Review artical

Fibroid: A common problem and its advanced management

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Abstract

Uterine fibroids are the most common gynaecological disorder, classically requiring surgery when symptomatic. Although attempts at finding a nonsurgical cure date back to centuries, it is only around the middle of the last century that serious attempts at a medical treatment were carried out. Initially, both progestins and estrogen–progestin combinations have been utilized, although proof of their usefulness is lacking. A major step forward was achieved when peptide analogues of the GnRH were introduced, first those with super agonist properties and subsequently those acting as antagonists. Because both types of analogues produce hypoestrogenism, their use is limited to a maximum of 6 months and, so they can't be used routinely but utilized as an adjuvant treatment before surgery with overall good results. Over the last decade, new, nonpeptidic, orally active GnRH-receptor blockers Elagolix and another development of selective progesterone receptor modulators, sometimes referred to as "antiprogestins of choice is Ulipristal acetate are promising.Large clinical trials have proven the effectiveness of Ulipristal in the long-term medical therapy of fibroids, caution must taken for liver complications. All selective progesterone receptor modulators produce unique endometrial changes that are today considered benign, reversible, and without negative consequences. Long-term medical treatment of fibroids seems possible today, especially in premenopausal women. Surgical treatments are myomectomy, radiofrequency ablation procedure, endometrial ablation, uterine artery embolization, magnetic resonance-guided focused ultrasound myolysis are effective and reserved for the women who desires to keep uterus, and morcellation . Still Hysterectomy is the definitive treatment for fibroid and the techniques of surgery is inclining towards minimum invasive surgery .

Keywords: uterine myomas, progestin, gonadotropin-releasing hormone receptor blockers, selective progesterone receptor modulators, antiestrogens.

Introduction

Uterine fibroids, also known as uterine leiomyomas (UL), are the most common benign neoplasm of the reproductive organs in women of reproductive age.[1] About 20% to 80% of women develop fibroids by the age of 50 and estimated that 171 million women were affected worldwide. Incidence of uterine leiomyoma is 2 to 3 times greater among black than white women after adjustment for age and other risk factors. The higher incidence among black women is evident at nearly all ages.[2] Uterine leiomyomas are 2.2 times more frequent in first degree relatives and risk for the development o fibroids when there was a family history of these tumors.[3] Estimates that prevalence and incidence come from epidemiologic studies that use universal ultrasound screening. However, the best measures of disease burden and health care expenditures come from studies of hospital discharged at or self-reported rates of clinical diagnosis.[4] Incidence rates of uterine leiomyoma diagnosis in US populations are based largely on data from national hospital discharge studies, nationally representative studies and large prospective cohort studies.[5] Uterine fibroids are monoclonal tumors that arise from uterine smooth muscle tissue. The use of estrogen agonists is associated with an increased incidence of fibroid tumors and growth hormone appears to act synergistically with estradiol in affecting the growth of fibroid tumors. Conversely, progesterone appears to inhibit their growth.[6] They are benign neoplasms composed of disordered "myofibroblasts" buried in abundant quantities of extracellular matrix that accounts for a substantial portion of tumor volume. The initiating events for fibroid genesis remain speculative. Myomas can be single or multiple and can vary in size, location and perfusion. Myomas are commonly classified into 3 subgroups based on their location: sub serosal, intramural and submucosal.[7]

The majority of uterine leiomyomas are asymptomatic and 20% to 50% are clinically symptomatic. The most

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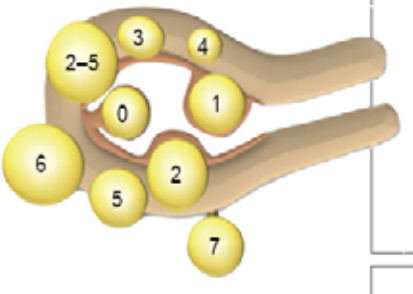
common presenting symptom is heavy menstrual bleeding, which can lead to anemia, fatigue and sometimes painful periods. Other symptoms include abdominal protuberance, pressure symptoms, painful intercourse and bladder or bowel dysfunction resulting in urinary incontinence or retention, pain or constipation.[8] On physical examination, an enlarged mobile uterus with irregular contour is consistent with fibroids. Ultrasonography is the most widely used modality because of its availability, ease of use and cost effectiveness. It is particularly helpful to assess myoma growth and the adnexa if these cannot be palpated separately with confidence. Contrast infusion saline or 3D sonohysterography are very accurate diagnostic procedures to detect submucosal lesions, all with sensitivity and specificity of 98% to 100%. CT scan is of limited value in delineating the location of myomas relative to the endometrium or myometrium, but MRI is the most accurate modality in assessing the adnexa and the uterus because it provides information on size, location, number and perfusion of leiomyomas.[9]

Treatment strategies are typically individualized based on the severity of the symptoms, the size and location of the leiomyoma lesions, the patient's age and their chronological proximity to menopause and the patient's desire for future fertility, the availability of therapy and the experience of the therapist. Symptomatic uterine fibroids may be treated medically, surgically or with a combination or both. Prospective imaging studies indicate that 3% to7% of untreated fibroids in premenopausal women regress over 6 months to 3 years.[10] Most women experience shrinkage of fibroids and relief of symptoms at menopause; therefore, depending on the severity of their symptoms, women who are approaching menopause may choose to wait for the onset of menopause before deciding in treatment.[11] Medical treatment is used mainly for temporary control of symptoms and for preoperative management. The purpose is to reduce the size of the fibroid and improve the hematological status of the patient. Several medications are available. Of these agents, gonadotropin releasing hormone analogues (GnRHa) are FDA approved agents for the temporary preoperative use to reduce leiomyoma related blood loss and to correct the ensuing iron deficiency anemia. Other agents, such as, selective estrogen receptor modulators (SERMs), antiprogestins, aromatase inhibitors (AIs), cabergoline, danazol and gestrinone have been evaluated for the treatment of leiomyoma with varying degrees success.[12] The gold standard of leiomyoma treatment is surgical intervention. Hysterectomy is the definitive surgical operation, 40% to 60% of all the hysterectomies performed are because of the presence of myomas but myomectomy is still commonly performed specially in women who desire future fertility. More recently developed techniques which include uterine artery embolization (UAE), magnetic resonance guided focused ultrasound surgery (MRgFUS) and myolysis are emerging as minimally invasive alternative procedures.[13]

Classification



SM – Submucosal	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
O – Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify eg, cervical, parasitic)
Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hypen. By convention, the first refers to the relationship with the endometrium, while the second refers to the relationship to the serosa. One example is given below	
	2–5	Submucosal and subserosal, each with less than half the diameter in the endometerial and peritoneal cavities, respectively

Figure 1 FIGO leiomyoma subclassification system.
Note: Reprinted from *Int J Gynaecol Obstet*. Vol 113(1). Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Pages 3–13. Copyright 2011, with permission from Elsevier.[1]
Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

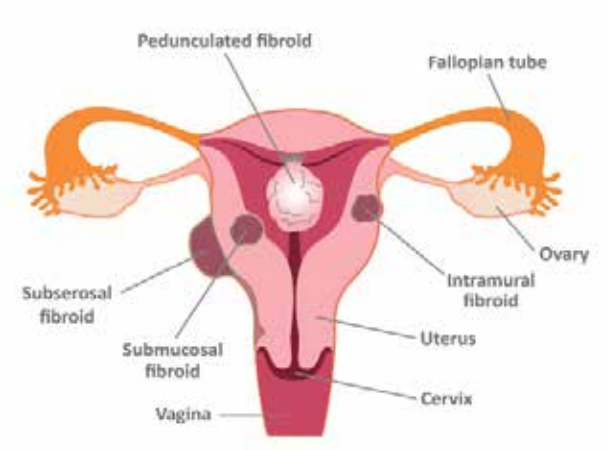


Figure 2: Different types of uterine fibroids

Risk factors

Both modifiable and nonmodifiable factors are associated with development of fibroids. These include age, race, endogenous and exogenous hormonal factors, obesity, uterine infection and lifestyle (diet, caffeine and alcohol consumption, physical activity, stress, smoking) .[15]

Age

Myomas do not occur before puberty and their frequency decreases with menopause. It is most often found in women aged 30-50 years.16-18

Race &Genetics

Myomas are the most common in women of the black race. Genetic factors can play a significant role in myoma development. The growth of multiple myomas in the same uterus implies that heritage plays an important role in myoma development, causing some women to be more predisposed than others.[17]

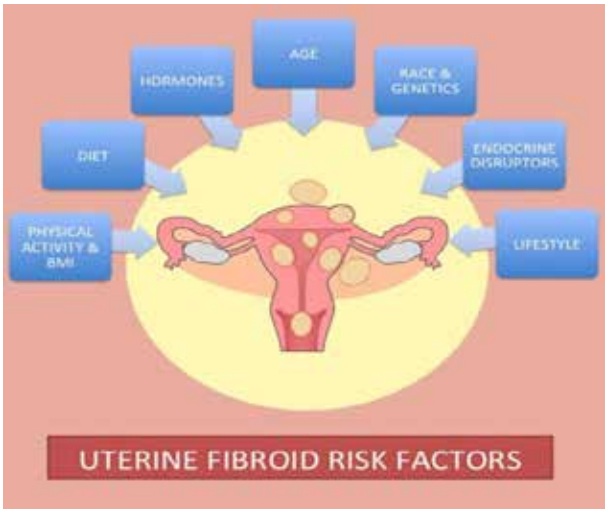


Figure 3: Risk factors affecting the incidence of uterine fibroids.

Hormonal factors

Both estradiol and progesterone are critical of leiomyoma growth, ovarian activity is essential for fibroid growth and most fibroid shrink after menopause.[20]

Endocrine disruptors

Many risk factors for these tumors have been identified, including environmental exposures to endocrine-disrupting chemicals (EDCs) such as genistein and diethylstilbestrol. Uterine development may be a particularly sensitive window to environmental exposures, as some perinatal EDC exposures have been shown to increase tumor genesis in both rodent models and human epidemiologic studies.[20]

Diet

The study results investigating the impact of diet on the occurrence of myomas are Inconclusive due to selection biases and the presence of confounding factors. In the Current study, fruit intake was inversely associated with UL risk, with the strongest reduction in risk observed for a high intake of citrus fruit. Dietary vitamin A was also Inversely associated with UL risk but the only intake derived from animal products (eg, liver and dairy products) appeared to be related to the reduction in risk.[19,21,22]

Lifestyle

Lifestyle factors such as diet, caffeine and alcohol consumption, smoking, physical activity and stress have a potential effect on the formation of myomas and their growth.[20]

Physical Activity & BMI

Higher body mass index (BMI) is associated with a modest increase in the risk of fibroids.20 But regular exercise may prevent fibroid.[23,24]

Epidemiology of leiomyoma

According to a 2010 World Health Organization report, leiomyomas affects between 20-25% of middle and later reproductive women and close to 235 million women which represent6.6% of global women population are estimated to have been affected worldwide.25 Leiomyomas are common and occur in >70% of women based on data from ultrasonography-screening studies and pathology data.19,21 The global prevalence rate compromises of 21.4% among 30-60 years age group and highest prevalence range of leiomyomas estimates is 3-20% , with African and American older women.[25] In the USA, women in their reproductive age (age group 18-49 years) who have ever experienced menstrual bleeding. 4,000 women meeting the inclusion criteria and the quotas were enrolled in the study. The self-reported prevalence of uterine leiomyomas is 4.5%.25In the UK,

women in their reproductive age (age group 15-49 years) who have ever experienced menstrual bleeding. 2,500 women meeting the inclusion criteria and the quotas were enrolled in the study. The self-reported prevalence of uterine leiomyomas are 4.6%.25 In France, women in their reproductive age (age group 15-49 years) who have ever experienced menstrual bleeding, 2,500 women meeting the inclusion criteria and the quotas were enrolled in the study. The self-reported prevalence of uterine leiomyomas are 9.8%.2 In Korea, women in their reproductive age (age group 15-49 years) who have ever experienced menstrual bleeding, 2,500 women meeting the inclusion criteria and the quotas were enrolled in the study. The self-reported prevalence of uterine leiomyomas are 9%.25

In Brazil, Canada, Germany and Italy, women in their reproductive age (age group 15-49 years) who have ever experienced menstrual bleeding, 2,500 women meeting the inclusion criteria and the quotas were enrolled in the study. The self-reported prevalence of uterine leiomyomas are 4.5%.25 In India, approximately 25% of women in their reproductive years have noticeable leiomyomas.[24]

Symptoms

Many fibroids are asymptomatic.[24] They also cause heavy or prolong menstrual bleeding that can lead to social embarrassment and the development of iron-deficiency anaemia.

Fibroids can also enlarge the uterus and can lead to urinary symptoms (such as frequent urination, nocturia or urinary retention) or gastrointestinal symptoms (such as diarrhea or constipation) in addition to abdominal distention or pain . They also cause menstrual cramps, infertility, miscarriage.[15,21-23,26,27]

Investigations

Traditionally, ultrasonography is used to confirm the diagnosis of leiomyoma after indicated by symptoms or physical examination.[24] Saline infusion sonography can be done.

A hysteroscopy may be required to differentiate intracavitary myomas and large endometrial polyp.[24]

MRI can provide more information on the number of fibroids, their size, vascularization, relationship with the endometrial cavity and serosal surface, and boundaries with normal myometrium.[24]

Blood Chemistry is done to assess the degree of anemia and other related factors if appropriate. Pap's smear is done routinely.

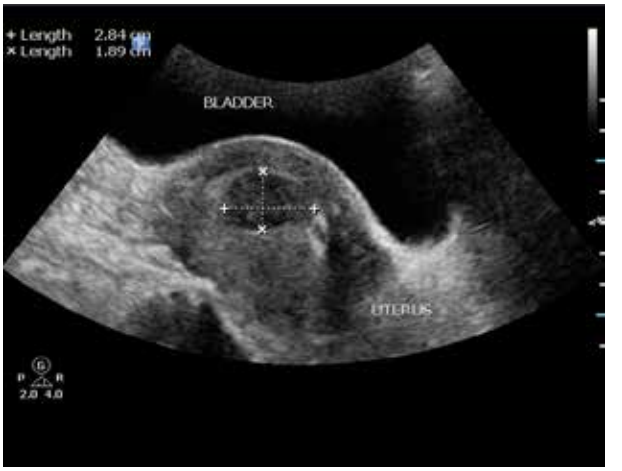


Figure 4: Ultrasonographic view of fibroid uterus

Treatment

Treatment options are-
Expectant treatment
Medical treatment
Surgical treatment

Medical treatment

Attempts at a nonsurgical treatment of uterine leiomyomas probably began hundreds of years ago, but scientifically validated modalities became available only some 40 years ago. During this relatively short period of time, several regimens were introduced using different categories of drugs. Today, the most promising ones belongs to two categories: PR modulators and orally active GnRH blockers.

Evidence on medical treatments has been systematically analysed in 2016. In a total of 75 randomized controlled trials (RCT), concluding that their overall quality was very low and that there was insufficient evidence to recommend any medical treatment in the management of fibroids.[27] Interestingly, the same year another systematic review, after evaluating 52 studies, reached a different conclusion, that proves the efficacy of a number of agents, opening-up promising avenues for the development of medical alternatives to surgery. Most available medical therapies includes androgenic agents (e.g., danazol, gestrinone), progestins (e.g., medroxyprogesterone acetate, depomedroxyprogesterone acetate, norethindrone), Mirena (IUD). Oral contraceptive pills have been used to control menorrhagia (prolonged and/or profuse blood flow) in women with leiomyomas, presumably by diminishing the endometrium (endometrial atrophy). Tranexamic acid is an anti-fibrinolytic medication that does not contain hormones that can also be used to treat heavy bleeding. None of these medications decrease uterus or fibroid volume signficantly. Progesteron receptor modulators and GnRHA are new promising drugs.[28]

Progesterone

This is widely used without any clear evidence. Today, guidelines usually specify that there is insufficient evidence of benefits from use of progestins and therefore they cannot be advocated as a medical therapy for uterine myomas.[29,30]

Recently, however, attention has been drawn again on the process of red degeneration: Nakai et al claimed that MRI can find out myomas undergoing this degenerative regression, including coagulative necrosis.31 Red degeneration has also been observed following GnRH analogue (GnRHA) treatment.[32]

The situation is complex because it seems that pprogesterone exerts a dual action on myomas: it stimulates their growth through up regulating expression of EGF and B-cell lymphoma 2 (Bcl-2) and it inhibits growth through down regulation of insulin-like growth factors (IGF) expression in the cells.[33]

Intrauterine progesterone device

Levonorgestrel releasing device is used for HMB, but now FDA has approved it for myoma as it diminishes the volume of myoma, decreases the bleeding and improves the haematocrit.

Oral Contraceptive pills (OCP)

It was reported that the prolonged use of an OC produced a significant shrinkage in myoma's size.34 However, immediately after, the journal published a formal retraction.[35]

Thus, at present, it is safe to state that whereas OC use does not carry any increased risk of developing a myoma, no valid data have been presented to support the concept that they can inhibit the growth or decrease the volume of existing fibroids. Some cohorts show they decrease fibroid formation.

Gonadotropin-releasing hormone receptor blockers

GnRH agonist do shrink most fibroids considerably, myoma's regrowth and recurrence of symptoms invariably follows discontinuation of treatment.36-38 Not only the effect seems to vanish after discontinuing therapy, the use of the analogue cannot be prolonged beyond 6 months, because of the untoward consequences of the hypoestrogenism first and foremost an increased risk of osteoporosis.[39]

To combat side effects

An RCT involving 100 women tested the addition of the selective estrogen receptor (SERM) raloxifene to the analogue over 6 months and, as expected, found that the drug produced a significant reduction in the volume of the myoma even in the no-SERM group. This effect, however, was significantly ($P<0.05$) more pronounced when both drugs were administered; in subjects treated with raloxifene, bone mineral density (BMD) and serum bone markers were unchanged.[40,41] Other addback therapies are estrogen, medroxyprogesterone acetate. OCP cannot be used.

Pre-treatment before surgery

The usefulness of a short (3-month) pre-treatment with a GnRHA has been extensively used in a variety of situations.

Adjunct to laparoscopic myomectomy

This will definitely be the case in the presence of a pedunculated or subserosal myoma; unfortunately, in the case of intramural tumors pre-treatment may make cleavage more difficult and excision more problematic. The advantages were recognized already in the early experience of pre-treatment in 150 laparoscopic myomectomies by Mettler and Semm.[42] Subsequently, the same group compared results obtained with leuprolide and triptorelin, observing at 3 months an identical reduction of myoma size (between 10% and 50%, in 88% of both groups).[43]

Adjuvant in hysteroscopic myomectomy

In view of the increasing use of the hysteroscopic approach for myomectomy, the usefulness of GnRHA has been carefully investigated. The combined approach has been pioneered by Donnez et al, who used Ng-YAG laser and made the interesting observation of a lower vascularity in the myometrium. They suggested that after pre-treatment, a two-step procedure should be carried out. This would consist of resecting first the protruding part of the tumor, followed by the intramural portion that at this stage would become accessible to the laser beam. GnRHA therapy would then be continued for another 8 weeks. [44,45]

Orally active antagonists of the gonadotropin-releasing hormone receptor-Elagolix

Elagolix allows for modulation of gonadotropin and ovarian hormone concentrations, with a partial suppression of FSH at lower doses and nearly full suppression at higher ones. With doses of at least 50 mg/day, circulating level also decreased and at the dosage of 50–200 mg/day or 50 mg twice daily, they remained low (17±3 to 68±46 pg/mL) in most women during late follicular phase. Importantly, effects were rapidly reversed after discontinuation. Elagolix was well tolerated at all doses; among side effects, worthy of mention are headache, abdominal pain, and hot flashes.

In a three-prong trial: elagolix vs placebo and elagolix plus low-dose estrogen/progestogen add-back therapy was carried out.[46]

This preliminary study documented that Elagolix significantly reduced heavy menstrual bleeding in women with fibroids.

Selective progesterone receptor modulators (SPRM)

Myoma's growth is highly dependent on the presence of estrogens and these tumors are exceptional before puberty and regress after menopause.[47]

Ulipristal (UPA) and mifepristone are SPRMs. The study dealt with the effectiveness and safety of UPA for 212-week cycles of 5 or 10 mg UPA daily in 451 women. They observed control of excessive bleeding in >80% of subjects, a mean reduction in fibroid volume of 54% and 58%, respectively, and an improvement in pain symptom and overall quality of life (QoL).[48]

A systematic meta-analysis of the effects of UPA in women having fibroids was conducted in 2016; it included four RCTs (three comparing the drug with placebo and one comparing it with a GnRHA) for symptomatic relief. The trials reported improvement in excessive uterine bleeding as evidenced by the very significant attainment of amenorrhea ($P<0.00001$). An improved QoL parameters and reduction in fibroid size were noted in the UPA group.[49]

A major advancement was made when an international group carried out a double-blind, RCT with on-and-off four 12-week courses of UPA (10 and 5 mg daily) for the long-term treatment of fibroids. Each treatment course was separated by a drug-free period of two spontaneous menstrual bleeds.[50]

They concluded, whereas the unique nature of endometrial changes produced by SPRMs on the endometrium is undeniable, its significance, possible long-term effects, and therefore regulatory aspects are still open to debate and to lack of agreement.

To minimize the occurrence of these changes one might try a mixed regimen using first a GnRHA and, after obtaining a proper volume reduction and an inactive endometrium, begin treatment with an SPRM.[51]

Danazol and Gestrinol may be effective but they are not used because of side effects.

Surgical treatment

Types- Conservative and definitive
Conservative: - Myomectomy.
Radiofrequency ablation procedure.
Endometrial ablation.
Fibroid or artery embolization.
Magnetic resonance-guided focused ultrasound surgery.
Morcellation
Definitive: - Hysterectomy.

Myomectomy is a surgical procedure that removes fibroids preserving the uterus. It can be done in following ways-

Abdominal Myomectomy

Also known as an "open" myomectomy, an abdominal myomectomy is a major surgical procedure. Infertility secondary to uterine fibroid is one of the indications for myomectomy;52other indications include symptoms such as AUB (abnormal uterine bleeding), menorrhagia, recurrent pregnancy loss, dysmenorrhea, lower abdominal swelling, urinary frequency or incontinence or pressure symptoms and constipation.53 Other unproven indications are prevention of obstetric complications, evaluation of malignancies.

Blood loss during the surgery may require a blood transfusion. So correction of anaemia and blood should be stored before surgery. Sometimes it becomes so difficult that hysterectomy may be required; so consent has to be taken from the couple.

After a myomectomy, we recommend a Caesarean section (C-section) for the delivery of future pregnancies.

It is also important to note that new fibroids may develop, resulting in recurrent symptoms and additional procedures.

Risks

Like any surgical procedure, an abdominal myomectomy does have some risks, as, preoperative haemorrhage, increased rate of blood transfusion, conversion to hysterectomy, febrile morbidities. About 5 percent of women develop a wound infection. Adhesion formation, and regrowth of fibroid may occur.54Scar dehiscence is rare in labour but C/S is recommended.

Laparoscopic Myomectomy

Only certain fibroids can be removed by a laparoscopic myomectomy. If the fibroids are large, numerous or deeply embedded in the uterus, then an abdominal myomectomy may be necessary. Expertise is important for this procedure.

Most women spend one night in the hospital and two to four weeks recovering at home

Risks

Like any surgical procedure, a laparoscopic myomectomy does have some risks, though rare. Complications may include injuries to internal organs and bleeding. New fibroids may develop, resulting in recurrent symptoms and additional procedures.

Hysteroscopic Myomectomy

Only women with sub-mucosal fibroids are eligible for a hysteroscopic myomectomy. This is an outpatient

surgical procedure; patient may go home after several hours of observation in the recovery room after the procedure.

Patient experiences cramping and light bleeding after the procedure. Typical recovery involves one to four days of resting at home.

Uterine Fibroid Embolization/ Uterine Artery Embolization

Uterine fibroid embolization (UFE), also known as uterine artery embolization (UAE) is an alternative to surgery that involves placing a catheter through a small incision in the groin into an artery in the leg and guiding the catheter via x-ray pictures to the arteries of the uterus. Once there, the catheter is used to deliver agents that block off the blood vessels that feed the uterine fibroids. Total radiation exposure during this procedure is comparable to that in one to two CT scans. UAE does not remove uterine fibroids, but causes them to shrink by 30 to 50 percent. Advantages of this procedure include no abdominal incisions and a shorter recovery time. After this procedure women may experience amenorrhea (lack of periods) depending on their age. Fibroids can recur or vascularize after this procedure, and up to 20 percent of women seek additional treatments in the five years following UAE.

Magnetic resonance guided focused Ultrasound Treatment

MRI-guided focused ultrasound (FUS) is a non-invasive treatment option for uterine fibroids that destroys fibroids while preserving the normal uterus. Focused high-frequency, high-energy sound waves are used to target the proteins in fibroids, until they are destroyed. Used in combination with MRI, FUS allows physicians to precisely target and monitor therapy. A single treatment session lasts approximately 3 hours. Although fibroids are treated and ultimately decrease in size, they are not removed. Women are able to resume normal activity within a day of the procedure; however, the long-term effectiveness of this treatment is not known and it is not recommended for women who want to preserve their fertility.

Hysterectomy

It is the only sure way to cure uterine fibroids completely. It is indicated when patient is near or past menopause and if the fibroids is very large or patient and patient is having very heavy bleeding not responding to medical treatment.

During a hysterectomy, the whole uterus is removed.

There are several ways to perform a hysterectomy.56,57

Abdominal hysterectomy

The surgeon removes the uterus through a cut in the abdomen. This type of hysterectomy requires a longer hospital stay and longer recovery time than others.55 Removal of the ovaries is not required for treatment of fibroid symptoms. Similarly, some women may desire to preserve the cervix if there is no history of abnormal Pap smears.

Vaginal hysterectomy

This method is less invasive than an abdominal hysterectomy, so recovery time is usually shorter (3 to 4 weeks). Vaginal hysterectomy may not be an option if fibroids are very large.

Laparoscopic hysterectomy

Minimally invasive approaches include laparoscopic hysterectomy, laparoscopy-assisted vaginal hysterectomy, and robotic-assisted laparoscopic hysterectomy. Not all cases of uterine fibroids can be treated with such approaches, but these methods may result in reduced postoperative recovery time.

Robotic hysterectomy

Robotic hysterectomy is becoming more common. The surgeon sits at a console near the patient and guides a robotic arm to perform laparoscopic surgery. The recovery can be shorter (3 to 4 weeks) than with more invasive procedures. More research is needed to understand how (and how well) these procedures work and to compare the outcomes with those of other established surgical treatments.

Women must know that Having a hysterectomy means that you will no longer be able to get pregnant.57 This process cannot be reversed, so be certain about your choice before having the surgery.

Myolysis

It refers to laparoscopic thermal, radiofrequency or cryoablation. This technique is easier to master than myomectomy which requires suturing. However, localized tissue destruction may increase the adhesions.

Conclusion

Uterine fibroids are highly prevalent in reproductive-aged women, and as women continue to delay childbearing, an increasing number of patients will require fertility-preserving treatment options. Medical management of uterine fibroids may provide symptomatic relief along with the opportunity to maintain fertility. A wide range is now available and some require further evaluation. Currently, GnRH agonists and SPRMs are the most effective medical therapies, with the most evidence to support their reduction of fibroid volume and symptomatic improvement in menstrual bleeding. Minimal invasive surgery for fibroid including Myomectomy and hysterectomy are very promising. Finally the choice of treatment depends on the patient's

personal treatment goals, as well as efficacy and need for repeated interventions.

Disclosure of Interests
No conflicts of interest

References

1. Sparić R. Uterine myomas in pregnancy, childbirth and peurperium. Srp Arh Celok Lek. 2014;142(1-2):118-24.
2. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM, High cumulative incidence of uterine leiomyoma in black and white women: Ultrasound evidence. Am J Obstet Gynecol. 2003;188(1):100-7.
3. Vollenhoven B. Introduction: the epidemiology of uterine leiomyomas. Baillikre's Clin Obslet Gynaecol. 1998;12(2):168-70.
4. Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of Uterine Leiommyomas in the First Trimester of pregnancy. Obslet Gynecol. 2009;113(3):630-5.
5. Whiteman MK, Kuklina E, Jamieson DJ, Hillis SD, Marchbanks PA. inpatient hospitalization for gynecologic disorders in the United States. AM J Obslet Gynecol. 2010;202(6):541.e1-541.e6.
6. Wise LA. Epidemiology of Uterine Fibroids : From Menarche to Menopause. 2016;59(1):2-24.
7. Flake GP, Anderson J, Dixon D, Flake GP, Anderson J, Dixon D. Brogan & Partners Etiology and Pathogenesis of Uterine Leiomyomas : A Review Published by : The National Institute of Environmental Health Sciences Stable URL : http://www.jstor.org/stable/3435420 REFFERENCES Linked references are available on JSTOR for th. 2016;111(8):1037-54.
8. Vilos GA, Allaire C, Laberge PY, Leyland N, Vilos AG, Murji A, et al. The Management of Uterine Leiommyomas. J Obslet Gynaecol Canada. 2015;37(2):157-78.
9. Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. Acta Obstet Gynecol Scand. 2003;82(6):493-504.
10. Dewaay DJ, Syrop CH, Nygaard IE, Davis WA, Voorhis BJ Van. Natural History of Uterine Polyps and Leiommyomata : Obstetrics & Gynecology 2002;100(1):3-7.
11. Yang CH, Lee JN, Hsu SC, Kuo CH, Tsai EM. Effect of hormone replacement therapy on uterine fibroids in postmenopausal women – A 3 years study. Maturitas. 2002;43(1):35-9.
12. Sabry M, Al-Hendy A. Medical treatment of uterine leiomyoma. Repord Sci.2012;19(4):339-53.
13. Evans P, Brunsell S. Uterine Fibroid Tumors: Diagnosis and Treatment. Am Fam Physician. 2007;75:1503-8.
14. Minute. H. Women's Quality of Life Reduced by Fibroids. Am J Obslet Gynecol. 2017;
15. Shen Y, Xu Q, Xu J, Ren ML, Cai YL. Environmental exposure and risk of uterine leiomyoma: An epidemiologic survey. Eur Rev Med Pharmacol Sci. 2013;17(23):3249-46.
16. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. BJOG An Int J Obslet Gynaecol. 2017;124(10):1501-12.
17. Sparic R, Mirkovic L, Ph D, Malvasi A, Tinelli A, Ph D. Epidemiology of Uterine Myomas: A review. 2016;9(4):424-35.
18. Segars JH. Uterine fibroid research: A work in progress. Reprod Sci. 2014;1-3.
19. Pavone D, Clemenze S, Sorbi F, Famfrini M, Petraglia F. Epidemiology and Risk Factors of Uterine Fibroids. Best Pract Res Clin Obslet Gynaecol. 2018;46:3-11.
20. Katz TA, Yang Q, Treviño LS, Walker CL, Al-Hendy A, Endocrine-disrupting chemicals and uterine fibroids. Fertil Steril. 2016;106(4):1-11.
21. Wise LA, Radin RG, Palmer JR, Kumanyika SK, Bogg DA, Rosenberg L. Intake of fruit, vegetables, and carotenoids in relation to risk of. Am J Clin Nutr. 2011;(7):1620-31.
22. Templeman C, Marshall SF, Clark CA, DeLellis Henderson K, Largent J, Neuhausen S, et al. Risk factors for surgically removed fibroids in a large cohort of teachers. Fertil Steril. 2009;92(4):1436-46.
23. Donnez J, Drlmans MM. Uterine fibroid management: From the present to the future. Hum Reprod Update. 2016;22(6):665-86.
24. Swain D, Yadav C, Kumari J, Rani M, Rongmei PD, Khurana SK. Predictors and symptomatic burden of uterine fibroids among women in

South-Easstern India: a cross-sectional survey analysis. Int J Reprod Contraception, Obslet Gynecol. 2019;8(2):524-30.

25. Zimmermann A, Bernuit D, Gerlinger C, Schaefers M, Geppert K. Prevalence, symptoms and management of uterine fibroids: An international internet-based survey of 21,746 women. BMC Womens Health. 2012;12:1-11.
26. Coyne KS, Margolis MK, Bardley LD, Guido R, Maxwell GL, Spies JB. Further validation of the uterine fibroid symptom and quality-of-life questionnaire. Value Heal. 2012;15(1):135-42.
27. Gurusamy KS, Vaughan J, Fraser IS, Best LMJ, Richards T. Medical therapies for uterine fibroids-a systematic review and network meta-analysis of randomised controlled trials. PLoS One. 2016;11(2):e0149631art.
28. Bartels CB, Cayton KC, Chuong FS, et al. An evidence-based approach to the medical management of fibroids: a systematic review. Clin Obstet Gynecol. 2016;59(1):30–52.
29. Farquhar C, Arroll B, Ekeroma A, et al. The Working Party of the New Zealand Guidelines Group. An evidence-based guideline for the management of uterine fibroids. Aust N Z J Obstet Gynaecol. 2001;41:125–140.
30. Lefebvre G, Vilos G, Allaire C, Jeffrey J. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2003;25:396–405.
31. Nakai G, Yamada T, Hamada T, et al. Pathological findings of uterine tumors preoperatively diagnosed as red degeneration of leiomyoma by MRI. Abdom Radiol. 2017;42(7):1825–1831.
32. Hachiya K, Kato H, Kawaguchi S, et al. Red degeneration of a uterine fibroid following the administration of gonadotropin releasing hormone agonists. J Obstet Gynaecol. 2016;36(8):1018–1019.
33. Xu Q, Ohara N, Liu J, et al. Progesterone receptor modulator CDB-2914 induces extracellular matrix metalloproteinase inducer in cultured human uterine leiomyoma cells. Mol Hum Reprod. 2008;14(3):181–191.
34. Friedman AJ, Thomas PP. Does low-dose combination oral contraceptive use affect uterine size or menstrual flow in premenopausal women with leiomyomas? Obstet Gynecol. 1995;85(4):631–635.
35. Pitkin RM. Does low-dose combination oral contraceptive use affect uterine size or menstrual flow in premenopausal women with leiomyomas [Retraction of Friedman and Thomas]. Obstet Gynecol. 1995;86:728.
36. Matta WHM, Shaw RW, Nye M. Long-term follow-up of patients with uterine fibroids after treatment with the LHRH agonist buserelin. Br J Obstet Gynaecol. 1989;96(2):200–206.
37. Letteri GS, Shawker TH, Coddington CC, Shawker TH, Loriaux DL, Collins RL. Efficacy of gonadotropin releasing hormone agonist in the treatment of uterine leiomyomata: long-term follow-up. Fertil Steril. 1989;51:951–956.
38. Benagiano G. Uterine fibroids: literature review and summary of posters. Horm Res. 1989;32(Suppl 1):120–124.
39. Roux C, Pelissier C, Listrat V, et al. Bone loss during gonadotropin releasing hormone agonist treatment and use of nasal calcitonin. Osteoporos Int. 1995;5(3):185–190.
40. Palomba S, Orio F Jr, Russo T, et al. Long-term effectiveness and safety of GnRH agonist plus raloxifene administration in women with uterine leiomyomas. Hum Reprod. 2004;19(6):1308–1314.
41. Palomba S, Orio F Jr, Morelli M, et al. Raloxifene administration in women treated with gonadotropin-releasing hormone agonist for uterine leiomyomas: effects on bone metabolism. J Clin Endocr Metab. 2002;87(10):4476–4481.
42. Mettler L, Semm K. Laparoscopic approach of fibroid excision after treatment with GnRH analogues. In Lunenfeld B, Carnforth IV, editors. Proceedings of the IIIrd International Symposium on GnRH Analogues in Cancer and Human Reproduction. UK: Parthenon Publ, London; 1993:95–98.
43. Mettler L, Alvarez-Rodas E, Semm K. Hormonal treatment and pelviscopic myomectomy. Diagn Ther Endosc. 1995;1(4):217–221.
44. Donnez J, Schrurs B, Gillerot S, Sandow J, Clerckx F. Treatment of uterine fibroids with implants of gonadotropin-releasing hormone agonist: assessment by hysterography. Fertil Steril. 1989;51(6):947–950.
45. Donnez J, Nisolle M, Grandjean P, Gillerot S, Clerckx F. The place of GnRH agonists in the treatment of endometriosis and fibroids by advanced endoscopic techniques. Br J Obstet Gynaecol. 1992;99(Suppl 7):31–3

46. Archer DF, Stewart EA, Jain RI, et al. Elagolix for the management of heavy menstrual bleeding associated with uterine fibroids: results from a phase 2a proof-of-concept study. Fertil Steril. 2017;108(1):152–160.
47. Zaloudek C, Norris HJ. In: Kurman RG, editor. Blaustein's Pathology of the Female Genital Tract. 5th ed. New York: Springer-Verlag; 2002:373–408.
48. Donnez J, Hudecek R, Donnez O, et al. Efficacy and safety of repeated use of ulipristal acetate in uterine fibroids. Fertil Steril. 2015;103(2):519–527.
49. Kalampokas T, Kamath M, Boutas I, Kalampokas E. Ulipristal acetate for uterine fibroids: a systematic review and meta-analysis. Gynecol Endocrinol. 2016;32(2):91–96.
50. Donnez J, Donnez O, Matule D, et al. Long-term medical management of uterine fibroids with ulipristal acetate. Fertil Steril. 2016;105(1):165–173.
51. Benagiano G, Primiero FM. The potential use of antiprogestins in gynaecological disorders. In: Motta M, Serio M, editors. Sex Hormones and Antihormones in Endocrine Dependent Pathology: Basic and Clinical Aspects. Amsterdam: Elsevier Science; 1994:391–399.
52. Obed JY, Babo B, Kadas S, et al. The benefit of myomectomy in women aged 40years and above: Experience in Urban Teaching Hospital in Nigeria. Niger Med J. 2011;52(3):158–162.
53. Ikeako CL, Hezegwu IU, Okeke T, et al. myomectomy in a Secondary Health Centre in Awka, South East Nigeria. Orient J Med. 2012;24(3):1–6.[Google Scholar]
54. Kemfang NJD, Kasia JM, Nke ZH, Neng HT. High incidence of adnexal adhesions formation after abdominal myomectomy among African women. J of Pharmaceutical and Biomedical Sci. 2012;18(06):1–4.[Google Scholar]
55. American Congress of Obstetricians and Gynecologists (ACOG). (2015). Patient FAQ: Hysterectomy. Retrieved August 7, 2018, from https://www.acog.org/Patients/FAQs/Hysterectomy
56. Agency for Healthcare Research and Quality (AHRQ). (2005). The FIBROID Registry: Report of Structure, Methods, and Initial Results. AHRQ Publication No. 05[06]-RG008. Retrieved June 13, 2017, from http://archive.ahrq.gov/research/fibroid/fibsum.htm
57. ACOG. (2011). Patient FAQ: Uterine fibroids. Retrieved June 13, 2017, from http://www.acog.org/~/media/For%20Patients/faq074.pdf?dmc=1 &ts=20121015T1425097855 (PDF-366 KB)