OPTIONS FOR MANAGEMENT OF UTERINE FIBROIDS

RAJ NARAYAN MD
MCW
BACKGROUND

• Fibroids affect*:
  • 60% reproductive age women
  • 80% of women during lifetime
• Fibroids account for 600,000 hysterectomies in US per year¹
• Public healthcare burden in the US is estimated to be between $5.9-34 billion/year!!
• Incidence 3-4 times higher in AA women compared to Caucasian

*Laughlin SK, Semin Reprod Med. 2010; 28:204-217
GENETICS OF LEIOMYOMA

• Benign monoclonal tumors
• May also occur as part of heritable cancer syndromes
  • HLRCC (hereditary leiomyomatosis and renal cell cancer) is autosomal dominant
  • Alport syndrome: X linked progressive nephropathy
• Up-regulation of genes involved in fibrosis and extracellular matrix production and transforming growth factor (TGF)β
BACKGROUND

• Fibroids cause
  • Menorrhagia
  • Pelvic pain
  • Pressure symptoms on bladder or bowel
  • Infertility (sole cause in 1-3%)
  • Pregnancy complications
  • Iron deficiency anemia

• Location of fibroids and size matter
  • Submucosal
  • Intramural
  • Subserosal
EFFECT OF FIBROID ON FERTILITY

- **Submucosal fibroid**
  - 70% decrease in implantation and clinical pregnancy rates after IVF*

- **Intramural fibroid**
  - Non cavity distorting intramural fibroids adversely affect fertility
  - Related to size of fibroids (>3cm)
  - Decreased implantation, clinical pregnancy and live birth**

- **Subserosal fibroid**
  - Does not negatively affect clinical pregnancy but may influence mode of delivery

*Somigliana E Hum Reprod Update. 2007;13:465-76
**Sunkara SK Hum Reprod. 2010;25:418-19
DIAGNOSIS

- Clinical examination
  - Essential to determine route of surgery
- Endometrial sampling
  - Important in most women
  - Risk factors for fibroids are similar to those of endometrial hyperplasia
    - Low parity
    - Obesity
    - AA race
- Sonohysterography
- Hysterosalpingography
- Hysteroscopy
• Ultrasonography
  • Transvaginal sonography
  • Sufficient for diagnosis in a vast majority of patients not considering uterine preservation
  • Saline sonohysterography outlines submucous fibroids
IMAGING - MRI

- Useful for precise anatomic mapping
- Especially useful to evaluate large uteri
- Obesity does not obscure
- Detects co-existing disease such as adnexal mass
- Distinguishes between adenomyosis and leiomyoma
- Outlines distortion of pelvic anatomy due to fibroids
MEDICAL MANAGEMENT

• Managing excessive bleeding
• Managing pelvic pressure/pain
• Managing anemia due to chronic blood loss
• Pre-operative shrinking of fibroids

There are currently no FDA approved agents for long term treatment of uterine fibroids.
MEDICAL MANAGEMENT

- GnRH analogues
  - Pre-operative Depot Leuprolide 3.75mg/month for 3 months is the only FDA approved GnRH analogue
  - 35-65% reduction in size of fibroids and uterus can be achieved
  - Amenorrhea
  - Reduces intra-operative blood loss, decreases hospital stay and helps convert some laparotomies into minimally invasive procedures
  - Re-growth of fibroids to pre-treatment size within months of cessation of GnRH therapy
  - May make surgical planes indistinct: myomectomy may be difficult
MEDICAL MANAGEMENT

- GnRH Analogue with Add-back
  - Progesterone
    - Relieves symptoms of hot flashes
    - Uncertain if it helps or opposes the effect of GnRH
  - Estrogen
    - Risk of unopposed estrogen effect on endometrium
- Estrogen-Progesterone
  - Comparable to Progesterone only add-back
MEDICAL MANAGEMENT

- Tibolone
  - Not available in the US
  - Selective tissue estrogenic activity modulator
  - Long term (24 months) use as add-back reduced hot flashes, prevented bone loss

- Raloxifene
  - More significant reduction in size of leiomyoma than GnRH alone
MEDICAL MANAGEMENT

- GnRH antagonist
  - Does not have the immediate flare effect of GnRH analogues
  - Needs daily injection
- Selective Estrogen Receptor Modulator*
  - Currently no evidence that they are effective
  - Raloxifene
    - Decreases collagen synthesis in leiomyomata
  - Tamoxifen
    - Not ideal since it will increase risk of endometrial cancer
    - May be a better choice in patients with history of breast cancer

*Deng L. The Cochrane Library, 2012, issue 10
MEDICAL MANAGEMENT

• Aromatase inhibitors
  • Currently available: letrozole and anastrozole
  • Significantly block ovarian and peripheral estrogen production
  • Reduction of leiomyoma size similar to GnRH analogue
  • Rapid onset of action without flare
  • Oral medication
SELECTIVE PROGESTERONE RECEPTOR MODULATORS

- Currently available: Mifepristone, ulipristal,
- Investigational: telapristone, asoprisnil
- Can cause endometrial thickening and hyperplasia

MIFEPRISTONE
- Improves fibroid specific quality of life without reducing fibroid size*
- Endometrial hyperplasia, risk is increased 16-55 fold* 

ULIPRISTAL: oral daily dose equivalent to GnRH analogue**

*Tristan M. The Cochrane Library. 2012:issue 8
**Croxtall J. Drugs. 2012; 72 (8):1075-85
MEDICAL MANAGEMENT

• Levonorgestrel IUS
  • FDA does not approve use in patients with uterine anomalies or distortion
  • Effective in reducing bleeding without reduction in myoma size *
  • Consider in pre-menopausal patients with menorrhagia

• Other agents
  • Danazol: no proven effectiveness
  • Gestrinone: side effect of androgen excess symptoms

• Acupuncture
  • Cochrane review** shows no effect but there were no RCTs

*Maruo T. Contraception. 2007; 75:S99-103
**Zhang Y. The Cochrane Library. 2012: Issue 1
UTERINE FIBROID EMBOLIZATION

- Performed by interventional radiologists
- Small particles of polyvinyl alcohol used to occlude blood supply to fibroids
- MRI used to map the uterus prior to procedure
UTERINE FIBROID EMBOLIZATION

- Indications
  - Symptomatic fibroids
  - Future fertility not desired
  - Wish to avoid surgery
  - Poor surgical risk

- Contraindications
  - Gynecologic cancer not ruled out
  - Pregnancy
  - Allergy to contrast
  - Coagulopathy
  - Renal insufficiency
UTERINE FIBROID EMBOLIZATION

- Adverse effects
  - Post-procedure pain
  - Post embolization syndrome
    - Fever
    - Nausea
    - Fatigue
    - Pain
  - Passage of fibroids through cervix 5%**
  - Premature menopause*
    - 1-2% under 45 years
    - 15-20% over 45 years
  - Re-intervention rate 5.3%**

*Stovall D. Menopause 2011;18(4):437-444
**Toor SS. AJR 2012; 199:1153-1163
UTERINE FIBROID EMBOLIZATION

• Effectiveness
  • Symptomatic improvement 78-90%*
  • Less blood loss compared to abdominal hysterectomy*
  • Shorter hospital stay*
  • Quicker return to work*
  • Cost $20,000 (compared to hysterectomy 17,800)**
  • If pregnancy does occur there is increased risk of miscarriage of up to 60%**

*Toor SS. AJR 2012; 199:1153-1163
**Stovall D. Menopause 2011;18(4):437-444
MR GUIDED FOCUSED ULTRASOUND

• Performed by radiologists
• High intensity US is focused on fibroids
• Temperature 65°C-85°C
• Takes several hours
• Patient has to lay still and prone
• No more than 2 sessions in a 2 week period
• Not for postmenopausal women
Indications
- Symptomatic fibroids
- Uterine size less than 24 week size

Contraindications
- Desire for future fertility
- Subserous or pedunculated fibroids
- Presence of any metal implant
- Presence of IUD
- Myoma close to bladder, bowel, sacral nerves
- Adenomyosis
- Inability to lie prone
- Weight >250 lbs
- Abdominal surgical scars
- Severe anemia
MR GUIDED FOCUSED ULTRASOUND

• Adverse effects
  • Pain
  • Potential bowel or bladder injury
  • Skin burns
  • Nerve injury

• Effectiveness
  • 85-95% symptoms relief in 12 months*
  • 21% recurrence of symptoms at 12 months*
  • If pregnancy occurs there is increased risk of spontaneous loss (28%)**
  • Cost: $12,000*

*Stovall D. Menopause 2011;18(4):437-444
ENDOMETRIAL ABLATION

- Treats menorrhagia
- Applicable
  - if cavity is not distorted
  - if submucous fibroid is less than 3.5cm
- Effectiveness data is mixed with DUB treatment
- Cost $3,000-8,000
MYOMECTOMY

- Open procedure through laparotomy
- Laparoscopic myomectomy
- Single port laparoscopy
- Robotic laparoscopic myomectomy
- Hysteroscopic myomectomy
MYOMECTOMY

• Indications
  • Desire to preserve fertility
  • Desire to preserve uterus
  • pedunculated subserous fibroid
  • Small symptomatic submucous fibroids

• Effectiveness
  • No difference between open and laparoscopic route for fertility
  • No RCT available to assess hysteroscopic route and fertility
HYSTERECTOMY

• Minimally invasive approach
  • Vaginal hysterectomy
  • Laparoscopic assisted vaginal hysterectomy
  • Total laparoscopic hysterectomy
  • Single-port laparoscopic hysterectomy
  • Robotic assisted total laparoscopic hysterectomy

• Open (Laparotomy)
  • Total hysterectomy
  • Supracervical hysterectomy
SUMMARY

- Only symptomatic fibroids need treatment
- Current data does not support using UAE, MRgFUS in patients desiring future fertility
- No RCT data showing myomectomy improves fertility
- If surgery is chosen, minimally invasive option results in quicker recovery and less blood loss.
- Hysterectomy offers the best long term solution when fertility is not desired