Management of Uterine Myomas

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Disclosures

I have no relevant financial relationships to disclose.

Objectives

- Describe options for management of symptomatic myomas in patients who desire future fertility.
- Describe indications for myomectomy in the setting of asymptomatic fibroids.
- Describe options for definitive therapy when fertility is not desired, including surgical and non-excisional alternatives.
FIGO Nomenclature

Epidemiology of Myomas

• By age 50, cumulative incidence 70-80%

• Prevalence 2.3x higher in black women
  • Increased number of myomas
  • Diagnosed at younger ages

• Women with 1st-degree relatives with myomas have 2.5-fold increased risk of developing myomas.

Hormone Sensitivity of Myomas

• ↑ number of estrogen and progesterone receptors

• High aromatase expression

• Progesterone stimulates mitotic activity, also affects cell replication and apoptosis

• Estrogen causes ↑progesterone receptor expression
Submucosal Myomas

• Dysfunctional uterine contractility
• Secretion of angiogenic factors
• Altered gene expression → decreased endometrial receptivity

Vollenhoven 1990

Rackow 2008

Strategy for Management Decisions

Symptomatic or asymptomatic?

Fertility desired?

Distortion of uterine cavity?

Overview of Management

• Medical management of symptomatic myomas
• Surgical management (fertility-sparing)
• Definitive therapies
Overview

- Medical management of symptomatic myomas
- Surgical management (fertility-sparing)
- Definitive therapies

Goals of Medical Management

- Decrease size of myomas preoperatively
- Reduce risk of transfusion
- Improve anemia
- Bridge to menopause?

Medical Management

- Options for medical management
  - Medications for control of HMB
  - GnRH agonists
  - Aromatase inhibitors
  - Levonorgestrel-releasing IUD
  - Selective progesterone receptor modulators (SPRM)
Medications for HMB

• Tranexamic acid
  • Anti-fibrinolytic, can reduce bleeding by ~40%
  • Dose TID for up to 5 days during menses
  • Some evidence to suggest necrosis of myomas

• Mefenamic acid
  • NSAID, blocks prostaglandin activity
  • 20-40% reduction in blood loss

GnRH Agonists

• Induce hypoestrogenic state

• Role in preoperative management
  • Reduction in uterine size (30-70%) at 3-6 mos.
  • May reduce operative blood loss

• ↑difficulty with surgical dissection during myomectomy?

• Side effects limit long-term use

Aromatase Inhibitors

• Increased aromatase expression in myomas

• Mechanism of action: reduction in estrogen levels

• Myoma volume reduced ~50%

• Off-label use for fibroids

• Better side effect profile vs. GnRH-a
LUS-IUD

- Decreased menstrual blood loss by 80-90% at 1 year
- Reduction in myoma volume and uterine size
- Higher rate of expulsion
  - Avoid if uterus > 12-wk size
  - Avoid if cavity distortion

Selective Progesterone Receptor Modulators

- Ulipristal acetate (UPA)
- Faster onset of amenorrhea vs. GnRH-a
- Unlike mifepristone, UPA not associated with ↑ risk of endometrial hyperplasia
- At doses of 5 and 10mg, induced amenorrhea in 47% and 58%, respectively

Preoperative Medical Therapy

- Cochrane review, 2017
  - 38 RCTs, 3623 patients (most GnRH-a, but 4 were SPRMs vs. placebo)
  - Comparisons included medical therapy vs. placebo, no treatment, or other medical therapy before myomectomy, hysterectomy, hysteroscopic resection for myomas
Preoperative Medical Therapy

- Cochrane review, 2017
  - Clear evidence that preop GnRH-a reduces uterine/myoma size and increases Hgb levels
  - SPRMs superior to placebo in reducing uterine/myoma size and bleeding, but replication of studies needed
  - Higher incidence of hot flushes with GnRH-a

Conclusions – Medical Management

- Benefit to preoperative use
- Side effects limit long-term utility of many agents
- Rapid re-growth after discontinuation

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Surgical Management

• Symptomatic myomas
  • Q: What is the best approach?

• Asymptomatic myomas
  • Q: Should I operate?

*Does myomectomy improve fertility outcomes in patients with asymptomatic myomas?*

Here’s where things get confusing.....

Limitations of the Literature

• Observational data
  • Selection bias, confounders

• Heterogeneity
  • Age
  • Size, location, and number of fibroids

• Inappropriate control groups; inconsistent primary endpoints
ASRM Guideline – Asymptomatic Myomas

- Insufficient evidence that myomas reduce the likelihood of achieving and maintaining pregnancy

- Insufficient evidence that a specific size, number, or location (excluding SM or cavity-distorting) is associated with reduced pregnancy or increased risk of early pregnancy loss

ASRM Guideline (continued)

- Insufficient evidence that myomectomy (laparoscopic or open) reduces miscarriage rates

- Fair evidence that hysteroscopic myomectomy for submucosal fibroids improves clinical pregnancy rates
ASRM Recommendations

• In asymptomatic women with cavity-distorting myomas (submucosal, or intramural with SM component), myomectomy (open or laparoscopic or hysteroscopic) may be considered to improve pregnancy rates.

• Myomectomy is generally not advised to improve pregnancy outcomes in asymptomatic infertile women with non-cavity-distorting myomas.

Data from AMIGOS Trial

• Styer et al, 2017
  • Secondary analysis from RCT investigating fertility outcomes after superovulation/IUI
  • 102 of 900 study participants had at least 1 myoma and normal uterine cavity
  • No difference in conception and LBR in those with non-cavity-distorting fibroids vs. those without fibroids
  • ↑ SAB rate in AA women with fibroids (may be due to type I error)

Limitations

• Overall prevalence of myomas only 11%
  • Study population: unexplained infertility
  • Under-detection during study screening?

• Did not record total number or total volume of myomas, only the largest; median volume 7.5 cm³

• Unknown if prior history of myomectomy
Summary – Surgical Management and Fertility

• For non-cavity-distorting myomas, literature does not support myomectomy to improve fertility.

• Fair evidence supporting myomectomy for removal of cavity-distorting myomas

Overview

• Medical management of symptomatic myomas

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• Definitive therapies

Definitive Therapies

• Hysterectomy

• Uterine artery embolization

• MR-focused ultrasound
**Hysterectomy**

- Surgical approach dependent on size, location, mobility of uterus, body habitus, etc.
- Strategies to facilitate minimally invasive approach
- Myomectomy patients should be counseled regarding risk of hysterectomy

**Uterine Artery Embolization**

- Catheterization of femoral artery under local anesthesia
- Occlusion of uterine arteries → necrosis of myomas
- Post-procedure N/V, pain, low-grade fever
- Less effective with larger fibroids

**Cochrane review, 2014**

- 7 RCTs, 793 patients
- Comparison of UAE and hysterectomy or myomectomy
- No difference in patient satisfaction rates at 2 or 5 years
- UAE had ↑ rate of minor complications
- 15-30% re-intervention rate in UAE group within 2 years
EMMY Trial

- Embolization vs. Hysterectomy (EMMY) trial
  - RCT of 177 patients, hysterectomy vs. UAE
- 10-year outcomes data recently published
- Conclusions:
  - Hyst can be avoided in 2/3 of UAE-treated patients
  - Similar QOL outcomes at 10 years

MR-Focused Ultrasound

- FDA approved MRI-guided system in 2004
- Focused, high-intensity ultrasound waves directed at myoma
- Penetrates soft tissue, causing necrosis of myoma
- Modest reduction in uterine size (less than 20%), but significant symptom reduction
- Minimal data on long-term efficacy

Summary – Definitive Treatments

- Alternatives to hysterectomy should be discussed with patients
- Avoid in patients who desire future fertility
- Long-term studies are needed to determine efficacy of MR-focused ultrasound
Conclusions (1 of 2)

• Medical treatment options may be appropriate preoperatively or in patients who wish to avoid surgery.

• Removal of submucosal and cavity-distorting myomas may improve pregnancy rates.

Conclusions (2 of 2)

• There is insufficient data to recommend myomectomy for asymptomatic patients with myomas that do not distort the uterine cavity.

• Consider non-excisional procedures as an alternative to hysterectomy in select patients who desire definitive management.

Questions