Review

The current place of mini-invasive surgery in uterine leiomyoma management

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ABSTRACT

Uterine leiomyomas are the most common benign tumors in women of reproductive age. Most of leiomyomas are asymptomatic. They are often found incidentally, and require neither monitoring nor treatment. For symptomatic women who wish to become pregnant, surgical myomectomy remains the conservative treatment of choice. It can be performed in various routes depending on the location and the number of leiomyomas and the experience of the surgeon. A minimally invasive procedure should always be the preferred option so as to improve woman satisfaction and to decrease perioperative morbidity. In selected patients, medical therapy prior to surgery can be useful to correct anemia, to improve the quality of life and to decrease the volume of the leiomyomas. The use of blood saving techniques need to be mastered to prevent or to treat perioperative haemorrhage. Patients must be aware of uterine rupture in case of subsequent pregnancy, even if the risk seems to be very low. Future research challenges include the development of three-dimensional models and augmented reality that could be able to specifically treat leiomyomas without damaging the unaffected part of the uterus.

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Introduction

Leiomyomas are the most common benign tumor in women of reproductive age. Their prevalence varies between 30% and 70% in non-menopausal women [1]. Most of uterine leiomyomas are asymptomatic. Only a part (approximately 1/3) leads to a range of symptoms that include abnormal uterine bleeding, pelvic pain or pressure, bowel or urinary tract issues (bulk-related symptoms), sexual disorders (dyspareunia), and impairment of fertility. The relationship between leiomyomas and infertility is controversial and difficult to establish. The proportion of women for whom the infertility is only related to the presence of a uterine leiomyoma is probably very low, in the order of 1% to 2% [2].

In case of symptomatic uterine leiomyomas, medical, surgical, or radiological therapies may be chosen depending on a range of criteria:

- the age,
- the desire to become pregnant,
- the desire to preserve the uterus,
- the number, the size and the location of the leiomyomas,
- the main symptom,
- the comorbidities,
- the anticipated surgical difficulties (multiple prior surgeries, multiple myomectomies),
- the level of experience of the therapist.

Various alternative treatment options need to be discussed individually with each woman, taking into account the risk/benefit ratio for each of the selected therapies. The surgical treatment can be conservative (myomectomy) or non-conservative (hysterectomy). Indications are summarized in Table 1.

In case of infertility, surgical treatment of submucosal leiomyomas by hysteroscopy significantly improves the pregnancy rate. Removal of subserosal leiomyomas with the sole aim of enhancing fertility is not recommended. In terms of leiomyomas with an intramural location in infertile women, the surgical treatment is controversial as there is no evidence that myomectomy increases spontaneous or IVF-assisted fertility [2].

Mini-invasive conservative surgical treatment

Surgical myomectomy remains the standard treatment for women who wish to become pregnant. It can be performed by hysteroscopy, by laparoscopy (robotically-assisted or not), by

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Table 1
Principles of surgical management of symptomatic uterine leiomyomas.
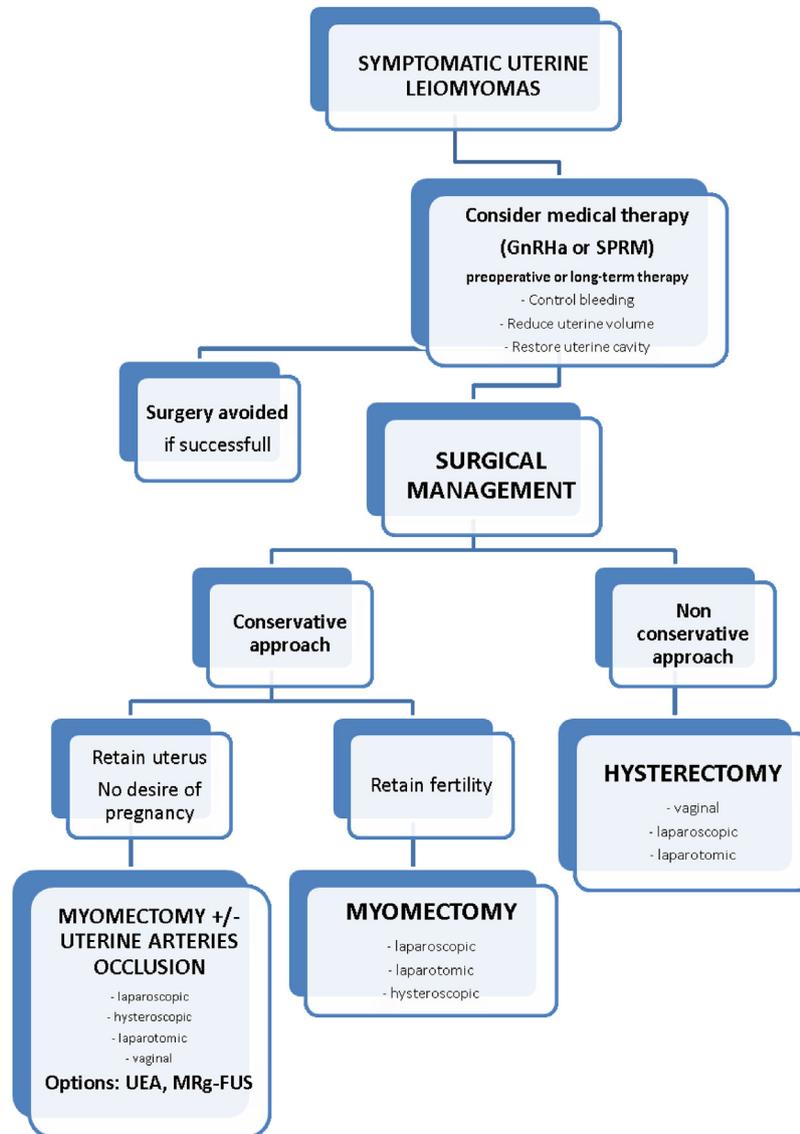
UEA: Uterine Artery Embolization; MRg-FUS: Magnetic Resonance-guided Focused Ultrasound.

laparotomy or, more rarely, by a vaginal route. A mini-invasive approach should systematically be the preferred option. The choice of the route in case of a conservative surgical treatment of the uterus depends on:

- the type, the size, and the number of leiomyomas to be treated,
- the associated comorbidities (anesthetic considerations),
- the surgeon experience,
- the local conditions according to the pelvic examination (uterine mobility, uterine volume, or associated endometriosis).

Determination of the exact location of the leiomyomas prior to surgery is paramount. This is done by pelvic ultrasound or Magnetic Resonance Imaging (MRI). At present, some authors suggest using augmented reality so as to improve the perioperative mapping [3].

Hysteroscopic myomectomy

Hysteroscopy is the standard route to treat submucosal leiomyomas that undergo intracavitary development, corresponding with FIGO (*Fédération Internationale des Gynécologues-Obstétriciens*) classification type 0, 1, and 2. The wire loop resectoscopic technique under permanent direct visual guidance is the standard procedure. It is suitable for submucosal leiomyomas of less than 4 cm. When the largest diameter exceeds 4 cm and/or in case of more than 3 leiomyomas of significant size in a submucosal position, hysteroscopy becomes technically difficult. A two-step resection, separated by two to four months, is occasionally necessary so as to avoid the perioperative risks of a long and laborious procedure. The safety margin with the uterine serosa needs to be at least 5 mm in order to minimize the risk of uterine perforation and visceral injury. Progress in terms of the size of the

instruments (5 French bipolar electrodes) now allows the procedure to be carried out in an office setting for leiomyomas up to 25 mm in diameter [4]. The borderline between diagnostic and operative hysteroscopy becomes hence blurred with the advent of "see-and-treat in an office setting" procedures. This way, intrauterine pathologies can be diagnosed and treated without anesthesia.

The energy chosen for operative hysteroscopy is a major issue as the media used for distension do not entail the same risks. Monopolar energy using a hypoosmolar and hypotonic solution is associated with a significant increased risk of hyponatremia in case of excessive intravascular fluid absorption, which can lead to irreversible neurological sequelae. Isotonic solutions used with bipolar energy do not entail this risk, although they can lead to a circulatory overload (pulmonary oedema) in case of excessive fluid absorption, particularly in women at risk of cardiovascular issues [5]. A strict fluid balance between outflow and inflow needs to be done every 15 minutes during the procedure.

Preoperative medical therapies, particularly Selective Progesterone Receptor Modulator (SPRM) or Gonadotrophin-releasing hormone agonists (GnRHa), play an important role in case of large submucosal leiomyomas of more than 3 cm. These agents can allow for a significant decrease in the volume of the leiomyoma and thereby make complete resection possible [6]. In more rare cases, huge submucosal leiomyomas (exceeding 6 cm) that do not respond to medical treatment can be approached by an abdominal route, preferably using laparoscopy, which requires opening of the endometrial cavity and a challenging suture of the wall defect.

The complication rate with hysteroscopic myomectomy is below 1%. The perioperative risks are uterine perforation (0.12–3%), excessive bleeding, excessive liquid absorption, and visceral injury (bowel, bladder). Close to half of the complications occur during the dilatation of the cervix prior to the introduction of the hysteroscope [7].

The use of bipolar energy during operative hysteroscopy may decrease the risk of postoperative intrauterine adhesions [8]. Primary prevention of synechias requires applying an anti-adhesion gel at the end of the procedure. Carrying out a diagnostic hysteroscopy at one or two months allows for secondary prevention of synechias, which can readily be cut using the endoscope. Post-operative hysteroscopy could also be useful in case of laparotomic myomectomy [9].

Laparoscopic and robotically-assisted myomectomy

Myomectomy by laparoscopy has been described since the 1970s for pedunculated leiomyomas, although it was not until the start of the 1990s that it was developed for intramural leiomyomas requiring a myometrial suture [10]. It is suitable for FIGO type 3 to 7 leiomyomas and for hybrid leiomyomas. In more rare cases, a laparoscopic approach is possible for huge submucosal leiomyomas that have not responded to preoperative treatment with ulipristal acetate or GnRHa. The choice of a laparoscopic approach depends on the surgeon experience. The procedure is limited by the volume and the number of leiomyomas to be removed. The technical difficulties are mainly in regard to uterine mobilization, management of the risk of hemorrhaging, the myometrial suture, and the length of the operation. In case of intramural or subserosal leiomyomas, the *Collège National des Gynécologues-Obstétriciens Français* (CNGOF) recommends a laparoscopic approach if the number of leiomyomas is limited to 3 and if their diameter is less than 8 cm [11]. Beyond a diameter of 10 cm, the longer duration of the operation, the risk of excessive bleeding, and the difficulty to extract the resected specimen need to be taken into account. For some authors, a threshold of 14 cm (obtained by adding the greatest diameter of all of the leiomyomas to be removed) determines the feasibility of the laparoscopic myomectomy [12].

The technique of myomectomy by laparoscopy is a standardized procedure. The placement of the trocars is the same as for other gynecological operations. In case of voluminous leiomyomas, particularly those that undergo abdominal development, the optical and the accessory trocars are placed as high as possible in the upper part of the abdomen. This allows for a proper endoscopic view and the necessary space to operate. An endo-uterine canulation is often used to mobilize the uterus.

Pedunculated and sessile subserosal (FIGO type 7) leiomyomas do not present specific surgical difficulties as they only require effective coagulation of the pedicle or of the base of the leiomyoma. Suture of the uterine serosa is most often not necessary and is performed only for hemostatic purposes. Huge leiomyomas of more than 10 cm can therefore be treated by laparoscopy, as the main issue lies with difficulty in regard to the extraction and the time required for morcellation. For intramural leiomyomas, hysterotomy is performed directly opposite the leiomyoma, in a sagittal or para-sagittal axis, until the right plane of the pseudocapsule is reached. A more oblique angle assists with suturing for anteriorly located leiomyomas. The energy used for hysterotomy needs to have a limited degree of necrosis and myometrial diffusion, particularly in women with a desire of pregnancy. A monopolar needle point with a cutting voltage of 10–15 W or more recently ultrasonic energy are our preferences. Leiomyoma enucleation requires the use of strong grasping forceps that allows traction and counter traction. Hemostasis is achieved with a bipolar coagulation forceps, in a selective and parsimonious manner. The use of ultrasonic energy is also possible, with potential benefits in terms of blood loss and operating time. The bed of the myomectomy needs to be minimally coagulated so as to limit myometrial necrosis. Hemostasis is mainly ensured by the quality of the laparoscopic suture. Uterine wall closure is carried out in one or two layers with running or interrupted sutures, according to the preference of the surgeon. A large caliber mono- or multifilament suture is generally used for the myometrial closure (caliber 0). The course of the fallopian tubes and its interstitial part needs also to be clearly identified. The uterine serosa is preferentially closed with a small caliber (2/0) monofilament suture. The knots are intra- or extracorporeal depending on surgeon's preference. As with laparotomy, an opened endometrial cavity needs to be sutured with small caliber (3/0) absorbable thread and an anti-adhesion gel should be applied to prevent synechias. Intracavity injection of methylene blue can help to visualize the opened cavity. Extraction of the leiomyoma is achieved by morcellation, using either a laparoscopic power morcellator or a cold laparoscopic scalpel (Chardonnens scalpel®). A vaginal extraction by a posterior colpotomy is also an option for leiomyomas up to 5–6 cm, if the vagina is accessible easily. Enlargement of the trocar incisions or performing a mini-laparotomy have been described as alternatives to power morcellation. Risks associated with laparoscopic power morcellation of resected specimens were recently highlighted by the Food and Drug Administration, particularly in case of an unsuspected leiomyosarcoma [13].

Peritoneal tumor spillage following power morcellation could be associated with an increase risk of recurrence and a decrease risk in overall survival in case of an unsuspected uterine leiomyosarcoma. The risk of visceral injury and parasitic leiomyomas in relation with the use of power morcellation is low, estimated to be less than 1%. Using a specific endoscopic bag for contained morcellation could be an alternative to prevent all these risks [14].

At the end of the procedure, it is recommended to place an anti-adhesion barrier at the site of the hysterotomy scar so as to prevent the risk of postoperative adhesions [15].

Robotic assisted laparoscopic myomectomy offers the same advantages as a totally laparoscopic technique in terms of

efficiency and pregnancy outcomes [16]. A robotic approach could provide benefits to reduce the estimated blood loss and the number of complications and conversions, but these results are only based on non-randomized studies [17].

Myomectomy by vaginal approach

Vaginal myomectomy applies to either prolapsed leiomyomas through the cervical canal or to subserosal/intramural leiomyomas. For the latter indication, it is necessary to perform an anterior or a posterior colpotomy by the vaginal route, depending on the topography of the leiomyomas. The posterior leiomyomas are easier to remove as a posterior colpotomy offers a large vaginal access. Exclusive vaginal access is therefore largely reserved for single posterior leiomyomas in women who have a compliant vaginal access and a mobile uterus. The vaginal route does however limit the visualization of the adnexa, particularly in the context of a desire to become pregnant and/or in case of infertility. Possible associated endometriotic lesions can also not be diagnosed or treated. There is no data in the literature on the subsequent fertility after a myomectomy by the vaginal route [18].

Medical therapy prior to surgery

It is essential to screen and to correct for anemia prior to surgery. Indeed, anemia has a negative impact on the postoperative morbi-mortality [19].

The purpose of the long-term preoperative hormonal therapy is to stop bleeding, to correct anemia, to improve the quality of life, and to decrease the volume of the leiomyomas. The surgical approach can be changed if the uterine volume decreases significantly, making a laparoscopy route possible when a laparotomy was scheduled initially. If medical therapy is completely successful, surgery could even be avoided. Two medical therapies have proven to be effective in this indication: GnRHa and SPRM (ulipristal acetate) [6]. Valaprisan, a novel promising powerful SPRM, is currently under investigation in phase III studies.

Perioperative blood-saving techniques

Perioperative haemorrhage is the main risk associated with surgical myomectomy. It is sometimes necessary to resort to a blood transfusion and/or a hemostatic hysterectomy, irrespective of the surgical route chosen. Several techniques have been developed to reduce the risk of haemorrhage, based on two principles:

- reduce uterine arteries blood flow: pericervical "tourniquet" technique, preoperative embolization, or preventive uterine arteries occlusion;
- use uterotonic or vasoconstrictive agents: ocytocine, misoprostol, or sulprostone, intramyometrial injection of vasopressin or epinephrine + bupivacaine [20].

Preventive uterine artery occlusion is of particular value with myomectomy by laparoscopy as it allows for a decrease in perioperative bleeding and it could reduce the risk of leiomyoma recurrence in case of permanent occlusion [21].

Informations to be provided to women

Recurrence

In case of myomectomy, women need to be informed of the risk of recurrence or persistence of the symptoms. The risk of recurrence has been determined to be approximately 15% [21].

Birth

Interval between myomectomy and a possible attempt conception has not been clearly established in the literature. The risk of uterine rupture during subsequent pregnancy after myomectomy has been determined to be less than 1%. Claeys et al., in an exhaustive review of the literature, described 29 cases of uterine rupture secondary to a myomectomy for the 3,685 pregnancies that were studied [22]. Endometrial cavity exposure, the number of suture planes, and the number of leiomyomas removed do not appear to be risk factors of uterine rupture.

An interval of more than 6 months after myomectomy is as reasonable timeframe to become pregnant. This delay is based solely on expert opinion. The route of delivery during subsequent pregnancy depends on several factors: the perioperative conditions, the postoperative complications, and the conditions regarding the pregnancy. Vaginal versus scheduled cesarean delivery is a shared decision making involving the patient, the obstetrician, and the surgeon. Prevention of uterine rupture is therefore based on:

- a correct uterine suture technique, preferably in two planes,
- a limited use of electrosurgery,
- checking for and suture of a opened endometrial cavity,
- limiting hematomas and postoperative infections.

Conclusion

Mini-invasive conservative surgery still has an important place in the management of uterine leiomyomas, although recent developments have promoted the use of SPRMs. For symptomatic women who wish to preserve their fertility, a combined treatment comprising medical treatment followed by a myomectomy appears to be an optimal therapeutic strategy. Therapy with SPRM is effective despite a recent European alert had transitory suspended the prescription of UPA. It has been shown to rapidly stop bleeding and correct anemia, improving the quality of life and the level of woman satisfaction. The potential decrease in the volume of leiomyomas after a treatment by SPRM or GnRHa increases the possibility to undertake myomectomy by a mini-invasive approach (laparoscopy or hysteroscopy). In some cases, the surgery can be avoided if medical therapy is completely successful. In the future, the use of augmented reality will expedite myomectomy by laparoscopy, particularly in case of multiple leiomyomas.

Disclosure of interest

The author declares that he has no competing interest.

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Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

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