



Fibroids and Fertility

What every practitioner should know

by Dr Kelly Loi

Uterine fibroids or leiomyomata are smooth muscle cell tumours. They are the most common benign gynaecologic tumour in women of reproductive age. The lifetime prevalence is around 30%. They are rarely found before menarche and usually regress after menopause. They are hormonally responsive, and oestrogens appear to promote their growth.

One in four women with fibroids is symptomatic. For women who are asymptomatic or with bearable symptoms, expectant management is usually sufficient. Median fibroid growth is around 9% over 6 months. Many women with fibroids have successful pregnancies. However, fibroids are often found as part of the investigation of a couple presenting with infertility. It is well established that submucosal fibroids have a negative impact on rates of implantation, clinical pregnancy, ongoing pregnancy, miscarriage, and live birth. Hence, an important aspect in evaluating fibroids is to determine if the fibroid is submucosal, and the degree to which it impinges on the endometrium. Imaging is important in the preoperative evaluation of fibroids, especially where fertility is a concern.^{1,2}

Evaluation of fibroids

Transvaginal ultrasound is effective and may identify fibroids of up to 4 to 5 mm in diameter. Ultrasound may, however, be suboptimal for multiple fibroids, because of acoustic shadowing.

Magnetic resonance imaging (MRI) has been well studied in the evaluation of fibroid uteruses, especially for fibroid localisation and degree of submucosal indentation. It was shown to be the most reliable method of evaluation when compared with vaginal ultrasound, hysterosonography, and hysteroscopy, with 100% sensitivity and 91% specificity (gold standard was pathological examination).³ The main drawback of MRI evaluation would be the high cost.

Hysterosalpingography is often performed to assess tubal patency in women with infertility. However, the sensitivity and positive predictive value of

this test for the identification of intrauterine lesions can be as low as 50% and 28%, respectively.⁴ Hysterosalpingography cannot therefore be considered reliable to exclude endometrial distortion secondary to submucosal fibroids.

Hysterosonography, which has the advantages of pelvic ultrasound, has been advocated as superior to transvaginal ultrasound alone and equal to hysteroscopy in the evaluation of endometrial impingement.⁵ It has been shown to be highly sensitive and specific in the identification of submucosal myomas. Its main drawbacks are discomfort and the risk of infection (approximately 1%).

In women with infertility, the extent to which any fibroids present are likely to affect the integrity of their endometrial cavity should probably be evaluated. However, it is unclear which should be the optimal method. It is likely that the results of studies attempting to clarify the relationships between fibroids and infertility and the impact of treatment is due to inadequate classification of fibroids, and in particular their impact on the endometrial cavity [Figure 1].

Impact of fibroids on fertility

Both infertility and age have been associated with the presence of fibroids and this may further

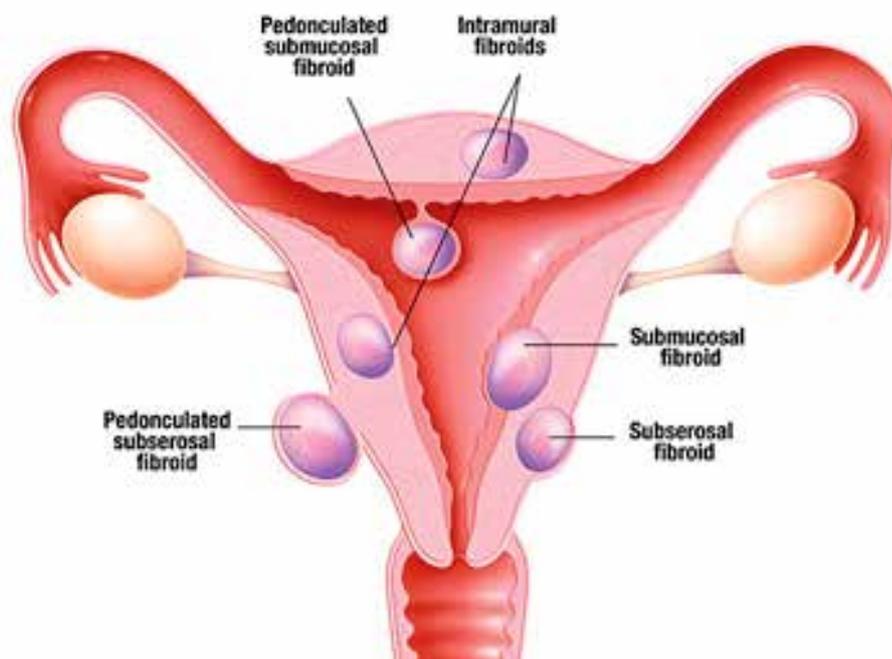


Figure 1. Types of fibroids (Source: www.nhs.uk/conditions/fibroids)

confound results of studies attempting to clarify the relationship between fibroids and infertility.

Many hypotheses have been generated to explain how fibroids might cause infertility. Perfusion studies have shown that blood flow to uterine fibroids is less than that to the adjacent myometrium. There may also be endometrial inflammation and an altered local hormonal environment which may affect embryo implantation. Large fibroids can potentially alter uterine contractility possibly interfering with sperm and ovum interaction or embryo migration.

In general, it appears that women with fibroids have decreased fertility. However, the impact appears to be related to fibroid location. Systematic reviews and meta-analyses published to date indicate that subserosal fibroids do not appear to have an impact on fertility. Available studies however are in agreement that submucosal fibroids (fibroids with

endometrial impingement) have a negative impact on rates of implantation, clinical pregnancy, miscarriage, ongoing pregnancy and livebirth. The greatest question remains on the impact and treatment of intramural fibroids. The most recent good quality meta-analyses appear to show that intramural fibroids do seem to have an impact on both implantation and clinical pregnancy rates but less than that of submucosal fibroids. Most studies included intramural fibroids < 5 cm.

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Another way of assessing whether a uterine pathology has an impact on conception rates is to evaluate whether pregnancy rates increase more after removal than after expectant management. However, studies on treatment for leiomyomas in women with infertility have been few and small. A meta-analysis of the small studies available found an apparent benefit of hysteroscopic myomectomy over fibroids left in situ on clinical pregnancy rates (RR 2.034, 95% CI 1.081 to 3.826, $P = 0.028$).⁶

Medical management

Current medical therapy is essentially a treatment option for the control of symptoms. Tranexamic acid helps with reduction in menstrual blood loss. The other medical options available are primarily hormonal agents which act on the oestrogen and progesterone responsiveness of fibroids and are unsuitable for fertility. GnRH analogues cause hypo- oestrogenic side effects and bone loss. They may be suitable for pre- operative therapy but because of the side effects, should be limited to a maximum use of 6 months. Novel therapies that are under study include aromatase inhibitors, mifepristone, selective estrogen receptor modulators, and selective progesterone receptor modulators. These have shown promise in symptom improvement and fibroid regression without the hypoestrogenic symptoms associated with GnRH analogues.

New treatment methods

Newer uterus-sparing treatments include uterine artery embolisation (UAE) and more recently, MRI-Guided focused ultrasonography (MRgFUS). UAE is a procedure where an interventional radiologist uses a catheter to deliver small particles that block the blood supply to the uterine

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body. MRgFUS involves the use of high- frequency ultrasound waves to produce heat and denature proteins leading to cell death and shrinkage of fibroids. MRI is used to help guide the ultrasound beams to target the fibroids. However, these techniques have not been used on a large scale, and data on their reproductive outcomes in patients trying to conceive are insufficient to make recommendations. There is some concern regarding development of pelvic adhesions following such treatments. Furthermore, ovarian reserve may be adversely affected.

Surgical management

Well-designed surgical intervention trials for myomectomy and infertility are sparse, with a single randomised controlled trial published to date.⁷ This study demonstrated an improvement in conception rates after the surgical removal of submucosal fibroids, but pregnancy rates following the removal of intramural or subserosal fibroids were no more improved than in the expectant management group of women with intramural-subserosal fibroids in situ. A meta-analysis demonstrated similar findings, with an improvement in pregnancy rates in infertile patients undergoing surgical removal of submucosal fibroids, but not in those undergoing surgical removal of intramural fibroids.⁶

Depending on the fibroid size and location, the surgical approach to fibroids can be either vaginal or abdominal. The abdominal approach may be either by laparotomy or laparoscopy.

Hysteroscopic myomectomy

Hysteroscopic myomectomy is the preferred treatment for patients with submucosal fibroids. Classification systems have been devised to enable accurate description of submucous fibroids and assist in assessing the likelihood of a successful hysteroscopic resection. The most widely used classification system is that adopted by the European Society of Gynaecological Endoscopy (ESGE). Submucosal fibroids which are likely to be successfully treated by hysteroscopic myomectomy are those completely within the uterine cavity (Type 0) or with at least 50% of the fibroid volume within the uterine cavity (Type I). Fibroids with less than 50% of the fibroid volume in the cavity (Type II) are much more difficult to resect completely and are more often associated with the need for repeated procedures. Additionally, it has generally been recommended

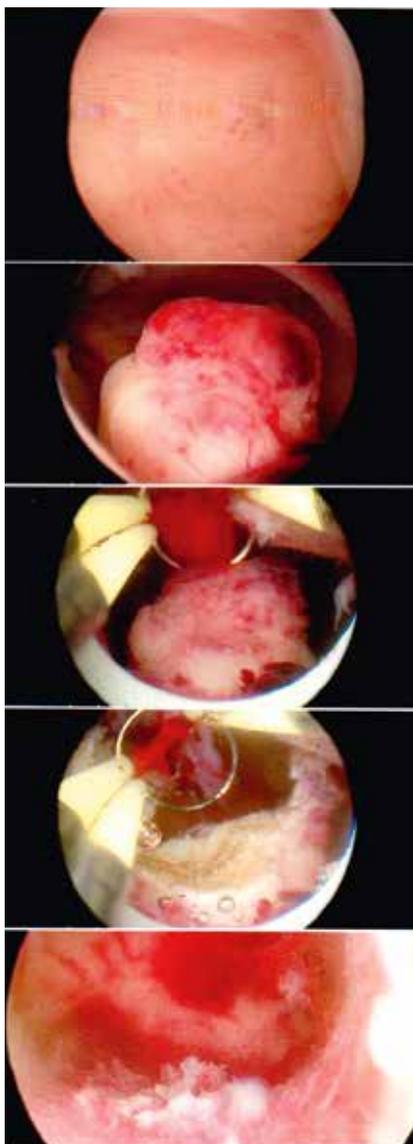


Figure 2. Hysteroscopic transcervical resection of submucous fibroid

that hysteroscopic myomectomy be undertaken for fibroids under 5 cm. For fibroids greater than 5 cm, and those classified as Type II fibroids, hysteroscopic resection may be possible but repeat procedures may be necessary [Figure 2].

The incidence of post surgery intrauterine adhesions has been a concern and the incidence was shown in one study to be 7.5%.⁸ Post surgery preventive measures including estrogen therapy or insertion of an intrauterine device have been used. However, there is little evidence to support the use of these therapies following hysteroscopic resection of submucosal fibroids.⁹

Laparoscopy or laparotomy

Two randomised controlled trials with a combined 267 patients compared reproductive outcomes of laparoscopic myomectomy and myomectomy by laparotomy. In the first study of patients undergoing myomectomy for infertility and at least 1 fibroid > 5 cm, pregnancy rates were similar following in the laparoscopy and laparotomy groups (53.6% vs. 55.9%).¹⁰ There was lower febrile morbidity in the laparoscopy group (26.2% vs. 12.1%), shorter hospital stay, and a lower postoperative drop in haemoglobin.

In the second study, 12 months postoperatively, cumulative pregnancy rates were similar in the laparoscopy and laparotomy groups (52.9% vs. 38.2%).¹¹ Again, the laparoscopic approach was associated with a quicker recovery, less postoperative pain, and less febrile morbidity.

Widespread use of the laparoscopic approach to myomectomy may be limited by the technical difficulty of this procedure. Patient selection should probably be individualized based on the number, size and location of uterine fibroids.

There may often, be instances when surgical removal of fibroids in an infertile patient is undertaken for reasons other than fertility enhancement, such as relief of pressure symptoms or surgical management of menstrual disturbances secondary to fibroids. However, surgical treatment of fibroids can be associated with morbidity. Where patients are asymptomatic, the decision for surgery should be weighed against potential risks. **MG**

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