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The Impact of Uterine Leiomyomas on Reproductive Outcomes

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Abstract

Uterine leiomyomas (fibroids, myomas) are a common benign disease of the uterus with a prevalence of 8–18%. Prevalence rates vary with race, and fibroids are most common in African American women. Uterine leiomyomas can also be present during pregnancy, which may occur more frequently than previously suspected, with prevalence rates reported of up to 10%. Recent evidence has emerged to clarify the relationship of uterine fibroids on fertility and obstetrical outcomes. In this paper we review evidence that uterine fibroids, specifically submucosal and intramural myomas, negatively impact fertility and are associated with adverse obstetrical outcomes such as: pain, preterm labor, placental abruption, malpresentation, postpartum hemorrhage, and cesarean section. Myomectomy performed for submucosal and intramural fibroids significantly improves fertility outcome, and current evidence suggests myomectomy is the treatment of choice in women desiring to conceive. For women that do not desire surgery, medical management of myomas is also available. Treatment with GnRH agonists may be considered, however newer medications with fewer side effects give practitioners and patients more options. Progesterone antagonists, selective progesterone receptor modulators, and aromatase inhibitors have all shown promise as effective therapies. Non-pharmacologic treatments such as uterine artery embolization and MRI-guided ultrasound have also emerged as effective treatments for uterine fibroids. With such a wide range of new and emerging treatment options, patients and providers will be even more likely to find an appropriate and effective treatment method for management of fibroids.

Introduction

Uterine leiomyomas (fibroids, myomas) are a common benign growth of the myometrium. The prevalence of fibroids varies depending on patient age, race, and the methods used to detect uterine leiomyoma. Pathologic examination of hysterectomy specimens detected a prevalence of 77%.¹ A much lower prevalence rate of 10% was found at the time of previously scheduled tubal sterilization.² In 2009, Laughlin et al.³ reported a similar prevalence of 10.7% in 4217 women undergoing ultrasound screening in the first trimester

of pregnancy. Many studies have detected higher prevalence rates in African American women ranging from 16–18% compared to 8–10% in white or Hispanic women.^{2,3} Baird et al.⁴ found that cumulative incidence of fibroids by age 50 was 80% for black women and 70% for white women. In another study, African American women were younger at the time their fibroids were diagnosed and also were more likely to have multiple fibroids than white women.⁵ Interestingly, uterine fibroids may have different growth patterns in different ethnic groups. Peddada et al.⁶ observed that fibroid growth rates over time were equivalent in white and black women under age 35. In women over age 35 however, fibroid growth rates declined for white women but did not decline in black women. This may explain the increased lifetime prevalence of fibroids in African American women.

While many women with fibroids are asymptomatic, symptoms most commonly associated with uterine fibroids include menstrual disorders such as menorrhagia and dysmenorrhea, pelvic pain, and pelvic pressure. Additional symptoms include urinary complaints or constipation. Acute abdominal pain may occasionally be caused by the degeneration of individual fibroids.^{7,8} Based on a study from 2009, symptom severity scores between black and white women with known fibroid disease were similar.⁵ Fibroids also have adverse effects on fertility and are associated with early pregnancy complications^{9–21} and adverse obstetric outcomes, such as preterm labor, placenta previa, IUGR, an increased rate of cesarean section, and postpartum hemorrhage.^{22–29} This review will discuss the impact of fibroids on reproductive outcomes, specifically infertility, pregnancy and obstetrical outcomes. We will also explore new available management strategies for treating uterine leiomyomas.

Classification and Diagnosis

Uterine leiomyomas are most commonly classified based on their location, however there is not widely accepted classification system to categorize these lesions.^{9,13} Also, although location is taken into account, the size and number of fibroids are not currently included in existing staging systems, making comparative assessments of treatments difficult.³⁰ Based on their location, fibroids are categorized as submucosal, intramural and subserosal.^{9,31} Submucosal fibroids are defined as those that are in contact with, or distort the endometrial cavity.³ A more specific subtype classification has been used by the European Society of Hysteroscopy. In this system, Type 0 submucosal myomas are pedunculated and do not extend intramurally; Type I are sessile with less than 50% intramural involvement; and Type II are sessile with more than 50% intramural extension.^{9,13,31} Intramural myomas are found in the myometrium and cause no endometrial or serosal distortion.³ Some investigators classify intramural fibroids as those that do not cause cavity distortion and have less than 50% protrusion into the serosal surface. Myomas are considered subserosal if they distort the serosal surface, often defined as more than 50% protrusion into the uterine serosa. Subserosal myomas may also be subclassified as sessile or pedunculated.^{9,13,31} The effects of fibroids on reproductive outcomes vary by location and are discussed later in the review.

Investigators have used various methods to diagnose uterine fibroids. Clearly, the diagnostic method employed by researchers to determine the presence and location of fibroids will influence diagnostic accuracy and may, in turn, affect study's conclusions.

Hysterosalpingography (HSG) and transvaginal ultrasound are the two most frequently used diagnostic modalities to assess the effects of fibroids on the endometrial cavity. However, the sensitivity and specificity of HSG for detection of intrauterine pathology can be as low as 50% and 20% (respectively) and precise fibroid localization is unlikely.^{15,32–34} Transvaginal ultrasound, which was initially reported to be both highly sensitive and specific (as high as 90–100% for sensitivity and 87–98% for specificity),^{35,36} was later found to have sensitivities of as low as 69%^{15,37–40} and specificity of 11% for precise localization of submucosal leiomyomas.⁴¹

As a result of these limitations, newer diagnostic techniques such as saline infusion sonography, in both two and three dimensional (3D) modes, has emerged as the diagnostic modality of choice for the assessment of uterine fibroid distortion of the endometrial cavity.^{40–42} One study reported misdiagnosis of only one of 22 intramural and submucosal myomas when sonohysterogram was used for evaluation.⁴³ Moreover, sonohysterography has reported specificity of 100% and has been shown to be comparable to hysteroscopy.⁴² Hysteroscopy is often considered the gold standard to diagnose intracavitary lesions and studies have reported sensitivity, specificity, and predictive values of up to 100%.³⁵ MRI was shown in some studies to be superior to hysteroscopy in localizing uterine fibroids³⁹ however, this may be true only in specific situations, such as when the number of fibroids per uterus is substantial,⁴⁴ or to differentiate a myoma from an adenomyoma.¹³ Considering the substantially higher cost, MRI is therefore usually performed as an adjunct measure in more complicated cases.^{39,44} Current evidence suggests that MRI may be useful for assessment of atypical appearing fibroids, which might be more cellular and possibly at greater risk for malignancy.

The Effects of Fibroids on Fertility

Uterine fibroids are detected in about 5–10% of women with infertility. Furthermore, in 1–2.4% of women affected with infertility, fibroids are the only abnormality detected.^{11,45,46} Many studies have evaluated the relationship between parity and fibroids. Parity does seem to be associated with a reduced risk of fibroids. However, this observation may be explained by a protective effect of pregnancy on the development and growth of fibroids, alternatively, the presence of fibroids may compromise fertility and therefore reduce parity.^{13,30} Recent studies suggest that in some cases fibroids may undergo substantial shrinkage during postpartum involution of the uterus, which might also explain, in part, the reduced prevalence of fibroids in parous women.

Many suggested mechanisms have been invoked to explain the adverse effects of fibroids on fertility. These include: impaired gamete transport or embryo implantation, chronic endometrial inflammation, anatomic distortion of the endometrial cavity, impairment of the endometrial blood supply, increased uterine contractility, and an abnormal local hormonal milieu.^{12,13,45,46,47} It is possible that depending on the location and size of the fibroid(s), one or more of these mechanisms, in varying degrees, might impair fertility. Slightly different considerations must be given to patients being treated with assisted reproductive technology (ART). Because ART techniques bypass gamete transports, adverse effects of fibroids on fertility for patients undergoing in vitro fertilization/intracytoplasmic sperm

injection (IVF/ICSI) are most likely due to problems with embryo implantation.^{12,13} Detrimental effects of fibroids on the endometrium have been noted since the 1970s. One of the most frequently cited histological changes attributed to fibroids is glandular atrophy in the endometrium that overlies individual leiomyomas.^{48,49} Furthermore, subsequent studies have suggested that these effects are proportional to the proximity of the fibroid to the endometrial surface.⁵⁰ Interestingly, histologic alterations have also been observed on the endometrium opposite the side of the fibroid, suggesting that myomas may cause more than just local endometrial effects. These changes might be explained by the mechanical pressure applied by the fibroids which may impair more distant endometrium.⁵⁰ A recent study of the endometrium in myoma patients noted a global reduction in endometrial HOX gene expression in the presence of submucosal and intramural fibroids. This was observed not only in the tissue overlying the fibroid, but throughout the endometrium.⁵¹

Based on the latest literature, there seems to be agreement that fibroids do impact fertility potential and that removal of certain types of fibroids improves fertility.^{13,15} When comparing IVF/ICSI cycles between women with fibroids, those who have had previous myomectomies, and controls, patients with fibroids have significantly lower pregnancy rates than controls, while myomectomy patients do not. Additionally, of all patients who undergo myomectomy for infertility, half of them will subsequently conceive.¹³ Important to remember is that fibroids are an extremely heterogeneous disease, ranging from a single small serosal lesion to multiple large lesions that may significantly distort total pelvic anatomy.^{13,15} Clearly, the impact on fertility will depend on the location of the fibroid.

Submucosal Fibroids

There is general agreement that submucosal fibroids negatively impact fertility. Compared to women without fibroids, women with submucosal myomas have reduced clinical pregnancy rate (RR 0.363, 95% CI 0.179–0.737), implantation rate (RR 0.283, 95% CI 0.123–0.649), and ongoing pregnancy/live birth rate (RR 0.318, 95% CI 0.119–0.850) with a significantly higher spontaneous abortion rate (RR 1.678, 95% CI 1.373–2.051).^{10–15} These findings are relevant to both patients undergoing IVF as well as those that conceive spontaneously. Bulletti et al.⁵² compared women with fibroids undergoing myomectomy with a control group of unoperated fibroid patients, and found a significantly higher pregnancy rate in the myomectomy group after nine months of natural cycle (42 versus 11%). Casini et al.⁵³ also observed similar results when comparing women undergoing myomectomy to those with no treatment. Pregnancy rates were 27.2% and 43.4% in the non-myomectomy versus myomectomy groups respectively ($p < 0.05$). In patients being treated with ART, submucosal fibroids similarly impair fertility. A review by Benecke et al.¹² reported a significantly lower implantation rate and pregnancy rate in patients with submucosal myomas compared to controls.

Intramural Fibroids

The effect of intramural fibroids on reproductive outcome has been a subject of debate in the past, but recent literature indicates that intramural myomas also negatively impact fertility. Farhi et al.⁵⁴ did not find a detrimental effect for fibroids that did not distort the uterine

cavity. However, in 1998 two separate groups, Eldar-Geva et al.⁵⁵ and Stovall et al.⁵⁶ reported reduced pregnancy rate and implantation rate in women with intramural fibroids, even in the absence of cavity distortion. Again, these findings seem to be true for patients being treated with IVF/ICSI and those that conceive without ART. In 2009, Pritts et al.¹⁵ conducted a systematic review of both IVF treated on non-IVF treated patients regarding the effect of fibroids on infertility. The authors evaluated a total of 23 studies and reported that women with intramural fibroids have significantly decreased rates of implantation (RR 0.792, 95% CI 0.696–0.901) and ongoing pregnancy/live birth (0.780, 95% CI 0.690–0.883) with significantly increased rates of spontaneous abortion (RR 1.891, 95% CI 1.473–2.428). These results supported previous reports.

Beneck et al.¹² published a literature review in 2005 of 6 selected reports analyzing the effects of fibroids on fertility for couples undergoing IVF. The authors noted a significant negative impact on implantation rate in the intramural fibroid group versus the control (16.4 vs. 27.7%), as well as a significantly lower delivery rate in the fibroid group (31.2 vs. 40.9%). The authors concluded that intramural fibroids, which by definition do not cause cavity distortion, exerted a negative impact on pregnancy outcome in IVF/ICSI cycles and that myomectomy should be considered for these fibroids, particularly in patients whose previous cycles were not successful. A more recent meta-analysis by Somigliana et al.¹³ which included 17 studies, also showed a statistically significant adverse effect on both the clinical pregnancy rate (OR 0.8, 95% CI 0.6–0.9) and the delivery rate (OR 0.7, 95% CI 0.5–0.8).

Subserosal Fibroids

The existing data on the effects of subserosal fibroids on fertility support the conclusion that these fibroids do not exert any detrimental effects on fertility outcomes. Both the original studies^{56–59} and the meta-analyses^{10–15} have failed to detect any adverse effects on ART outcome attributable to subserosal fibroids. This conclusion is further supported by the fact that no beneficial effect on fertility is noted when myomectomy is performed for subserosal leiomyomas.⁵³

The Effects of Fibroids on Obstetric Outcomes

The prevalence of fibroids during pregnancy was commonly believed to range from 0.1–3.9%.^{28,29} However, a recent prospective study of 4217 patients enrolled for first trimester obstetrical ultrasound, showed a much higher prevalence rate of 10.7%.³ Although it is often stated that fibroids tend to grow as pregnancy progresses, most longitudinal studies have not supported this belief.^{14,29} One study noted growth in only 15% of fibroids throughout pregnancy and, in fact, showed regression in 62% of fibroids with a diameter of less than 5 cm.⁶⁰ Despite this, fibroids may cause a significant amount of pain during pregnancy for some patients if they undergo red degeneration. Approximately 5–15% of women with fibroids will require hospitalization during pregnancy for pain control, with the risk increasing for fibroids larger than 5cm.^{14,29}

Fibroids are also a source of several obstetrical complications. It has been noted that pregnant patients with myomas have an antepartum complication rate of 10–40%.²⁹ There is

still debate regarding the certainty of fibroid association with the numerous pregnancy complications that are commonly mentioned in the literature. Most studies suggest that preterm labor and delivery, placental abruption, malpresentation and breech presentation, and postpartum hemorrhage are complications of fibroids in pregnancy.^{13,14,28,29} Many different mechanisms have been proposed to explain these different complications. For example, some authors propose that fibroids cause a less distensible uterus causing preterm labor and delivery, while others suggest that increased levels of oxytocin in the fibroids uterus may lead to myometrial contractility.²⁹ Placental abruption seems to be highly related to fibroid location. Coronado et al.²⁵ found a 57% likelihood of having a placental abruption if the myoma was retroplacental in location. This may be explained by reduced placental perfusion in the area of the fibroid.^{14,29} Malpresentation is thought to be caused by distortion of the uterine cavity by large uterine fibroids, similar to outcomes in mullerian anomaly patients. Uterine myomas may also predispose to postpartum hemorrhage due to suboptimal uterine contractions following delivery.²⁹ Other adverse obstetrical outcomes have been reported, however studies are conflicting. These outcomes include placenta previa, intrauterine growth restriction, and premature rupture of membranes. Chorioamnionitis, retained placenta and pre-eclampsia have not been shown to be related to fibroids.^{13,14,28,29}

An increased rate of cesarean sections is perhaps the most commonly cited adverse obstetrical outcome associated with fibroids. A recent review of the literature showed a significantly increased rate of cesarean section in women with uterine fibroids compared to those without, 48.8% versus 13.3%.¹⁴ Qidwai et al.²⁸ found this to be true even when controlling for only those patients that were labor eligible. The increased rate of cesarean section in women with myomas is likely due to a number of factors such as increased risk for malpresentation, dysfunctional labor and placental abruption. Also, it seems that women with fibroids in the lower uterine segment are more likely to undergo cesarean section than those with fibroids in other locations.²³ It is important to note however, that despite the increased risk of cesarean section in women with fibroids, high vaginal delivery rates are still expected and patients should not be routinely counseled against a trial of labor.

Clinical Management of Uterine Fibroids

The strategy for clinical management of uterine fibroids should be tailored based on the specific symptoms and location of fibroids, as well as priorities of individual patients. The traditional treatment for fibroids has been surgery; however considering the inherent risks associated with any surgery, there has been an increasing interest in recent years towards development of non-surgical approaches. This new initiative involves attempts at both medical therapies as well as methods employing interventional radiology. An examination of the evidence for the effectiveness of surgical treatment will be followed by a brief discussion of these treatments.

Myomectomy

Myomectomy has long been regarded as the standard treatment for the various symptoms associated with fibroids, such as pelvic pressure, pain or menorrhagia. Myomectomy is often

the best option for women who are interested in preserving their fertility,⁶¹ however, considering the high recurrence rate of myomas, hysterectomy remains the definitive treatment for women who have completed childbearing. Myomectomy performed for fertility purposes has been evaluated in several studies, which examined both efficacy and safety of the procedure. It is important to bear in mind that the value of myomectomy is likely dependent on the location of fibroid, and may vary depending on whether or not IVF/ICSI is being pursued. Vercellini et al.⁶² published a systematic review in 1998 and reported a pregnancy rate of 57% (95%CI 48–65) after abdominal myomectomy. This success rate was even higher at 61% (95%CI 51–70) among women with otherwise unexplained infertility. Similar success rates have been reported for laparoscopic and hysteroscopic myomectomies.^{63–68} When location of the fibroid was considered, Pritts et al.¹⁵ found that submucosal myomectomy increased pregnancy rates compared to infertile women who did not undergo myomectomy for their fibroids (RR 2.03, CI 1.08–3.82). Also, when myomectomy patients were compared to those women without fibroids, pregnancy rates were shown to be similar between the two groups.¹⁴ This was not found to be true with either intramural or subserosal fibroids. A randomized trial of myomectomy for fertility was reported in 2006. Casini et al.⁵³ recruited 181 women with submucosal, intramural or subserosal fibroids and randomized subjects either to surgery or expectant management. Pregnancy rates were substantially higher in women with submucosal fibroids after myomectomy compared to expectant management (43% vs. 27%). Pregnancy rates were also significantly improved in those patients with a combination of submucosal and intramural fibroids after myomectomy (36% vs. 15%). For patients with only intramural myomas, there was a trend towards a higher likelihood of pregnancy after myomectomy (56% vs. 41%), however this difference did not reach statistical significance.

In patients undergoing treatment with IVF/ICSI, the beneficial effects of myomectomy appear similar. Bulletti et al.⁵² compared patients with intramural and subserosal fibroids greater than 5 cm in diameter who chose to undergo myomectomy prior to IVF treatment with those patients that decided against myomectomy. A significant improvement was seen in both pregnancy rate (34% v 15%) and delivery rate (25% v 12%) in those patients that underwent myomectomy. Myomectomy is likely to be beneficial for women with submucosal fibroids, and possibly intramural fibroids > 4cm, but further studies are needed to confirm this conclusion. It is important to bear in mind that myomectomy carries risks common to major surgical interventions; specifically bleeding, infection and damage to adjacent structures. Myomectomy is also associated with significant adhesion formation, particularly for leiomyomas on the posterior aspect of the uterus.^{69–71} Although this might not be a concern for women pursuing ART, it may impact the likelihood of spontaneous conception. The possible need for cesarean section following myomectomy should also be considered.^{72–73} In conclusion, current evidence suggests that myomectomy is beneficial in women with submucosal and intramural fibroids and should be considered in women who are pursuing fertility treatments.

Medical Management of Fibroids

Gonadotropin releasing hormone (GnRH) agonists down regulate GnRH receptors on the pituitary gonadotropes, leading to diminished secretion of LH and FSH with a subsequent

reduction in estrogen and progesterone. The induced hypogonadotropic, hypoestrogenic state can result in a significant reduction of between 35–65% in myomas volume within 3–6 months.⁷⁴ However, due to the side effects associated with prolonged use (such as osteoporosis), these agents should not be administered for longer than 6 months. Unfortunately, when treatment is discontinued, the fibroids rapidly return to their pretreatment size.⁷⁴ Also, because GnRH agonists inhibit ovulation, they are of limited use in women desiring pregnancy, unless they are given within an IVF protocol. More recently, GnRH antagonists have been introduced to the market. Unlike GnRH agonists, GnRH antagonists exert their effect by competing with endogenous GnRH for receptor binding site in the pituitary.⁷⁵ Due to the lack of any intrinsic activity with the use of GnRH antagonists, the characteristic initial 'flare-up' effect of GnRH-agonist administration is avoided. This results in a more rapid suppression of gonadotropin release from the pituitary gland, and a 30% reduction in fibroid size within 2 weeks.⁷⁵ Like GnRH agonists, GnRH antagonists cannot be used on a long term basis and their beneficial effects will disappear upon discontinuation. Despite the previously mentioned limitations of GnRH agonist and antagonist treatment, some women may benefit from the significant and rapid reduction in the fibroids' size achieved with either GnRH analogue. GnRH agonist or antagonists may be particularly valuable prior to initiation of ART cycles or to reduce fibroid volume prior to surgery.

Other medical treatments for fibroids have been used and new compounds are being studied. Progesterone receptor modulators are one such compound. Mifepristone, a pure progesterone antagonist, was reported for myoma treatment in 2003. Doses from 5 to 100 mg daily were effective in decreasing fibroid volume. A dose of 50 mg, for example, reduced fibroid volume by 50% after 12 weeks of treatment.⁷⁷ In 2006, Fiscella et al.⁷⁸ randomized 37 women suffering from uterine fibroids to treatment with mifepristone or placebo. After 26 weeks of treatment, women who took mifepristone had significant improvement in quality of life scores, decreased uterine volume by 47%, increased hematocrit levels, and 41% were amenorrheic. Closely related to the progesterone antagonists are the selective progesterone receptor modulators (SPRMs). Asoprisnil was one of the first such compounds to be studied. In doses of 5, 10 or 25 mg per day, Asoprisnil reduced uterine volume by an average of 36% after 12 weeks of treatment in women with uterine fibroids.⁷⁷ There is some concern regarding the effect of Asoprisnil on the endometrium, as some studies have suggested that anti-progesterone drugs may lead to endometrial hyperplasia. More studies are needed to evaluate effects on endometrium, breast stimulation and risk of tumor regrowth after discontinuation of treatment.⁷⁷ In 2009, Levens et al.⁷⁹ studied a new SPRM called CBD-2914. In this three month study, 18 patients with a documented fibroid uterus were randomized to receive CDB-2914 or placebo. CDB-2914 eliminated menstrual bleeding and ovulation and was also found to decreased fibroid volume significantly compared to the placebo (29% v 6%, $p < 0.01$).

Aromatase inhibitors are also gaining popularity as a medical treatment for fibroids. A prospective study of Anastrozole in women with myomas reported a 59.7% reduction in fibroid volume and a 29.9% reduction in uterine volume.⁸⁰ In this study Anastrozole was associated with very few side effects and reduced bleeding and pain. Parsanezhad et al.⁸¹ conducted a randomized control trial comparing the aromatase inhibitor, Letrozole 2.5 mg

per day, with a GnRH agonist for the treatment of fibroids. This multicenter trial included a total of 70 patients each with a single fibroid larger than 5 cm in diameter. Myoma volume was decreased by 45.6% in the aromatase inhibitor group, which was significantly greater than the 33.2% decrease in the GnRH agonist group. Also, after 12 weeks of aromatase inhibitor use, no significant changes from baseline were seen in levels of FSH, LH or estradiol. However, significantly decreased levels of FSH, LH and estradiol were noted in the GnRH agonist group. Overall, medical management of fibroids is an effective option for women seeking fertility who do not desire surgical management. Short courses of these medications may help to decrease myoma size enough to allow for conception. With ongoing investigation into new medications, the medical management of fibroids should continue to improve while minimizing the side effects associated with the current treatments.

Uterine artery embolization

Uterine artery embolization (UAE) has emerged as an alternative therapeutic option for patients with uterine fibroids who do not want surgery or are not good surgical candidates. This procedure, if performed properly, results in 77–86% of patients with symptomatic relief three months after the procedure.⁸² However, in a review of UAE, myoma volume only reduced by 40–75%.⁸³ Shorter hospital stay and a quicker recovery are advantages of UAE compared to myomectomy, however, minor complications occur more frequently with UAE.⁸⁴ An important concern regarding UAE, particularly for patients desiring future fertility, is impairment of the ovarian blood supply with the resultant detrimental effect on ovarian reserve and diminution of the oocyte supply.^{85,86} Furthermore, permanent endometrial atrophy has been reported following UAE.⁸⁷ Several studies have also reported a significantly increased risk of obstetric complications such as: preterm delivery, malpresentations, IUGR, and abnormal placentation. An increased likelihood of miscarriage has also been suggested as a complication in women who have undergone UAE.^{84–86,88,89} Taking into account these considerations, most providers do not recommend UAE for women who desire future pregnancy.

MRI-guided focused ultrasound

MRI-guided focused ultrasound is the latest therapeutic modality among the non surgical management options for symptomatic fibroids.⁹⁰ This procedure is performed by directing energy from multiple elements of a phased array transducer through the anterior abdominal wall. The ultrasound waves converge at the fibroid and cause it to undergo a coagulative necrosis. Two year follow up data for 359 women who have undergone this treatment indicated that MRI-guided ultrasound can provide sustained relief of fibroid symptoms that is equivalent to more traditional treatment options.⁹⁰ Reported outcomes, however, were focused on bleeding and pain symptoms and not on fertility-related issues or pregnancy. A plausible advantage of MRI-guided focused ultrasound compared to UAE, is that ovarian and endometrial blood supply should be unaffected, making this technique beneficial for women who desire future childbearing. Successful pregnancies have been reported after MRI-guided focused ultrasound surgery,^{91,92} but so far there have been no studies to address

its application as an adjunct for fertility enhancement. Moreover, the safety of pregnancy following the procedure has not been established.

Conclusion

Leiomyomas are highly prevalent and vary by age and race, with the highest incidence in African American women. Fibroids in pregnancy are also very common, and may be more prevalent than previously suspected, with prevalence rates reported of up to 10%. Although most women with fibroids will have uncomplicated pregnancies, myomas are associated with a number of adverse pregnancy outcomes such as pain, preterm labor/delivery, placental abruption, malpresentation, and postpartum hemorrhage. An increased risk of cesarean section is also a recognized complication. Leiomyomas, specifically submucosal and intramural myomas, are also associated with reduced fertility. Myomectomy does improve fertility outcome in patients with submucosal and intramural fibroids, and is currently the treatment of choice in women desiring to conceive. For women with symptomatic fibroids who have completed childbearing, hysterectomy may be the treatment of choice. For patients who do not desire surgery, medical management for the treatment of uterine fibroids is available. Standard medical therapy includes treatment with GnRH agonists, however these medications should only be used for several months and may be associated with menopausal symptoms. Newer medications, such as progesterone antagonists, SPRMs, and aromatase inhibitors, are now being used with promising results. Non-pharmacologic treatments, such as uterine artery embolization and MRI-guided ultrasound, have been shown to be effective in treating uterine leiomyomas, however these treatments are not currently recommended in patients desiring future fertility.

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