CLINICAL GUIDELINE

This document is intended to guide clinical care without changing the responsibility of the health care team or the patient.
It never replaces clinical judgment and individualized care.

Developed and endorsed by SASOG as part of the BetterGYN® programme

TREATMENT OF UTERINE LEIOMYOMATA

Definition:

A leiomyoma is a benign spherical solid tumour of cells from the Mullerian duct, composed of smooth muscle interlaced with fibrous strands, and occurs mostly in the uterine myometrium and is hormonally sensitive. Women can present at any age, with single or multiple tumours and with or without symptoms.

Risk factors include:

- Black race;
- A family history;
- Advanced age at first pregnancy;
- Low parity;
- Hypertension.

Use of hormonal contraceptives and smoking may reduce risk.

Commonly used synonyms include "myoma" and "fibroid".

Genetic and epigenetic factors; sex steroids; growth factors; cytokines; chemokines and extra cellular matrix (ECM) components have all been implicated in the pathogenesis of leiomyomas. Progesterone plays a crucial role in the development and growth of leiomyomas and studies have reported an increased expression of progesterone receptors A & B in leiomyomas compared to the adjacent myometrium.

Impact:

The reported prevalence varies widely from about 5% to 60%, but there is a great likelihood of underestimating the frequency of the condition because leiomyomas are asymptomatic in many women. Heavy menstrual bleeding is the most common presenting symptom, and can lead to anaemia, fatigue and painful periods. Other symptoms include non-cyclic pain, dyspareunia, abdominal protuberance, pelvic pressure and bladder- or bowel-dysfunction. Reproductive problems such as impaired fertility, pregnancy complications, loss, and adverse obstetric outcomes lead to morbidity and can have a major negative impact on the sufferer's quality of life.

Leiomyomata remain one of the leading causes of hospitalisation for gynaecological disorders and are the most frequent reason for hysterectomy. It is not associated with malignancy nor is it an important reason for loss of life. About 25% of women who present with clinically apparent leiomyomas which require treatment do so during reproductive age.

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Clinical assessment:

The clinical history may suggest the presence of uterine leiomyomas. The aim is to understand the impact of the disease on the patient's life and consider treatment choices. General examinations must prioritise anaemia and other co-existing conditions including abnormal blood-pressure. Abdominal examinations, followed by pelvic examinations may reveal an enlarged uterus or pelvic mass. The size, position, and mobility of the mass are all relevant findings.

Special tests:

At the time of examination, **cervical screening** should be offered. **Endometrial sampling** is appropriate in peri- and post-menopausal bleeding. Further tests, including imaging, could be recommended depending on the findings of the initial evaluation.

Pelvic ultrasound is done to confirm the presence of round solid uterine tumours. It allows accurate assessment of the size, position and number of fibroids. Co-existing adnexal or endometrial abnormalities are important and may be missed due to the density of leiomyomas.

Saline infusion into the uterine cavity can delineate submucosal myomas and indicate the proximity of intramural tumours to the endometrial cavity. In the presence of larger myomas the test is best performed both transvaginally and transabdominally.

Hysteroscopy may be required to differentiate intracavitary myomas from polyps; but both conditions can be treated at the same time.

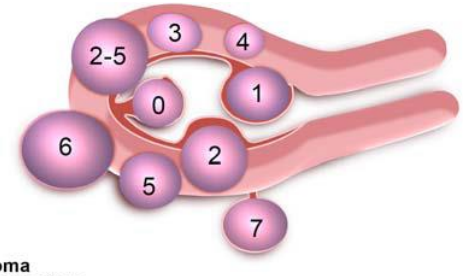
Blood tests should include a full blood count and assessment of iron status, a beta-HCG, if appropriate, and an endocrine evaluation consisting of FSH, ovulation and ovarian reserve, if fertility assessment is needed.

Magnetic resonance imaging can provide extra information on the number of fibroids, their size, vascularisation, their relationship with the endometrial cavity, serosal surface and boundaries with normal myometrium in cases where that is not clear from the ultrasound evaluation and needed to plan treatment.

Classification:

The FIGO classification (Munro 2011) is as follows:

0. *Pedunculated intracavitary*
1. *Submucosal, < 50% intramural*
2. *Submucosal, ≥ 50%*
3. *Contact with endometrium*
4. *Intramural*
5. *Subserosal > 50%*
6. *Subserosal <50%*
7. *Subserosal pedunculated*
8. *Other (eg. cervical; parasitic)*



Leiomyoma subclassification system

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Treatment options:

1 Myomectomy:

Myomectomy is generally successful at reducing menstrual blood loss and pressure symptoms while aiming to retain fertility potential or at least the uterus. The access route for myomectomy is determined mostly by the position and size of tumours. Leiomyomas may recur as new tumours develop.

Hysteroscopic myomectomy is suitable for submucosal tumours and may be done by cutting the base in small tumours (Betocchi's method), or by slicing in a single or two-step procedure for larger tumours. The risk for fluid overload is reduced by use of bipolar energy and saline solution.

Laparoscopic myomectomy is suitable for subserosal or intramural myomas. The procedure requires more skill in cases where posterior tumors, larger tumors or multiple tumours are to be removed, and also if numerous incisions and suturing are required. Recovery is faster than after laparotomy, but the reproductive outcomes are similar and the usual complications of laparoscopic procedures can occur.

All uterine wall defects must be sutured carefully to help prevent uterine rupture, and all tumour fragments must be removed from the peritoneal cavity to prevent dispersion.

Open myomectomy via laparotomy is preferred if the skill or equipment for laparoscopic surgery is not available, if the number or size of the tumours is considered too large, or if there is a contra-indication for the use of morcellation.

Measures to limit blood loss, myometrial damage and peritoneal adhesions should be taken.

2 Hysterectomy:

Hysterectomy provides a permanent solution but removes all hopes of future fertility. Usually one or both ovaries can be retained for hormonal function or oocyte harvesting. The surgery can also be done via the vaginal, endoscopic or laparotomy routes, or a combination of these. The choice is determined by technical and anatomical factors, as well as the patient's and surgeon's preferences, and availability of equipment. Large myomas usually necessitate an abdominal incision to enable their removal.

The most typical complications vary according to the access route used, but the complication rates are similar. Usual recovery time is shorter for vaginal and endoscopic surgery, but recovery after the initial weeks is similar.

3 Uterine artery obstruction:

Uterine artery obstruction reduces the blood supply of the total uterus, and can be done surgically or by intravascular embolization via arterial catheterization. Uterine artery embolization was developed in 1995. It is now reported that only 15-20% of women require repeat surgery after successful embolization. As with all therapies, the patient must be fully informed before giving written consent.

Controversy remains about the fertility outcomes after the procedure and it is important for gynaecologists to convey this uncertainty. Other complications include those of arterial catheterisation (including bleeding and migration of embolising material), and the morbidity and complications of tissue ischemia and necrosis (including severe pain, uterine discharge and systemic signs of the inflammatory response).

4 Tumour ablation:

Magnetic resonance guided focused ultrasound surgery (MRgFUS) is a form of thermal or physical energy ablation that uses MRI to visualize and define the target. It can also be guided by ultrasound imaging. The energy is directed to a central point inside the fibroid, and coagulation tissue necrosis is induced.

The procedure is currently costly and time-consuming if multiple tumours are treated. The tissue necrosis is similar to that following UAE, but the damage to normal myometrium may be less. Repeated treatments may be needed, and the longer-term outcomes of these promising options are still being studied.

5 Hormonal treatment:

Gonadotrophin releasing hormone agonists (GnRHa) have a direct suppressive impact on the pituitary. They induce temporary menopause by totally suppressing all ovarian hormone production. Their use may lead to shrinkage of myomas and restoration of iron levels and blood count if used for a sufficiently long period of time. Add-back therapy is needed to ameliorate the extreme symptoms and bone loss, and this is achieved using low dose estrogen, tibolone, raloxifene or medroxy-progesterone acetate. This therapy is occasionally recommended pre-operatively.

Selective progesterone receptor modulators (SPRMs) are synthetic compounds with an agonist or antagonistic effect on progesterone receptors. . Ulipristal acetate has shown best results with effective fibroid volume reduction after four courses of three months of ulipristal acetate (UPA), 5 mg daily, with two natural cycles between courses.

4 Symptomatic treatment or no treatment:

The most common symptom of leiomyomas is heavy menstrual bleeding and this can be treated by hormonal therapy, NSAIDS, tranexamic acid, and sometimes by a progestogen containing IUCD. Dysmenorrhoea can be treated with NSAIDS and analgesia. Asymptomatic women do not require any intervention.

Choice of treatment:

Following thorough assessment, all available treatment options must be discussed in detail with the patient. Conservative management can be followed by interventions if needed.

Prognosis:

Leiomyomas are benign tumours and have a good prognosis but can nevertheless have devastating psychosocial and medical consequences. Treatment outcomes are good and there are several options available.

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