No. 128, May 2003

The Management of Uterine Leiomyomas

The following clinical practice guideline has been reviewed by the Clinical Practice Gynaecology Committee and approved by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: The objective of this document is to serve as a guideline to the investigation and management of uterine leiomyomas.

Options: The areas of clinical practice considered in formulating this guideline are assessment, medical treatments, conservative treatments of myolysis, selective artery occlusion, and surgical alternatives including myomectomy and hysterectomy. The risk-to-benefit ratio must be examined individually by the woman and her health-care provider.

Outcomes: Implementation of this guideline should optimize the decision-making process of women and their health-care providers in proceeding with further investigation or therapy for uterine leiomyomas, having considered the disease process and available treatment options, and reviewed the risks and anticipated benefits.

Evidence: English-language articles from MEDLINE, PubMed, and the Cochrane Database were reviewed from 1992 to 2002, using the key words "leiomyoma," "fibroid," "uterine artery embolization," "uterine artery occlusion," "uterine leiomyosarcoma," and "myomectomy." The level of evidence has been determined using the criteria described by the Canadian Task Force on the Periodic Health Examination.

Benefits, Harms, and Costs: The majority of fibroids are asymptomatic and will not require intervention or further investigations. For the symptomatic fibroid, hysterectomy offers a definitive solution. However, it is not the preferred solution for women who wish to preserve their uterus. The predicted benefits of alternative therapies must be carefully weighed against the possible risks of these therapies. In the properly selected woman with symptomatic fibroids, the result from the selected treatment should be an improvement in the quality of life. The cost of the therapy to the health-care system and to women with fibroids must be interpreted in the context of the cost of untreated disease conditions and the cost of ongoing or repeat treatment modalities.

Recommendations:

1. Medical management should be tailored to the needs of the woman presenting with uterine fibroids and geared to alleviating the symptoms. Cost and side effects of medical therapies may limit their long-term use. (III-C)
2. In women who do not wish to preserve fertility and who have been counselled regarding the alternatives and risks, hysterectomy may be offered as the definitive treatment for symptomatic uterine fibroids and is associated with a high level of satisfaction. (II-A)
3. Myomectomy is an option for women who wish to preserve their uterus, but women should be counselled regarding the risk of requiring further intervention. (II-B)

Key Words

Leiomyoma, fibroid, myomectomy, uterine artery embolization

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4. Hysteroscopic myomectomy should be considered as first-line conservative surgical therapy for the management of symptomatic intracavitary fibroids. (I-B)
5. It is important to monitor ongoing fluid balance carefully during hysteroscopic removal of fibroids. (I-B)
6. Laparoscopic myolysis may present an alternative to myomectomy or hysterectomy for selected women with symptomatic intramural or subserous fibroids who wish to preserve their uterus but do not desire future fertility. (II-B)
7. Uterine artery occlusion may be offered as an alternative to selected women with symptomatic uterine fibroids who wish to preserve their uterus. (I-C)
8. Women choosing uterine artery occlusion for the treatment of fibroids should be counselled regarding possible risks, and that long-term data regarding efficacy, fecundity, pregnancy outcomes, and patient satisfaction are lacking. (III-C)
9. Removal of fibroids that distort the uterine cavity may be indicated in infertile women, where no other factors have been identified, and in women about to undergo *in vitro* fertilization treatment. (III-C)
10. Concern of possible complications related to fibroids in pregnancy is not an indication for myomectomy, except in women who have experienced a previous pregnancy with complications related to these fibroids. (III-C)
11. Women who have fibroids detected in pregnancy may require additional fetal surveillance when the placenta is implanted over or in close proximity to a fibroid. (III-C)
12. In women who present with acute hemorrhage related to uterine fibroids, conservative management consisting of estrogens, hysteroscopy, or dilatation and curettage may be considered, but hysterectomy may become necessary in some cases. (III-C)
13. Hormone replacement therapy may cause myoma growth in postmenopausal women, but it does not appear to cause clinical symptoms. Postmenopausal bleeding and pain in women with fibroids should be investigated in the same way as in women without fibroids. (II-B)
14. There is currently no evidence to substantiate performing a hysterectomy for an asymptomatic leiomyoma for the sole purpose of alleviating the concern that it may be malignant. (III-C)

Validation: This guideline was reviewed and accepted by the Clinical Practice Gynaecology Committee, and by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

Sponsor: The Society of Obstetricians and Gynaecologists of Canada.

J Obstet Gynaecol Can 2003;25(5):396–405.

INTRODUCTION

Uterine leiomyomas are the most common gynaecological tumours and are present in 30% of women of reproductive age.[1-3] Treatment of women with uterine leiomyomas must be individualized, based on symptoms, size and rate of growth of the uterus, and the woman's desire for fertility. The majority of uterine leiomyomas are asymptomatic and will not require therapy. However, in Canada, 75% of hysterectomies are performed for menorrhagia and fibroids.[4] In the last decade, several new conservative therapies have been introduced, but there remains a paucity of randomized controlled trials evaluating these therapies. Evidence arising from cohort and case-based reports allows the outline of known risks and benefits. Women should consider their options with the understanding that high levels of evidence are not yet available. The quality of evidence reported in this guideline has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Examination (Table).[5]

CLINICAL FEATURES

The vast majority of leiomyomas are asymptomatic.[2,6] The most common symptom of uterine leiomyoma is abnormal uterine bleeding.[2,6] In published series of myomectomies, 30% of women suffered from menorrhagia.[6] The mechanism of fibroid-associated menorrhagia is unknown. Vascular defects, submucous tumours, and impaired endometrial hemostasis have been offered as possible explanations.[7,8]

Pelvic pain is rare with fibroids and it usually signifies degeneration, torsion, or, possibly, associated adenomyosis.[1,2,6] Pelvic pressure, bowel dysfunction, and bladder symptoms such as urinary frequency and urgency may be present.[9] Urinary symptoms should be investigated prior to surgical management of fibroids to exclude other possible causes.[1,2,6] In the postmenopausal woman presenting with pain and fibroids, leiomyosarcoma should be considered.[10,11]

EVALUATION

Clinical examination is accurate with a uterine size of 12 weeks (correlating with a uterine weight of approximately 300 g) or larger. Ultrasonography is helpful to assess the adnexa if these cannot be palpated separately with confidence.[12] Although reliable in measuring growth, routine ultrasound is not recommended as it rarely affects clinical management. In women with large fibroids, diagnostic imaging will occasionally demonstrate hydronephrosis, the clinical significance of which is unknown. Complete ureteric obstruction is extremely rare.[1,13]

In women who present with abnormal uterine bleeding, it is important to exclude underlying endometrial pathology.[4]

MEDICAL MANAGEMENT

Treatment should be tailored to the needs of the woman presenting with uterine fibroids and geared to alleviating the symptoms. The medical management of abnormal uterine bleeding has been reviewed in a separate guideline.[4] There is no evidence that low-dose oral contraceptives cause benign fibroids to grow, thus uterine fibroids are not a contraindication

to their use. Gonadotropin-releasing hormone (GnRH) agonists are available in nasal spray, subcutaneous injections, and slow release injections.[2,14,15] In general, fibroids may be expected to shrink by up to 50% of their initial volume within 3 months of therapy.[13,16] GnRH agonist treatment should be restricted to a 3- to 6-month interval, following which regrowth of fibroids usually occurs within 12 weeks.[13,16] GnRH agonists are indicated preoperatively to shrink fibroids and to reduce menstrual-related anemia.[16] Tranexamic acid may reduce menorrhagia associated with fibroids.[17] Progestins may be associated with fibroid growth.[7] Danazol has been associated with a reduction in volume of the fibroid in the order of 20% to 25%.[18] Although the long-term response to danazol is poor, it may offer an advantage in reducing menorrhagia.

RECOMMENDATION

1. Medical management should be tailored to the needs of the woman presenting with uterine fibroids and geared to alleviating the symptoms. Cost and side effects of medical therapies may limit their long-term use. (III-C)

SURGICAL MANAGEMENT

HYSTERECTOMY

The only indications for hysterectomy in a woman with completely asymptomatic fibroids are rapidly enlarging fibroids or, after menopause, when enlarging fibroids raise concerns of leiomyosarcoma even though it remains very rare.[1,19,20] Hysterectomy was once recommended to prevent ureteric obstruction but silent ureteric obstruction is rare.[1,19]

A recent study showed no increase in perioperative complications in women with a uterus greater than 12 weeks' size compared to smaller uteri.[19] Hysterectomy need not be recommended as a prophylaxis against increased operative morbidity associated with future growth.[19] In women who have completed childbearing, hysterectomy is indicated as a permanent solution for leiomyomas causing substantial bleeding, pelvic pressure, or anemia.[21]

When considering hysterectomy for menorrhagia attributed to fibroids, other causes should be ruled out. Endometrial biopsy should be considered, to exclude endometrial lesions.[4] Leiomyomas rarely cause pelvic pain, and therefore, if pain is a major symptom, other causes should be excluded.[22] Hysterectomy is not expected to offer a cure for symptoms of incontinence in the presence of uterine fibroids.[2,6]

RECOMMENDATION

2. In women who do not wish to preserve fertility and who have been counselled regarding the alternatives and risks, hysterectomy may be offered as the definitive treatment for symptomatic uterine fibroids and is associated with a high level of satisfaction. (II-A)

CONSERVATIVE SURGICAL THERAPIES

MYOMECTOMY THROUGH A LAPAROTOMY INCISION

Although myomectomy allows preservation of the uterus, available data suggest a higher risk of blood loss and greater operative time with myomectomy than with hysterectomy.[9] The risk of

QUALITY OF EVIDENCE ASSESSMENT[5]	CLASSIFICATION OF RECOMMENDATIONS[5]
The quality of evidence reported in these guidelines has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam. I: Evidence obtained from at least one properly randomized controlled trial. II-1: Evidence from well-designed controlled trials without randomization. II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group. II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category. III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	Recommendations included in these guidelines have been adapted from the ranking method described in the Classification of Recommendations found in the Canadian Task Force on the Periodic Health Exam. A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination. B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination. C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination, but recommendations may be made on other grounds. D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination. E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

ureteric injury may be decreased with myomectomy.[9] There is a 15% recurrence rate for fibroids[9] and 10% of women undergoing a myomectomy will eventually require hysterectomy within 5 to 10 years.[9] Women should be counselled about the risks of requiring a hysterectomy at the time of a planned myomectomy. This would be dependent on the intraoperative findings and the course of the surgery. Hysterectomy remains the treatment of choice for the vast majority of women who require a surgical solution.[22]

RECOMMENDATION

3. Myomectomy is an option for women who wish to preserve their uterus, but women should be counselled regarding the risk of requiring further intervention. (II-B)

LAPAROSCOPIC MYOMECTOMY

For several pelvic disorders, gynaecologists have resorted to minimal access surgery in an effort to reduce hospital stay and improve recovery time. Myomas may be removed by a laparoscopic approach.[18,23-25] The challenges of this surgery rest with the surgeon's ability to remove the mass through a small abdominal incision and to reconstruct the uterus. A few case series have been published encompassing more than 500 women with fibroids ranging from 1 cm to 17 cm.[23-25] When compared to a laparotomy, the laparoscopic approach appears to take longer but is associated with a quicker recovery.[23-25] Concerns have been raised regarding the ability to suture the uterus with an adequate multilayer closure laparoscopically. Uterine rupture during a subsequent pregnancy has been reported.[24] The risk of recurrent myomas may be higher after a laparoscopic approach, with a 33% recurrence risk at 27 months.[26] In one case-control series there were fewer postoperative adhesions in women who had undergone myomectomy laparoscopically,[18] but adhesion formation after laparoscopic myomectomy has still been reported to occur in 60% of cases.[18,24]

The choice of surgical approach is largely dependent on surgical expertise. Morcellators have permitted removal of larger myomas, but there is a danger of injury to surrounding organs.[18,23,24] In a review of available recommendations, most suggest a laparotomy for fibroids exceeding 5 cm to 8 cm, multiple myomas, or when deep intramural leiomyomas are present.[18,23,24] Laparoscopic-assisted myomectomy presents an opportunity to enucleate the myoma partially by laparoscopy, deliver the tumour through a small abdominal incision, then close the uterine defect through this laparotomy.[18] Long-term outcomes of these new approaches are lacking.

HYSTEROSCOPIC MYOMECTOMY

Intracavitary or submucous myomas have been observed in 30% of 2049 completed outpatient diagnostic hysteroscopies in women with abnormal uterine bleeding.[27] Hysteroscopic myomectomy is feasible and very effective,[28,29] and it should be considered in women with symptomatic intracavitary or submucous narrow-based intrauterine myomas.[28,29] Indications include infertility, multiple pregnancy losses, and abnormal uterine bleeding.[28,29] The pregnancy rate in women undergoing *in vitro* fertilization (IVF) may be reduced when myomas are submucosal or when they distort the uterine cavity.[28,29] If fertility is not desired and abnormal uterine bleeding is the main symptom, concomitant endometrial ablation or resection may provide better resolution of abnormal bleeding than myomectomy alone.[30] Recently, electrosurgical loop electrodes using bipolar technology, as well as vaporizing electrodes using both monopolar[31] and bipolar technology, have been described as new technologies to facilitate hysteroscopic myomectomy.[32]

Pretreatment with a GnRH analogue for 3 months prior to myomectomy may increase the preoperative hemoglobin and hematocrit in women with anemia and may result in shrinkage of the fibroid and decrease of uterine blood flow and endometrial cavity size, as well as thinning of the endometrium.[33]

Hysteroscopic myomectomy has been associated with significant complications.[33,34] Intraoperative bleeding may lead to an emergency hysterectomy. Electrical burns to the genital tract,[34] return electrode site,[35] and bowel[36] have been reported. Hyponatremia, blindness, coma, and death from excessive irrigant fluid absorption have also been reported.[37] Fluid absorption is related to the intrauterine pressure during the procedure, the size of the uterine cavity, the duration of the procedure, and the vascularity of the myoma and the uterus itself.[30]

Prolonged surgical procedures require careful monitoring of irrigant fluid balance. Several fluid monitoring systems are now available. Surgeons should be realistic about their expertise and ability to resect multiple and large intrauterine myomas.

Data describing the fertility and pregnancy outcomes following hysteroscopic myomectomy are limited, but results appear to be similar to those following laparoscopic and abdominal myomectomies.[36,38-40]

Hysteroscopic myomectomy was clinically effective for treatment of abnormal uterine bleeding in five series involving 1422 women. Failure rates ranged from 14.5% to 30% at 3 to 4 years of follow-up.[41]

RECOMMENDATIONS

4. Hysteroscopic myomectomy should be considered as first-line conservative surgical therapy for the management of symptomatic intracavitary fibroids. (I-B)

5. It is important to monitor ongoing fluid balance carefully during hysteroscopic removal of fibroids. (I-B)

LAPAROSCOPIC MYOLYSIS

Myolysis refers to the procedure of delivering energy to myomas in an attempt to desiccate them directly or disrupt their blood supply.[42-48] Myomata deprived of their blood supply would presumably shrink or completely degenerate as they receive less nutrients, sex hormones, and growth factors. Laparoscopic

myoma coagulation was first explored as an alternative to myomectomy or hysterectomy in the late 1980s.[43,44] The indications for myolysis include symptomatic myomas requiring surgical treatment for abnormal uterine bleeding and pelvic pain and pressure to adjacent organs.[45-47] Women may be considered candidates for myolysis if they have fewer than four myomas of ≤5 cm or if their largest myoma measures less than 10 cm in diameter.[45,47]

Other concomitant pelvic surgery such as adhesiolysis, excision of endometriosis, or adnexal surgery, can be carried out at the same time. As a rule, concomitant hysteroscopic endometrial ablation or resection is recommended to further assist in the management of menorrhagia and can be performed at the end of laparoscopic myolysis. Complications consisting of pelvic infection, bacteremia, and bleeding have been reported in less than 1% of cases.[46]

In general, 3 months of GnRH agonist pretreatment reduces the total uterine myoma volume by approximately 35% to 50%.[33] Following myoma coagulation, the total uterine myoma volume is reduced by an additional 30% for a total reduction of approximately 80%, appearing to be permanent. Repeat diagnostic laparoscopy in a limited number of women has demonstrated various degrees of adhesion formation over the coagulated myomas.[46,49]

The integrity and tensile strength of the uterine wall has not been determined following laparoscopic myolysis, and it is recommended that pregnancy should not be undertaken by women who have undergone myolysis.[45-47,49] Although some women who underwent the procedure have conceived and have uneventfully delivered by Caesarean section, the fertility and pregnancy outcomes after laparoscopic myolysis remain unknown. Three cases of uterine rupture during the third trimester of pregnancy, one with catastrophic results for the fetus, have been reported.[50] Thus, myolysis can be considered only after a woman expresses certainty she desires no further children.

RECOMMENDATION

6. Laparoscopic myolysis may present an alternative to myomectomy or hysterectomy for selected women with symptomatic intramural or subserous fibroids who wish to preserve their uterus but do not desire future fertility. (II-B)

SELECTIVE UTERINE ARTERY OCCLUSION

Selective uterine artery occlusion is a global treatment alternative to hysterectomy for women with symptomatic uterine fibroids, in whom other medical and surgical treatments are contraindicated, refused, or ineffective.[51]

Fibroids have been treated effectively by laparoscopic occlusion at the origin of the uterine arteries using vascular clips[52] or bipolar electrocoagulation.[53] Since the uterine arteries are located less than 2 cm away from the vaginal lateral fornices, transvaginal uterine occlusion by surgery or colour Doppler-directed ultrasonic probe appears feasible and several approaches are currently undergoing investigation.

The most popular approach to uterine artery occlusion is selective uterine artery catheterization and embolization. Embolotherapy to treat uterine fibroids was introduced in France in 1990,[51] in the United States in 1995,[51] and in Canada soon after.[54] Eligible women include those with symptomatic fibroids who wish to avoid surgical therapy.

Before undergoing uterine artery embolization, all women should be counselled that this procedure is less than 10 years old, and its long-term effects and durability, including fertility and pregnancy outcomes, are not yet known. It is associated with the side effects and complications described below. Preoperative evaluation should include a thorough history, physical and pelvic examination, complete blood count (CBC), electrolytes, and renal and coagulation function tests. Routine cervical cytology and endometrial sampling should be performed according to established guidelines when clinically indicated and technically feasible.[4] Uterine artery embolization is performed in a medical imaging suite by interventional radiologists using aseptic sterile techniques.

PERIOPERATIVE RISKS AND COMPLICATIONS

Perioperative risks and complications include infection, bleeding, and hematomas at the femoral artery puncture site,[55-58] allergic or anaphylactic reactions to the iodinated contrast dye,[55-58] and incomplete uterine artery occlusion as well as misembolization of nontarget organs.[51,55-58] Such complications occur in approximately 1% to 2% of procedures.[51,55-58]

POST–UTERINE ARTERY OCCLUSION SIDE EFFECTS AND COMPLICATIONS

Early or Acute Abdominal Pelvic Pain

Virtually all women experience some degree of acute pain, often requiring hospitalization with intensive pain management protocols and monitoring. No correlation has been established between uterine size, myoma number or size, duration of procedure, quantity of polyvinyl alcohol (PVA) particles used, or clinical outcome of the treatment.[54] The pain is thought to be due to nonspecific ischemia of the uterus and fibroids, and responds to pain control including opiates and nonsteroidal anti-inflammatory drugs (NSAIDs).[51]

Postembolization Syndrome

Up to 40% of women experience a constellation of signs and symptoms including diffuse abdominal pain, generalized malaise, anorexia, nausea, vomiting, low-grade fever, and leukocytosis.[55] The syndrome is self-limiting and usually resolves within 48 hours to 2 weeks with conservative and supportive therapy, consisting of intravenous fluids and adequate pain control, including NSAIDs.

Infection

The incidence of febrile morbidity and sepsis following embolization has been reported to be between 1.0% and 1.8%.[57,59] The infections have included pyometria with endomyometritis, bilateral chronic salpingitis, tubo-ovarian abscess, and infected myomas.[57] The most frequent pathogen isolated has been *Escherichia coli*.[59] Some women have responded to antibiotic therapy but others have required prolonged hospitalization, intensive therapy, and hysterectomy. One woman died of sepsis following uterine artery embolization, despite an abdominal hysterectomy performed 7 days after embolization and intensive therapy.[60] Prophylactic antibiotics have not been shown to be effective and their use should be reserved for women at higher risk of infection, according to established guidelines.[61]

Persistent or Chronic Pain

In 5% to 10% of women, the pain persists for more than 2 weeks. Persistent pain in the absence of infection or pain lasting longer than 2 to 3 months may require surgical intervention. Hysterectomy for postembolization pain has been reported in up to 2% of women within 6 months of the embolization.[58,62]

Ovarian Dysfunction

Transient and permanent symptoms indicative of ovarian failure have been reported by up to 10% of women after uterine artery embolization.[57,63-66] Underlying factors leading to ovarian dysfunction are unknown, but the evidence indicates that women over the age of 45 are more likely to experience postembolization ovarian failure.[63-66] Ovarian failure is of greater consequence when preservation of fertility is desired.

Menstrual Dysfunction

Improvement in menstrual bleeding in up to 90% of women following uterine artery embolization has been reported.[54] The menstrual improvement is age dependent, the highest being after age 50. Transient and permanent amenorrhea have been reported in 15% and 3% of women, respectively.[57,58,67] Amenorrhea after embolotherapy is also highly age dependent and is reported to be related to waning ovarian function.[57,58,67,68]

Transcervical Myoma Expulsion

Following artery embolization, spontaneous expulsion of myomas through the cervix has been reported to occur in approximately 5% to 10% of women.[59,69] Sixty percent of women with submucous myomas, confirmed by hysteroscopy, passed myomas vaginally, following uterine artery embolization.[69]

Uterine Wall Integrity

The physical characteristics, integrity, and the histopathologic features of the uterine wall after uterine artery embolization remain unknown. Uterine wall defects,[70] uterine fistula,[71] and one case of diffuse uterine necrosis[72] following uterine artery embolization have been reported. Although normal pregnancies and deliveries following uterine artery occlusion have been reported, there is insufficient long-term data regarding reproductive outcome following this procedure and it would be prudent to reserve embolization for women who will not wish pregnancy.[73]

Hysterectomy

The number of women who proceed to hysterectomy following uterine artery embolization has been used as an indicator for the measurement of treatment failure.[54] The rate of hysterectomy within 6 months of embolization has been reported to be 1% to 2%, and the indications have included infection, persistent bleeding, persistent pain, fibroid prolapse, and uterine malignancies.[12,56,57,59]

Mortality

In the United Kingdom, one fatality was associated with septicemia,[60] and in Italy, one death was attributed to pulmonary embolism from a clot in the pelvic veins following uterine artery embolization.[74] No fatality has been reported following the approximately 10 000 to 12 000 procedures performed in the United States and Canada.[18,59] The combined mortality is estimated to be approximately 0.1 to 0.2 per 1000 procedures.

RECOMMENDATIONS

7. Uterine artery occlusion may be offered as an alternative to selected women with symptomatic uterine fibroids who wish to preserve their uterus. (I-C)

8. Women choosing uterine artery occlusion for the treatment of fibroids should be counselled regarding possible risks, and that long-term data regarding efficacy, fecundity, pregnancy outcomes, and patient satisfaction are lacking. (III-C)

SPECIAL CONSIDERATIONS

FIBROIDS AND INFERTILITY

The impact of fibroids on fertility is controversial. As a sole factor, fibroids probably account for only 2% to 3% of infertility cases.[2] The impression that fibroids cause infertility arises from a number of case series where removal of fibroids resulted in improved conception rates.[2,6] A comprehensive review of the literature on outcomes after abdominal myomectomy for fertility showed a combined pregnancy rate of 57% in the prospective studies.[75] The overall conception rate was 61% when no other infertility factors were identified.[75] A recent meta-analysis of all the studies looking at this question found that only women whose myomas had an intracavitary component had lower pregnancy rates and implantation rates than controls and were the most appropriate candidates for

surgical intervention.[76] No randomized controlled trials of myomectomy for infertility have been published.

Various theories have been advanced to explain the potential subfertility effect of fibroids[2,77]: dysfunctional uterine contractility, focal endometrial vascular disturbance, endometrial inflammation, secretion of vasoactive substances, or enhanced endometrial androgen environment. The published evidence suggests that submucous fibroids are more likely to cause subfertility.[77,78] Fibroids larger than 5 cm, and those close to the cervix or tubal ostia, are also thought to be more problematic.[77]

Studies of women undergoing IVF cycles have found that submucous or intramural myomas, which distort the uterine cavity, have a negative impact on implantation and pregnancy rates.[78,79] Other studies have shown an impact of fibroids on IVF implantation rates, even when there was no distortion of the uterine cavity.[80,81]

RECOMMENDATION

9. Removal of fibroids that distort the uterine cavity may be indicated in infertile women, where no other factors have been identified, and in women about to undergo *in vitro* fertilization treatment. (III-C)

FIBROIDS AND PREGNANCY

It is estimated that in 4% to 5% of women undergoing prenatal ultrasounds, uterine fibroids are detected. An increasing number of women are delaying pregnancy until their late thirties, which is also the most likely time for fibroids to develop. Most of these fibroids (80%) remain the same size or become smaller during the pregnancy.[82] There is conflicting evidence in the literature regarding the impact of fibroids on pregnancy.[82-85] The risk and type of complication appear to be related to the size, number, and location of the myomas. If the placenta implants over or in close proximity to a myoma, there may be an increased risk of miscarriage, preterm labour, abruption, prelabour rupture of membranes, or intrauterine growth restriction.[83] Fibroids located in the lower uterine segment may increase the likelihood of fetal malpresentation, Caesarean section, and postpartum hemorrhage.[83]

However, a large retrospective review of ultrasounds and medical records of 12 708 pregnant women concluded that mode of delivery, fetal growth, and risk of prelabour rupture of membranes were generally unaffected by the presence of fibroids.[84] The review did find a statistically significant increase in threatened preterm labour and treatment with intravenous tocolytics.[84] Large fibroids, defined as greater than 20 cm in diameter, were more likely to cause abruption and abdominal pain.[84]

Myomectomy should not be performed in pregnant women because of the increased risk of uncontrolled bleeding. The exception may be symptomatic subserosal fibroids on a pedicle less than 5 cm thick, in which case the risk of hemorrhage may be reduced.[85]

RECOMMENDATIONS

10. Concern of possible complications related to fibroids in pregnancy is not an indication for myomectomy, except in women who have experienced a previous pregnancy with complications related to these fibroids. (III-C)

11. Women who have fibroids detected in pregnancy may require additional fetal surveillance when the placenta is implanted over or in close proximity to a fibroid. (III-C)

ACUTE BLEEDING

Rarely, women with fibroids present with an acute hemorrhage, which can become life-threatening. There are only a few case reports in the English literature regarding management of this situation.[14,15] After resuscitation is initiated, the usual hormonal manipulation for dysfunctional uterine bleeding may be helpful.[14,86] High-dose estrogens may help cause vasoconstriction and stabilize the endometrium.[14] A dilatation and curettage may help slow down the bleeding.[86] If a submucous fibroid is found prolapsing through the cervix, its removal will usually stop the bleeding.[87] On occasion, a submucous fibroid may bleed heavily after initiation of GnRH agonist therapy.[14,15] Hysteroscopic resection of an intracavitary submucous fibroid that is bleeding is an option, but may be technically difficult due to poor visualization.[15] If the woman does not respond to conservative measures, uterine artery occlusion can be performed if it is readily available. Ultimately, hysterectomy may become necessary in some cases.

RECOMMENDATION

12. In women who present with acute hemorrhage related to uterine fibroids, conservative management consisting of estrogens, hysteroscopy, or dilatation and curettage may be considered, but hysterectomy may become necessary in some cases. (III-C)

FIBROIDS IN MENOPAUSE

Fibroids will usually shrink to about half their original size after menopause. A review of the literature found 5 randomized controlled trials looking at the effect of HRT on fibroids in postmenopausal women.[88] This review found that combined HRT, particularly using transdermal estrogen, can cause myoma growth, however, the myoma growth did not cause any clinical symptoms in these women.[88] A recent prospective study confirmed these findings in the first 2 years of HRT use, but noted a decline in fibroid volume in the third year.[89]

RECOMMENDATION

13. Hormone replacement therapy may cause myoma growth in postmenopausal women, but it does not appear to cause clinical symptoms. Postmenopausal bleeding and pain in women with fibroids should be investigated in the same way as in women without fibroids. (II-B)

FIBROIDS AND UTERINE LEIOMYOSARCOMAS

Uterine sarcoma is a rare gynaecologic malignancy, occurring in 1.7 per 100 000 women over the age of 20 years.[10] Sarcomas represent 1.2% to 6% of all uterine malignancies, with leiomyosarcomas representing approximately 25% of these. The mean age at diagnosis for uterine leiomyosarcoma has been reported to be between 44 and 57 years.[90] In one series, 47% of women were between the ages of 41 and 50 years.[91]

Women found to have a leiomyosarcoma have experienced symptoms for a median of 2.7 months.[91] Fifty percent of the women had experienced abnormal bleeding, more likely if the lesion was submucous. Other symptoms in descending order of frequency were pain, an enlarging abdomen, or abnormal vaginal discharge.[90]

A uterine mass increasing in size in a postmenopausal woman suggests a leiomyosarcoma rather than a benign leiomyoma. Also, leiomyosarcomas tend to be present as a singular large uterine mass or to be confined to the largest of the multiple uterine masses. The masses tend to be softer due to tissue necrosis and internal cystic degeneration and hemorrhage. Leiomyosarcomas tend to be difficult to separate from the surrounding myometrium at attempted myomectomy because of their invasive nature. Fewer than 1 in 10 leiomyosarcomas arise within the cervix.[90]

Preoperative diagnosis of leiomyosarcoma is infrequent. Cervical cytology, endometrial sampling, and ultrasound (including colour Doppler) have not been found to be reliable.[11,91] Preliminary studies assessing the efficacy of percutaneous needle biopsy, leading to the diagnosis of a malignant smooth muscle tumour, have been reported, but require further evaluation.[92,93] There is insufficient evidence to support routine biopsy of uterine fibroids. Magnetic resonance imaging (MRI) is promising in distinguishing between benign and malignant smooth muscle tumours. An ill-defined margin of a uterine smooth muscle tumour on MRI is more in keeping with a malignant process.[94]

There is currently no evidence to substantiate performing a hysterectomy or myomectomy for an asymptomatic uterine leiomyoma for the sole purpose of alleviating the concern that it may be malignant. The prevalence of leiomyosarcomas found incidentally in this setting is 1 in 2000, or approximately the surgical mortality rate of hysterectomy (1:1000 to 1.6:1000) for benign disease.[1] The clinical diagnosis of a rapidly growing leiomyoma prior to menopause has not been shown to predict uterine leiomyosarcoma in the absence of any other symptomatology, and thus should not be used as the sole indication for myomectomy or hysterectomy.[95] In women for whom hysterectomy is warranted because of significant signs and symptoms, the incidence of uterine leiomyosarcoma ranges between 0.3% and 0.7%.[1,90,91] In women between 41 and 50 years of age, the incidence may be as high as 0.89%.[91] The index of suspicion for malignancy should increase with age and a past history of pelvic irradiation.[10,90,91]

Women considering uterine conserving treatment, for leiomyomata, should be counselled regarding the potential risk of leiomyosarcoma, as a delay in diagnosis in those rare instances may compromise ultimate survival.[11,91,96] Close follow-up of conservative management of fibroids, such as hysteroscopic intrauterine ablative and resection techniques, GnRH agonists, and uterine artery occlusion, are recommended.[96,97]

Intraoperative or postoperative diagnosis of leiomyosarcoma warrants an oncologic consultation. Intraoperative frozen sections of smooth muscle tumours have not been shown to be helpful in giving a definitive diagnosis at the time of surgery.[11,91,95] Successful treatment via myomectomy alone has been reported in women where fertility conservation was desired, but this must be considered exceptional.[89] Adnexal metastases have been reported,[90] but in young women the role of adnexectomy should be individualized. The conventional operation for a diagnosis of uterine leiomyosarcoma includes an abdominal hysterectomy and bilateral salpingo-oophorectomy. These tumours have a propensity for hematogenous dissemination. The incidence of lymph node metastases, at the time of diagnosis, is less than 5%.[90] Routine lymphadenectomy has not been shown to affect survival.[10,90] Currently, with the best treatment modalities available, survival for stage I disease is 50%.[10,90]

RECOMMENDATION

14. There is currently no evidence to substantiate performing a hysterectomy for an asymptomatic leiomyoma for the sole purpose of alleviating the concern that it may be malignant. (III-C)

CONCLUSION

Thirty percent of women have uterine fibroids and the majority of them will not require intervention. For those women who present with symptoms, the menu of options for the treatment of uterine leiomyomas is expanding. These technologies are relatively new and although many are promising, they often lack long-term data, which interferes with our ability to present all risks and benefits with assurance. Ongoing research and data collection will help us assess the relative merit of newer options as the technology continues to expand.

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