



Surgery in adenomyosis

Marco Aurelio Pinho Oliveira^{1,4} · Claudio Peixoto Crispi Jr.² · Leila Cristina Brollo¹ · Claudio Peixoto Crispi² · Rudy Leon De Wilde³

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Abstract

Introduction Adenomyosis is defined as the presence of endometrial glands and stroma within the myometrium. The true prevalence is unknown and has been reported to range from 1 to 70%. It has a significantly negative impact on women's quality of life, causing abnormal uterine bleeding, dysmenorrhea, and chronic pelvic pain. The definitive treatment for adenomyosis is hysterectomy, although it does not contemplate patients who wish to preserve their fertility. The aim of this paper is to discuss the latest evidence on the surgical techniques for the treatment of adenomyosis published in medical–scientific databases.

Method A comprehensive literature search for articles published from 1996 to 2017 related to surgery for adenomyosis was made in Pubmed, Medline, the Cochrane Library, and Google Scholar, in English, by the following MeSH terms: adenomyosis, surgery, pathogenesis, dysmenorrhea and infertility.

Results There is extensive evidence on several surgical approaches for the improvement of adenomyosis-related symptoms; however, there is no robust evidence that they are effective for infertility.

Conclusion The management of adenomyosis is quite complex and controversial. Complications after extensive uterine reconstruction, such as uterine rupture, should be considered and discussed with the patient. There are still limited data to support surgery effectiveness, especially for infertility, and further well-designed studies are required.

Keywords Adenomyosis · Treatment · Review

Introduction

Endometriosis and adenomyosis are considered as variants of the same disease and often-coexisting conditions [2]. There is evidence showing that endometriosis and adenomyosis have in common an endometrial dysfunction involving eutopic and heterotopic endometrium [3].

Although there are some similarities, including some pathogenic mechanisms with endometriosis, there is enough evidence (including molecular mediators) to corroborate that adenomyosis is an independent disease [24, 43, 44]. However, both diseases often coexist and around 20% of patients undergoing surgery for the treatment of endometriosis have uterine adenomyosis [7].

Adenomyosis is defined as the presence of endometrial glands and stroma within the myometrium. The true prevalence is unknown and has been reported to range from 1 to 70%. This large range is due to lack of standard diagnostic criteria by imaging modalities and pathological analysis [37]. It is most often diagnosed in middle-aged and multiparous women [3, 34].

The evaluation of myometrial junctional zone provided non-invasive diagnostic criteria for adenomyosis, when patients present a diffuse or focal non-uniform thickness more than 12 mm [3, 9]. However, diffuse thickening of the junctional zone should be carefully distinguished from

✉ Marco Aurelio Pinho Oliveira
endometriose@gmail.com

¹ Department of Gynecology, State University of Rio de Janeiro, Rio de Janeiro, Brazil

² Crispi Institute of Minimally Invasive Surgery, Rio de Janeiro, Brazil

³ Clinic of Gynecology, Obstetrics and Gynecological Oncology, Pius Hospital, University Hospital for Gynecology, Carl von Ossietzky University Medical School, Oldenburg, Germany

⁴ Rua Dois de Dezembro 78/803, Flamengo, Rio de Janeiro, Brazil

physiological changes, since the thickness of junctional zone varies considerably during the menstrual cycle [15].

The use of preoperative imaging has shown that adenomyosis may also occur in adolescents, but diagnosis is based on histologic examination, especially after hysterectomy [2, 37]. Magnetic resonance imaging findings may be more helpful than transvaginal ultrasound in distinguishing adenomyosis from a leiomyoma and more effective for both diffuse and focal adenomyosis [16].

Diffuse adenomyosis should be differentiated from nodular adenomyosis [35]. Diffuse adenomyosis is an ectopic and diffuse growth of the endometrium cells into the myometrium with either diffuse or focal enlargement of junctional zone. Nodular adenomyosis is a focal form, circumscribed within the myometrium [9].

Adenomyosis has a significantly negative impact on women's quality of life, causing abnormal uterine bleeding, dysmenorrhea and chronic pelvic pain. There is a lack of consensus in the literature regarding the relationship between adenomyosis and fertility [42].

The treatment depends on the symptoms, severity and fertility desire and there are several methods, such drug therapy with gonadotropin-releasing hormone agonists (GnRHa) and nonsteroidal anti-inflammatory drugs (NSAIDs), levonorgestrel intrauterine system (LNG-IUS), danazol-loaded intrauterine devices, uterine artery embolization, and hysterectomy. For women who require fertility, there are conservative surgeries, and many surgical techniques have been proposed [8, 17, 29].

Medical treatment

Several medical treatments have already been evaluated in patients with abnormal uterine bleeding and/or pain related to adenomyosis. The studies are quite heterogeneous, especially in diagnosis criteria [36].

Some authors consider progestins as the first line of medical treatment, mainly in the form of intrauterine system with levonorgestrel. This therapeutic modality is effective in reducing the symptoms related to adenomyosis with improvement of the quality of life. GnRH agonists appear as a second option for patients with symptoms refractory to progesterone use. GnRH-a reduce inflammation and angiogenesis but their use is limited due to side effects [36]. Combined oral contraceptives may also be effective in treating symptoms related to adenomyosis especially when used continuously [33].

Adenomyosis is associated with a negative impact on fertility, decreasing the rate of spontaneous pregnancy and increasing the rate of abortion. It also has a negative impact on the results of assisted reproduction techniques. However, there is no evidence that medical treatment can improve pregnancy rates [36].

Sonographic interventions

The use of high intensity ultrasound (ultrasound guided or magnetic resonance guided) in the treatment of adenomyosis has grown in the last years. Some studies present interesting results regarding the improvement of symptoms associated with pain and bleeding, as well as in the reduction of uterine volume [1]. There is no evidence on the improvement of infertility with those therapeutic options. Reports of pregnancy after sonographic interventions are anecdotal [5].

Radiologic interventions

Uterine artery embolization, initially used for fibroids, has also been used in the treatment of symptoms associated with adenomyosis. Some authors have shown promising results with this technique that represents an alternative to hysterectomy [1].

Surgical treatment

Hysterectomy is the gold standard treatment for women who have no desire for future fertility. Any form of hysterectomy offers the advantage of no chance of recurrence [1]. The procedure may be performed abdominally, vaginally or laparoscopically depending on several factors. However, it is important to emphasize that subtotal hysterectomy should be avoided, as there are reports of recurrence of the disease in the cervical stump or in the rectovaginal septum [31].

Presently, minimally invasive techniques are preferred to laparotomic techniques. Vaginal hysterectomy is an option because it is a safe option and with good postoperative results [31]. Interestingly, in an earlier comparative study of complications during vaginal hysterectomy in patients with adenomyosis or fibroids, there was an increased risk of bladder injury during the procedure in the adenomyosis group [11].

There are few specific comparative studies of hysterectomy route on outcomes in patients with adenomyosis. However, laparoscopic approach does not seem to increase the risks of perioperative complications [47]. Even when the single-port technique is performed, the procedure appears to be safe, with no increase rates of conversions or complications [20].

Hysterectomy obviously can permanently resolve symptoms related to abnormal uterine bleeding. As for the pain-related symptom, hysterectomy also presents good results, although there is a chance of persistence of pain, especially if there is the concomitant presence of endometriosis [25, 27, 46].

However, in a recent prospective study of laparoscopic supracervical hysterectomy in premenopausal women with cyclic pelvic pain, the presence of endometriosis did not alter the satisfaction indexes [4].

Endometrial ablation/resection

Endometrial ablation/resection is widely used in the treatment of abnormal bleeding and may include patients with adenomyosis. It is an alternative to hysterectomy and is not indicated to patients who desire pregnancy. However, clinical failure is high and this procedure reduces the chance of hysterectomy by only 30%. The combination of endometrial resection and the LNG-IUS is a possible alternative to hysterectomy in women who have completed their childbearing, while in women who wish to retain their fertility the LNG-IUS alone is a reasonable choice [8]. Results may be better in superficial endometriosis and when levonorgestrel IUS is inserted after the resection [41].

Conservative (fertility-sparing procedures)

In recent years, the desire of getting pregnant with advanced age has increased, which leads to a greater chance of being affected by adenomyosis, which can affect fertility in several ways. Some studies have suggested that adenomyosis may interfere with embryo implantation, but few data on the epidemiology of adenomyosis in pregnancy and fetal loss are available [12, 42]. The reproductive performance of women with adenomyosis seems to have a lower implantation rate per embryo transfer, lower clinical pregnancy and live birth rates and a higher spontaneous abortion rate [42]. There is growing evidence that a pre-pregnancy disorder of the myometrial junctional zone is the mechanism that affects reproductive and obstetrical outcomes [6].

After failure of clinical treatments for infertility, including assisted reproductive therapies, women with adenomyosis may be offered fertility-sparing surgery. Some authors even suggest the term “hysteroplasty” for this type of technique, which is so challenging for gynecological surgeons. However, conservative surgery, or uterine-sparing surgery, is not considered the standard treatment of this disease. First, there are several non-standard techniques available. Secondly, none of the techniques can guarantee complete excision of the disease from within the myometrium due to its infiltrative pattern. These characteristics lead invariably to damage to healthy uterine musculature during this type of procedure, which can increase uterine rupture in case of pregnancy [13].

The main indication for performing conservative surgery is the preservation or even improvement of fertility in patients with symptomatic adenomyosis and who wish to get pregnant. Combined conservative surgery with GnRHa or

conservative surgery alone has been reported in the management of sub-fertile women with adenomyosis. GnRHa has a synergistic effect in improving fertility and pregnancy for women with adenomyosis. Successful pregnancies following combined cytoreductive surgery with GnRHa were reported in several small studies and case reports [6], but an increased woman's age has an adverse impact for fertility outcomes, regardless of conservative surgery for the focal or diffuse disease forms. Among women ≤ 39 years and ≥ 40 years of age, clinical pregnancy rates were 41.3 and 3.7%, respectively, following conservative surgery [21]. The maintenance of future fertility in women treated with conservative surgery should be considered, especially in those less than 40 years of age [42].

A large meta-analysis included 64 studies and 1049 patients undergoing conservative surgeries for symptomatic adenomyosis. Significant reduction of dysmenorrhea after conservative surgery ranges from 54.6 (non-excisional techniques) to 84.6% (complete adenomyomectomy). Significant reduction of menorrhagia ranges from 50 to 68.8% (myometrectomy) or even 73.7% (non-excisional techniques). The pregnancy rate ranges from 46.9 (partial adenomyomectomy) to 60.5% (myometrectomy) [13].

There are two basic types of conservative techniques [13, 16]: (1) non-excisional techniques such as thermal coagulation of the diseased myometrium and (2) excisional techniques including adenomyomectomy with complete removal of the focal disease, usually adenomyoma, and myometrectomy, with partial removal of the diseased myometrium, usually diffuse type.

The non-excisional techniques preserve the anatomical structure, without surgical removal of adenomyotic tissue and adjacent myometrium. These techniques include, for example, laparoscopic electrocoagulation of the diseased myometrium and radiofrequency technology [13]. Phillips et al. [32] treated ten patients with symptomatic adenomyosis with laparoscopic bipolar electrocoagulation of the disease. Twelve months postoperatively, seven women had continued resolution or significant reduction of dysmenorrhea and resolution of menorrhagia. One woman with unresolved dysmenorrhea and menorrhagia required hysterectomy and two with recurrent menorrhagia required resection of the endomyometrium.

More recently, radiofrequency technology was used in 15 women with symptomatic nodular adenomyosis, who had no plans for pregnancy but declined hysterectomy. A 14-gauge needle, with an exposed tip, and seven extendible prongs (secondary electrodes) at the distal end (Fig. 1) is laparoscopically inserted in the suspected area. That device produces a spherical area of coagulative necrosis, with a maximum diameter of 5 cm. The target temperature of the radiofrequency was 98 °C. The median adenomyosis reduction in volume was 32, 49.4, 59.6, and 65.4% at 3, 6, 9, and

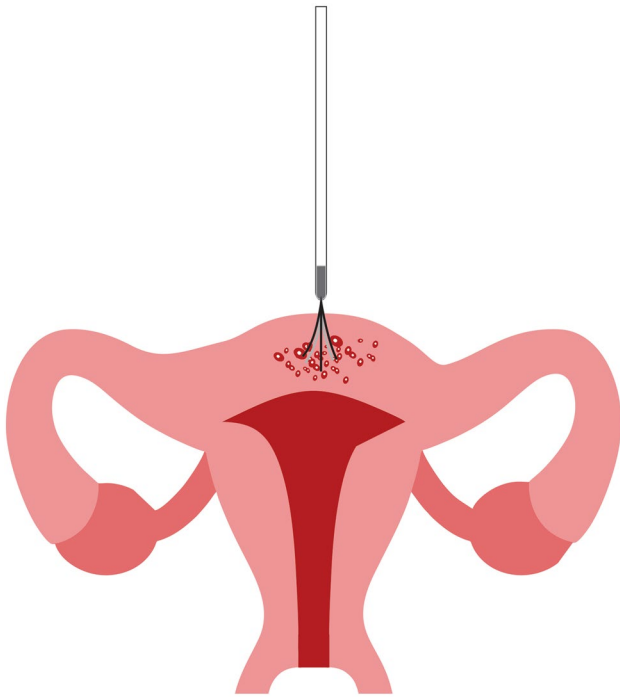


Fig. 1 A 14-gauge needle with seven extendible prongs (secondary electrodes) are inserted laparoscopically in the suspected area

12 months, respectively. A significant progressive improvement in the symptoms score was observed at follow-up, with 71.3% of VAS score reduction in 12 months [35].

The development of non-excisional surgical techniques supports the major concern in maintaining a functional uterus after conservative surgery. Sometimes the myometrial defect after excision becomes too large and may be difficult to maintain an adequate uterus for future pregnancy [13].

Excisional techniques (adenomyomectomy or myometrectomy)

Horng et al. [16] classified the excisional conservative procedures as: type 1, which includes complete removal of the lesion (adenomyomectomy) and type 2, which comprises cytoreductive surgery in the treatment of diffuse adenomyosis (myometrectomy). According to this study, type 1 can better preserve the integrity of the uterine wall; whereas type 2, there is a greater risk of uterine rupture in future pregnancies, because of the size of the defect.

Adenomyomectomy (type 1)

Adenomyomectomy is the preferred technique in cases of focal disease (adenomyoma) and may be used in some cases of diffuse disease (Figs. 2a, b, 3). Basically the

affected region is identified and all macroscopic lesions are usually completely removed. The uterine wall is sutured at the end [29]. Adenocystectomy is reserved for rare cases of the disease in its focal cystic form; and consists of the complete removal of this form of disease presentation [39].

Adenomyomectomy has long been described by Hyams [18]. In this study, the classical technique was used, very similar to myomectomy. After a longitudinal incision of the uterine wall they performed dissection and extraction of the lesion and, finally, closure of the uterine wall.

Using the same technique, laparoscopically, Morita et al. [26] performed an excision of adenomyomata in three women with severe dysmenorrhea and hypermenorrhea. There were no intraoperative or postoperative complications. Dysmenorrhea and hypermenorrhea disappeared by the end of the first postoperative menses.

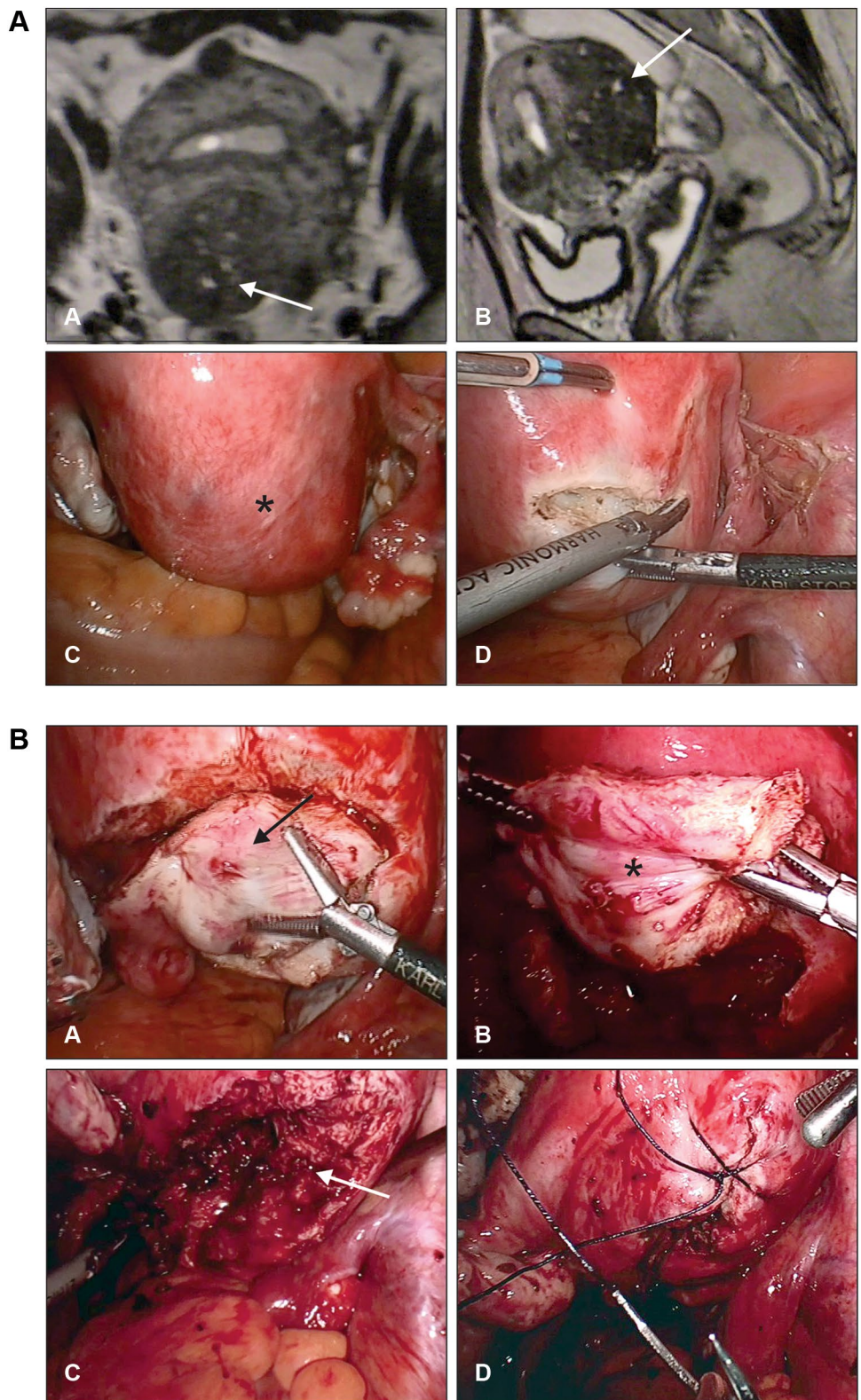
Another study with six consecutive cases of patients undergoing classic laparoscopic surgery for focal adenomyosis had excellent results: there were no intraoperative or postoperative complications and there was a complete regression of the symptoms in a mean follow-up of 13.7 months [14].

Sun et al. [38] performed resection of adenomyoma with monopolar needle laparoscopically, after removal of the adenomyomatous tissue. The cave like wall wound is approximated by U-shape sutures at the muscular layer; the seromuscular layer is closed by figure-eight sutures. Of the patients who underwent this modified technique, 91.2% showed improvement of dysmenorrhea and 40% improved menorrhagia. Of the infertile patients, the pregnancy rate after surgery was 23.1% for natural pregnancy and 45.5% for assisted reproductive techniques.

Another modified laparoscopic technique for reconstruction of the uterine wall was developed by Takeuchi et al. [40]. In this technique of overlapping flaps, the transverse incision is made in the adenomyotic tissue, and the lesion is excised with a monopolar needle, after diluted vasopressin is locally injected into adenomyotic tissue. The remaining seromuscular layers are overlapped and sutured to cover the excised layer of the uterus. In this study, all cases of abnormal bleeding had improvement and there was a significant reduction in the pain scale during menstruation.

In a study of laparoscopic partial resection of symptomatic adenomyosis combined with uterine artery occlusion, 37 patients with symptomatic adenomyosis and history of failed medical treatment, menorrhagia was improved in all women at 6-month follow-up. Median score of dysmenorrhea was 8 before surgery and only 4 at 12 months after surgery. This combined technique may be an alternative method for the treatment of symptomatic adenomyosis, instead of hysterectomy and/or uterine artery embolization [19].

Fig. 2 a 34 years, nulliparous woman. **A** MRI axial view of adenomyoma in the posterior uterine wall (white arrow). **B** MRI sagittal view of adenomyoma in the posterior uterine wall (white arrow). **C** Laparoscopic view of adenomyoma in the posterior uterine wall (black asterisk). **D** Transverse incision of the posterior uterine wall with harmonic scalpel (courtesy of Oliveira, MAP). **b** Same case from previous figure. **A** Wedge resection of the adenomyoma (black arrow). **B** Resection completed (black asterisk). **C** Uterine defect after resection (white arrow). **D** Laparoscopic suture of the defect (courtesy of Oliveira, MAP)

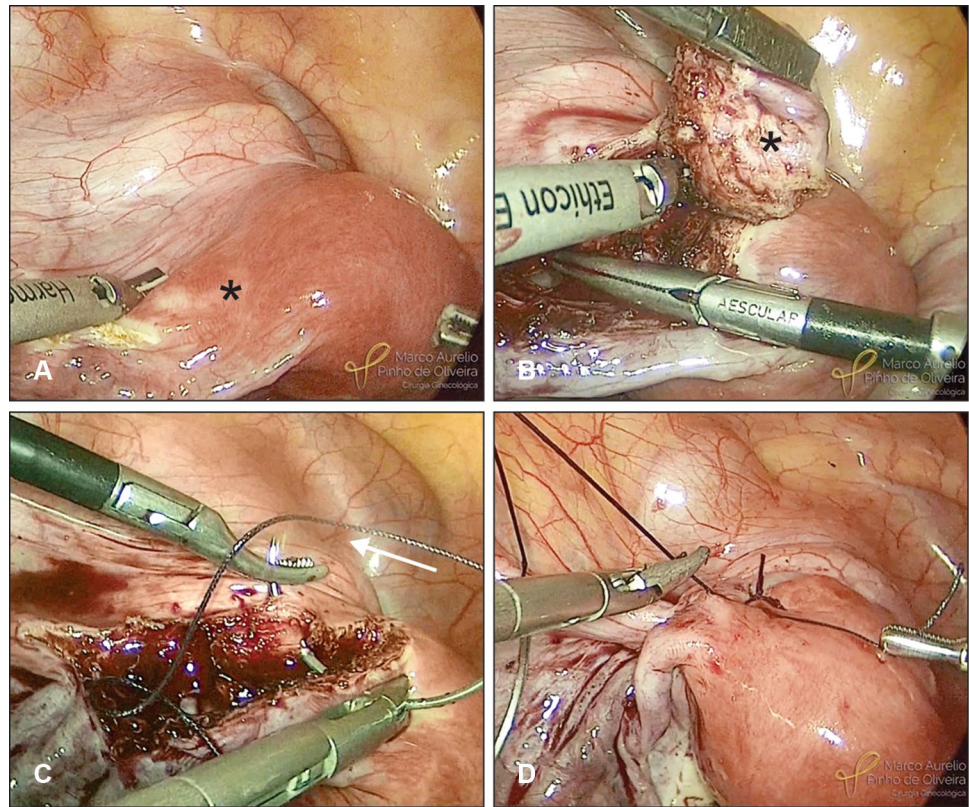


Myometrectomy (type 2)

Preferably used in the treatment of diffuse/severe adenomyosis. This technique consists of removing as much

of the macroscopic lesion as possible. Sometimes it is not possible to remove all the disease and the surgery is considered cytoreductive only. If a large amount of healthy

Fig. 3 31 years, nulliparous woman. **a** Adenomyoma (black asterisk). **b** Resection of adenomyoma with harmonic scalpel (black asterisk). **c** Uterine defect after resection (beginning closure). **d** Laparoscopic suture completed (courtesy of Oliveira, MAP)



myometrium is excised, the result could lead to a “functional” hysterectomy [13].

In the classical technique, the steps are like an abdominal myomectomy. A transverse or vertical uterine incision is applied, then adenomyotic tissue is resected; the uterine wall is inspected for macroscopic adenomyotic lesions. Uterine closure is done by two or three layers of suturing by interrupted technique. Hematoma should be prevented taking care to close the base of the uterine defect [10].

Fujishita et al. [10] compared the classical technique with their technique, a transverse H incision technique, in which two transverse incisions are made perpendicularly to one vertical incision, to achieve the affected myometrium. There were no differences in blood loss and operation time between the two groups. Postoperative relief of pain was more evident in the modified than in the classical group. There was no case of pregnancy in the classical group; however, one patient conceived spontaneously 4 months after operation by this H incision procedure.

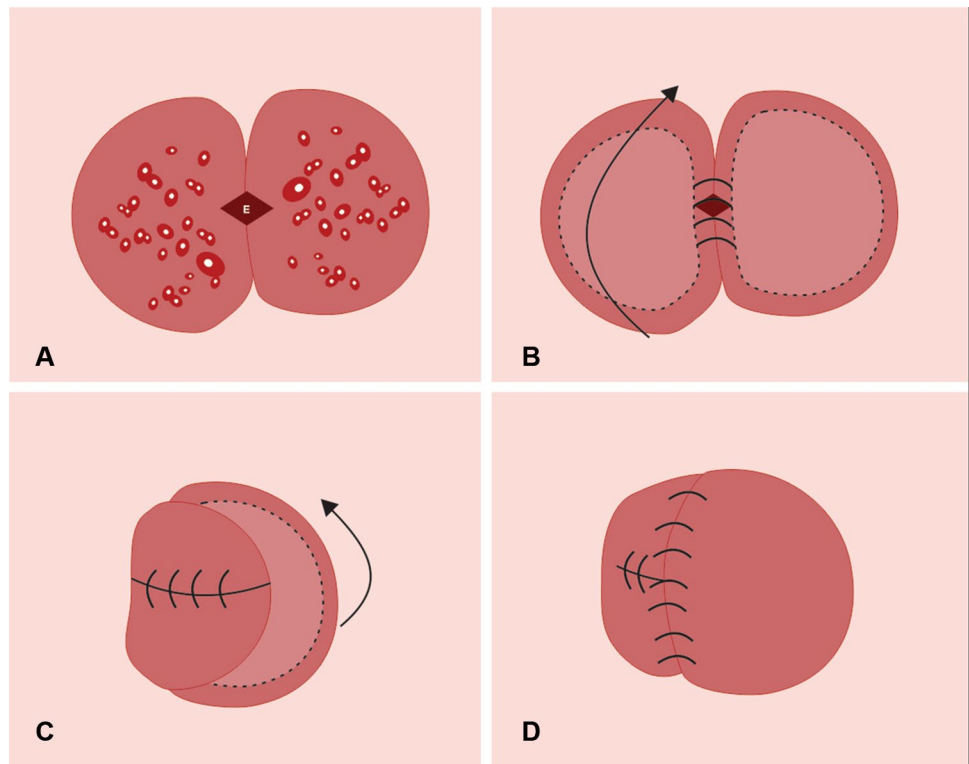
In another laparotomic technique, after diluted vasopressin injection, uterine fundus was retracted upward with a number 1 silk suture and then was transected longitudinally to divide inside and outside. An asymmetric dissection of the uterus was performed preserving both the uterine cavity and the uterine arteries. From the incision, the myometrium was dissected diagonally, as if hollowing out the uterine cavity. Next, a transverse incision was made to open the uterine

cavity. While inserting the index finger in the uterine cavity, the adenomyotic lesion was excised using a loop electrode to a thickness of 5 mm of the inner myometrium. The procedure continues with excision of adenomyosis to a thickness of 5 mm of the serosal myometrium. Endometrial cavity was then closed, and the uterine flaps were rejoined in layers. Using this procedure, Nishida et al. [28] have obtained some good results: the mean VAS score of dysmenorrhea decreased from 9.4 to 0.8, and anemia due to menorrhagia improved in all women. Two patients became pregnant.

Complete removal of the disease is more feasible in focal disease. However, Osada et al. [29] developed a laparotomic technique for the treatment of the severe diffuse form of the disease, known as the “triple-flap method”. It consists of radical excision of adenomyosis (leaving 1 cm margin of tissue above the endometrium and 1 cm margin of tissue below the serosal surface), with subsequent triple-flap reconstruction of the uterus (Fig. 4). A rubber tourniquet is placed before resection to reduce blood loss. This technique was used in 104 women, with a significant reduction of symptoms related to bleeding and pain. Of the 26 women who desired pregnancy, 16 could get pregnant and 14 went to term and all of them delivered a healthy baby. There were no cases of uterine rupture.

A prospective study included 103 Iranian women with symptomatic uterine adenomyosis. Conservative surgery removed as much of the adenomyotic lesion as possible. The

Fig. 4 Osada procedure (adapted from [29]). **a** Diffuse adenomyosis (*E* endometrium). **b** Resection of adenomyosis with cold scalpel (leaving 1 cm margins at serosa and endometrium) and suture of defect in multiple layers. **c** Closure of one of the flaps. **d** Uterus after mobilization and suture of all flaps



surgical procedure involved resection of lesions with a thin (≤ 0.5 cm) margin (wedge-shaped removal) after sagittal incision in the uterine body. Reconstruction was performed in layers. Of 70 patients who attempted pregnancy, naturally or by assisted reproductive therapies, 30% achieved a clinical pregnancy and 16 resulted in a full-term live birth. Dysmenorrhea and menorrhagia were reduced post-surgery. Only one patient had a recurrence of adenomyosis. In this study cytoreductive surgery proved to be an effective procedure to treat severe adenomyosis [34]. The main difference between this technique and that of Nishida et al. [28] is the non-opening of the endometrium.

Cytoreductive surgery has been shown to be more effective than medical treatments, both in symptomatic improvement and in infertility. Wang et al. [45] performed a comparative study of the cytoreductive surgery outcomes using the classical technique (with or without the use of GnRH-a prior to surgery) and the use of GnRH-a therapy alone. Cumulative 3-year clinical pregnancy and successful delivery rates were significantly higher in surgery group, compared with those in GnRH-a therapy only group (46.4 versus 10.8%, $p = .002$, and 32.1 versus 8.1%, $p = .022$, respectively).

Myometrectomy with transient occlusion of uterine arteries may be used for conservative surgical treatment in patients with severe diffuse adenomyosis. Kwon et al. [23] performed this procedure by laparotomy in 26 patients with symptomatic diffuse uterine adenomyosis. They used

a similar technique described by Nishida et al. [28]. After arteries occlusion, the uterus was bisected perpendicular to the axis, also opening the endometrial cavity. They preserved a minimal of 5-mm depth of the tissues underlying the endometrium, as it was done also in serosa. For suturing, the uterus layers were approximated with interrupted sutures. There were no major complications during the mean follow-up period of 13.5 months. At the 7-month follow-up, no patient complained of menorrhagia and complete remission of dysmenorrhea was observed in 94.4% of women. Kwack et al. [22] treated successfully a patient with diffuse adenomyosis using the technique described by Kwon et al. [23]. After in vitro fertilization, she achieved an intrauterine twin pregnancy and delivered at 32 weeks of gestation by an uncomplicated cesarean section.

Maintaining a healthy uterus is of paramount importance in conservative surgeries for adenomyosis. Otsubo et al. [30] evaluated the uterine wall thickness using magnetic resonance and/or sonography in women who underwent uterine-sparing surgery for diffuse uterine adenomyosis prior to conception. Of the 23 women, 10 had an early miscarriage and 13 proceeded to delivery. Of the miscarriage cases, two had a uterine rupture probably caused by wide excision of the uterine wall. They concluded that the optimum wall thickness should be from 9 to 15 mm to allow conception and prevent uterine rupture during pregnancy.

Conclusion

The management of adenomyosis is quite complex and controversial. Clinical treatment offers a variable response to abnormal uterine bleeding and dysmenorrhea. Although hysterectomy remains the definitive treatment for women with severe symptoms, conservative surgery should be offered to women who desire to preserve fertility. Conservative surgical may improve the associated symptoms in case of clinical treatment failure. With respect to infertility, clinical treatments are not very effective and conservative excisional techniques are an option. Obstetrics complications after extensive uterine reconstruction, such as uterine rupture, should be considered and discussed with the patient. There are still limited data to support surgery effectiveness and further well-designed studies are required.

Author contributions MAPO: Project development, manuscript writing. CPCJ: Project development, manuscript writing. CPC: Manuscript editing. LCS: Manuscript editing. RLDW: Project development, manuscript reviewing. We confirm that the manuscript has been written and approved by all named authors.

Compliance with ethical standards

Conflict of interest All authors declare that they do not have any potential conflict of interest relevant to this article.

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