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BRIEFINGS FROM
MINIMALLY INVASIVE AND GYNECOLOGIC SURGEONS

Evidence Based Management of Uterine Fibroids

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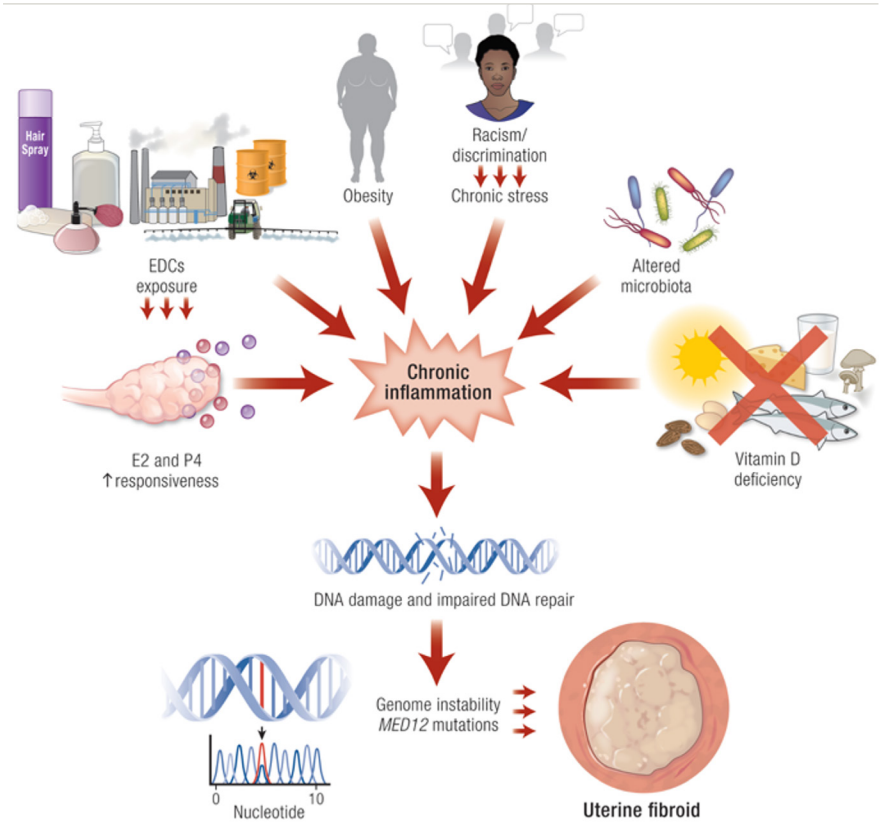
Uterine fibroids (UFs) are benign soft tissue tumors of the uterus that affect up to 80% of women in the US and cost the US economy up to $34.4 billion annually [1, 2]. UFs disproportionately affect Black women who tend to have earlier onset of disease and more severe symptoms [3]. UFs are hormone dependent and tend to occur in reproductive age women and regress to varied degrees after menopause. Some risk factors for developing UFs include Black race (racism), nulliparity, obesity, family history of UF, hypertension, vitamin D deficiency, exposure to endocrine disrupting chemicals (EDCs) [4]. Recent studies suggest that UF development is mediated by chronic inflammation which leads to DNA damage and impaired DNA repair [5].

Approximately 25% of women with UFs will have symptoms that may include:

- Heavy menstrual bleeding (HMB)
- Pelvic pain
- "Bulk"-related symptoms caused by large myoma(s), such as pressure in the abdomen and pelvis
- Urinary symptoms (urinary urgency, frequency, and incontinence)
- Bowel symptoms (constipation and tenesmus)
- Persistent HMB can induce iron-deficiency anemia and associated fatigue [4].

Symptomatic UFs can impact women's psychological and emotional health, leading to anxiety, depression, social isolation and feelings of hopelessness and helplessness. UFs can severely impact multiple facets of a women's quality of life such as sexuality, emotional and physical well-being, productivity, and relationships [4].



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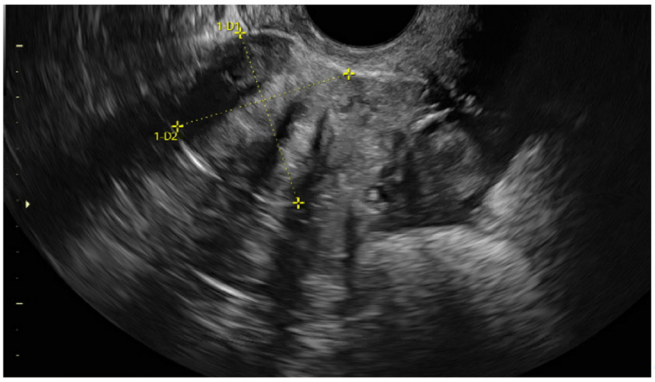
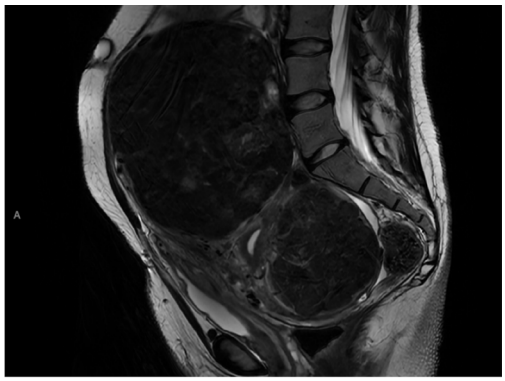
UFs are often diagnosed on physical exam. Different imaging modalities are utilized for UF diagnosis and evaluation including ultrasounds, saline sonograms, and MRIs.

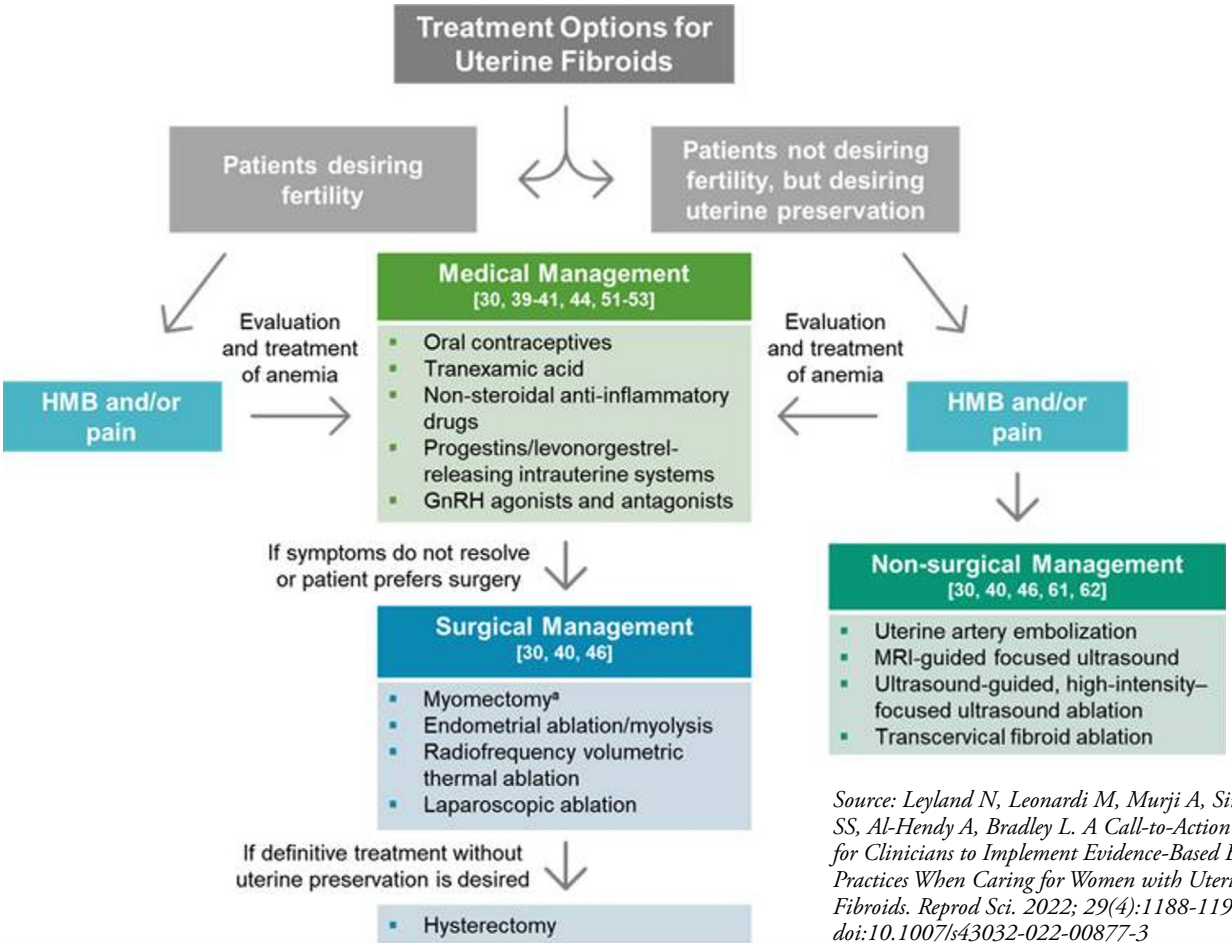


Pelvic ultrasound of UF



Pelvic MRI of UF

Treatment options for UFs can be broadly categorized into: (1) surgery, (2) non-surgical/minimally invasive procedures (e.g., uterine artery embolization, magnetic resonance-guided focused ultrasound, and radiofrequency ablation), or (3) medical treatment. The algorithm below represents an evidence-based approach to UF management, which should be tailored according to the patients' clinical scenario [6].



Source: Leyland N, Leonardi M, Murji A, Singh SS, Al-Hendy A, Bradley L. A Call-to-Action for Clinicians to Implement Evidence-Based Best Practices When Caring for Women with Uterine Fibroids. Reprod Sci. 2022; 29(4):1188-1196. doi:10.1007/s43032-022-00877-3

At the University of Chicago Center for Advanced Treatment and Research (CATeR) of Uterine Fibroids, **https://www.uchicagomedicine.org/conditions-services/obgyn/uterine-fibroids**, our expert team of obstetricians, gynecologists, advanced pelvic surgeons, fertility specialists, hematologists, radiologists, sonologists, pelvic and mental health experts value the importance of shared- decision making and are committed to implementing best practice guidelines in fibroid treatment.

(continued from page 2)

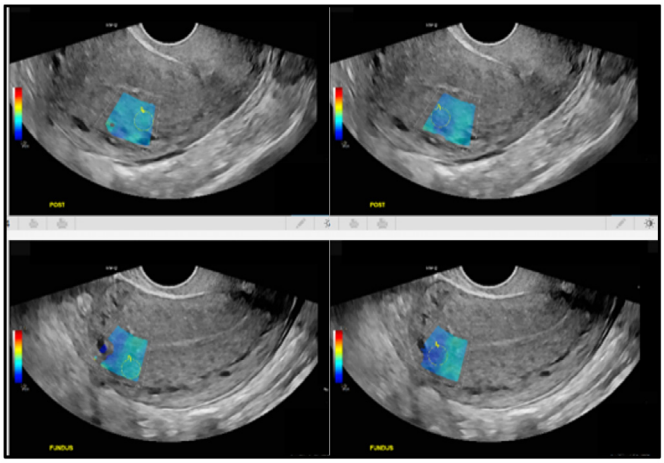
The CATeR Fibroid Center hosts an annual Hands-On CME training event for OBGYN specialists in the surrounding community and teaching hospitals. This **event** is proctored by fellowship trained Minimally Invasive Gynecologic Surgeons (MIGS) at the University of Chicago. Additionally, we host quarterly patient **webinars** on the basics of uterine fibroids and abnormal uterine bleeding. Our surgical team offers second opinions and surgical consults for complex surgical candidates including patients with high BMIs, multiple comorbid conditions, advanced pelvic adhesive disease, large multi-fibroid uterus etc. We also care for special populations including Bloodless patients. **Referring physicians can contact us here.**

Emerging Treatments for Secondary Prevention of UF

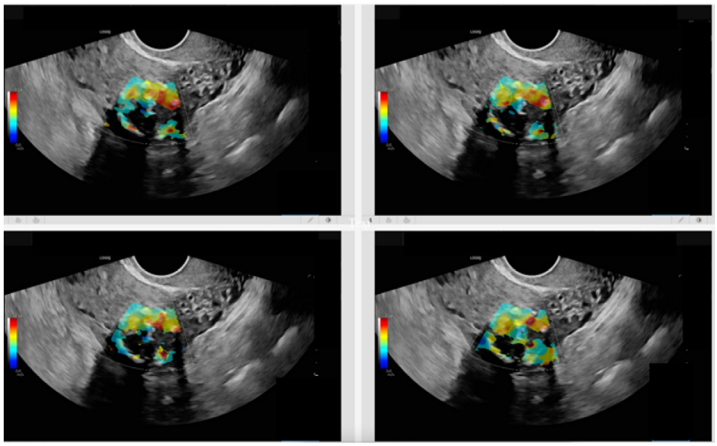
A key feature of UFs is fibrosis which is characterized by excessive accumulation of extracellular matrix (ECM). Research thus supports that inhibition of fibrotic processes may restrict UF growth. Epigallocatechin gallate (EGCG), a green tea compound with powerful antioxidant properties, is an investigational drug for uterine fibroids. Early phase clinical trials show that EGCG is effective in reducing fibroid size and its associated symptoms. The mechanism of action is the anti-fibrotic effects of EGCG in fibroid cells [7]. Another naturally occurring compound that has shown promising results in inhibiting UF growth and mitigating symptoms is Vitamin D. It is well recognized that diet and micronutrients play a role in the biology and pathophysiology of UFs. Many studies have demonstrated a strong correlation between vitamin D deficiency and potential development of UF. Vitamin D's effect on UF is mediated by the regulation of progesterone receptors (PR) and estrogen receptors (ER); as well as the ability of vitamin D to control Vitamin D receptor (VDR) expression [8]. Early clinical trials investigating the use of vitamin D and/or green tea extract (EGCG) for UF management have shown promising results. The favorable safety profiles of these naturally occurring products make utilization of these supplements potentially safe, efficacious, and economically viable for secondary prevention of UF. **Some authors suggest vitamin D (4000 IU/day), EGCG (800 mg/day).**[9]

Clinical Research in UF – *Investigating a new approach to managing an old disease.*

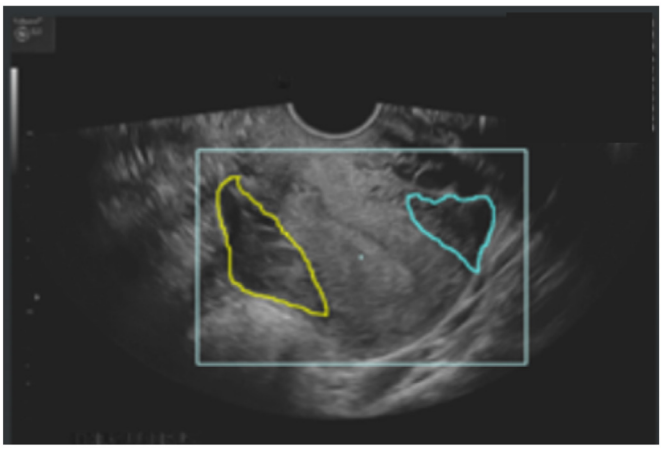
The variability of UF symptomatology is a unique and poorly understood feature of the disease. This unpredictability of UF morbidity influences variable treatment decisions, thus perpetuating disparities in care [10]. The clinical research at University of Chicago is geared towards understanding and predicting UF behavior with a goal to design precision medicine for UF management. Precision medicine is a new approach to medicine that offers tailored treatments to affected populations based on an increased understanding of the molecular mechanism of the disease in question [11]. By investigating the use of an ultrasound-based technology called shear wave elastography (SWE) to assess uterine and UF stiffness and integrating machine learning (ML) and artificial intelligence (AI) to basic gynecologic ultrasounds, we aim to advance UF diagnostics, prognostication, and precision management. We are currently enrolling patients into our clinical trials. Please see the next page for ongoing studies and inclusion/exclusion criteria.



SWE of normal myometrium; sagittal view



SWE of posterior wall UF; sagittal view



Machine Learning station; outlined UF

Ongoing Fibroid Research Studies

Evaluating shear wave elastography (SWE) for use in the diagnosis and management of Uterine Fibroids

Objective: To investigate the use of shear wave elastography (SWE) for myometrial and UF imaging.

Aim 1: To design an SWE image acquisition protocol and validate in vivo stiffness against ex vivo mechanical tissue measurements.

Aim 2: To correlate uterine fibroid stiffness with fibroid symptom severity and quality of life as measured using a validated questionnaire.

Aim 3: To describe the SWE characteristics of the normal myometrium and to assess their variability by race and menstrual phase.

Who can participate?

- Women aged 18 years and older,
- Must speak and understand English,
- Should have a previous ultrasound report for comparison,
- No fibroids (normal uterus) or have 5 or fewer fibroids,
- No diagnosis of endometriosis,
- Premenopausal with a BMI ≤ 40,
- Have not used hormonal therapy within a month of the SWE scan.

CLICK TO VIEW THE BROCHURE FOR THIS STUDY

Surgical myomectomy Followed by Oral Myfembree Versus Standard of Care Trial (SOUL Trial)

Objective: To determine if Relugolix combination therapy (Myfembree) can slow or even delay fibroid growth and symptoms after myomectomy.

Aim 1: To determine if there is a difference in fibroid recurrence (defined as a new fibroid identified on ultrasound with volume >1 cm3), symptom recurrence (defined as either moderate-heavy menses with PBAC score ≥ 120, pelvic pain during menses measured on NRS ≥ 4 or score of 25 on symptom severity scale) or need of reintervention between women receiving myomectomy plus Relugolix combination therapy (Myfembree) compared to those receiving standard of care after myomectomy.

Aim 2: To determine if there is a difference in quality-of-life scores as measured by Patient Reported Outcome and Quality of life questionnaires (UFS-QOL, WPAI: SHP, Female Sexual Function Index,) in patients receiving myomectomy plus Relugolix combination therapy compared to those receiving standard of care after myomectomy.

Who can participate?

- Women aged 18 years and older,
- Must speak and understand English,
- Have had a robotic, laparoscopic, or open myomectomy within 4 to 6 weeks,
- Does not desire to conceive for at least 12 months.

There are a few additional inclusion & exclusion criteria to join each study. We will ensure that patients meet criteria before they are enrolled.

CLICK TO VIEW THE BROCHURE FOR THIS STUDY

To learn more about these clinical trials, contact Sumeyra Agambayev at sumeyra.agambayev@bsd.uchicago.edu or Dr. Laveaux at slaveaux@bsd.uchicago.edu.

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