Contemporary management of uterine fibroids

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CASE

A woman, aged 41 years, presented with primary infertility. She described regular, heavy menstrual bleeding without dysmenorrhoea. Infertility investigations demonstrated iron deficiency anaemia with a haemoglobin level of 101 g/L and age-appropriate ovarian reserve parameters. Early follicular ultrasound showed a 30-mm×42-mm×45-mm intramural fibroid distorting the uterine cavity; otherwise, normal uterine size, a regular and thin endometrium, no abnormal ovarian findings and patent uterine tubes were observed. The semen analysis parameters were within the normal range.

QUESTION 1

How are fibroids evaluated and classified?

QUESTION 2

What are the clinical implications of fibroids?

QUESTION 3

What are the available therapies for fibroids?

QUESTION 4

Should fibroids be removed in asymptomatic infertile patients?

ANSWER 1

The investigation of uterine fibroids is based on the patient's symptoms. Fibroids can also be an incidental imaging finding in asymptomatic women. Transvaginal ultrasound is the preferred initial modality for fibroids assessment.[1] Sonohysterography or hysteroscopy can be added to improve the sensitivity of diagnosis of submucosal fibroids and their impact on the uterine cavity. Magnetic resonance imaging can be a complementary modality in surgical planning, determining vascularity, degeneration and the possibility of malignant transformation (leiomyosarcoma).[2] There are several fibroid classification systems; the most recently published International Federation of Gynecology and Obstetrics (FIGO) classification describes nine types of fibroids based on their relationship to the endometrium and serosal surfaces.[3]

ANSWER 2

Only 30–40% of women with fibroids experience symptoms, which vary depending on the location, size and number of fibroids, as well as other patient-specific factors. Submucosal and intramural fibroids can cause abnormal uterine bleeding associated with leiomyoma (AUB-L) and subsequent iron deficiency anaemia. Large fibroids can cause symptoms due to pressure on adjacent organs, presenting as bowel or bladder dysfunction or dyspareunia.[2] Evidence suggests a detrimental effect of fibroids on natural fecundity, with 3.5-fold increased odds for the presence of fibroids in subfertile compared with fertile women.[4] The presence of submucosal or intramural cavity-distorting fibroids has been reported to be associated with lower clinical pregnancy rates in women undergoing in vitro fertilisation (IVF) treatment.[4] The impact of non-distorting cavity intramural fibroids on IVF outcomes depends on their size. A recent meta-analysis demonstrated a reduced live birth rate in patients with 2- to 6-cm intramural fibroids undergoing IVF treatment compared with patients with no fibroids.[5] Conversely, subserosal fibroids have minimal impact on fertility outcomes. The size of fibroids might change throughout pregnancy. Fibroid size might increase in 20–30% of all cases, especially during the first trimester.[6] In cases of fast-growing fibroids, vascular abnormalities might lead to ischaemia, necrotic degeneration and pain. Moreover, fibroids are associated with obstetrics complications, such as an increased risk of miscarriage (odds ratio [OR] 1.2; 95% confidence interval [CI]: 0.8–1.5), placenta praevia (OR 2.2; 95% CI: 1.5–2.9), placental abruption (OR 2.6; 95% CI: 1.4–3.9), preterm birth (OR 2.6; 95% CI: 1.8–3.8), fetal malpresentation (OR 2.7; 95% CI: 1.6–2.7), caesarean section (OR 2.6; 95% CI: 2–3.2) and growth restriction (OR 1.4; 95% CI: 1.1–1.7).[4]

ANSWER 3

The treatment options for fibroids include medical (Table 1) and surgical therapies (Table 2) guided by patient-specific symptoms and the desire to preserve the uterus and fertility. Medications primarily address AUB-L, although evidence to guide first-line treatment recommendations is lacking.[7] It must be noted that the majority of medical interventions are unsuitable for patients actively trying to conceive, and surgical intervention might be required in this setting. Hysteroscopic myomectomy is indicated for small (usually ≤3 cm)

intrauterine or submucosal fibroids, FIGO Type 0–3. Other fibroids can be removed with laparoscopy or open surgery.[2] Hysterectomy provides a definitive cure for women with symptomatic fibroids who do not wish to preserve fertility, resulting in complete resolution of symptoms and improved quality of life. A total hysterectomy with the removal of the fallopian tubes can be performed either vaginally, abdominally or laparoscopically, depending on the local expertise and the size of the fibroids. Laparoscopic or vaginal approaches are preferred because they result in shorter recovery and fewer complications in experienced hands, but might not be feasible due to the size of the fibroids.[8] Asymptomatic fibroids where fertility is not actively pursued might not require any treatment and might be followed up with annual ultrasound.[9]

ANSWER 4

In asymptomatic infertile women with >3- to 4-cm intramural or submucosal cavity-distorting fibroids, myomectomy (open, laparoscopic, hysteroscopic) might be considered to improve pregnancy rates.[12] A systematic review with stratified analysis comparing infertile women with submucosal fibroid removal versus no intervention found higher rates of clinical pregnancy among the intervention group compared with women with myomas in situ (relative risk 2.03; 95% CI: 1.08–3.82; *P*=0.28).[13]

A recent systemic review and meta-analysis concluded that 2- to 6-cm non-cavity-distorting intramural fibroids are associated with decreased live births after IVF treatment.[5] However, high-quality studies are needed before myomectomy might be offered to women with non-distorting intramural fibroids before undergoing IVF treatment. In those cases, myomectomy might be offered after multiple failed assisted reproductive technology cycles.[12]

Key points

- Fibroids are extremely common in the population of women of childbearing age. Their impact on fertility, both naturally and with various fertility treatments, largely depends on the size, position and number of fibroids present.
- Medical therapies primarily address dysfunctional bleeding and are commonly effective, although most of them cannot be used while actively trying to conceive. Although non-invasive modalities such as embolisation and magnetic resonance imaging-guided ultrasound show promise,

Table 1. Medical therapies for uterine fibroids[2,7]

Treatment	Description	Comments
Tranexamic acid	• Prevents fibrin degradation	• Reduces menstrual blood loss • Safe for use in patients trying to conceive
NSAIDs	• Inhibit cyclo-oxygenase enzyme, diminishing the production of prostaglandins	• Reduce pain and menstrual blood loss • (Less effective than tranexamic acid or hormonal treatment)
Combined oral contraceptives	• Control AUB-L by suppressing endometrial growth	• Reduce menstrual blood loss after several months of use
52-mg levonorgestrel-releasing IUD (Mirena; Bayer Australia Ltd)	• Controls AUB-L by stabilising the endometrium	• Reduces menstrual blood loss • High rate of expulsion in patients with fibroids that distort the uterine cavity • Hormone-secreting IUDs with lower doses of levonorgestrel are not indicated as AUB-L treatment
Oral GnRH antagonist agents with hormonal add-back therapy (elagolix, relugolix)	• Suppress pituitary GT secretion • Can be used with add-back therapy for up to 2 years	• Second-line medial treatment • Reduce menstrual bleeding loss as early as the first month of treatment • Amenorrhoea in more than half of patients after 12 months of use • Improve quality of life
GnRH agonists (goserelin, nafarelin)	• Suppresses pituitary GT secretion • Short-term treatment as a bridge to operative treatment strategies	• Second-line medial treatment • Reduce fibroid size • Reduce menstrual bleeding loss
Selective progesterone receptor modulators (ulipristal acetate)	• Currently restricted for use due to rare but serious liver injury, despite proven short-term efficacy	

AUB-L, abnormal uterine bleeding associated with leiomyoma; GnRH, gonadotropin-releasing hormone; GT, gonadotropin; IUD, intrauterine device; NSAIDs, non-steroidal anti-inflammatory drugs.

Table 2. Non-surgical and surgical interventions[10,11]

Uterine artery embolisation	Embolic agent is catheterised through uterine arteries and causes fibroid devascularisation and involution	• Uterine preserving interventions • Should be recommended with caution to patients who desire fertility due to potentially higher rates of abortion and pregnancy complications • 20–30% of women treated with those methods require further fibroid surgery
High-frequency MRI-guided focused ultrasound	Thermal ablation using MRI to visualise the fibroids while the ultrasound energy is directed to the fibroids and coagulation tissue necrosis is induced	
Hysteroscopic fibroid resection	Indicated for FIGO Type 1–3 fibroids	
Laparoscopic or open myomectomy		• Laparoscopic myomectomy is associated with less postoperative morbidity and faster recovery than open myomectomy, with no significant difference in recurrence risk or reproductive outcomes
Hysterectomy	Vaginal, laparoscopic or abdominal	• Vaginal and laparoscopic approaches are preferred due to shorter recovery, but the surgical approach depends on the size of the uterus and local expertise

FIGO, International Federation of Gynecology and Obstetrics; MRI, magnetic resonance imaging.

they need to be used with caution due to the paucity of data regarding long-term obstetric outcomes.

- Minimally invasive hysteroscopic and laparoscopic approaches are well-established modalities that preserve fertility and constitute first-line surgical treatment of fibroids. In cases where future fertility is not desired and medical interventions do not adequately manage symptoms, a total hysterectomy could be an appropriate option, with laparoscopic and vaginal approaches being preferred.

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