American College of Radiology
ACR Appropriateness Criteria®
Management of Uterine Fibroids

Variant 1: **Reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and a desire to preserve fertility. Initial therapy.**

Procedure	Appropriateness Category
Hysteroscopic myomectomy	Usually Appropriate
Laparoscopic or open myomectomy	Usually Appropriate
Medical management	Usually Appropriate
MR-guided high-frequency focused ultrasound ablation	Usually Appropriate
Uterine artery embolization	Usually Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate
Endometrial ablation	Usually Not Appropriate
Hysterectomy	Usually Not Appropriate

Variant 2: **Reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bowel, or bladder symptoms), and no desire for future fertility. Initial therapy.**

Procedure	Appropriateness Category
Laparoscopic or open myomectomy	Usually Appropriate
Medical management	Usually Appropriate
MR-guided high-frequency focused ultrasound ablation	Usually Appropriate
Uterine artery embolization	Usually Appropriate
Hysterectomy	May Be Appropriate
Hysteroscopic myomectomy	May Be Appropriate
Endometrial ablation	Usually Not Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate

Variant 3: **Reproductive age patient with uterine fibroids and concurrent adenomyosis, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and no desire for future fertility. Initial therapy.**

Procedure	Appropriateness Category
Medical management	Usually Appropriate
Uterine artery embolization	Usually Appropriate
Hysterectomy	May Be Appropriate
MR-guided high-frequency focused ultrasound ablation	Usually Not Appropriate
Endometrial ablation	Usually Not Appropriate
Hysteroscopic myomectomy	Usually Not Appropriate
Laparoscopic or open myomectomy	Usually Not Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate

Variant 4: **Reproductive age patient with pedunculated submucosal uterine fibroids, symptomatic with heavy uterine bleeding. Initial therapy.**

Procedure	Appropriateness Category
Hysteroscopic myomectomy	Usually Appropriate
Medical management	Usually Appropriate
Uterine artery embolization	May Be Appropriate
MR-guided high-frequency focused ultrasound ablation	May Be Appropriate
Hysterectomy	Usually Not Appropriate
Endometrial ablation	Usually Not Appropriate
Laparoscopic or open myomectomy	Usually Not Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate

Variant 5: **Postmenopausal patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms). Negative endometrial biopsy. Next step.**

Procedure	Appropriateness Category
Hysterectomy	Usually Appropriate
Laparoscopic or open myomectomy	May Be Appropriate
Uterine artery embolization	May Be Appropriate
Hysteroscopic myomectomy	May Be Appropriate
MR-guided high-frequency focused ultrasound ablation	Usually Not Appropriate
Endometrial ablation	Usually Not Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate
Medical management	Usually Not Appropriate

Variant 6: **Reproductive age patient with uterine fibroids desiring pregnancy and experiencing reproductive dysfunction. Initial therapy.**

Procedure	Appropriateness Category
Hysteroscopic myomectomy	Usually Appropriate
Laparoscopic or open myomectomy	Usually Appropriate
Uterine artery embolization	May Be Appropriate
Medical management	May Be Appropriate (Disagreement)
MR-guided high-frequency focused ultrasound ablation	May Be Appropriate
Laparoscopic uterine artery occlusion	Usually Not Appropriate
Endometrial ablation	Usually Not Appropriate
Hysterectomy	Usually Not Appropriate

MANAGEMENT OF UTERINE FIBROIDS

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Summary of Literature Review

Introduction/Background

Uterine fibroids, also called leiomyomas or myomas, arise from the smooth muscle cells and fibroblasts of the myometrium and are the most common benign tumor in patients of reproductive age. Fibroid-associated symptoms are greatest leading up to menopause and typically decline in postmenopausal patients. These symptoms include heavy and prolonged uterine bleeding, which can lead to anemia, pelvic pain, bulk symptoms, and reproductive dysfunction. Physical examination, including an abdominal examination, speculum examination, and bimanual pelvic evaluation, are performed to characterize the location, shape, and mobility of the fibroids. Diagnosis is made with pelvic ultrasound (US) or MRI, which further characterize fibroid location, size, and number. Additional workup may include pregnancy testing, hemoglobin levels, and endometrial biopsy if features of the patient's presentation raise concern for other causes of heavy menstrual bleeding. See the ACR Appropriateness Criteria® topic on "Fibroids" [1] for further guidance. This document addresses both cisgender females (birth assigned female with female gender identity) and transgender and gender diverse individuals assigned female at birth.

Initial Therapy Definition

Initial therapy is defined as a first-line treatment option for the medical condition defined by the variant. More than one option can be considered usually appropriate as the initial therapy when:

- There are equivalent alternatives (ie, only one option will be planned to effectively manage the patient's care).

OR

- There are complementary therapies (ie, more than one treatment option is planned to be performed simultaneously or in sequence during the same setting, wherein the therapies provide synergistic or complementary benefits to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and a desire to preserve fertility. Initial therapy.

Endometrial Ablation

There is no relevant literature regarding the use of endometrial ablation in the treatment of uterine fibroids in patients desiring to preserve fertility. Endometrial ablation is associated with a high risk of pregnancy complications [2].

Hysterectomy

There is no relevant literature regarding the use of hysterectomy in the treatment of uterine fibroids in patients desiring to preserve fertility. Infertility is permanent and irreversible following hysterectomy.

Hysteroscopic Myomectomy

Hysteroscopic myomectomy involves the transvaginal, transcervical placement of a hysteroscope and removal of submucosal uterine fibroids by an electrosurgical wire loop or other instruments and is indicated in patients with submucosal fibroids desiring uterus preservation. Patients with significant intramural or subserosal fibroid burden

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causing bulk symptoms or heavy menstrual bleeding with concomitant adenomyosis are less likely to experience symptom relief from hysteroscopic myomectomy. Risks include uterine perforation, fluid overload, need for blood transfusion, bowel or bladder injury, endomyometritis, and a need for reintervention [3]. The procedure is associated with shorter hospitalization and a faster return to usual activities compared to laparoscopic or open myomectomy. Improvement in symptom scores and quality of life is equivalent to other surgical approaches at 2 to 3 months [4]. In a randomized trial of myomectomy versus uterine artery embolization (UAE), myomectomy using any approach was shown to have improved quality of life scores at 2 years, although this difference was no longer significant at 4 years [5,6].

Whether hysteroscopic myomectomy improves fertility is a matter of debate, because high-quality evidence on live birth rates following hysteroscopic myomectomy is lacking. Two single-center randomized controlled trials have been performed to date. The first demonstrated no difference in pregnancy rates between patients undergoing hysteroscopic myomectomy and controls [7]. The second demonstrated improved pregnancy rates after myomectomy; however, data could not be externally validated due to internal inconsistencies in reporting [8,9]. Neither study reported live birth rates. The miscarriage rate was reported in one study and found to be between 30% and 50% [7]. Retrospective studies demonstrate pregnancy rates of 85% after hysteroscopic myomectomy with live birth rates of 65% [10]. Large prospective registries show no significant difference in fertility outcomes among hysteroscopic, laparoscopic, and open myomectomy [11].

Laparoscopic or Open Myomectomy

Laparoscopic or open myomectomy is performed through abdominal incisions and is indicated for subserosal or intramural fibroids. Open myomectomy is preferred over laparoscopic approaches in patients with multiple fibroids or very large uteri. Laparoscopy is associated with shorter hospital stays and a faster return to usual activities compared to open myomectomy [4,12]. Both procedures are associated with an improved quality of life at up to 10 years [13]. Of note, there is increasing utilization of robotic-assisted laparoscopic myomectomy, and outcomes appear similar to traditional laparoscopy in terms of operative time, hospital stay, and postoperative complications.

Large prospective registries show no significant difference in fertility outcomes among hysteroscopic, laparoscopic, and open myomectomy [11]. Of patients trying to conceive, less than half achieve pregnancy after myomectomy at up to 3 years of follow-up. Of these, less than half of these pregnancies will result in a live birth [11]. Case reports have associated laparoscopic and open myomectomy with uterine rupture during subsequent pregnancy [14].

Laparoscopic Uterine Artery Occlusion

Laparoscopic uterine artery occlusion (LUAO) is occasionally used as an adjunct to hysterectomy or myomectomy as a means of decreasing intraoperative blood loss. When performed in isolation for uterine fibroids, it is associated with decrease in heavy menstrual bleeding and fibroid diameter. LUAO was compared to uterine fibroid embolization in a prospective nonrandomized clinical trial, which demonstrated greater reduction in fibroid diameter with UAE (53% versus 39%) and higher frequency of complete infarction with UAE (82% versus 23%). On the other hand, LUAO was associated with decreased postprocedural complications and rehospitalizations. Total pregnancy rates (69% for UAE versus 67% for LUAO), live births (50% versus 46%), and abortion rates (34% versus 33%) were not significantly different between groups [15].

Medical Management

Agents used in the medical management of fibroids include anti-inflammatory medications (eg, nonsteroidal anti-inflammatory drugs [NSAIDs]) and medications that work by suppressing the reproductive axis to decrease symptoms associated with fibroids such as bleeding and pain. First-line medical management includes estrogen-progestin oral contraceptive pills and progestin-containing intrauterine devices (IUDs), which reduce bleeding symptoms [16]. Tranexamic acid is a nonhormonal alternative agent that may reduce bleeding symptoms in patients with fibroids [17].

Second line medical management includes parenteral gonadotropin-releasing hormone (GnRH) agonists (eg, leuprolide acetate) and oral GnRH antagonists (eg, elagolix, linzagolix, and relugolix) [18-23]. In addition to reducing bleeding symptoms, both GnRH agonists and antagonists are effective at significantly reducing tumor volume and are commonly used for short courses to decrease fibroid size in preparation for surgery [24]. As monotherapy, both GnRH agonists and antagonists are associated with hypoestrogenic effects including headaches, hot flushes, hypertension, and loss of bone mineral density. Combination treatment with low doses of estrogen and progestin mitigates these symptoms and is an FDA-approved treatment option for fibroid-related heavy menstrual bleeding [19,25]. Although these agents are often chosen by patients interested in uterus-preserving therapy or

preservation of future fertility, fertility is suppressed during treatment and cessation of therapy leads to rapid recurrence of symptoms.

There are growing data supporting the efficacy of progesterone receptor modulators such as ulipristal acetate. These agents reduce both bleeding and bulk symptoms and can be administered intermittently, allowing for menstruation during medication breaks [26,27]. Efficacy of continuous use after 3 months and intermittent use for 2 years with comparison to both placebo and GnRH agonists has been demonstrated in randomized controlled trials [28-30]. However, reports of hepatotoxicity are a barrier to its approval for use in the United States [31,32].

MR-Guided High-Frequency Focused Ultrasound Ablation

MR-guided focused US surgery (MRgFUS) uses high-intensity US waves to target and thermally ablate uterine fibroids, resulting in coagulative necrosis without damage to intervening tissues. Complications are rare and include skin burns, nerve damage, vaginal discharge, bowel injury, deep vein thrombosis, and abdominal wall pain and swelling [33].

A recent randomized controlled trial compared MRgFUS to placebo and demonstrated significantly greater improvement in quality of life, significantly greater decrease in fibroid diameter (−18% versus no change), and a reintervention rate of 33% at 2 years [34].

The randomized controlled Fibroid Interventions: Reducing Symptoms Today and Tomorrow (FIRSTT) trial compared UAE to MRgFUS and demonstrated that MRgFUS was associated with a higher reintervention rate (30% versus 13%) and decreased symptom control compared to UAE [35]. Reinterventions included hysterectomy, myomectomy, or UAE. Uterine Fibroid Symptom and Quality of Life (UFS-QOL) improved in both groups, with UAE demonstrating a significantly greater improvement in scores at all time points (6-, 12-, and 24-months). Compared to UAE, MRgFUS is also longer (6.75 hours versus 2.3 hours) and is occasionally performed over 2 days. MRgFUS is associated with decreased postprocedural pain and narcotic and anti-inflammatory use as well as a faster recovery. Frequency and severity of adverse events is similar for both procedures, with a low rate of major adverse events for both [36]. Compared to myomectomy or hysterectomy, a recent large prospective trial demonstrated a major adverse event rate of 0.2% for focused US and 12.6% for surgical approaches. In this study, MRgFUS also demonstrated a greater improvement in symptoms and quality of life scores compared to baseline at 6 and 12 months [37].

Reintervention rates similar to UAE have been reported. One study reported a reintervention rate of 4% at 1 year, 13% at 2 years, 19% at 3 years, and 23% at 4 years [38], although other studies have reported reintervention rates as high as 30% at 2 years [39]. In cohort studies, quality of life and rates of reintervention are similar between patients undergoing laparoscopic myomectomy and MRgFUS at 5 years [40].

No randomized controlled trials assessing fertility have been performed for MRgFUS. The best evidence comes from a prospective cohort of 51 women who underwent MRgFUS. Among these women, 54 pregnancies were recorded with a mean time of conception 8 months after treatment. Live births were achieved in 41%. There was a 28% spontaneous abortion rate, an 11% rate of elective termination, and a 20% rate of ongoing pregnancy beyond 20 weeks at follow-up [41]. The FIRSTT trial reported anti-Mullerian hormone levels, a surrogate marker of ovarian reserve, in UAE versus MRgFUS, and found that both procedures decreased anti-Mullerian hormone, with UAE decreasing anti-Mullerian hormone significantly more at 1 year [35].

Uterine Artery Embolization

UAE is a technique using a transfemoral or transradial arterial approach to introduce a catheter into the uterine arteries. Embolic materials (eg, gelatin, microspheres, or coils) introduced through the catheter cause arterial occlusion, ischemic necrosis, and involution of fibroids. Indications for UAE include bulk symptoms and heavy menstrual bleeding. Side effects of UAE include pelvic pain, vaginal expulsion of submucosal fibroids, and postembolization syndrome, a flu-like syndrome that presents with pain, nausea, fevers, and leukocytosis. Since the first published study in 1995, UAE has been shown to cause persistent decreases in pain, heavy menstrual bleeding, and an average decrease in uterine fibroid size of >50% at 5 years [42]. Randomized controlled trials have demonstrated that compared to myomectomy, UAE is equally effective at reducing heavy menstrual bleeding at 4 years [5]. Further, UAE is associated with a decreased risk of blood transfusion and shorter hospital stays, and rates of new fibroid formation are significantly lower with UAE than with myomectomy [42]. Quality of life scores and reintervention rate at 4 years are not significantly different between myomectomy and UAE [5]. Ten year follow-up from the Embolization vs Hysterectomy (EMMY) trial, which did not permit repeat embolization after initial treatment, reported secondary hysterectomy rates of 28% at 5 years and 35% at 10 years [13].

In a meta-analyses comparing UAE and MRgFUS, UAE has been associated with improved symptom relief, improved quality of life, lower reintervention rates, and lower pregnancy rates [43].

Historically, fertility after UAE has been a topic of debate, but a growing number of studies demonstrated high rates of live birth following UAE in patients trying to conceive. Recent prospective studies demonstrate high live birth rates (10/12 pregnancies, 1 ongoing pregnancy) with low miscarriage rates (1/12) [44]. The randomized FEMME (Treating Fibroids with Either Embolisation or Myomectomy to Measure the Effect on Quality of Life Among Women Wishing to Avoid Hysterectomy) trial found no significant different in levels of biomarkers of ovarian reserve between UAE and myomectomy [6]. At 4-year follow-up, pregnancy and birth rates were too low for statistical analysis but demonstrated that a majority of pregnancies in UAE resulted in live births (9/15). The miscarriage rate was 33% (5/15) [5]. A retrospective cohort study of reproductive outcomes for women who underwent UAE for fibroids, adenomyosis, or both demonstrated a live birth rate of 73% (109/148) with a miscarriage rate of 17.5% (26/148) [45]. These findings are consistent with another retrospective study reporting a spontaneous pregnancy rate of 29.5% and 40.1% following UAE at 1 and 2 years, respectively, with a live birth rate of 81% (148 live births following 182 pregnancies) [46].

Despite these findings, the question of fertility after UAE is haunted by an early randomized controlled trial, which demonstrated a higher miscarriage rate after UAE (9/15) compared with myomectomy (6/33) [47]. This study should be interpreted with caution because it excluded patients with submucosal fibroids from the myomectomy arm, represented midterm results with a short follow-up time, and had a low number of women attempting conception in the UAE arm compared to myomectomy. Further, the high rate of miscarriage was inconsistent with data reported from prospective trials at the time. In light of these shortcomings, and newer evidence to date which contradicts these findings, there is promising evidence that UAE is comparable to myomectomy with regards to fertility, and future trials are needed.

Variant 2: Reproductive age patient with uterine fibroids, symptomatic with abnormally heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bowel, or bladder symptoms), and no desire for future fertility. Initial therapy.

Endometrial Ablation

Endometrial ablation is a minimally invasive technique that can be performed for patients with uterine fibroids associated with heavy menstrual bleeding who are refractory or intolerant to medical therapy. This technique uses thermal energy to irreversibly destroy the uterine lining and is only indicated in patients who do not desire future pregnancy. In a small randomized controlled trial of hysterectomy versus thermal balloon ablation, ablation was associated with amenorrhea or hypomenorrhea in all patients for up to 2 years [48]. However, endometrial ablation is not a form of contraception, and large population-based linkage studies demonstrate an elevated risk of extrauterine pregnancy, preterm delivery, and stillbirth with this procedure [49]. Given these risks, endometrial ablation should only be performed after failure of medical therapy.

Hysterectomy

Hysterectomy, whether transvaginal, laparoscopic, or abdominal, remains the most common treatment for uterine fibroids, accounting for three-quarters of fibroid treatment in the United States [50], and provides definitive resolution of all fibroid-related symptoms for patients who do not desire future pregnancy. Hysterectomy eliminates the risk of new fibroid formation and allows for simultaneous treatment of concomitant intrauterine disease such as adenomyosis, endometriosis, high-risk cervical dysplasia, uterine prolapse, or intrauterine malignancy. If there is not another indication for removal, the ovaries are left in place to avoid precipitating menopause and associated cardiovascular risks. Even with bilateral ovarian conservation, hysterectomy alone is associated with elevated risk of subsequent cardiovascular disease and mood disorders. Some studies report increased mortality, especially when performed at a young age [51-53]. Short-term complications may include abscess, venous thromboembolism, damage to ureter, bowel, or bladder, bleeding requiring transfusion, and vaginal cuff complications. Randomized studies have demonstrated increased rate of severe complications, longer hospitalization, and a longer return to regular activities with hysterectomy compared to UAE despite similar symptom relief [54], suggesting that hysterectomy should be avoided if a less invasive procedure is available. Cohort studies and registries have reported long-term effects of hysterectomy, including increased risk of cardiovascular disease [51], osteoporosis and bone fracture [55], and dementia [56]. Thus, unless there are other reasons for hysterectomy, an alternative to hysterectomy should be first-line treatment.

If hysterectomy is indicated, the least invasive route for hysterectomy should be performed. Abdominal hysterectomy is associated with longer hospital stay, recovery time, and greater pain and risk of infection compared to other approaches. Vaginal hysterectomy is associated with shorter operating times, a faster return to normal activities, and a better quality of life compared to abdominal hysterectomy. Laparoscopic hysterectomy is associated with a faster return to normal activities, shorter hospital stays, and lower rates of wound infection compared to abdominal hysterectomy [57]. Of note, there is increasing utilization of robotic-assisted hysterectomy, and outcomes appear similar to traditional laparoscopy in terms of operative time, hospital stay, and postoperative complications [58].

Hysteroscopic Myomectomy

Hysteroscopic myomectomy involves the transvaginal, transcervical placement of a hysteroscope and removal of submucosal uterine fibroids by an electrosurgical wire loop and other instruments and is indicated in patients with submucosal fibroids desiring uterus preservation. Patients with significant intramural or subserosal fibroid burden causing bulk symptoms or heavy menstrual bleeding with concomitant adenomyosis are less likely to experience symptom relief from hysteroscopic myomectomy. Risks include uterine perforation, fluid overload, the need for blood transfusion, bowel or bladder injury, endomyometritis, and the need for reintervention [3]. The procedure is associated with shorter hospitalization and a faster return to usual activities compared to laparoscopic or open myomectomy. Improvement in symptom scores and quality of life is equivalent to other surgical approaches at 2 to 3 months [4]. In a randomized trial of myomectomy versus UAE, myomectomy using any approach was shown to have improved quality of life scores at 2 years, although this difference was no longer significant at 4 years [5].

Patients with no desire for future fertility should be counseled that pregnancy is possible after hysteroscopic myomectomy.

Laparoscopic or Open Myomectomy

Laparoscopic or open myomectomy is performed through abdominal incisions and is indicated for subserosal or intramural fibroids. Open myomectomy is preferred over laparoscopic approaches in patients with multiple fibroids or very large uteri. Laparoscopy is associated with shorter hospital stays and a faster return to usual activities compared to open myomectomy [4,12]. Both procedures are associated with an improved quality of life at up to 10 years [13]. Of note, there is increasing utilization of robotic-assisted laparoscopic myomectomy, and outcomes appear similar to traditional laparoscopy in terms of operative time, hospital stay, and postoperative complications.

Patients with no desire for future fertility should be counseled that pregnancy is possible after laparoscopic or open myomectomy.

Laparoscopic Uterine Artery Occlusion

LUAO is commonly used as an adjunct to hysterectomy or myomectomy as a means of decreasing intraoperative blood loss. When performed in isolation for uterine fibroids, it is associated with decreased heavy menstrual bleeding and fibroid diameter. LUAO was compared to uterine fibroid embolization in a prospective nonrandomized clinical trial, which demonstrated greater reduction in fibroid diameter with UAE (53% versus 39%) and higher frequency of complete infarction with UAE (82% versus 23%). On the other hand, LUAO was associated with decreased postprocedural complications and rehospitalizations. Total pregnancy rates (69% for UAE versus 67% for LUAO), live births (50% versus 46%), and abortion rates (34% versus 33%) were not significantly different between groups [15].

Patients with no desire for future fertility should be counseled that pregnancy is possible after LUAO.

Medical Management

Agents used in the medical management of fibroids include anti-inflammatory medications (eg, NSAIDs) and medications that work by suppressing the reproductive axis to decrease symptoms associated with fibroids such as bleeding and pain. First-line medical management includes estrogen-progestin oral contraceptive pills and progestin-containing IUDs, which reduce bleeding symptoms [16]. Tranexamic acid is a nonhormonal alternative agent that may reduce bleeding symptoms in patients with fibroids [17].

Second line medical management includes parenteral GnRH agonists (eg, leuprolide acetate) and oral GnRH antagonists (eg, elagolix, linzagolix, and relugolix) [18-23]. In addition to reducing bleeding symptoms, both GnRH agonists and antagonists are effective at significantly reducing tumor volume and are commonly used for short courses to decrease fibroid size in preparation for surgery [24]. As monotherapy, both GnRH agonists and antagonists are associated with hypoestrogenic effects including headaches, hot flushes, hypertension, and loss of

bone mineral density. Combination treatment with low doses of estrogen and progestin mitigates these symptoms and is an FDA-approved treatment option for fibroid-related heavy menstrual bleeding [19,25]. Although these agents are often chosen by women interested in uterus-preserving therapy or preservation of future fertility, fertility is suppressed during treatment and cessation of therapy leads to rapid recurrence of symptoms.

There is growing data supporting the efficacy of progesterone receptor modulators such as ulipristal acetate. These agents reduce both bleeding and bulk symptoms and can be administered intermittently, allowing for menstruation during medication breaks [26,27]. Efficacy of continuous use after 3 months and intermittent use for 2 years with comparison to both placebo and GnRH agonists has been demonstrated in randomized controlled trials [28-30]. However, reports of hepatotoxicity are a barrier to its approval for use in the United States [31,32].

MR-Guided High-Frequency Focused Ultrasound Ablation

MRgFUS uses high-intensity US waves to target and thermally ablate uterine fibroids, resulting in coagulative necrosis without damage to intervening tissues. Complications are rare and include skin burns, nerve damage, vaginal discharge, bowel injury, deep vein thrombosis, and abdominal wall pain and swelling [33].

A recent randomized controlled trial compared MRgFUS to placebo and demonstrated significantly greater improvement in quality of life, significantly greater decrease in fibroid diameter (−18% versus no change), and a reintervention rate of 33% at 2 years [34].

The randomized controlled FIRSTT trial compared UAE to MRgFUS and demonstrated that MRgFUS was associated with a higher reintervention rate (30% versus 13%) and decreased symptom control compared to UAE [35]. Reinterventions included hysterectomy, myomectomy, or UAE. UFS-QOL improved in both groups, with UAE demonstrating a significantly greater improvement in scores at all time points (6-, 12-, and 24-months). Compared to UAE, MRgFUS is also longer (6.75 hours versus 2.3 hours) and is occasionally performed over 2 days. MRgFUS is associated with decreased postprocedural pain and narcotic and anti-inflammatory use as well as faster recovery. Frequency and severity of adverse events is similar for both procedures, with a low rate of major adverse events for both [36]. Compared to myomectomy or hysterectomy, a recent large prospective trial demonstrated a major adverse event rate of 0.2% for focused US and 12.6% for surgical approaches. In this study, MRgFUS also demonstrated a greater improvement in symptoms and quality of life scores compared to baseline at 6 and 12 months [37].

Reintervention rates similar to UAE have been reported. One study reported a reintervention rate of 4% at 1 year, 13% at 2 years, 19% at 3 years, and 23% at 4 years [38], although other studies have reported reintervention rates as high as 30% at 2 years [39]. In cohort studies, quality of life and rates of reintervention are similar between patients undergoing laparoscopic myomectomy and MRgFUS at 5 years [40].

Patients with no desire for future fertility should be counseled that pregnancy is possible after MRgFUS.

Uterine Artery Embolization

UAE is a technique using a transfemoral or transradial arterial approach to introduce a catheter into the uterine arteries. Embolic material (eg, gelatin, microspheres, or coils) introduced through the catheter cause arterial occlusion, ischemic necrosis, and involution of fibroids. Indications for UAE include bulk symptoms and heavy menstrual bleeding. Side effects of UAE include pelvic pain, vaginal expulsion of submucosal fibroids, and postembolization syndrome, a flu-like syndrome that presents with pain, nausea, fevers, and leukocytosis. Since the first published study in 1995, UAE has been shown to cause persistent decreases in pain, heavy menstrual bleeding, and an average decrease in uterine fibroid size of >50% at 5 years [42]. Randomized controlled trials have demonstrated that compared to myomectomy, UAE is equally effective at reducing heavy menstrual bleeding at 4 years [5]. Further, UAE is associated with a decreased risk of blood transfusion and shorter hospital stays, and rates of new fibroid formation are significantly lower with UAE than with myomectomy [42]. Quality of life scores and reintervention rate at 4 years are not significantly different between myomectomy and UAE [5]. Ten year follow-up from the EMMY trial, which did not permit repeat embolization after initial treatment, reported secondary hysterectomy rates of 28% at 5 years and 35% at 10 years [13].

In a meta-analysis comparing UAE and MRgFUS, UAE has been associated with improved symptom relief, improved quality of life, lower reintervention rates, and lower pregnancy rates [43].

Patients with no desire for future fertility should be counseled that pregnancy is possible after UAE.

Variant 3: Reproductive age patient with uterine fibroids and concurrent adenomyosis, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and no desire for future fertility. Initial therapy.

Endometrial Ablation

There is no relevant literature regarding the use of endometrial ablation in the treatment of uterine fibroids in patients with concomitant adenomyosis. Treatment failure of endometrial ablation for heavy menstrual bleeding has been associated with the presence of adenomyosis [59].

Hysterectomy

Hysterectomy, whether transvaginal, laparoscopic, or abdominal, remains the most common treatment for uterine fibroids, accounting for three-quarters of fibroid treatment in the United States [50], and provides definitive resolution of all fibroid-related symptoms for patients who do not desire future pregnancy. Hysterectomy eliminates the risk of new fibroid formation and allows for simultaneous treatment of concomitant intrauterine disease such as adenomyosis, endometriosis, high risk cervical dysplasia, uterine prolapse, or intrauterine malignancy. If there is not another indication for removal, the ovaries are left in place to avoid precipitating menopause and associated cardiovascular risks. Even with bilateral ovarian conservation, hysterectomy alone is associated with elevated risk of subsequent cardiovascular disease and mood disorders. Some studies report increased mortality, especially when performed at a young age [51-53]. Short-term complications include abscess, venous thromboembolism, damage to ureter, bowel, or bladder, bleeding requiring transfusion, and vaginal cuff complications. Randomized studies have demonstrated increased rate of severe complications, longer hospitalization, and longer return to regular activities with hysterectomy compared to UAE despite similar symptom relief [54], suggesting that hysterectomy should be avoided if a less invasive procedure is available. Cohort studies and registries have reported long-term effects of hysterectomy including increased risk of cardiovascular disease [51], osteoporosis and bone fracture [55], and dementia [56].

If hysterectomy is indicated, the least invasive route for hysterectomy should be performed. Abdominal hysterectomy is associated with longer hospital stay, recovery time, and greater pain and risk of infection compared to other approaches. Vaginal hysterectomy is associated with shorter operating times, faster return to normal activities and better quality of life compared to abdominal hysterectomy. Laparoscopic hysterectomy is associated with a faster return to normal activities, shorter hospital stays, and lower rates of wound infection compared to abdominal hysterectomy [57]. Of note, there is increasing utilization of robotic-assisted hysterectomy and outcomes appear similar to traditional laparoscopy in terms of operative time, hospital stay, and postoperative complications [58].

Hysteroscopic Myomectomy

There is no relevant literature regarding the use of myomectomy alone in the treatment of uterine fibroids in patients with concurrent adenomyosis. Adenomyosis is unlikely to be effectively addressed with this technique.

Laparoscopic or Open Myomectomy

There is no relevant literature regarding the use of myomectomy alone in the treatment of uterine fibroids in patients with concurrent adenomyosis. Adenomyosis is unlikely to be effectively addressed with this technique.

Laparoscopic Uterine Artery Occlusion

There is no relevant literature regarding the use of LUAO alone in the treatment of uterine fibroids in patients with concurrent adenomyosis.

Medical Management

Although studies specifically exploring the question of heavy menstrual bleeding in patients with fibroids and concurrent adenomyosis are lacking, progestin IUDs and combined oral contraceptives have both been shown to reduce painful and heavy menstrual bleeding in randomized controlled trials [60-62]. Progestin IUDs are clinically favored due to local mechanism of action, lower levels of systemic hormones, long duration of action after placement, and user independence. A recent randomized controlled trial demonstrated significant improvement in pain and bleeding in women with adenomyosis treated with progestin IUD versus combined oral contraceptives [63]. Additionally, pooled analysis of 2 randomized controlled trials demonstrated that the presence of concomitant adenomyosis does not decrease the effectiveness of oral GnRH antagonist combinations in the treatment of heavy menstrual bleeding [64]. These therapies will not treat associated bulk symptoms.

MR-Guided High-Frequency Focused Ultrasound Ablation
There is no relevant literature regarding the use of MRgFUS ablation in the treatment of uterine fibroids in patients with concurrent adenomyosis.

Uterine Artery Embolization
Evidence from prospective cohort studies supports the use of UAE for patients with adenomyosis and fibroids who fail conservative measures and desire uterus-preserving therapy. Prospective cohort studies of women with adenomyosis and fibroids demonstrate improvement in quality of life and symptom scores, especially when fibroids predominate [65]. In patients with adenomyosis with or without fibroids, UAE improved symptom scores and quality of life at up to 7 years follow-up. Eighteen percent of patients underwent hysterectomy for persistent symptoms [66,67]. A recent meta-analysis reported short-term (<12 months) and long-term (>12 months) improvement in symptoms in 94% and 85%, respectively, with a 7% rate of hysterectomy for persistent symptoms [68]. Successful pregnancy has been reported after UAE for adenomyosis with fibroids symptoms [68]; however, comprehensive data on fertility and pregnancy is lacking, and patients should be counseled accordingly.

The results of the ongoing multicenter nonblinded randomized controlled QUESTA trial (Quality of Life after Embolization versus Hysterectomy in Adenomyosis) aims to provide a comparison of UAE and hysterectomy outcomes in patients with adenomyosis [69].

Variant 4: Reproductive age patient with pedunculated submucosal uterine fibroids, symptomatic with heavy uterine bleeding. Initial therapy.

Endometrial Ablation
There is no relevant literature regarding the use of endometrial ablation as the initial treatment of pedunculated submucosal uterine fibroids.

Hysterectomy
Hysterectomy, whether transvaginal, laparoscopic, or abdominal, remains the most common treatment for uterine fibroids, accounting for three-quarters of fibroid treatment in the United States [50], and provides definitive resolution of all fibroid-related symptoms for patients symptomatic with heavy uterine bleeding. However, there is no relevant literature regarding the use of hysterectomy as the initial treatment of pedunculated submucosal uterine fibroids as less invasive and equally effective approaches are available.

Hysteroscopic Myomectomy
Hysteroscopic myomectomy is the procedure of choice for pedunculated submucosal uterine fibroids <5 cm. The procedure is associated with shorter hospitalization and faster return to usual activities compared to laparoscopic or open myomectomy. Data from large registries demonstrate that improvement in symptom scores and quality of life is equivalent to more invasive surgical approaches at 2 to 3 months [4].

Laparoscopic or Open Myomectomy
There is no relevant literature regarding the use of laparoscopic or open myomectomy in the treatment of pedunculated submucosal uterine fibroids.

Laparoscopic Uterine Artery Occlusion
There is no relevant literature regarding the use of LUAO in the treatment of pedunculated submucosal uterine fibroids.

Medical Management
Some forms of medical management can be considered for patients with pedunculated submucosal uterine fibroids associated with heavy bleeding. First-line medical management includes NSAIDs and estrogen-progestin oral contraceptive pills, which reduce bleeding symptoms [16]. Tranexamic acid is a nonhormonal alternative agent that may reduce bleeding symptoms in patients with fibroids [17].

Second line medical management includes parenteral GnRH agonists (eg, leuprolide acetate) and oral GnRH antagonists (eg, elagolix, linzagolix, and relugolix) [18-23]. In addition to reducing bleeding symptoms, both GnRH agonists and antagonists are effective at significantly reducing tumor volume and are commonly used for short courses to decrease fibroid size in preparation for surgery [24]. As monotherapy, both GnRH agonists and antagonists are associated with hypoestrogenic effects including headaches, hot flushes, hypertension, and loss of bone mineral density. Combination treatment with low doses of estrogen and progestin mitigates these symptoms and is an FDA-approved treatment option for fibroid-related heavy menstrual bleeding [19,25]. Although these

agents are often chosen by patients interested in uterus-preserving therapy or preservation of future fertility, fertility is suppressed during treatment and cessation of therapy leads to rapid recurrence of symptoms.

There is growing data supporting the efficacy of progesterone receptor modulators such as ulipristal acetate. These agents reduce both bleeding and bulk symptoms and can be administered intermittently, allowing for menstruation during medication breaks [26,27]. Efficacy of continuous use after 3 months and intermittent use for 2 years with comparison to both placebo and GnRH agonists has been demonstrated in randomized controlled trials [28-30]. However, reports of hepatotoxicity are a barrier to its approval for use in the United States [31,32].

MR-Guided High-Frequency Focused Ultrasound Ablation

Evidence for MRgFUS for pedunculated submucosal fibroids is limited and derives from case reports and small prospective studies [70]. One prospective study demonstrated a 66% decrease in volume of perfused fibroid with a corresponding 30% decrease in diameter of pedunculated submucosal fibroids at 6 months. Treatment was associated with a significant improvement in symptom score, with 89% of women reporting an improvement in bulk symptoms [71]. These findings are consistent with prior data on pedunculated submucosal fibroids treated with UAE [72].

Uterine Artery Embolization

The literature on therapeutic outcomes of patients undergoing UAE for fibroids does not distinguish patients with pedunculated submucosal fibroids. Patients undergoing UAE for submucosal fibroids can experience fibroid expulsion. One retrospective study demonstrated a 50% rate of complete expulsion, with low complication rates [73].

Variant 5: Postmenopausal patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms). Negative endometrial biopsy. Next step.

With rare exception, the natural history of fibroids is shrinkage and symptom resolution with menopause due to decreased circulating estrogen and the cessation of menses. Given this natural history and the elevated incidence of cancer in this group, suspicion for malignancy should be increased in postmenopausal patients with fibroids and persistent abnormal uterine bleeding, fibroid growth, or both. It is essential to pursue endometrial biopsy prior to intervention because it can rule out endometrial neoplasia and, in some cases, diagnose sarcoma. There is no evidence in favor of any one approach for symptomatic uterine fibroids in postmenopausal patients with a negative endometrial biopsy.

Endometrial Ablation

There is no relevant literature regarding the use of endometrial ablation in the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

Hysterectomy

Hysterectomy may be helpful in postmenopausal patients with symptomatic fibroids and a negative endometrial biopsy. In this setting, benefits of hysterectomy include the ability for pathologic evaluation of the uterus to confirm absence of malignancy. Additionally, postmenopausal patients are less likely to pursue fertility sparing treatments. These considerations must be weighed against the potential for increased surgical risk in this older cohort of patients.

Hysterectomy, whether transvaginal, laparoscopic, or abdominal, remains the most common treatment for uterine fibroids, accounting for three-quarters of fibroid treatment in the United States [50], and provides definitive resolution of all fibroid-related symptoms for patients who do not desire future pregnancy. Hysterectomy eliminates the risk of new fibroid formation and allows for simultaneous treatment of concomitant intrauterine disease such as adenomyosis, intrauterine endometriosis, or intrauterine malignancy. Short-term complications include abscess, venous thromboembolism, damage to ureter, bowel, or bladder, bleeding requiring transfusion, and vaginal cuff complications. Randomized studies have demonstrated increased rate of severe complications, longer hospitalization, and a longer return to regular activities with hysterectomy compared to UAE despite similar symptom relief [54], suggesting that hysterectomy should be avoided if a less invasive procedure is available. Cohort studies and registries have reported long-term effects of hysterectomy, including increased risk of cardiovascular disease [51], osteoporosis and bone fracture [55], and dementia [56].

If hysterectomy is indicated, the least invasive route for hysterectomy should be performed. Abdominal hysterectomy is associated with longer hospital stay, recovery time, and greater pain and risk of infection compared to other approaches. Vaginal hysterectomy is associated with shorter operating times, a faster return to normal activities, and a better quality of life compared to abdominal hysterectomy. Laparoscopic hysterectomy is associated

with a faster return to normal activities, shorter hospital stays, and lower rates of wound infection compared to abdominal hysterectomy [57].

Hysteroscopic Myomectomy
Hysteroscopic myomectomy may be helpful in postmenopausal patients with symptomatic fibroids and negative endometrial biopsy when fibroids are submucosal and associated with postmenopausal bleeding. Hysteroscopic myomectomy involves the transvaginal, transcervical placement of a hysteroscope and removal of submucosal uterine fibroids by an electrosurgical wire loop or other instruments and is indicated in patients with submucosal fibroids. Risks include uterine perforation, fluid overload, a need for blood transfusion, bowel or bladder injury, endomyometritis, and a need for reintervention [3]. The procedure is associated with shorter hospitalization and a faster return to usual activities compared to laparoscopic or open myomectomy. Improvement in symptom scores and quality of life is equivalent to other surgical approaches at 2 to 3 months [4]. In a randomized trial of myomectomy versus UAE, myomectomy using any approach was shown to have improved quality of life scores at 2 years, although this difference was no longer significant at 4 years [5]. There is no additional relevant literature regarding the use of hysteroscopic myomectomy specific to the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

Laparoscopic or Open Myomectomy
Laparoscopic or open myomectomy may be helpful in postmenopausal patients with fibroids causing bulk symptoms and negative endometrial biopsy. There is no additional relevant literature regarding the use of laparoscopic or open myomectomy specific to the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

Laparoscopic Uterine Artery Occlusion
There is no relevant literature regarding the use of LUAO in the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

Medical Management
There is no relevant literature regarding the use of medical management in the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

MR-Guided High-Frequency Focused Ultrasound Ablation
There is no relevant literature regarding the use of MRgFUS ablation in the treatment of postmenopausal patients with fibroids and negative endometrial biopsy.

Uterine Artery Embolization
In postmenopausal patients with abnormal uterine bleeding, even in the presence of fibroids, uterine sarcoma and endometrial cancer must be ruled out as the underlying cause prior to treatment with minimally invasive therapy. Evidence from a small retrospective study supports UAE as a safe and effective procedure for the treatment of fibroids in postmenopausal patients. Complete fibroid necrosis was seen in all patients with accompanying symptom resolution (urinary frequency and vaginal bleeding) in 89% [74]. Given the increased risk of uterine malignancy in this population, all postmenopausal patients with abnormal uterine bleeding should undergo workup to rule out endometrial cancer prior to proceeding with UAE.

In addition to endometrial cancer, there is a risk that presumed fibroids actually represent uterine sarcoma. Retrospective studies estimate the risk of unexpected uterine sarcoma following surgery for presumed fibroids at 2.94 per 1,000. However, stratification by age reveals lower risk in patients <30 years of age and a higher risk in older patients (up to 10.1 per 1,000 in patients 75-79 years of age) [75]. Fibroids and uterine sarcoma can present similarly, and although MRI is a useful tool to distinguish the two, there is no way to definitively diagnose them prior to surgery. As a result, continued fibroid growth or bleeding after menopause should raise suspicion for uterine sarcoma [76].

Variant 6: Reproductive age patient with uterine fibroids desiring pregnancy and experiencing reproductive dysfunction. Initial therapy.

Endometrial Ablation
There is no relevant literature regarding the use of endometrial ablation in the treatment of fibroids in patients desiring pregnancy and experiencing reproductive dysfunction. Endometrial ablation is associated with a high risk of pregnancy complications [2].

Hysterectomy
There is no relevant literature regarding the use of hysterectomy in the treatment of fibroids in patients desiring pregnancy and experiencing reproductive dysfunction. Infertility is permanent and irreversible following hysterectomy.

Hysteroscopic Myomectomy
If a complete infertility workup fails to identify another source of infertility, hysteroscopic myomectomy may be offered to patients with fibroids who desire pregnancy and are experiencing reproductive dysfunction. However, whether hysteroscopic myomectomy improves fertility is a matter of debate, and high-quality evidence on live birth rates following hysteroscopic myomectomy is lacking. Two single center randomized controlled trials have been performed to date. The first demonstrated no difference in pregnancy rates between patients undergoing hysteroscopic myomectomy and controls [7]. The second demonstrated improved pregnancy rates after myomectomy; however, data could not be externally validated due to internal inconsistencies in reporting [8,9]. Neither study reported live birth rates. The miscarriage rate was reported in one study and found to be between 30% and 50% [7]. Retrospective studies demonstrate pregnancy rates of 85% after hysteroscopic myomectomy with live birth rates of 65% [10]. Large prospective registries show no significant difference in fertility outcomes among hysteroscopic, laparoscopic, and open myomectomy [11].

Laparoscopic or Open Myomectomy
Evidence for laparoscopic or open myomectomy in patients with fibroids and otherwise unexplained infertility comes from two historic randomized controlled trials. Both demonstrated similar pregnancy and live birth rates between patients with infertility and at least 1 fibroid >5 cm undergoing laparoscopic versus open myomectomy [77,78]. The combined miscarriage rate was comparable to the general population at 14% and was not significantly different between groups. Laparoscopic myomectomy was associated with decreased postoperative fever, shorter hospital stays, and a smaller decrease in postoperative hemoglobin [78].

Laparoscopic Uterine Artery Occlusion
There is no relevant literature regarding the use of LUAO in the treatment of fibroids in patients desiring pregnancy and experiencing reproductive dysfunction.

Medical Management
Although most accepted medical therapies suppress fertility, a recent study of ulipristal acetate in patients with infertility and submucosal fibroids undergoing in vitro fertilization demonstrated a 41% reduction in fibroid volume and a pregnancy rate similar to matched controls without fibroids [79].

MR-Guided High-Frequency Focused Ultrasound Ablation
Evidence for MRgFUS for fertility enhancement in patients with fibroids and reproductive dysfunction is limited to case reports [80,81]. A randomized controlled trial to investigate the efficacy and safety of MRgFUS for this indication was terminated due to lack of enrollment [82].

Uterine Artery Embolization
Pisco et al [46] retrospectively studied a population of patients with infertility and fibroids or adenomyosis who underwent UAE. Patients included in the study had failed to conceive for at least 1 year, and some had previously undergone myomectomy or attempted in vitro fertilization. The spontaneous pregnancy rate at 1 and 2 years following UAE was 29.5% and 40.1%, respectively, with a live birth rate of 81% (148 live births following 182 pregnancies). The authors did not find a statistically significant difference in pregnancy outcome between partial UAE and conventional UAE.

Summary of Recommendations

- **Variant 1**: Laparoscopic or open myomectomy, medical management, MRgFUS, or UAE is usually appropriate for the initial therapy of a reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and a desire to preserve fertility. In most cases, medical management should be trialed prior to pursuing more invasive therapies. The procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2**: Laparoscopic or open myomectomy, medical management, MRgFUS, or UAE is usually appropriate for the initial therapy for a reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bowel, or bladder symptoms), and no desire for future

fertility. In most cases, medical management should be trialed prior to pursuing more invasive therapies. The procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).

- **Variant 3**: Medical management or UAE is usually appropriate for the initial therapy for a reproductive age patient with uterine fibroids and concurrent adenomyosis, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms), and no desire for future fertility. In most cases, medical management should be trialed prior to pursuing more invasive therapies.
- **Variant 4**: Hysteroscopic myomectomy or medical management is usually appropriate for the initial therapy for a reproductive age patient with pedunculated submucosal uterine fibroids that is symptomatic with heavy uterine bleeding. In most cases, medical management should be trialed prior to pursuing more invasive therapies.
- **Variant 5**: Hysterectomy is usually appropriate as a next step for a postmenopausal patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (eg, pressure, pain, fullness, bladder, or bowel symptoms) and negative endometrial biopsy. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 6**: Hysteroscopic myomectomy or laparoscopic or open myomectomy is usually appropriate for the initial therapy for a reproductive age patient with uterine fibroids desiring pregnancy and experiencing reproductive dysfunction. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care). The panel did not agree on recommending medical management for this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from this procedure in this scenario. Intervention with this procedure in this patient population is controversial but may be appropriate.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

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