UTERINE FIBROIDS (LEIOMYOMAS)

FLAME LECTURE: 227
BURNS / CAROL 8.29.19
LEARNING OBJECTIVES

- Discuss the prevalence of uterine leiomyomas
- Describe the symptoms and physical findings of a patient with uterine leiomyomas
- Describe the diagnostic methods to confirm uterine leiomyomas
- List the management options for the treatment of uterine leiomyomas
- Prerequisites: NONE
- See also: NONE
EPIDEMIOLOGY

- Extremely common benign growth of uterine smooth muscle cells
  - Lifetime risk: 70% in Caucasian women and >80% of African American women
- Most common indication for surgery in women (~1/3 of all hysterectomies)
- They are hormonally sensitive - grow and shrink in response to fluctuating levels of estrogen/progesterone
  - Most will regress after menopause when circulating hormones decrease
EPIDEMIOLOGY

Risk Factors:
- African American
- Hypertension
- Early menarche
- Peri-menopausal
- Increased alcohol
- Family History

Protective Factors:
- Increasing parity
- Oral contraceptive use
- Injectable DMPA
Uterine leiomyomas are *monoclonal tumors* meaning they arise from a single progenitor smooth muscle cell.

Uterine fibroids are *benign* and can remain asymptomatic in many women.

- They do NOT have malignant potential to transform into leiomyosarcomas.

However, *leiomyosarcomas* are malignant tumors that can also arise from smooth muscle cells of the uterus independently.

- Notably, many women who develop leiomyosarcoma also have leiomyomas.
PATHOPHYSIOLOGY

- Symptoms and classification depend on the location of fibroid on the uterus

A. Subserosal
B. Intramural
C. Submucosal (SM)
D. SM (Pedunculated / Intracavitary type)
E. Parasitic
Most fibroids are asymptomatic and discovered incidentally.

Others require intervention because they cause discomfort, bleeding, or infertility.

- 3 classes of symptoms:
  - Abnormal uterine bleeding
  - Bulk-related symptoms: Pelvic pressure/pain
  - Reproductive difficulties: infertility, pregnancy loss, obstetric complications

### CLINICAL SYMPTOMS

<table>
<thead>
<tr>
<th>F</th>
<th>Frequency/retention of urine</th>
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<tbody>
<tr>
<td>I</td>
<td>Iron deficiency anemia</td>
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<tr>
<td>B</td>
<td>Bleeding abnormalities</td>
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<tr>
<td>R</td>
<td>Reproductive difficulties (preterm/difficult labor, increased C-section rate)</td>
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<tr>
<td>O</td>
<td>Obstipation/rectal pressure</td>
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<tr>
<td>I</td>
<td>Infertility</td>
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<tr>
<td>D</td>
<td>Dysmenorrhea</td>
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<td>S</td>
<td>Symptomless (most common)</td>
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Clinical presentation

- Clinical symptoms depend on size and location of fibroid
  - Submucosal fibroids (C/D) which protrude into the uterine cavity can disrupt the endometrium causing abnormal uterine bleeding (the most common symptom), infertility, or problems with placental implantation (like miscarriage)
  - Large subserosal fibroids (A) can put pressure on surrounding structures causing hydronephrosis, urinary frequency, constipation, and venous stasis
DIFFERENTIAL & DIAGNOSIS

- When symptomatic, the most common presentation of uterine fibroids is abnormal uterine bleeding, thus differential = PALM COEIN
  - Structural causes
    - P: polyps
    - A: adenomyosis
    - L: leiomyoma
    - M: malignancy/hyperplasia
  - Non-structural causes
    - C: coagulopathy
    - O: ovulatory dysfunction
    - E: endometrial factor
    - I: iatrogenic
    - N: not yet classified
- Also, in a reproductive age woman with enlarging uterus, always check for pregnancy

Adenomyosis vs. Fibroids:
- Both cause AUB and have enlarged uteri. However:
  A) Fibroids are surrounded by pseudo-capsule separating abnormal tissue from surrounding myometrium
  B) Fibroids lead to an *irregularly* enlarged uterus, adenomyosis generally causes symmetrical enlargement
A SIDENOTE ON POLYPS...

- Localized benign overgrowth of *endometrial* tissue (different origin tissue from fibroids)
- Can be pedunculated and prolapse into vagina
- Risk factors:
  - Usually occur in age 40-50, but can occur after menopause
  - Obesity
  - Tamoxifen increases risk by causing endometrial proliferation due to estrogen agonism (but more concerning is potential for hyperplasia/malignancy development)
- Most common symptom is abnormal uterine bleeding (the ‘P’ in PALM-COEIN) but they can also cause dyspareunia and post-coital bleeding if prolapses into vagina
- Diagnosis: Ultrasound or sonohystogram can visualize polyp but hysteroscopy can concurrently remove polyp. Even with confirmed polyp + AUB in woman >45, should still do EMB to rule out malignancy.
- Polyps, though benign, should be removed because their bleeding can mask underlying malignancy. Can also contribute to infertility.
  - Removed via *hysteroscopic polypectomy* for full visualization of polyp origin even if prolapsed through cervix
DIAGNOSIS OF FIBROID

- **Pelvic Exam**
  - Enlarged, mobile, irregularly shaped uterus without any corresponding ovarian masses

- **Transvaginal Ultrasound**
  - First Line Test: High sensitivity, low cost
  - For better visualization, can inject saline into uterus to visualize extent of disruption of endometrial cavity if concern for a submucosal fibroid (Saline Sonohysterogram)
  - Calcifications in fibroid suggests fibroid is undergoing necrosis (degenerating fibroids)

- **Hysteroscopy**
  - Can visualize inside uterine cavity but difficult assessing size and fibroids that are not submucosal or pedunculated

- **MRI**
  - Best for distinguishing between fibroids and other causes of enlarged uterus (adenomyosis, or even concern for leiomyosarcoma) but is expensive and not as widely used. Best used pre-operatively to guide surgery.
Small intramural fibroid seen on ultrasound
Large subserosal fibroid seen on ultrasound
Submucosal fibroid seen on hysteroscopy
TREATMENT
PHARMACEUTICAL OPTIONS

- **Combined Hormonal Contraceptives**
  - Pros: can reduce bleeding in setting of fibroids and can prevent occurrence of new fibroids
  - Cons: may exacerbate pressure/bulk-related symptoms

- **Progestins (helpful for patients with contraindications to estrogen)**
  - Medroxyprogesterone acetate, Etonorgestrel implant (Nexplanon), Progestin-only pills
    - Pros: reduce bleeding and fibroid size via vaginal atrophy
    - Cons: will not resolve fibroid or aid fertility; may have breakthrough bleeding

- **Levonorgestrel-releasing IUD (i.e. Mirena, Liletta)**
  - Pros: reduce bleeding/menorrhagia and uterine volume
  - Cons: will not resolve fibroid or aid fertility, intracavitary leiomyomas may make placement difficulty or not possible
TREATMENT

PHARMACEUTICAL OPTIONS

- GnRH agonist (leuprolide) or antagonists (elagolix)
  - **Pros**: effective at shrinking fibroids due to decreased estrogen, best used to shrink fibroids prior to surgery
  - **Cons**: can only be used for short time, <6 months, due to side effects (essentially causes functional menopause and decreased bone mineral density). Fibroids will again enlarge when medication is stopped
  - **Note**: can consider add-back hormonal therapy to improve these cons

- Progesterone receptor modulators (Ullipristal acetate & Mifepristone)
  - **Pros**: Temporary use to shrink fibroid size before surgery
    - Equal efficacy at decreasing bleeding and anemia + safer side effect profile than GnRH agonists
  - **Cons**: Not as effective at shrinking uterus compared to GnRH agonists, currently not available in daily low dosing and available doses are too high, have adverse effects when used regularly
**TREATMENT**

**PHARMACEUTICAL OPTIONS**

- **Uterine Artery Embolization (UAE)**
  - Pros: minimally invasive option, good option for fibroids with heavy bleeding
  - Cons: limited data on fertility after UAE, some data to support increased acute and chronic pelvic pain following procedure

- **Myomectomy (Laparoscopic, including robotic-assisted, or Open Approach)**
  - Pros: fertility-sparing, can be minimally-invasive
  - Cons: high chance of recurrence of fibroids, can cause adhesions

- **Hysterectomy**
  - Pros: only definitive treatment for fibroids
  - Cons: not fertility-sparing
TREATMENT OVERVIEW

Uterine Fibroids

Asymptomatic
- Expectant management
  - If desiring pregnancy and has submucosal fibroid, can consider hysteroscopic resection if concerning size/location

Premenopausal
- If desiring pregnancy and has submucosal fibroid, can consider hysteroscopic resection if concerning size/location
- Fibroids usually atrophy after menopause
- Thus existing pelvic mass or bleeding should be worked up for possible malignancy (EMB, imaging)

Desire pregnancy now
- Hysteroscopic myomectomy

Desire pregnancy later
- OCP’s, LNG IUD to decrease bleeding
- Hysteroscopic myomectomy if still needed when pregnancy desired

Done child-bearing
- Hysterectomy most definitive treatment
  - GnRH agonist can be added prior to surgery if needed to shrink fibroid/uterus size, however side effects should be monitored
  - Less invasive: use LNG- IUD until menopause or UAE to decrease bleeding

Postmenopausal
- Fibroids usually atrophy after menopause
- Thus existing pelvic mass or bleeding should be worked up for possible malignancy (EMB, imaging)
REFERENCES

1. UpToDate