

Uterine Fibroids

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Agenda

- **▶** Background
- ▶ Epidemiology
- ► Etiology
- ▶ Types of Uterine Fibroids
- ▶ Natural History
- ► Risk Factors

- **▶** Symptoms
- **▶** Diagnosis
- ► Impacts on quality of life, fertility, pregnancy
- ► Treatment options

Case Presentation

▶ MB is a 33 yo AA woman who presents to your office with complaints of increasing fatigue. Her only significant past medical history is Class 1 obesity. While obtaining her history she reveals that she has a long history of very heavy menstrual cycles. She states that she has to wear multiple pads at one time and changes them frequently during her menses. She often passes large clots and soils her clothing. She also states that she misses work often during her menstrual cycle due to severe cramping. Her cycles occur every 28 days and last for 5-6 days. She feels like her bleeding has increased in the last year. She does not use any contraception and is not sexually active. She does state she feels increasing bladder pressure. She says her mother and sister both had hysterectomies for uterine fibroids.

Case Presentation Cont.

► PMH: Class 1 obesity

▶ PSH: none

▶ Social: Negative

► FH: HTN in mother.

▶ Vitals: normal

▶ Physical exam:

► General: Well appearing

►CV: RRR

► Resp: CTAB

► Abd: obese, nontender throughout. Palpable mass at the umbilicus.

▶ Pelvic: Enlarged uterus up to the umbilicus

▶ Labs

▶TSH: normal

▶ CBC: Hgb 8.9, MCV 65, Plts 200

Background: Uterine Fibroids

- ▶ Leiomyoma, Fibroids, Fibroid tumors, Myomas
- Definition = Benign solid neoplasms composed to smooth muscle and fibroblasts
- ▶ Vary in size and location within the uterus
- Most common solid and symptomatic neoplasm in women
- Leading indication for hysterectomy



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Epidemiology

- ► Estimated to occur in up to **70%** of women by menopause. The true incidence difficult to determine because most cases are asymptomatic and go undiagnosed
- ▶ Approximately 25% become clinically significant enough to require any intervention.
- ▶ Prevalence increases until menopause, then declines
- ▶ Black women have a 2-3x higher incidence at all age groups as compared to all other women
 - ▶ Black women are typically diagnosed at earlier ages, are more likely to be anemic, develop clinically significant symptoms earlier, and have larger uteri at the time of diagnosis.

Etiology

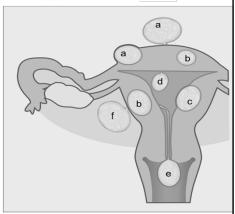
- ▶ The exact cause is unknown
- ▶ Advances have been made in understanding the molecular biology of fibroids and their dependence on genetic, hormonal and growth factors
 - ▶ **Genetic** more than 100 genes and genetic abnormalities have been studied and may have implications in leiomyoma development. Research is ongoing.
 - ▶ Hormones Both increase in number and responsiveness of receptors for estrogen and progesterone appear to promote fibroid growth
 - ▶ Found more in hyper estrogenic states such as obesity, HRT use menopausal women, early menarche or late menopause, anovulatory states, etc.
 - Growth decreases after menopause and with medications that cause a menopausal state

▶ Growth Factors

▶ Growth factors produced locally by smooth muscle cells and fibroblast appear to promote fibroid growth

Types of Uterine Fibroids

- ▶ A standardized leiomyoma sub-classification system was developed by the International Federation of Gynecology and Obstetrics (FIGO) to describe fibroid location in relation to the endometrial and serosal surfaces of the uterus.
- <u>Submucosal</u> project into the cavity of the uterus
- <u>Intramural</u> Growth within the myometrium or muscle of the uterus
- <u>Subserosal</u> Growth on the outermost serosal layer of the uterus (outside of the muscle)
- <u>Pedunculated</u> Hang off of a stalk (outside or inside the uterus)



Schematic drawing of various types of uterine fibroids: a=subserosal fibroids, b=intramural fibroids, c=submucosal fibroid, d=pedunculated submucosal fibroid, e=cervical fibroid, f=fibroid of the broad ligament

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Natural History of Fibroids

- ▶ Most grow slowly 9% growth rate over 12 months
- ▶ Growth rate decreases after age 35 years in white women, but not in black women
- ▶ Most reduce in size with the onset of menopause
- Rapid growth in premenopausal women generally does not indicate sacromatous change
- ► Fibroids become calcified or degenerate in menopausal women

Risk Factors

- ▶ Both modifiable and non-modifiable risk factors have been associated with leiomyoma development
- ▶ These include
 - ▶ Age
 - ▶ Race
 - ▶ Family History 1st degree relatives with fibroids confer 3.5x increased risk
 - ► Endogenous/Exogenous hormonal factors
 - ▶ Obesity High BMI is associated with a modest increase risk of fibroids by way of increasing endogenous estrogen production.
 - ▶ Parity several studies suggest a protective effect of pregnancy on development of fibroid with 3 or more deliveries decreasing risk up to 5-fold

Risk Factors

- ▶ Lifestyle factors Have been demonstrated to potentially modify signaling pathways and molecular mechanisms involved in fibroid development and growth
 - ▶ Diet diet rich in red meat, ham, beef increase risk of fibroids
 - ▶ Exercise woman who exercise regularly are at lower risk than those who do not exercise
 - ▶ Caffeine Use increased use at earlier age increases risk
 - ➤ **Smoking** variable data on if this increases or decreases risk. Research ongoing
 - **▶** Alcohol Consumption
 - **▶** Stress

Symptoms

- Abnormal Uterine Bleeding (most common presenting symptom)
 - ► Heavy or prolonged menstrual cycles
 - With or without associated anemia
- Increased pelvic cramping or pain

- Sequelae of uterine enlargement (Bulk Symptoms)
 - ▶ Pelvic Pressure
 - ▶ Urinary frequency or pressure
 - Constipation or change in bowel habits
- ▶ Abdominal distension
- ▶ Infertility*

Diagnosis

- ► Complete medical history
- ▶ Physical Exam → Abdominal and Pelvic Exam
 - Incidentally found or in exam for a woman with symptoms
 - ▶ Not all fibroids can be palpated
 - ▶ Generally a uterus that is enlarged to the size of 12 or 14 week pregnancy is readily palpated on exam



Diagnosis

▶Imaging

- ▶ Transvaginal ultrasound
 - ▶ is a useful screening test to assess for leiomyoma and should be your initial imaging modality of choice
 - ▶ Provides good assessment of size and number of fibroids
- ► Submucosal fibroids (intracavitary)
 - ▶ Saline Sonography
 - ► Hysterosalpingogram
 - ► Hysteroscopy

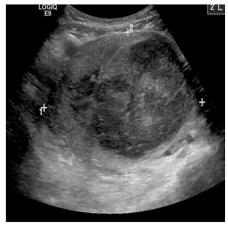


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Diagnosis

▶Imaging

- ▶ Pelvic MRI
 - ► Useful for surgical planning
 - ▶ allows evaluation of number, size location and proximity to bladder, rectum, tubal opening in uterine cavity and endometrium
 - ▶ Not generally required
- ▶ CT scan
 - ► Generally less useful in the evaluation of fibroids
- ▶ Diagnostic evaluation should exclude other causes of AUB and pelvic masses based on history and physical exam findings



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Impacts on Fertility, Pregnancy, and quality of life

Fibroids and Fertility

- True cause of infertility in only 1-3% infertile patients
- ▶ Many women experiencing infertility or recurrent miscarriage are found to have fibroids
 → May not be related to their infertility
- ▶ All other causes of infertility should be ruled out before fibroids implicated as the cause
- ▶ Procedural removal of fibroids => Myomectomy
 - ▶ Data inconclusive as to if this increases fertility
 - ▶ Depends on location of the fibroids
 - ▶ **Submucosal** Data suggest that removal can improve fertility outcomes
 - ▶ Subserosal –Have not been shown to be implicated in fertility
 - ▶ Intramural Located in the muscle of the uterus. Can decrease fertility depending on size and location. Removal has not been shown to IMPROVE fertility
- ► Take Away Until fibroids proven to be the cause of infertility, removal may not improve fertility.

Fibroids and Pregnancy

- ▶ Found in 18% of first trimester ultrasounds
- ▶ Often have NO impact on pregnancy
- ▶ Most do not increase in size during pregnancy, but they can due to hormonal stimulation
 - ► Can Degenerate (necroes in center) in pregnancy → intense pain, fever
- ▶ Fibroids can affect pregnancy by increasing rates of
 - ▶ Fetal growth restriction
 - ▶ Malpresentation
 - ► Early Labor
 - ▶ Prolonged or dysfunctional labor
 - ▶ Hemorrhage after delivery
 - ► Early pregnancy loss (miscarriage)

Quality of Life Issues

- ▶ Heavy bleeding and pain and impact all aspects of life
 - ► Anemia
 - ► Hospitalizations
 - ▶ Impaired work productivity
 - **▶** Embarrassment
 - ▶ Increased cost of pads/tampons
 - ▶ Emotional distress
 - ▶ Avoidance of social engagement
 - ► Financial burdens

Treatment options

Treatment options - overview

- ▶ Variety of options available which include
 - **► Expectant Management** → watchful waiting
 - ► Medical therapies
 - ► Hormonal therapies
 - ▶ Non-Hormonal medical therapies
 - **▶** Surgical treatments
 - ▶ Myomectomy
 - ▶ Hysterectomy
 - ► Interventional Therapies
 - ► Radiologic procedures
- Alternative therapies
 - ► Complementary and alternative therapies such as acupuncture, herbal preparations, alternative medicines lack data in effectiveness

Expectant Management

- Appropriate in women who have no or minimal symptoms or do not desire therapy
- ▶ Rarely results in harm. Fibroids do not become cancerous and data has not shown clinical meaningful change in symptoms with short term follow up of 1 year.
- ▶ In asymptomatic patients or those who do not desire intervention, it is appropriate to consider expectant management as a long term management plan.
- ▶ Can monitor based on symptoms or changes in physical exam

Medical Therapies

- Generally treat bleeding symptoms as they do not decrease the size of fibroids
- There is insufficient comparative evidence currently to guide recommendations on first-line medical therapies, thus decision on medical therapy should be individualized

Hormonal

- ▶ Contraceptive pills
- ▶ Progesterone pills
- Depot Provera
- Levonorgestrel Intrauterine Devices
 - Expulsion rates are higher (11% vs 0-3%) in women with leiomyoma, particularly those with submucosal fibroids.

Non-Hormonal

- ► NSAIDs → not shown to improve bleeding related to fibroids
- ► Gonadotropin Releasing Hormone Antagonist
 - ▶ Reversible suppression of gonadotropins and ovarian sex hormones → temporary menopausal state
 - ► Can be used up to 2 years with add back therapy → reduce impacts of hypoestrogenic state
 - ▶ Can Decrease size temporarily
 - ▶ Generally used as bridge to surgery or interventional procedure
- Tranexamic Acid
 - ➤ Antifibrinolytic medication that prevents fibrin degradation → slows heavy bleeding

Surgical Therapies - Myomectomy

Procedural intervention and surgical approaches treat bulk symptoms and bleeding by decreasing fibroid mass

- Myomectomy
 - Removal of the fibroids from the uterus
 - ▶ Uterus remains intact
 - ▶ Types
 - ▶ Hysteroscopic
 - ▶ Laparoscopic
 - ▶ Abdominal

- Advantages
 - ▶ Retains uterus for future fertility or personal preference
 - ▶ Will improve bleeding and pressure symptoms
 - ▶ Depending on location can improve fertility
- ▶ Disadvantages
 - ► Fibroids may grow back
 - ► Increased blood loss during procedure and general surgical risks
 - ▶ Creation of adhesions/scar tissue
 - ▶ May require cesarean section if becomes pregnant
 - ▶ Increased rates of re-intervention in younger women

Hysterectomy

- Complete removal of the uterus and fibroids
- ► For women who have completed child bearing
- ▶ Types
 - ▶ Abdominal
 - ▶ Laparoscopic
 - ▶ Vaginal
 - ▶ Total removal of uterus and cervix
 - ► Supracervical removal of uterus and leave cervix

- ▶ Advantages
 - ► True definitive management of fibroids and symptoms
- Disadvantages
 - ▶ Depending on approach can have a longer hospitalization.
 - ▶ Longer recover 4-6 weeks
 - ▶ Surgical risks
 - ▶ Loss of fertility

Interventional Therapies

- ▶ Radiologic procedures that reduce size of fibroids and bleeding
- ▶ Recommended for women who wish to maintain their uterus
- ▶ Procedures
 - ▶ Uterine Artery Embolization
 - ▶ Radiofrequency ablation
 - ▶ Focused ultrasound

Deciding on the treatment

- Decision should be individualized based
 - ▶ Patient preferences
 - ► Symptoms severity
 - ▶ Patient short and long term goals
- ▶ Providers should discuss ALL options and have a in depth discussion on recommendations for therapy based on the individuals needs

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Uterine Artery Embolization for Symptomatic Leiomyomas: Who, Why, How

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Objectives

- 1. Patient evaluation: Initial work-up and how to optimize patient selection for uterine artery embolization (UAE) ${\sf UAE}$
- 2. Uterine arterial anatomy: Learn to identify and work around arterial anomalies
- 3. UAE technical aspects: Learn the proper tools for technical success
- 4. Synergistic analgesia and managing postprocedural pain
- 5. Postprocedure Care: How to manage patients post-embolization
- 6. Outcomes: Defining technical and clinical success and expected patient outcomes
- 7. Comparison of treatment modalities: Exploring the objective data





Focused History

- · Characterize abnormal bleeding
- Evaluate for bulk symptoms
- Pelvic pain
- Symptomatic anemia
- Pre- or Postmenopausal?
- Fertility



Physical Exam

- An enlarged, mobile uterus (correlating to a weight of approximately 300 g or 12 weeks of pregnancy) with irregular contour is consistent with fibroids
- Recent gynecologic examination by an OB/GYN



Laboratory Studies

- CBC
- Basic chemistry panel
- PT/INR
- Pregnancy test prior to intervention
- Documentation of recent Pap smear and endometrial biopsy in instances of abnormal uterine bleeding



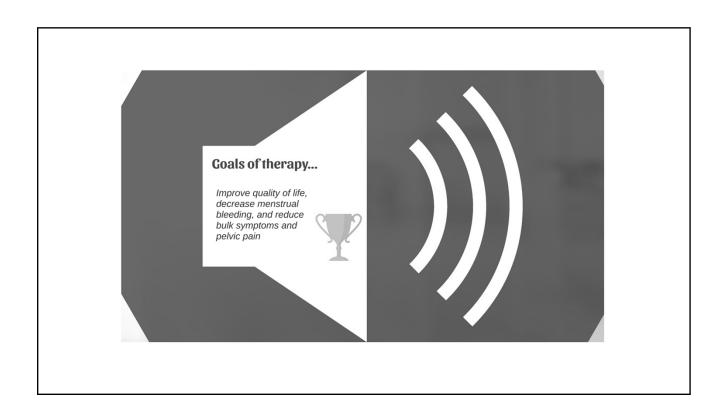


- **Ultrasound is the gold standard**: 90% to 99% sensitivity, but it may not detect subserosal or diminutive fibroids
 - Advent of 3D imaging technology can improve spatial resolution with coronal reconstruction of uterus
- Ultrasonography after infusion of saline into the uterine cavity can delineate submucousal myomas and indicate the proximity of intramural myomas to the endometrial cavity
- MRI provides highest spatial resolution and more information on number of fibroids, size, vascularization, relationship with the endometrial cavity and serosal surface, and boundaries with normal myometrium
 - · May help exclude other uterine pathology, particularly adenomyosis
 - Suboptimal in excluding malignancy

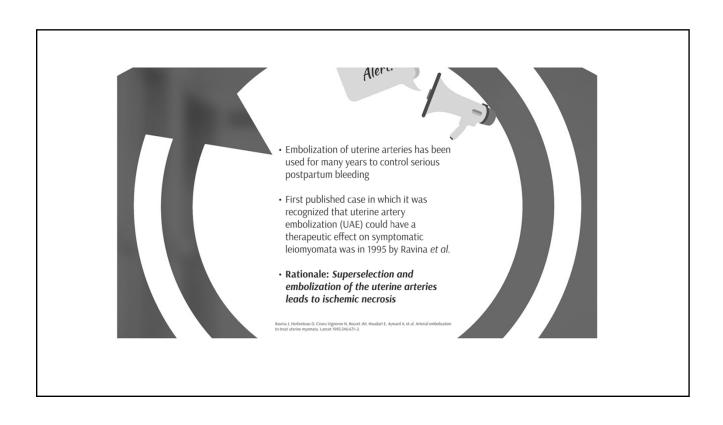


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Patient Selection



- **Inclusion criteria:** patients with symptomatic leiomyomatous uterus confirmed by imaging and low-probability of malignant etiology
 - May consider endometrial biopsy for all postmenopausal women with vaginal bleeding, for all women with irregular vaginal bleeding, and for all women over 40 years of age with regular menorrhagia.
- Exclusion criteria: malignancy, tortuosity and advanced atherosclerosis of iliac or uterine arteries or both on preprocedural imaging, active salpingitis or endometritis, and unregulated coagulation parameters

Vedantham et al. Uterine Fibroid Embolization: Preprocedure AssessmentTechniques in Vascular and Interventiona Radiology, Vol 5, No 1 (March), 2002: pp 2-16

Pre-Intervention Imaging

Ultrasound

- Highly sensitive: 90% to 99% sensitivity, though suboptimal for subserosal or diminutive fibroids
- In patients with extremely large uteri, ultrasound may not be capable of visualizing the entire uterus
- Ultrasonography after infusion of saline into the uterine cavity can delineate submucousal myomas and indicate the proximity of intramural myomas to the endometrial cavity

MRI

- · MRI provides highest spatial resolution and more information on number of fibroids, size, vascularization, relationship with the endometrial cavity and serosal surface, and boundaries with normal myometrium
- May help exclude other uterine pathology, particularly adenomyosis
 Suboptimal in excluding malignancy

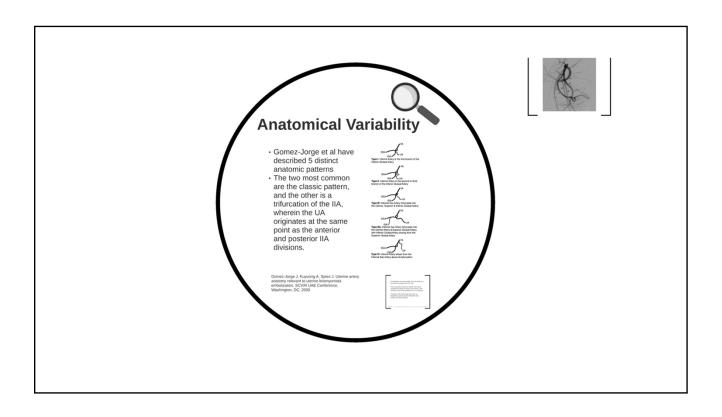


 Useful to identify the characteristics of the main artery supplying the uterus and any arterial atherosclerosis or obstruction that could contraindicate catheter-directed therapy

Vascular Anatomy

- · Internal iliac artery (IIA) bifurcates into anterior and posterior division
- Generally, the posterior division gives rise to the superior gluteal, iliolumbar and lateral sacral arteries
- · Uterine artery is typically the first branch of the anterior division of the internal iliac artery, arising anteromedially



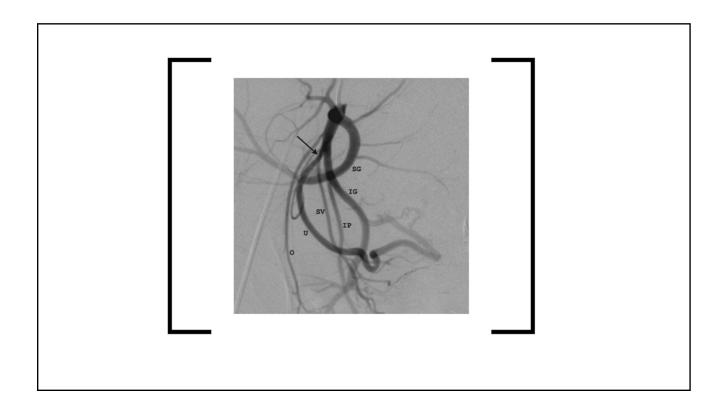


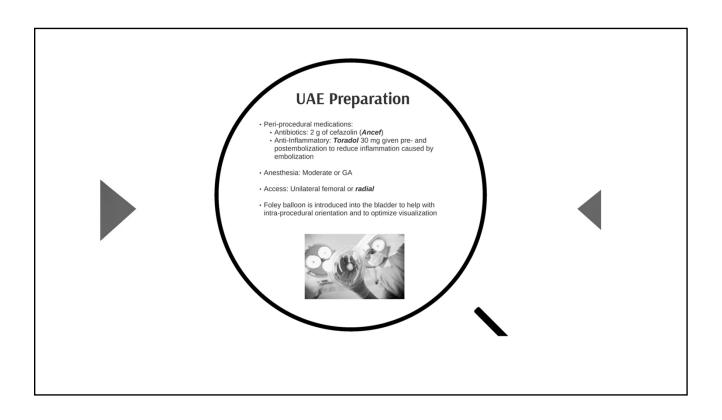
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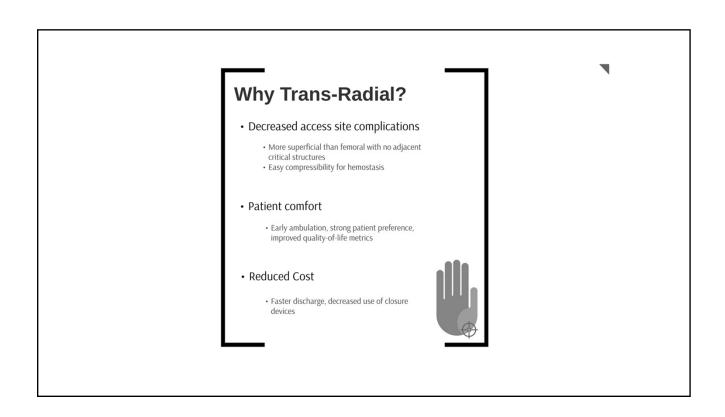
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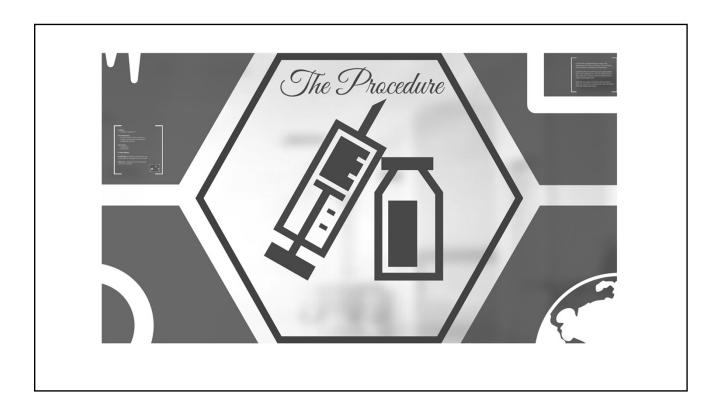
- UA diameter can vary greatly, from as small as 1 to 2 mm to as large as 5 or 6 mm.
- The intrauterine branches of both UAs freely anastomose within the body of the uterus, with excellent cross-filling between the 2 circulations
- Treatment with GnRH agonists such as leuprolide (Lupron) tend to make the UAs smaller and more spastic.

Vorthington-Kirsch et al. Uterine Fibroid Embolization: Technical Aspects. Techniques in Vascular and Interventional Radiology, Vol 5, No 1 (March), 2002: pp 17-34





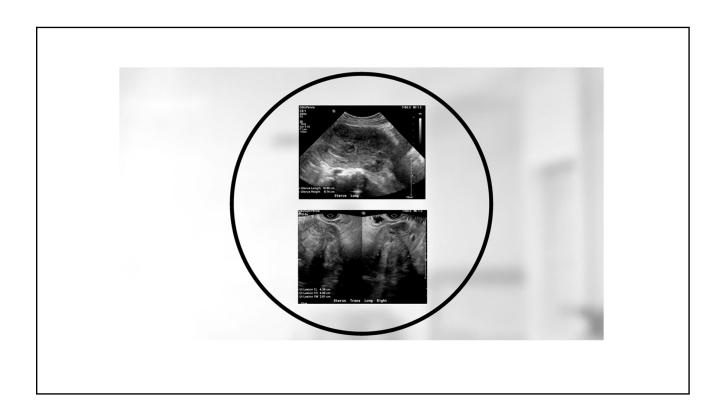


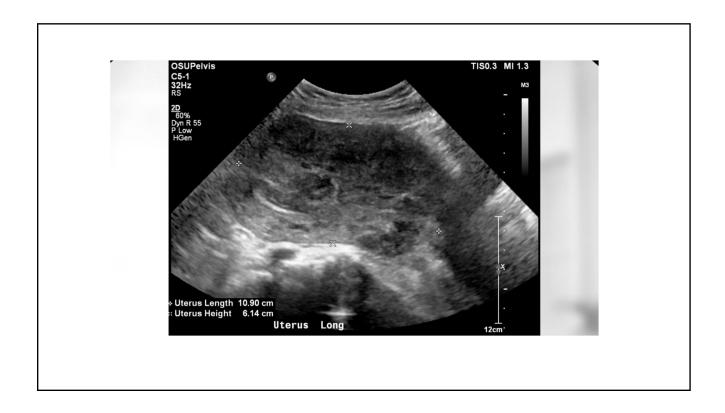


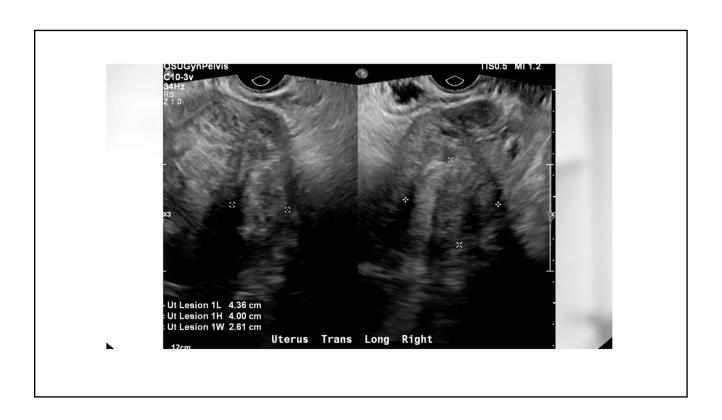


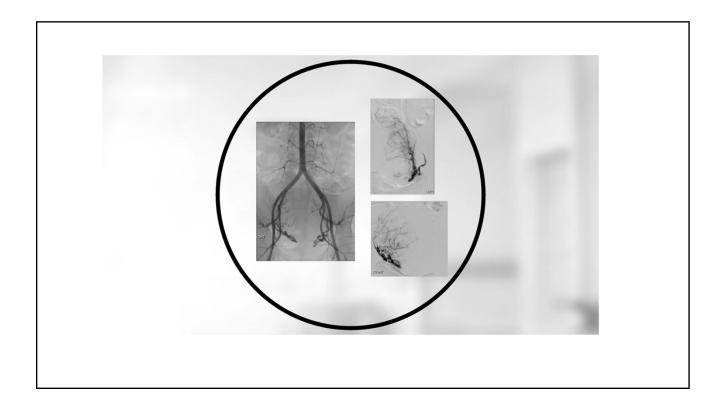


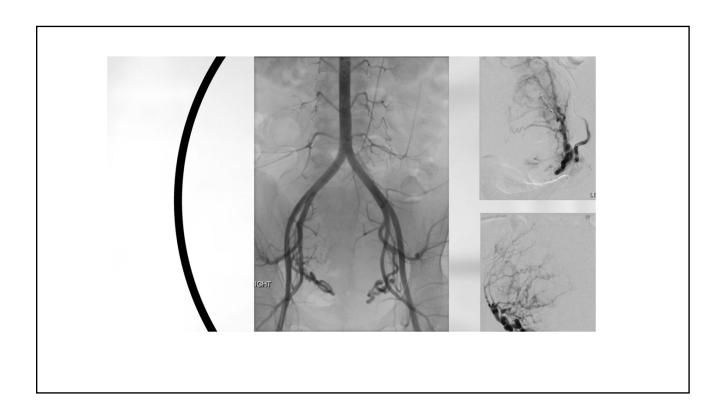


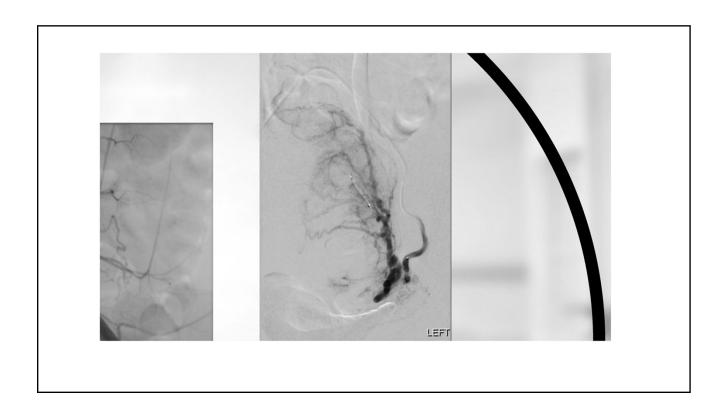


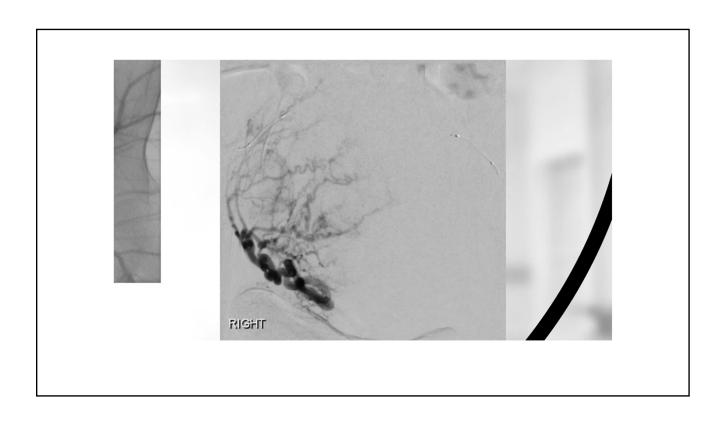






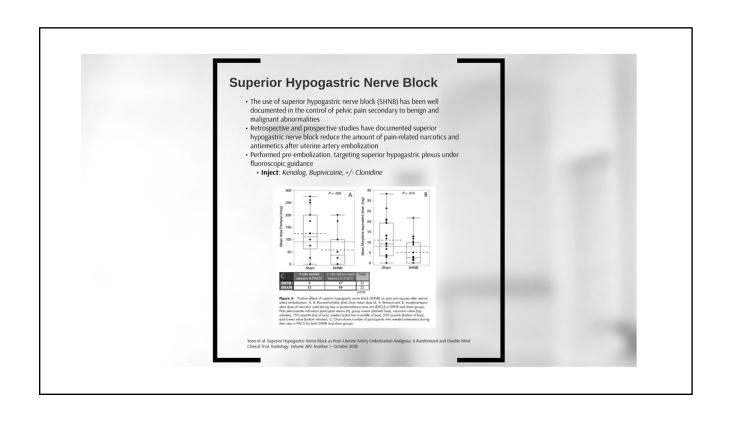


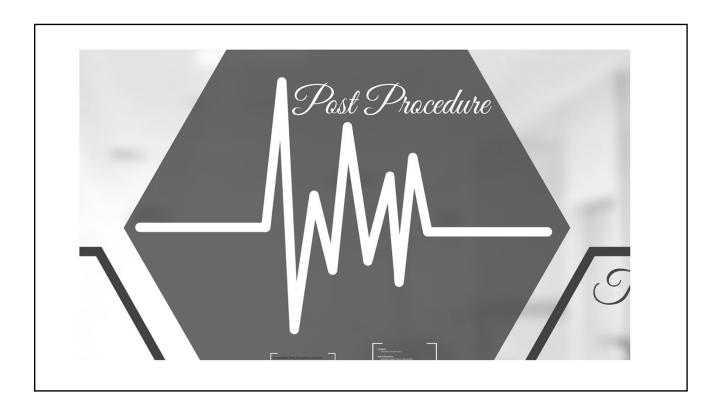












Immediate Post Procedure Course

- Control the symptoms associated with the acute ischemia of the uterus: abdominal cramps, nausea, and pain (**Postembolization Syndrome**)
- Manifests in first 12 to 24 hours after the procedure, as tissue necrosis begins to release breakdown products
- Overnight admission recommended
- Monitor for vascular complications

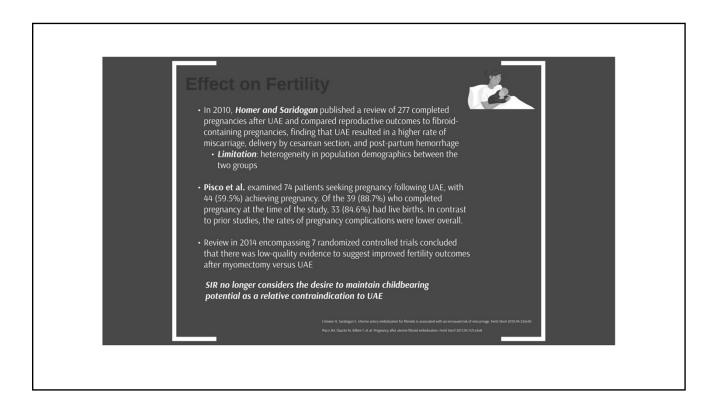


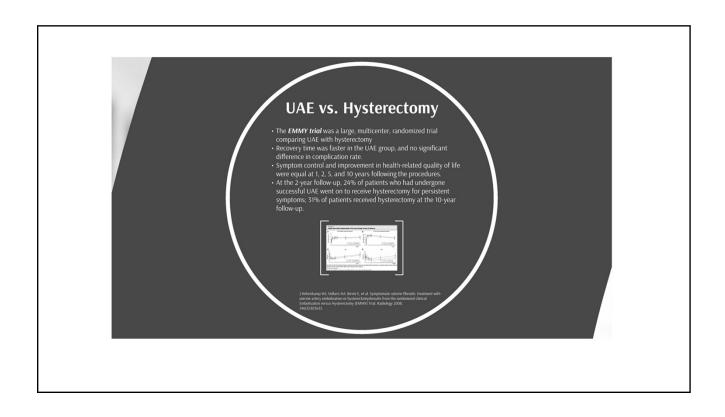


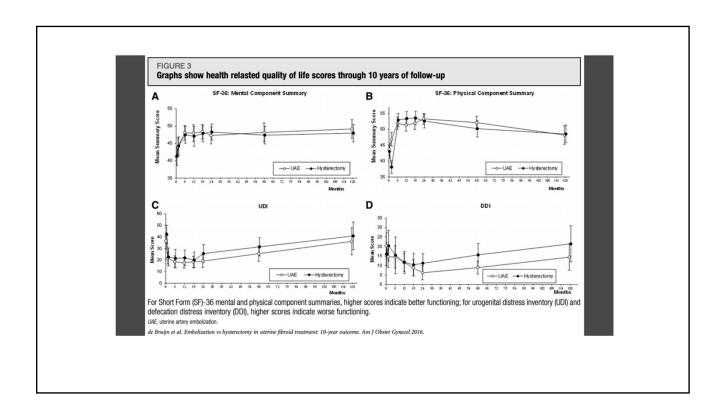


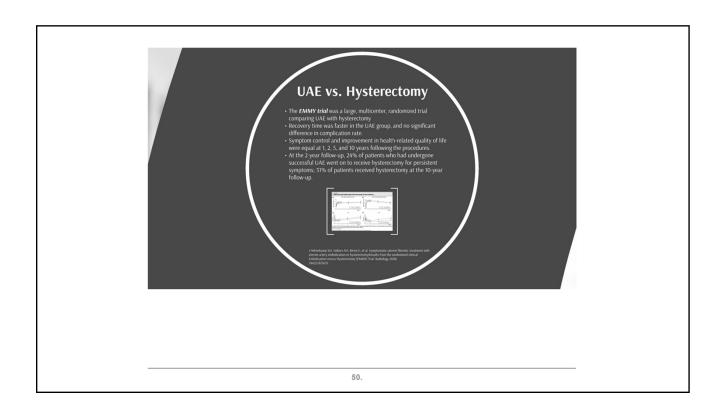


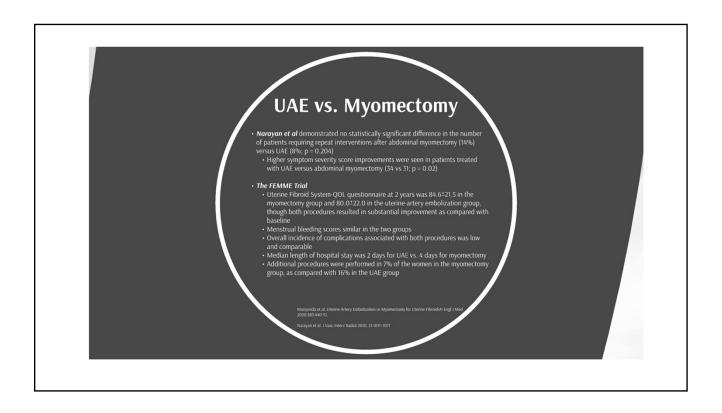














- Current body of published literature about UAE demonstrates the safety and efficacy of this procedure for the treatment of symptomatic leiomyomata
- In patients who do not wish to pursue surgical options, UAE is well-established as a safe and viable alternative with comparable symptom control and improvement in health-related quality of life
- While the vast majority of patients achieve symptom relief, it is important to counsel patients about possibility for further surgical intervention

Where do we go from here?

- More multidisciplinary collaboration
- Dispersion of more information on UAE to patients & clinicians
- Further large, prospective studies investigating UAE versus surgical interventions
- Techniques to augment more traditional UAE such as hypogastric nerve block and radial artery access may improve patients' experience and recovery time.