical treatment (25).

No: Technical challenges

Adenomyosis is characterized by the diffuse invasion of endometrial tissue into the myometrium, making it difficult to clearly identify and isolate lesions during surgery (**Figure 2**) (27). Unlike fibroids, which are well-defined and encapsulated, adenomyotic lesions often infiltrate into the surrounding tissue, complicating their removal. Consequently, the effectiveness of lesion excision remains limited, with success rates estimated at approximately 50% (45). Conservative surgical procedures for adenomyosis require highly experienced surgeons, specialized skills, and a multidisciplinary approach due to their technical complexity, risk of complications, and significant impact on fertility and pregnancy outcomes

disrupt normal uterine contractions (10)—potentially impairing sperm transport and embryo implantation—surgical excision may help restore regular uterine contractility, further supporting implantation. Also, adenomyosis is associated with chronic inflammation in the uterine environment, characterized by increased levels of pro-inflammatory cytokines, prostaglandins, and immune cells (17). This inflammatory milieu can affect endometrial receptivity (18). By removing adenomyotic lesions, conservative surgery can reduce the source of inflammation, creating a more favourable environment for embryo implantation. Additionally, surgery may help reverse some of the epigenetic changes observed in the endometrium, such as the downregulation of Hox-A10 (19, 20). This alteration in gene expression is thought to contribute to disordered decidualization, which can compromise implantation.

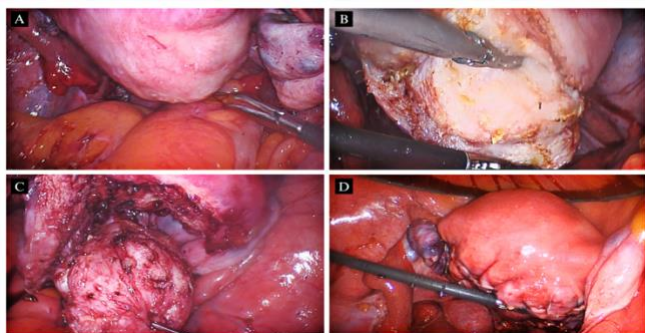


Figure 1. Surgical steps of laparoscopic adenomyomectomy

Yes: Symptom relief

While not directly related to fertility, surgical intervention for adenomyosis can significantly enhance quality of life by alleviating symptoms such as heavy menstrual bleeding, chronic pelvic pain, and dysmenorrhea (4). Numerous studies have emphasized the dual benefits of conservative surgical procedures for adenomyosis, demonstrating significant symptom relief alongside improved reproductive outcomes. Osada et al. reported that all patients experienced immediate relief from symptoms of hypermenorrhea and dysmenorrhea following surgical intervention (4). Similarly, a study by Al Jama demonstrated that combined conservative surgery with GnRH agonist therapy provided more effective symptom relief compared to GnRH agonist therapy alone (6). Additionally, findings from Wang et al. highlighted that conservative surgery, whether performed alone or in combination with GnRH agonists, offers superior and longer-lasting symptom control for women with extensive uterine adenomyosis compared to GnRH agonist therapy alone (5).

(46). Given the steep learning curve of adenomyomectomy, surgeons with high case volumes and specialized training are more likely to achieve optimal results (43, 44).

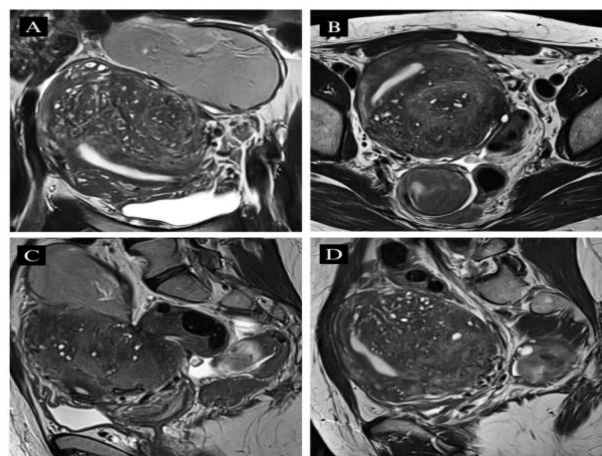


Figure 2. T2-weighted MRI of the Pelvis

No: Recurrence or persistent symptoms

Based on available evidence, recurrence or persistent symptoms following conservative adenomyosis surgery are relatively common. Studies on adenomyosis recurrence have shown that it can occur at varying rates. A recent systematic review and meta-analysis of studies from January 2000 to January 2022 assessed adenomyosis recurrence, defined as the return of symptoms or adenomyotic lesions, and found a 12.6% recurrence rate after adenomyomectomy (47). A study analyzing 133 patients who underwent adenomyosis surgery reported a recurrence rate of 39.1% over a mean follow-up of 52 months (48). Several factors influence the recurrence of adenomyosis after conservative surgery, including the location and extent of adenomyosis, with involvement of the posterior uterine wall being associated with higher recurrence rates (48).

Co-existing conditions, such as endometriosis, further increase the risk of recurrence (21). Surgical technique is also a key determinant, with complete excision showing the lowest recurrence rate (9%) compared to partial excision (19%) (37). Postoperative use of adjuvant hormone therapy can reduce recurrence, with a study indicating an 8.0% recurrence rate with hormone therapy versus 16.6% without it (47). Longer follow-up periods also tend to show higher recurrence rates, particularly in studies with follow-up times exceeding 24 months (47). A systematic review found that complete and partial excision of adenomyosis reduced dysmenorrhea by 82.0% and 81.8%, with persistence rates of 18.0% and 18.2%, respectively (43). Menorrhagia control

Yes: Long-term efficacy

Studies have shown that the benefits of conservative surgical procedures for adenomyosis can be long-lasting. In a study by Zhu et al., long-term outcomes of adenomyomectomy using a modified double-flap technique via either laparoscopy or laparotomy were assessed over a 6-year follow-up period (21). The study evaluated remission or recurrence of menorrhagia, dysmenorrhea, serum CA125 levels, and uterine size as key factors (21). Results demonstrated that the modified double-flap adenomyomectomy method yielded effective outcomes in treating severe diffuse adenomyosis, with effectiveness rates exceeding 60% at the 6-year follow-up (21).

The recurrence rate within three years after double-flap adenomyomectomy, followed by 3–6 courses of GnRH agonist therapy, was observed in only 5.1% in a study by Zhou et al. (8). Thirty-three patients underwent laparoscopic or robotic adenomyomectomy for adenomyosis, with and without three courses of postoperative GnRH agonist therapy (22). Over a three-year follow-up, patients had significant symptom relief, though four (12%) had symptom recurrence (22).

Yes: Conclusion

Adenomyosis can significantly impair IVF outcomes, particularly in severe cases. Uterine-sparing surgeries offer a valuable option for fertility preservation, improving reproductive outcomes, and symptom relief, **making them a critical consideration for individuals with severe adenomyosis or those who have experienced repeated IVF failures.** However, surgical intervention must be **individualized and** carefully considered based on factors like age, disease severity, and prior fertility treatments. While these procedures provide meaningful benefits, patient selection and choosing an optimal approach are crucial. Adenomyomectomy remains a promising strategy, but its use should be tailored to each patient's clinical and reproductive needs.

varied more significantly, with reductions of 68.79% after complete excision and 50.00% after partial excision, leaving residual rates of 31.21% and 50.00% (43).

No: Medical management ensures safety

GnRH agonist therapy has an antiproliferative effect on adenomyotic tissue, reducing inflammation, promoting apoptosis, and enhancing endometrial receptivity (1, 49). It can provide a safer, non-invasive alternative to conservative surgery for patients with diffuse adenomyosis, who are suboptimal surgical candidates, due to the inherent complexity of intervention and increased risk of disease recurrence (12, 50). Pretreatment with long-acting GnRH agonists for 3–6 months improved clinical pregnancy rates in fresh IVF/ICSI cycles (OR 1.49, 95% CI 1.15–1.92) but did not significantly improve live birth rates or reduce miscarriage rates (51). Frozen embryo transfer following GnRH agonist pretreatment tended to increase the pregnancy rate in patients with adenomyosis in a study by Parker et al. (52).

No: Long-term considerations

Long-term consideration following adenomyosis surgery often includes postoperative hormonal therapy to suppress residual disease, minimize recurrence risk, and manage symptoms. Several studies have showed the effectiveness of GnRH agonists (8, 22, 53, 54) and Levonorgestrel Intrauterine System (54, 55) in reducing the risk of recurrence following conservative adenomyosis surgery. The long-term use of GnRH agonists is restricted due to hypoestrogenic side effects, such as hot flashes, mood swings, headaches, urogenital atrophy, and osteoporosis, which can result in treatment discontinuation (56). To mitigate these effects, add-back therapy is recommended, particularly when GnRH agonists are used for extended periods (56). Despite conservative surgical management, hysterectomy may ultimately be necessary for some patients with adenomyosis due to persistent or recurrent symptoms (57). Notably, the reintervention rate due to symptomatic recurrence has been reported as 2.6% (47). Conservative surgical treatment of adenomyosis may also delay the initiation of IVF, which is a critical consideration, particularly for individuals of advanced reproductive age. Recovery and uterine healing time vary based on the extent of surgery, surgical approach, and individual healing rates. Delaying IVF is often recommended to optimize uterine healing and reduce the risk of pregnancy complications (37). Additionally, postoperative hormonal therapy, typically lasting 3–6 months, may delay the initiation of IVF (34).

No: Conclusion

Conservative surgery for adenomyosis carries a higher risk of complications, requiring careful patient selection. A thorough assessment of individual factors is essential to balance potential fertility benefits and symptom relief against surgical risks. For patients prioritizing fertility preservation, a tailored, interdisciplinary approach involving reproductive specialists and experienced surgeons can help optimize outcomes while minimizing invasiveness.

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