# Medical management and minimally invasive interventions for uterine fibroids: a perspective

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Uterine fibroids are found in up to 70% of women by the age of 50 years, of whom up to 40% experience symptoms including heavy menstrual bleeding, urinary or bowel dysfunction, pelvic discomfort, pressure symptoms, reproductive dysfunction, and mood disturbances. Uterine fibroids have a detrimental effect on quality of life and cause a large proportion of gynaecological hospitalisations. Although hysterectomy is the definitive treatment, up to 3% and 4% of patients experience intra- and post-operative complications, respectively. Moreover, hysterectomy is unacceptable in women who wish to preserve their fertility. Medical management of uterine fibroids includes hormonal and nonhormonal (tranexamic acid) medications. Commonly used hormonal medications include combined oral contraceptives and progestogens, levonorgestrel-releasing intrauterine devices, selective progesterone receptor modulators, and gonadotrophin-releasing hormone agonists and antagonists. Other less commonly used agents include androgens, selective oestrogen receptor modulators, and aromatase inhibitors. Minimally invasive interventions include uterine artery embolisation, high-intensity focused ultrasound, and radiofrequency ablation. Treatment should be personalised to suit each woman's needs without compromising fertility, reproductive, or obstetric outcomes. Surgery must still be considered when symptoms are intractable, malignancy is suspected, or in an emergency setting in which fibroid-related complications such as torsion or obstructive uropathy arise. Shared decision making is essential, particularly in women of reproductive age, to balance efficacy, fertility goals, and treatment risks.

Keywords: Leiomyoma; Uterus

## Introduction

Uterine leiomyomata (also known as fibroids) are steroid hormone-responsive, benign, smooth muscle tumours found in up to 70% of women by the age of 50 years, of whom up to 40% experience symptoms<sup>1,2</sup>. Fibroids may present with a variety of symptoms including heavy menstrual bleeding, urinary or bowel dysfunction, pelvic discomfort, pressure symptoms, reproductive dysfunction, and mood problems such as depression. Moreover, fibroids account for up to 29% of gynaecological hospitalisations<sup>3,4</sup> and significantly affect the quality of life<sup>5</sup>. In a Hong Kong study in 2023, fibroids attributed to an increase in disabilityadjusted life-years from 90 389 in 1990 to 159 558 in 2019<sup>5</sup>. In the US, fibroids were estimated to incur US\$4.1 to US\$9.4 billion in direct annual costs, US\$1.55 to US\$17.2 billion in lost work costs, and US\$238 million to US\$7.76 billion in associated obstetric outcome costs<sup>3,4</sup>. Thus, given the ever-increasing health and economic burden of fibroids, prompt and effective treatment is imperative.

The definitive treatment of uterine fibroids is a hysterectomy. A 2014 audit of obstetric and gynaecological services in Hong Kong revealed that 56.3% of abdominal and 48.6% of laparoscopic hysterectomies were performed for uterine fibroids<sup>6</sup>. Among these hysterectomies, the

blood loss ranged from 100 to 400 mL, and the hospital stay ranged from 3 to 5 days. Nearly 2% of open hysterectomies and >3% of laparoscopic hysterectomies had intraoperative complications, with the most common being haemorrhage requiring transfusion (1.25% of open hysterectomies) and visceral injury (0.7% of open and laparoscopic hysterectomies). Indeed, postoperative complications occurred in 3.86% of open hysterectomies, 1.50% of laparoscopic hysterectomies, and 4.19% of vaginal hysterectomies. Hysterectomy is associated with significant risks of intra- and post-operative complications. Moreover, most women experience symptomatic fibroids before the menopause, and hysterectomy is unacceptable for women who wish to preserve fertility. Thus, nonsurgical management for uterine fibroids is warranted.

## **Medical management**

Medical management of uterine fibroids includes hormonal and non-hormonal medications. Leiomyoma cells demonstrate a dependency on steroid hormones such as oestrogen; thus, the disruption of the hypothalamic-

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pituitary-ovarian axis with hormonal medication can lead to a decrease in the production of steroid hormones and subsequent symptomatic relief.

#### Non-hormonal medications

Tranexamic acid, which inhibits fibrinolysis and stabilises blood clots, is the most prescribed non-hormonal agent for treating fibroids, because up to 40% of women with uterine fibroids present with heavy menstrual bleeding<sup>7</sup>. A Cochrane systematic review in 2018 demonstrated that, compared with placebo, tranexamic acid led to a reduction in mean blood loss of 53.20 mL per cycle and higher rates of symptom improvement in 43% to 63% of women<sup>8</sup>. The finding of reduction in menstrual blood loss was supported by a randomised controlled trial (RCT)9. Moreover, tranexamic acid was superior to progestogens and nonsteroidal anti-inflammatory drugs in terms of symptom improvement and reduction in mean blood loss per cycle. Nevertheless, contraindications to tranexamic acid include previous or current thromboembolic disease, epilepsy, severe renal impairment, subarachnoid haemorrhage, and active variceal bleeding. Tranexamic acid should not be used in pregnancy. It must be noted that tranexamic acid does not ameliorate pressure symptoms or reduce the size of uterine fibroids.

## Hormonal medications

Hormonal medications for treating uterine fibroids include combined oral contraceptives and progestogens (COCP), levonorgestrel-releasing intrauterine devices, aromatase inhibitors, androgens, selective oestrogen receptor modulators, selective progesterone receptor modulators, and gonadotrophin receptor agonists and antagonists (Table).

## Combined oral contraceptives and progestogens

COCPs contain varying levels of oestrogen and progesterone that disrupt the hypothalamic-pituitary-ovarian axis and reduce the amount of endogenous oestrogen and progesterone, resulting in reduction of menstrual blood loss by up to 53.5%<sup>10</sup>, but they have limited efficacy in reducing fibroid volume or uterine size. A meta-analysis showed that COCPs have a role in prevention of uterine fibroids; the risk reduced by 57% in current users and by 17% in those who have ever used COCPs (a persistent effect even after cessation of treatment)<sup>11</sup>. The use of COCPs may, however, be limited by age and contraindications such as obesity, smoking, hypertension, and migraines. COCPs, unlike progestogens, cannot be used together with tranexamic acid owing to an increased risk of venous thromboembolism.

Progestogens are structurally similar to progesterone and often used in the treatment of abnormal uterine bleeding through an oral (ie, norethisterone acetate) or intramuscular (ie, depot medroxyprogesterone acetate) route. A RCT comparing norethisterone acetate and leuprolin showed a 7.3% reduction in uterine fibroid volume 16 weeks after treatment<sup>12</sup>; however, the study quality was low. Another study comparing promegestrone, nomegestrol acetate, and depot medroxyprogesterone acetate did not demonstrate significant reductions in menstrual bleeding or fibroid size<sup>13</sup>. Indeed, a Cochrane review concluded that there is insufficient evidence to support the efficacy of progestogen treatment for uterine fibroids<sup>14</sup>.

#### Levonorgestrel-releasing intrauterine device

The levonorgestrel-releasing intrauterine device is a T-shaped thermoplastic device inserted into the uterus through the cervix; it releases levonorgestrel to thin the endometrium and induce endometrial decidualisation, thus inhibiting the proliferation of leiomyoma cells. The National Institute for Health and Care Excellence recommends it as first-line treatment for women with heavy menstrual bleeding, except in those with fibroids >3 cm and uterine cavity distortion. However, its overall effect is mixed; compared with COCPs and other progestins, the device has no strong evidence of benefit in premenopausal women, with inconsistent results in change of uterine and fibroid volumes<sup>14,15</sup>.

## Gonadotrophin-releasing hormone agonists and antagonists

Gonadotrophin-releasing hormone (GnRH) agonists have demonstrated efficacy in treating symptomatic fibroids. They are structurally akin to endogenous GnRH and, after an initial flare effect that elevates folliclestimulating hormone and luteinising hormone levels, induce receptor downregulation, leading to a hypogonadotrophic hypogonadal (ie, hypo-oestrogenic) state. GnRH agonists are well established for preoperative preparations; a Cochrane review demonstrated improvements in preand post-operative haemoglobin levels and reductions in uterine and fibroid volumes, uterine size, and duration of hospitalisation<sup>16</sup>. Patients undergoing GnRH agonist injection before surgery have better perioperative outcomes including a lower rate of midline laparotomy, less blood loss and blood transfusion, and reduced operative time and difficulty. However, GnRH agonists are not used for prolonged periods owing to a significant and rapid loss of bone mineral density of up to 6% annually, secondary to the ensuing hypo-oestrogenic state, which may not recover after discontinuation<sup>17</sup>.

Table. Hormonal medications and minimally invasive interventions for uterine fibroids.

Treatment	Mechanism	Reduction in bleeding, %	Reduction in fibroid size, %	Reduction in uterine size, %	Improvement in quality of life	Sustained response	Reproductive outcome	Adverse effects
Commonly used hormonal medications								
Tranexamic acid	Antifibrinolytic	40-60	No	No	Yes (reduced heavy menstrual bleeding)	Recurrence after cessation	-	Mild (gastrointestinal tract symptoms, thrombosis risk in high doses)
Combined oral contraceptives and progestogens	Disrupt hypothalamic- pituitary-ovarian axis, reduce endogenous oestrogen and progesterone	30-40	Minimal (low-quality evidence)	No	Limited	Recurrence after cessation	-	Moderate (venous thromboembolism risk, headaches, breast tenderness, weight gain, acne, mood changes)
Progestogens	Inhibit endometrial proliferation	30-50	Minimal (low-quality evidence)	No	Limited	Recurrence after cessation	-	Mild (weight gain, bloating, mood changes)
Levonorgestrel- releasing intra- uterine device	Localised progestin effect, inhibits endometrial proliferation	70-90 (for heavy menstrual bleeding in those without uterine fibroids)	Minimal (low-quality evidence)	No	Yes (reduced heavy menstrual bleeding)	Effective for 5 years	-	Mild (irregular bleeding, amenorrhoea)
Gonadotrophin- releasing hormone agonists	Induces hypo- oestrogenic state	80-90	30-60	30-50	Significant	Fibroid regrowth after cessation	-	Major (vasomotor symptoms, accelerated loss in bone mineral density)
Gonadotrophin- releasing hormone agonists + add-back therapy	Induces hypo- oestrogenic state Replenishes steroid hormones to prevent bone loss	70-90	10-30	10-30	Significant	Fibroid regrowth after cessation	-	Mild (vasomotor symptoms)
Selective progesterone receptor modulators	Direct reduction in fibroid proliferation	70-90	30-70	30-40	Significant	Yes	-	Major (benign endometrial changes, rare liver toxicity)
Less commonly used hormonal medications								
Aromatase inhibitors	Inhibit local aromatase activity	Yes	Up to 46	Up to 21	-	-	-	Moderate (arthralgia, vasomotor symptoms, follicular hormonal profile over study period)
Androgens	Binds to and decreases sex hormone- binding globulin, suppresses hypothalamic- pituitary-ovarian axis	69 (in amenorrhoea)	23.6-37.6	-	-	-		Moderate (acne, weight gain, permanent voice changes, muscle cramps, oily skin)
Selective oestrogen receptor modulators	Oestrogen receptor agonist/antagonist effect	No	9.1-31 greater shrinkage than gonadotrophin- releasing hormone	-	-	-	-	Mild (vasomotor symptoms)
Minimally invasive interventions								
Uterine artery embolisation	Direct occlusion of blood supply	85-90	35-60	30-50	Significant	Yes	Worse, compared with myomectomy	Moderate (post- embolisation syndrome, ovarian failure, pelvic pain)
High-intensity focused ultrasound	Direct thermal ablation with ultrasound waves	70-80	30-50	20-40	Moderate to significant	Yes, but higher reintervention rate.	Better, compared with uterine artery embolisation	Moderate (skin burns, pelvic pain, visceral and nerve injury)
Radiofrequency ablation	Direct thermal ablation with radio waves	75-85	40-60	30-50	Significant	Yes	Better, compared with uterine artery embolisation	Mild (pain, infection, visceral injury)

In 2021, oral GnRH antagonists such as relugolix and elagolix were approved for the treatment of fibroid-induced abnormal uterine bleeding by the US Food and Drug Administration (FDA). Oral GnRH antagonists have a faster onset of action and can avoid the initial flare effect<sup>17-20</sup>. Loss in bone mineral density can be mitigated with oestrogen and progestogen add-back therapy. Multiple RCTs (namely ELARIS UF-I, UF-II, UF-EXTEND, LIBERTY I, II, and III, Extended LIBERTY, and LIBERTY randomised withdrawal) have demonstrated significant reductions in menstrual blood loss, increase in haemoglobin levels, decrease in fibroid numbers and volume, and improvement in quality-of-life scores.

In LIBERTY I and LIBERTY II double-blinded phase III trials, patients with fibroid-associated heavy menstrual bleeding were randomised to receive daily relugolix combination therapy (ie, add-back therapy of 1 mg of oestradiol and 0.5 mg of norethindrone acetate daily), relugolix with delayed combination therapy (relugolix alone for 12 weeks and then combined with add-back therapy for the remaining 12 weeks), or placebo<sup>20</sup>. At 6 months, 73% of patients with relugolix combination therapy attained a reduction in menstrual bleeding ≥50% and a total volume of menstrual blood loss <80 mL, whereas 80% of patients with a delayed relugolix combination achieved the same outcomes. Bone mineral density loss in the respective groups was 0.4% and 1.9% to 2.4% at the lumbar spine and 0.1% to 0.5% and 1.1% to 1.6% at the hip. Patients with relugolix combination therapy had an 84.3% to 89.4% decrease in menstrual blood loss volume from baseline; 50% to 61% of those with anaemia had an increase in haemoglobin levels of >2 g/dL; the volume of the primary fibroid reduced 12.4% to 30.2%; and the Bleeding and Pelvic Discomfort scores improved 28.9% to 33.4%. When the treatment was extended to 76 and 104 weeks, 78.4% and 69.8% of patients maintained a menstrual blood loss of <80 mL, respectively<sup>21</sup>. The mean loss in bone mineral density from week 52 to week 104 of treatment was 0.8% at the lumbar spine and 0.3% at the hip. Thus, a combination of relugolix and add-back therapy is effective for treating symptomatic uterine fibroids.

## Selective progesterone receptor modulators

Selective progesterone receptor modulators such as ulipristal acetate (UPA) exhibit variable agonist and antagonist activities on progesterone receptors, decreasing endogenous oestrogen through inhibition of the hypothalamic-pituitary-ovarian axis, resulting in antiproliferative, proapoptotic, and antifibrotic changes in leiomyomata. RCTs have shown significant decreases

in fibroid and uterine volumes and menstrual blood loss; the effects and improvement in quality-of-life scores and serum oestradiol levels in the mid-follicular range were maintained 6 months after cessation, thereby negating the hypo-oestrogenic state of GnRH agonist drugs<sup>22</sup>.

The PEARL trials evaluated the efficacy and safety of UPA in the treatment of symptomatic uterine fibroids. PEARL I demonstrated the efficacy of UPA in controlling heavy menstrual bleeding and pain, without significant adverse effects<sup>23</sup>. PEARL II compared UPA with a GnRH agonist (leuprolide acetate); patients with UPA achieved amenorrhoea 2 weeks earlier, with better pain control and fewer adverse effects<sup>24</sup>. Only 10% to 11% of those with UPA experienced moderate to severe hot flashes, compared with up to 40% in those with leuprolide acetate. The mean serum oestradiol was maintained at 70 to 79 pg/mL in those with UPA, compared with 24 pg/mL in those with leuprolide acetate. PEARL III showed that long-term (18 months) UPA resulted in shrinkage of uterine leiomyomata by up to 72% and an amenorrhoea rate of nearly 90%<sup>25</sup>. At 3 months after cessation of UPA, the volume of the three largest leiomyomata decreased by 60%, and up to 45% of patients experienced a reduction in uterine volume by ≥25%. Fibroid-specific quality-of-life scores improved from 22.7 to 31.4 and were maintained even after treatment cessation. The PEARL IV compared two doses of UPA (5 and 10 mg) given as two 12-week courses separated by two menstrual cycles and showed reductions in fibroid volume by 54% and 58%, respectively, with no increase in adverse effects<sup>26</sup>. UPA can, therefore, maintain amenorrhoea and fibroid and uterine volume reduction, with superior adverse effect profile and quality of life, compared with GnRH agonist alone. In a case series of 47 women (mean age, 36 years) with pregnancy after UPA (75% were nulliparous), 85% conceived spontaneously, and 64% resulted in live births after a mean gestational age of 38 weeks<sup>27</sup>. There were no fetal malformations, and 43% of patients did not require myomectomy after UPA treatment.

Up to 12% of patients treated with UPA had thickened endometria (>16 mm) and progesterone receptor modulator–associated endometrial changes. Long-term follow-up with endometrial sampling showed no atypia in any patients, and these endometrial changes were reversible 1 to 2 months after treatment cessation. However, the European Medicines Agency recommends restricting UPA use due to cases of serious liver injury<sup>28</sup>. It stipulates that UPA can only be used to treat uterine fibroids in premenopausal women for whom surgical procedures (including embolisation) fail or are not appropriate; UPA

must not be used to control symptoms of uterine fibroids while awaiting surgical treatment<sup>29</sup>. It is argued, however, that the associations between UPA and acute liver injury are overblown. According to the FDA's Drug-Induced Liver Injury Guidance<sup>30</sup>, indicators of drug-induced liver injury (ie, Hy's law) include tripling or more of alanine aminotransferase or aspartate aminotransferase levels compared with the upper limit of normal (ULN), and doubling or more of total bilirubin levels in such patients without evidence of cholestasis, underlying liver disease, or any other explanation for the deranged liver function other than exposure to the drug. In the phase I trials for UPA, 160 patients received up to 50 mg of UPA daily for up to 10 days-up to ten times the marketed dose-and none showed any derangement of liver function. In the phase II trials, 152 patients (excluding those with alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, or bilirubin more than double the ULN, and those with alcohol abuse) received up to 20 mg of UPA daily for 3 months and none experienced any elevation of liver transaminases more than double the ULN or a total bilirubin >1.5 times the ULN. In the phase III trials, 1556 patients received 5 and 10 mg UPA daily for up to eight 3-month courses; only eight patients had liver transaminase levels more than three times the ULN<sup>31</sup>.

## Other medical treatments

Other less commonly used agents include androgens, selective oestrogen receptor modulators, and aromatase inhibitors (Table). Androgens such as danazol (a synthetic testosterone derivative that binds to and decreases sex hormone-binding globulin production) and gestrinone (a synthetic steroidal hormone with androgenic and antioestrogenic properties) have been used with some efficacy. Studies have shown a reduction in fibroid volume of up to 38% and amenorrhoea in up to 69% of women<sup>32-35</sup>. However, persistent androgenic adverse effects such as weight gain, permanent voice deepening, oily skin, and acne limit widespread use of androgens. Raloxifene is a selective oestrogen receptor modulator that binds to oestrogen receptors with varying degrees of agonist and antagonist effects; it has an antiproliferative effect on leiomyoma cells and hence reduces fibroid size. A Cochrane review reported that selective oestrogen receptor modulators did not significantly reduce the duration or severity of uterine bleeding or improve haemoglobin levels, despite being effective in reducing the mean leiomyoma size<sup>36</sup>, but existing data are limited and of low quality. Aromatase inhibitors, which block local aromatase activity and prevent extragonadal and intratumoural oestrogen conversion, are effective in fibroid size reduction and symptom improvement<sup>37-39</sup>. An RCT comparing aromatase inhibitors and GnRH agonists demonstrated a reduction in mean fibroid volume of up to 45.6% without any adverse effects or changes in bone mineral density, follicle-stimulating hormone, or oestrogen levels. Additionally, prospective studies have shown a reduction in mean fibroid and uterine volumes by approximately 47% and 22%, respectively, and a decrease in mean blood loss from 315 to 151 mL<sup>37-39</sup>. However, the evidence is limited, and none shows whether treatment response is sustained after cessation.

## Minimally invasive interventions

#### Uterine artery embolisation

Uterine artery embolisation (UAE) is a minimally invasive, interventional radiological procedure, in which microparticles (made of tris-acryl gelatin or polyvinyl alcohol) are delivered to the uterine arteries under image guidance via a catheter through the common femoral artery. Occlusion of one or both uterine arteries leads to ischaemia with subsequent necrosis and shrinkage of the uterine fibroids.

According to the Society of Interventional Radiology guidelines, noticeable reductions in uterine and fibroid volumes occur weeks after UAE and continue for 3 to 12 months after treatment; the rates of leiomyoma size reduction were 50% to 60%; there were 88% to 92% reduction of bulk symptoms,>90% elimination of abnormal uterine bleeding, and up to 75% elimination of symptoms<sup>40</sup>.

A systematic review and meta-analysis in 2024 comparing UAE and myomectomy for symptomatic uterine fibroids reported that UAE had superior postprocedural outcomes including fewer major complications (infection, pulmonary embolism, uterine ischaemia, fibroid expulsion, and sepsis) within 30 days of discharge (odds ratio [OR]=0.44), fewer readmissions due to complications (OR=1.16), and shorter hospital stay (mean difference [MD]= -47.07)<sup>41</sup>. UAE was not inferior to myomectomy in terms of obstetric outcomes, with comparable rates of amenorrhoea, pregnancy, live birth, and miscarriage. However, the quality-of-life scores did not improve significantly at 2 or 4 years of follow-up. At 1, 2, and 4 years of follow-up, UAE was associated with higher rates of reintervention (OR=1.77, 3.44, and 1.84, respectively) and greater risks of hysterectomy (OR=2.67, 4.06, and 4.04, respectively). Common post-procedural adverse effects include pain, nausea, groin haematoma, fever, and post-embolisation syndrome (fever, pain, and nausea).

### High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) guided by ultrasound or magnetic resonance imaging transmits energy to a targeted lesion, raising its temperature to >60°C and leading to localised coagulative necrosis within 1 to 3 mm of boundaries of the lesion without damaging surrounding tissue<sup>42</sup>.

In a meta-analysis of 10 studies involving 4450 women comparing outcomes of HIFU with myomectomy<sup>43</sup>, HIFU showed better fibroid symptom control, with significant improvements in uterine fibroid symptomrelated quality-of-life scores at 6 months (MD= -4.16, 95% confidence interval [CI]= -7.39 to -0.94) and 12 months (MD = -2.44, 95% CI = -3.67 to -1.20) and in overall qualityof-life scores at 6 months (MD=2.13, 95% CI=0.86-3.14) and 12 months (MD=2.34, 95% CI=0.82-3.85). HIFU showed significantly shorter duration of hospital stay (MD= -3.41 days, 95% CI= -5.11 to -1.70 days) and time to return to work (MD= -11.61 days, 95% CI= -19.73 to -3.50 days), as well as a significantly lower incidence of severe complications (including fever, transfusion, and re-hospitalisation) within 42 days (risk ratio=0.33, 95% CI=0.13-0.81). The rate of reintervention at 60 months, however, was 53.9% after HIFU, compared with 12.2% after myomectomy and 14.4% after UAE<sup>44</sup>.

In a systematic review of 14 studies assessing reproductive outcomes after magnetic resonance imaging—guided HIFU (n=124) or ultrasound-guided HIFU (n=366)<sup>28</sup>, in the respective groups, pregnancy rates were 7% to 36% and 10% to 69%; live birth rates were 73% to 84% and 91%; conception occurred within 0 to 36 months and 4 to 16 months of treatment; miscarriage rates were 30% to 50% and 4% to 15%; and rates of Caesarean section were 36% to 64% and 72% to 80% (although most were performed for social reasons). Overall, the pregnancy rates were lower after HIFU than after myomectomy, but live birth rates were comparable. There were eight cases of placenta praevia without any invasive placentation but no reports of uterine rupture.

HIFU is generally safe; absolute contraindications include pregnancy, malignant or suspected malignant pelvic masses, active pelvic infections, intrauterine contraceptive device in situ, severe abdominal adhesions, interposed bowel/bladder, and submucosal fibroids with a significant intracavity component, whereas relative contraindications include pedunculated fibroids, fibroids >10 cm, numerous or diffuse fibroids, previous uterine surgery, and very thick abdominal walls. With appropriate patient selection, HIFU can deliver effective treatment of uterine fibroids.

### Radiofrequency ablation

Radiofrequency ablation (RFA) applies an alternating current in the radiofrequency range of 450 to 500 kHz, through a transvaginal, transcervical, percutaneous, or laparoscopic approach. It induces local tissue destruction, coagulative necrosis, and hence fibroid shrinkage.

In a systematic review and meta-analysis of 30 studies that evaluated clinical outcomes after RFA, the mean fibroid volume reduced by 46% at 3 months and 65.4% at 12 months, with substantial improvement in abnormal menstrual bleeding within the first 3 months, which was maintained up to 24 months<sup>45</sup>. Uterine fibroid symptomrelated quality-of-life scores peaked at 6 months after RFA (88.0, 95% CI=83.0-92.9; 11 studies), with a significant increase in quality-of-life scores (53.4, 95% CI=48.2-58.5; 20 studies) and a significant decrease in symptom severity scores (52.2, 95% CI=46.2-58.1; 17 studies). The symptom severity scores were lowest at 12 months (12.8, 95% CI=7.0-18.6; 11 studies) and were sustained for up to 5 years. The mean hospital stay was 2.5 to 12 hours; the mean time for return to normal activity was 2.2 to 16.3 days, averaging 5.8 days; and the rates of secondary hysterectomy were 1% to 24.1%, with the longest followup being 74 months.

A systematic review of 10 studies involving 923 patients with RFA reported a total of 50 pregnancies<sup>46</sup>. The mean age of patients ranged from 27 to 46 years; conception occurred within 3.5 to 33 months of RFA; 44 of the pregnancies were full term and delivered vaginally (55%) or through Caesarean section (45%); the spontaneous miscarriage rate was 12%. There were no reports of uterine rupture, placental abruption, or invasive placentation. Nevertheless, RFA has not yet been approved by the FDA for women seeking future fertility.

RFA is generally safe and well tolerated. Absolute contraindications include pregnancy, malignant or suspected malignant pelvic masses, active pelvic infections, intratubal or other metal implants, and intrauterine contraceptive device in situ. Relative contraindications include nickel allergy, coagulopathy, numerous or diffuse fibroids, interposed bowel or bladder, and significant abdominal adhesions. With appropriate patient selection, RFA can be effective treatment for uterine fibroids.

## Conclusion

Treatment for uterine fibroids should be personalised to suit each woman's needs with minimal compromise to

fertility, reproductive, or obstetric outcomes. Leiomyomata, however, do not exist in isolation and are commonly found as a constellation of gynaecological pathologies including endometriosis, adenomyosis, and endometrial hyperplasia or even malignancy. Surgery must still be considered when symptoms cannot be adequately controlled or in an emergency setting in which fibroid-related complications such as torsion or obstructive uropathy arise. Malignancy should be suspected in cases of rapidly growing fibroids (particularly in postmenopausal women), when suspicious features (irregular margins, intralesional vascularity, central necrosis, or haemorrhage) are seen on imaging or when there are associated symptoms. Prompt surgical evaluation to exclude leiomyosarcoma is warranted. Although minimally invasive techniques preserve fertility and avoid surgical morbidity, myomectomy or hysterectomy remains the definitive treatment. Shared decision making is essential, particularly in women of reproductive age, aiming at balancing efficacy, fertility goals, and procedural risks.

## **Contributors**

JL designed the study, acquired and analysed the data, drafted the manuscript, and critically revised the manuscript. MC critically revised the manuscript. Both authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy.

## Conflicts of interest

Both authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author upon reasonable request.

## References

- Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188;100-7. crossref
- Wise LA, Laughlin-Tommaso SK. Epidemiology of uterine fibroids: from menarche to menopause. Clin Obstet Gynecol 2016;59:2-24. Crossref
- 3. Al-Hendy A, Lukes AS, Poindexter AN 3rd, et al. Treatment of uterine fibroid symptoms with relugolix combination therapy. N Engl J Med 2021;384:630-42. Crossref
- Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. Am J Obstet Gynecol 2012;206:211.e1-9. Crossref
- Yeung SY, Kwok JWK, Law SM, Chung JPW, Chan SSC. Uterine fibroid symptom and health-related quality of life questionnaire: a Chinese translation and validation study. Hong Kong Med J 2019;25:453-9. Crossref
- The Hong Kong College of Obstetricians and Gynaecologists.
   Territory-Wide Audit in Obstetrics & Gynaecology 2014.
   Accessed 3 August 2025. Available from https://www.hkcog.org.hk/hkcog/Download/Territory-wide\_Audit\_in\_Obstetrics\_Gynaecology\_2014.pdf
- Gupta S, Jose J, Manyonda I. Clinical presentation of fibroids. Best Pract Res Clin Obstet Gynaecol 2008;22:615-26. Crossref
- Bryant-Smith AC, Lethaby A, Farquhar C, Hickey M. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev 2018;4:CD000249. Crossref

- Lukes AS, Moore KA, Muse KN, et al. Tranexamic acid treatment for heavy menstrual bleeding: a randomized controlled trial. Obstet Gynecol 2010;116:865-75. Crossref
- 10. Sayed GH, Zakherah MS, El-Nashar SA, Shaaban MM. A randomized clinical trial of a levonorgestrel-releasing intrauterine system and a low-dose combined oral contraceptive for fibroid-related menorrhagia. Int J Gynaecol Obstet 2011;112:126-30. crossref
- Qin J, Yang T, Kong F, Zhou Q. Oral contraceptive use and uterine leiomyoma risk: a meta-analysis based on cohort and case-control studies. Arch Gynecol Obstet 2013;288:139-48. Crossref
- Verspyck E, Marpeau L, Lucas C. Leuprorelin depot 3.75 mg versus lynestrenol in the preoperative treatment of symptomatic uterine myomas: a multicentre randomised trial. Eur J Obstet Gynecol Reprod Biol 2000;89:7-13. crossref
- 13. Donnez J. Uterine fibroids and progestogen treatment: lack of evidence of its efficacy: a review. J Clin Med 2020;9:3948. Crossref
- 14. Sangkomkamhang US, Lumbiganon P, Pattanittum P. Progestogens or progestogen-releasing intrauterine systems for uterine fibroids (other than preoperative medical therapy). Cochrane Database Syst Rev 2020;11:CD008994. Crossref
- Jiang W, Shen Q, Chen M, et al. Levonorgestrel-releasing intrauterine system use in premenopausal women with symptomatic uterine leiomyoma: a systematic review. Steroids 2014;86:69-78. Crossref
- 16. Puscasiu L, Vollenhoven B, Nagels HE, Melinte IM, Showell MG, Lethaby A. Preoperative medical therapy

- before surgery for uterine fibroids. Cochrane Database Syst Rev 2025;4:CD000547. Crossref
- 17. Sauerbrun-Cutler MT, Alvero R. Short- and long-term impact of gonadotropin-releasing hormone analogue treatment on bone loss and fracture. Fertil Steril 2019;112:799-803. Crossref
- Simon JA, Al-Hendy A, Archer DF, et al. Elagolix treatment for up to 12 months in women with heavy menstrual bleeding and uterine leiomyomas. Obstet Gynecol 2020;135:1313-26. Crossref
- Carr BR, Stewart EA, Archer DF, et al. Elagolix alone or with add-back therapy in women with heavy menstrual bleeding and uterine leiomyomas: a randomized controlled trial. Obstet Gynecol 2018;132:1252-64. Crossref
- 20. Venturella R, Al-Hendy A, Lukes AS, Kang J, McKain L, Stewart EA. Relugolix combination therapy significantly reduced menstrual blood loss associated with first treatment cycle in women with heavy menstrual blood loss with first treatment cycle in women with heavy menstrual bleeding associated with uterine fibroids: results from the liberty phase 3 program. Fertil Steril 2020;114(Suppl):E85. crossref
- Al-Hendy A, Venturella R, Arjona Ferreira JC, et al. LIBERTY randomized withdrawal study: relugolix combination therapy for heavy menstrual bleeding associated with uterine fibroids. Am J Obstet Gynecol 2023;229:662.e1-25. Crossref
- Chabbert-Buffet N, Esber N, Bouchard P. Fibroid growth and medical options for treatment. Fertil Steril 2014;102:630-9. Crossref
- Donnez J, Tatarchuk TF, Bouchard P, et al. Ulipristal acetate versus placebo for fibroid treatment before surgery. N Engl J Med 2012;366:409-20. Crossref
- Donnez J, Tomaszewski J, Vázquez F, et al. Ulipristal acetate versus leuprolide acetate for uterine fibroids. N Engl J Med 2012;366:421-32. Crossref
- Donnez J, Vázquez F, Tomaszewski J, et al. Long-term treatment of uterine fibroids with ulipristal acetate. Fertil Steril 2014;101:1565-73.e1-18. Crossref
- Donnez J, Donnez O, Matule D, et al. Long-term medical management of uterine fibroids with ulipristal acetate. Fertil Steril 2016;105:165-73.e4. Crossref
- 27. De Gasperis-Brigante C, Singh SS, Vilos G, Kives S, Murji A. Pregnancy outcomes following ulipristal acetate for uterine fibroids: a systematic review. J Obstet Gynaecol Can 2018;40:1066-76.e2. Crossref
- Anneveldt KJ, van 't Oever HJ, Nijholt IM, et al. Systematic review of reproductive outcomes after high intensity focused ultrasound treatment of uterine fibroids. Eur J Radiol 2021;141:109801. Crossref
- European Medicines Agency. Ulipristal acetate 5mg medicinal products 2020. Accessed 3 August 2025. Available from: https://www.ema.europa.eu/en/medicines/human/ referrals/ulipristal-acetate-5mg-medicinal-products
- U.S. Food and Drug Administration. Guidance for Industry Drug-Induced Liver Injury: Premarketing Clinical Evaluation. Accessed 3 August 2025. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/

- drug-induced-liver-injury-premarketing-clinical-evaluation
- 31. Donnez J. Liver injury and ulipristal acetate: an overstated tragedy? Fertil Steril 2018;110:593-5. Crossref
- 32. La Marca A, Musacchio MC, Morgante G, Petraglia F, De Leo V. Hemodynamic effect of danazol therapy in women with uterine leiomyomata. Fertil Steril 2003;79:1240-2. Crossref
- De Leo V, la Marca A, Morgante G. Short-term treatment of uterine fibromyomas with danazol. Gynecol Obstet Invest 1999;47:258-62. Crossref
- Coutinho EM. Treatment of large fibroids with high doses of gestrinone. Gynecol Obstet Invest 1990;30:44-7. crossref
- La Marca A, Giulini S, Vito G, Orvieto R, Volpe A, Jasonni VM. Gestrinone in the treatment of uterine leiomyomata: effects on uterine blood supply. Fertil Steril 2004;82:1694-6. Crossref
- Deng L, Wu T, Chen XY, Xie L, Yang J. Selective estrogen receptor modulators (SERMs) for uterine leiomyomas. Cochrane Database Syst Rev 2012;10:CD005287. Crossref
- 37. Gurates B, Parmaksiz C, Kilic G, Celik H, Kumru S, Simsek M. Treatment of symptomatic uterine leiomyoma with letrozole. Reprod Biomed Online 2008;17:569-74. Crossref
- 38. Hilário SG, Bozzini N, Borsari R, Baracat EC. Action of aromatase inhibitor for treatment of uterine leiomyoma in perimenopausal patients. Fertil Steril 2009;91:240-3. crossref
- Song H, Lu D, Navaratnam K, Shi G. Aromatase inhibitors for uterine fibroids. Cochrane Database Syst Rev 2013;2013:CD009505. Crossref
- 40. Dariushnia SR, Nikolic B, Stokes LS, Spies JB; Society of Interventional Radiology Standards of Practice Committee. Quality improvement guidelines for uterine artery embolization for symptomatic leiomyomata. J Vasc Interv Radiol 2014;25:1737-47. Crossref
- Peng J, Wang J, Shu Q, Luo Y, Wang S, Liu Z. Systematic review and meta-analysis of current evidence in uterine artery embolization vs myomectomy for symptomatic uterine fibroids. Sci Rep 2024;14:19252. crossref
- Izadifar Z, Izadifar Z, Chapman D, Babyn P. An introduction to high intensity focused ultrasound: systematic review on principles, devices, and clinical applications. J Clin Med 2020;9:460. Crossref
- 43. Liu L, Wang T, Lei B. High-intensity focused ultrasound (HIFU) ablation versus surgical interventions for the treatment of symptomatic uterine fibroids: a meta-analysis. Eur Radiol 2022;32:1195-204. Crossref
- 44. Sandberg EM, Tummers F, Cohen SL, van den Haak L, Dekkers OM, Jansen FW. Reintervention risk and quality of life outcomes after uterine-sparing interventions for fibroids: a systematic review and meta-analysis. Fertil Steril 2018;109:698-707.e1. Crossref
- 45. Chen I, Berman JM, Balk EM, et al. Radiofrequency ablation for the treatment of uterine fibroids: a systematic review and meta-analysis by the AAGL Practice Committee. J Minim Invasive Gynecol 2025;32:74-91. Crossref
- Polin M, Hur HC. Radiofrequency ablation of uterine myomas and pregnancy outcomes: an updated review of the literature. J Minim Invasive Gynecol 2022;29:709-15. Crossref