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# Operative Management of Adenomyosis

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**Abstract:** ***The complex pathogenesis of adenomyosis makes it one of the most difficult groups of FIGO PALM-COEIN abnormal uterine bleeding to diagnose and treat. Clinical symptoms of pain, abnormal uterine bleeding, and subfertility are the main symptoms of adenomyosis. Treatment is aimed at managing symptoms and improving fertility. Management by hysterectomy is not always desirable for women and it is often unreasonable to consider this radical option. Treatment requires a lifelong management plan because this disease negatively impacts the quality of life from menstrual symptoms, fertility, pregnancy outcome, as well as a high risk for miscarriage and obstetriccomplications.***

**Keywords:** Adenomyosis, infertility, management

## 1. Introduction

Adenomyosis is a benign uterine disorder with presence of heterotopic endometrial tissue (glands and stroma) in the myometrium and it associated with smooth muscle cell hyperplasia.[1] Affected women may present with abnormal uterine bleeding (AUB), dysmenorrhea, dyspareunia, or infertility. But one-third of that case are asymptomatic. Adenomyosis usually occurs in reproductive age women, especially in menorrhagia and dysmenorrhea. Adenomyosis is divided into diffuse and localized (focal). This depends on the extent of myometrial invasion.[2] Over the years, the diagnosis of adenomyosis has remained based on histopathological analysis after hysterectomy procedure in perimenopausal women with heavy menstrual bleeding (HMB) or pelvic pain.[3] Based on the current management of adenomyosis, there are no international guidelines to perform surgical or medical treatment of adenomyosis. However, recent technological advances regarding diagnostic methods and treatment options are changing the way of the doctors to treat adenomyosis. This becomes important in the future because a life-long management plan is needed in the management of this disease, including pain and bleeding control, maintenance of fertility, and pregnancy outcomes.[1,4]

## 2. Treatment and Management Adenomyosis

The standard treatment for adenomyosis is hysterectomy. However, challenges come in treating women who are symptomatic, with either conservative medical or surgical options. This treatment option depends on maintaining female fertility and sorting women who can get a surgical procedure based on risk factors. Medical treatment using hormonal suppressants can temporarily cause adenomyosis regression. Furthermore, the treatment options regarding surgical options and medical therapy will be described in more detail.[5]

## 3. Medical Treatment

### 3.1 Oral Contraception and Progestins

Although there are no randomized controlled trials that have to evaluate oral contraceptives continuously in patients with adenomyosis, patients with dysmenorrhea and menorrhagia may get a benefit from amenorrhea induction. This can relieve the symptoms of adenomyosis. The use of high-dose progestins such as oral norethindrone acetate or subcutaneous depot medroxyprogesterone has not been studied in the treatment of adenomyosis. However, their role as hormonal suppression agents may also help temporarily induce regression of adenomyosis.[5]

### 3.2 Levonorgestrel Intrauterine Device

The LNG IUD releases 20 mg of levonorgestrel per day. It has been shown effective in the treatment of adenomyosis. Use of the LNG IUD is associated with endometrial decidualization to reduce bleeding and is associated with acting directly on adenomyotic deposits by downregulating estrogen receptors. This reduces focal size, increases uterine contractility to reduce blood loss, improves dysmenorrhea by reducing prostaglandin production in the endometrium, and by inducing amenorrhea.[2] Studies have shown that the use of the LNG IUD improves the symptoms of menorrhagia and dysmenorrhea and there are good radiological changes in uterine adenomyosisn and may be beneficial for women who want to pregnant after treatment.[6]

### 3.3 Danazol

Danazol (19-nortestosterone androgen derivate) has a progestin-like effect that can induce direct inhibition of ovarian enzymes. This enzyme is responsible for producing estrogen and secretion of pituitary gonadotropin. Experience with the use of this systemic therapy in adenomyosis patients is limited. This occurs due to the drug's adverse effects such as weight gain, muscle cramps, reduced breast size, acne, hirsutism, oily skin, decreased HDL levels elevated liver enzymes, mood swings, depression, and a deepening of the voice. Systemic

treatment with danazol causes decreased estrogen receptors, which may reduce the uterine size and improve symptoms.[7]

### 3.4 GnRH Agonists

GnRH agonists bind to GnRH receptors in the pituitary gland, which results in downregulation of GnRH activity. Therapy is administrated by intramuscu lar injection, subcutaneous injection, or nasal spray twice daily. Usually, therapy is given in a limited period of time (from 3 to 6 months). This due to the adverse effects of hot flashes and decreased bone mineral density. Several case series reported that infertile patients with adenomyosis who had received GnRH agonists short-term treatment became pregnant within 6 months after discontinuation of therapy.[8]

### 3.5 Aromatase Inhibitors

Expression of cytochrome P-450 aromatase has been observed in endometriosis implants.[9] This enzyme converts androgens into estrogens. In several case reports and randomized trials, aromatase inhibitors have been used to treat severe endometriosis, which relieved the pain sensation.[10] However, there are no studies that describe this to be the choice of treatment for adenomyosis.

## 4. Surgical Treatment

### 4.1 Hysterectomy

Hysterectomy has become the main diagnostic and treatment option for adenomyosis. Vaginal hysterectomy is preferred over abdominal hysterectomy because of the lower morbidity and faster recovery. However, in a retrospective study of 14 women with adenomyosis from 1,246 women who undergo vaginal hysterectomies has shown an increased incidence of bladder injury. We concluded that the reason for injury was unknown, but we hypothesized that there may be greater difficulty in identifying the supravaginal septum and the vesicovaginal and vesicocervical planes. Laparoscopic hysterectomy can facilitate dissection of this field to prevent injury. Compared with vaginal hysterectomy, the rate of bladder injury occurs lower than the laparoscopic approach. However, urete ral injury occurred slightly higher.[11] Laparoscopic hysterectomy is preferred because of postoperative pain relief.[12,13]

***Complete Excision of Adenomyosis/ Adenomyomectomy***

**1) Classic technique**

These techniques have a same step as myomectomy (open or laparoscopic). These techniques include:[2]

- Inspection and/or palpation location and borders of the lesion,
- Longitudinal incision of the uterine wall along the adenomyoma (Figure 1Aa),
- Sharp and blunt dissection of the lesions with scissors, graspers, and/or diathermy (Figure 1Ab),
- Suturing of the uterine wall in a seromuscular layer or in two or more layers[4,10] (Fig.1Ad), and suturing the endometrial cavity with absorbable sutures if needed only.
- In laparoscopic adenomectomy (Figure 1Ac), the adenomyotic mass was removed using a morcellator. In cases where the recognition of intraoperative adenomyosis lesions is difficult, it's recommended to use ultrasound guidance, either in the form of monitoring hydro-ultrasonography or trans-trocarultrasound.[14]

**2) Mofidication in wall reconstruction: U-shaped suturing**

In this laparoscopic modification, after adenomyomatous tissue was removed, the wall's cavelike wound is approximated by U shape sutures at the muscle layer; the seromuscular layer is closed by figure-eight sutures.[15]

**3) Modification in wall reconstruction: overlapping flaps**

In this laparoscopic modification, a transverse incision is made in the adenomyotic tissue. Then, the lesion was excised with a monopolar needle. The remaining seromuscular layers are overlapped and sutured to counteract the lost muscle layer of the uterus (Fig. 1Ba–d).

**4) Triple-flap method**

This laparotomy technique includes;

- Extraperitonealization of the uterus and rubber tourniquet placement for hemostasis;
- Bisection of the uterus in the midline and sagittal plane with a scalpel until it reaches the uterine cavity (Fig. 1Ca);
- Opening the endometrial cavity to allow the index finger to guide excision of adenomyosis tissue;
- Using Martin forceps to grasp adenomyosis tissue, then remove the tissue from the myometrium. So that the thickness of the myometrium becomes 1 cm above from the serosa and below the endometrium.(Fig. 1Cb);
- Closure endometrium with 3-0 Vicryl (Fig.1Cc);
- Closure of the flaps of the uterine wall approximating the myometrium and serosa of the one side of the bisected uterus in the anteroposterior plane with interrupted 2 –0 Vicryl (Fig. 1Cd), while the contralateral side of the uterine wall is brought over the reconstructed first side in such a way as to coverit (Fig. 1Ce)

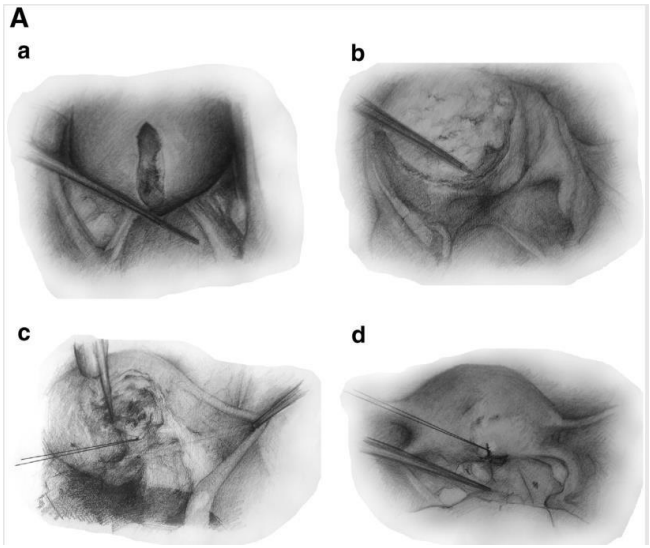


**Figure 1:** Complete adenomyomectomy classic technique: (a) Longitudinal incision along the adenomyoma. (b) Sharp and blunt dissection with scissors, graspers and/or diathermy. (c) Suturing of the endometrial cavity. (d) Suturing of the uterine wall.

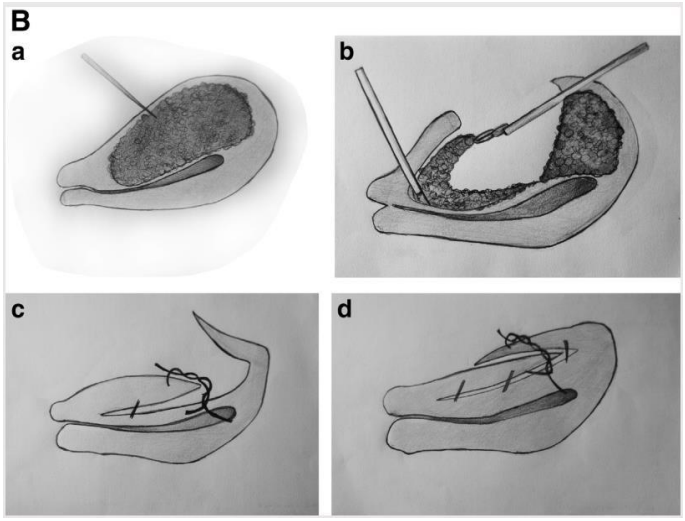


**Figure 2:** Complete adenomyomectomy classic technique with overlapping flaps: (a) Transverse incision. (b) The lesion is excised with monopolar needle. (c, d) The remaining seromuscular layers are overlapped and sutured to counteract the lost muscle layer of the uterus.

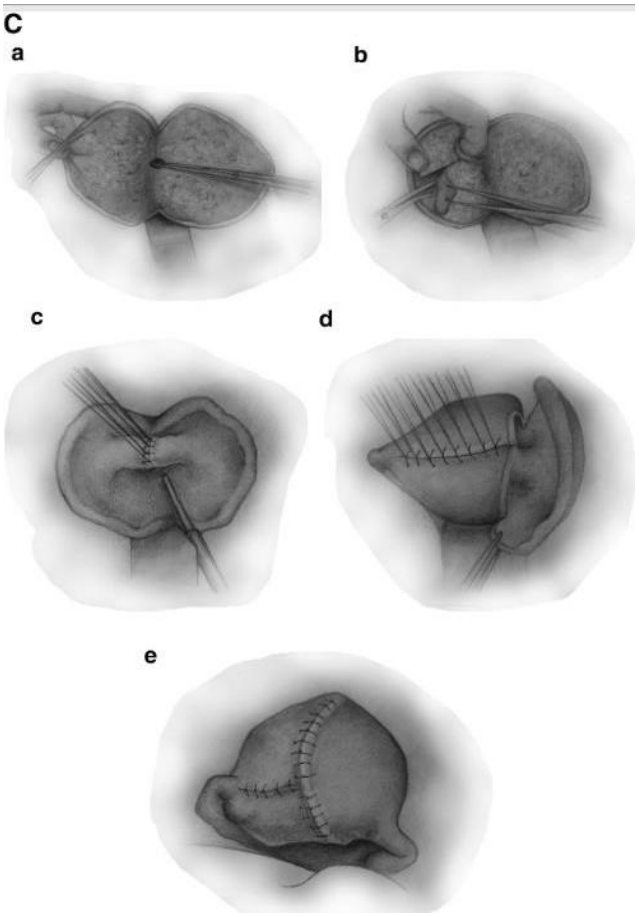


**Figure 3:** Complete adenomyomectomy with triple flap technique: (a) Bisection of the uterus in the midline and in the sagittal plane. (b) Opening of the endometrial cavity and excision of adenomyotic tissues leaving a myometrial thickness of 1 cm. (c) Closure of the endometrium. (d) Closure of the flaps approximating the myometrium and serosa of the one side of the bisected uterus in the anteroposterior plane. (e) The contralateral side of the uterine wall is brought over the reconstructed first side in such a way as to cover it.

### 4.2 Cytoreductive Surgery/Partial Adenomyomectomy

#### 1) Classic technique

Cytoreductive surgery for adenomyosis includes these following steps:[16]

- Vertical or transverse incision is applied in the middle of the anterior or posterior uterine wall;
- Ford T clamps (or an equivalent instrument) are applied to the wound edges so as myometrium of the subserous layer, which is rarely affected by adenomyosis (up to _10 mm), can be preserved;
- Uterine wall is examined for non-microscopic adenomyotic lesions. This can be recognized clinically by the presence of rough and white trabeculation. The lesion is excised piece by piece to keep as much as possible normal myometrium;
- If the adenomyosis extends to the contralateral wall of the uterus, the incision is extended over the uterus and down into the bladder of the pouch of Douglas. Closure of myometrium is carried out in one or more layers. Serous closure in one layer is carried out with interrupted

sutures. Be careful not to leave any defects in the uterus that could increase the risk of a hematoma.

**2) Transverse H incision technique**

In laparotomy modification especially adenomyosis of the anterior uterine wall, uterine cervix ligation is performed throughout the broad ligament and vasoconstricting agents are used to minimizing blood loss. A vertical incision is made in the uterine wall and two transverse incisions are made perpendicular to the initial incision along the upper and lower edges of the uterus (H incision). A 5-mm thickness of intestinal serosa is resected from the uterine myometrium through a vertical incision. This resection is extended, then the uterine serosa is opened wide bilaterally in the area under the H incision. Then, a slice of adenomyotic tissue is removed using manual palpation to determine the healthy myometrial margin. The chromopertubation test using indigo-carmine allows the assessment of endometrial perforation. As above, myometrial closure is performed in one or more layers and serous closure in one layer with an interrupted suture.[16]

**3) Wedge resection of the uterine wall**

In this technique (open or laparoscopic), the seromuscular layer in which adenomyosis present is removed by wedge resection of the uterine wall. Then, the operation was completed with the traditional closure of the uterine wound as described in the classic partial adenomyomectomy technique.[17]

**4) Asymmetric dissection of uterus**

In this laparotomy technique, the uterus will be dissected longitudinally with an electric scalpel. It performed asymmetrically to divide the inside from the outside so that the uterine cavity and bilateral uterine arteries are maintained. Then from this incision, the myometrium is dissected diagonally, as if to make a hole in the uterine cavity. With a transverse incision, the uterine cavity is opened. The index finger is inserted into the cavity. Next, an adenomyotic lesion was excised using a loop of electrodes up to 5 mm thickness from the inner myometrium. This procedure is followed by excision of the adenomyosis up to 5 mm thickness from the serosal myometrium. Then the endometrial cavity is closed and the uterine flap is recombined into the lining (muscle and serosa).[18]

**5) Laparoscopically assisted vaginal excision**

In this technique, the surgeon must ensure that the uterus is free from any adhesions. Then, the bilateral uterosacral ligaments were removed laparoscopically and followed by a posterior colpotomy. Through a vaginal incision, the uterus is extracted. Subsequently, under direct manipulation by the surgeon, the adenomyotic fragments were removed. The residual of the myometrium is closed in two layers. The advantage of this method is it comparable to open adenomectomy because the excision of the adenomyotic tissue is performed by touch and knotted manually with sufficient tension.[19]

## 5. Prognosis

There is a lot of evidence to suggest an association of adenomyosis with infertility and miscarriage. Currently, infertility is considered one of the clinical symptoms of adenomyosis, and several theories have explained this underlying mechanism. Fertility depends on the size and type of adenomyosis, which is classified as focal (usually embedded in the myometrium) and diffuses [characterized by foci of the endometrial mucosa (glands and stroma) scattered throughout the uterine muscle].[20] The association of adenomyosis with an increased risk of miscarriage has been shown to be significant. Miscarriage rates were observed in 31.8% of pregnancies in women with adenomyosis and 12.5% (29/224) in women without adenomyosis.[21]

Several medical treatments, both hormonal and non-hormonal are used off-label to treat pain, bleeding, and increase fertility. The use of GnRHa is indicated before fertility treatment to increase the chances of pregnancy in infertile women with adenomyosis and the highest pregnancy rates are reported in patients undergoing frozen embryo transfer after initial GnRHa treatment.[22] In contrast, the use of GnRHa to reduce pain and bleeding should be considered only for short-term treatment due to the effects of menopause.[1]

The use of progestins has anti-proliferative and anti-inflammatory effects, decidualization, and endometrial tissue atrophy which shows a significant reduction in the incidence of bleeding. Recently, a randomized, double-blind, multicentre, placebo-controlled trial of dienogest (DNG) administered daily for 16 weeks in women with adenomyosis reported good tolerability as evidenced by reduced pain relief and higher quality of life scores.[23] The intrauterine device that releases levonorgestrel (LNG-IUD) is also an effective treatment and has been used successfully to treat adenomyosis. The results showed a reduction in menstrual bleeding, pain, and uterine volume by 72%.[6]

Although conservative surgery has not becomethe standard treatment for adenomyosis, several reports have mentioned the success of the pregnancy process after conservative surgery in women with adenomyosis. The advantages of removing the affected area must be offset by the disadvantages of leaving the uterine wall which is likely to be damaged. Study by Tamura *et* al showed, 89 patients who underwent conservative surgery (open: 65 patients; laparoscopy: 24 patients), as many as 41.6% could return to pregnancy after infertility treatment. Because the surgical techniques differ by the facility, it is difficult to analyze the relationship between the results obtained with each surgical technique. However, there are no data to suggest that conservative surgery as a pretreatment for adenomyosis increases pregnancy rates in infertile women.[20] Tskhay *et al* in their study used adenomectomy, developed by Osada(24) as a promising solution for reducing symptoms and planning pregnancy in patients with severe adenomyosis. Within 12 months after surgery, uterine size and volume decreased significantly in all patients. In addition, all patients reported normal menstrual cycle and sexual function with reduced pain. During the 5 years of follow-up, there was no severe postoperative complications or disease recurrence. In

addition, two operated patients which had full-term pregnancies ended in cesarean section and there wasn't pathological changes in their uterus.[25]

The most challenging surgical treatment is a conservative treatment in order to maintain (perhaps even enhancing) fertility. A recent meta-analysis reported that 1,049 women who underwent total surgical removal showed an 82% reduction in dysmenorrhea, 69% red uction in heavy menstrual bleeding, and an increase in pregnancy by 60%. When only partial excision was possible, the yield was reduced to 82%, 50%, and 47% [62]. It is likely that partial excision occurs in a large proportion of women, with more extensive disease leading to worse clinical outcomes. Neither of these data came from randomized trials, and most came from small, retrospective series.[26,27]

One of the largest studies reporting fertility outcomes was a 10-year study including 104 women with extensive adenomyosis who described a technically challenging triple -flap technique for cytoreduction adenomyosis and uterine reconstruction with the specific aim to maintain fertility [88]. Postoperatively, reports show as many as 61% of women wishing for fertility became pregnant and 54% of women had full-term labor without uterine rupture.[24]

## References

[1] Vannuccini S, Petraglia F. Recent advances in understanding and managing adenomyosis. F1000Research. 2019;8.
[2] Farquhar C. I. Brosens Medical and surgical management of adenomyosis Best Pract. Res Clin Obs Gynaecol. 2006;20:603–16.
[3] Taran FA, Wallwiener M, Kabashi D, Rothmund R, Rall K, Kraemer B, et al. Clinical characteristics indicating adenomyosis at the time of hysterectomy: a retrospective study in 291 patients. Arch Gynecol Obstet. 2012;285(6):1571–6.
[4] Vannuccini S, Luisi S, Tosti C, Sorbi F, Petraglia F. Role of medical therapy in the management of uterine adenomyosis. Fertil Steril. 2018;109(3):398–405.
[5] Garcia L, Isaacson K. Adenomyosis: review of the literature. J Minim Invasive Gynecol. 2011;18(4):428–37.
[6] Sheng J, Zhang WY, Zhang JP, Lu D. The LNG-IUS study on adenomyosis: a 3-year follow-up study on the efficacy and side effects of the use of levonorgestrel intrauterine system for the treatment of dysmenorrhea associated with adenomyosis. Contraception. 2009;79(3):189–93.
[7] Ishihara H, Kitawaki J, Kado N, Koshiba H, Fushiki S, Honjo H. Gonadotropin- releasing hormone agonist and danazol normalize aromatase cytochrome P450 expression in eutopic endometrium from women with endometriosis, adenomyosis, or leiomyomas. Fertil Steril. 2003;79:735–42.
[8] Ozaki T, Takahashi K, Okada M, Kurioka H, Miyazaki K. Live birth after conservative surgery for severe adenomyosis following magnetic resonance imaging and gonadotropin-releasing hormone agonist therapy. Int J Fertil Womens Med. 1999;44(5):260–4.
[9] Bulun SE, Fang Z, Imir G, Gurates B, Tamura M, Yilmaz B, et al. Aromatase and endometriosis. In: Seminars in reproductive medicine. Thieme; 2004. p. 45–50.
[10] Patwardhan S, Nawathe A, Yates D, Harrison GR, Khan KS. Systematic review of the effects of aromatase inhibitors on pain associated with endometriosis. BJOG An Int J Obstet Gynaecol. 2008;115(7):818–22.
[11] Garry R, Fountain J, Mason SU, Hawe J, Napp V, Abbott J, et al. The eVALuate study: two parallel randomised trials, one comparing laparoscopic with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. Bmj. 2004;328(7432):129.
[12] Ghezzi F, Uccella S, Cromi A, Siesto G, Serati M, Bogani G, et al. Postoperative pain after laparoscopic and vaginal hysterectomy for benign gynecologic disease: a randomized trial. Am J Obstet Gynecol. 2010;203(2):118-e1.
[13] Candiani M, Izzo S, Bulfoni A, Riparini J, Ronzoni S, Marconi A. Laparoscopic vs vaginal hysterectomy for benign pathology. Am J Obstet Gynecol. 2009;200(4):368-e1.
[14] Gordts S, Brosens JJ, Fusi L, Benagiano G, Brosens I. Uterine adenomyosis: a need for uniform terminology and consensus classification. Reprod Biomed Online. 2008;17(2):244–8.
[15] Moghadam R, Lathi RB, Shahmohamady B, Saberi NS, Nezhat CH, Nezhat F, et al. Predictive value of magnetic resonance imaging in differentiating between leiomyoma and adenomyosis. JSLS J Soc Laparoendosc Surg. 2006;10(2):216.
[16] Fujishita A, Masuzaki H, Khan KN, Kitajima M, Ishimaru T. Modified red uction surgery for adenomyosis. Gynecol Obstet Invest. 2004;57(3):132–8.
[17] Ai-jun SUN, Min LUO, Wei W, Rong C, Jing-he L. Characteristics and efficacy of modified adenomyomectomy in the treatment of uterine adenomyoma. Chin Med J (Engl). 2011;124(9):1322–6.
[18] Nishida M, Takano K, Arai Y, Ozone H, Ichikawa R. Conservative surgical management for diffuse uterine adenomyosis. Fertil Steril. 2010;94(2):715–9.
[19] Wada S, Kudo M, Minakami H. Spontaneous uterine rupture of a twin pregnancy after a laparoscopic adenomyomectomy: a case report. J Minim Invasive Gynecol. 2006;13(2):166–8.
[20] Tamura H, Kishi H, Kitade M, Asai-Sato M, Tanaka A, Murakami T, et al. Clinical outcomes of infertility treatment for women with adenomyosis in Japan. Reprod Med Biol. 2017;16(3):276–82.
[21] Youm HS, Choi YS, Han HD. In vitro fertilization and embryo transfer outcomes in relation to myometrial thickness. J Assist Reprod Genet. 2011;28(11):1135–40.
[22] Park CW, Choi MH, Yang KM, Song IO. Pregnancy rate in women with adenomyosis undergoing fresh or frozen embryo transfer cycles following gonadotropin -releasing hormone agonist treatment.

Clin Exp Reprod Med. 2016;43(3):169.
[23] Osuga Y, Fujimoto-Okabe H, Hagino A. Evaluation of the efficacy and safety of dienogest in the treatment of painful symptoms in patients with adenomyosis: a randomized, double-blind, multicenter, placebo-controlled study. Fertil Steril. 2017;108(4):673–8.
[24] Osada H, Silber S, Kakinuma T, Nagaishi M, Kato K, Kato O. Surgical procedure to conserve the uterus for future pregnancy in patients suffering from massive adenomyosis. Reprod Biomed Online. 2011;22(1):94–9.
[25] Tskhay VB, Schindler AE, Mikailly GT. Diffuse massive adenomyosis and infertility. Is it possible to treat this condition? Horm Mol Biol Clin Investig. 2019;37(1).
[26] Grimbizis GF, Mikos T, Tarlatzis B. Uterus-sparing operative treatment for adenomyosis. Fertil Steril. 2014;101(2):472–87.
[27] Abbott JA. Adenomyosis and abnormal uterine bleeding (AUB-A)—pathogenesis, diagnosis, and management. Best Pract Res Clin Obstet Gynaecol. 2017;40:68–81.