Management of Uterine Fibroids: Review of Literature

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ABSTRACT
Leiomyomas or fibromyomas, commonly called uterine fibroids, are the most common tumors that originate from the smooth muscle of the uterus (myometrium). Uterine fibroids are generally classified into four main types based on their location, namely: intramural fibroids, subserosal fibroids, pedunculated fibroids and submucosal fibroids. The actual cause of leiomyomas is unknown but the hormone estrogen is found to be the possible stimulus to their proliferation which is proven by the increase in the size of these fibroids during pregnancy and high dose estrogen therapy. The most common signs and symptoms of uterine fibroids include heavy menstrual bleeding, menstrual periods lasting longer than a week, pelvic pressure or pain, frequent urination, difficulty emptying the bladder, constipation and backache or leg pain. Some of the factors that may increase the risk of women having uterine fibroids are old age, women of African- American race, obesity, family history of Leiomyomas, high blood pressure, nulliparity, vitamin D deficiency, excess eating leading to weight gain and consumption of estrogen rich foods. Routine examination, ultrasound, saline hysterosonography, lab tests, MRI, hysteroscopy and hysterosalpingography are some of the tests used to diagnose uterine fibroids. Symptomatic treatment of uterine fibroids may include medical management, surgical treatment or a combination of the two. Hence, the treatment of women with uterine fibroids must be tailored according to their symptoms, number, size and location of the fibroids, the patient’s age, need, and desire to preserve their fertility or their uterus, the availability of the treatment and the physician’s experience.

Keywords: Fibromyomas, Fibroids, Hysterosonography, Hysterosalpingography, Leiomyomas.

INTRODUCTION
Leiomyomas or fibromyomas, commonly called uterine fibroids, are the most common tumors that originate from the smooth muscle of the uterus (myometrium). They often contain a variable amount of fibrous tissue and their growth is dependent on the hormones estrogen and progesterone. The occurrence of fibroids is rare before puberty. They are most prevalent during the reproductive years in varying size and are observed to decrease in size post menopause.

They are often benign tumors and do not cause any symptoms. Less than 0.5% of cases have shown malignant transformation of leiomyomas. Fibroids vary greatly in their size, shape and location.

The uterus has three different layers, namely: the outer layer called the perimetrium, the middle and thickest layer called the myometrium and the inner layer which lines the uterus called the endometrium. Fibroids may be found in the uterus, uterine wall or on its surface and may also be attached to the uterus by a stalk or stem-like structure.2 Uterine fibroids are generally classified into four main types based on their location, namely: 3

1. Intramural fibroids.
2. Subserosal fibroids.
3. Pedunculated fibroids.
4. Submucosal fibroids.

Intramural fibroids are the most common type of fibroids which grow in the muscular wall of the uterus. They can grow larger and stretch the uterus because of their location.

Subserosal fibroids grow outside the uterus on the serous membrane (also called serosa), which forms the outer lining of all the organs and internal body cavities. These fibroids grow to such a large extent that they can cause the uterus to stretch and make it look bigger on one side.

Pedunculated fibroids form when a Subserosal fibroid develops a stem or stalk-like structure. This stem goes on to become a slender base that can support a tumor. A pedunculated fibroid grows from such a stem.

Submucosal fibroids grow in the middle muscular layer of the uterine wall called the myometrium. These fibroids are not as common as the other types of fibroids.
Uterine fibroids are more commonly observed in women of African-American race than in white women and they also bear the tendency to show up earlier and grow quicker in African-American women.

**Etiology**

The actual cause of leiomyomas is unknown but the hormone estrogen is found to be the possible stimulus to their proliferation which is proven by the increase in the size of these fibroids during pregnancy and high dose estrogen therapy. Fibroids usually develop during the reproductive years when estrogen levels are observed to be at their highest and they tend to shrink in size when estrogen levels are low, such as after menopause. Other possible factors that may cause leiomyomas are human growth hormone and sterility.  

**Symptoms**

Many women who have uterine fibroids usually do not experience any symptoms. In women who do experience symptoms, they can be influenced by the location, size and the number of fibroids.  

The most common signs and symptoms of uterine fibroids include:

1. Heavy menstrual bleeding
2. Menstrual periods lasting longer than a week
3. Pelvic pressure or pain
4. Frequent urination
5. Difficulty emptying the bladder
6. Constipation
7. Backache or leg pain.

A fibroid rarely causes acute pain but may occur when the fibroid outgrows its blood supply and begins to die.

**Risk Factors**

Uterine fibroids are commonly known to grow in women of childbearing age and may shrink in size after menopause. There are numerous factors that may increase the risk of women having uterine fibroids, like:  

1. Old age (they are at a higher risk when compared to younger women).
3. Obesity.
4. History of Leiomyomas in the family.
5. High blood pressure.
7. Vitamin D deficiency.
8. Excess eating leading to weight gain.

The following factors may lower the risk of Leiomyomas:

1. Pregnancy (with an increasing number of pregnancies, the risk decreases)
2. Using oral or injectable contraceptives for a long period of time.

**Pathophysiology**

The pathophysiology of fibroids is poorly understood but disordered angiogenesis and altered smooth muscle cell proliferation are believed to play an important role.  

The inappropriate growth of uterine smooth muscle tissue, also called myometrium, results in the growth of fibroids. Their growth depends on the estrogen and progesterone levels in the body. The underlying pathophysiology is uncertain.

**Clinical Presentation**

Uterine fibroids are mostly asymptomatic in most of the affected women, whereas in other women they cause significant complications and affect their quality of life. Affected women may exhibit the following symptoms:  

1. Menstrual disturbances like menorrhagia
2. Dysmenorrhoea
3. Mid-cycle bleeding
4. Pelvic pain not related to menstruation
5. Feeling bloated
6. Increase in urinary frequency
7. Bowel disturbances

Leiomyomas may also affect reproductive function leading to delay in conceiving, early loss of pregnancy, complications later in pregnancy like preterm labour, pain, malpresentations, increase in the need for caesarean section, and postpartum haemorrhage. Fibroids larger in size may lead to abdominal distension. Abnormal bleeding is observed in some of the symptomatic women, along with symptoms like bloating, pelvic discomfort due to the presence of fibroids. Clinically significant uterine fibroids are more prevalent during the perimenopausal years and eventually shrink after menopause. The clinical presentation of Leiomyomas greatly depends on their size, number and location.

**Diagnosis**

Myomas are frequently found unexpectedly during a routine pelvic examination. Irregularities in the shape of the uterus suggest the presence of fibroids.  

The following tests are used to diagnose uterine fibroids:

**Ultrasound**

An ultrasound uses sound waves to get an image of the uterus to confirm the diagnosis and to locate and measure the fibroids. The transducer is moved over the abdomen to confirm the diagnosis and to locate and measure the fibroids.
(transabdominal) or is placed inside the vagina (transvaginal) to get the images of the uterus. In a transvaginal ultrasound, a special ultrasound probe is placed inside the vagina which is usually not painful. Closer images of the uterus, endometrium and ovaries are then taken.

**Saline Hysterosonography**

This is an ultrasound procedure that does not use radiation. This ultrasound aids in better visualization of the inside of the uterus and endometrium as well as easy identification of submucosal fibroids and polyps. This examination is often performed after the end of a woman’s menstrual period. In this procedure, a small catheter is inserted through the cervix and a small balloon is inflated to hold it in place. With the help of this catheter sterile saline is injected into the uterus to expand the uterine cavity which makes it easier to take ultrasound images of submucosal fibroids and the endometrium especially in women trying to get pregnant or those who experience heavy menstrual bleeding. During the procedure, some cramping maybe experienced which may last for a short period after the procedure is done.

**Lab Tests**

In case of abnormal menstrual bleeding, the physician may order a Complete Blood Count (CBC) to determine if the patient has anemia due to chronic blood loss, and other blood tests to rule out thyroid problems or bleeding disorders.

**Magnetic Resonance Imaging (MRI)**

This test shows the size and location of the fibroids in detail, helps in the identification of the different kinds of tumors, and help determine the best treatment plans. MRI is comparatively more expensive than ultrasound but it gives an accurate and elaborate picture of the size, number and the precise location of the myomas. Oftentimes, an MRI is required only in those women with a larger uterus, or in perimenopausal women or those who are being assessed for a uterine artery embolization (UAE). Prior to the procedure, a special dye called a contrast media is intravenously administered which helps to clearly view certain parts in the body. MRI does not use radiation but it mainly uses a very strong magnetic field, radiofrequency pulses and computer to produce very clear images of internal structures of the pelvic area. 13

**Hysteroscopy:**

This is another diagnostic tool used to view the inside of the uterus. This test helps to easily identify submucosal fibroids and polyps. During this procedure, a speculum is placed in the vagina, and a long, slender telescope known as a hysteroscope is inserted through the cervix into the uterine cavity. Sterile saline is injected into the uterus through the hysteroscope to expand the uterine cavity which helps in better examination of the uterine walls, the openings of the fallopian tubes, polyps and submucosal fibroids whose images are then displayed on a monitor. Mild cramps maybe experienced during the procedure which can be alleviated by taking Ibuprofen one hour before the procedure.

**Hysterosalpingography**

In hysterosalpingography, a contrast media is used to highlight the uterine cavity and the fallopian tubes on X-ray images. A physician may recommend this test if the patient has infertility issues. This test is used to ascertain whether the fallopian tubes are open or are blocked and is used to view some submucosal fibroids as well.

**Management**

As the majority of uterine fibroids in women are asymptomatic, therapy is unnecessary. However, in symptomatic cases, characterized by iron deficiency anemia, abnormal uterine bleeding, reproductive issues, etc., treatment may be necessary. The treatment of uterine fibroids should be modified based on the size and location of the myomas, the age and symptoms of the patient, the patient’s desire to maintain fertility and preserve the uterus, experience of the physician, availability of the therapy. An ideal treatment plan should accomplish four goals, namely, alleviation of the signs and symptoms, continued reduction in the size of the fibroids, preserving the patient’s fertility (if desired), and avoiding harm. 14, 15

Symptomatic treatment of uterine fibroids may include medical management, surgical treatment or a combination of the two.

**Medical management:**

Thus far, the options for medical management of uterine leiomyomas have been limited due to their moderate efficacy and/or the adverse effects they produce.

**The following are some recommended Pharmacological therapies for the treatment of uterine fibroids:**

**Gonadotropin-releasing hormone agonists**

Treatment with these agents is given before the surgery in order to reduce the size of the tumors or it is also preferred in women approaching menopause.

**Benefits**

Gonadotropin-releasing hormone agonists decrease blood loss (due to menorrhagia), duration of surgery as well as recovery time.

**Risks/ Disadvantages**

Long-term treatment with GnRH agonists is not feasible due to higher cost and it is also not advisable as it produces menopausal symptoms, causes bone loss and increases the risk of fibroid recurrence with myomectomy.

**Fertility**

The procedure performed post GnRH agonist therapy determines whether or not the patient’s fertility is preserved.
Progestins/Levonorgestrel-releasing intrauterine system

This is used to treat abnormal uterine bleeding (AUB) by stabilizing the endometrium.

Benefits

This treatment is considered to be most efficacious in reducing blood loss. It also leads to considerable reduction in the volume of the fibroid.

Risks/Disadvantages

Progestins/Levonorgestrel-releasing intrauterine system causes irregular uterine bleeding and there is an elevated risk of device expulsion.

Fertility

Fertility is preserved if treatment with Progestins/Levonorgestrel-releasing intrauterine system is discontinued upon resolution of symptoms.

Non-steroidal Anti-Inflammatory Drugs (NSAIDs)

Non-steroidal Anti-Inflammatory Drugs possess anti-inflammatory properties and they also act as prostaglandin inhibitors.

Benefits

NSAIDs are used in the symptomatic treatment of uterine fibroids to reduce pain. They are also known to reduce loss of blood from fibroids.

Risks/Disadvantages

These drugs do not cause any reduction in the volume of the fibroids and on the other hand cause severe gastrointestinal adverse effects.

Fertility

There is no evidence of NSAIDs affecting the fertility of the patient.

Oral Contraceptives (OCs)

OCs are one of the most commonly preferred drugs in the treatment of AUB, and they do this by stabilizing the endometrium.

Benefits

Treatment with OCs are used to reduce blood loss that occurs due to fibroids. In the event of treatment with OCs being unsuccessful, the patient can switch to an alternate therapy without any hassle or adverse effects.

Risks/Disadvantages

OCs are not known to decrease the volume of the fibroid(s).

Fertility

The fertility of the patient gets restored upon discontinuation of treatment with OCs once the symptoms get resolved.

Selective Progesterone Receptor Modulators (SPRM)

The patient is treated with SPRMs before surgery in order to reduce the size of the tumors. They are also prescribed to women who are approaching menopause.

Benefits

Treatment with SPRMs reduces loss of blood, surgery duration and recovery time. SPRMs do not cause any hypoestrogenic adverse effects.

Risks/Disadvantages

SRPMs cause headache, breast tenderness, progesterone receptor modulator-associated endometrial changes and also increases the risk of fibroid recurrence with myomectomy.

Fertility

The patient’s fertility depends on the procedure done post SPRM therapy.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent which is used to prevent or reduce hemorrhage. Tranexamic acid works by competitively and reversibly inhibiting the activation of plasminogen by binding to four or five low-affinity sites and one high-affinity site which is involved in binding with fibrin. Plasminogen upon binding with fibrin induces fibrinolysis. Tranexamic acid occupies the necessary binding sites which prevents the dissolution of fibrin, thereby sustaining the clot and preventing hemorrhage.

Benefits

Tranexamic acid reduces/prevents hemorrhage caused by the presence of fibroids and allows the ease of switching to an alternate therapy.

Risks/Disadvantages

Tranexamic acid does not decrease the volume of the fibroid(s) and has medical contraindications.

Fertility

Tranexamic acid does not affect the patient’s fertility.

Surgical Management

Surgical management of uterine leiomyomas may be necessary in women who have severe pressure symptoms, who do not respond to medical therapies or in case of large pedunculated subserosal or submucosal fibroids. Surgical management of uterine fibroids include hysterectomy and myomectomy, one of which is chosen based on the size and location of the fibroid as well as the patient’s desire for future fertility or lack thereof. Various routes which may be utilized to remove uterine fibroids include laparoscopy, hysteroscopy, vagina or laparotomy. Although myomectomy may lessen the symptoms in majority of women with uterine leiomyomas, it can still lead to complications like uncontrollable severe hemorrhage which will then need to be rectified with
hysterectomy. Careful counseling prior to any surgical intervention is extremely vital to prevent such complications.

The following are the different types of surgical procedures involved in the management of uterine fibroids.

**Hysterectomy**

Hysterectomy can be defined as a surgical procedure done to remove all or part of the uterus either transabdominally or transvaginally or laparoscopically. It is a permanent solution for symptomatic myomas in women who do not wish to retain their fertility. Enlarging fibroids in postmenopausal women who aren’t undergoing Hormone Replacement Therapy, despite being rare, cause major concerns for leiomyosarcoma, which is the sole indication for hysterectomy in women with entirely asymptomatic fibroids. Therefore, there is no evidence to confirm the risk of malignancy in women with asymptomatic fibroids and they should be assured that hysterectomy is not indicated in them.

**Types of Hysterectomy**

The different types of hysterectomies based on the route through which they are done are namely abdominal, laparoscopic, and vaginal hysterectomy. The type of hysterectomy is chosen based on clinical practice guidelines, and the surgeon’s training, experience and comfort. The least invasive procedure should be chosen.

There are no significant advantages of abdominal, supracervical or total hysterectomy, but studies show that there may be less blood loss and complications associated with supracervical hysterectomy.

**Benefits**

Transvaginal and laparoscopic hysterectomies are known to be less painful, cause decreased blood loss and have a shorter recovery period when compared with transabdominal hysterectomy.

**Risks/Disadvantages**

Transabdominal hysterectomy is associated with higher surgical risks like infection, pain, fever, increased loss of blood and longer recovery period. There is an increased risk of iatrogenic dissemination of tissue due to morcellation by laparoscopic approach.

**Fertility**

The patient loses her fertility due to partial or complete removal of the uterus.

**Magnetic resonance-guided focused ultrasound surgery**

Magnetic resonance-guided focused ultrasound surgery works by employing high intensity ultrasound waves (also called sonications) to heat up and destroy the fibroid in situ. It accurately targets the uterine fibroids while sparing the healthy tissue. It is a non-invasive procedure which does not require incision. This procedure is also called focused ultrasound surgery or focused ultrasound ablation. In this procedure, a contrast media is injected intravenously and then Magnetic Resonance Imaging (MRI) is used to accurately locate and target uterine fibroids while sparing the surrounding healthy tissues. A Foley’s catheter is inserted into the bladder to drain it during the procedure as a filled bladder would displace the position of the uterus, making it difficult to locate the fibroids. The ultrasound transducer is placed exactly under the fibroids and repeated sonications are delivered using MRI as guidance to destroy the fibroids while avoiding the surrounding healthy tissues. Each sonication lasts between 15 to 25 seconds. As each sonication targets a very small area, these ultrasound waves are sent repeatedly until the entire fibroid is completely destroyed. The entire procedure generally requires about 50 sonications or more and might take a really long time depending on the number and size of the fibroid(s) being treated. Once the procedure is completed, a contrast media is once again administered intravenously to check and ensure the fibroid(s) are completely destroyed. 17

**Benefits**

It is a non-invasive procedure and it has a shorter recovery period with satisfactory symptom improvement. This procedure is a non-invasive alternative to more invasive procedures like hysterectomy, uterine artery embolization and myomectomy.

**Risks/Disadvantages**

Magnetic resonance-guided focused ultrasound surgery leads to heavy menstrual periods, causes pain due to the sciatic nerve being irritated and has a higher reintervention rate. 18

**Fertility**

The patient’s fertility whether or not being preserved is unknown.

**Myomectomy**

Myomectomy is surgical procedure done to remove fibroids from the wall of the uterus. The fibroids may also be endoscopically excised. It is an alternative to hysterectomy in women who want to retain their uterus and in turn their fertility if they desire. In women experiencing symptoms like heavy menstrual bleeding, pelvic pain and/or pressure symptoms, and other reproductive issues, surgical excision of fibroids should be considered.

Despite being able to retain the uterus by opting for myomectomy, the duration of the procedure might be longer when compared with hysterectomy and there is also a higher risk of blood loss, but a decreased risk of ureteric injury is observed. There is a recurrence of fibroids in women who undergo myomectomy and may eventually need to undergo hysterectomy at some point.

Age, number of fibroids present prior to myomectomy, size of the uterus, associated diseases and having children post
myomectomy may be risk factors for recurrence of uterine fibroids.

Benefits
Myomectomy definitively resolves the symptoms while preserving the patient’s fertility.

Risks/Disadvantages
The uterine fibroids are known to recur at five years post myomectomy, depending on the size and extent of these fibroids.

Fertility
Myomectomy does not affect the patient’s fertility.

Uterine Artery Embolization (UAE)
Uterine Artery Embolization is an interventional radiologic procedure done to occlude the uterine arteries. It is a new treatment option for symptomatic women who desire to preserve their fertility. This procedure is done by interventional radiologists, which involves cutting off the blood supply to the fibroids so that they shrink in size. Aterial Embolization reduces uterine blood flow which in turn reduces the growth of fibroids. 19

A long, thin plastic tube, called a catheter which is about 1/8 inch in diameter, is inserted through the groin into the femoral artery using a high definition x-ray camera and then maneuvered through the uterine artery. After this, the embolic agent is injected into both the right and left uterine arteries which supply blood to the fibroids and the uterus. The fibroids then die and begin to shrink, which results in the full recovery of the uterus. This entire procedure requires just one small skin puncture. It takes about 90 minutes to complete the procedure.20

Uterine Artery Embolization uses many different kinds of embolic agents. They act alike but their composition differ. Some of them are:
- Polyvinyl alcohol (a coarse sand like plastic material),
- Gelfoam (a spongy material made up of gelatin),
- Microspheres (polyacrylamide spheres with a gelatin coating).

Benefits
UAE is a minimally invasive procedure which does not need further surgical intervention and requires a shorter hospital stay.

Risks/Disadvantages
The fibroids have a significant recurrence rate at around three years after the procedure. UAE is known to cause post embolization syndrome.

Fertility
Whether the patient’s fertility is preserved or not is unknown.
site of myolysis during pregnancy, which is why this technique is not widely used.

**Cryomyolysis**

Cryomyolysis is another conservative surgical technique used to treat uterine fibroids in which the uterus is retained. The uterine fibroids can be accessed laparoscopically or hysteroscopically. In this procedure, a cryoprobe is inserted into the fibroid which is then frozen. There are not many studies done about cryomyolysis. 23

**CONCLUSION**

Uterine fibroids are the most common type of tumors found in women of reproductive age. Despite being benign tumors, women with uterine fibroids may present with a variety of complications and challenges, especially in terms of fertility, depending on the size, number and location of the fibroids. There are medical and surgical methods to manage uterine fibroids. In symptomatic women who experience abnormal uterine bleeding, pelvic pain, etc., medical treatments with levonorgestrel intrauterine system, gonadotropin-releasing hormone analogues, selective progesterone receptor modulators, oral contraceptives, progestins, danazol as preoperative treatment have shown to be greatly effective in tackling these symptoms and causing a considerable and short-term reduction in the size of uterine fibroids in women who are scheduled to undergo surgery. Among the different methods of surgical management of uterine fibroids, hysterectomy remains the most effective treatment for symptomatic fibroids. Myomectomy is a minimally invasive surgical method which can be considered as an option for symptomatic women who wish to preserve their uterus and fertility, but this procedure may eventually require surgical intervention in the long run. Hysteroscopic myomectomy can be considered as the first-line surgical treatment for the management of fibroids within the uterine cavity.

Among the conservative surgical treatments currently available, Uterine Artery Embolization has the longest history of being a very effective and successful surgical option for treating uterine fibroids in the right candidates, although, women undergoing this procedure may experience challenges related to conception and may also run the risk of abnormal placentaion, low or very low birth weights, preterm labour, etc . Newer surgical methods such as Laser-Induced Interstitial Thermotherapy (LIIT), Myolysis and Cryomyolysis show promising results but there aren’t many long term studies proving their outcomes in terms of safety, efficacy and future fertility.

In conclusion, treatment of women with uterine fibroids must be tailored according to their symptoms, number, size and location of the fibroids, the patient’s age, need, and desire to preserve their fertility or their uterus, the availability of the treatment and the physician’s experience and they should also be counseled about the possible risks and benefits of their treatment options so that they can make an informed decision.

**ABBREVIATIONS**

GnRH- Gonadotropin Releasing Hormone.

NSAIDs- Non Steroidal Anti Inflammatory Drugs.

OCs- Oral Contraceptives. 

SPRM- Selective Progesterone Receptor Modulator.

UAE- Uterine Artery Embolization. 

LIIT- Laser-Induced Interstitial Thermotherapy.

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