The Surgical Treatment of Adenomyosis

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Adenomyosis has a significantly negative impact on women's quality of life, causing abnormal uterine bleeding, dysmenorrhea, and chronic pelvic pain [1, 2]. Like endometriosis, adenomyosis is a benign disease, and although the definitive treatment of adenomyosis is hysterectomy, it is against many patients' desire to retain fertility. At present, there are currently no international guidelines to follow for either surgical or medical treatment for adenomyosis. But there is a growing consensus that adenomyosis needs long-term management plans, including pain and bleeding control, fertility preservation, and pregnancy assistance. In this context, the effect of conservative surgical treatment for long-term symptomatic relief, the benefit from the uterus-sparing surgery, and the pregnancy outcome after conservative surgery have become hot issues in the clinical treatment of adenomyosis. This chapter will discuss the surgical treatment of adenomyosis.

11.1 Indications of Surgery

The treatment of adenomyosis depends on the symptoms, severity, and fertility desire. Several medical treatments have been evaluated in adenomyosis, such as progestin [3], gonadotropin-releasing hormone agonists (GnRHa), nonsteroidal anti-inflammatory drugs (NSAIDs), levonorgestrel intrauterine system (LNG-IUS) [4], and combined oral contraceptives especially when used continuously [5]. These drug treatments are effective in reducing menstrual volume and pain in adenomyosis and are safe in long-term management. Therefore, the many experts' consensus in the diagnosis and treatment of adenomyosis agrees that we should give enough attempts to drug therapy before the decision of surgery.

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M. Xue et al. (eds.), *Adenomyosis*, https://doi.org/10.1007/978-981-33-4095-4_11

Since in 1965, the first conservative surgical treatment for adenomyosis in young women was reported [6]; several new surgical methods for adenomyomectomy has been tried and reported. But the management of these women with adenomyosis-associated pain or subfertility is still highly controversial. So far we have not been able to reach a consensus on (a) who will definitively benefit from conservative surgery, (b) when is the appropriate time for patients to choose surgery, and (c) whether there will be an improvement in reproductive performance after the use of medical and/or surgical management. At present, the indications of surgery for adenomyosis should include (a) dysmenorrhea and hypermenorrhea that are difficult to control with medication and (b) intolerability or contraindications to long-term medication. For older patients who do not have fertility requirements, they can choose a total hysterectomy; for younger patients who desire to preserve fertility or the uterus, they can select conservative surgery, that is, fertility-sparing operations. For patients undergoing conservative surgery, they should be fully informed of the possibility of recurrence of symptoms, because the uterus is preserved.

11.2 Preoperative Assessment

The preoperative evaluation of adenomyosis should first summarize the symptoms, previous treatment, and its results, to judge the indication and timing of the operation.

11.2.1 Age

Age should be an important factor to consider before surgery, especially before the decision-making of patients with adenomyosis associated infertility, because it might be the most critical factor of fertility. It is well-known that fertility declines after 35 years of age, and the chance of miscarriage increases [7].

11.2.2 Infertility

For every patient, detailed medical history should be inquired, including years of infertility, clinical symptoms, diagnosis, and previous medical and surgical treatment, as well as whether there is a history of repeated abortion or repeated embryo transfer failure. At the same time, we should carefully check whether the patients have the previous diagnosis of pelvic endometriosis, myoma, endometrial polyp, hydrosalpinx, etc. The ovulation function (combined with menstrual history, B-ultrasonic monitoring, and urine LH measurement) and the ovarian function (age, Antral Follicle Count (AFC), Anti-Mullerian Hormone (AMH), and basic endocrine) also should be evaluated in patients complaining of infertility. Other auxiliary examinations, if indicated, can also include hysteroscopy, CA125, MRI, and semen analysis. The evaluation of ovarian reserve function is very important. In the case of

basic follicle stimulating hormone (FSH) is more than 12 IU/L, and ultrasonography shows that bilateral Antral Follicle Count Score (AFCS) is less than 5, and/or AMH is less than 1.1 ng/ml, the ovarian reserve function failure can be considered.

Therefore, the surgical plan for patients with adenomyosis and infertility problem should insist that the gynecologist and the reproductive medicine specialist, if possible, cooperate to jointly develop a treatment plan for the patient, rather than the unilateral decision of the gynecologist.

11.2.3 Laboratory Examinations

Preoperative laboratory examination and evaluation includes routine blood tests and CA125 measurements. For patients with moderate anemia before surgery, pretreatment before surgery to correct anemia will improve the safety of surgery and help patients to recover quickly after surgery. GnRHa is a drug commonly used before the operation for uterine adenomyosis, which can correct anemia and reduce the uterine volume. Usually, three monthly GnRHa injections can be given before surgery. Preoperative anemia can also be improved through supportive treatment, such as iron supplements.

11.2.4 Preoperative Imaging

The preoperative imaging of adenomyosis is more important than the preoperative diagnosis. It can help to predict the operation approach, the effectiveness of the operation, and the risk of the surgery.

11.2.5 Preoperative Pelvic Ultrasound Evaluation

Pelvic ultrasound examination is the most commonly used auxiliary examination before adenomyosis surgery, and it is also the preferred imaging examination [8, 9]. A recent meta-analysis has shown that the sensitivity and specificity of 2D transvaginal ultrasound scanning (TVUS) to diagnose adenomyosis was 83.8% and 63.9%, while the sensitivity and specificity of 3D TVUS are 88.9% and 56.0% [10], respectively. Not only the rate of diagnosis of adenomyosis is high, but ultrasound is also the basis for the classification of adenomyosis [11, 12]. Symptoms of uterine motility detected during an ultrasound scan also help predict the condition during the operation. A negative uterine motility sign indicates that adenomyosis may involve the uterine serosa with adhesion to surrounding organs (such as the bowels). The assessment of whether the disease is accompanied by deep invasive endometriosis at the same time has a reference effect on the choice of laparoscopic or open surgery before surgery.

Some ultrasound diagnosticians have put forward an ultrasonic report system of adenomyosis, aiming to report the ultrasonic results of adenomyosis more regularly and systematically. A new reporting system for adenomyosis was proposed by

Van den Bosch et al. 2019 [11] which described the location of the adenomyosis, into anterior, posterior, left, right, and fundus, and the involvement <25%, 25%–50%, and > 50% of uterine volume and the size of adenomyosis. The scoring system can provide a more detailed ultrasound description of the adenomyosis image. However, other scholars have proposed a definition of adenomyosis severity scoring system [13]. Tellum et al., 2018 [14] also developed a clinical prediction model that uses the most relevant features, like myometrial cysts, fan-shaped echo, hyperechoic islets, globular uterus, thickness/thinnest ratio, etc., to identify the disease. These ultrasound-based assessment systems not only help to standardize the ultrasound description of adenomyosis but also provide a better assessment of the severity of adenomyosis before surgery and the prediction of improved fertility outcomes after surgery. They also make it easy for preoperative preparation and communication with patients. However, these models currently require external validation and more evidence to support its reliability. Such verification requires the joint participation of clinical gynecologists, ultrasound doctors, obstetricians, and reproductive medicine doctors, which will be worthwhile for us to work in this direction in the future.

11.3 Preoperative MRI Evaluation

Because of its advantages of intuitive images, not operator dependence, multi-parameter imaging, and multi-planar imaging, MRI is increasingly applied for preoperative evaluation of uterine adenomyosis [15]. At this time, the information provided by MRI is not only a diagnosis of adenomyosis but also offers detailed information for surgery. For example, MRI can give a more precious classification to refine the surgical treatment of different adenomyosis. In the previous chapter on diagnosis, the imaging-clinical classification based on MRI appearance has been described. The four subtypes proposed by Kishi et al. 2012 [12] and the complex 11 subtypes from A to K proposed by Bazot et al. 2018 [16] are conducted under the guidance of imaging experts. We need to further correlate these subtypes with clinically effective treatment outcomes, especially the improvement of symptoms after uterine-sparing surgery and the relationship between pregnancy outcomes of infertile patients and different types of adenomyosis.

Besides, MRI can still provide additional details about the preoperative evaluation of adenomyosis. For example, on the T2-weighted MRI, there are multiple spot-like high signals in the muscle layer. These spot-like high signals correspond to histopathological endometrial tissue with hyperplasia, with or without changes in the bleeding. The surrounding low-signal area corresponds to smooth muscle hyperplasia of the myometrium [17]. Small endometrial cysts can also be found, which are very helpful for the localization of preoperative adenomyomas (see Fig. 11.1). The T1-weighted sequence also helps identify high-signal-intensity lesions [18] that represent bleeding areas, with a positive predictive value of 95% [19]. The detection of these adenomyosis lesions before surgery is very instructive to detect and define the lesions as much as possible and reduce residual lesions after surgery.

Fig. 11.1 Adenomyosis of the posterior uterine wall with cystic changes (reproduced with permission from reference)

MRI can also be used to determine the presence or absence of intrapelvic endometriosis before surgery, especially deep infiltrates lesions. A typical example is the "hourglass sign." Local fibrous tissue hyperplasia in the posterior cervix or vaginorectal endometriosis leads to adhesion of surrounding structures, partial or complete closure of the uterine rectal fossa, thickening of the uterine and sacral ligaments, and invasion of the rectum causing teardrop-like traction and forward involving the uterine serosa layer (Fig. 11.2), leading to external adenomyoma, resulting in a classic "hourglass"-like appearance. This sign indicates severe adhesion of the posterior pelvic cavity and may be combined with deep infiltrating endometriosis of the uterosacral ligaments and the pouch of Douglas. The evaluation of these imaging details before surgery has important reference and significance for judging the difficulty of operation, choosing an open or laparoscopic approach, and also involving rigorous preoperative bowel preparation.

11.4 Surgical Treatment

11.4.1 Total Hysterectomy

Total hysterectomy is a radical cure for adenomyosis and the gold standard for treating patients without fertility requirements. After a hysterectomy, there is theoretically no chance of recurrence. Hysterectomy can be performed by abdominal, vaginal, or laparoscopic approaches. In recent years, it can also be a single-port laparoscopic [20, 21] and transvaginal natural orifice transluminal endoscopic

Fig. 11.2 External adenomyosis shows the hourglass sign (reproduced with permission from reference)

assisted hysterectomy [22]. It must be emphasized that subtotal hysterectomy should be avoided, and there have been more cases of continuous vaginal bleeding after hysterectomy [23], recurrent dysmenorrhea, and occurrence of the cervical stump or recto-vaginal adenomyosis. This management of these conditions can be tricky. Patients may need to have repeated medical treatment. Residual cervical resection is accompanied by an increased risk of bladder and rectal injury. Cochrane's analysis also found no evidence that subtotal hysterectomy is superior to total hysterectomy in reducing pelvic support disorders or decreased sexual function [24].

For different surgical approaches, minimally invasive surgery is preferable to traditional open surgery from the perspective of doctors or patients. Transvaginal hysterectomy is also a safe option for patients without severe pelvic adhesions [25] and have good postoperative results. Clinical studies report that laparoscopic surgery does not appear to increase the risk of perioperative complications. Single-port laparoscopy, which has started in recent years, is also safe, without increasing the rate of laparotomy or risk of complications [26]. It should also be noted that adenomyosis is often associated with pelvic endometriosis and may be accompanied by complicated pelvic deep-infiltrating endometriosis lesions, including recto-vaginal endometriosis nodule and complete obliteration of recto-vaginal fossa.

In the study of the risk factors of laparoscopic hysterectomy, some researchers have reported that type II adenomyosis is one of the independent high-risk factors for laparoscopic hysterectomy [27]. In an early comparative study of the complications of vaginal hysterectomy in patients with adenomyosis or uterine fibroids, the adenomyosis group had an increased risk of bladder injury during surgery [28]. Therefore, a total

hysterectomy for adenomyosis can be a difficult hysterectomy. The transabdominal hysterectomy is still a relatively safe procedure in patients with adenomyosis with severe pelvic adhesions and deeply infiltrating endometriosis (DIE).

There are a few specific comparative studies on the prognosis of patients with a total hysterectomy. Total hysterectomy obviously can permanently resolve the complications of abnormal uterine bleeding. As for pain-related symptoms, total hysterectomy also works well. It is possible that in patients with endometriosis, there is a risk of recurrence of symptoms after uterine removal alone. However, in a recent prospective study, laparoscopic hysterectomy for premenopausal women with cyclic pelvic pain associated with endometriosis, the satisfaction index after hysterectomy remained high [29]. Therefore, the use of hysterectomy for patients with adenomyosis can be confirmed.

11.5 Conservative Surgery

From the perspective of alleviating symptoms and promoting fertility, patients with adenomyosis should initially choose drug treatment. For patients of reproductive age who cannot tolerate long-term drug treatment or failed drug treatment, they have fertility requirements or need to retain the uterus. Surgery is fertility-sparing procedures.

The purpose of conservative surgery is to remove the adenomyosis lesion, preserve the uterus, and even preserve fertility. Conservative surgery for adenomyosis was reported in 1965 [30]. Before the 1970s, the most common suture materials were silk and gut, which could lead to strong foreign body reactions after surgery, increasing complications, such as suture failure. Despite this, surgical resection of adenomyoma continues to improve. Furthermore, the development of absorbable sutures has significantly reduced severe tissue reactions. The development of energy devices, such as electric, ultrasonic, and high-frequency scalpels, has reduced intraoperative bleeding and improved surgical safety. But today, conservative surgery compared with total hysterectomy remains a challenge for gynecologists and patients. There are, however, still authors who believe that the uterus-sparing surgery [31] or fertility-sparing surgery cannot be considered a standard treatment for adenomyosis [1]. The reason is that (a) although the existing clinically reported procedures are effective in improving symptoms, no standard procedure has yet been established. When the literature is reviewed, a total of 2365 cases of adenomyosis resection were reported from 1990 to 2018, of which Japanese scholars reported 2123 (89.8%). It can be seen that the validity of regional clinical studies is relatively limited, and more extensive clinical data are needed. Therefore international studies are required to verify problems associated with multiple interventions in conservative surgery [31]. (b) Due to the infiltration pattern and unclear border of adenomyosis, no surgical technique can guarantee the complete removal of the adenomyosis lesions from the uterine myometrium. (c) Any conservative procedure will damage the healthy uterine muscle, and it will increase the risk of uterine rupture and placental implantation during pregnancy.

11.5.1 Types of Conservative Surgeries for Adenomyosis

Conservative surgery for adenomyosis is divided into (a) adenomyomectomy for focal adenomyosis (1), (b) cytoreductive surgery for diffuse adenomyosis, and (c) endometrial ablation or resection for intrinsic adenomyosis.

11.5.2 Adenomyomectomy

There have been reports of various surgical approaches involving laparotomy and laparoscopic and robotic adenomyoma resections [32–34]. Adenomyoma resection includes wedge resection of adenomyoma and resection of cystic adenomyoma. Wedge resection was to remove part of the myometrium and its underlying adenomyosis. In this procedure, the wound cavity after resection is relatively small, and some adenomyoma tissue will remain on one or both sides of the incision. The wound of the uterine wall is repaired by suturing the remaining muscular layer with the serosa. According to the tension of the wound wall of the muscular wall, the suture method can be a continuous suture, interrupted suture, or U-type reduction suture reinforcement (see Fig. 11.3) [35] and muscle layer overlap suture to fill the wound cavity [36].

11.5.3 Cytoreductive Surgery for Diffuse Adenomyosis

Focal debulking of diffuse adenomyosis is based on a new concept completely different from traditional surgical methods. This surgical technique mainly includes two parts: (a) try to remove the lesions of the muscular layer and (b) repair the huge defect of the uterine wall and reconstruct the uterine wall, which is called "uterine reconstruction," and establish the endometrium with a different technique. The methods of constructing the muscle flap and the myometrial muscle flap are slightly different, and their purposes are to repair a large defect of the uterine wall and reconstruct the uterus. This procedure is mainly used in diffuse adenomyosis and

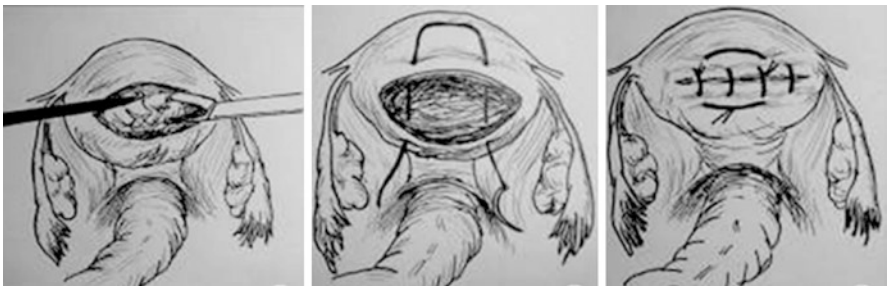

Fig. 11.3 shows U-shaped reduction suture reinforcement to close the wound cavity of the uterine wall. (reproduced with permission from Sun et al. 2011, Chinese medical journal)

severe adenomyosis. Different scholars have reported different techniques for excision and uterine reconstruction. Japanese scholars have made significant contributions to this technique, and they have explored many different methods of resection and reconstruction. The incision on the uterine wall can be vertical, diagonal, and H-shaped incisions [37, 38]. Uterine reconstruction methods include U-shaped sutures, "overlapping flaps," "triple flaps," and so on. In order to delay or reduce the postoperative recurrence in these procedures, it is necessary to remove as many adenomyosis lesions as possible, and they are likely to enter the uterine cavity. It is more difficult to remodel the uterine muscle wall after the adenomyosis lesions are removed. Therefore open abdominal surgery is easier to perform than this procedure.

11.5.4 Symptom Relief After Conservative Surgery

In terms of the improvement of symptoms and infertility, the efficacy of conservative surgery is positive. The smaller the remaining lesion, the more successful the symptom relief is. A systematic literature review published in 2014 [31] included 64 studies and 1049 patients who underwent conservative surgery for symptomatic adenomyosis. After complete excision of adenomyosis, the postoperative dysmenorrhea response rate was 82.0%, the menstrual period reduction response rate was 68.8%, the pregnancy rate was 60.5%, postoperative remission rate of dysmenorrhea was 81.8%, the menstrual reduction rate was 50.0%, and the pregnancy rate was 46.9%. Younes and Tulandi, 2018 [39] also confirmed that after conservative surgery, over three-fourths of women would experience symptom relief; on the other hand, the pregnancy rates varied widely with or without adjuvant medical treatment. The conservative surgery can be comparable with drug treatment in terms of symptom relief and pregnancy rate during postoperative follow-up.

11.5.5 Recurrence of Symptoms After Conservative Surgery

Surgery is effective in relieving symptoms; however, the recurrence of symptoms after surgery reflects the two sides of a problem. Relapse is due to the presence of residual adenomyosis tissue. Unlike uterine fibroids, the boundary between adenomyosis lesions and the normal myometrium is not clear, and the lesion is difficult to remove completely. This is the main reason for pain recurrence after conservative surgery, and it has a certain correlation with the size of residual lesions [35].

11.5.6 Uterine Rupture After Conservative Surgery

Symptom relief, recurrence, fertility outcomes, and risk of uterine rupture after uterine-preserving surgery are issues that should be addressed. Osada et al. 2018 [1] reviewed a total of 2365 cases of adenomyoma resection reported since 1990, including 2123 (89.8%) in Japan. In a total of 397 postoperative pregnancies, there

were 337 (84.89%) live births and 23 uterine ruptures. A meta-research showed that the highest pregnancy rates were reported after resection of cystic adenomyosis and focal adenomyosis, having a higher pregnancy rate than diffuse adenomyosis and lower uterine rupture rates [2, 40]. The risk of uterine rupture (6.8%) after conservative surgery for adenomyosis is much higher than that for uterine fibroid removal (about 0.26%) [1, 41]. This point should be taken seriously by all surgeons who undergo conservative surgery for adenomyosis.

For conservative surgery for adenomyosis, it is important to maintain the firmness of the uterine wall. Otsubo et al. 2016 [42] used MRI and/or ultrasonography to examine the thickness of the uterine wall before pregnancy in women undergoing conservative surgery for diffuse adenomyosis. As a result, 10 of the 23 women had premature births, and 13 had continued pregnancy. The uterine rupture occurred in two cases of abortion. They found that the thickness of the uterine wall is related to the risk of uterine rupture during pregnancy. The optimal uterine wall thickness before pregnancy should be between 9 and 15 mm to reduce the risk of uterine rupture during pregnancy. Morimatsu et al. 2007 [43] reported a case of pregnancy that occurred 1 month after conservative surgery, and the uterine rupture occurred after 28 weeks of gestation. Kodama et al. 2015 [44] reported the results of 71 cases of laparoscopic adenomyoma resection, including one case of uterine rupture, which was pregnancy at 4 months after surgery.

Wound healing is usually a complex process involving inflammation, angiogenesis, new tissue formation, and tissue remodeling. After myomectomy or cesarean section, the uterine rupture in the scar area is usually manifested by abnormally high collagen concentration in the uterine muscle wall tissue near the ruptured site, and smooth muscle fibers are reduced, so the tension of the uterine muscle layer is damaged [45]. Cold knife, scissors, etc. are commonly used in open surgery for conservative adenomyosis operation, while electrosurgical equipment, such as monopolar electric diathermy and laser knife, is commonly used in laparoscopy. Although energical equipment can reduce the bleeding and speeds up the procedure, yet, it also can cause thermal injury at the incision wound in the muscular layer, resulting in poor healing of the incised tissue. As a result, there are many cases of tissue fibrosis at the uterine boundary between the abnormal tissue and normal tissue. Histological studies have shown that thermal injury had greatly affected the wound healing, which can lead to suture failure, because tissue necrosis, scarring, and excessive collagen deposition increase the risk of wound dehiscence.

The adverse effect of any thermal injury on wound healing is even more detrimental in the healing wounds after adenomyosis surgery. An analysis of 23 cases of uterine rupture after conservative surgery for adenomyosis, 15 patients had surgery using monopolar cautery, high-frequency electrosurgery, laser knife, and other high-energy instruments; two cases used monopolar electrosurgery knife. The remaining six patients did not have information on the type of intraoperative cutting instruments used. There have been no reports of uterine rupture due to the use of a scalpel. Therefore, there seems to be a clear link between uterine rupture and the use of high-energy power instruments. Thus, if the safety of laparoscopic and open conservative surgery in terms of uterine rupture and technical difficulty are to be

compared, laparoscopic surgery with its use of high-energy thermal devices may increase the risk of uterine rupture during pregnancy [46, 47].

To summarize the possible risk factors for uterine rupture after conservative surgery of adenomyosis, it may include: the electrosurgical instruments used (such as cold knife or energy device), the amount of adenomyosis removed, the extent and size of uterine muscle defects, the uterine reconstruction technique, wound hematoma and infection, contraceptive time, and the surgical procedure. Besides, there are reports of high-risk pregnancy, such as placental implantation after adenomyosis surgery. Therefore, the consensus of experts on adenomyosis recommends a detailed communication of the pros and cons and possible risks of conservative surgery for the adenomyosis. From the safety and technical perspective of facilitating the removal of the adenomyosis and repairing the uterine muscle layer, open surgery is even more suitable.

11.6 Conservative Surgery Improves Adenomyosis-Related Infertility

There is currently insufficient evidence to support the benefits of conservative surgery to improve the adenomyosis-related infertility. Kishi et al. 2014 [48], however, reported that in 102 women who wished to become pregnant, the total clinical pregnancy rate was 31.4% (32/102) after conservative surgery. When grouped by age (under 40 and above 40), the clinical pregnancy rates were 41.3% and 3.7%, respectively. Of the six patients in the >40-year-old group, five had abortions. Therefore, this study showed that in women over 40 years of age, the benefits of surgery were not obvious.

Although surgery is not recommended as a first-line treatment for the treatment of adenomyosis with infertility, conservative surgery is recommended for patients with severe symptoms or failure of repeated assisted reproductive assistance [49]. If the patient is unwilling to receive assisted reproductive assistance after surgery, spontaneous natural pregnancy after GnRHa treatment can be attempted.

11.7 Conclusion

Treatment of adenomyosis is quite complex and controversial. Although hysterectomy is still the ultimate treatment for women with severe symptoms, conservative surgical options should be offered for women who wish to maintain fertility. Conservative surgery can improve symptoms associated with clinical treatment. In patients with adenomyosis, conservative surgery can be an option when clinical treatment fails. Obstetric complications after extensive uterine reconstruction can increase, such as uterine rupture, placental implantation, placenta previa, etc. These complications should be paid attention to and fully discussed with patients before surgery. At present, there are many conservative surgical procedures, and there is still a lack of standardized surgical procedures. Data supporting the effectiveness of these surgical procedures are still limited, and further elaborate clinical studies are needed.

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