



A Review of Treatment Options Available for Women with Uterine Fibroids

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Authors' contributions

This work was carried out in collaboration between all authors. Author TCO designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors TCO, CTE and LCI searched literature and reviewed the paper. All authors read and approved the final manuscript.

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ABSTRACT

Background: The quest for ideal treatment and understanding of fibroid biology has resulted in further studies in pharmacological, radiological and surgical options with the goals of being safe, less invasive, cost-effective and enhancing reproductive potentials. However, surgery remains the mainstay of present effective management for large symptomatic fibroids.

Aim: The aim is to review the treatment options available for women with uterine fibroids.

Methods: Publications on the management of uterine fibroids were accessed using medline, google scholar and pubmed databases. Relevant materials on treatment of uterine fibroids, selected references from internet services, journals, textbooks and lecture notes on management of uterine fibroids were also accessed and critically reviewed.

Results: The mainstay of management for large symptomatic fibroids is surgical (myomectomy or hysterectomy). Minimally invasive procedures are becoming more commonly performed via both laparoscopic or hysteroscopic approaches, minimizing recovery time, postoperative pain and

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morbidity. Uterine artery embolization (UAE) carries a risk of pelvic infection with limited evidence regarding the risks for future pregnancies. Levonorgestrel-releasing intrauterine system (LNG-IUS) is effective as a treatment for heavy menstrual bleeding. However, it is not recommended if the uterine cavity is markedly enlarged or distorted by fibroids. Gonadotrophin releasing hormone analogue (GnRHa) is the most widely used medical option. It can reduce the size of fibroids by about 30-35%, but only used for short-term course or preoperative mode of management since the resulting hypoestrogenic state can cause osteoporosis in long-term course.

Furthermore, it can restore haemoglobin levels and apparently reduce blood loss at operation but notorious for rebound growth of fibroids upon cessation of therapy with major adverse effects. Newly introduced treatment options are poorly understood, still unclear with lots of theoretical advantages not fully backed with long-term effects. Little is known about their risks, cost and adverse effects.

Conclusion: Fibroids are commonly found in women of reproductive age. Most women do not require treatment because fibroids are benign and most times asymptomatic. For symptomatic fibroids, many treatment options exist and should be considered before the decision to perform hysterectomy which precludes future fertility.

Keywords: Fibroid; treatment; options; women; myomectomy; hysterectomy.

1. INTRODUCTION

Uterine fibroids or uterine leiomyomata commonly referred to as fibroids are benign smooth muscle tumours commonly found in women of reproductive age in up to 75% of all women [1]. Fibroids are the most common female pelvic tumour of unknown aetiology [2]. Most of the women that harbour fibroids, are asymptomatic and in general, they do not need any treatment [3]. In the past, fibroids were a frequent indication for gynaecological surgery, most commonly hysterectomy [4]. Many hysterectomies were carried out for asymptomatic fibroids but with advances in imaging, diagnosis has improved and enabled more women to be managed conservatively [4]. For those women with symptomatic uterine fibroids that interfere with quality of life, many treatment options exist and must be considered before the decision to perform hysterectomy.

Currently, it is difficult to find out pharmacological agent that will result in fibroid shrinkage and reduce menstrual blood loss while maintaining fertility and oestrogenic state [5,6]. The ideal treatment would be minimally invasive, cost effective, efficacious, tolerable with minimal side effects and have a low incidence of fibroid recurrence [5]. The optimal management for the patient is based on a number of factors: age, desire for future fertility, previous obstetrical performance, location and size of the fibroid, patient's preference and lifestyle [7]. Risks and benefits of each option must be carefully explained. The options available for women with uterine fibroids include observation (watchful

waiting), medical therapy, radiologic therapy and surgical treatment. The quest for ideal management of uterine fibroids has resulted in this review for options available for women with uterine fibroids.

2. METHODOLOGY

A systematic search of literature on the management of uterine fibroids published in English was conducted. Relevant materials on treatment options were selected. Selected references, conference papers, technical reports, journal articles, abstracts, relevant books, lecture notes and internet articles using medline, google scholar, and pubmed databases were critically reviewed.

2.1 Observation

Observation with "watchful waiting" is indicated in women with asymptomatic fibroids and in late perimenopause regardless of their size [8]. The women can be managed expectantly by annual pelvic examination [9]. If assessment of the adnexa is hindered by uterine size or contour, annual sonographic surveillance is advised [10]. A study by the National Institute of Health found the average annual increase in fibroid volume to be 9%, but with a variable change in fibroid size from 25% shrinkage to 138% growth in a single year [11]. Watchful waiting can be considered in late perimenopause because after menopause, bleeding will stop and fibroids will shrink.

2.2 Medical Therapy

In some women with symptomatic fibroids (such as dysmenorrhoea, heavy menstrual bleeding, dyspareunia, pelvic pressure) and infertility, medical therapy may be preferred [12]. Medical therapy avoids complications associated with surgery and permits uterine preservation. However, symptoms usually recur after discontinuation of therapy. Medical treatment is indicated mainly for temporary control of symptoms and preoperative status of the patient. The aim is to reduce the size of the fibroid and improve the haematological status of the patient. The following medications are available for women with symptomatic uterine fibroids:

Oral contraceptives and progesterone only pills are effective for the treatment of abnormal uterine bleeding and dysmenorrhoea but not for uterine fibroids [12,13,14].

2.3 Long Acting Progesterone

Depo-provera 150 mg/month for 6months decreased uterine bleeding in 30-70% of patients [15]. The volume of the fibroid is reduced but the effect is temporary and is not as effective as GnRHa [15,16]. Long term use of depot medroxy- progesterone acetate (MPA) protects against development of fibroids [17].

2.4 Progesterone-releasing Intrauterine Device

Women with fibroid associated heavy menstrual bleeding will benefit from treatment with levonorgestrel-releasing intrauterine system (LNG-IUS). It is associated with a reduction in the amount and duration of menstrual blood loss. It is an effective treatment for dysfunctional uterine bleeding. However, the incidence of spontaneous expulsion is higher in women with submucosal fibroids which may limit its therapeutic use [18]. Therefore, the use of LNG-IUS is considered in women with fibroid-associated heavy menstrual bleeding, where there is no significant cavity distortion or with uterine size <12 weeks gestational size [18].

2.5 Anti-progestin (Mifepristone, RU486)

Mifepristone is a derivative of norethindrone and has both antiprogestone and antiglucocorticoid activities. Mifepristone has proved effective in decreasing fibroid volume and clinical symptoms

[12,19]. Morales et al. [20] reported that mifepristone 25mg daily for three months resulted in 50% decrease in the size of uterine fibroid. Eisinger [21], and Murphy [22] had a similar 50% reduction in fibroid volume in their studies [12]. Compared with GnRHa, its use is associated with less hypoestrogenic side effect [20,21]. Mifepristone therapy is associated with several draw-backs such as vasomotor symptoms, simple hyperplasia and elevation of serum levels of hepatic transaminases in about 4% of women, but these return to normal after discontinuation of the drug [19,21].

2.6 Selective Progesterone Receptor Modulator (SPRM)

SPRM is a new class of progesterone receptor modulators. Preliminary study with SPRM showed that it reduced the duration and amount of uterine bleeding in a dose dependent manner [23]. Such modulators include Ulipristal acetate and Asoprisnil. Oral ulipristal acetate 5 mg daily for more than 13 weeks of treatment, controlled excessive uterine bleeding in at least 90% and was shown to be non-inferior to leuprolide acetate injected monthly over 3 months [23]. The incidence of hot flushes was significantly lower than for women given leuprolide acetate.

2.7 Selective Estrogen Receptor Modulators (SERM)

Raloxifene is one of the SERMS evaluated in women with uterine fibroids. In postmenopausal women, it reduces the volume of the fibroid [6,24]. However, due to the spontaneous shrinkage in fibroid after menopause and for the fact that evidence was insufficient to show any improvement in fibroid size or clinical symptoms and its associated significant side effects, it might not be relevant clinically [6,24-26].

2.8 Aromatase Inhibitors

Aromatase inhibitors inhibit the conversion of androgen to oestrogen. Aromatase inhibitors only appear to be effective in postmenopausal women. They have significant long-term side effects and experience with their use is also limited [6].

2.9 Gestrinone

Few studies have shown that gestrinone treatment leads to a reduction in uterine fibroid of

up to 40% [27]. However, it is associated with significant androgenic side effects and not compatible with reproduction.

2.10 Danazol

Danazol is an isoxazole derivative of 17 alpha ethinyl testosterone (ethisterone). It has multiple effects at different levels of the hypothalamic-pituitary-ovarian axis by binding to intracellular steroid receptors for androgens, progesterone, and glucocorticoids. It reduces the volume of fibroids by 23.6% and improves uterine bleeding but its use is limited by the side effects of acne, hirsutism, and weight gain and are not compatible with reproduction [6,28-29].

2.11 GnRH Agonists

GnRHa is the most effective and widely used medical treatment for uterine fibroids [5,6]. These compounds are synthetic derivatives of the GnRH decapeptide. Amino acid substitution makes them resistant to degradation, thereby increasing their half-life and resulting in prolonged receptor binding. They are inactive when taken orally, but intramuscular, subcutaneous and intranasal routes are available. Examples are Triptorelin, Leuprolide acetate, Goserelin and Nafarelin. These agents initially stimulate receptors on pituitary gonadotropes to cause a supraphysiologic release of both luteinizing hormone (LH) and follicle stimulating hormone (FSH). The initial stimulation of receptors on pituitary gonadotropes to cause a supraphysiologic release of both LH and FSH is called a "flare". This phase lasts 1week. With their long-term action, however, agonists down regulate receptors in gonadotropes, thus creating desensitization to further GnRH stimulation. Decreased gonadotropin secretion leads to suppressed oestrogen and progesterone levels one to two weeks after initial GnRHa administration [30]. Another possible mechanism is that fibroids themselves may contain GnRH receptors, and agonists may directly decrease fibroid size [31].

Treatment with GnRH agonist induces amenorrhoea and shrinkage of fibroids, thus avoidance of midline incisions at laparotomy and rendering vaginal hysterectomy more likely [32]. These changes are secondary to temporary ovarian suppression and long-term treatment with GnRHa is contraindicated due to the risk of

bone loss. Most authors recommend treatment for a total of 3 to 6 months.

Currently, the role of GnRH agonist is largely limited to preoperative shrinkage of fibroids except with the addition of hormonal add-back therapy for their long term use [4,33]. GnRH agonists have been shown to reduce uterine volume by 35% and bleeding in 95% of women [34]. One non randomized, controlled study [35] reported a significant reduction in operating time, blood loss, volume of distending medium and treatment failure following pre-treatment with a GnRH agonist. Massive fibroids can be reduced in size and morbidity with use of GnRH agonist and thus, easily removed vaginally, laparoscopically, hysteroscopically, or through a smaller more cosmetic incision [36,37]. Enucleation of GnRH agonists treated fibroids is said to be difficult because the capsules are thinner and not well delineated [37]. GnRH agonists have significant costs, risks and side effects (pseudomenopause, vasomotor symptoms, bone resorption) [4,5,38]. Because of the limitations of GnRH agonist therapy, the American College of Obstetricians and Gynecologists [9] (ACOG) currently recommends it only as a temporizing agent in women nearing menopause or as a surgical pretreatment in selected women.

2.12 GnRH Antagonists

GnRH antagonist acts by competitive binding of the GnRH receptors. Their profound hypoestrogenic effects are similar to those of GnRH agonists but they are not associated with an initial "flare up phenomenon" and have a more rapid action [5,12,39]. In spite of its faster effect than that of GnRH agonist, GnRH antagonist is not widely used for uterine fibroid due to the requirement of daily treatment. Daily subcutaneous injection of GnRH antagonist ganirelix results in a 29% reduction in fibroid volume within 3 weeks [40]. If longer acting GnRH antagonists becomes available, preoperative treatment with GnRH antagonist would be preferable [41].

2.13 Alternative Medicine Treatment

Published and circulated studies on alternative medicine treatments have been non-randomized, non-blinded and small. A study with traditional Chinese medicine reported a failure in fibroid growth or shrank in 59% of patients after 6 months of treatment when compared with 8% of

control [42]. In another study with traditional Chinese medicine, heavy menstrual bleeding declined in 95% and dysmenorrhoea improved in 94% [43].

2.14 Radiologic Therapy

2.14.1 Uterine Artery Embolization (UAE)

This is an angiographic interventional procedure that delivers polyvinyl alcohol (PVA) microspheres or other particulate emboli into both uterine arteries. An angiographic catheter is placed in either femoral artery and advanced under fluoroscopic guidance to selectively catheterize both uterine arteries. Uterine blood flow is therefore obstructed resulting in ischaemia and necrosis. Uterine artery embolization (UAE) is effective for uterine fibroids symptoms. In a study of 538 women after UAE, Pron and associates found a clinical success rate of 80% for bleeding and pain and 91% for patient satisfaction [44]. UAE is associated with shorter hospital stays and quicker postoperative recovery than hysterectomy. However, rates of readmission and further treatment for bleeding are higher with UAE [45-47]. Long term data following UAE are limited. The ACOG [48] currently recommends UAE for short-term relief of bleeding or pressure symptoms. Contraindications for UAE are women who would not accept hysterectomy even for a life threatening complication. Others are active genital infection, genital tract cancer, compromised immune status, allergy to intravenous contrast, impaired renal function and severe vascular disease limiting access to the uterine arteries. Complications observed in women during pregnancy subsequent to UAE are preterm delivery, malpresentation and increased incidence of abnormal placentation [44,49]. Due to lack of long-term outcome data, women who desire future child bearing are not currently considered for UAE [48,50-52]. The ACOG recommends that women who are considering UAE have a thorough evaluation with gynecologist to facilitate collaboration with an interventional radiologist and that responsibility for patient care be clear [53].

2.14.2 Magnetic Resonance Imaging (MRI) guided Focused Ultrasound (MRI-FUS)

MRI-FUS is an outpatient-based treatment that is technically feasible, reproducible and significantly reduces symptoms in more than 75% of women treated with fibroids [54]. It is the therapeutic use

of ultrasound waves to induce focal thermal effects, ablation or thermo-coagulation in vivo. Recently, a combination of diagnostic ultrasound guidance and therapeutic high intensity focused US (HIFU) made soft tissue targeting and sonication possible [55]. Patients with symptomatic fibroids undergo a thorough clinical assessment evaluation including history, physical examination (special attention to lower abdominal wall scar), and assessment of her clinical symptoms. A validated symptom severity questionnaire (a useful tool for establishing a baseline and for monitoring treatment response) can be objectively performed for the assessment of her clinical symptoms. All women should also be screened for MR incompatibility and to rule out those who have contraindications to MR examination such as cardiac pacemaker implantation, metallic implants like Berry aneurysm chips, incompatibility with MR, severe claustrophobia and pregnancy [54]. To ensure a safe procedure, the woman should be able to lie prone on the MR table for about 3 hours and communicate sensation during the procedure. Pre-procedure pelvic MRI is done to confirm the diagnosis of fibroids, rule out adenomyosis, and assess the fibroid number, size, location, tissue character and enhancement characteristics. For large fibroids, pre-treatment with GnRH agonists allows shrinkage and shortens treatment times. Thus, GnRH agonist treatment prior to MRI-FUS will increase efficacy [56]. The rate of adverse effects is generally low which include mild skin burn, nausea, short-term buttock or leg pain and transient sciatic nerve palsy [57-59]. The procedure has few major adverse effects such as full thickness burns of the abdominal wall [12,60]. The advantages of MRI-FUS, are very low morbidity and very rapid recovery however, currently, the procedure is not recommended for women wishing future fertility. The current FDA stand on MRI-FUS is that the device should be limited only to those who have completed their family size. Further efficacy and safety studies are needed for this procedure [61].

2.14.3 Surgical treatment

Surgery is the conventional treatment of uterine fibroid. Surgery is the mainstay of present management for large symptomatic fibroids [7]. Surgical treatment options currently include hysteroscopic myomectomy, abdominal myomectomy, laparoscopic myomectomy, endometrial ablation and hysterectomy and myolysis.

2.14.4 Myomectomy (abdominal, laparoscopic, hysteroscopic)

Myomectomy is the standard conservative surgical treatment for women who wish to retain their fertility. It is the traditional procedure. Myomectomy can be performed laparoscopically. This procedure was developed by the desire to create a minimally invasive approach that would avoid a major laparotomy. Minimally invasive abdominal procedures offer many advantages over open techniques. When comparing laparotomy, mini-laparotomy, and laparoscopic-assisted mini-laparotomy for myomectomy, they all showed similar operating times [62]. Laparoscopic assisted mini-laparotomy, however, offered a reduced time of paralytic ileus and quicker discharge from hospital [62]. Laparoscopic myomectomy has also been shown to result in reduced post operative pain and requirements for analgesia compared with laparotomy in the first 3 days after surgery [63]. However, open myomectomy is sometimes the procedure of choice where uterine fibroid is large and fertility is desired [64]. A recent prospective trial that compared the triple tourniquet technique (applied to uterine and ovarian vessels) to temporary occlude uterine blood supply at the time of surgery with pre-operative gonadotrophin releasing hormone analogue has shown that the triple tourniquet technique is more effective in reduced intra-operative blood loss to a minimum and reducing morbidity for the patient [65]. Submucous myomectomy is performed by hysteroscopy while intramural or subserous fibroid is performed by laparoscopy or laparotomy [66,67]. Hysteroscopic myomectomy is now the standard minimally invasive surgical procedure for treating submucosal fibroids that are thought to contribute to abnormal uterine bleeding or infertility [68]. It is safe and effective, avoids a scar and opening the uterine cavity [69]. A recent study found that hysteroscopic myomectomy for submucous fibroids in women with unexplained primary infertility improved pregnancy rates [70]. The most common complications are uterine perforation, false cervical canal and excessive absorption of distension media [71,72].

2.14.5 Hysterectomy

This is most common and definitive surgical treatment for uterine fibroids [12]. Hysterectomy for uterine fibroid can be performed vaginally, abdominally or laparoscopically. However laparoscopic hysterectomy requires special skills and training [73]. Many studies have shown the

safety and efficacy of laparoscopic hysterectomy [5,73]. A study of 418 women undergoing hysterectomy for benign gynaecologic conditions [74] found hysterectomy for women with symptomatic fibroids resulted in satisfaction rates greater than 90%. There were marked improvements in pelvic pain, urinary symptoms, fatigue, psychological symptoms and sexual dysfunction [74].

2.14.6 Myomectomy versus hysterectomy

Traditionally, hysterectomy was reserved for women who have completed their family size. It was thought that hysterectomy carried a greater risk for perioperative morbidity than myomectomy. However, with advances in operative exposure, hysterectomy has been shown to be effective and carry perioperative risks comparable with myomectomy. In some studies, blood loss, intraoperative injuries, and morbidity were similar [75]. Postoperative intra-abdominal adhesions and recurrence of uterine fibroids are more common after myomectomy than with hysterectomy [76].

2.14.7 Uterine artery ligation

Bilateral uterine artery ligation is a safe and effective procedure for the treatment of symptomatic uterine fibroids especially in areas where access to high level medical technology is restricted [77]. The mean fibroid volume, mean uterine volume, and mean menstrual pain rating showed statistically significant reductions at six, 12, and 36 months following trans-vaginal bilateral uterine artery ligation for the treatment of uterine fibroids in fifty women at LASUTH, Ikeja, Lagos, Nigeria. The mean haemoglobin level and patients' satisfaction rating showed a statistically significant increase after six, 12, and 36 months [77].

2.14.8 Endometrial ablation

Endometrial ablation is effective for women with dysfunctional bleeding but when used as a sole technique for uterine fibroid related bleeding, the failure rate approaches 40% [78]. Endometrial ablation is also used as an adjunct to hysteroscopic fibroid resection in women with abnormal uterine bleeding.

2.14.9 Cryotherapy

Uterine fibroid coagulation or myolysis has been advocated. A number of techniques are available to induce fibroid necrosis and shrinkage such as

mono or bipolar cautery, laser vaporization or cryotherapy. These techniques are used laparoscopically and consume a lot of operating time, incite variable degree of necrosis within the fibroid and surrounding normal myometrium with resultant significant postoperative pain, fever and abscess formation [79]. However, this procedure is associated with adhesion formation and possible uterine rupture in pregnancy. Prophylactic antibiotics administration is recommended. Follow-up studies showed variable results with volume reduction of fibroids ranging from 31%-80% [80]. This has led to most gynaecologists abandoning cryotherapy [81,82].

2.14.10 Radiofrequency Ablation (RFA)

RFA is a minimally invasive procedure for control of local tumors. It was first used in 2005 in the management of uterine fibroid via surgical laparoscopic approach [83], subsequently with ultrasound guidance [84,85]. This ablation of fibroid tumor results from heating which causes coagulation necrosis of local tissue. A large area of necrosis can be achieved in a single access with RFA. RFA when compared with cryotherapy, it is relatively time efficient. However, due to the incompatibility of RFA to magnetic resonance [86], the currently used image guiding modalities for RFA are ultrasound or CT. RFA while good for lesion targeting, is unable to provide accurate temperature monitoring [54]. The real ablation area could not be seen during the treatment, and thermal mapping is now possible [54]. More recent volumetric techniques in concert with sonography, minimize the need for multiple punctures through fibroids; in the case of transcervical or transvaginal radiofrequency ablation, the serosa is entirely avoided [85,87,88].

2.14.11 Role of vitamin D in treatment of uterine fibroids

Fibroids are four times more likely to affect African-American women [89]. Studies have shown that vitamin D deficiency can promote fibroid growth and African-American women are particularly susceptible to vitamin D deficiency [89]. In a recent study by Baird et al. [90], women with adequate vitamin D levels are 32% less likely to develop uterine fibroids [90]. In this study, circulating levels of vitamin D (25-hydroxy D) were measured using blood samples. Women who have more than 20 nanograms/ml were accepted as having sufficient levels of the

vitamin. Those women who spent more than one hour outside per day had a decreased risk of fibroids with an estimated reduction of 40%. Fibroids are more common in black women and black women also tend to have lower levels of vitamin D as skin pigmentation reduces the formation of vitamin D in their skin [89].

Researchers noted that treatment of cultures of human uterine fibroid tissue with a form of vitamin D resulted in decreased cell proliferation accompanied by inhibition of molecular pathways for fibrosis. Thus vitamin D was found to play active role in slowing the growth of fibroid tissue. There is need for further studies on the role of vitamin D in treatment of uterine fibroid.

2.14.12 Role of green tea in treatment of uterine fibroids

Green tea extract has a significant positive effect in the reduction of uterine fibroid burden in both weight and size and symptom severity [91,92]. Recent studies by Zhang et al. [93] and Roshdy et al. [92] found that epigallocatechin inhibits the proliferation of HuLM cells (fibroid cells) and induces apoptosis. Thus, the green tea extract may be potential anti-uterine agent acting through multiple signal transduction pathways. Tea extracts are best absorbed when taken on an empty stomach. The subjects that used green tea extracts for 4 months experienced significant shrinkage in their total fibroid volume, significant reduction in symptom severity and significant consistent improvement in their quality of life. Thus, oral administration of green tea could possibly be an effective treatment for uterine fibroid. However, this requires larger multicentre trials confirmation [92]. Green tea is not approved by FDA and is therefore not recommended for treatment of uterine fibroid.

2.15 Controversies

Controversies exist regarding the natural course of untreated fibroids, uterine fibroid and infertility, the efficacy of medical management, unresolved questions regarding surgery and myomectomy at caesarean section.

The aetiology of fibroid is poorly understood. The genetic basis of fibroid development or the molecular mechanism of myometrial proliferation is poorly understood and still unclear, and the non-surgical therapeutic intervention that will be ideal for fibroid treatment is still awaited. The clinicians are then challenged with the following

(a) to determine an effective prevention strategy in genetically predisposed individuals. (b) To slow the growth of fibroid. (c) To identify the mechanism of infertility. (d) To improve early detection. (e) To develop better surgical techniques. (f) To reduce recurrence after myomectomy and to evaluate their long term results [94].

Women with unexplained infertility may present with fibroid as an incidental finding. This is often regarded as a cause of infertility because it has been postulated that fibroid may cause infertility by mechanical means. That is by alteration of normal transport of gametes or embryos through the genital tract. Also, it may alter the normal pattern of uterine contractility and uterine receptivity [5,95,96]. From studies, it is assumed that all types of myomectomy (laparoscopy, laparotomy or hysteroscopy) increase pregnancy rates. However, fertility enhancing effects of removal of intramural fibroids remains unclear.

Further questions in the management of fibroids include the role of fibroids in infertility. Do fibroid cause infertility? Should women with infertility who have fibroids as incidental finding at ultrasound be offered myomectomy? It is very clear that submucous fibroids are associated with infertility while subserous fibroids hardly interfere with fertility.

A lot of therapies are currently available for women with uterine fibroid with their merits and demerits. The alternatives to the traditional hysterectomy are newly introduced and poorly studied. Little is known about their risks, cost and adverse effects. There are lots of theoretical advantages not fully backed with long-term follow up effects [94].

A number of newly introduced surgical options for treatment of fibroids are being explored. Some are poorly understood with a lot of complications and not safe on humans. Short term results may be good but long term effects not properly guaranteed. Overall data are extremely limited and larger prospective studies are needed [97].

Myomectomy is generally contraindicated during caesarean section. This is due to excessive bleeding intraoperatively. However, with the effective use of tourniquet it is possible to perform myomectomy in selected cases during caesarean section [94].

Traditionally, women who had their endometrium breached during myomectomy, should be delivered by Caesarea section. However, there are instances where such women had normal vaginal deliveries without complications. It is well known that healing of a non-pregnant uterus produces a scar of better integrity than that of a pregnant uterus [37]. The healing of the pregnant uterus may be impaired by the retractile contractions of the involuting uterus resulting in a weaker scar with possibility of subsequent rupture during labour [37].

In African tradition, certain cultures may be a hindrance to hysterectomy. The acceptance rate for hysterectomy among African women is relatively low [98]. Women refuse hysterectomy to preserve their uteri and menstrual function for cultural and religious reasons. Our women treasure their uterus so much that they are not ready to part with this God given organ. The reason for this is that in African tradition, marriage is revered and respected [99]. Any marriage without a child is viewed with contempt [99]. However, hysterectomy is associated with depression and altered self image [100,101].

3. CONCLUSION

Uterine fibroid or uterine leiomyomata commonly referred to as fibroids are benign smooth muscle tumours commonly found in women of reproductive age. Fibroids impact negatively on women's health and quality of life and have significant cost implications for their management. The aetiology is unknown and most times they are asymptomatic. For asymptomatic fibroids, no treatment is required while in symptomatic fibroids, many treatment options exist. The current mainstay of management for large symptomatic fibroids are surgical (myomectomy or hysterectomy). Newly introduced treatment options are poorly understood, still unclear with lots of theoretical advantages not fully backed with long term effects. Little is known about their risks, cost and adverse effects. Hysterectomy is the definitive surgical treatment for uterine fibroids. However, other options should be considered before the decision to perform hysterectomy which precludes future fertility whereas the impact of the other treatments on reproduction is uncertain.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Lee HJ, Norwitz ER, Shaw J. contemporary management of fibroids in pregnancy, *Rev. Obstet Gynecol.* 2010;3:20-27.
2. Levy BS. Modern management of uterine fibroids (Journal Articles, review) *Acta Obstet Gynecol Scand.* 2008;87(8):812-823.
3. Tulandi T. Uterine fibroids. Embolisation and other treatments. Cambridge University Press, London; 2003.
4. West CP. Uterine fibroids and Menorrhagia. In: Luesley DM, Baker PN (eds) *obstetrics and gynaecology: An evidence based text for MRCOG*, London Arnold. 2004;526-531.
5. Tulandi T, Kabli N. Update on management of uterine fibroid. Department of obstetrics and gynaecology, McGill University, Montreal, Quebec, Canada; 2011.
6. Sankaran S, Manyonda IT. Medical management of fibroids. *Best Pract Res Clin Obstet Gynaecol.* 2008;22(4):655-676.
7. Munro KI, Critchley HOD. Advances in the management of uterine fibroids. *F1000 Medicine Reports* 2009;1:74. DOI:10.34 10/M1-74.
8. Parker WH, Fu YS, Berek JS. Uterine sarcoma in patients operated on for presumed leiomyoma and rapidly growing leiomyoma. *Obstet Gynecol.* 1994;83:414-418.
9. American College of Obstetricians and Gynecologists committee on practice bulletin's-gynecology: ACOG practice bulletin. Surgical alternatives to hysterectomy in the management of leiomyomas, May 2000. *Int J Gynaecol Obstet.* 2001;73(16):285.
10. Guarnaccia MM, Rein MS. Traditional surgical approaches to uterine fibroids: Abdominal myomectomy and hysterectomy. *Clin Obstet Gynecol.* 2001;44:385.
11. Peddada SD, Laughlin SK, Miner K, et al. Growth of uterine leiomyomata among premenopausal black and white women. *Proc Natl Acad Sci USA.* 2008;105:19887-19892.
12. Hoffinan BL. Pelvic Mass. In: Schorge JO, Schaffar JI, Halvorson LM, Hoffman BI, Bradshaw KD, Cunningham FG.(eds). *Williams Gynecology, Access Medicine Section 1-Benign Gynecology*, chapter 9 Pelvic Mass, McGraw Hills; 2008.
13. 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;85:631.
14. Orsini G, Laricchia L, Fanelli M. (low-dose combination oral contraceptive use in women with uterine leiomyomas). (Italian). *Minerva Ginecologica.* 2002;54:253.
15. Venkatachalam S, Bagratee JS, Moodley J. Medical management of uterine fibroids with medroxyprogesterone acetate (Depo-Provera): A pilot study. *J Obstet Gyneacol* 2004;24:798-800.
16. Johnson N, Fletcher H, Raid M. Depo Medroxy Progestrone Acetate (DMPA) therapy for uterine myomata prior to Surgery-Int *J Gynaecol Obstet.* 2004;85:174-176.
17. Lumbiganon P, Rugsao S, Phandhu-Fung S, Laopaiboon M, Vudhika-mraksa N, Werawatakul Y. Protective effect of depot medroxyprogesterone acetate on surgically treated uterine leiomyomas: A multicentre case control study. *BJOG.* 1995;103:909-914.
18. Mercorio F, et al. The effect of a levonorgestrel-releasing intrauterine device in the treatment of myoma-related menorrhagia. *Contraception.* 2003;67:277-280.
19. Steinauer J, Pristts EA, Jackson R, et al. Systematic review of mifeprostone for the treatment of uterine leiomyoma. *Obstet Gynecol.* 2004;103:1331.
20. Morales AJ, Kettel LM, Murphy AA. Mifepristone: Clinical application in general gynecology. *Clin Obstet Gynecol.* 1996;39:451-460.
21. Eisinger SH, Meldrum S, Fiscella K, et al. Low dose mifepristone for uterine leiomyomata. *Obstet Gynecol.* 2003;101:243-250.
22. Murphy AA, Kettel LM, Morales AJ, et al. Regression of uterine leiomyomata in

- response to the antiprogestosterone RU486. *J Clin Endocrinol Metab.* 1993;76:513.
23. Croxtall JD. Ulipristal acetate: In uterine fibroids. *Drugs.* 2012;72:1075-1085.
 24. Walker CL. Role of hormonal and reproductive factors in the etiology and treatment of uterine leiomyoma. *Recent Prog Hormone Res.* 2002;57:277-294.
 25. Palomba S. Long-term effectiveness and safety of GnRH agonist plus Raloxifene administration in women with uterine leiomyomas. *Hum Reprod* 2004;6:1308-1314.
 26. Wu T, Chen X, Xie L. Selective Estrogen Receptor Modulators (SERMS) for uterine leiomyomas. *Cochrane Database of Systematic Reviews;* 2007.
 27. La Marca A. et al. Gestrinone in the treatment of uterine leiomyomata: Effects on uterine blood supply. *Fertil Steril.* 2004;82:1694-1696.
 28. De Leo V, LaMarca A, Morgante G. short term treatment of uterine fibromomas with danazol. *Gynecol Obstet Invest.* 1999;47(4):258.
 29. Brown WW III, Coddington CC III. Expectant and medical management of uterine fibroids. In uterine fibroids. Embolization and other treatments (Ed. T. Tulandi), Cambridge University Press, London; 2003.
 30. Broekmans FJ. GnRH agonists and uterine leiomyomas. 1996;11(suppl 3):3.
 31. Parker WH: Etiology, symptomatology, and diagnosis of uterine myomas, *Fertil Steril.* 2007;87:725-736.
 32. Lethaby A, Vollenhoven B, Sowter M. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. *Cochrane Database Syst Rev* 2001;(2):CD000547.
 33. Pierce SJ, Gazvani MR, Farguharson RG. Long-term use of gonadotropin releasing hormone analogues and hormone replacement therapy in the management of endometriosis: Randomized trial with a 6-year follow up. *Fertil Steril.* 2000;74:964-968.
 34. Schlaff WD, Zerhouni EA, Huth JA, Chen J, Damewood MD, Rock JA. A placebo-controlled trial of a depot gonadotropin-releasing hormone analogue (leuprolide) in the treatment of uterine leiomyomata. *Obstet Gynecol.* 1989;74:856-862.
 35. Perino A, Chianchino N, Petronio M, Ciltadini E. The role of leuprolide acetate depot in hysteroscopic surgery: A controlled study. *Fertil Steril.* 1993;59:507-510.
 36. Crosignani PG, Vercellini P, Meschia M, et al. GnRH agonists before surgery for uterine leiomyomas. A review: *J Reprod Med.* 1996;41:415.
 37. Ogedengbe OK. Uterine fibroids. In: Okonofua F, Odunsi K (eds). *Contemporary obstetrics and gynaecology for developing countries.* WHARCS, Benin City. Intec printers Ltd. 2003;202-213.
 38. Scharla SH, Minne HW, Waibel-Treber S, et al. Bone mass reduction after estrogen deprivation by long-acting gonadotropin-releasing hormone agonists and its relation to pretreatment serum concentrations of 1,25-dihydroxy vitamin D3. *J Clin Endocrinol Metab.* 1990;70:1055.
 39. Kettel LM, Murphy AA, Morales AJ, et al. Bone mass reduction after estrogen deprivation by long-acting gonadotropin releasing hormone antagonist. *Fertil Steril.* 1993;60:642.
 40. Flierman PA, Oberye JJ, vander Hulst VP, deBlok S. Rapid reduction of leiomyoma volume during treatment with the GnRH antagonist ganirelix. *BJOG.* 2005;112:638-642.
 41. Parker WH. Managing uterine fibroids: Alternatives to hysterectomy. *Medscape Obstetrics and Gynecology.* Posted 07/20/2012.
 42. Mehl-Mdrona L. Complementary medicine treatment of uterine fibroids: A pilot study. *Altern Ther Health Med.* 2002;8:34-36,38-40,42,44-46.
 43. Sakamoto S. Yoshino H, Shirahata Y, Shimodairo K, Okamoto R, Pharmacotherapeutic effect of kuei-chih-fu-ling-wan (Keishi-bukuryo-gan) on human uterine myomas. *Am J Chin Med.* 1992;20:313-317.
 44. Pron G, Mocarski E, Bennett J, et al. Pregnancy after uterine artery embolization for leiomyomata: The Ontario multicentre trial. *Obstet Gynecol.* 2005;105:67-76.
 45. Pinto I, chimeno P, Romo A, et al. Uterine fibroids: Uterine artery embolization versus abdominal hysterectomy for treatment: A prospective, randomized and controlled clinical trial. *Radiology.* 2003;226:425.
 46. Hehenkamp WJ, Volkers NA, Donderwinkel PF, et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): Peri and postprocedural

- results from a randomized controlled trial, *Am J Obstet Gynecol.* 2005;193:1618-1629.
47. Edward RD, Moss JG, Lumsden MA, et al. Committee of the randomized trial of embolization versus surgical treatment for fibroids. Uterine artery embolization versus surgery for symptomatic uterine fibroids. *N Engl Med.* 2007;356(4):360-370.
 48. Walker WJ, Pelage JP. Uterine artery embolisation for symptomatic fibroids. Clinical results in 400 women with imaging follow-up. *Br J Obstet Gynaecol.* 2002;109:1262-1272.
 49. Goldberg J, Pereira L, Berghella V, et al. Pregnancy outcomes after treatment for fibromyomata: Uterine artery embolisation versus laparoscopic myomectomy. *Am J Obstet Gynecol.* 2003;191:18-21.
 50. Mickey M, Hammond I. What is the place of uterine artery embolisation in the management of symptomatic uterine? *Aust NZJ Obstet Gynaecol.* 2008;48:360-368.
 51. NHS. National Institute of Clinical Excellence: Uterine artery embolisation for the treatment of fibroids. *Interventional Procedure Guidance.* 2004;94.
 52. Spies JB, Cooper JM, Worthington-Kirsch R, et al. Outcome of uterine embolization and hysterectomy for leiomyomas: Results of a multicenter study. *Am J Obstet Gynecol.* 2004;191:22-31.
 53. ACOG. Committee of gynecologic practice: ACOG Committee Opinion uterine artery embolization. *Obstet Gynecol.* 2004;103:403-404.
 54. Shen S, Fennessy F, McDannold N, Jolesz F, Tempny C. Image-guided thermal therapy of uterine fibroids. *Semin Ultrasound CT MR.* 2009;30(2):91-104.
 55. Dubinsky TJ, Cuevas C, Dighe MK, et al. High-intensity focused ultrasound: Current potential and oncologic applications. *AJR Am J Roentgenol.* 2008;190(1):191-199.
 56. Smart OC, Hindley JT, Regan L, et al. Gonadotrophin-releasing hormone and magnetic-resonance-guided ultrasound surgery for uterine leiomyomata. *Obstetrics & Gynecology.* 2006;108(1):49-54.
 57. Mikami K, Murakami T, Okada A, et al. Magnetic resonance imaging-guided focused ultrasound ablation of uterine fibroids: Early clinical experience. *Radiat Med.* 2008;26:198-205.
 58. Funaki K, Fukunishi H, Funaki T, et al. Magnetic resonance-guided focused ultrasound surgery for uterine fibroids: Relationship between the therapeutic effects and signal intensity of preexisting T2-weighted magnetic resonance images. *Am J Obstet Gynecol.* 2007;196:184.e1-184.e6.
 59. Fennessy F, Tempny CM, McDannold N, et al. MRI-guided focused ultrasound surgery of uterine leiomyomas: Results of different treatment guideline protocols. *Radiology.* 2007;243:885-893.
 60. Chan AH, et al. An image guided high intensity focused ultrasound device for uterine fibroids treatment. *Med Physic* 2002;29:2611-2620.
 61. Cowan BD. Myomectomy and MRI directed cryotherapy. *Sem Reprod Med* 2004;22:143-148.
 62. Cagnacci A, Pirillo D, Malmusi S, Arangino S, Alessandrini C, Volpe A. Early outcome of myomectomy by laparotomy, minilaparotomy and laparoscopically assisted minilaparotomy. A randomized prospective study. *Hum Reprod.* 2003;18:2590-2594.
 63. Holzer A, Jirecek ST, Illievick UM, Huber J, Wenzl RJ. Laparoscopic versus open myomectomy: A double-blind study to evaluate postoperative pain. *Anaesth Analg.* 2006;102:1480-1484.
 64. Seracchioli R, Rossi S, Govani F, Rossi E, Venturoli S, Bulletti C, Flamigni C. Fertility and obstetric outcomes after laparoscopic myomectomy of large myomata: A randomized comparison with abdominal myomectomy. *Hum Reprod.* 2000;15:2663-2668.
 65. Al-shabibi N, Chapman L, Madari S, Papandimitriou A, Papalampros P, Magos A. Prospective randomized trial comparing gonadotrophin-releasing hormone analogues with triple tourniquets at open myomectomy. *BJOG.* 2009;116:681-687.
 66. Benard G et al. Fertility after hysteroscopic myomectomy. *Eur J Obstet Gynecol Reprod Biol.* 2000;88:85-90.
 67. Seidman DS, Nezhat CH, Nezhat F, Nezhat C. Laparoscopic management of uterine myoma. In uterine fibroids. Embolization and other treatments (Ed.T.Tulandi), Cambridge University Press, London; 2003.
 68. Pritts EA, Parker WH, Olive DL. Fibroids and Infertility: An updated systematic review of the evidence. *Fertile Steril.* 2009;91:1215-1223.
 69. Di Spiezio Sardo A, Mazzon I, Bramante S, Bettocchi S, Bifulco G, Guida M, Nappi C.

- Hysteroscopic myomectomy: A comprehensive review of surgical techniques. *Hum Reprod Update*. 2008;14:101-119.
70. Shokeir T, El-Shafei M, Yousef H, Allam AF, Sadek E. Submucous myomas and their implications in the pregnancy rates of patients with otherwise unexplained primary infertility undergoing hysteroscopic myomectomy: A randomized matched control study. *Fertil Steril*; 2009. (Epub ahead of print).
 71. Jansen FW, Vredevoogd CB, Van Ulzen K et al. Complications of hysteroscopy: A prospective multicenter study. *Obstet Gynecol*. 2006;96:266-270.
 72. Propst AM, Liberman RF, Harlow BL, et al. Complications of hysteroscopic surgery: Predicting patients at risk. *Obstet Gynecol*. 2000;96:517-520.
 73. Sarmini OR, Lefholz K, Froeschke HP. A comparison of laparoscopic supracervical hysterectomy and total abdominal hysterectomy outcomes. *J Min Inv Gynecol*. 2005;12:121-124.
 74. Carlson KJ, Miller BA, Fowler FJ Jr. The maine women's health study: II. Outcomes of nonsurgical management of leiomyomas, abdominal bleeding and chronic pelvic pain. *Obstet Gynecol*. 1994;83:566-572.
 75. Sawin SW, Pilevsky ND, Berlin JA, Barnhart KT. Comparability of perioperative morbidity between abdominal myomectomy and hysterectomy for women with uterine leiomyomas. *Am J Obstet Gynecol*. 2000;183:1448-1455.
 76. Stricker B, Blanco J, Fox HE. The gynecologic contribution to intestinal obstruction in females. *J Am Coll Surg*. 1994;178:617.
 77. Akinola OI, Fabamwo AO, Akinola RA, Ottun TA, Akinniyi A, Akpan AE. Uterine artery ligation for the treatment of fibroids. *Acta Obstet Gynecol Scand*. 2009;88(1):59-62.
 78. Yin CS, Wei RY, Chao TC, et al. Hysteroscopic endometrial ablation without endometrial preparation. *Int J Gynaecol Obstet*. 1998;62:167.
 79. Sakuhara Y, Shimizu T, Kodama Y, et al. Magnetic resonance-guided percutaneous cryoablation of uterine fibroids: Early clinical experiences. *Cardiovascular Intervention Radiol*. 2006;29:552-555.
 80. Pease GR, Wong ST, Roos MS, et al. MR image-guided control of cryosurgery. *J Magn Reson Imaging*. 1995;5:753-760.
 81. Goldfarb HA. Myoma coagulation (myolysis). *Obstet Gynecol Clin North Am*. 2000;30:421-427.
 82. Dubuission JB, et al. Reproductive outcome after laparoscopic myomectomy in infertile women. *J Reprod Med*. 2000;45:23-30.
 83. Milic A, Asch MR, Hawrylyshyn PA, et al. Laparoscopic ultrasound-guided radiofrequency ablation of uterine fibroids. *Cardiovasc Intervent Radiol*. 2006;29:694-698.
 84. Recaldini C, Carrafiello G, Lagana D, et al. Percutaneous sonographically guided radiofrequency ablation of medium sized fibroids: Feasibility study. *AJR Am J Roentgenol*. 2007;189:1303-1306.
 85. Cho HH, Kim JH, Kim MR. Transvaginal radiofrequency thermal ablation: A day-care approach to symptomatic uterine myoma. *Australian and New Zealand Journal of Obstetrics and gynaecology*. 2008;48:296-301.
 86. Fry WJ, Fry FT. Fundamental neurological research and human neurosurgery using intense ultrasound. *IRE Trans Med Electron*. 1960;ME-7:166-181.
 87. Kim CH, Kim SR, Lee HA. Transvaginal ultrasound-guided radiofrequency myolysis for uterine myomas. *Human Reproduction*. 2011;26(3):559-563.
 88. Carrafiello G, Recaldini C, Fontana F, et al. Ultrasound-guided radiofrequency thermal ablation of uterine fibroids: Medium term follow-up, *Cardiovascular and Interventional Radiology*. 2010;33(1):113-119.
 89. Harris S. Vitamin D and African Americans. *Am Soc Nutr*. 2006;136(4):1126-1129.
 90. Baird D, et al. Vitamin D and the risk of uterine fibroids. *Epidemiology*. 2013;24(3):447-453.
 91. Zhang D, Al-Hendy M, Richard-Davis G, Montgomery-Rice V, Sharan C, Rajaratnam V, et al. Green tea extract inhibits proliferation of uterine leiomyoma cells in vitro and in nude mice. *Am J Obstet Gynecol*. 2010;202(3):289.e1-9.
 92. Roshdy E, Rajaratnam V, Maita S, Sabry M, Allah ASA, Al-Hendy A. Treatment of symptomatic uterine fibroids with green tea extract: A pilot randomized controlled clinical study. *Int J Womens' Health* 2013;5:477-486.

93. Zhang D, Al-Hendy M, Richard-Davis G, Montgomery-Rice V, Rajaratnam V, Al-Hendy A. Anti proliferative and proapoptotic effects of epigallocatechin gallate on human leiomyoma cells. *Fertil Steril*. 2010;94(5):1887-1893.
94. Kwawukume EY. Uterine leiomyomas. In: Kwawukume EY, Emuveyan EE. (eds) *Comprehensive gynaecology in the tropics*. 1st edition. Accra, Graphic Packaging Ltd. 2005;124-137.
95. Pritts EA. Fibroids and infertility: A systematic review of the evidence. *Obstet Gynecol Survey*. 2001;56:483-491.
96. Kelly SM, Tulandi T. Should myomectomy be performed for intra mural fibroids on infertile women? Controversies in OB/GYN. *Comtemp Obstet Gynecol*. 2005;50:76-86.
97. ACOG. Committee Opinion. Committee on gynecology practice, American College of Obstetricians and Gynecologists. Uterine artery embolization. *Obstetrics and Gynecology*. 2004;103(2):403-404.
98. Ogunbode O. Environmental factors in the management of uterine fibroids. *Trop J Obstet Gynecol*. 1981;2:199-200.
99. Balogun SK. Age as correlate of incidence of vesico-vaginal fistula (VVF): The Nigerian example. *Issues Health Psychol*. 1995;2:44-51.
100. John ME. Psychosocial needs and perceived support of pregnant and adolescents in South Eastern Nigeria. *J Humanities*. 2000;3:111-119.
101. Udoma EJ, John ME, Ekanem AD, Etuk SJ. Hysterectomies amongst teenagers in Calabar, Nigeria. *Tropical Doctor*. 2004;34:110-112.

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