

# Uterine fibroids: Investigation and current management trends

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## Background

Uterine leiomyomas, or fibroids, represent a large proportion of gynaecological presentations in both general and specialist gynaecology practice. The diagnosis is relatively simple with current imaging modalities. The management of fibroids, however, is not always straightforward and can present many challenges.

## Objective

This article reviews current approaches to the management of uterine fibroids, including novel techniques, and highlights important patient counselling points.

## Discussion

Many fibroids cause debilitating symptoms that greatly affect a woman's quality of life. Traditional surgical treatment options include myomectomy and hysterectomy. Minimally invasive surgical and radiological techniques, as well as symptomatic treatment, including the use of hormonal medication, intrauterine devices, and endometrial ablation, have become increasingly popular treatment choices. While these treatments are associated with reduced perioperative morbidity and shorter hospital stays, patients should be carefully counselled regarding the risks and the benefits. General practitioners may often help to initiate discussions to assist women considering their management options.

Fibroids are common, benign smooth muscle tumours originating from uterine myometrial cells. They are estimated to affect 40–80% of women by age 50 years.<sup>1,2</sup> Symptomatic fibroids are associated with great costs to the patient and the healthcare system; it was estimated that uterine fibroids incurred a total direct cost of US\$10.3 billion in the United States in one year alone.<sup>3,4</sup>

Fibroids are the most common indication for a hysterectomy.<sup>4,5</sup> Although highly effective, hysterectomy is associated with perioperative and postoperative morbidity and, very rarely, mortality (estimated one in 2000).<sup>5</sup> More conservative management techniques allowing women to preserve the uterus have become increasingly popular. The aim of this article is to provide an overview of current therapies, and insights into risks and benefits for general practitioners (GPs) to consider in patient consultations.

## Malignancy risk

Differential diagnosis of a malignancy should be considered in women presenting with a uterine mass, particularly if they are postmenopausal.<sup>6</sup> One to two in 1000 women with uterine masses are estimated to have a uterine malignancy.<sup>7</sup>

Suspicion for malignancy is raised for rapidly growing fibroids, particularly in postmenopausal women who are not on hormone replacement therapy, and women responding poorly to gonadotrophin-releasing hormone (GnRH)

agonists. A history of tamoxifen use for more than five years is associated with a threefold increase in the risk of leiomyosarcoma, and uterine sonographic surveillance is recommended in such cases, especially in patients who have had prior pelvic irradiation.<sup>8–17</sup>

Preoperative differentiation between benign fibroids and uterine malignancy is extremely difficult, yet increasingly important because of trends for using conservative and minimally invasive treatments. Occasionally, morcellators are used in laparoscopic fibroid resection. These instruments divide tissue into smaller sections that are otherwise too large to remove via portholes or the vaginal outlet. Shorter operating times and smaller incisions reduce postoperative morbidity.

In 2014, the US Food and Drug Administration (FDA) released a statement discouraging the use of laparoscopic power morcellation following a case of inadvertent morcellation of a leiomyosarcoma and subsequent malignant upstaging.<sup>18</sup> Many have since considered the therapeutic challenges and risks of minimally invasive surgery. A large retrospective trial showed that the risk of unintended morcellation of a uterine leiomyosarcoma following preoperative selection of women with fibroids is one in 4791 women.<sup>19</sup> While seemingly low, the risks of minimally invasive surgery should be carefully conveyed to patients to help them make fully informed decisions.

## Clinical evaluation

### History

Following a detailed medical and gynaecological history, consider if the patient has had the following:<sup>7</sup>

- abnormal uterine bleeding: menorrhagia, dysmenorrhoea, breakthrough bleeding
- symptoms of anaemia and iron deficiency from long-term menorrhagia
- pressure symptoms, such as urinary frequency, retention, tenesmus or evidence of hydronephrosis
- a history of subfertility: distortion of the uterine cavity may be associated with implantation failure and even later stage pregnancy losses
- acute pelvic pain: this can occur in the setting of fibroid degeneration as its vascular supply is outgrown.

### Examination

Abdominal and pelvic examination may reveal a firm palpable uterine mass. Fibroids may palpate as smooth and be similar to a gravid uterus, or irregular and nodular if there are multiple fibroids. Larger fibroids may distend the abdomen. Differential diagnoses are listed in Box 1.

## Investigations

### Biochemical

There are no specific blood tests to diagnose fibroids. Depending on symptoms, tests that may help in the patient workup include a full blood count, iron studies, thyroid function tests and measurement of follicular stimulating hormone, luteinising hormone, oestrogen and  $\beta$ -human chorionic gonadotropin levels. The usefulness of assessing levels of Ca-125 and other tumour markers is debatable in a routine workup. Elevation of Ca-125 levels with benign large fibroids has been observed and is likely to be due to peritoneal irritation or concurrent adenomyosis.<sup>20</sup> Tumour markers may have a more accurate role in follow-up after treatment.<sup>20</sup>

### Ultrasonography

Ultrasonography is a non-invasive, highly tolerable diagnostic technique

and is usually the modality of choice for detailed evaluation of the endometrium and myometrium. It provides information about the number, size and position of fibroids, and the uterine vasculature. Serial assessments can improve accuracy and positive predictive value in distinguishing benign from malignant uterine masses.<sup>21</sup>

### Magnetic resonance imaging (MRI)

MRI has a prominent evolving role in assessing uterine masses. MRI provides more accurate morphological soft-tissue detail when compared with computed tomography (CT), and has a useful pre-operative role in some cases, particularly in monitoring fibroid degeneration and identifying sarcomatous changes.<sup>9,22,23</sup>

### Computed tomography

CT is not believed to be as specific as other imaging modalities in differentiating between fibroids and malignancy,<sup>24-26</sup> and is generally reserved for postoperative follow-up to assess the extent of metastatic disease.<sup>27</sup>

## Management

### Conservative

Asymptomatic women, or those with small or slow-growing fibroids, usually benefit from expectant management.

#### Box 1. Differential diagnoses for fibroids

##### Uterine

- Pregnancy
- Haematoma
- Leiomyosarcoma

##### Extra-uterine

- Ovarian cyst
- Ovarian malignancy
- Ectopic pregnancy
- Pyosalpinx
- Hydrosalpinx
- Primary fallopian tube neoplasm
- Pelvic abscess
- Colorectal carcinoma
- Bladder carcinoma

Women with larger fibroids who decline medical treatment and have no significant complications may only require annual serial ultrasounds to monitor growth.<sup>28</sup>

### Medical

Tranexamic acid and non-steroidal anti-inflammatory drugs used alone are marginally effective in managing fibroid-related menorrhagia.<sup>29</sup> Intrauterine devices can help with abnormal uterine bleeding. Depending on fibroid size and position, associated cavity distortion may create difficulty with insertion and retention of the device.

GnRH agonists reduce oestrogen production and may reduce fibroid size and decrease vascularity. These effects are transitory and fibroids usually grow back to the pre-treatment size several months after treatment cessation. Additionally, they carry significant side effects, such as hot flushes, sleep disturbances, vaginal dryness and headaches. Long-term use (>6 months) can predispose to osteoporosis.<sup>28</sup> GnRH analogues are currently recommended for temporary symptomatic relief and pre-operative fibroid size reduction.

### Radiological

#### Uterine artery embolisation (UAE)

UAE involves an embolic agent introduced via angiography to occlude the vascular supply of a fibroid, causing degeneration. UAE is considered to be safe and minimally invasive, with demonstrable improvement in menstrual bleeding, pressure and urinary symptoms, as well as dysmenorrhea for most patients.<sup>30,31</sup>

In comparison to myomectomy, UAE is associated with shorter procedural times and hospital stays, and faster resumption of usual activities.<sup>32,33</sup> Patient satisfaction with fibroid symptom relief after UAE or hysterectomy are closely comparable.<sup>32,34</sup> However, UAE is associated with higher rates of minor postoperative complications and increased likelihood of surgical re-intervention within two years.<sup>32</sup> The overall failure rate is estimated to be around 32% within the first two years, compared

with 7% of patients after hysterectomy or myomectomy.<sup>33</sup> The higher re-intervention rate may balance out an initial cost advantage, for which patients should be carefully counselled.<sup>33</sup>

Effects of UAE on premature ovarian failure, overall fertility and pregnancy outcomes are not well established.<sup>35</sup> Women undergoing this treatment are believed to receive a radiation dose equivalent to approximately 10 times that of a pelvic CT scan.<sup>5</sup> Patients should be aware of the risk that, although rare, complications of UAE may ultimately necessitate a life-saving hysterectomy.<sup>28,35</sup>

### MRI-guided focused ultrasound

This is a relatively new technique that has been trialled with promising effects. Ultrasonic energy is focused to generate heat at focal points in the fibroid to denature proteins and cause cell death, thus reducing fibroid size. MRI is used for precise tissue targeting and temperature monitoring.<sup>36,37</sup> The procedure is associated with low morbidity and quick recovery. Published results have shown reductions in fibroid volume of up to 33% at six months after the procedure.<sup>28,38</sup>

The disadvantages of MRI are similar to those of UAE, with a risk of requiring further surgical treatment. At this stage there is insufficient evidence for pregnancy outcomes after MRI-guided focused ultrasound, and the procedure should be recommended with caution for women who are planning to become pregnant.<sup>28</sup>

### Surgical Myomectomy

Myomectomy is a uterine-sparing procedure involving surgical removal of fibroids from the uterine wall. Some women may require this to improve their reproductive chances if there is a suggestion that the fibroid is causing recurrent miscarriages, fallopian tube compression or significant distortion of the uterine cavity.

Myomectomy may be performed via laparotomy, laparoscopy or hysteroscopy in the case of submucosal fibroids. The laparoscopic approach is associated with decreased peri-operative and postoperative morbidity and shorter hospital stays when performed by a skilled laparoscopic surgeon, particularly when compared with open myomectomy.<sup>5,39</sup> However, this approach may have a higher recurrence rate of fibroids, compared with open myomectomy.<sup>40</sup>

Submucosal fibroids can be removed hysteroscopically with a resectoscope or morcellator. This is usually a day procedure and is minimally invasive with reduced surgical trauma and positive outcomes. Most women avoid further surgery and experience improved heavy menstrual bleeding symptoms, sometimes without combined endometrial ablation.<sup>41,42</sup> A recent Cochrane review suggested that hysteroscopic myomectomy may improve reproductive chances, but the evidence is not conclusive.<sup>43</sup>

### Hysterectomy

Women with symptomatic fibroids who do not desire future fertility may be candidates for a hysterectomy. Complete removal of the uterus has the best outcome for symptom reduction, recurrence of fibroids and requirements for further surgery.

There are three main surgical approaches to a hysterectomy: vaginal, abdominal (laparotomy) and laparoscopic with or without the use of a surgical robot. A vaginal hysterectomy is the preferred option when possible. In the cases of large fibroids, this may not be technically achievable.

A laparoscopic hysterectomy has similar benefits to the vaginal approach in terms of reduced post-operative pain, cosmetic results, shorter hospitalisation and speedier return to work. It uses expensive equipment, but most costs are offset by savings in hospital stays and post-operative care when compared with an abdominal hysterectomy. Further evolution of technology may allow cheaper and more accessible options to become available.

## Conclusion

Women may perceive their fibroids differently and have various treatment expectations. Minimally invasive treatments increase the range of options available, and gynaecological input is recommended for individual cases. Differential diagnosis of malignancy is important, particularly with ever-increasing conservative modalities. Careful counselling aids women with their treatment choices; discussions may begin with their GPs.

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