

REVIEW

Conservative surgical treatment of uterine fibroids in women of childbearing age

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Abstract

Uterine fibroids are benign gynecologic tumors, and women aged between 30 to 50 years are known to have a high incidence of uterine fibroids. A growing number of pharmacotherapies and minimally invasive organ-preserving treatments have been designed and conducted over the past few years. However, there has not been any therapeutic drugs exhibiting an ideal therapeutic effect and low recurrence rate, such that the surgical treatment continues to be primarily employed in the actual clinical treatment. In general, surgical treatment has been performed as the organ- and fertility-preserving hysteroscopic or laparoscopic resections of the fibroids. Minimally invasive surgical equipment (e.g., hysteroscopy, traditional porous laparoscopy, trans-umbilical laparoscopy, transvaginal laparoscopy, as well as robot-assisted laparoscopy) has been extensively applied to clinical treatment. Compared with traditional laparotomy, minimally invasive surgical equipment is characterized by minimally invasive surgery, high efficiency and safety. As medical technology has been leaping forward, interventional therapy and radiofrequency ablation can also be employed for treating uterine fibroids. In accordance with the research progress worldwide, the current situation, limitations, and advantages of the treatment of uterine fibroids in patients with fertility requirements are reviewed in this study.

Keywords

Uterine fibroids; Myomectomy; Uterine artery embolization; High-Intensity focused ultrasound; Radiofrequency ablation; Pregnancy; Fertility

1. Introduction

Uterine fibroids are formed by hyperplasia of uterine smooth muscle tissues. They are benign tumors with a high incidence in the female reproductive system. Uterine fibroids are common in women aged between 30 and 50 years. They grow with the increase of age. Women aged around 40 years have been found as the main population of uterine fibroids. These tumors can be detected in nearly 80–90% of women aged 50 years [1]. Women of color (e.g., non-Hispanic Black/African American women and Hispanic/Latinas) are known with a higher uterine fibroid prevalence, incidence, and disease burden than non-Hispanic white women [2]. Patients with uterine fibroids may be subjected to more menstruation, frequent urination, constipation, and other pelvic compression symptoms, sexual pain, and other symptoms, as well as reduced quality of life. It has become a social trend that women postpone childbearing to later ages [3]. When the peak of uterine fibroids symptoms commonly occurs, infertility, pregnancy loss, and placental abruption can be caused [4, 5]. As a result, women have a rising demand of treatment options that preserve both the uterus and their fertility. Accordingly, the pursuit of the

optimal treatment choice takes on a critical significance. In this study, the current situation, limitations and advantages of the treatment of uterine fibroids patients with fertility requirements are reviewed in accordance with the research progress worldwide [4–6].

2. Hysteroscopic myomectomy (HM)

In 2022, the International Society of Gynecological Endoscopy (ISGE) [7] developed 10 1A–C recommendations and four 2A–C recommendations, thus suggesting that hysteroscopic surgery is the most effective conservative minimally invasive gynecological intervention for treating submucous uterine fibroids. Since hysteroscopy has been extensively applied to clinical surgical treatment, a new path has been opened for the surgical treatment of submucosal uterine fibroids patients. The location of submucosal fibroids and the deformation of the endometrium (submucous fibroids or deeply infiltrated intramural fibroids) serve as the optimal predictors of impaired fertility and the possible benefits of surgical resection, such that hysteroscopic myomectomy should be applied to the treatment for infertile patients [8]. In 2022, Yang Y

et al. [9] have suggested that hysteroscopic myomectomy achieves effective long-term pregnancy outcomes, and it is an effective surgical choice for treating submucosal fibroids patients. Hysteroscopic submucosal myomectomy has been confirmed as an effective alternative to hysterectomy, and it is capable of meeting the requirements in women of child-bearing age to preserve their uterus and reproductive function. Hysteroscopy shows the advantages that it does not require an open abdomen, thus facilitating rapid postoperative recovery. Moreover, the absence of an incision in the uterus reduces the rate of cesarean delivery. Furthermore, hysteroscopic myomectomy has potential side effects, which may reduce fertility, *i.e.*, intrauterine and peripheral adhesions. Thus, for patients with fertility requirements, more attention should be placed on protecting the normal endometrium around the fibroids.

3. Open myomectomy (OM) and laparoscopic surgery

In 2022, Tinelli A *et al.* [10] have suggested that previous laparoscopic myomectomy and open myomectomy are correlated with uterine rupture during pregnancy, hysteroscopic myomectomy is associated with early pregnancy, and uterine rupture does not increase exponentially with the increase in the number of previous scars. The incision should be cautiously closed in a multi-layer manner to minimize the risk of uterine rupture during pregnancy after myomectomy [11]. Although laparotomy surgery is more traumatic compared with laparoscopic surgery, it is advisable for those with considerable fibroids, large diameter (*e.g.*, >10 cm), fibroids in special parts, and severe pelvic adhesion surgery, or may increase the risk of uterine rupture in a future pregnancy. There may be a risk of tumor spread during uterine fibroids crushing for leiomyosarcoma or even smooth muscle tumors exhibiting uncertain malignant potential, such that laparotomy should also be selected [12]. However, in 2022 Wang W *et al.* [13] presented a novel laparoscopic power crushing multiport airtight system to prevent tumor spread, which is capable of further addressing this risk. Traditional laparoscopic myomectomy has become progressively applied to the treatment of uterine fibroids, which usually has a lower incidence of perioperative complications and shows several advantages (*e.g.*, shorter hospital stay, smaller incisions, as well as reduced pain) [14]. Over the past few years, the robot-assisted surgery has been applied to various gynecological operations (*e.g.*, hysterectomy and hysteromyomectomy), whereas there has been scarce randomized research [15]. Although RM may not be preferred for its long operative time, increased blood loss, and cost, in 2021, Özbaşı E *et al.* [16] have suggested that robot-assisted myomectomy (RM) is recommended for women carrying large uterine sizes and large-size of fibroids since it includes three-dimensional imaging, facilitates more precise surgery, and has significantly less postoperative pain. Robot-assisted myomectomy is a safe minimally invasive surgery in terms of skilled surgeons. Robot-assisted surgery is recognized as a novel and innovative minimally invasive method, and robot-assisted technology is expected to be optimized through the continuous progress of technology in years ahead to facil-

itate the treatment for patients.

4. Laparoscopic surgery *via* natural cavity

Endoscopy through the natural cavity has recently been further developed using minimally invasive technology, and the safety or feasibility of transumbilical laparoendoscopic single-site myomectomy (LESS-M) has aroused the wide attention of scholars. The outstanding advantage of LESS-M is the use of the natural channel. It can not only reduce the complications caused by abdominal wall surgery but also maintain skin integrity, which is more consistent with the concept of minimally invasive and more easily accepted by patients [17]. In 2021, L. Jiang *et al.* [18] have suggested that LESS-M is safe and feasible, which is capable of shortening operation time, reducing intraoperative bleeding, reducing the risk of complications, significantly alleviating patients' pain, facilitating patient recovery, and achieving a better cosmetic effect. In 2018, Liu J *et al.* [19] have confirmed that Transvaginal-Natural orifice transluminal endoscopic surgery (V-NOTES) can also have certain effects in subserous, intermuscular and pedicled leiomyomas. Notably, it applies to patients with obesity, diabetes or unable to tolerate laparotomy or laparoscopic surgery. In general, it is indicated for patients with a loose vagina, no pelvic adhesions, relatively good uterine mobility, preferably with a single fibroid. The operation of V-NOTES has some limitations, including narrow surgical field, poor exposure, difficulty in surgery for patients with combined pelvic adhesions or large fibroids, high risk of intraoperative complications (*e.g.*, internal bleeding and adjacent organ damage), as well as high demands on surgeon's skills. However, patients undergoing transvaginal myomectomy show certain advantages (*e.g.*, faster postoperative recovery and less treatment cost). Besides, its effect on fertility has not been reported thus far. V-NOTES is a novel choice for myomectomy, whereas its effect on pregnancy and fertility has been rarely investigated.

5. Other surgical procedures

5.1 Uterine artery embolization (UAE)

Uterine artery embolization is a vascular interventional therapy. UAE treatment of uterine fibroids primarily involves the inhibition of fibroid growth by causing ischemic necrosis of the fibroid lesions, followed by dissolution and absorption. Lastly, the lesions can be shrunk or even disappear, such that clinical symptoms are mitigated. In 2022, Russ M *et al.* [20] have suggested that UAE is beneficial to remove uterine fibroids in patients with enlarged uterine parenchyma. Compared with no intervention before myomectomy, the high blood loss (≥ 500 mL), postoperative blood transfusion demand and postoperative complications in patients with multiple leiomyomas after UAE were significantly reduced. Existing clinical research has suggested that the UAE is a safe and effective treatment. However, the side effects (*e.g.*, pain) are severe, and the reintervention rate is relatively high at nearly 24% [21]. Moreover, existing research has suggested that up to 5% of patients can experience ovarian dysfunction

from this treatment [22]. Some retrospective research has suggested that the UAE may increase the risk of miscarriage and other adverse pregnancy outcomes [23, 24]. Compared with traditional myomectomy, uterine artery embolization has been largely employed to mitigate the symptoms of uterine fibroids by reducing the volume of myoma, or destroying the endometrium. Some research has suggested that there is no difference in pregnancy outcomes between myomectomy and UAE treatment, and high-quality randomized controlled trials have been rare for further demonstration. Accordingly, the risk of potential adverse pregnancy outcomes should be carefully considered before UAE treatment for women with fertility requirements.

5.2 High-intensity focused ultrasound (HIFU)

In high intensity focused ultrasound, another new minimally invasive therapy, the low-intensity ultrasound *in vitro* is concentrated on the target area *in vivo* under the guidance of ultrasound or magnetic resonance. On that basis, the focus of high energy density is formed, causing the tissue in the focus area to heat up rapidly. Moreover, the thermal effect of ultrasound is employed to cause local coagulation necrosis of solid tumor, *i.e.*, ablation. Since the Food and Drug Administration (FDA) has approved magnetic resonance-guided high intensity focused ultrasound for the treatment of uterine fibroids in 2004, the safety and effectiveness of HIFU in the treatment of uterine fibroids have been extensively proven. However, HIFU only applies to a select group of patients. The fibroids should be smaller than 10 cm and preferably located in the anterior wall region [25]. Available evidence suggests that HIFU can be considered uterine retention therapy for women with uterine fibroids of different races, especially for those who want to maintain fertility [26].

5.3 Transcervical ultrasound-guided radiofrequency ablation (TRFA)

Interventional radiology methods (*e.g.*, UAE and HIFU) have not brought a breakthrough. The transcervical ultrasound-guided radiofrequency ablation (TRFA) has been proposed as a novel and innovative procedure to the treatment of symptomatic uterine fibroids. TRFA has been applied in Germany since 2013. Thus far, over 1200 people have performed TRFA treatments in Germany, Austria and Switzerland [27]. The procedure allows for optimization of the ablated volume in the targeted fibroid. TRFA is an excellent choice for the Federation International of Gynecology and Obstetrics (FIGO) type 2, 3 and 4 fibroids and of FIGO 2–5 transmural fibroids [28]. Compared with surgery, this procedure has the advantage of preserving uterine continuity while protecting the endometrium and avoiding the occurrence of intrauterine adhesions. Although this technique outperforms conventional methods, there has not been any safe method for presurgical identification of a patient with a uterine sarcoma, particularly for patients carrying large fibroids [29]. To prevent misdiagnosis or treatment of an unexpected sarcoma, the number, size and type of fibroids should be clearly evaluated using ultrasound and magnetic resonance imaging. Experts have

recommended that it is possible to schedule a pregnancy within 3 months of the TRFA after a follow-up ultrasound has been performed [30]. It is noteworthy that no prospective controlled trials have been performed on patients willing to have children.

6. Conclusion

According to the existing reports worldwide, myomectomy can be used to treat symptomatic uterine fibroids and infertile women, and symptomatic submucosal myoma can usually be treated by hysteroscopy. TRFA is an option that should be offered to patients for its benefits compared with surgical procedures and interventional radiology procedures. Symptomatic intermural and subserous myoma can be treated using various pathways of laparoscopic myomectomy. However, current evidence does not reveal that there are better surgical methods (laparotomy, hysteroscopy, or laparoscopy) to increase live birth, premature birth, clinical pregnancy, persistent pregnancy, abortion, or cesarean section.

In brief, minimally invasive surgery is increasingly used for women of childbearing age undergoing conservative surgery for uterine fibroids, the more minimally invasive treatment has brought new options to the treatment of uterine fibroids, improved the cure rate of uterine fibroids, and promoted the minimally invasive techniques for facilitating the treatment of uterine fibroids. However, different minimally invasive treatment options have different indications and contraindications (Table 1), and it is recommended that the optimal treatment option should be selected based on the shared medical decision to ensure the treatment effect and reduce the treatment risk (*e.g.*, patient's fertility needs, personal constitution, individual psychological assessment, fibroid size and location, economic status, as well as hospital medical equipment). Moreover, evaluation of patient age-related fertility and ovarian reserve are vital factors to consider for the evaluation of the potential fertility benefit of myomectomy. Despite minimally invasive techniques of uncertainty and controversy, it is believed that with the advance of minimally invasive techniques and the accumulating experience of clinicians, when counseling the subfertile woman carrying uterine fibroids, minimally invasive techniques will serve as the main clinical treatment for uterine fibroids among women of childbearing age.

AUTHOR CONTRIBUTIONS

HY, RS and BX—designed the research study. SZ, WZ, HT, YC and ZD—performed the research. ZQ, JL, HW and MB—conducted the selection of relevant studies. HY, WW and JC—drafted the paper. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

TABLE 1. Conservative surgical treatment.

	Indications	Limitations	Prognosis for Fertility
HM	Submucosal fibroids, intermuscular fibroids that affect the uterine cavity		Uterine cavity adhesion endometrial damage
OM	Multiple fibroids, fibroids in special parts, severe pelvic adhesion	More traumatic	
Laparoscopic surgery	Intermural and subserous myoma		
RM	Large uterine sizes, large-size and complex fibroids	Untouched, difficulty in suture	The risk of uterine rupture, pelvic adhesions, there were no statistically significant differences in postoperative pregnancy rates and pregnancy outcomes.
LESS-M	Fibroids location: anterior wall of the uterus, the base of the uterus		
V-NOTES	Patients: obesity, diabetes or unable to tolerate laparotomy surgery fibroids location: cervix, isthmus of the Cervix, posterior wall of the uterine, lower segment of the uterus		
UAE	Patients: postoperative recurrence, cannot tolerate or unwilling to surgery	No pathology	UAE should be carefully considered.
HIFU			Available evidence suggests that HIFU can be considered.
TRFA			Experts have recommended that pregnancy can be planned 3 months after TRFA.

HM: hysteroscopic myomectomy; OM: open myomectomy; RM: robot-assisted myomectomy; LESS-M: laparoendoscopic single-site myomectomy; V-NOTES: Transvaginal-Natural orifice transluminal endoscopic surgery; UAE: uterine artery embolization; HIFU: high-intensity focused ultrasound; TRFA: transcervical ultrasound-guided radiofrequency ablation.

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CONFLICT OF INTEREST

All authors approved the manuscript and have agreed to submit it to your esteemed journal. The authors declare no conflict of interest.

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