Chapter

Benefits of Surgical Intervention in Women with Endometriosis-Related Infertility

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Abstract

Endometriosis is one of the most common gynecological diseases in the world with a great variety of symptoms and clinical features. The true prevalence rates in the general population are not known, but according to different authors, endometriosis is to be found in 10% in women of reproductive age. According to different publications, around half of the patients with infertility were diagnosed with endometriosis which change the significance of this disease from the only female to a socio-economical problem. In this chapter, we will focus on the current view on endometriosis-associated infertility, from superficial to adenomyosis, with a closer view of surgical treatment, as it is still the standard of care for diagnosis and in severe cases—treatment of the disease.

Keywords: adenomyosis, DIE, deep infiltrative endometriosis, endometrioma, peritoneal endometriosis, infertility, IVF

1. Introduction

Today, the medical community considers endometriosis as a significant disease and problem. According to different resources, about 176 million women are suffering from the disease worldwide. In multination, multicenter study [1] about 50% of gynecologists polled in Russia in 2007 examined 7–28 patients with endometriosis per month (240 patients per year). The number was almost equal to that of patients with myoma.

Endometriosis is known to be found in 60% of women aged under 30. More important is the fact that there is a 7-year delay from the first disease manifestation to the diagnosis [2].

The physician should suspect the endometriosis if the following complaints are present [3]:

- Dysmenorrhea, acyclic pelvic pain, deep dyspareunia, and infertility
- If a woman of reproductive age has the following symptoms: dyschesia, dysuria, hematuria, and rectorrhagia

Even though the exact mechanism of endometriosis-associated infertility is still unknown, some aspects are well studied. Endometriosis has an influence on the

quality of peritoneal fluid with growing macrophage concentration as well as proteases and cytokines negatively influencing the quality of oocytes, sperm, embryo, and fallopian tube potential.

It is difficult to recommend the optimal treatment as the development of the disease is unpredictable—from asymptomatic to very aggressive though pelvic pain and infertility usually called "active endometriosis" [4].

The American Society of Reproductive Medicine (ASRM) classification of endometriosis describes four stages of the disease. But that does not always correlate with the actual symptoms (pain, infertility, etc.) [5–7]. The more you work with this classification, the more it becomes obvious that patients with the same stages of the disease by ASRM classification, in fact, are incomparable. The ideal approach to endometriosis treatment should take into consideration how active the disease is. The "active" disease requires a combined treatment. The combination of surgical, hormonal treatment, and in vitro fertilization (IVF) could be individually chosen in each specific case of infertile patients.

For an easier understanding of how to treat endometriosis-associated infertility, it is better to separate the disease in four different phenotypes: superficial, endometrioma, deep infiltrated endometriosis, and adenomyosis.

2. Superficial endometriosis

The "gold" standard of superficial endometriosis treatment is laparoscopy. The common indications for surgery are pelvic pains and infertility. Hysteroscopy and biopsy, laparoscopy with fallopian tube perturbation, adhesiolysis, endometriosis staging with ablation, and/or removal lesions could be recommended. Pregnancy rate (PR) after laparoscopic treatment is the same for all stages [5].

However, if pelvic pain dominates, empirical conservative medical treatment could be applied. Infertile patients should be informed of alternative methods of treatment. Pregnancy can be achieved with IVF without surgery.

Laparoscopic treatment of minimal and mild endometriotic lesions (stage 1 and 2 ASRM) is justified in the case of pelvic pain because their destruction significantly decreases the pain compared with diagnostic laparoscopy alone. In this context, ablation and excision give identical results in terms of pain reduction. It is not recommended to treat asymptomatic patients. Literature shows no interest in uterine nerve ablation in case of dysmenorrhea due to minimal and mild endometriosis. With regard to treatment of minimal and mild endometriosis in infertile patients, only two studies can be selected, and both show that laparoscopy with excision or ablation and ablation of adhesions is superior to diagnostic laparoscopy alone also in terms of pregnancy rate [8].

The effectiveness of adjuvant hormonal treatment after surgery is not improved. Most hormonal medications have a contraceptive effect and make spontaneous pregnancy almost impossible.

IVF should be recommended in cases of fallopian tubes' low potential and/or male infertility. The spontaneous PR is very low if there are several simultaneous infertility factors. The very important factor is also the maternal age. At present, there is no generally accepted age for patients who should be recommended to go straight to ART after surgery and who could try to achieve spontaneous pregnancy. But a lot of surgeons agree that the maternal age of 35 and higher should be considered in favor of ART after surgery.

de Ziegler's et al. in the review [9] presented an algorithm for the management of infertility associated with endometriosis. This algorithm is presented in **Figure 1**.

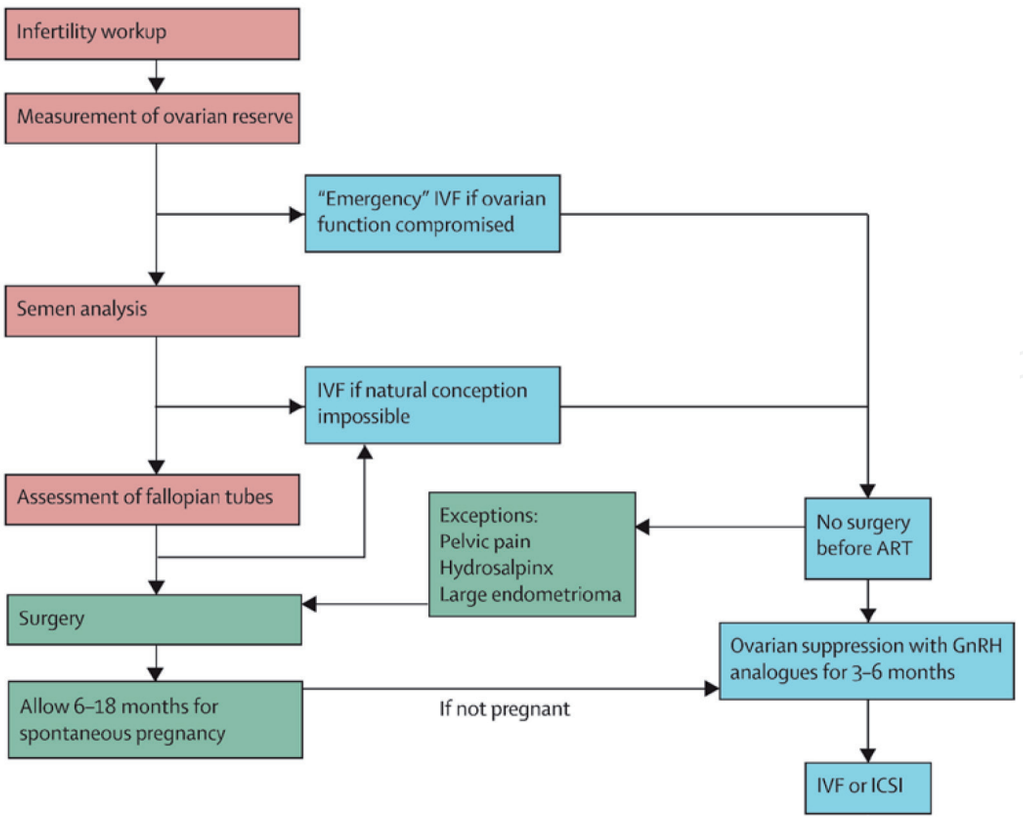

Figure 1.
Algorithm for management of infertility associated with endometriosis [9]. IVF, in vitro fertilization; ART, assisted reproductive technologies; GnRH, gonadotropin-releasing hormone; ICSI, intracytoplasmic sperm injection.

The repeated surgery is not recommended due to low spontaneous PR. The second (third, fourth, etc.) laparoscopy results in further IVF. This is not because of the bad surgery performed but because endometriosis is a chronical complex disease, which is associated with pelvic inflammation and profound alterations of peritoneal fluid, which surrounds the pelvic organs [10]. These alterations could affect natural conception.

3. Deep infiltrating endometriosis

Recently, the number of patients with deep infiltrating endometriosis (DIE) has been steadily increasing. It is estimated to affect up to 12% of all women with endometriosis. DIE is detected in 50–70% of patients of reproductive period with pain syndrome. This disease is diagnosed when there is an infiltration of 5 mm or more beneath the peritoneal surface [11] and/or an involvement of muscular layer of affected organ into the pathologic process is found [12].

DIE is characterized by multifocal distribution with the involvement of peritoneum, pelvic spaces, uterus ligaments, rectovaginal septum, vagina, intestine, bowel, ureters and bladder, and diaphragm. The feature of such dissemination is the lymphovascular invasion, the degree of which one is correlated with sizes of the primary endometrioid nodules. It is also estimated that endometriotic lesions seem to infiltrate the bowel wall preferentially along the nerves, even at distance from palpated nodules, while the mucosa is rarely and only focally involved [13].

There is no correlation between the stage of endometriosis, how deep it is, the number of symptoms, and their duration. Infertility is the most frequent symptom. Development of infertility in DIE is multifactorial: pelvic adhesions, the decrease in ovarian reserve, and a poor quality of oocytes in case of involvement of the ovaries. It is assumed that changes in ectopic endometrium are not as pronounced in patients with DIE as in cases of severe adenomyosis. This conclusion could be made on the basis that in patients with DIE, the frequency of miscarriages is less, and the frequency of successful IVF attempts is satisfactory.

In cases of lesions difficult location (myometrium, bowel and ileum, pararectal space), where removal is technically impossible or highly risky, the combination of surgery and medication is very promising. According to the data of Darai et al., spontaneous PR after surgical treatment is 51.1%, whereas IVF PR is 18.9% [14].

The medical treatment of deep infiltrating endometriosis may decrease symptoms and is often associated with such side effects as noncyclic bleedings, weight increase, libido loss, and headaches. It doesn′t provide the control of disease course in a long-term period, and when the treatment is over, the disease progresses. Moreover, the medical options have contraceptive effects and can′t be used when pregnancy is attempted [15].

Surgical treatment of DIE and infertility in most cases is preferable. Spontaneous pregnancy rate (PR) after surgical treatment of DIE is close to 50% [15]. It means that every second patient with DIE and infertility will not require IVF.

At the same time, we must not forget that the rate of severe postoperative complications of DIE treatment (rectal bleeding, anastomosis insufficiency, rectovaginal fistulas, abscesses, fecal peritonitis) is 10% [16]. Patients must be informed about the possible complications and results of DIE infertility treatment. IVF is preferable if other symptoms (pain, dyspareunia, dyschezia, low urinary tract symptoms) are absent.

There are no doubts about the removal of such endometriotic nodules in the bladder and parametrium, but the choice of ideal surgical approach to the treatment of bowel endometriosis is more controversial. Three types of surgical removal of endometrioid nodules are described: shaving, discoid, and bowel resection. According to the data of Abrao et al. [17], the treatment algorithm for deep endometriosis compromising the bowel must be individualized (**Figure 2**). "Conservative" surgery (shaving) is more appropriate in reproductive medicine due to its less risk. Surgery of DIE including bowel resection should be considered as a second-line treatment after failed IVF and in cases when there is a presentation of such symptoms as pelvic pain, dyspareunia, dyschezia, and bowel stenosis.

We can't recommend the anticipating spontaneous pregnancy after surgery for more than 9–12 months. It is attended with the risk of recurrent endometriosis and pelvic pain, which will make IVF more complicated.

In Malzoni et al. [18] publication, indications for radical colorectal surgery are described and clearly stated. Absolute indications are severe pain, bowel stenosis with functional organ compromise, and infertility in patients after unsuccessful IVF attempts even asymptomatic. The relative indications to radical surgery are the following: infertility in young patients (<35 years), infertility (even aged >35 years) after two or more IVF failures before the oocyte donation, and increased risks of pregnancy and delivery complications.

The last indication is one of the most disputable. Exacoustos et al. [19] described the obstetrical complication in patients with colorectal endometriosis. The number of premature delivery <37 weeks was five times more in colorectal endometriosis group than the control group. Placenta previa was diagnosed in every six patients with posterior endometriosis (only 1 case from 300 patients in control group).

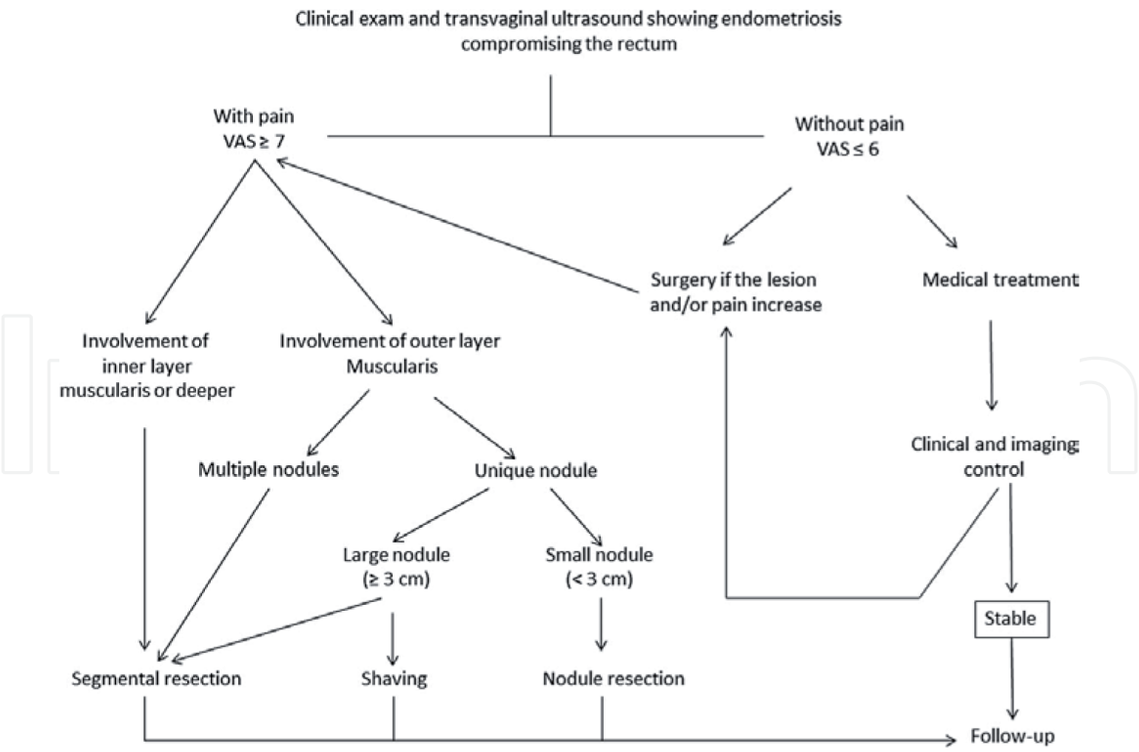

Figure 2.
Treatment algorithm for deep endometriosis compromising the bowel by Abrao et al. [17] (VAS—visual analog scale).

Cesarian section was performed in 68.3% in colorectal endometriosis group. Hysterectomy, hemoperitoneum, bowel resection, and bladder injury were described in 3.6–7.1% of patients with colorectal endometriosis.

The pathogenic mechanisms of pregnancy complications can be the following: endometriosis-related chronic inflammation, adhesions and their mechanical implications, and invasion of decidualized ectopic endometrium to the vessel walls.

Taking into account the risks of surgical intervention in cases of DIE, it′s reasonable to perform the operation in the specialized medical centers by multidisciplinary team, including gynecologist, urologist, colorectal surgeon, and fertility specialist. But endometriosis is a gynecological disease, and the gynecologist should be the leader of this team.

A very important practical question is what would be the recommendations if an unexperienced surgeon found DIE with diagnostic laparoscopy? In such case no one has repealed one of the basic rules of medical practice—"primum non nocere"—do not harm. If the surgeon is not enough experienced, to prevent complications, it would be better to stop the surgery after doing those steps, which could be done, according to the experience and send the patient to the clinic, which is focused on DIE treatment. Providing all the information about the presence of the disease to the patient is essential.

4. Endometrioma

In recent years, indications for surgical treatment of endometriomas in infertile patients are reconsidered due to the negative impact of surgery on the ovarian reserve, especially in recurrent cysts and bilateral localization. The surgeon faces the question which patients should be operated and if expectant management is chosen and then what period is appropriate. Comparative evaluation of cystectomy of non-endometriotic cyst (dermoid, serous, and mucinous cystadenoma) and

endometriomas highlighted that some ovarian tissue was removed only in 6% during surgical treatment of non-endometriotic cysts. In contrast, in the resection of endometriomas, ovarian tissue was present in the specimen in 54% of cases [1].

Nowadays, there is no consensus on the size of endometriomas which should be treated surgically. International recommendations indicate surgical treatment for cysts larger than 3–4 cm [3, 20] and according to some other guidelines, more than 6 cm.

According to some published data, surgery on the ovaries before IVF does not improve reproductive outcomes. The exception is large endometriomas which are difficult to puncture [21]. Asymptomatic endometriotic cysts of small size do not require surgical treatment, especially in patients older than 35 years. Surgical treatment must be performed in patients with long-term infertility in the presence of cysts greater than 4 cm [3].

In patients with a high risk of ovarian reserve damage (second ovarian surgery, bilateral localization, late reproductive age), it is necessary to consider cryopreservation of embryos or vitrification of oocyte before surgical treatment.

Surgical treatment can be performed in three ways—aspiration, sclerotherapy, and laparoscopic/open removal. The endometriotic lining of endometrioma may undergo pressure atrophy, and that spontaneous resolution of cyst can be achieved by simple aspiration by ultrasound or laparoscopic control. In difficult cases (adhesions, high risks of anesthesia, recurrence of small endometrioma), transvaginal puncture by ultrasound guidance could be recommended. According to different publications, the recurrence rate for sclerotherapy is 9.1–66.7% and could be decreased to 12% by the use of 95% ethanol in situ [22]. However, this procedure has been associated with postoperative pelvic abscesses.

If the surgery is to be performed, then the "gold" standard in case of endometrioma and infertility is laparoscopic cystectomy. Cystectomy can be performed in two ways: cyst ablation and enucleation. Laparoscopic cystectomy demonstrates the best results in achieving pregnancy for the first identified unilateral endometriomas. The spontaneous PR after cystectomy is more than 60%.

However, in the second surgery, partial capsule removal and ablation are the better options (to save ovarian reserve). In case of bilateral endometriomas in more advanced reproductive age and recurrent endometrioma, urgent IVF is indicated (the risk of decreased ovarian reserve). The removal of small endometrioma does not have an impact on cumulative PR. In some cases (recurrent endometrioma, difficulty in follicle puncture), sclerotherapy by ultrasound control could be recommended.

There are pitfalls of endometrioma's surgery. Surgery should be performed in the follicular phase to prevent recurrence. High power electrosurgical technique should be avoided. Bipolar coagulation (max 30 Watts) and/or suturing of the ovarian tissue is safer. Ablation can be applied for recurrence endometrioma in particular. New energies (PlasmaJet, CO_2 laser, argon-spread).

In our unpublished study, from 2010 to 2018, we performed 1187 laparoscopic procedures with removing of endometriomas in Moscow Regional Scientific Research Institute of Obstetrics and Gynecology. The average age of patients was 31.6 years old. Among them we make a follow up in 530 patients, and only 259 were included in the study. From 259 patients 105 have primary infertility before surgery (40.5%), 45 (17.37%) have secondary infertility, and 93 (35.9%) did not desire a pregnancy. In total, infertility was detected in 150 cases (57.9%). Laparoscopy and cyst removal (stripping) were done in the majority of cases—211 (81.6%); in 48 (18.4%) ovarium resection with the cyst was performed. Spontaneous pregnancy was registered among 77 women (51.3%). In 16 cases pregnancy was unexpected. Twenty-eight patients (18.6%) became pregnant after IVF. Cumulative pregnancy rate was 70% (105 patients). Ineffective attempts of spontaneous conception were

30, and IVF attempts were also unsuccessful in 36 cases (24%). After surgery, hormonal therapy was prescribed: dienogest in 34.3%, COC in 15%, and gonadotropin-releasing hormone agonists (GnRH-a) in 1.9% cases. The recurrence rate of the disease was 13.1% (34 cases).

There are the risks of nonsurgical management of patients with cysts and infertility [23]. The conditions with an expected high risk of complications, if patients go to IVF without surgical treatment, are the following: low ovarian responsiveness to the stimulation, low quality of oocytes, technical difficulties for ovarian puncture, endometrioma rupture, injury to adjacent organs, infection of the endometrioma, follicular fluid contamination, progression of endometriosis, pregnancy complications, the opportunity to miss the malignancy, and/or cancer development after IVF.

However, the meaning of surgery was overestimated. Surgical treatment did not improve an ovarian responsiveness to the stimulation, quality of oocytes, rate of technical difficulties during ovarian puncture, rate of injury to adjacent organs during this procedure, follicular fluid contamination, progression of endometriosis, and pregnancy complication rate.

5. Adenomyosis and infertility

Adenomyosis is a common gynecological disease, defined as the presence of ectopic endometrial epithelium and stroma in the myometrium.

Through the twentieth century before the widespread of transvaginal ultrasound (TVU) and magnetic resonance imaging (MRI) techniques, adenomyosis remained the disease, whose diagnosis was based on histological examination of the specimen after hysterectomy. As this examination was held after the surgery, the connection between infertility and adenomyosis was not well established. However, over the last three decades, the introduction of new diagnostic tools, mentioned above (TVU and MRI), made it possible to study adenomyosis without performing surgery. The measuring of the inner myometrium or myometrial junctional zone (JZ) described by Hricak group [24], provided new noninvasive diagnostic criteria for adenomyosis [25]. These new diagnostic tools allow us to diagnose the adenomyosis from early to advanced stages and see the progressing of the disease with high sensitivity and specificity. By different authors, the sensitivity and specificity range is 53–89% and 65–98% respectively. Although there is a great success in noninvasive diagnosis, the real incidence of adenomyosis is still unknown. The prevalence has been reported to range from 1 to 70%. This large range primarily reflects the lack of agreed diagnostic standards both by imaging tools and pathological analyses.

Even though many classifications, as well as scoring systems, have been proposed since the first mentioning of endometriosis as a disease, no widespread agreement on a classification for endometriosis has been reached. Unfortunately, there is no ideal classification of endometriosis that would be able to reflect all the aspects of the disease, the pathogenesis, anatomical distribution, clinical manifestation, progression, and recurrence.

The clinical presentation of adenomyosis can vary from patient to patient, but the main symptoms are abnormal uterine bleeding and dysmenorrhea, occurring in approximately 65% of patients [26]. Today there is a strong data that there is a correlation between the type, localization, and the number of endometriotic lesions and painful symptoms [27]. Despite the fact that the link between infertility and adenomyosis is still a subject of debate, the association between these two processes is clinically recognized [28]. Infertility is found in 11–12% of patients with adenomyosis [29].

The effect of adenomyosis on fertility has been assessed by examining its prevalence in infertility in patients or its effect on the outcomes of assisted reproduction

technologies (ART). In a review by Campo et al. [30], several pathogenesis hypotheses of infertility in patients with adenomyosis are described. The first one was proposed by Kunz et al. [31, 32], which points out the idea of thickening and disruption of the myometrial JZ which can result in perturbed uterine peristalsis. In 1984 Birnholz [33] has published his data about the presence of contraction waves in the myometrium: using transabdominal ultrasound, he showed that uterine peristaltic activity originates exclusively from the JZ, while the outer myometrium remains static. During the follicular and periovulatory phases, contraction waves have a cervico-fundal orientation, and their amplitude and frequency increase significantly towards the time of ovulation. There is an idea that adenomyosis causes infertility by impairing sperm transport.

The second hypothesis is focused on biochemical and functional alterations in both eutopic and heterotopic endometrium in individuals with adenomyosis [34]. These alterations could lead to lower receptivity, as suggested by the presence of "implantation marker" defects. This increased knowledge has created new therapeutic options, including the block of local aromatase production through the use of selective estrogen receptor modulators, estrogen-progestin combinations, and gonadotropin-releasing hormone super agonists.

The third hypothesis proposes that the presence of an abnormal concentration of intrauterine free radicals [35] and of altered decidualization [36] is also suggestive of altered receptivity. The authors propose that free radicals may adversely affect eggs and fertilized eggs in adenomyosis by a similar mechanism to that in endometriosis. The exaggerated expression of these enzymes suggests a crucial role of superoxide in infertility and/or miscarriage in these diseases.

A lot of studies showed the effect of adenomyosis on fertility in patients, who underwent ART. Recent reviews by Vercellini et al. [37] and Younes et al. [38] allowed to shed light on many questions, even though the number of publications analyzed in these reviews is small. In Vercellini review 1865 women were enrolled in the 9 selected studies, and in Younes paper only 15 studies were analyzed.

The prevalence of adenomyosis in the infertility population undergoing IVF/ICSI varies widely, from 6.9% [39] to 34.3 [40]. A clinical pregnancy after IVF/ICSI happens in 40.5% of women with adenomyosis and in 49.8% in those without this disease. The effect of adenomyosis on implantation rate per cycle is still controversial, and different authors have different data, related to that topic [40, 41]. According to Piver's publication [42], JZ thickness could be a predictive factor of repeated implantation failure in women who underwent IVF, suggesting that adenomyosis may impair embryo implantation in IVF cycles. As for the miscarriage rate, we now know that adenomyosis almost doubles this index: 31.9%, compared to 14.1% in women without adenomyosis. There could be also a connection between the miscarriage rate and a live birth rate per cycle. Martínez-Conejero et al. [40] reported 26.8% in the adenomyosis group and of 37.1% in the no adenomyosis group.

Despite the fact that now we have such meta-analysis data, it is still hard to understand the exact influence of the adenomyosis on the fertility, as in some analyzed studies there were groups of patients with both adenomyosis and endometriosis, so it is difficult to identify whether IVF failure and early pregnancy complications were directly related to the presence of endometriosis or the presence of adenomyosis. However, Vercellini and his team concluded that adenomyosis has a negative effect on the outcome of IVF/ICSI, which leads to reduced rates of clinical pregnancy and implantation and an increased risk of early pregnancy loss. To sum up, it seems logical to screen for adenomyosis before starting assisted reproduction procedures [43].

Another publication shows that there is a heightened risk of preterm delivery in patients with adenomyosis. A case–control study of Juang et al. [44] reveals the

connection between adenomyosis and preterm birth, and two other studies show poor pregnancy and perinatal outcomes in adenomyosis patients [45, 50].

According to Sandberg's study [46], the prevalence of adenomyosis in women in the time of delivery is quite high (17.8%), but complications during spontaneous pregnancy in such patients are rare. They can include rapid growth in pregnancy [47], spontaneous rupture of an unscarred uterus [48], and delayed postpartum hemorrhage [49]. Also, there is data that women with adenomyosis are at an increased risk of second-trimester miscarriage, small-for-gestational-age, preeclampsia, fetal malpresentation, placental malposition, and postpartum hemorrhage [50]. However, there are no large studies investigating the influence of adenomyosis on perinatal complications, and further accumulation of data is required to reveal this issue. Taking into account that the majority of pregnancies will be uneventful, it may be best that available information should be given to pregnant women in a way that would avoid raising unnecessary anxiety [43].

5.1 Fertily-sparing treatment

Treatment of adenomyosis could be conservative and surgical. Medical treatment for adenomyosis follows the principles for medical treatment of endometriosis, which aim is to reduce the production of endogenic estrogen or induction of endometrial differentiation with progestins. The principles are inhibition of ovulation, abolition of menstruation, and establishment of a stable steroid milieu [51].

Nowadays there are several different options of conservative treatment, mainly against menstruation-related symptoms such as dysmenorrhea and heavy menstrual bleeding. According to Streuli et al. review [52], there are almost no well-conducted randomized controlled trials on the pharmacological treatment of adenomyosis, and the information collected from published studies is insufficient. However, experts' opinion in this review says that the use of levonorgestrel-releasing intrauterine system, oral contraceptive pills, and danazol can improve those symptoms. Also, there are very few reports showing therapeutic effects of these drugs for infertility. Despite the fact that there are many therapeutic options, the majority of them inhibits the ovulation and\or inducts of necrosis, which is unacceptable in infertile patients. So, in this chapter, we will discuss options, which could be applied in such a group of patients.

The use of gonadotropin-releasing hormone agonists (GnRH-a) and its effect on infertility were described in several studies. In two IVF studies [53] in which a long protocol GnRH-a was admitted, there were no lower pregnancy rates in women with adenomyosis. GnRH-a could be admitted in women with moderate to severe symptomatic adenomyosis, especially in women with failed implantation of embryos of high quality. The weak point of these studies is that both of them were retrospective, and other factors may also have contributed. In patients with adenomyosis who plan to have frozen embryo transfer, one study [54] showed that 2-month GnRH analog pretreatment improved rates of implantation, clinical pregnancy, and ongoing pregnancy.

There is also data that the treatment of an intrauterine device containing danazol resulted in the successful conception of infertile patients [55].

5.2 Surgical treatment

Grimbizis reviewed studies on uterus-sparing surgical treatment options for adenomyosis and concluded that this kind of treatment is feasible and efficient [56].

There are several options nowadays: adenomyomectomy for diffuse or focal adenomyosis, cytoreductive surgery (partial adenomyomectomy), or a variety of non-excisional techniques (endometrial ablation, high-intensity focused ultrasound (HIFU) and uterine artery embolization (UAE)). Non-excisional techniques result in tissue necrosis, which is unacceptable in patients who desires pregnancy.

In patients with adenomyosis who desires pregnancy, surgery should only be chosen if the medical treatment is no effect. In patients with the localized process (adenomyoma) it is possible to perform an adenomyomectomy and remove all pathologic tissue. Nowadays it is the most popular surgical technique, performed through the laparoscopic or open approach. Laparoscopic surgery (adenomyosis resection) might be proper for women younger than 40 years old with focal adenomyosis who failed infertility treatments including assisted reproductive technology [57]. Several kinds of incisions are proposed for such procedure—transverse, longitudinal, wedge-shaped, and transverse H-shaped incisions [58], which could be chosen according to the size and location of the lesion. As well as for the incisions, for suturing wounds, there are several different techniques, including double- and triple-flap methods [59, 60].

In **Figure 3** you can see the different types of complete adenomyomectomy.

In patients with the diffuse process, cytoreductive surgery is performed. The main aim of the uterine preservation surgery is quite challenging—to remove the adenomyotic tissue as much as possible and to preserve the functional myometrium to save a functional uterus. In cases of diffuse process, it could be quite difficult to find the right plane and the border between those two layers in the adenomyotic uterus, as the pathologic tissue invades the myometrium. On one side of the scale, there is a radical treatment and on the other a functional uterus.

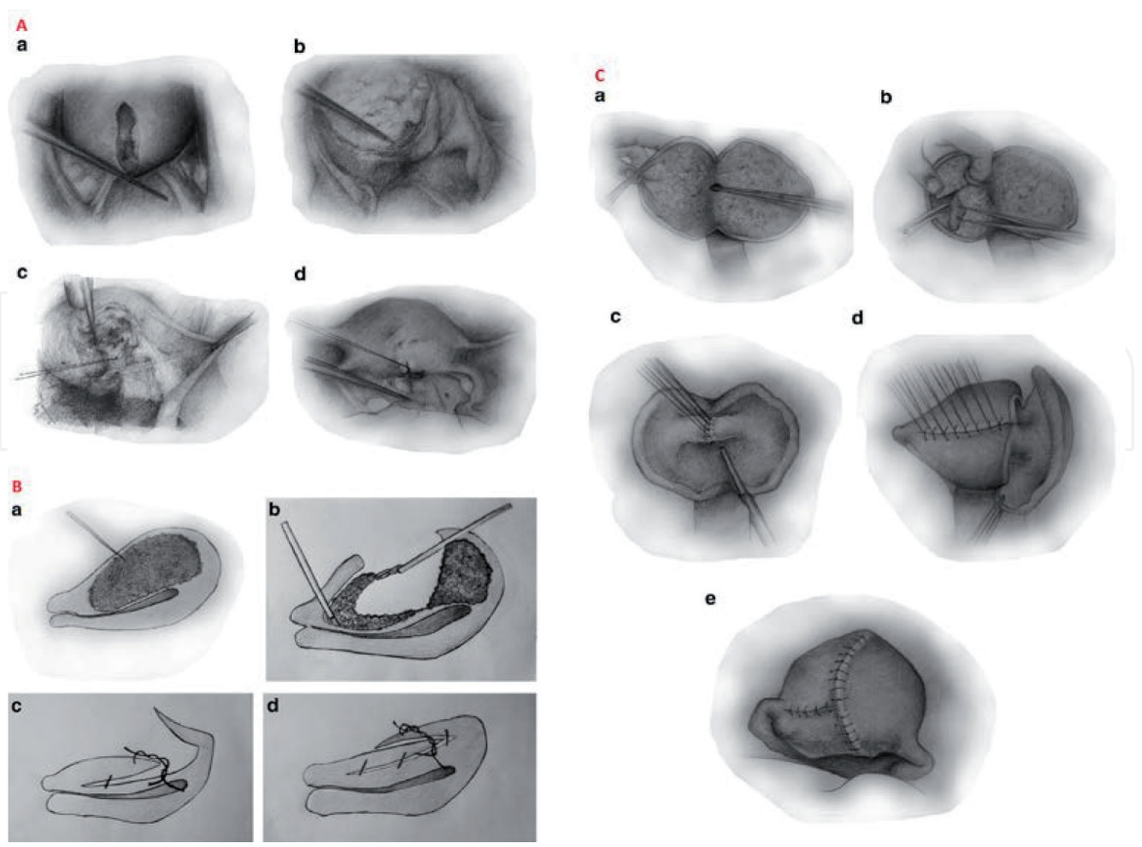

Figure 3.
Different complete adenomyomectomy techniques. (A) Classic technique, (B) classic technique with overlapping flaps, and (C) triple-flap technique [56].

In the recent review of fertility-sparing treatment for adenomyosis by Rocha et al. [61], there is also an analysis of combined medical and surgical treatment. The overall pooled clinical pregnancy rate after surgical resection of adenomyosis was 38.8%, ranging from 12.5 to 61.5%. The pooled miscarriage rate was 17.9% and pooled live birth rate 30.4%. As for spontaneous pregnancies, the overall clinical pregnancy rate was very low (18.2%). However, when using GnRH-a for 24 weeks after surgery [62, 63], the pooled spontaneous pregnancy rate was higher than not using adjuvant GnRH-a. There was no significant difference between pooled results with or without GnRH-a after adenomyomectomy for pregnancy rate, live birth rate, IVF pregnancy rate, or miscarriage rate. Two studies examined the effect of combined treatment with the use of adenomyomectomy and GnRH-a versus GnRH-a treatment alone [62, 64]. Even though the number of patients in the studies was small, it appears that surgery is associated with increased pregnancy rate. To sum up, adenomyomectomy alone has low spontaneous pregnancy rates and should be followed by ART or medical therapy with GnRH-a. Assisted reproductive technologies have good pregnancy rates in women with adenomyosis, and data suggest that long stimulation protocol is superior to short protocol. Most authors agree that there is currently no convincing evidence of the superiority of one of the methods of treatment over another and further prospective studies are needed to elucidate the usefulness of adenomyosis cytoreductive surgery as a fertility treatment. Also at the moment, literature data on such complications like uterine rupture and placenta accrete after surgery is scarce.

There is also a place for treatment adenomyosis with hysteroscopic techniques [65]. This method could be performed in patients with adenomyotic cysts, and crypts are suggested before treatment for fertility [66]. However, this procedure and its effect on adenomyosis are described only in case reports.

Dueholm et al. [51] in the recent review proposed an algorithm of how the patient with adenomyosis should be treated in infertility clinic. This algorithm is presented in **Figure 4**. However, authors make a conclusion that this algorithm is based on limited evidence and further randomized controlled trials are necessary to define the best strategy for patients with adenomyosis who want to conceive.

In the twenty-first century, new technologies come for patients suffering from uterine infertility, and without the option of surrogate motherhood, uterine

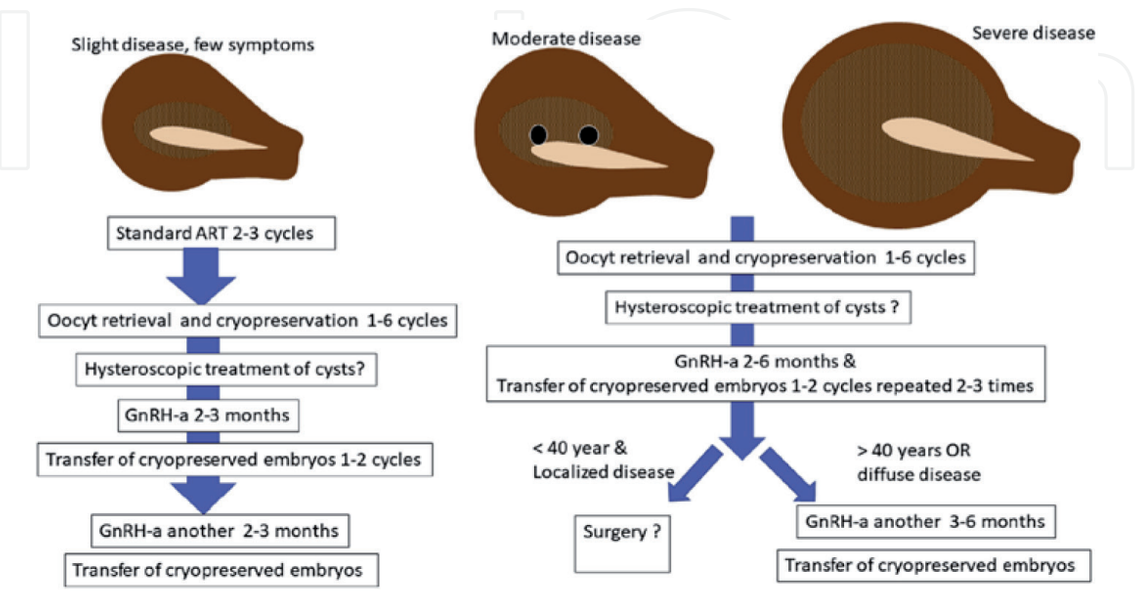

Figure 4.
Treatment algorithm for the patient with adenomyosis in an infertility clinic [51].

transplantation could be the only way to parenthood. Since the report in 2014 of a successful pregnancy [67] in the transplanted uterus, research interest in this field has been steadily growing with an increasing number of surgical teams training on the technique. Thirty-seven transplantations have already been realized worldwide setting the stage for a complex new research area in gynecological surgery, which needs to address technical, ethical, social, and economic issues [68]. These new technologies in the nearest future could also give a chance to become a mother for patients with uterine infertility caused by adenomyosis, resistant to other types of treatment.

6. Summary

In spite of huge achievements both in reproductive surgery and assisted reproductive technologies, endometriosis as a disease is very actual today. It is known that the number of ART centers has been increased recently, the majority of which do not have facilities to perform surgery. This fact seems quite controversial. It resulted in the situation when the importance of reproductive surgery is neglected. Most of the studies are originally oriented to a recognition of ART as a major method of infertility treatment. We think this practice leads to the loss of reproductive surgery quality and professional degradation. Spontaneous pregnancy rate occurs in 30–70% infertile patients after an adequate operation performed just in time. That means one- or two-thirds of patients with endometriosis-associated infertility do not need ART at all. However, surgery is not the only possible kind of infertility treatment. It is important to diminish the number of the second (third, fourth, etc.) surgery. The reproductologist should be involved in the treatment and ART could be recommended promptly. The best option is to find a balance between surgery and ART, which could be reached through the organization of the multidisciplinary team, "brother in arms" professional connections between the surgeon and the reproductologist. Only working together with a constant search of the best solution on how to reach the pregnancy and informing the infertile patient about all ways of the treatment could lead to success.

Conflict of interest

The authors declare no conflict of interest.

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