

REVIEW

Adenomyosis: the missed disease



BIOGRAPHY

Felice Petraglia is Professor and Chairman of Obstetrics and Gynecology and Director of the Residency Program in Obstetrics and Gynecology at the University of Florence, Italy. He is also past-President of the Society for Endometriosis and Uterine Disorders, the Society for Gynecological Investigation and the Society for Reproductive Investigation.

Pietro Santulli^{1,2,3}, Silvia Vannuccini^{4,5}, Mathilde Bourdon^{1,2,3},
Charles Chapron^{1,2,3}, Felice Petraglia^{4,5,*}

KEY MESSAGE

Adenomyosis often remains a 'missed' disease, frequently overlooked or misdiagnosed, despite the advancement of non-invasive diagnostic tools, such as transvaginal ultrasonography or magnetic resonance imaging. The heterogeneity in clinical presentation, imaging criteria and treatments still poses a great challenge for the management of adenomyosis.

ABSTRACT

Adenomyosis, a menstruation-related uterine disorder, refers to the presence of endometrial stroma and glands within the myometrium and is typically observed in reproductive-age women. The pathogenesis explaining the migration, persistence, proliferation and differentiation of ectopic endometrial cells includes a genetic and epigenetic background, an oestrogen/progesterone receptor imbalance and an inflammatory reaction driven by local immune dysfunction, along with fibrosis and neuroangiogenesis within the myometrium. In the past, it was thought that adenomyosis almost exclusively affected multiparous women after 40 years of age and the diagnosis was generally confirmed upon hysterectomy. Nowadays, using imaging techniques such as transvaginal ultrasonography and magnetic resonance imaging, adenomyosis is increasingly identified in young women with dysmenorrhoea, dyspareunia, abnormal uterine bleeding and heavy menstrual bleeding, and also in infertile patients. Furthermore, adenomyosis often coexists with other gynaecological conditions, such as endometriosis and uterine fibroids. Despite the improvement of non-invasive diagnostic tools, the awareness of the condition is still poor and the diagnosis is often missed, due also to a heterogeneity in clinical presentation and imaging criteria. In addition, medical and surgical management do not follow shared recommendations, even though adenomyosis requires a lifelong management plan, including pain and bleeding control, fertility preservation and pregnancy complications.

INTRODUCTION

Adenomyosis was first described in 1860 by an Austrian pathologist, Karl von Rokitansky, who stated that endometrial stroma and glands were unexpectedly present in the myometrium. In the last century, adenomyosis was defined by the infiltration of the endometrial basalis layer (glands and stroma) into the myometrium

through an altered junctional zone, a highly specialized hormone-responsive layer of the uterine architecture located in the inner third of the myometrium. Endometrial migration is accompanied by myometrial hypertrophy/hyperplasia and fibrosis. The diagnosis of adenomyosis was for decades made only by histology after hysterectomy, with focal, diffuse, cystic and adenomyoma being the main types of adenomyotic lesion. The scenario has now completely changed

thanks to the enhanced imaging techniques, in particular transvaginal ultrasonography (TVUS) and magnetic resonance imaging (MRI), making it possible to diagnose adenomyosis non-invasively.

In the past, it was thought that adenomyosis almost exclusively affected women in their forties and fifties, whereas adenomyosis is currently increasingly identified in young women with pain,

KEYWORDS

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¹ Faculté de Santé, Faculté de Médecine Paris Centre, Université Paris-Cité, Paris, France.

² Department of Gynecology Obstetrics II and Reproductive Medicine, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Universitaire Paris Centre (HUPC), Centre Hospitalier Universitaire (CHU) Cochin, Paris, France.

³ Department of Development, Reproduction and Cancer, Institut Cochin, INSERM U1016, Paris, France.

⁴ Department of Experimental, Clinical and Biomedical Sciences 'Mario Serio', University of Florence, Florence, Italy.

⁵ Department of Maternal and Child Health, Careggi University Hospital, Florence, Italy.

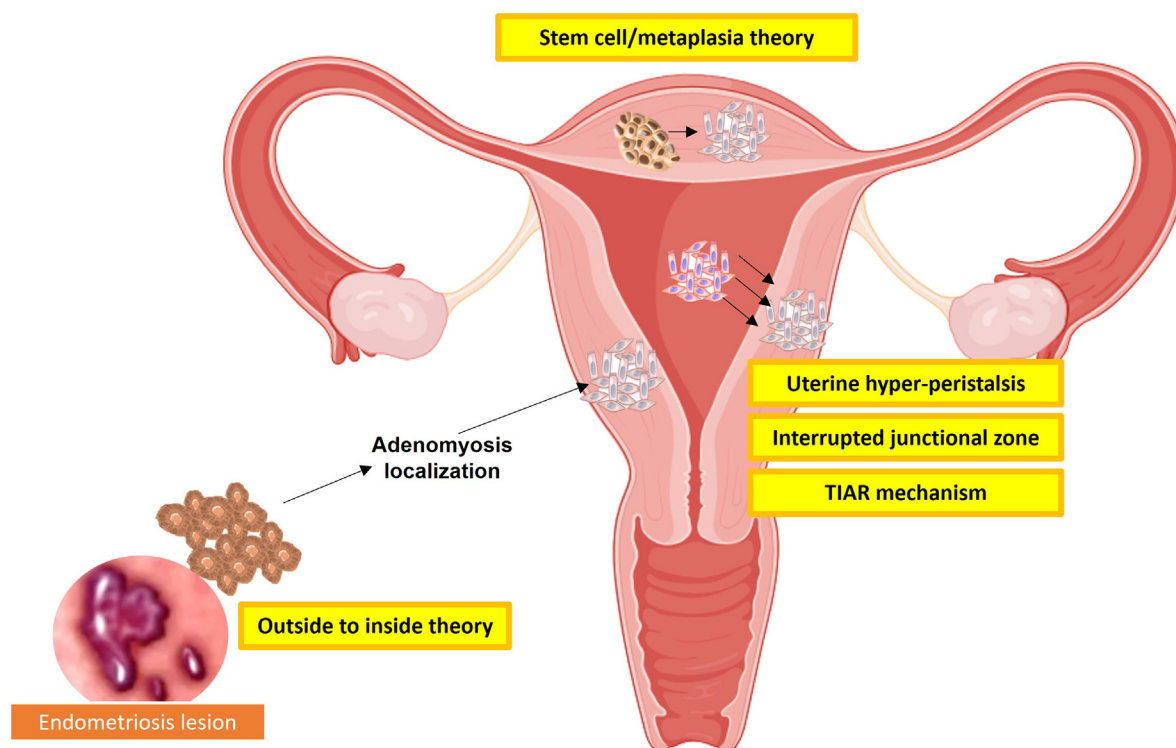


FIGURE 1 Pathogenesis of adenomyosis: the inside-to-inside theory with invagination of the endometrium into the myometrium, due to hypercontractility and/or a tissue and injury repair (TIAR) mechanism through an interrupted junctional zone; the stem cell/metaplasia theory; and the outside-to-inside theory, with migration and implantation of endometrium into the myometrium from endometriotic lesions.

abnormal uterine bleeding or infertility (*Vannuccini and Petraglia, 2019*). Thus, adenomyosis has turned into a heterogeneous clinical condition, rather than a histopathological finding. Despite the new diagnostic tools, adenomyosis often remains a 'missed' disease, poorly known in both primary and secondary care; it is overlooked or misdiagnosed as common gynaecological comorbidities such as uterine fibroids and endometriosis.

The enormous heterogeneity in clinical presentation and imaging findings and the low awareness of this condition among clinicians make it challenging to diagnose. Furthermore, the management of adenomyosis does not follow shared recommendations, given the lack of approved drugs and tailored treatment approaches, even though adenomyosis requires a lifelong management plan, including symptom control, fertility and pregnancy complications.

HOW ADENOMYOSIS DEVELOPS

Different theories have been proposed for the origin of adenomyosis (*Vannuccini et al., 2017; Zhai et al., 2020*) (**FIGURE 1**).

First is the invagination hypothesis, which is related to uterine hyperperistalsis. Contractions of the myometrium and the resultant trauma to the endometrial–myometrial junctional zone may lead to adenomyosis through invagination of the endometrial basal layer into the myometrium. The tissue injury and repair mechanism is activated in response to an injury/trauma (mechanical, thermal), and oestrogen is locally released due to local paracrine activity, altering the junctional zone and invading the myometrium, which may in turn decrease the cell-mediated immunity. A chronic hypercontractility and auto-traumatization may contribute to the development of adenomyosis. The menstruation process itself may increase the endometrial ectopic migration, and further repetitive bleeding episodes represent a number of iterative events including hypoxia, necrosis, myometrial contractions, angiogenesis and regenerative processes (*Vannuccini et al., 2022b*). The metaplasia theory involves migration and differentiation within the myometrium of embryonic pluripotent Müllerian cells or endometrial or mesenchymal stem cells normally located in cell niches, ensuring cell regeneration and the replacement of healthy endometrium. From these cells de-novo adenomyotic foci may develop.

The 'outside-to-inside theory' suggests that ectopic endometrial cells may penetrate the uterine wall from the outside, creating an adenomyotic focal localization. Adult endometrial cells may be displaced into the myometrium as a result of retrograde menstruation and the ability of ectopic endometrial cells to migrate from endometriosis lesions and implant (*Chapron et al., 2020, 2017*). The strong association between posterior focal adenomyosis and deep infiltrating endometriosis nodules in the posterior compartment in endometriosis/adenomyosis patients supports this hypothesis. Adenomyosis is the result of a series of complex pathogenic mechanisms: sex steroid hormone dysfunction, inflammation, abnormal immune response, cell migration, invasion and proliferation, fibrosis and neuroangiogenesis (*Vannuccini et al., 2017*). However, the pathophysiology is still poorly understood.

The imbalance between oestrogens and progesterone is the promoter of adenomyosis by (*Vannuccini and Petraglia, 2022*): (i) increased oestrogen receptor beta activity and local oestrogen production (related to increased aromatase activity) with normal peripheral

serum oestradiol concentrations; and (ii) decreased activity of progesterone receptors. The increased oestrogen activity stimulates the proliferative response, leading to changes in the expression of various other genes related to the increased anti-apoptotic activity of the basal layer, promoting the invagination process and the 'spreading' of adenomyosis into the myometrium, in the presence of decreased type B progesterone receptors. In addition, the abnormal expression of DNA methyltransferases causing epigenetic changes in oestrogen receptors and progesterone receptors contributes to the hormonal dysregulation (Bulun et al., 2021). In fact, genetic and epigenetic factors should be considered in the pathogenesis of adenomyosis, such as the new finding of activating somatic mutations of the KRAS gene (Inoue et al., 2019), also identified in endometriosis.

Following their proliferation, endometrial cell invasion of the myometrium and epithelial-to-mesenchymal transition (EMT) are the critical mechanisms, and some microRNA (miRNA; miR-124-3p or miR-145-5p) play a role in enhancing the migration and the EMT process of endometrial stromal cells. Adenomyosis is also considered a chronic inflammatory disease characterized by an abundance of inflammatory mediators in adenomyotic lesions: cyclooxygenase 2, prostaglandins, interleukins and urocortin are the main mediators. Changes in innate and adaptive immune defences also contribute to the inflammatory reaction in the eutopic and ectopic endometrium (Bourdon et al., 2021). Increased neoangiogenesis in adenomyosis is confirmed by increased microvessel density and by increased vascular endothelial growth factor expression. Adenomyotic tissues express high concentrations of neurogenic factors, such as nerve growth factors, regulating the secretion of inflammatory factors and causing pain symptoms. Furthermore, EMT and collagen production through transforming growth factor- β and Smad2/3-dependent signalling lead to smooth muscle metaplasia and ultimately to fibrosis, which determines the stiffness of adenomyosis lesions (Vannuzzi et al., 2022).

THE EPIDEMIOLOGICAL SCENARIO OF ADENOMYOSIS

The prevalence and risk factors of adenomyosis are still controversial (Upson

and Missmer, 2020). Historically, the disease has been identified as a pathological entity from histological reports after hysterectomy; however, the prevalence ranges from 9% to 62%, because of the lack of consistent criteria, even for histopathological diagnosis. The recent diagnostic advances have enabled the detection of adenomyosis by imaging, leading to the identification of the disease in adolescence and among young women (Chapron et al., 2020). According to TVUS, the overall prevalence of adenomyosis ranges from 12% to 34%, depending on age, symptoms and membership of the general versus a selected population, with similar results on MRI (Chapron et al., 2017; Vannuccini et al., 2024b). Thus, the traditional risk factors, being age 40–49 years, multiparity and prior uterine surgery, need to be updated as adenomyosis is commonly identified in completely different populations such as infertile women, adolescents and young women, as well as in symptomatic and asymptomatic individuals. Furthermore, the uniformity of diagnostic criteria in non-invasive tools is of the utmost importance to determine the true prevalence of adenomyosis across the reproductive life course and the developmental time-specific risk factors.

THE CHALLENGES OF ADENOMYOSIS DIAGNOSIS

The introduction of MRI and two-dimensional/three-dimensional Doppler TVUS has represented a major breakthrough, although there are still many controversies in terms of diagnostic criteria. However, the diagnosis of adenomyosis may already be suspected from the clinical data, especially the gynaecological and menstrual history (Chapron et al., 2020). Clinically, adenomyosis is considered as one of the causes of abnormal uterine bleeding in the International Federation of Gynecology and Obstetrics PALM-COEIN (Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, iatrogenic and Not yet classified) classification. This condition, being a menstruation-related disorder, is frequently associated with heavy menstrual bleeding (HMB), prolonged bleeding or pre-menstrual or post-menstrual bleeding, frequently causing iron deficiency anaemia. Furthermore, gynaecological pain symptoms are frequently reported by

women with adenomyosis, especially dysmenorrhoea, dyspareunia and chronic pelvic pain, impairing quality of life. There is also increasing evidence of links with infertility, recurrent pregnancy loss and adverse obstetric outcomes, such as preterm birth, pre-eclampsia and abnormal placentation.

The precise diagnosis of adenomyosis is based on the presence of ectopic endometrial tissue in the myometrium by pathological analysis; however, there are discrepancies even in a method that has always been thought to be the gold standard. In the last 15 years, the diagnosis of adenomyosis has been accessible by TVUS and MRI, even though some limitations in imaging accuracy and standardization still remain. Ultrasound criteria for diagnosing adenomyosis using morphological uterine sonographic assessment (MUSA) are well defined (Van den Bosch et al., 2015). Direct signs reflect the presence of ectopic endometrial tissue within the myometrium: echogenic subendometrial lines and buds in the inner myometrium, echogenic islands within the myometrium and intramyometrial cysts. Indirect signs are secondary features caused by the ectopic tissue, namely globular uterus, asymmetrical thickening of the uterine walls, translesional vascularity, fan-shaped shadowing and an irregular or interrupted junctional zone. The diagnosis is made by the presence of at least one of the direct MUSA criteria (Harmsen et al., 2022). However, there are different phenotypes, the main ones being diffuse or focal, and cystic or non-cystic; in addition, grading of adenomyosis severity depends on the extent of myometrial involvement. The inner, the middle or the outer myometrium can be affected by the disease, so three different forms can be described, showing how heterogeneous the TVUS appearance of adenomyosis is.

However, scarce evidence has so far been available on the link between the features of morphological uterine sonographic evaluation and clinical presentation. More information originates from MRI studies, where diffuse or intrinsic adenomyosis, focal (posterior or anterior) or extrinsic adenomyosis, and adenomyoma are described (Kishi et al., 2012). Diffuse adenomyosis is more frequently associated with HMB and older age, whereas the focal phenotype is usually observed in younger patients, coexisting with endometriosis

(*Chapron et al., 2017*). Furthermore, the imaging diagnosis of adenomyosis may be skewed by the frequent coexistence with uterine fibroids, altering junctional zone and uterine morphology.

The heterogeneity of the disease and non-specificity of symptoms often makes the achievement of an accurate diagnosis challenging, but it may guide the clinician to a suspicion of this uterine disorder in a wide epidemiological scenario, ranging from adolescence (*Vannuccini et al., 2024b*) to menopause (*Vannuccini et al., 2024a*).

THE IMPACT OF ADENOMYOSIS ON FERTILITY AND PREGNANCY OUTCOME

While adenomyosis often causes HMB and pain, its impact on fertility and pregnancy outcomes has gained increasing attention. The underlying pathophysiology that links adenomyosis to reproductive and obstetric challenges involves chronic inflammation, abnormal uterine contractility and altered endometrial receptivity, all of which create a less favourable environment for conception and progression of a healthy pregnancy (*Vercellini et al., 2023*). Understanding the mechanisms by which adenomyosis affects fertility, its influence on pregnancy and the treatment principles is crucial for improving both quality of life and reproductive outcomes (*Chapron et al., 2020*).

The mechanisms underlying adenomyosis-related infertility

The primary mechanisms by which adenomyosis contributes to infertility are rooted in structural and functional changes within the uterus. Studies suggest that these changes lead to disruption of sperm transport, embryo implantation and endometrial receptivity, cumulatively reducing fertility potential. Numerous different mechanisms have been discussed and could explain the negative impact of adenomyosis on conception chances.

First, the presence of endometrial tissue within the myometrium disrupts the normal structure and function of the uterus, leading to an altered junctional zone which can interfere with embryo implantation. Second, the effect of adenomyosis on myometrial contractility results in dysregulated uterine peristalsis (*Rees et al., 2024*). This dysperistalsis may

impair the utero-tubal transport of spermatozoa or embryos, thus reducing the likelihood of both fertilization and implantation.

In addition, aberrations in the eutopic endometrium include changes in steroid hormone receptors, decreased expression of implantation-related molecules and increased oxidative stress. These factors disrupt the endometrium–embryo dialogue, potentially leading to altered endometrial receptivity. The chronic inflammatory environment and the immune dysfunction of the adenomyotic uterus is marked by the recruitment of dysfunctional macrophages and other immune cells, and increased concentrations of cytokines, growth factors and prostaglandins in the myometrium. These proinflammatory mediators are thought to create a hostile environment for gamete survival and fertilization, as well as for early embryo development and implantation (*Bourdon et al., 2021*).

Next, chronic inflammation within the myometrium can trigger fibrosis through EMT processes, leading to the transdifferentiation of fibroblasts into myofibroblasts. The remodelling of the uterine structure by fibrotic tissue and subsequent chronic hypoxia may also contribute to an altered uterine architecture less prone to normal embryo implantation (*Vercellini et al., 2023*).

Finally, adenomyosis-related vascularization abnormalities, such as increased microvessel density and hypoxia, may compromise endometrial receptivity by reducing oxygenation in the myometrium and disrupting endometrium–myometrium signalling.

Clinical evidence on the link between adenomyosis and fertility

The association between adenomyosis and infertility remains insufficiently characterized in human populations, although animal studies have demonstrated a robust link between adenomyosis and impaired fertility. In murine models, adenomyosis has been associated with reduced fertility rates, along with local and systemic immune changes during the implantation window (*Bourdon et al., 2023*).

In human studies, there is accumulating evidence that adenomyosis may negatively impact fertility. Clinical data have shown

reduced pregnancy rates following colorectal surgery for endometriosis in patients with concurrent adenomyosis (*Ballester et al., 2012*). Furthermore, studies suggest that distinct adenomyosis phenotypes (focal versus diffuse) may differentially affect fertility outcomes. For example, focal adenomyosis of the outer myometrium has been significantly associated with primary infertility, whereas diffuse adenomyosis did not demonstrate a similar relationship with infertility (*Bourdon et al., 2020*).

Among infertile women undergoing IVF or intracytoplasmic sperm injection, the prevalence of adenomyosis is notably high, reaching up to 1 in 3. The literature on the impact of adenomyosis on assisted reproductive technology (ART) outcomes presents mixed results, with some studies reporting reduced pregnancy and live birth rates alongside increased miscarriage rates (*Cozzolino et al., 2022*), while others report no significant effect on outcomes (*Neal et al., 2020*). Additionally, in patients with adenomyosis undergoing ART, such as oocyte donation, higher miscarriage rates have been reported, further complicating fertility outcomes (*Cozzolino et al., 2024b*). Variability in these findings may stem from differences in ovarian stimulation protocols, inconsistent diagnostic criteria and the lack of standardized categorization for adenomyosis phenotypes, complicating cross-study comparisons (*Cozzolino et al., 2024a, 2025*).

These findings highlight the need for comprehensive, imaging-based diagnostic approaches in infertile women, which could facilitate improved management and prognostic strategies for adenomyosis-related infertility.

Impact of adenomyosis on pregnancy outcomes

Emerging data link adenomyosis to adverse pregnancy outcomes, including increased risks of miscarriage, preterm birth, small-for-gestational age infants, conditions such as pre-eclampsia, increased Caesarean section rates and postpartum haemorrhage (*Nirgianakis et al., 2021; Vercellini et al., 2023*). Proposed mechanisms include localized and systemic inflammation, increased myometrial prostaglandin production, altered uterine contractility and defective spiral artery remodelling, leading to abnormal placentation (*Horton et al., 2019; Vannuccini et al., 2017, 2016*). Structural uterine changes, such as myometrial

hypertrophy and hyperplasia, may restrict uterine cavity expansion, increasing the likelihood of preterm birth. Vascular irregularities, particularly in adenomyotic regions, may impair placental development and function. Abnormal vascularization can reduce fetal blood flow and nutrient delivery, heightening the risk of intrauterine growth restriction ([Vannuccini et al., 2016](#)).

Preliminary studies suggest that the impact of adenomyosis on obstetric and perinatal outcomes may be influenced by the presence of coexistent endometriosis and the specific adenomyosis phenotype (e.g. diffuse versus focal). For instance, in a retrospective analysis of data collected prospectively, the incidence of small-for-gestational-age infants was 10.8% in women with endometriosis alone, compared with 40% in those with both endometriosis and diffuse adenomyosis. In contrast, no statistically significant difference was found when comparing women with endometriosis alone with those with focal adenomyosis ([Scala et al., 2018](#)). This highlights the importance of a standardized classification system that could include adenomyosis pattern, location, histological variants and degree of myometrial involvement to advance the understanding of adenomyosis and enhance clinical management.

Given the substantial reproductive implications of adenomyosis, careful monitoring of pregnancies complicated by adenomyosis is essential. It is notable, however, that no standardized treatment exists for adenomyosis-related pregnancy complications; management primarily involves surveillance and supportive therapies to mitigate risk.

MANAGEMENT OF ADENOMYOSIS

Treatment of adenomyosis, particularly in women desiring to conceive, involves managing the symptoms while preserving fertility. Hormonal therapies have shown efficacy in reducing adenomyosis symptoms by inducing a hypo-oestrogenic state that shrinks adenomyotic lesions ([Vannuccini et al., 2022a](#)). However, there are currently no drugs that are specifically approved for the treatment of adenomyosis. For severe disease or when conservative treatments have failed, surgical options may be considered. This procedure targets the resection of

adenomyotic tissue to improve uterine function, but it poses significant risks for pregnancy.

Medical treatment options

Medical treatments for adenomyosis primarily involve hormonal therapies aimed at reducing symptoms and creating a more favourable uterine environment for conception. These treatments focus on manipulating hormonal concentrations to decrease oestrogen concentrations, as adenomyosis is oestrogen dependent, thereby managing inflammation and reducing lesion size. While hormonal therapies are effective in alleviating pain and HMB, they exert anti-gonadotrophic effects and inhibit ovulation, limiting their suitability for women actively seeking to conceive ([Vannuccini et al., 2018](#)). These treatments include the following.

Progestins

Progestins, such as dienogest, induce a pseudo-pregnant state with anti-oestrogenic effects, thereby minimizing the oestrogen-driven growth of adenomyotic lesions. Dienogest has a high affinity for progesterone receptors and exerts direct anti-inflammatory and antiproliferative effects on adenomyotic tissue. It has demonstrated efficacy in reducing pain scores, analgesic use and uterine volume ([Guo, 2023](#)).

The levonorgestrel-releasing intrauterine system

The levonorgestrel-releasing intrauterine system (LNG-IUS) provides localized hormonal therapy by releasing levonorgestrel directly into the uterine cavity. This system promotes endometrial atrophy and significantly reduces menstrual bleeding, which is particularly beneficial for women with adenomyosis-associated HMB. Although primarily intended for symptom relief, the LNG-IUS may also improve uterine conditions indirectly by reducing lesion volume.

Gonadotrophin-releasing hormone analogues

Gonadotrophin-releasing hormone (GnRH) analogues, including agonists and antagonists, are commonly used to induce a hypo-oestrogenic state by down-regulating the hypothalamic–pituitary–ovarian axis, thereby significantly reducing oestrogen production and causing adenomyotic lesions to regress. Additionally, GnRH agonists exert a direct antiproliferative effect through GnRH receptors expressed

on adenomyotic lesions within the myometrium, contributing to both local and systemic hypo-oestrogenic effects. They also modulate other pathogenic mechanisms by reducing inflammation and angiogenesis, leading to a substantial decrease in uterine volume and alleviation of symptoms such as bleeding and pain.

However, the hypo-oestrogenic effects of GnRH analogues can lead to side effects, including vasomotor symptoms and bone density loss, making them suitable primarily for short-term use or with 'add-back' therapy to mitigate these adverse effects. GnRH analogues have proved effective in preparing the uterus for conception, particularly before ART techniques.

Surgical approaches to preserve fertility

Conservative surgery may be considered in select patients who are unresponsive to medical therapy or have severe symptoms. Surgical treatment aims to excise or reduce adenomyotic tissue while preserving the structural integrity of the uterine wall.

Adenomyomectomy is a procedure designed to remove adenomyotic lesions from the uterus; several techniques are available, including wedge resection, modified reduction and the triple-flap method. While adenomyomectomy has shown promise in improving fertility outcomes, it carries certain intraoperative risks, such as haemorrhage, a need for transfusion, infections and adhesions. There is also a risk of uterine rupture during a subsequent pregnancy, underscoring the need for careful patient selection and surgical expertise ([Osada, 2018](#)).

In cases of diffuse adenomyosis, the procedure is typically more invasive and performed via laparotomy. For focal adenomyosis, minimally invasive options, such as laparoscopic adenomyomectomy, may be appropriate, providing shorter recovery times ([Osada, 2018](#)).

Optimizing ART outcomes

ART is a viable option in managing adenomyosis-related infertility. Despite the lower success rates associated with adenomyosis, adjusting the timing of embryo transfer to align with optimal endometrial receptivity may further enhance pregnancy rates. A 'freeze-all' strategy, delaying embryo transfer to avoid the potential detrimental impact of ovarian

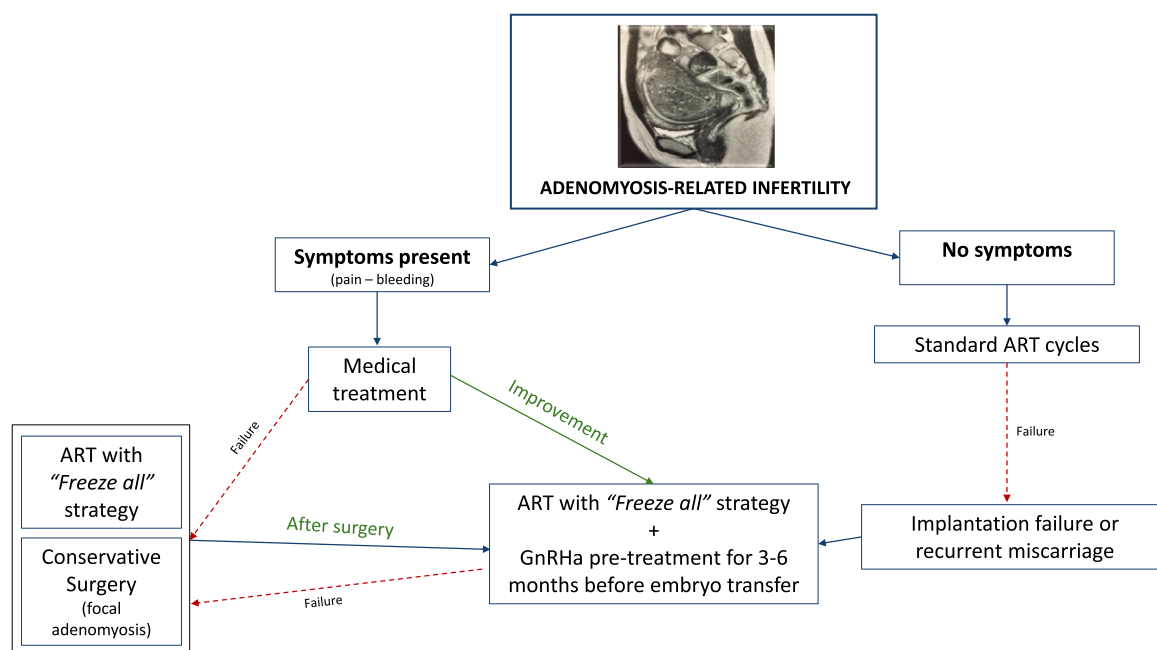


FIGURE 2 Management algorithm for adenomyosis-related infertility. In women with adenomyosis who present with symptoms such as pain and bleeding, management may begin with medical treatment to alleviate symptoms and modulate the uterine environment. If symptoms improve, assisted reproductive technology (ART) cycles with a ‘freeze-all’ strategy and deferred embryo transfer may be proposed. For individuals with persistent or recurrent symptoms, conservative surgery may be considered to enhance reproductive outcomes, especially in cases of focal adenomyosis. In patients who are asymptomatic or have mild symptoms, standard ART cycles are recommended. However, in cases of implantation failure or recurrent miscarriage, a freeze-all strategy with pre-treatment using a gonadotrophin-releasing hormone analogue (GnRHa) for 3–6 months before embryo transfer is proposed to optimize endometrial receptivity and improve pregnancy outcomes. Furthermore, if the ART freeze-all strategy fails, conservative surgery may be considered.

stimulation on endometrial receptivity, has shown promise in increasing cumulative live birth rates in individuals with adenomyosis (Bourdon *et al.*, 2024). In addition, pre-treatment with suppressive hormonal therapies, such as GnRH agonists with or without an aromatase inhibitor (Cuzzolino *et al.*, 2025), can improve implantation rates and overall pregnancy outcomes by decreasing the uterine volume, modulating endometrial receptivity (Wu *et al.*, 2022).

The management of adenomyosis-related infertility can be tailored according to symptom presentation and previous ART outcomes (FIGURE 2). However, the available data are derived primarily from retrospective studies, and there is an urgent need for more robust evidence, such as randomized controlled trials, to reach definitive conclusions on the effectiveness of these strategies.

Future treatments

Advances in understanding the pathogenesis of adenomyosis have sparked interest in non-hormonal therapies.

Experimental treatments, including selective progesterone receptor modulators, aromatase inhibitors and anti-angiogenic drugs, are under investigation. These therapies offer potential benefits by directly targeting inflammation and lesion growth, although they remain investigational (Guo, 2023; Vannuccini *et al.*, 2018).

Emerging non-invasive procedures such as high-intensity focused ultrasound (HIFU) present promising alternatives but require further study to establish their safety and efficacy. HIFU uses focused ultrasound waves to ablate adenomyotic tissue, potentially reducing symptom burden without requiring incisions. Preliminary findings suggest that HIFU may improve fertility outcomes, yet additional research is needed to confirm its long-term efficacy and safety during pregnancy (Guo, 2023).

CONCLUSIONS

Adenomyosis poses substantial challenges to women’s reproductive health. Despite

the improvement of non-invasive diagnostic tools, the awareness of the condition is still poor and the diagnosis is often missed, due also to a heterogeneity in clinical presentation and imaging criteria. Adenomyosis presents with various subtypes, distinct epidemiological profiles and symptoms, and thus it is frequently overlooked or misdiagnosed as common gynaecological comorbidities, such as uterine fibroids and endometriosis. Furthermore, the lack of approved drugs represents a considerable challenge in its clinical management. In addition, medical and surgical management do not follow shared recommendations, even though adenomyosis requires a lifelong management plan, including pain and bleeding control, fertility preservation and pregnancy complications. Thus, efforts are needed to raise awareness among healthcare professionals, aiming for early diagnosis of the condition for timely management and a tailored treatment strategy.

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