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Review Article

**OVERVIEW OF MANAGEMENT APPROACHES OF UTERINE
FIBROID**

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Abstract:

In this review we discuss possible management approaches of uterine fibroid. Electronic search of journal articles relevant to the management approaches of uterine fibroids was performed through PubMed, and Embase up to 2018, with the following MeSH key words (uterine fibroid, interventions) within PubMed. Uterine fibroids (leiomyomas or myomas) are the most popular pelvic tumors and one of the most widespread benign tumors in women. A large number of women with uterine fibroids either remain asymptomatic or develop syndromes progressively over time. When patients are symptomatic, the number, size, and/or area of fibroids are critical factors of its clinical indications. Typically reported indicators consist of hefty menstruation bleeding, dysmenorrhea, noncyclic ache, urinary symptoms, exhaustion, and constipation.

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INTRODUCTION:

Uterine fibroids (UFs), also referred to as uterine leiomyomas, are benign smooth muscle tumors of the uterus that impact women of reproductive age [1]. They might be asymptomatic or induce a range of serious and chronic signs and symptoms. One of the most widespread presenting indicator is hefty menstrual bleeding, which can lead to anaemia, and exhaustion and painful periods. Additional UF symptoms consist of non-cyclic ache, abdominal protrusion, painful intercourse or pelvic pressure, and bladder or intestinal dysfunction leading to urinary incontinence or retention, ache or constipation. UFs might also be connected with reproductive problems, including damaged fertility, maternity complications and loss, and undesirable obstetric results. UFs are among the major causes of hospitalisations for gynaecological ailments, and are one of the most common reason for hysterectomy in the USA [1].

Uterine fibroids are the most popular tumor affecting females, and it has been postulated that they occur in over 70% of women by the beginning of menopause [2]. They are estimated to be clinically obvious in 25% of women of reproductive age and induce signs and symptoms severe enough in about 25% of women with UFs to require therapy [2]. The frequency of the condition is, nevertheless, most likely to be undervalued because in lots of females it is asymptomatic, or symptoms improve insidiously, and consequently remains undiagnosed. The unknown degree and effect of undiscovered UFs bias the epidemiological data and proof on connected elements to reflect serious ailment [3]. Although lots of studies on the epidemiology of UFs have been published, articles of the incidence and prevalence of UFs vary broadly relying on the method of medical diagnosis and the population examined; for instance, approximations of the incidence of UFs range from 5.4% to 77% of females of reproductive age [3]. Moreover, many different risk elements have been related to the advancement of UFs, consisting of biological, demographic, reproductive and lifestyle factors. Real occurrence and prevalence of UFs, and hence their worldwide effect on females' health and wellness, and the function of suppositional danger factors, are as a result currently unidentified.

Hysterectomy was considered the only alleviative approach for fibroids; nevertheless, alternative medical treatments that preserve fertility and evade invasive surgery, with high efficiency, and a

preferable negative effects profile are currently offered. Nevertheless, each carries its specific safety and effectiveness side view, and the treatment of fibroids should be individualized relying on such details as the patient's age, signs and symptoms, sustained reduction of fibroid dimension, and upkeep or improvement of fertility, while minimizing side effects. In this review we discuss possible management approaches of uterine fibroid.

METHODOLOGY:

Electronic search of journal articles relevant to the management approaches of uterine fibroids was performed through PubMed, and Embase up to 2018, with the following MeSH key words (uterine fibroid, interventions) within PubMed, we limited our search to only English language studies with human subjects.

Discussion:**• Background**

Numerous females have curable (non-cancerous) expansions known as fibroids in or on their womb (uterus). Most fibroids are tiny and do not cause any kind of concerns. They are normally discovered by chance. Depending on where fibroids are located, they may lead to duration discomfort, heavy menstruation bleeding or different symptoms.

There are various manners to treat fibroids [2]. The most suitable treatment will substantially rely on a woman's individual circumstances-such as whether she would still prefer to have children.

Fibroids are composed of muscle cells and connective tissue. Their dimension, form and area vary. Fibroids are mostly categorized based on where they are:

- Directly under the lining of the womb (submucosal fibroids)
- In the wall of the womb (intramural fibroids)
- On the outer wall of the womb (subserosal fibroids)
- In the cervix (cervical fibroids)
- In the connective tissue next to the womb (intra-ligamentary fibroids)

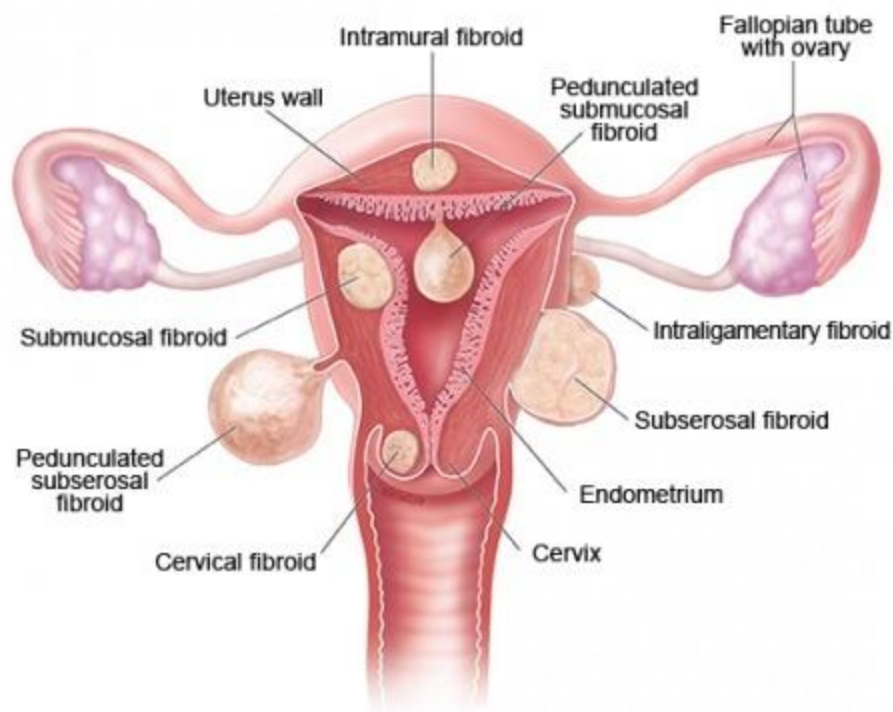


Figure 1. Different types of uterine fibroid

Many women that have fibroids don't discover that they have them. Some may simply have one, while others have a number of. Fibroids most frequently induce signs and symptoms in females among the ages of 30 and 50 [5]. Regular signs include the following:

- Severe or prolonged menstrual bleeding
- Severe, cramp-like duration ache
- Diffuse pain and tension in the abdominal area

Fibroids generally provoke signs and symptoms if they influence the function of the womb, for example during menstrual bleeding [5]. Fibroids that grow just under the cellular lining of the womb are specifically most likely to cause heavy menstrual bleeding. Routine hefty durations can lead to anemia. Women

who have anemia often look light and experience tired.

Larger fibroids sometimes push against bordering organs like the bladder or bowel. This can lead to a grown desire to urinate or food digestion problems (constipation, pain). Back pain or trouble urinating (urinary system retention) are feasible also, but uncommon.

"Pedunculated fibroids might trigger sudden and extreme pain. These fibroids can expand on the inner and external wall surface of the womb. They are connected to the womb by a thin, stem-like framework. Abrupt motions can generate pedunculated fibroids to turn on these stems. This interrupts the blood circulation to the fibroid, which can be very excruciating [4].

Table 1.Factors That Affect the Risk of Uterine Fibroids [5],[4].

<i>DECREASED RISK</i>	<i>INCREASED RISK</i>
Increased parity	African descent
Late menarche (older than 16 years)	Age greater than 40 years
Smoking	Early menarche (younger than 10 years)
Use of oral contraceptives	Family history of uterine fibroids
	Nulliparity
	Obesity

- **Management of uterine fibroids**

A number of methods are available for the management of uterine fibroids. The strategy may be dictated by aspects such as the patient's wish to become pregnant in the future, the significance of uterine conservation, symptom severeness, and tumor features.

Pharmacologic options

Pharmacologic treatments appropriate for treating all sorts of uterine fibroids. A variety of options are obtainable, consisting of hormonal treatments, such as oral contraceptives (OCs), progestins, the progesterone receptor antagonist mifepristone, the selective progesterone receptor modulator (SPRM) asoprisnil, which has blended progesterone agonist/antagonist action, and gonadotropin-releasing hormonal agent (GnRH) agonists/antagonists. OCs and progestins are used to regulate bleeding, but no evidence sustains their effectiveness in treating myomas.

Oral progestogens are described to lessen their syndromes or prevalence by 25- 50%, when carried out during the subsequent part of the cycle or as 21-day contraceptives; there are no data regarding constant regulation [6], [1]. The levonorgestrel intra-uterine device (LNGUS) is successful in lowering menstruation blood loss and rejuvenating hemoglobin levels and can be another option to surgical treatment, nevertheless its result on the size of uterine myoma is still uncertain [6]. Researches recommend that it can be a possibly good choice for symptomatic women with no endometrial distortion [6]. COC demonstrated upgrade in menstrual blood loss,

although no substantial change in the amount of the tumors [6]. Gonadotropin-releasing hormonal agent (GnRH) antagonists, such as, cetrorelix and ganirelix are not regularly operated to heal UFs, nevertheless have actually been explored preoperatively in females with fibroids with beneficial results in tumor reduction. Danazol causes endometrial hypotrophy and enhances fibroids shrinking, but also reveals dramatically a lot more negative results (including weight gain, acne, bone and joint pain, hot flushes and hirsutism) than other clinical therapies due to its androgenic activity [7].

Gonadotropin-releasing hormone analogs (GnRHa) constantly reduce UFs volume and control indicators and are particularly useful pre-operatively in lowering fibroid volume, enhancing hematocrit, reducing the need for blood transfusion and enabling fewer invasive medical techniques [7]. Nevertheless, their use is limited to temporary treatment mainly as a result of the fact that: (i) control of blood loss is medically pertinent just after three months of therapy; (ii) deep reductions of estrogen levels unnaturally induces post-menopausal indicators (hot flushes, mood swings, bone mineral density loss) and (ii) after medication withdrawal, fibroids usually re-grow to pre-treatment dimension. Association of other drugs throughout treatment with GnRH analogues (i.e., add-back therapy) is used to limit negative effects; however, some addback therapies (e.g., medroxyprogesterone acetate, tibolone and conjugated estrogens) might moderate vasomotor syndromes however they are connected with larger uterine quantity as an unfavorable effect [7].

Aromatase preventions have been revealed to readily minimize UFs size (as much as 71% in 2 months) [8] and appear to be as reliable as GnRH with fewer side effects; however robust proof regarding their efficiency is missing. The selective estrogen receptor modulator (SERM) raloxifene has also been investigated for therapy of symptomatic UFs; nevertheless, the few studies that are available are of poor quality and supply irregular results [9]. Extra recently, the duty of vitamin D and ecological tee remove (epigallocatechin gallate, EGCG) was explored as possible precautionary and anti-uterine fibroid choices, specifically, with appealing results [9].

The arrival of selective progesterone receptor modulators (SPRMs) has included an updated armamentarium to the clinical options for UFs. Unlike GnRH analogues, these drugs do not have the downside of causing estrogen shortage and lower in bone mineral density to name a few adverse events [10]. Several researches have established the prospective role of SPRMs in the treatment of UFs and their affiliation with a decrease hurting, bleeding, dimension of fibroids and total upgrade in quality of life [10]. Ulipristal acetate (UPA), the most recent medication of this class, is a reliable and well-tolerated choice for the preoperative and lasting therapy of moderate and serious syndromes of UFs in females of reproductive age.

Hysterectomy

Hysterectomy can be applied to heal all sorts of fibroids and is considered the conclusive treatment for uterine fibroids, due to the fact that elimination of the tumors in addition to their site of origin eliminates the existing pathology and the potential for additional fibroid development. In the USA, uterine fibroids are the leading indicator for hysterectomy, and hysterectomy has been associated with a patient satisfaction rate of over 90% [11]. Nevertheless, hysterectomy may not be a desirable method for lots of females; as a result, other approaches have progressed with the objective of sparing the womb and decreasing morbidity. Although hysterectomy is the definite therapy for fibroids, it results in a permanent loss of fertility and requires significant surgical procedure. In one current research study, as several as 43% of women that underwent hysterectomy revealed regret about their loss of fertility [11]; as a result, prior to option of this approach, females must thoroughly evaluate their sensations concerning this issue. Issue rates connected with hysterectomy have been reported to be as reduced as 1.5% and as high as 29.3% [11]. Surgical morbidity/mortality such as blood loss,

bowel injury, bladder and urethral injury, infection, postoperative distress, and death have all been reported with hysterectomy [11]. Typical recuperation times for hysterectomy are around 6-8 weeks; better, it has been reported that the mean procedural cost for a hysterectomy was about \$7,707 [12].

Myomectomy

Myomectomy, which such as hysterectomy has been offered for over 150 years, limitations surgical treatment to elimination of the fibroids alone and therefore preserves fertility. Myomectomy is generally performed through hysteroscopy, laparoscopy or via laparotomy. Laparotomy, or abdominal myomectomy, is beneficial for healing subserosal or intramural fibroids, while the hysteroscopic route is better for submucosal fibroids [13]. Laparoscopic myomectomy is effective for handling conveniently available tumors, such as superficial or pedunculated subserosal fibroids [13]. A prolapsed submucous myoma might also be resected transvaginally. A contrast of outcomes after myomectomy executed by laparotomy or laparoscopy in infertile patients acknowledged that laparoscopic myomectomy was superior in terms of febrile morbidity, hemoglobin levels, blood transfusion demands, and postoperative hospital stay. Nonetheless, no differences in post-surgery maternity rate, abortion rate, preterm delivery rate, or Cesarean area were seen [13]. It ought to be kept in mind that myomectomy might be rather difficult for women with large, numerous myomas, or for females that have previously gone through numerous myomectomies; in these situations, hysterectomy may be preferable [13]. Myomectomies in these women might be reached by specialists with appropriate ability and experience to handle the considerable blood loss and uterine reconstruction demanded by the considerable breakdown.

As with hysterectomy, myomectomy is a surgery; therefore, medical morbidity and death are disadvantages to this method. There is also the potential for considerable blood loss throughout the procedure. As a result, a selection of approaches for reducing blood loss have been employed, including preoperative embolization, misoprostol, intramyometrial injection of bupivacaine plus epinephrine, vasopressin, and tourniquets. Other disadvantages consist of a high threat of adhesion forming and the capacity for uterine rupture while pregnant. Typical healing times vary by the procedure done; a six- to eight-week healing time is related to abdominal muscle myomectomy, whereas patients undergoing a laparoscopic surgical treatment

might return to typical activities within one to pair of weeks, and patients getting a hysteroscopic procedure may recuperate within seven to ten days. The procedural prices for abdominal or laparoscopic treatments have been located to be comparable, with approximated expenses ranging from \$4,610 to \$8,860 for the abdominal treatment, and \$4,317 to \$8,018 for the laparoscopic techniques [14]. Hysteroscopic myomectomies have been approximated to be slightly less expensive, with costs varying from \$4,291 to \$7,704 [14].

Myolysis/Cryomyolysis

Myolysis refers to the damage of uterine fibroids by focused energy that is believed to disrupt blood supply to the tumors. Originally, neodymium: yttrium-aluminum-garnet (Nd: YAG) lasers were applied to effect coagulative necrosis of fibroids by thermomyolysis. Subsequently, a bipolar electrosurgery needle was created to achieve the very same treatment using radiofrequency. Cryomyolysis entails the use of a supercooled probe to cause sclerohyaline degeneration of fibroids. Myolysis procedures are usually done through laparoscopy, and multiple applications of the myolysis probe are used on each fibroid going through treatment. The results of a study considering the effects of thermomyolysis in symptomatic females (N167), 164 of whom had received ternary months of pretreatment with depot leuprolide acetate, and 52 of whom had chronic menorrhagia and concomitant transcervical endometrial resection, showed a mean 77.7% decrease in uterine volume at 7-12 months of followup. Of the females that had chronic menorrhagia at standard, 33 (63.5%) came to be amenorrhagic. Hysterectomy was obligated for six women (3.6%) for persistent menorrhagia, ache, and pressure [15].

One drawback of this technique is that it is not suitable for females who desire to become pregnant. Although two women in the study by Phillips and workmates had the ability to become pregnant after undertaking thermomyolysis, the substitute of fibroid tissue by scar tissue introduces the possibility for uterine rupture and abnormal placentation. On top of that, pelvic adhesion development after myolysis/cryomyolysis can influence reproductive ability [15]. With thermomyolysis, the lack of ability to determine the extent of damages introduces a danger of undertreatment or overtreatment. These techniques are likewise limited by the fact that the

medical professional can treat just a limited variety of fibroids each time; small intramyometrial fibroids might be missed with the laparoscopic strategy unless intraoperative imaging is utilized to discover the much deeper lesions.

Uterine artery embolization (UAE)

With UAE, the uterine arteries are accessed under fluoroscopic assistance and injected with a mass of trisacryl gelatin microspheres or polyvinyl alcohol particles for occlusion. Because the uterine arteries answer for around 94% of the blood supply to uterine fibroids, with the remainder obtained from the ovarian arteries by means of the infundibulopelvic ligament, this procedure considerably disrupts the blood supply to the fibroids [16]. It is considered that through the induction of transitory uterine ischemia, the tiny vessels in the myometrium ended up being occluded with clots, which are lysed in time as fibrinolytic substances from the adjunctive blood circulation in the womb perfuse the region. As the fibroids cannot lyse coagulums, they infarct and undertake ischemic necrosis [17]. Consequently, this procedure has the advantage of treating the uterus around the world. Generally, UAE is most useful in treating intramural fibroids, whereas a hysteroscopic approach would be more appropriate for submucosal myomas. Pedunculated tumors should not be treated with UAE, as a result of the potentiality for the stalk to infarct and detach from the uterus. Finally, compared to hysterectomy, UAE has been connected with a shorter recuperation time (B10 days) and a lower procedural cost (\$5,698) [12].

Fibroid ablation

The term ablation describes tissue damage with concentrated energy. It is also referred to as myolysis, and there are various sources of energy, such as ultrasound, radiofrequency (RF), and laser. Originally, surgical procedures were necessitated, however nowadays ultrasound or MRI chooses the point where the energy have to be directed [19]. Ultrasound-guided puncture with RF or/and high-frequency magnetic resonance-guided focused ultrasound surgery (MRgFUS) are minimally intrusive options that decrease menstrual blood loss and the dimension of UFs [18]. However, fertility appears not to be risked with these methods and surgical treatment might be required at a greater rate than UAE. According to our experience, both treatments are more suitable for UFs with an element of pain or compression.

Table 2. Comparison of Recommended Therapies for Uterine Fibroids [20-24].

<i>TREATMENT</i>	<i>DESCRIPTION</i>	<i>ADVANTAGES</i>	<i>DISADVANTAGES</i>	<i>FERTILITY PRESERVED?</i>
Medical therapies				
Gonadotropin-releasing hormone agonists	Preoperative treatment to decrease size of tumors before surgery or in women approaching menopause	Decrease blood loss, operative time, and recovery time	Long-term treatment associated with higher cost, menopausal symptoms, and bone loss; increased recurrence risk with myomectomy	Depends on subsequent procedure
Levonorgestrel-releasing intrauterine system (Mirena)	Treats abnormal uterine bleeding, likely by stabilization of endometrium	Most effective medical treatment for reducing blood loss; decreases fibroid volume	Irregular uterine bleeding, increased risk of device expulsion	Yes, if discontinued after resolution of symptoms
Nonsteroidal anti-inflammatory drugs	Anti-inflammatories and prostaglandin inhibitors	Reduce pain and blood loss from fibroids	Do not decrease fibroid volume; gastrointestinal adverse effects	Yes
Oral contraceptives	Treat abnormal uterine bleeding, likely by stabilization of endometrium	Reduce blood loss from fibroids; ease of conversion to alternate therapy if not successful	Do not decrease fibroid volume	Yes, if discontinued after resolution of symptoms
Selective progesterone receptor modulators	Preoperative treatment to decrease size of tumors before surgery or in women approaching menopause	Decrease blood loss, operative time, and recovery time; not associated with hypoestrogenic adverse effects	Headache and breast tenderness, progesterone receptor modulator-associated endometrial changes; increased recurrence risk with myomectomy	Depends on subsequent procedure

<i>TREATMENT</i>	<i>DESCRIPTION</i>	<i>ADVANTAGES</i>	<i>DISADVANTAGES</i>	<i>FERTILITY PRESERVED?</i>
Tranexamic acid (Cyklokapron)	Antifibrinolytic therapy	Reduces blood loss from fibroids; ease of conversion to alternate therapy	Does not decrease fibroid volume; medical contraindications	Yes
Surgical therapies				
Hysterectomy	Surgical removal of the uterus (transabdominally, transvaginally, or laparoscopically)	Definitive treatment for women who do not wish to preserve fertility; transvaginal and laparoscopic approach associated with decreased pain, blood loss, and recovery time compared with transabdominal surgery	Surgical risks higher with transabdominal surgery (e.g., infection, pain, fever, increased blood loss and recovery time); morcellation with laparoscopic approach increases risk of iatrogenic dissemination of tissue	No
Magnetic resonance-guided focused ultrasound surgery	In situ destruction by high-intensity ultrasound waves	Noninvasive approach; shorter recovery time with modest symptom improvement	Heavy menses, pain from sciatic nerve irritation, higher reintervention rate	Unknown
Myomectomy	Surgical or endoscopic excision of tumors	Resolution of symptoms with preservation of fertility	Recurrence rate of 15% to 30% at five years, depending on size and extent of tumors	Yes
Uterine artery embolization	Interventional radiologic procedure to occlude uterine arteries	Minimally invasive; avoids surgery; short hospitalization	Recurrence rate > 17% at 30 months; postembolization syndrome	Unknown

CONCLUSION:

Uterine fibroids (leiomyomas or myomas) are the most popular pelvic tumors and one of the most widespread benign tumors in women. A large

number of women with uterine fibroids either remain asymptomatic or develop syndromes progressively over time. When patients are symptomatic, the number, size, and/or area of fibroids are critical

factors of its clinical indications. Typically reported indicators consist of hefty menstruation bleeding, dysmenorrhea, noncyclic ache, urinary symptoms, exhaustion, and constipation. Uterine fibroids are highly common in reproductive-aged females, and as females remain to postpone childbearing, an increasing number of patients will request fertility-preserving treatment alternatives. Medical supervision of uterine fibroids may supply symptomatic alleviation of the uterine fibroid-related symptoms in addition to the opportunity to keep fertility. A large range is currently available and some require additional analysis. Presently, GnRH agonists and SPRMs are the most effective clinical therapies, with one of the most evidence to support their reduction of fibroid quantity and symptomatic renovation in menstruation bleeding. The choice of treatment relies on the patient's individual treatment goals, in addition to efficiency and need for repeated interventions.

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