NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Management of Uterine Fibroids in Gynaecology

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Title : Management of Uterine Fibroids in Gynaecology (512)

Objectives : To describe current evidence based management of non-pregnant women found to have uterine fibroids

Scope :

Audience : This guideline is intended for use by healthcare professionals working within GGC who are involved in the care of non-pregnant women with uterine fibroids.

Body of Guideline

Uterine fibroids (leiomyomas) are common benign tumours found in 1 in 3 women of reproductive age. By age 50 nearly 70% of white women and more than 80% of black women have had at least one fibroid. They will commonly shrink following menopause. They may be associated with heavy menstrual bleeding (HMB), pelvic pressure symptoms, pelvic pain, dyspareunia, subfertility and can have implications during pregnancy.

The malignant potential of fibroids is extremely low (<1%) with leiomyosarcomas typically occurring in women above the age of 60years.

Investigations

Abdominal and vaginal examinations should be performed.

Pelvic ultrasound (Transabdominal, transvaginal or both) is useful first line imaging of uterine fibroids.

Magnetic resonance imaging (MRI) is indicated when ultrasound is inconclusive and fibroids are suspected. Additionally, it should be performed to help radiology planning if patient is considering undergoing a fibroid embolisation procedure.

An endometrial biopsy should be taken where there is concern regarding an endometrial abnormality or malignancy. This is outlined in the GGC guideline, [CG] Menstrual disorders including heavy menstrual bleeding (nhsggc.org.uk)

Consideration of blood tests should be undertaken. These include FBC for assessment of Haemoglobin and platelet levels, and UE for renal function, particularly if there are concerns regarding ureteric compression.

Management

Management will be dependent upon the patients' wishes, current symptoms, and fertility plans. It will also be influenced by the size, location and number of fibroids which are present.

Treatment options include -

- Conservative management with observation
- Medical therapies
- Surgical procedures

Observation

In women who are asymptomatic (estimated at 3 in 4 women with fibroids), the majority require no further investigation or treatment once diagnosed unless there is rapid growth or a reason to suspect pelvic malignancy.

This option is appropriate for women who do not desire treatment. When individual fibroids are > 5cms, it is suggested a follow up ultrasound scan should be repeated after 6 to 12 months. If at time of review fibroid size is reduced or stable, no further routine ultrasound assessment is required.

Medical therapies

Medical therapies should be tailored to help symptoms. For management of Heavy Menstrual bleeding please see GGC guideline, [CG] Menstrual disorders including heavy menstrual bleeding (nhsggc.org.uk). Medical options will include NSAIDs, Tranexamic Acid, Hormonal Contraceptives and hormonal intrauterine systems.

Pharmacological Hormonal Management - Fibroids 3 cm or more in diameter, normal endometrial histology

Gonadotrophin Releasing Hormone Analogue (GnRHa) injections

- The use of GnRHa may be considered prior to surgery or when other treatment options for uterine fibroids are not suitable.
- Used pre-operatively, it is associated with reduced pre-operative anaemia and intra-operative blood loss.
- These preparations will stop the menstrual cycle as they induce a temporary menopause by binding to the receptors in the pituitary.
- They can also reduce uterine volume by 35-40% and help with pelvic pressure effects.
- Vasomotor symptoms are very common but add-back HRT can be used to treat side effects.
- HRT should also be offered for bone protection (estimated 6% loss in 6 months) if treatment extended more than 6 months
- These preparations are licensed for 6 months of use and should only be used in the context of a formal management plan following discussion with a consultant.
- Injections can be given monthly or every 12 weeks

Gonadotrphin Releasing Hormone Antagonist oral tablet with add back HRT

Ryeco® (Relugolix 40mg, Estradiol 1mg and Norethisterone Acetate 0.5mg)

- Ryeco® is an oral tablet preparation containing GnRH-receptor antagonist combined with add-back HRT therapy (Relugolix 40mg, Estradiol 1mg and Norethisterone Acetate 0.5mg). It is licenced for the treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age. Fibroids must be at least > 2cms size (no maximum size limit).

- Currently, use is restricted to specialist initiation for use in patients who have failed or are unsuitable for conventional therapies described above.

- It is reasonable to assess symptomatic benefit at 6 months and assess need for continued therapy. Discontinuation of therapy should be considered when the patient enters menopause, as uterine fibroids are known to regress when menopause begins.

- **Benefits** include significant reduction in menstrual blood loss (50% reduction at 4 weeks), Amenorrhoea (50% at 6months and 71% at 12 months), reduction in anaemia and pelvic pain, and a small non-significant reduction in fibroid volume (up to 14%)

- **Common side effects** include hot flushes, headaches and abnormal uterine bleeding. Additionally, bone loss occurs in 3-8% women (average of 0.04% at 1 year)

- Menstruation and ovulation return quickly after treatment is stopped and no associated endometrial changes have been reported.

- **Advice on use**

    - One tablet should be taken daily at the same time each day
    - Treatment should be commenced during the first 5 days of menstrual cycle
    - Pregnancy should be excluded prior to commencing treatment.
    - Hormonal contraception should be stopped prior to starting treatment. Of note, Ryeco® will inhibit ovulation after at least 1month of correct treatment. Barrier contraception is recommended for the first month's use.
    - If two or more consecutive tablets are missed, barrier contraception is advised for 7 days.
    - Start contraception immediately after stopping treatment, if required.

- ***Bone Density Assessment***
  Owing to the small risk of bone loss, a DEXA scan is advised pre-treatment IF at high risk of osteoporosis. Otherwise, a DEXA scan is advised 52 weeks after treatment.

  The clinician initiating treatment is responsible for organising the DEXA scan investigation.

- **Contraindications:** current or previous venous thromboembolism, arterial thromboembolic cardiovascular disease, (e.g. myocardial infarction, cerebrovascular accident, ischemic heart disease), osteoporosis, known thrombophilic disorders, migraine with aura, pregnancy, severe liver problems, hormone-related malignancy.

Gonadotrphin Releasing Hormone Antagonist oral tablet

Yselty® (Linzagolix 100mg and 200mg dosing options)

- Linzagolix is an oral GnRH receptor antagonist. Unlike Ryeco®, it does not contain add back HRT so may be more suitable as an alternative for women where they do not wish to take HRT, or are not suitable for oral HRT preparations.

- Add back therapy can be initiated separately at clinician discretion, note Primrose Trial data are based on oral HRT only (estradiol 1 mg/ norethisterone acetate 0.5 mg) [7]

- Linzagolix has been accepted by SMC for the treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age [8].

- Currently, use is restricted to specialist initiation for use in patients who have failed or are unsuitable for conventional therapies described above in this guideline.

- It is reasonable to assess symptomatic benefit at 6 months and assess need for continued therapy. Discontinuation of therapy should be considered when the patient enters menopause, as uterine fibroids are known to regress when menopause begins.

- **Treatment regimes**

  Partial suppression (100mg daily dosing) +/- add back HRT

  Full suppression (200mg daily dosing) +/- add back HRT

  Following 6 months of treatment at either the 100mg or 200mg daily dose, if treatment with Linzagolix is to continue, the addition of add back HRT therapy is recommended.

- **Benefits**
  – *blood loss reduction* - Linzagolix, with and without hormonal add-back therapy, resulted in statistically significant reductions in menstrual blood loss, compared with placebo. This reduction was greater with the 200mg dosing, with blood loss declining rapidly to statistically significant reduction at 24 weeks, which was maintained at 52 weeks.
  -fibroid volume – reduction in volume of fibroids was observed with a 43-49%reduction at 6 months. This was only observed when the full suppression with 200mg daily dosing was undertaken without add back HRT. This effect was not maintained where add back therapy was initiated after 6 months.

- **Advice on use**

Contraception and exclusion of pregnancy

Linzagolix with or without concomitant add back HRT has not been demonstrated to provide contraception. Based on current data, manufacturer suggests women of childbearing potential at risk of pregnancy should use effective non-hormonal contraception while on treatment with Linzagolix.

Use of hormonal contraceptive options (for contraception or add back hormone therapy) is off label.

Current data suggests return of menstruation around 30 days after stopping therapy.

Pregnancy must be excluded prior to initiation of treatment with Linzagolix.

Bone Density Assessment

Owing to the small risk of bone loss, a DEXA scan is advised pre-treatment IF at high risk of osteoporosis. Otherwise, a DEXA scan is advised 52 weeks after treatment.

The clinician initiating treatment is responsible for organising the DEXA scan investigation.

- **Contraindications:** Known osteoporosis, pregnancy or breastfeeding, hormone-related malignancy, undiagnosed vaginal bleeding, severe hepatic impairment

- **Cautions:** consider recognised contraindications to add back HRT therapy

Surgical Management - Fibroids 3 cm or more in diameter, normal endometrial histology

Women who wish to preserve their uterus

- **Hysteroscopic Resection of sub-mucous fibroids**
    - Referral to gynaecologist with special interest for management
- **Myomectomy**
    - Suitable for women who wish to preserve her fertility.
    - There is a small risk that emergency hysterectomy may be performed.
    - Consider pre-treatment with a GnRHa for 3 to 4 months.
    - The uterus and fibroids should be assessed by ultrasound prior to the procedure, with MRI considered where information about fibroid position, size, number and vascularity is required
- **Uterine Artery Embolisation (UAE)/Fibroid Embolisation**
    - Women who wish to avoid surgery may be referred to interventional radiology for assessment.
    - Embolisation can be considered as a fertility sparing procedure with no difference in markers of ovarian reserve when compared with myomectomy.
    - There is an approximately 5% risk of ovarian failure due to the effect of embolisation on the collateral supply of the ovary. It is believed that women in their 40s - as opposed to in their 20s - have an increased risk of ovarian failure from the procedure. Reports show the majority of women younger than 40 who experience any disruption in ovarian circulation post-embolisation only experience this temporarily, whereas women who are closer to menopause may already be vulnerable to ovarian damage, leaving a small percentage not as capable of recovering normal ovarian function.
    - Referrals should be made to **Dr Ram Kahsturi or Dr Andrew Christie, Consultant Interventional Radiologists, Glasgow Hospitals**
    - It is useful to organise MRI imaging at the same time as referring to the interventional radiology team as it allows full counselling and assessment.

Major surgical procedures

Hysterectomy

- Total hysterectomy is the only procedure that will guarantee amenorrhoea and is a definitive procedure for removal of the enlarged uterus. It has high patient satisfaction rates.
- Hysterectomy has a 4 in 100 risk of major complication.
- Preoperative consideration should be given to smear history (where a subtotal procedure is required) and previous surgery, particularly caesarean delivery.
- Oophorectomy should not be performed routinely if ovaries are healthy.
- Patients should be advised that ovarian failure is earlier following hysterectomy.

- Where there is a suggestion of ovarian dysfunction e.g. premenstrual syndrome, a trial of pharmaceutical ovarian suppression for at least 3 months should be used as a guide to the need for oophorectomy.
- The optimal surgical approach (abdominal, vaginal or laparoscopic) will depend on discussion between the patient and her gynaecologist.
- Ensure patient understands the differences between sub-total, total hysterectomy and hysterectomy with bilateral salpingo-oopherectomy (BSO).
- In the context of fibroids, the size, number and location will determine operative approach (laparoscopy or laparotomy)

VTE risk and Fibroids

Women with fibroids have a multifactorial increased incidence of venous thromboembolism due to:

· Pelvic vein compression
· Associated anaemia
· Increased Factor VIII levels secondary to bleeding
· Iatrogenic use of high dose progestin therapy has associated VTE potential.

It is important to reduce simple risk factors in the first instance e.g. stopping smoking, reducing weight if BMI elevated and avoiding severe anaemia with iron supplementation.

In the presence of large fibroids, an early recourse to surgical intervention if there is evidence of pelvic vein compression on imaging. Additionally, avoidance of high dose Norethisterone is advised due to the associated thrombosis potential.

In women with large fibroids where surgery is neither an immediate choice nor an option, they should be counselled regarding the small increased risk of venous thromboembolism.

For the very small group of women who have large fibroids and are immobile, anticoagulation with low molecular weight heparin prophylaxis may be considered whilst awaiting surgery. This should be stopped 24 hours before surgery. Advice may be sought from Haematology.

HRT and fibroids

The decision to manage menopausal symptoms with HRT will be led by the woman following discussion of the risks and benefits as for all other women.

It is thought that HRT can in some women lead to a modest increase in the size of fibroids. At review appointments, clinicians should enquire about symptoms related to fibroids.

Contraception and fibroids

In women where there is no distortion of the uterine cavity, all options for contraception are available. However, access for laparoscopic sterilisation may be difficult.

In women where there is distortion of the uterine cavity, all options for contraception are available. However, special consideration must be given to insertion of intrauterine devices and intrauterine systems due to difficulty in the insertion and higher expulsion rates.

References :

1. Fibroids: diagnosis and management. Lumsden MA, Hamoodi I, Gupta J, Hickey M, BMJ 2015;351:h4887

2. A review of evidence-based management of uterine fibroids K Younas, E Hadoura, F Majoko, A Bunkheila. The Obstetrician & Gynaecologist, 2016;18:33–42

3. NICE Clinical Knowledge Summaries, Management of Fibroids, May 2022

4. Liberty 1 & 2 Al-Hendy A *et al. N Engl J Med* 2021;38:630-642;

5. Liberty 3 Study Al-Hendy A, *et al.* Long-term Relugolix Combination Therapy for Symptomatic Uterine Leiomyomas. Obstet Gynecol. 2022 Dec 1;140(6):920-930.

6. Scottish Medicines Consortium (SMC) advice on new medicines. SMC2442, relugolix 40mg, estradiol 1mg, norethisterone acetate 0.5mg film-coated tablets (Ryeqo®) May 2022. relugolix-estradiol-norethisterone-acetate-ryeqo-final-may-2022-for-website.pdf (scottishmedicines.org.uk)

7. Linzagolix with and without hormonal add-back therapy for the treatment of symptomatic uterine fibroids: two randomised, placebo-controlled, phase 3 trials. Donnez, Jacques et al. The Lancet, Volume 400, Issue 10356, 896 – 907

8. Scottish Medicines Consortium (SMC) advice on new medicines. SMC2631, linzagolix (Yselty), November 2024. linzagolix-yselty-final-april-2024-issued-oct-2024-for-website.pdf

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