

(REVIEW ARTICLE)



## Literature Review on the Modern Management of Adenomyosis

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### Abstract

This review article discusses the current modern management of adenomyosis. Adenomyosis is common amongst women of child bearing age and it has many implications on quality of life. These women struggle with symptoms of dysmenorrhoea, menorrhagia and infertility. We discuss the medical, interventional and surgical management of adenomyosis. There are numerous medical treatments which involve hormonal and non-hormonal methods. The interventional methods consist of High intensity focus ultrasound (HIFU), percutaneous microwave ablation (PWMA) and radiofrequency ablation (RA). This paper also discusses the role of surgical technique and whether it has a role in the management of adenomyosis, currently surgical options are not routinely offered to patients. There have been promising studies which have identified that surgery has improved fertility, menorrhagia and dysmenorrhea for patients with adenomyosis.

**Keywords:** Adenomyosis; Menorrhagia; Dysmenorrhoea; Infertility; Management of Adenomyosis

### 1. Introduction



**Figure 1a:** Ultrasound image of diffuse adenomyosis (left) [1]. **1b:** MRI image of diffuse Adenomyosis (right) [2].

Adenomyosis is defined as the presence of endometrial glands and stroma in the myometrium [3]. The invasion can be accompanied with hypertrophy and hyperplasia of surrounding muscle cells, forming either diffuse or localised lesions.

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Adenomyosis is very common, and women present with menorrhagia, dysmenorrhoea, infertility and related pregnancy complications [4].

Adenomyosis is commonly diagnosed using pelvic ultrasound and Magnetic Resonance Imaging (MRI). Typical features on ultrasound are the presence of irregular endometrial-myometrial junction, hyperechoic islands, focal or diffuse myometrial bulkiness and increased vascular flow on doppler [5].

In this review article we will discuss the current modern management of adenomyosis. Management of adenomyosis is dependent on the symptoms, severity and fertility desire [4].

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## 2. Overview of Modern Management

There are multiple different options for managing symptoms of adenomyosis. In this article we will discuss medical, interventional and surgical management for adenomyosis.

### 2.1. Medical Management

Medical treatment consists of hormonal and non-hormonal methods. Non-hormonal methods consist of Non-Steroidal Anti-Inflammatory drugs (NSAIDs) which would be used to treat symptoms of dysmenorrhoea. Hormonal methods such as progestins and oral contraceptives are used to treat dysmenorrhoea and menorrhagia associated with adenomyosis [6]. Sharara et al. [7], summarised the effectiveness of GnRH antagonists which improved pelvic pain and size of adenomyotic lesions in a few case reports. However more work is required to investigate this further [7].

Levonorgestrel releasing - intrauterine system (LNG-IUS) has been used for its non-contraceptive benefits of improving dysmenorrhoea and menorrhagia. It has been identified in a few studies that LNG-IUS has been shown to be more effective than oral contraceptives. It reduces the uterine volumes, reduces pain scores and haemoglobin levels increased with use of LNG-IUS [7].

Danazol, is an androgenic hormone, has also been trialled in adenomyotic patients. Danazol-loaded IUS was used in one study where it improved dysmenorrhoea and there was a decrease in myometrial thickness in comparison to oral danazol. They also identified better fertility after removal of danazol-IUS [7].

Aromatase inhibitors (which stop the production of oestrogen) and GnRH agonists were compared for use in adenomyosis and identified that both were effective in reducing uterine and adenomyoma volumes, therefore reducing progression and improving symptoms [7].

Ulipristal acetate, a potent progesterone receptor modulator, has conflicting results in terms of its use. In some studies, it has shown an improvement in symptoms but in others it has identified worsening of symptoms. It also has adverse side effect of liver injury requiring liver transplantation, which removed its use from the European market. Therefore, this drug is not commonly used as treatment for adenomyosis [7].

There have been some mice studies on antiplatelet therapy for adenomyosis which suppressed myometrial infiltration, improved generalised hyperalgesia and reduced uterine contractility. However, there is no human data on its use [7].

Dopamine agonists such as bromocriptine is thought to be effective in adenomyosis as prolactin and its receptors are found in adenomyotic tissue. In a study it was identified that the use of dopamine agonists showed thinner maximal junction zone six months post treatment on ultrasound, however the results were insignificant on MRI. Its use has been shown in small pilot studies and bigger studies are required to identify if it makes a significant improvement in symptoms [7].

All the above medical treatments are not definitive treatments but manage the symptoms temporarily and with stopping the treatment, symptoms usually flare back. None the less in patients who would like to conceive and want relief of symptoms outside of pregnancy, medical treatments have been effective and widely used.

### 2.2. Interventional Management

There are newer minimally invasive techniques which use thermal energy sources on adenomyotic lesions to improve symptoms. There are three types: High intensity focus ultrasound (HIFU), percutaneous microwave ablation (PWMA) and radiofrequency ablation (RA) [8].

HIFU ablation is performed under either ultrasound or MRI. Patients are treated in a prone position and ultrasound waves are directed at a target lesion and causes instant coagulative necrosis. Patients are routinely admitted for one day, following a period of observation. During PMWA and RFA patients are supine, and an antenna are directed to the target lesion.

PMWA uses electromagnetic energy and RA uses high frequency alternating electrical current. Both these procedures produce heat energy which causes tissue necrosis. HIFU although its less invasive and doesn't use an electrode, there is a limitation of penetration of ultrasound for lesions that are deep. MWA and RFA, was identified to be more advantageous in comparison to HIFU due to shorter operator times, reduction in uterine and adenomyosis volume [8].

The non-invasive methods are desirable for patients and have brought interest amongst clinicians as an alternative for invasive methods. Although there have been short term benefits in improvement of symptoms, long term results are limited and there have been recurrence of symptoms [4].

### *2.2.1. Uterine Artery Embolization (UAE)*

In a review article by Popovic et al. [9], they looked at the effects of uterine artery embolization (UAE) on adenomyosis and identified that there is significant symptomatic relief in women undergoing UAE however the studies they reviewed, in some cases there was a combination of women having adenomyosis and leiomyoma, so it was difficult to ascertain if the effects were on leiomyoma or adenomyosis. There was also a lack of standardised method of identifying improvement in symptoms across all the different studies, making it difficult to make effective comparison across the studies. Although this method seems a viable option for treatment, more robust data are required to assess if this would be a potential for first-line treatment [9].

## **2.3. Surgical Management**

There are multiple surgical techniques that have been used in adenomyosis with newer techniques which also has come to fruition. They can be broadly categorised into laparoscopic and laparotomic techniques.

### **2.4. Laparotomic Techniques: Partial Excision**

#### *2.4.1. Wedge Resection*

The classical technique of wedge resection of the uterine wall entails removal of the focal adenomyoma as well as the seromuscular layer in a 'V' shape. The wound is closed with remaining muscular and serosal layer. This technique would be suitable for focal adenomyosis. However there have been limited benefits for symptoms of menorrhagia and dysmenorrhoea and high recurrence due to leaving behind some adenomyotic tissue [10].

#### *2.4.2. Modified Reduction Surgery*

In the 1990s there were a few studies where they performed partial excision of adenomyotic tissue, and 6 women went on to conceive later and none miscarried. Whereas in another study out of the 28 patients who had this procedure, 50% had live births and 38.8% had a miscarriage [10].

#### *2.4.3. Transverse H Incision of the Uterine Wall*

Another modified laparotomic procedure has been described whereby a transverse H incision is performed on the uterine fundus using electro-surgical scalpel separating the uterine serosa to uterine myometrium and then removing adenomyoma tissues. They then completed the procedure by suturing the myometrial edges in one or two layers. In a later study they identified that women who had undergone this procedure 38% achieved clinical pregnancy, 16.1% miscarried and 22.5% had live births [10].

## **2.5. Laparotomic Techniques: Complete Excision**

### *2.5.1. Triple Flap Method*

This technique is effective in diffuse adenomyosis and has potential to prevent uterine rupture in future pregnancies. This technique involves palpating and identifying the areas of adenomyosis and performing adenomyomectomy by opening the uterine cavity and then reconstruction of the uterine wall resistant to rupture. A study looked into women who had undergone this procedure and identified that in 81.4% the blood flow in the operated area had gone back to normal within six months. Also, out of the 46 who conceived 32 had delivered a healthy baby by elective caesarean section. With no cases of uterine rupture. Over the 27 years of the study, only 3.5% of the cases relapsed and required

a second surgery. The limitation of this technique is that it has to be done under open technique as it requires the palpation of the adenomyosis, and delicate suturing of the hand is required [10].

### 2.5.2. Asymmetric Dissection Method

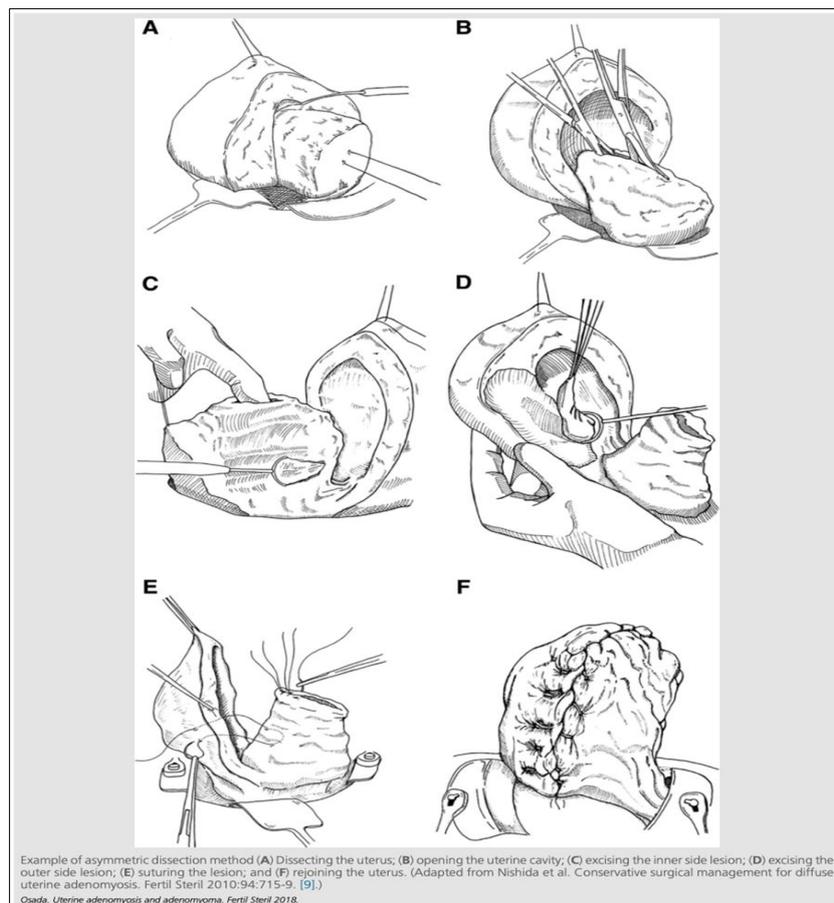
This technique involves excising the adenomyoma by opening the uterine cavity in a diagonal manner by inserting an index finger and palpating for the lesion and ensuring to excise >5mm of inner myometrium as well as >5mm of the serosal myometrium. The uterine cavity is then reconstructed. Figure 2 shows the step-by-step approach of this method. However, the main limitation of this technique is the risk of uterine rupture. There was spontaneous uterine rupture identified in 5 cases out of the 1,349 operated on [10].

### 2.5.3. Hysterectomy

This method is the gold-standard treatment for adenomyosis, and it has been used for many years as a treatment of adenomyosis. However, this method is not preferable in patients who wish to preserve their fertility.

## 2.6. Laparoscopic Techniques

Laparoscopic techniques should be used for focal adenomyosis as there is limited use of instruments and direction of movement. Moreover, the surgeon cannot palpate to identify adenomyotic lesions.



**Figure 2** The step-by-step method of asymmetric dissection [10]

There are several techniques that can be used laparoscopically, a longitudinal or transverse incision is performed across the adenomyoma. The adenomatosis is resected using monopolar needle or laser knife. If there is a breach to the endometrial cavity, this is sutured and the area excised is sutured in two or more layers. The adenomyotic mass is removed either by morcellator or a removal bag. There have been concerns that using a morcellator may disperse undetected malignant tumours and therefore spread it throughout the abdominal cavity [10].

In a study performed in 2017, 74 patients who had undergone this surgery 13 (41.9%) had conceived, 4 had a miscarriage and 9 (29.0%) had live births. There were no reports of any uterine rupture. In another study where they looked at pregnancy's in <40s and in >40s following laparoscopic adenomyomectomy. Although the rate of pregnancy was higher in women <40 years, from those who conceived in the older age group, two cases ended up with a hysterectomy for placenta accrete [10]. There have been benefits of both laparoscopic and laparotomic procedures in relieving symptoms of menorrhagia and dysmenorrhoea without limiting fertility. However, despite these benefits, due to the scar on the uterus the risk of uterine rupture increases in any women having any surgery to the uterus whether that is laparoscopic or laparotomic. In addition to that, it also poses risk for abnormal placentation in pregnancy.

### **2.7. Robot-Assisted Laparoscopic Adenomyomectomy**

Four cases of robotic assisted laparoscopy are discussed by Chung et al. 2016 [11], where they used robotic assisted laparoscopy to treat adenomyosis in 4 women who wished to preserve their fertility. They all had improvement in pelvic pain and no residual adenomyotic tissues were seen post-operatively after a pelvic MRI. The advantages of robotic surgery is that it has better visual field, with 3D high definition and the robotic arm has an endowrist with better range of movement in comparison to standard laparoscopy, allowing better suturing similar to laparotomic suturing. Therefore, this method has been suggested to be preferential to standard laparoscopy, however there is limited data on its use and bigger trials are required to identify benefits of robotic surgery over laparoscopy [11].

### **2.8. Combining Laparoscopy and Levonorgestrel Releasing-Intrauterine System (LNG-IUS)**

There was a study performed by Sun et al, 2021[12] that investigated the efficacy of combining laparoscopic adenomyomectomy and insertion of levonorgestrel releasing-intrauterine system (LNG-IUS). They looked at whether there would be a difference in scores for dysmenorrhea, menorrhagia and uterine volume using ultrasound. They identified that in the 50 women in their study there were clinical effectiveness in pelvic pain amongst patients where 98%, 96% and 96% at 3, 12 and 24 months post-operatively, respectively. The clinical effectiveness for menorrhagia were 97.6%, 95.2% and 95.2% at 3, 12 and 24 months postoperatively, respectively. The main adverse effects were uterine perforation, which occurred in one case and expulsion which occurred in 2 cases [12].

This study shows that combination therapy could be a beneficial method for patients as there is not one technique that has been proven to be therapeutic, except for the traditional hysterectomy method, therefore this can potentially reduce risk of recurrence and treat symptoms in patients with diffuse adenomyosis who do not wish to have laparotomy.

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## **3. Discussion**

Adenomyosis is very common in women of fertile age and is associated with menorrhagia, dysmenorrhoea and infertility which significantly affects quality of life. The traditional treatment has been hysterectomy, but this is not favourable in the younger population as it is not fertility preserving hence, we looked into the newer techniques available that will enable fertility preservation and which are less invasive. These two qualities would be very appealing to our patients and much more favourable if they prove to be beneficial in treating adenomyosis.

There are multiple therapies to treat adenomyosis that has been discussed, medical therapies mainly have symptomatic relief and restricted to duration of treatment for example: NSAIDs, progestins, COCP, GnRH agonists and antagonists, LNG-IUS, Danazol, aromatase inhibitors, ulipristal acetate and dopamine agonists. Furthermore, newer less invasive techniques such as HIFU, PWMA, RA and UAE have been used which has shown benefit for symptomatic relief. These newer techniques have shown to be promising, but they come with their risks and side effects and more studies are required to identify long term benefit and recurrence rates. There are also multiple surgical techniques which range from laparotomic, laparoscopic and robot-assisted laparoscopy. Laparotomy unfortunately is associated with longer hospital stay, higher estimated blood loss and longer recovery in comparison to laparoscopic techniques. The latter have been favoured especially in patients with comorbidities and obesity and has therefore broaden the spectrum of patients who could benefit from this technique.

In one systematic review by Grace Younes, MD, and Togas Tulandi [13], where they have evaluated 27 studies: 10 prospective and 17 retrospective studies including a total of 1398 patients. They found that excision of adenomyosis is effective for symptom control such as menorrhagia and dysmenorrhea and most probably for adenomyosis-related infertility [13]. For preserving fertility and relieving symptoms, medical treatment is usually the first choice, whereas excisional surgery could be performed for refractory adenomyosis. The results show that over three-fourths of women will experience symptom relief after conservative surgery. The pregnancy rates after conservative surgical treatment vary widely. However, three-fourths of them conceived after surgery with or without adjuvant medical treatment. Depending on the duration of follow-up, recurrence rates differ from no recurrence to almost one-half of patients.

Conservative surgery for adenomyosis improves pelvic pain, abnormal uterine bleeding, and possibly fertility but the best method of surgery is yet to be seen. Robot-assisted laparoscopy has very limited studies in its use but has been proposed to be better than standard laparoscopy for its increased range of movement and enables suturing like laparotomy. In all of these surgical techniques the main advantages were that there was significant improvement in symptoms and patients were able to conceive and have healthy live births after surgery. Which is a massive breakthrough in surgery, however there are associated risks, one of which is spontaneous uterine rupture and there have been cases where this has occurred in patients following surgery. Therefore, more studies are required to assess long term benefits and risk of recurrence as to whether fertility preserving surgery should become the gold standard.

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#### 4. Conclusion

As discussed above the management of adenomyosis is very complex and it has different elements. The most important of which that we have identified is that surgical treatment can have a role in the management of difficult cases, therefore, it should be considered by the clinician from now on and offered to the patient as an option for managing adenomyosis.

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#### Compliance with ethical standards

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##### *Disclosure of conflict of interest*

Both authors declare that they have no conflict of interest.

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