

Fibroids

Synonyms: uterine leiomyomas; myomas

Women with fibroids or symptoms suggestive of fibroids experience significant distress that reduces quality of life, particularly among racial minorities and women in lower income brackets.^[1] Among diagnosed women, around 71% use pharmacological therapy for symptom relief, and 30% undergo surgical-type treatment.

Pathogenesis

Fibroids are extremely common benign monoclonal tumours of the smooth muscle cells of the uterine myometrium, containing a large amount of extracellular matrix with disordered collagen. They start as multiple, single-cell seedlings distributed throughout the uterine wall. These then increase in size very slowly over many years, stimulated by oestrogens and progestogens. As the fibroid grows, the central areas may not receive an adequate blood supply and then undergo benign degeneration often followed by calcification.

The cause of fibroids is debated but it is thought to be a combination of acquired genetic change plus the effects of hormones and growth factors, possibly related to a response to ischaemic injury at the time of menses.

Classification

Fibroids, which are often multiple, are classified according to their position within the uterine wall:

- Intramural (the majority).
- Submucosal: growing into the uterine cavity. They may be pedunculated and may protrude through the cervical os.
- Subserosal: growing outwards from the uterus - can be:
 - Uterine
 - Cervical
 - Intraligamentous
 - Pedunculated subserous (abdominal)

Most uterine fibroids are asymptomatic but in perimenopause or menopause, they typically manifest as abnormal uterine bleeding, which represents up to 70% of all gynecological consultations.^[2] Additionally they can cause pelvic pressure or pain and also occasionally they may contribute to reproductive dysfunction. Fibroids don't undergo malignant change to a sarcoma except in very rare circumstances but tumours assumed to be benign fibroids may occasionally later be identified as uterine sarcomas.^[3] Most women with sarcoma have symptoms of a suspected gynaecological malignancy: abdominal pain and abnormal bleeding.

Epidemiology^[4]

The prevalence of symptomatic fibroids is low in women younger than 30 years of age - fibroids occur in 20-50% of women older than 30 years.

Peak incidence is in women in their 40s, with a crude incidence of 22.5 per 1,000 women-years.

The prevalence of fibroids is higher in black women than in white women.

Uterine fibroids are the most common non-cancerous tumours in women of childbearing age. Nearly 70% of white women and more than 80% of black women have had at least one fibroid by the age of 50 years.

Approximately 40% of white women and 60% of black women have had fibroids by the age of 35 years.

Risk factors^{[1] [5]}

Fibroids are more common in obese women and women with an early menarche - factors which increase lifetime exposure to oestrogen. Having a first-degree affected relative increases the risk of fibroids.

Additional factors increasing risk include:

- Having hypertension
 - Alcohol consumption
 - Poor diet
-

Protective factors include:

- Exercise
- Increased parity
- Cigarette smoking (possibly)

There is no definite relationship between the use of oral contraceptives and the presence or growth of fibroids. In the majority of menopausal women with fibroids, [hormone replacement therapy \(HRT\)](#) will not have any effect but in those where the fibroids do grow, this appears to be proportional to the dose of progestogen.

Presentation

Fibroids usually present between the ages of 30 and 50 years. Up to half of women with fibroids have no symptoms. The presence of symptoms depends on their size, position and condition.

They may cause excessive or [prolonged heavy periods](#), leading to [iron-deficiency anaemia](#) and therefore lethargy and pallor. Larger fibroids, no matter their position, appear to be more likely to cause [menorrhagia](#), possibly due to a variety of growth factors promoting angiogenesis.

Pedunculated submucosal fibroids may cause persistent [intermenstrual bleeding](#). Women with fibroids are slightly more likely than women without, to experience [pelvic pain](#) but this is unrelated to the size or number of myomas. An enlarging uterus may cause lower abdominal discomfort and heaviness due to pressure effects. Pressure on the bowel may cause [constipation](#) and pressure on the bladder may cause urinary symptoms.

Fibroids may present with [recurrent miscarriage](#) or [infertility](#). However, only submucous fibroids decrease fertility but their removal restores fertility to baseline rates.

- Examination:
 - Palpable abdominal mass arising from the pelvis.
 - Enlarged, often irregular, firm, non-tender uterus palpable on bimanual pelvic examination.
 - Signs of anaemia due to menorrhagia.

Differential diagnosis^[4]

Fibroids are so common that other more serious causes of abnormal bleeding or pelvic mass can often co-exist and need to be excluded. The differential diagnosis for fibroids depends on the symptoms they are causing but includes:

- [Dysfunctional uterine bleeding](#).
- Endometrial polyps, [endometrial cancer](#).
- [Endometriosis](#).
- Chronic [pelvic inflammatory disease](#).

- Tubo-ovarian abscess.
- Uterine sarcoma.
- [Ovarian tumour](#).
- Pelvic masses (other causes of a pelvic mass include tumour of the large bowel, appendix abscess, and diverticular abscess).
- Pregnancy.

Investigations

- Pregnancy test may be indicated.
- FBC (anaemia), iron studies.
- Pelvic ultrasound may be indicated to exclude other causes of a pelvic mass, to confirm the presence and size of a fibroid and to exclude possible complications such as urinary tract obstruction causing hydronephrosis. [6]
Transvaginal ultrasound (TVUS) is more accurate.
- Saline infusion ultrasound is superior to TVUS and hysteroscopy, in detecting submucous fibroids
- MRI is highly sensitive and specific and is occasionally required if ultrasound is not definitive in assessing the fibroid(s) when myomectomy is being considered.
- [Endometrial sampling](#) (Pipelle[®]): for histology in the assessment of abnormal uterine bleeding.
- Hysteroscopy: with biopsies.

Management

Treatment is only required if symptomatic, as long as other causes of pelvic masses and abnormal bleeding have been excluded. Expectant management is a valid option, especially in the perimenopause.

Pharmacological

- Non-steroidal anti-inflammatory agents (eg, ibuprofen) may be tried. They reduce menstrual blood loss when the cause is unknown but there is little evidence for their effectiveness in fibroid-related bleeding.
- Antifibrinolytic agents (eg, tranexamic acid) may also also reduce menorrhagia.

- Combined hormonal contraception (CHC): despite the 'pill' previously being considered a risk factor for fibroid growth, CHC is helpful if the patient requires contraception, although it is not as effective as a levonorgestrel-releasing intrauterine system (LNG-IUS).
- **LNG-IUS (Mirena):**
 - A prospective comparative study of 54 women with fibroid-related menorrhagia showed that not only does the LNG-IUS reduce the amount of menstrual loss but also reduces the uterine size in women with fibroids, although women with uterine distortion were excluded.^[7] In this study fibroids were associated with a higher expulsion rate, especially if submucous.
 - A Cochrane review states that LNG-IUS appears to reduce fibroid-related bleeding but the studies were small and of poor quality.^[8]
- Danazol: a Cochrane review could not find any evidence regarding the use of danazol in the management of fibroids.^[9]
- Gonadotrophin-releasing hormone (GnRH) agonists:
 - Produce reduction in the size of fibroids, in the region of 50% within three months but, once discontinued, fibroids regrow to their former size within about two months; therefore, they are mainly useful pre-hysterectomy. A Cochrane review concluded that their use leads to shorter operation times and shorter hospital stays, and increases the likelihood of a vaginal hysterectomy.
 - They are associated with significant side-effects, including significant menopausal symptoms and also bone loss, which can lead to osteoporosis in long-term use.

Editor's note

Dr Krishna Vakharia, 21st October 2022

Relugolix-estradiol-norethisterone acetate for treating moderate to severe symptoms of uterine fibroids^[10]

The National Institute for Health and Care Excellence (NICE) has recommended a combination drug called relugolix-estradiol-norethisterone acetate as an option for treating moderate to severe symptoms of uterine fibroids in adults of reproductive age. Relugolix is a gonadotropin-releasing hormone (GnRH) receptor antagonist that prevents follicular growth and development, thereby reducing production of oestrogen and progesterone. Relugolix is then combined with the oestrogen estradiol to reduce symptoms related to lowered levels of oestrogen. It is also combined with the progestogen norethisterone to counteract estradiol-induced endometrial hyperplasia. This combination has been shown to work well in reducing heavy menstrual bleeding.

Other benefits include:

A non-surgical option and thereby preserving the uterus.

It is well tolerated.

It is taken orally.

- Mifepristone is a progesterone receptor inhibitor which is effective at reducing fibroid-related bleeding but, as it results in exposure of the endometrium to unopposed oestrogen, it may cause [endometrial hyperplasia](#). It does not reduce uterine volume and hence has no role pre-surgery.
- [Ulipristal acetate](#): the indication of ulipristal acetate 5 mg for uterine fibroids has been restricted due to the risk of serious liver injury and liver failure, with some cases requiring liver transplantation. ^[11] Although the temporary suspension has been lifted, this medicine should only be used for intermittent treatment of moderate-to-severe symptoms of uterine fibroids before menopause and when surgical procedures (including uterine fibroid embolisation) are not suitable or have failed.
- Aromatase inhibitors, such as letrozole: a Cochrane review concluded that there is insufficient evidence to support their use in the treatment of uterine fibroids. ^[12]

Surgical

Surgery is indicated when:

- There is excessively enlarged uterine size.
- Pressure symptoms are present.
- Medical management is not sufficient to control symptoms.
- The fibroid is submucous and fertility is reduced.

Surgical options include:

- Myomectomy - this is used in patients who wish to maintain their reproductive potential or keep their uterus:
 - Abdominal myomectomy is a safe alternative to a hysterectomy. However, there is a risk of excessive bleeding and a risk of requiring hysterectomy at the time of the operation. Therefore, blood should be cross-matched pre-operatively and the patient needs to give their consent to hysterectomy should the need arise. Also 4-17% of women will later go on to have a hysterectomy.
 - Laparoscopic myomectomy is associated with less pain, shorter hospital stay and reduced recovery time.
 - An estimated 15-33% of fibroids recur after myomectomy, and approximately 10% of women undergoing myomectomy will undergo a hysterectomy within 5-10 years. ^[6]

- Laparoscopic removal of uterine fibroids with power morcellation shows potentially serious risk of spreading undiagnosed malignant tissue and evidence on efficacy is limited. Therefore this procedure should not be used for people who are postmenopausal or over 50, and only used with special arrangements for clinical governance, consent and audit or research for those under 50 years.^[13] Similarly, hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids has well recognised, infrequent but potentially serious side-effects and is similarly restricted.^[14]
- Hysteroscopic myomectomy is an established surgical procedure for women with submucosal fibroids and excessive uterine bleeding, infertility or repeated miscarriages.^[15] When performed for treatment of abnormal bleeding, this resolves in 74-94% at two years. 12% subsequently require hysterectomy.
- Laparoscopic laser myomectomy is not recommended by NICE, other than for research, due to lack of evidence for its safety and efficacy.^[16]
- Pedunculated vaginal fibroids may be removed vaginally but histology is essential to exclude a sarcoma in women aged over 60 years.
- Hysteroscopic endometrial ablation - for women presenting with menorrhagia.
- Total hysterectomy:
 - This has been the mainstay of treatment for many years, eliminating both symptoms and the possibility of recurrence, and fibroids are the indication for approximately one third of hysterectomies in the USA.
 - In women who have completed their family, hysterectomy remains the most effective treatment for excessive uterine bleeding.^[17]
 - It is also indicated when there are many fibroids.
 - If these are small then the vaginal route is appropriate but if they are large (especially if intraligamentous) then laparotomy is indicated with preservation of ovaries if possible.^[18]
 - The risk of blood loss is directly related to the uterine size. This may be reduced by pre-treatment with GnRH agonists.
 - NICE recommends that laparoscopic techniques for hysterectomy (eg, laparoscopically assisted vaginal hysterectomy, laparoscopic hysterectomy, laparoscopic supracervical hysterectomy and total laparoscopic hysterectomy) appear to be sufficiently safe and effective to support their use. There is, however, a higher risk of urinary tract injury and of severe bleeding in comparison with open surgery.^[19]

- Uterine artery embolisation (UAE):
 - This procedure has been shown to be both effective (for short- and medium-term symptom relief) and safe for women who wish to keep their uterus, although the effects on fertility and pregnancy are uncertain. [20] [21]
 - If patients are considering pregnancy, there is a theoretical risk of placental insufficiency leading to small-for-gestational-age babies, increased caesarean section and prematurity.
 - Ensuring the tumour is a benign fibroid and not a malignant sarcoma is essential prior to UAE. [3]
 - Women should be informed during consenting that symptom relief may not be achieved for some women and that symptoms may return.
 - Although complications are rare, they may necessitate life-saving hysterectomy, consent for which is required prior to the procedure.
 - The REST trial was a randomised controlled trial (RCT) comparing UAE with surgery in 157 women followed for five years. There was no difference in reduction in symptoms or patient satisfaction but a third of women having UAE required re-intervention. [22]
 - UAE is a cost-effective option compared with hysterectomy at one year, saving £1,000 per patient but this gain is lost by five years due to greater rates of secondary intervention. The faster, shorter recovery time needs to be weighed against the need for further treatment in a third of patients. [21]
- MRI-guided transcutaneous focused ultrasound:
 - This procedure has low morbidity and very rapid recovery. High-power pulses of ultrasound are used to ablate the fibroid - there may be skin burns as a result. Long-term outcome (fertility and the need for further treatments) is as yet uncertain.
 - NICE advises that short-term safety and efficacy evidence is now adequate to support the use of MRI-guided transcutaneous focused ultrasound, although notes that further treatment may be required and effects on subsequent pregnancy are uncertain. [23]

A 2021 systematic review looked at 84 studies involving minimally invasive techniques, including 10 randomised controlled trials and 74 observational studies. [24] Six studies on myomectomy demonstrated overall bleeding symptom improvement in up to 95.9% of patients, although there was no significant difference between mode of myomectomy. Forty-one studies on uterine artery embolisation reported significant reduction of fibroid-related bleeding, with symptomatic improvement in 79-98.5% of patients. Three studies suggested that embolisation may be superior to myomectomy in reducing fibroid-related bleeding. Six studies reported that laparoscopic uterine artery occlusion combined with myomectomy led to greater reduction of bleeding than myomectomy alone. Fifteen studies demonstrated significantly reduced bleeding severity after radiofrequency ablation (RFA).

Complications

- [Iron-deficiency anaemia](#).
- [Bladder frequency, constipation](#) (due to increased pelvic pressure).
- Hyaline degeneration (asymptomatic).
- Torsion of pedunculated fibroid.
- Ureteral obstruction causing hydronephrosis.
- [Infertility](#): this may occur as a result of narrowing of the isthmic portion of the Fallopian tube or as a consequence of interference with implantation (submucosal fibroids).
- In pregnancy:
 - [Recurrent miscarriage](#).
 - Fetal malpresentation.
 - Red degeneration: presents with fever, pain and vomiting. 8% of pregnant women with fibroids experience fibroid degeneration. [25]
 - [Intrauterine growth restriction](#).
 - [Premature labour](#).
 - [Postpartum haemorrhage](#).
 - Hydronephrosis.

Prognosis

Typically, fibroids regress with the menopause and symptoms resolve.

Further reading

- [British Fibroid Trust](#)
- [Heavy menstrual bleeding: assessment and management](#); NICE Guideline (March 2018 - updated May 2021)

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