

Uterine Fibroids

Tim Chang September 2016

Benign monoclonal tumours composed of

1. Smooth muscle
2. Connective tissue forming a pseudo capsule (Extra Cellular Matrix ECM).

Prevalence

- 25-70% of women by age 50 have fibroids
- Fibroids found in up to 80% of Hysterectomy specimens (depending on how carefully pathologist looks for them)
- Vary in size from a few mm to >65kg

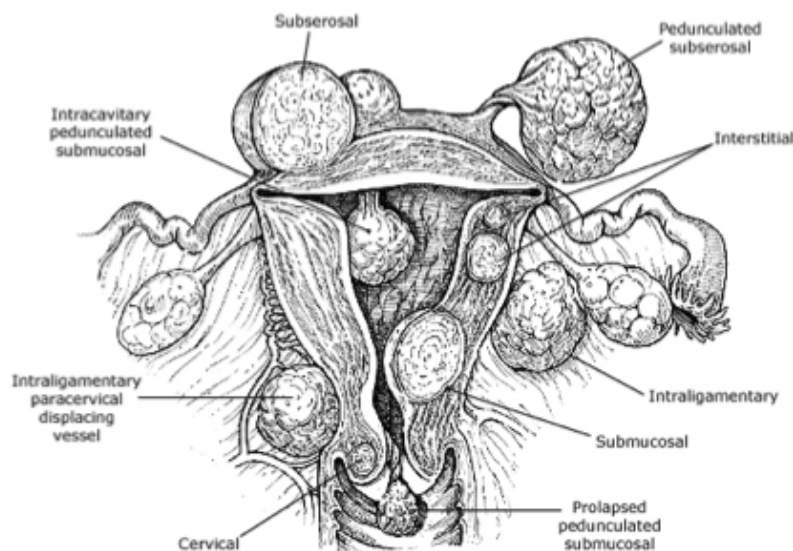
The risk factors :

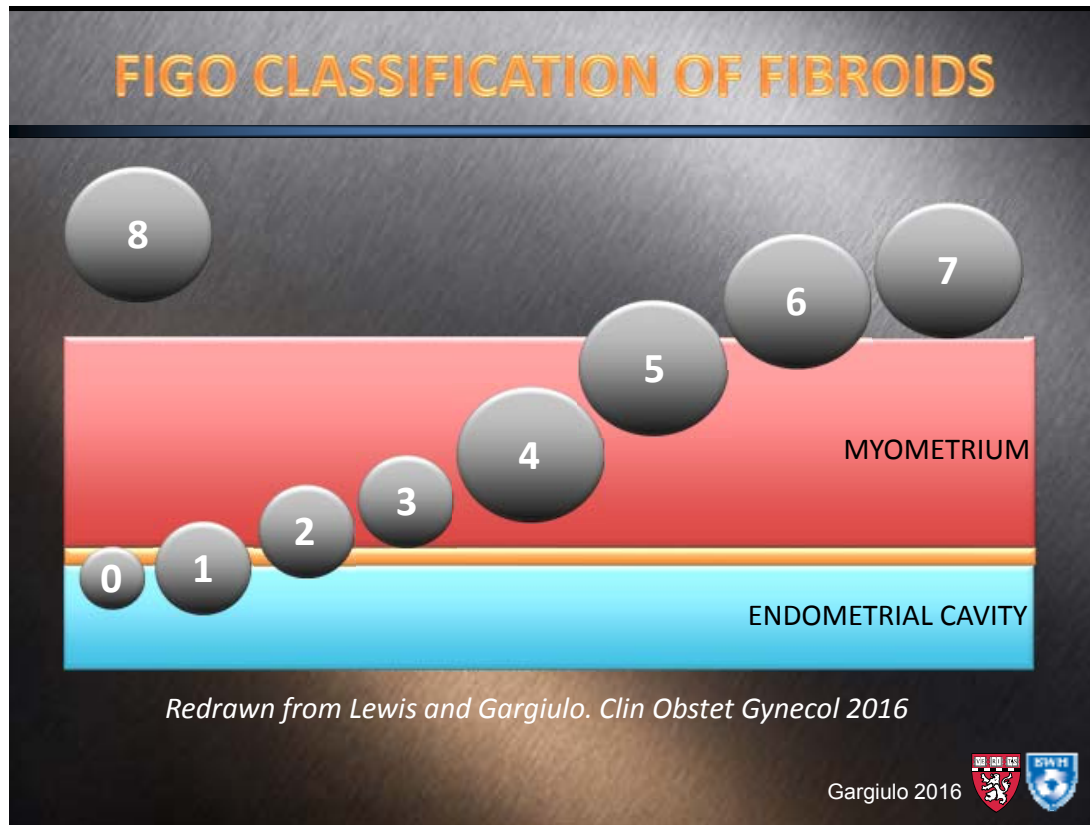
- Age more common in the forties (except blacks)
- Race (blacks RR2-3) > Caucasians > Asians
blacks experience fibroids younger age, larger size and have surgery younger and have greater recurrence after surgery ? genetic differences cf caucasian
- Family history (genetic component)
- high sex steroid environment:
 - Early menarche and late pregnancy
 - Infertility
 - Obesity Weight > 70kgs 3 times relatively risk of <50kgs
 - PCOS
- Smoking reduces risk
- Alcohol increase risk
- Hypertension increase risk
- Diet (fruits / vegetables / low fat) may reduce the risk
- Uterine infection increases risk (myometrial injury predisposes myoma formation?)
- OCP has conflicting data on the risk of fibroids (most show protective effect unless high doses taken at early age)

Sites:

- Intramural IM
- Subserous SS (may be pedunculated)
- Submucous SM 10%
- Cervical 5%
- Intra ligamentous 2.5%

Classification of uterine myomas by location





Variants of fibroids

- Parasitic eg omentum, bowel
typically from pedunculated fibroids gaining new blood supply
- Iatrogenic esp risk with morcellation (laparoscopic and vaginal)
Typically present with pain and / or mass
Can be found pelvis and upper abdomen and port sites
Cases reported after GnRHa and MRgFUS (related to reduced uterine blood supply)
- Intravenous leiomyomatosis: leiomyoma in blood vessels up to the heart → RH failure.
Case report success use aromatase inhibitor to treat this
- Leiomyomatosis peritonealis disseminata (LPD)
where multiple nodules stud the peritoneum simulating disseminated cancer
causes:
metaplasia in hyper oestrogenic environment e.g pregnancy, granulosa tumours,
OCP and often disappears after oestrogen removal.
Iatrogenic morcellation
- Benign metastising leiomyoma eg Lung . BSO cures this

Note

- Hereditary Leiomyomatosis and renal cell carcinoma syndrome .
Autosomal dominant condition characterized by cutaneous leiomyomas + uterine fibroids + renal cell cancer
- Leiomyosarcomas
Incidence 1/1000 fibroids & 1/500 rapidly enlarged fibroids

AETIOLOGY

Myomas derived from a single clone of smooth muscle.

50% of myomas are cytogenetically abnormal? this predisposes to myoma ?

however the exact cause is essentially unknown

Growth promoted by

1. Oestrogen
2. Progesterone now thought to be major growth factor (high concentration Progesterone Receptor PR-A and PR-B in fibroids)
3. paracrine growth factors

1 theory E2 activation leads to expression PR which control cell proliferation and ECM production

Smokers have a reduce risk of fibroids secondary to reduced oestrogen levels

Pathology

Most fibroids asymptomatic characterised by

- Whorled pattern smooth muscle
- Connective tissue pseudocapsule
- <5 mytotic figures per high HPF
- little cytological atypia

Discrepancy between growth and blood supply leads to degeneration.

2/3 of all myomas show some degeneration

Types of degeneration

- Hyaline degeneration in 65% (replacement with fibrous tissue) most common
- Myxomatous 15%
- Calcific 10%
- Cystic
- Fatty degeneration
- Red generation

especially in pregnancy because of acute infarction.

Prevalance of fibroids in pregnancy 1% - 10% of pregnant woman

up to 10% undergo degeneration

75% of fibroids do not increase or decrease with pregnancy i.e. 25% of myomas enlarge most of them do not cause symptoms.

- Malignant degeneration 1:1000 leiomyosarcoma (more common SM fibroids)

NB controversy over criteria sarcoma vs STUMP vs benign tumours

Malignant potential based on : mitotic index, cytology atypia and cell necrosis

Clinical presentation

Symptoms depend on

- Site / location
- Size
- Number
 - 1) Uterine bleeding
 - 2) pressure , bulk effects
 - 3) pain
 - 4) Reproductive effects
 - 5) Others

50% of fibroids asymptomatic and up to 80% may be asymptomatic

i.e. only 30 %- 50% of fibroids produce symptoms

Symptoms of fibroids:

- Bleeding
- Pain
- Pelvic mass
- Reproductive effects ie infertility, miscarriage
- Obstetric effects

30% have morbidity requesting treatment

Abnormal uterine bleeding

30% of woman with fibroids have increased menstrual blood loss
greater MBL the higher the incidence of fibroids
blood loss determined by location then size esp submucous
Characterised by menorrhagia heavy MBL not typically IMB
Mechanism

1. Compression of uterine vessels leading to ectasia
2. Interference with contractility of myometrium
3. Ulceration
4. Increase surface area of uterine cavity (normal SA =15cm²)
5. molecular dysregulation angiogenic factors
6. hyperplasia and polyps

1/3 of women with abnormal bleeding and myomas have other endometrial pathology eg hyperplasia, therefore the importance of endometrial sampling

Pressure symptoms

Related to size and impingement on various organs

- Urinary tract
 - Retention
 - Frequency
 - Ureteric obstruction
- Bowel
- Rectal pressure
- Tenesmus
- Constipation
- Increased abdominal girth

Pain

Experienced in 30% of women with fibroids

- dysmenorrhoea secondary to heavy MBL
- Oedema
- Dyspareunia
- Degeneration
- Torsion of pedunculated fibroid
- Cervical dilation of pedunculated sub mucous fibroid
- Infection (Pyomyoma)

Reproductive effects

- Infertility
- recurrent pregnancy loss.

1/3 of myomectomies performed for infertility

Obstetric effects

- PTL
- IUGR
- Abnormal presentation
- Increased CS

Others

- Polycythaemia
Mechanism:
Autonomous erythropoietin synthesis
Back pressure on renal parenchyma leading to increased erythropoietin secretion
- HyperPTH
- Hyperprolactinaemia
- Pseudo Meigs syndrome (ascites)
- Associated with endometrial hyperplasia secondary to local hyperoestrogen

Fibroids and infertility

- Do fibroids cause infertility? (1-2% infertility due to fibroids)
- If so, what type of fibroids?
- Does treatment improve reproductive outcome?

Proposed Mechanism

1. Mechanical obstruction distortion of anatomy
2. Altered peristalsis (normal quiescent luteal phase for successful implantation) with Impaired sperm and ovum transport as fibroids do not contract properly to semen PGs
3. prevents proper nidation / implantation of conceptus secondary abnormal vascular, paracrine inflammatory local effects

When assessing studies on fibroids and fertility:

- Control group matched esp age, duration of infertility and other causes of infertility
- How were fibroids diagnosed eg SSG and hysteroscopy more accurate than TVUS, HSG
- Type, size and mixture of the fibroids

Do fibroids cause infertility?

Fibroids (SM and IM) lead to reduced PR, LBR and increased MC

Av RR 0.8 (PR + LBR)

TABLE 2				
Effect of fibroids on fertility: all locations.				
Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	18	0.849	0.734–0.983	$P=.029$
Implantation rate	14	0.821	0.722–0.932	$P=.002$
Ongoing pregnancy/live birth rate	17	0.697	0.589–0.826	$P<.001$
Spontaneous abortion rate	18	1.678	1.373–2.051	$P<.001$
Preterm delivery rate	3	1.357	0.607–3.036	Not significant
<i>Pritts. Fibroids and infertility. Fertil Steril 2009.</i>				

What type of fibroids ?

SM have significantly poorer outcomes:

TABLE 3				
Effect of fibroids on fertility: submucous fibroids.				
Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	4	0.363	0.179–0.737	$P=.005$
Implantation rate	2	0.283	0.123–0.649	$P=.003$
Ongoing pregnancy/live birth rate	2	0.318	0.119–0.850	$P<.001$
Spontaneous abortion rate	2	1.678	1.373–2.051	$P=.022$
Preterm delivery rate	0	—	—	—
<i>Pritts. Fibroids and infertility. Fertil Steril 2009.</i>				

av RR 0.3 PR + LBR)

MC 1.7-3.8

IM fibroids also have poorer outcome:

TABLE 5**Effect of fibroids on fertility: intramural fibroids.**

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
A. All studies				
Clinical pregnancy rate	12	0.810	0.696–0.941	$P=.006$
Implantation rate	7	0.684	0.587–0.796	$P<.001$
Ongoing pregnancy/live birth rate	8	0.703	0.583–0.848	$P<.001$
Spontaneous abortion rate	8	1.747	1.226–2.489	$P=.002$
Preterm delivery rate	1	6.000	0.309–116.606	Not significant
B. Prospective studies				
Clinical pregnancy rate	3	0.708	0.437–1.146	Not significant
Implantation rate	2	0.552	0.391–0.781	$P=.001$
Ongoing pregnancy/live birth rate	2	0.465	0.291–0.744	$P=.019$
Spontaneous abortion rate	2	2.384	1.110–5.122	$P=.002$
Preterm delivery rate	0	—	—	—
C. Studies using hysteroscopy in all subjects				
Clinical pregnancy rate	2	0.845	0.666–1.071	Not significant
Implantation rate	1	0.714	0.547–0.931	$P=0.013$
Ongoing pregnancy/live birth rate	2	0.733	0.383–1.405	Not significant
Spontaneous abortion rate	2	1.215	0.391–3.774	Not significant
Preterm delivery rate	1	6.000	0.309–116.606	Not significant

Pritts. Fibroids and infertility. Fertil Steril 2009.

av RR 0.8 (PR + LBR)

meta analysis Sunkara et al.

N=6087 IVF cycles from 19 observational studies comparing women with non cavity distorting IM fibroids vs no fibroids confirmed:

Reduced LBR 0.79

Reduced PR 0.85

Trend increase MC 1.24 NSD

IM fibroids trend to increasing MC (RR 1.2-1.7)

Major issue is inconsistency assessment of uterine cavity IM fibroids in studies.

Does removal of fibroids improve outcomes?

Older case series show PR 40-60%

Comparative studies show improved LBR from 10-15% to 25-30% (control groups diverse and mixed location of fibroids)

Meta-analysis Pritts

Removal of Submucosal fibroids significantly improve PR rates with tendency to improved LBR and reduced MC (but NSD due to limited studies).

TABLE 6**Effect of myomectomy on fertility: submucosal fibroids.**

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
A. Controls: fibroids in situ (no myomectomy)				
Clinical pregnancy rate	2	2.034	1.081–3.826	$P=.028$
Implantation rate	0	—	—	—
Ongoing pregnancy/live birth rate	1	2.654	0.920–7.658	Not significant
Spontaneous abortion rate	1	0.771	0.359–1.658	Not significant
Preterm delivery rate	0	—	—	—
B. Controls: infertile women with no fibroids				
Clinical pregnancy rate	2	1.545	0.998–2.391	Not significant
Implantation rate	2	1.116	0.906–1.373	Not significant
Ongoing pregnancy/live birth rate	3	1.128	0.959–1.326	Not significant
Spontaneous abortion rate	2	1.241	0.475–3.242	Not significant
Preterm delivery rate	0	—	—	—

Pritts. Fibroids and infertility. Fertil Steril 2009.

overall expect doubling PR + LBR with removal SM fibroids

Removal of intramural fibroids does not improve outcome (due to limited studies??? But there is a trend)

TABLE 7				
Effect of myomectomy on fertility: intramural fibroids (fibroids in situ controls).				
Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	2	3.765	0.470–30.136	Not significant
Implantation rate	0	—	—	—
Ongoing pregnancy/live birth rate	1	1.671	0.750–3.723	Not significant
Spontaneous abortion rate	1	0.758	0.296–1.943	Not significant
Preterm delivery rate	0	—	—	—

Pritts, Fibroids and infertility. Fertil Steril 2009.

Conclusions on fibroids and fertility:

- SM fibroids strongly associated with reduced fertility and improved with removal.
- IM fibroids less association with infertility but there is no good evidence myomectomy improves outcomes
- SS is not associated with infertility and removal does not improve outcomes.

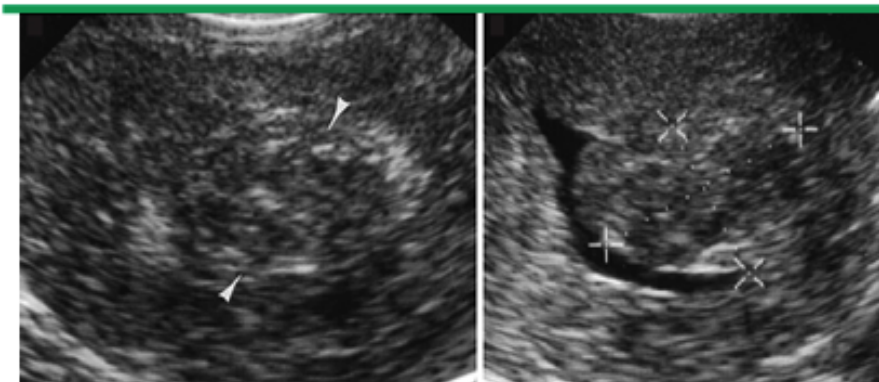
Management of fibroids in the infertile woman (IM) needs to be individualised:

- Age
- Other infertility factors including duration of infertility taken into account.
- Couples should have full infertility workup prior to any fibroid surgery for infertility
- Size / location/ number of fibroids
- Other fibroid symptoms
- Previous treatments eg multiple failed IVF cycles
- Consider impact of fibroids in pregnancy especially larger size.

Investigations

- Transvaginal Ultrasound
sensitivity 0.8
specificity 0.7 with PPV 0.5
can assess depth of fibroid and other pelvic pathology
- Saline sonography
very accurate in assessing the endometrium and myometrium with sensitivity, specificity and PPV 100% for fibroids >0.5cm

Fibroid in 53-year-old woman who presented with postmenopausal bleeding



Sagittal transvaginal sonogram shows hypoechoic endometrial thickening (arrowheads) (A). Sagittal sonohysterogram shows submucosal fibroid with thin overlying endometrium (cursors) (B). Reproduced with permission from Joizzo, JR, Chen, MY, Riccio, GJ, Endometrial Polyps: Sonohysterographic Evaluation. AJR Am J Roentgenol 2001; 176:617. Copyright © 2001 American Journal of Roentgenology.

- MRI
Sensitivity 100% specificity 94% low PPV with up to 100% NPV
Dynamic MRI may distinguish degeneration in fibroids and sarcomas
Potentially good screening tool + assessment exact anatomy especially prior to surgery
- Hysteroscopy
Excellent sensitivity for submucosal fibroids esp assessment size, depth, topography etc
Caveate: occasionally SM fibroid may be missed due to raise intrauterine pressure causing temporary regression of uterine contour
Important to exclude other endometrial pathology esp AUB
Sensitivity 30% detecting sarcomas (need to reach endometrial surface)
- Needle biopsy under US guidance
Useful if fibroids to be treated non surgically to exclude sarcoma
theoretical concern seeding needle tract and spread
Kawamura et al 2002 N= 435 patients MRI suggested suspicious changes
Underwent transcervical needle biopsy under US guidance
7 uterine sarcomas found (selected patients FU 2 years n= 141 hysterectomy / myomectomy
n= 294 managed conservatively)
all scored ≥ 2 ie 100% sensitivity with cut off 1

TABLE 1
Histopathologic Variables and Scores for Needle Biopsy Specimens

Variable	Score				
	0	1	2	3	4
Mitotic index (mf/10 hpf)	0	1-9	≥ 10	---	---
Cytologic atypia	Absent to mild	---	Moderate to severe	---	---
Coagulative tumor cell necrosis	Absent	Suspected	Present	---	---
Variant (myxoid, epithelioid)	Absent	Present	---	---	---
Endometrial stromal origin	Absent	Present	---	---	---
Vascular extension	Absent	Present	---	---	---
Marginal infiltration	Absent	Suspected	---	---	Present

mf/10 hpf: mitotic figures per 10 high-power fields.

Specimens with a total score of ≥ 4 corresponded to leiomyosarcoma according to the criteria established for the common type (spindle cell type) of uterine smooth muscle tumors.¹⁵

Relation between Histopathologic Scores, and Sarcoma Status Based on Histopathology of Surgical Specimens or Outcomes after 2 years of Follow-Up

Total histopathologic score	Sarcoma (n = 7)	No sarcoma (n = 365)
0	0	354
1	0	6
2	3	5
3	0	0
4	1	0
≥ 5	3	0

from Kawamura et al 2002

- Laparoscopy
For assessment of intramural and subserosal fibroids
Indicated when other pathology is suspected
- HSG
For SM fibroids
sensitivity 50%. Specificity 20% and PPV 30%

Excluding malignancy in uterine mass

Fibroids are common with lifetime risk 70%

Prevalence sarcoma:

- in general population $<1/10,000$
- undergoing surgery for uterine mass $1/352-1/2000$
- Uterine masses in prospect studies (presumed younger population) $1/8300$

Risk factors

- Age
- Race blacks x2 incidence
- Pelvic irradiation
- Tamoxifen
- Others eg renal cancer syndrome, childhood retinoblastoma

Incidence uterine cancer Based on age women undergoing surgery:

▪ <40	$1/2337$
▪ $40-49$	$1/702$
▪ $59-59$	$1/154$
▪ >60	$1/31$

Approaches:

- clinical suspicion eg growing mass in PM woman
- endometrial sampling may detect 30% sarcomas
- needle biopsy
- LDH esp LDH3 isoenzyme
- Dynamic MRI

ANY concerns malignancy ideally extirpative surgery without morcellation

Management

Depends on:

- Symptoms
- Fertility desire
- Patient preference
- Fibroid anatomy
 - Size
 - location of fibroids
 - Number
 - Uterine size
- Experience of the surgeon (for surgical treatment)

Management of Asymptomatic fibroids

Fertility NOT desired

Myomas <12 week size

Stable or slow growing over time

May be observed every 3 to 6 months and then eventually annually is all that is required.

Fertility desired

Patient advised to attempt conception for 6 to 12 months

If unable to conceive consider myomectomy

For submucous or large intramural / subserous fibroids consider immediate myomectomy prior to conception.

If patient wants to delay conception $>12/12$:

- a) if there is rapid growth consider myomectomy
- b) fibroids are stable observation is reasonable

Management of Symptomatic fibroids

Depends on fertility desires:

Desires fertility

Exclude other causes of infertility and

determine the site and size of the fibroid to determine optimal management.

Myomectomy gold standard esp submucous fibroids

No desire fertility

Hysteroscopy/D & C to exclude malignancy ±. Uterine biopsy

Treatment depends on severity of symptoms and patient desires and menopause status

TYPES OF THERAPY

- Medical
- Non surgical
- Surgical therapy

Timing and type of therapy should be individualized and factor to consider:

- Symptoms
- Reproductive desires
- Likelihood of regression or progression of fibroids

Size alone is not an absolute indication for treatment.

Medical therapy

Most medical therapy aimed at reducing menorrhagia and less likely to improve bulk symptoms or fertility.

Upto 75% patient have some relief of bleeding at 12 months but upto 60% will have surgery by 2 years (Cochrane 2006)

- OCP
Induce endometrial atrophy may help AUB, but not bulk symptoms
Useful if patient also need contraception
Reduce risk of fibroids but may increase the growth of existing fibroids
- Mirena
Observational studies show:
 - Reduced bleeding
 - Improved Hb
 - However less effective submucous fibroids
 - Minimal change in fibroid volume
 -
- Progestins (orally / implants / injectables)
May improve bleeding inducing endometrial atrophy, but does not change fibroid volumes
- GnRHa
maximum effect at 3 months
reduces fibroids size by 25 % after 3 months
reduced uterine volume by 40-60%
SE flushes, dryness, mood changes. Irreversible osteoporosis if used >12 months
The effects are only temporary as once GnRHa is stopped the fibroids regrow.
Role of add back therapy at 3 months may allow longer use of GnRHa
- GnRH antagonists
Theoretically useful but not practical requires daily injections
- Danazol
Induces amenorrhoea less effective in GnRHa
No effect uterine volume

- Gestrinone
Amenorrhoea rates 50%
May reduce uterine volume
- SERMs
Limited data Raloxifene may have clinical efficacy fibroids, but SE flushes etc.
- Aromatase inhibitors
Limited data shows letrozole may reduced fibroid volume 45% vs 30% GnRHa. No data on AUB.

Progesterone receptor modulators (PRM)

- has agonist / antagonist activities
- Inhibits ovulation via hypothalamus with little impact oestradiol levels
- Direct effect myoma induces apoptosis myoma cells
- Direct effect endometrium induces amenorrhoea + Induces progesterone receptor modulator associated endometrial changes (PAECs) with cystic glandular dilatation aka tamoxifen changes with endometrial thickening on US

Hyperplasia has not been observed and no reported cases endometrial cancer

Ulipristal (UPA)

PEARL I Donnez NEJM 2012

PGL4001 (Ulipristal Acetate) Efficacy Assessment in Reduction of Symptoms Due to Uterine Leiomyomata

5-10mg UPA for 13 weeks RCT vs placebo

UPA started first 4 days cycle

n=242 (95; 94; 48)

Inclusion criteria:

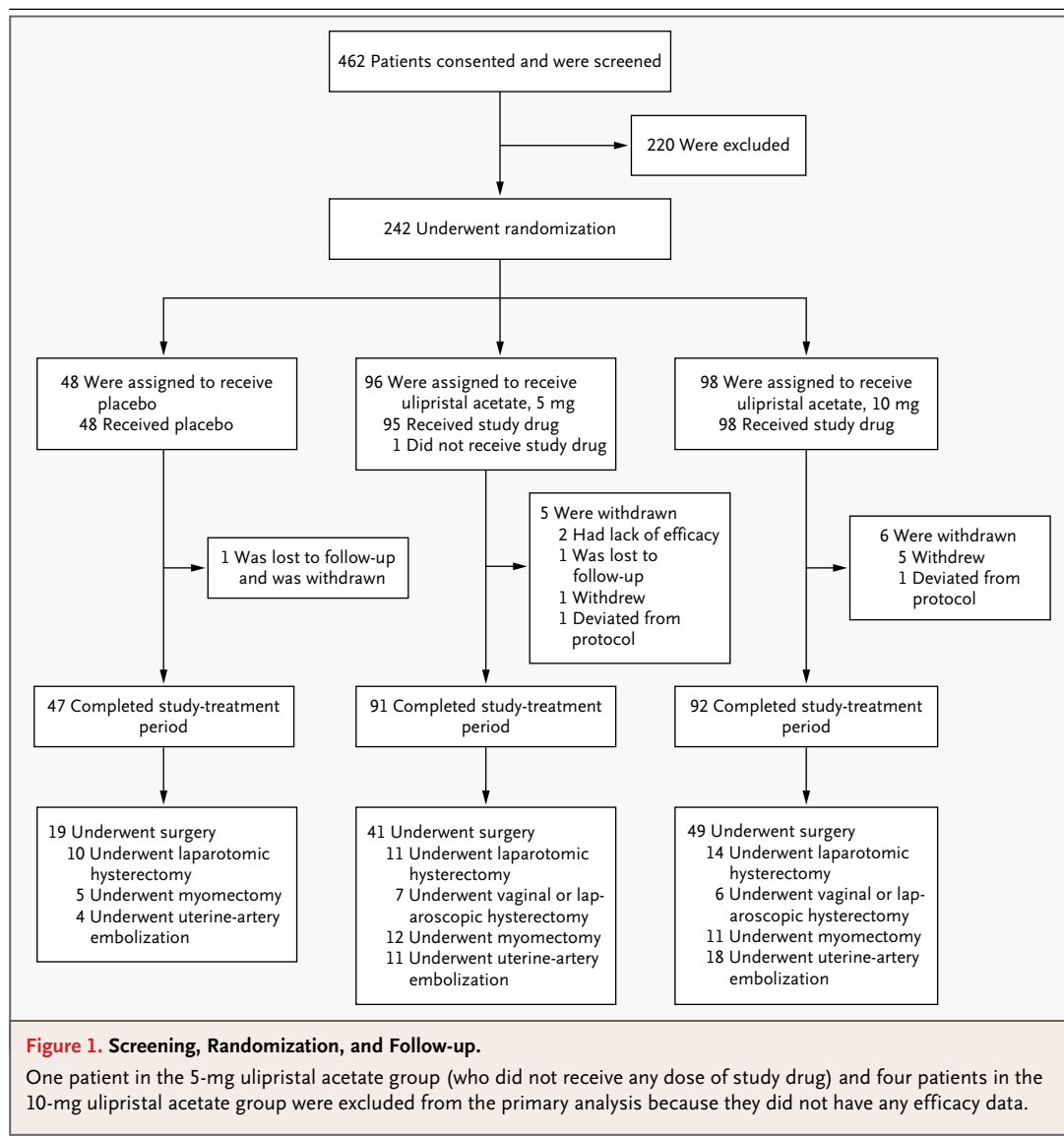
- Aged 18-50
- AUB eg PBAC >100; anaemia < 10.2
- Size 3-10cm; <16 week size mixture SM / IM / SS types
- BMI 18-40

FU

- SE recorded each visit upto week 17 any adverse SE upto week 38
- MRI at 13 weeks ; 26 and 38 weeks (if no HE or ablation)
- Endometrial biopsy at week 13 and 38 if no HE or ablation

Results:

- Resolution menorrhagia (91%; 92%; 19%)
- Improved Hb (4.2; 4.1; 3.1)
- Reduced fibroid volume (-21%; -12%; +3%)
- Amenorrhoea by week 13 (73%; 82%; 6%)
- Reduction in pain + discomfort symptoms
- Increased incidence endometria thickness >16mm at 13weeks all reversed by week 38
- Progesterone receptor modulator associated endometrial changes (PAEC) Non physiological changes increased (62%; 57%; 6%) disappeared at week 38
- No endometrial hyperplasia
- patients had further intervention after therapy (46% with 26% TAH ; 53% with 28% TAH; 40% with 52% TAH)



PEARL II trial (Donnez 2012)

RCT ulipristal 5+ 10mg vs leuprolide (3.75 monthly) for 13 weeks prior to surgery (non inferiority trial)

N= 307 (5mg vs 10mg vs GnRHa)

Aged 18-50

Symptomatic fibroids <16 weeks (3-10cm)

- comparable resolution menorrhagia PBAC <75 (90; 98;89%)
- quicker to achieve amenorrhoea (7 days; 5 days vs 21 days)
- less flushes (11%; 10%; 40%)
- similar reduction 3 largest fibroids (-36%; -42%; -53%) however more sustained reduction in fibroid volume 6 months after cessation therapy (-45%; -55%; -16%) related apoptosis myoma cells?
- equal relief pain, pressure symptoms
- 50% subsequently had surgery
- increased mean endometrial thickness (9.4mm/10.7mm/ 5.1mm)
- increased non physiologic endometrial changes (58%; 59%; 12%) all benign and returned to normal histology at week 38 with only 6% showing non physiologic changes.

PEARL III (Donnez 2014)

Demonstrated the efficacy and safety of 4 courses 12 weeks 10mg UPA with break WTB

N=209 symptomatic fibroids 3-10cm in women 18-48

4x3 monthly courses UPA 10mg with 10 days NETA 10mg or placebo break and waited for WTB (15 days vs 30 for placebo)

less bleeding with NETA after cessation 4th UPA course (PBAC 13 vs 55)

	After Course 1	2	3	4
Number women	209	131	119	107
amenorrhoea	79%	89%	88%	90%
Mean days to A	4	2	3	3
Reduction fibroid volume	-45%	-63%	-67%	-72%

No hyperplasia or cancer after 4 cycles

PAEC 25% after treatment, but 80% resolve 3 month after cessation treatment.

Reduction in pain / improved QoL + reduced fibroid volume maintained at 3 months after treatment

NB 107/209 (51%) completed 4 courses

PEARL IV Donnez 2016

N=451 RCT 5 vs 10mg UPA for 4 x12 week treatment cycles with 2 cycles break through menstruation between treatment cycles (average duration 20/12 with treatment interval 51-56 days). 75% completed 4 courses

	After course 1	2	3	4
Amenorrhoea (5/10mg)	72 %/ 83%	74% / 82%	73% /78%	70%/75%
Reduction fibroid volume >25%	62% / 66%			78% / 80%
NPEC	Baseline 8% / 8%	16% / 19%		16% / 10% 286 biopsies 3 /12 after 4 th course returned baseline

Non physiological endometrial changes

- amenorrhoea all 4 cycles 50% / 60%
- reduction pain scores
- common SE headache (<10%) ; mastalgia (<3%)

demonstrated long term efficacy and safety of both 5mg and 10mg UPA (4 x12 week cycles)

Luyckx 2014 FU PEARL II/III trials reported 18 pregnancies in 15/21 (71%) women wanting to conceive after UPA (19 had myomectomy 11 LM; 8 AM ; 2 had no further treatment) with LBR 12/18 (66%) and 6/18 MC (33%) with no regrowth fibroids during pregnancy and 1 patient requiring HE 4 years after treatment (1/15 = 7%).

1 LBR in UPA alone (original fibroid 10/40 size) fell pregnant on 5th course UPA!

Potential preop UPA to reduce growth fibroids during pregnancy and recurrence rate?

Indications for UPA

- prior to surgery (fertility or non fertility)
 - hysteroscopic >3cm / type 2
 - > 10cm
 - anaemia
- medical treatment for fibroids esp. perimenopausal women
- medical treatment for fertility?
- Post surgery adjuvant therapy?

Mifepristone

reduces uterine volume by 25-75% (similar GnRHa) in high doses (10-50mg/day)

with up to 50% amenorrhoea rates

reduced MBL >90%

theoretically can be used longer term (longest study 12 months to date 2010)

concern PRM associated endometrial changes which may be confused with hyperplasia

Indications for medical therapy

- Patient / doctor Choice hoping to avoid surgery or augment surgery
- Unfit for surgery
- Pre operative therapy
- Treatment alone or preoperatively for infertility ???
- Post op therapy to reduce recurrence fibroids???

Pre operative GnRH analog

- Improves preoperative and post operative Hb
- Reduce size of fibroids to allow less invasive Surgery
- reduce the intra operative blood loss
- More difficult to shell out
- Increases recurrence rate from 15% to up to 60% (no RCT)

Non Surgical treatment of Fibroids

- Uterine artery (UAE)
- MRI focused US (MRgFUS)
- Transvaginal temporary Uterine artery occlusion

UAE

UAE is percutaneous image guided procedure injecting particles (biodegradable and non biodegradable 150 to 1000 microns) to block the blood supply of the fibroids (bilateral uterine aa and sometimes utero-ovarian aa) causing infarction. (Ideally particles >500microns to avoid infarction of myometrium and ovaries)

First described by Ravina 1995

Takes about 1 hour

Most patients have pain for 12-24 hours

Typical recovery and return to activities 1-2 weeks

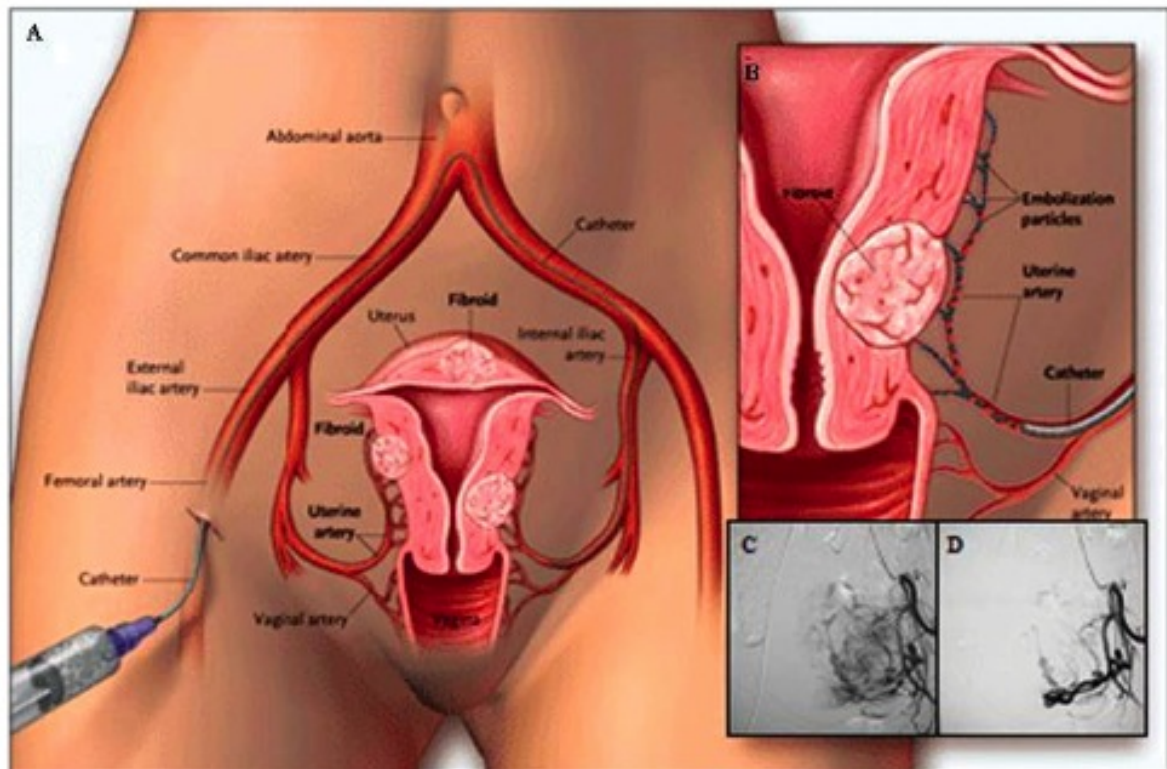


Figure 1: The UAE procedure. Drawings (A) and (B) illustrate the path of the catheter to deliver embolization particles to occlude the uterine arteries. Angiograms show the fibroid blood supply before (C) and after (D) UAE.

indications:

- bulk symptoms
- AUB

Absolute CI

- Pregnancy
- Active infection (pelvic or urinary tract)
- Severe vascular disease (including previous internal iliac artery ligation)

Relative CI

- Fertility desires
- Postmenopausal woman or use GnRHa
- Pedunculated or submucous fibroids
- Extensive adenomyosis
- Large fibroid (? What size fibroids >10cm? fibroids up to 24 weeks size have been treated)

Workup

- Exclude malignancy eg
 - Endometrial sampling
 - MRI /US
 - Myometrial biopsy?
- Assess anatomy eg US / MRI
- Baseline FBC /EUC and coags

Complications

In hospital complication rate 3% with 25% post discharge complications

Estimated mortality 0.05/1000 ie 1/20,000 compared with hysterectomy mortality 0.4/1000

- Pain
 - Almost universal related to ischaemic necrosis of fibroid
 - Treated with opiates and NSAIDs
- Vaginal discharge
 - Short term DC up to 2 weeks. Sometimes may last months
- Vaginal expulsion of fibroid
 - esp submucous component
 - typically occurs within 6 months but reported upto 4 years
- Post embolization syndrome
 - Severe pain / fever myalgia / raised WCC
 - Usually occur within 48 hours and resolved by 1 week
 - Need to differentiate from sepsis
- Sepsis (uterine infection)
 - Incidence <1%
 - May be refractory to AB requiring hysterectomy
 - Mortality reported
- Hysterectomy (risk <1%)
- Undetected sarcoma
 - Post menopausal women with increasing fibroid is CI
- Ovarian dysfunction
 - <45 2-3% premature menopause
 - ≥45 8%
- Adhesions
 - Intra-abdominal and intra-uterine
 - Amenorrhoea (transient or permanent) related ovarian failure 5%
 - Uterine necrosis and endometrial atrophy

Reproductive complications

most studies are case reports or series with poor controls

many confounding factors in uncontrolled trials e.g maternal age, reproductive history and severe fibroid history in UAE patients

limited studies suggests:

- Miscarriage increased from 16% to 35% (RR 2.8)
- Preterm delivery 3% to 16-22%
- Abnormal placentation
 - IUGR
 - Abruptio
 - PPH 5% to 18%

If fertility desired after UAE hysteroscopy to assess intrauterine adhesions advisable.

Outcomes

98-100% completion of procedure

>90% improved QoL (short term)

- Improved AUB 90% with 30% amenorrhoea
- Improved dysmenorrhoea 80%
- Improved bulk symptoms 60-90%
- Reduced uterine volume 30-60%

80% improved symptoms at 5 years

Reoperation rate 10% up to 2 years and 20% up to 5 years

Failures related to :

- New fibroids
- Regrowth of incompletely infarcted fibroids
- UAE of 1 artery (RR 2)
- Prior fibroid Surgery
- Adenomyosis

Patient selection is critical in obtaining successful outcome UAE:

- No desire fertility
- Avoid surgery eg multiple previous sx, Jehovah's witness etc
- No absolute CI UAE

Comparative trial of UAE vs surgical treatment:

Several comparative trials including UAE vs surgical intervention

Note in the studies:

- patient characteristics eg number fibroids, previous sx , size etc
- technical success UAE (EMMY trial 17.5 % technical failure UAE: related to radiologist experience)
- length of follow up
- type of surgery esp laparoscopic vs open

Cochrane 2014

7 trials n=793 with follow up >1 years

UAE vs surgery (HE + myomectomy)

Results of UAE

- similar patient satisfaction rates at 24 months but inconclusive at 5 years
- reduced PR 0.29 and LBR 0.26 poor quality data
- reduce length of stay circa 2 -4 days less
- quicker return to normal activities 10-23 days less
- higher minor complications and readmission rates OR 1.99 (eg PV DC, pain, post embolization syndrome)
- NSD major complication rates
- Reduced blood loss OR 0.07 for blood transfusion
- Increased reintervention rates after UAE OR 3.72 at 2 years 5.79 at 5 years (15-32% estimated absolute risk)
- Lower initial cost UAE balanced by higher cost later intervention

REST trial (Randomization of Embolization vs Surgical Treatment of Fibroids) 2007

Multicentre trial 106 UAE compared to 51 surgical cases (43 AH and 8 open myomectomies)

Symptomatic Fibroids >2cm on MRI

3 technical failures UAE with 1 failure surgery group myomectomy converted to hysterectomy

FU at least 12 months looking at QoL measures (SF36) and other measures morbidity:

- Improved activities at 1 month but NSD in SF36 at 12 months
- Shorter hospital stay (1 vs 5 days)
- Higher minor complication rate (34% vs 20%) but NSD major complications (15 vs 20%): most complications UAE after discharge vs in hospital for surgical treatment
- 10% failure at 12 months up to 20% thereafter
- lower immediate cost

criticisms

- small number fibroids
- most were open surgery

1 small RCT (n=66) UAE vs myomectomy (open or lap) Mara 2006 and 2007 concluded:

significant uterine pathology ie fibroids 57% vs 18%

37% reintervention rate vs 6% at 6 months

with more pregnancies (78% vs 50%) and deliveries (48% vs 19%) with less MC (23% vs 64%) in myomectomy group

Summary UAE

Suitable option in selected older patients ideally with no desire fertility and wish to avoid major surgery or have CI to surgery. Improved QoL similar to surgery with Shorter recovery with similar major complications with open surgery and reintervention rate 20% -30% at 5 years. Requires counseling if desires fertility as potentially reduced LBR and increased pregnancy complications

Transvaginal Temporary Uterine Artery Occlusion

Using Doppler US guided transvaginal clamping uterine aa. For 6 hours

Short term 6 months

- 50% reduction uterine volume
- 90% symptom reduction
- less post op pain

unknown long term effects

cases ureteric obstruction and hydronephrosis

MRI guided focused US (MRgFUS)

FDA approved 2004

Based on high intensity US focused thermal ablation of fibroids raising temp 55-90C causing coagulative necrosis performed under IV sedation.

Treatment consists of exposure to US energy typically lasting 20s (sonication) ablating 0.5ml tissue with pause of 90s

Tissue volume limited 150cm³ typically treated volume of fibroid 10-20% of total with fibroids typically <10cm

Procedure may take >3 hours

Improved results with GnRHa pretreatment

Results from case series

Most data short term 6 -12 months up to 24 months

- Reduction fibroid volume 13%
- 70% improved QoL
- 30% sought further treatments after 2 years

Severe pain during procedure 16% with post op severe pain 8%

Skin burns 5%

Sciatic nerve injury

Compared to UAE:

- No radiation exposure
- Less post op pain
- No risk non target embolization
- Less effect on reduction fibroid volume and restricted size and anatomy of fibroids for therapy e.g cannot be used close to bowel / bladder etc

Concerns

Area tissue necrosis from hysterectomy specimens 3x greater than MRI

Long term results of MRgFUS and incidence of recurrence

High rate Pregnancy complications

Surgical treatments for fibroids

Typical indications for Surgery

- abnormal bleeding
- pain
- pressure symptoms (including obstructed ureters)
- growth after menopause or concern of malignancy
- infertility
- RPL
- Size >12-16/40??

Hysterectomy

For those symptomatic and completed family, hysterectomy is gold standard

- VH
- AH (SAH)
- TLH / LAVH
- RLH

Myomectomy

Approaches:

- Abdominal myomectomy
- Laparoscopic myomectomy
- Robotic (RALM)
- Minilaparotomy
- vaginal myomectomy
- Hysteroscopic myomectomy

Depends on:

- Size
- Location and number
- *Experience of the surgeon*

Abdominal myomectomy

Principles:

- Midline anterior incision and avoid posterior incision
 - Minimize number of incisions to maximize removal of fibroids
 - Correct plane enucleate the fibroid (pseudocapsule)
 - Techniques to reduce blood loss
 - Restore anatomy
 - Adhesion prevention
- NB no studies on adhesion prevention with pregnancy as outcome

Bleeding is the major concern of myomectomy

Blood loss at myomectomy related to:

- Preoperative fibroid size
- Total weight of fibroids removed
- Operating time

Techniques to reduce blood loss at myomectomy:

- Preop GnRHa

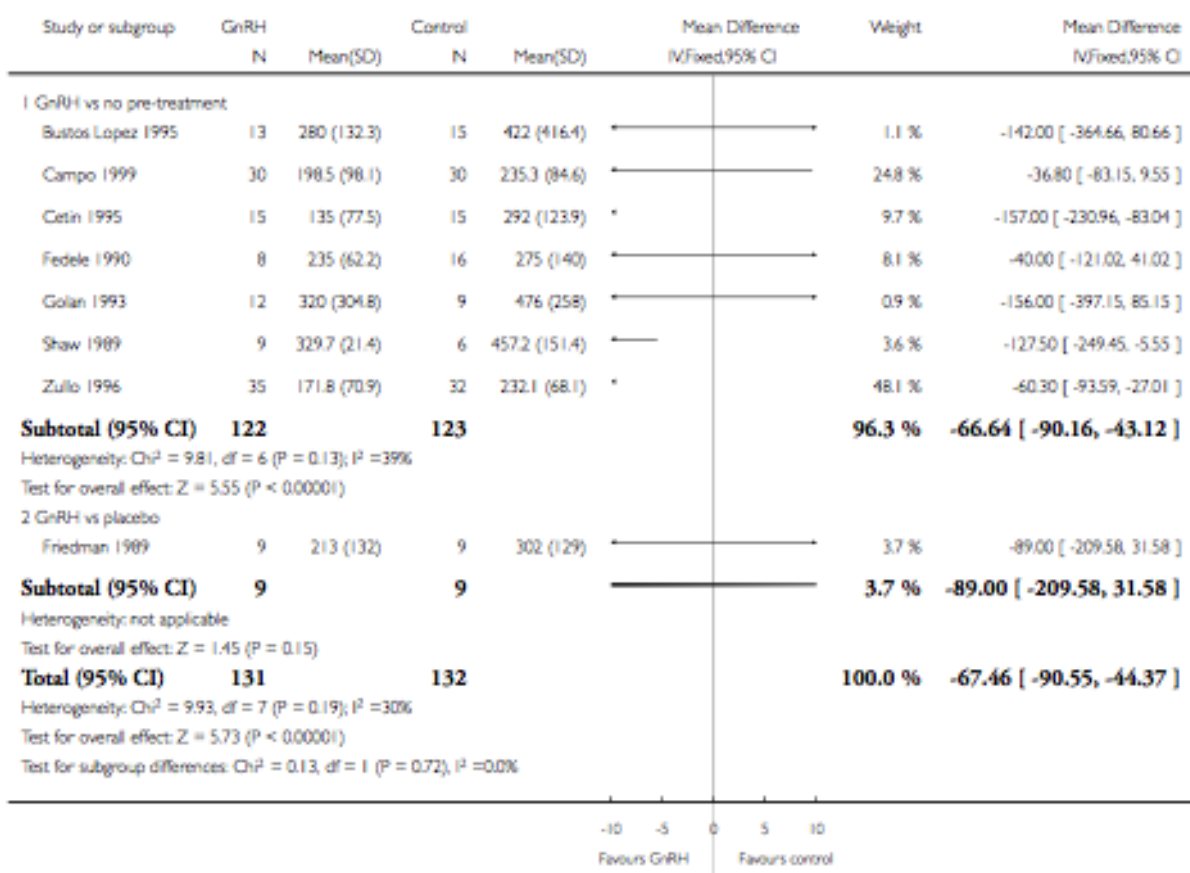
Cochrane 2001

Analysis 2.1. Comparison 2 GNRH ANALOGUE TREATMENT VS NO PRE-RX OR PLACEBO PRIOR TO MYOMECTOMY (OPERATIVE AND POST-OPERATIVE OUTCOMES), Outcome 1 Intra-operative blood loss (mls).

Review: Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids

Comparison: 2 GNRH ANALOGUE TREATMENT VS NO PRE-RX OR PLACEBO PRIOR TO MYOMECTOMY (OPERATIVE AND POST-OPERATIVE OUTCOMES)

Outcome: 1 Intra-operative blood loss (mls)



Reduced blood loss -67ml

less vertical incisions OR 0.11 (1study with n=28)

blood Tf OR 0.86 NSD

improved post op Hb +0.8

increased cost

- Vasopressin

reduced blood loss and blood TF

effects last 30mins

Cochrane

Reduced blood loss -298ml

Blood Tf OR 0.05

- Misoprostol

400mcg PV 1 hour preop

Cochrane

Reduced blood loss -149ml

Blood Tf OR 0.36

- Bupivacaine with adrenaline
Cochrane
Reduced blood loss -68mls
- Intravenous tranexemic acid
Reduced blood loss -243ml
Blood Tf OR 1.71 (NSD)
- Tourniquet
Occluding uterine and ovarian vessels (arterial and venous occlusion important)
Maximum length of time before permanent tissue ischaemia unknown
Cochrane 2006 (1 study n=14 each arm)
Pericervical tourniquet :
Reduced blood loss -1870ml
Reduced TF OR 0.02
- Uterine artery ligation / clipping
- UAE
- UPA

Results of myomectomy

Most will have resolution of symptoms

- reduce bleeding especially of sub mucus fibroid >80%
- reduction in pain less so due to other causes of pain
- reduction in uterine fibroid size

Improve fertility

- RR 1.7
- 50% conception rate
- 3/4 of those will conceive within 12 months
- advise not to fall pregnant for 3 to 6 months after surgery depending on the extensiveness of the surgery for

miscarriages

- RR 0.5
- Reduction MC from 40% to 20%

Complications of myomectomy (incidence 20-40%)

Compared to hysterectomy

1. Increased blood loss
2. Increased operative time technically more difficult
3. Increased post operative morbidity especially haematoma & seroma formation leading to fever and pain

Short term complications:

- Haemorrhage
Increase bleeding compare with hysterectomy with TF rates up to 20%
Routine Hb post op
Unplanned hysterectomy <1%
- Febrile morbidity and infection (<5%)
Unexplained fever up to 36% related to pyogenic factors released at myomectomy / haematomas?
Related to extensiveness of surgery
- Others eg Bowel, bladder wound complications etc

Long term complications

- Recurrence of fibroids
As many as 50-60% will have recurrent fibroids on US at 5 years and
10 to 25% will require repeat surgery
recurrence rates increase with length of time post original surgery
most occur > 3 years after initial operation
increased with use GnRHa pre operatively

- adhesions
leading to obstruction and infertility
most studies based on selected second look laparoscopies
incidence 50-90% vs 30-40% at LM esp posterior incisions and previous adhesions
less with laparoscopic approach
- obstetric complications
scar rupture increasing need of Caesarean section. Absolute risk of scar rupture unknown

Laparoscopic myomectomy

Aim of myomectomy :

Remove completely all fibroids

Restore anatomy and function

If this can be achieved laparoscopically, there is less short term morbidity vs open myomectomy

Conversion rates 0-8% (depends skill surgeon)

Issues with laparoscopic approach:

- larger the size and number and certain anatomy more difficult
- reduced tactile sensation replaced by better visualization (preop mapping fibroids important)
- enucleation fibroid more difficult
- laparoscopic suturing
- removal of the specimen
morcellation
posterior colpotomy
- Iatrogenic parasitic myomas after morcellation
- obstetric outcomes

Compared to open myomectomy (most case series with a few small RCTs):

- Quicker recovery (LOS + Return to activities)
- Less pain
- Less blood loss
- Less adhesions
- Longer operating times? (some report NSD)
- Recurrence NSD
- Fertility NSD (circa 50% PR) wait 3-6/12 prior to conception
- Obstetric outcome NSD

Meta analysis Jin et al 2009:

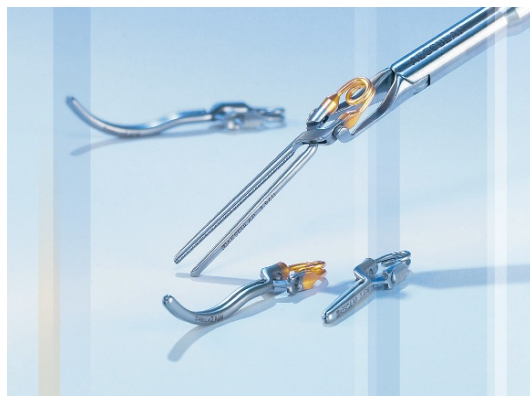
6 RCT n= 576

FU 6-52 months concluded:

- Reduced drop Hb -1.07g/dl
- Reduced blood loss (-34ml av 200ml vs 230ml)
- Reduced pain (lower VAS)
- Greater proportion patient fully recovered by 15
- Longer operating times (13 minutes av 100min vs 90min)
- Less overall complications (OR 0.47) with NSD major complications ie less minor complications
- Recurrence of fibroids NSD
- Pregnancy rates NSD

Criteria for laparoscopic myomectomy (personal opinion)

- Sub serous intra mural fibroids up to 10cm
- Max 3 fibroids
- Pedunculated fibroids
- Not located cervical broad ligament
- No other CI to laparoscopy



Laparoscopic Bulldog clips

Techniques of laparoscopic myomectomy

- Port location
- Techniques to reduce blood loss e.g vasopressin, cytotec, uterine a clipping, haemolock, bulldog clips

Alborzi et al 2009

Non randomized CT N=152 LM ± uterine artery ligation (Silk) with FU over 2years concluded:

- Reduced blood loss 173ml vs 402ml
- Reduced blood Tf 0% vs 17%
- Longer OT 112min vs 95min
- Similar febrile morbidity
- Improved symptoms 98% vs 83%
- Reduced recurrence 6% vs 20%
- Similar LBR 35% each group
- Single vertical incision
- Minimise diathermy use
- Enucleate fibroid with traction (myoma screw)
- Suturing defect : barbed sutures
- Morcellation fibroid / techniques to remove fibroid
- Thorough irrigation peritoneal cavity to reduce risk iatrogenic seeding
- Adhesion prevention

Cochrane 2014

Review comparison MIS techniques vs AM

N= 808

- Less post operative pain
- Less fever post op
- Reduced hospital stay

Complications of LM

Multicentre Italian study N=2050 LM by 5 experienced surgeons (1998-2004)

Overall complication 11% (compares favourably with open myomectomy complications)

Major 2%

Minor 9%

Table 2 Complications (total procedures: N = 2050)		
	No.	%
Major complications		
Hematomas*	10	0.48
Hemorrhages	14	0.68
Sarcomas	2	0.09
Repeat surgeries	2	0.09
Postoperative kidney failure	1	0.04
Bowel injury	1	0.04
Uterine rupture†	1	0.26‡
Procedure failings	7	0.34
Total	38	2.02
Minor complications		
Cystitis	70	3.41
Fever > 38°C	105	5.11
Manipulator injuries	12	0.58
Total	187	9.11
Total complications	225	11.1

*Two cases with double complication.
†Adenomyosis.
‡Data on uterine rupture are reported using the number of pregnancies (386 cases) as the denominator.

from Sizzi et al JMIG 2007

blood TF 1 case

failure to complete myomectomy 7 cases (0.34% conversion rate)

complications associated with:

- number of fibroids
- size
- location (intramural and intraligamentous)
- prolonged OT time

reduced with:

- vasopressin
- higher preop Hb

True incidence of uterine rupture after LM unknown

Incidence uterine rupture reported 0-1% (expert hands)

Risk factors for uterine rupture:

- Adenomyosis
- Excessive use diathermy / thermal injury
- Single layer closure or no closure (rupture reported after pedunculated fibroid removed)
- Use of fine sutures 3(0)

Cases reported as early as 17 weeks up to 40 weeks (mean 31 weeks)

19 case reports of uterine rupture after LM documented

Table 1
Identified cases of uterine rupture after laparoscopic myomectomy

Case [reference]	Year of Surgery	Myoma size, cm	Myoma type	Cavity entered	Uterine incision	Hemostasis	Closure	Uterine rupture, wk	Fetal survival	Maternal survival
1 [5]	1992	DM	IM	Yes	Sharp	ENC	1 Layer	28	DM	Yes
2 [6]	1992	3	SS	No	MP	MP	Serosa	34	Yes	Yes
3	1995	3	IM	No	MP	BP, S	1 Layer	34	Yes	Yes
4 [7]	1998	5	IM	Yes	MP	BP, S	1 Layer	28	Yes	Yes
5 [8]	1996	5	IM	Yes	DM	S	DM	28	Yes	Yes
6 [9]	1996	DM	IM	Yes	MP	BP	2 Layers	29	Yes	Yes
7	1997	9	IM	No	MP	BP, S	2 Layers	33	Yes	Yes
8 [10]	1997	5	SS	No	MP	BP	No	33	No	Yes
9 [11]	1997	11	SS-P	No	MP	MP	No	34	Yes	Yes
10 [12]	2000	4	SS	No	MP	MP	No	17	No	Yes
11	DM	2.5	DM	No	UC	S	3 Layers	28	No	Yes
12 [13]	2000	8	SS	No	BP	BP	No	40	Yes	Yes
13 [14]	2001	1.2, 1.2	SS-P	No	MP	MP	No	29	Yes	Yes
14 [15]	2001	3	IM	Yes	DM	BP	1 Layer	26	Yes	Yes
15	2002	2	SS	No	MP	BP	1 Suture	33	Yes	Yes
16	2002	4	SS-P	No	BP	BP	No	35	Yes	Yes
17 [16]	2003	4	SS-P	No	MP	MP	No	36	Yes	Yes
18 [17]	DM	2.5	IM	No	MP	MP	1 Figure-of-8	36	Yes	Yes
19 [18]	2004	4	IM	No	MP	BP	1 Figure-of-8	35	Yes	Yes

BP = bipolar electrosurgery; DM = data missing; ENC = endocoagulator; IM = intramural; MP = monopolar electrosurgery; S = suture; SS = subserosal; SS-P = subserosal pedunculated; UC = UltraCision [ultrasonic scissors].

from Parker et al JMIG 2010

most cases rupture deviated from open techniques:

- 7 cases no suture repair
- 3 cases single suture
- 5 cases 1 layer closure
- 16/19cases monopolar bipolar used haemostasis

recurrence fibroids after LM

- similar to AM
- 50% at 5 years
- 7% reoperation at 5 years

Conclusion:

In selected cases performed by suitably skilled surgeons, LM is a better choice for myomectomy than laparotomy.

Morcellation undiagnosed sarcoma

- Incidence 0.3%-0.06%
- Increased with age (<30 1/500 vs age 75-78 1/98)

Robotically assisted laparoscopic myomectomy (RALM)

- 3-D magnification
- articulation “7 degrees freedom”
- reduced tremor and scaling movements
- ergonomically better for surgeon

allows for more precise surgery

may expand criteria for MIS for fibroids

no prospective RCTs

limited data on RALM:

- reduced blood loss / LOS / improved short term morbidity with increased OR times vs AM
- comparable short term morbidity with LM (observation retrospective data with potential selection bias)
- reported pregnancy outcome similar to LM (uterine rupture rate 1.1%)

NB skill experience surgeon important in studies esp. robotic surgery experience.

Laparoscopically assisted Mini laparotomy myomectomy

Improved short term morbidity with open technique of suturing

Technique

- uterine manipulator
- 3-6cm skin incision with LA
- vertical rectus sheath incision
- vasoconstrictor
- Alexis soft abdominal wall retractor
- Conventional enucleation and suturing

Results:

MGlasser 2005 n= 136 cases audit

Myoma weight	275g
EBL	300ml
ORtime	110min
LOS	6 hours (range 2-48 hours)

Hysteroscopic resection of fibroids TCRM

Indications:

- AUB
- Recurrent miscarriage
- Infertility
- Others eg leucorrhoea, necrotic fibroid after UAE, dysmenorrhoea, need for histology

Patients with significant bulk symptoms are unlikely to have significant relief with TCRM

Criteria for TCRM (Submucous fibroids)

- Depth of penetration
Ideally Type 0 or 1 fibroids
Type 2 in expert hands
Ideally 8-10mm myometrium thickness (TVUS or SSG)
Correlation depth with:
 - Rates of complete resection type 0>95% / type 1 90% / type 2 70%
 - Fluid absorption 450ml / 950ml / 1700ml
- Size
≤ 3cm (risk subsequent fibroid surgery 10% vs 60% for >4cm)
- Ideally only one fibroid
- Experienced hysteroscopist

classification of submcous fibroids

Wamsteker / ESGE

G0	all intracavitary
G1	>50% intracavitary
G2	<50% intracavitary

Lasmar

points	Penetration	Size cm	Base	Third	Lateral wall +1
0	0	≤ 2	≤ 1/3	lower	
1	≤ 50%	> 2-5	>1/3-2/3	middle	
2	>50%	> 5	>3/3	upper	

Base refers to the extension of the base of the nodule with respect to the uterine wall on which the myoma is located.

Score 0–4 (Group I): low complexity hysteroscopic myomectomy.

Score 5–6 (Group II): complex hysteroscopic myomectomy, consider preparing with GnRH analogue and/or two stage surgery.

Score 7 – 9(Group III):recommend an alternative non-hysteroscopic technique.

Operative considerations:

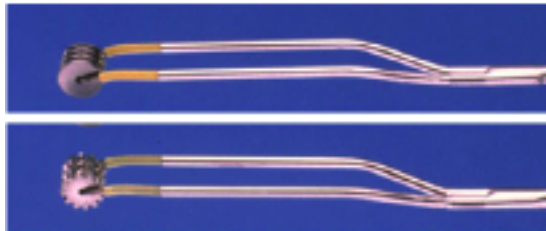
- Prophylactic antibiotics
- Endometrial preparation eg GnRHa, gestrinone or danazol
GnRHa / UPA
 - improves preop anaemia
 - Prepares endometrium better visibility and no need for scheduling
 - Reduction size fibroid
- SE
 - Expensive
 - Increase risk recurrence?
 - Increased cervical resistance and perforation
 - severe haemorrhage from flare effect
- Intraoperative vasopressin reduces blood loss and fluid absorption
- Cervical preparation eg cytotec 400-800mcg
- Fluid monitoring
- Intra operative US guidance
- 2 step procedure for complex procedure
- UPA preop for fibroids >3cm
 - Reduce fibroid volume
 - Improve anaemia

Instrumentation

- Resectoscope



- Vaportrode



Higher power setting (150-300W pure cut) with edge density to create high power density

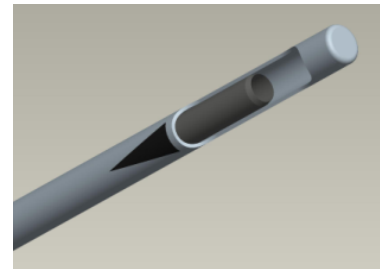
Quicker, less blood loss and fluid deficit

No tissue specimen (should have some tissue for histology exclude sarcoma)

Avoid cornua

Production Gas bubbles watch end tidal CO2 for gas embolism

- Bipolar electrodes
 - Uses saline
 - Different technique resect fibroids
- Hysteroscopic morcellator (myosure)
mechanical morcellator (6000rpm) incorporated into operative hysteroscope with fluid balance system to remove fibroids and polyps.
1 study suggest morcellator hysteroscopy easier to learn than hysteroscopic resection.



Techniques for challenging resections

- Enucleation fibroid
- Use of uterine massage techniques to stimulate contractions eg interrupting then restarting distension liquid several times, manual massage.
- US guidance
- 2 step procedure

Outcomes

Difficult to compare lack of RCT or comparative studies

Most studies show high patient satisfaction rates around 95% in selected cases

- Incomplete resection
 - 5-20% esp fibroids >3cm and type 2
 - many with incomplete resection do NOT have repeat surgery
 - left over lesions may shrink with US
- Recurrent fibroid / AUB
 - Improved bleeding 70-99%
 - Up to 20% over 3 years
 - Combined with EA amenorrhoea rates 95%
- Infertility
 - Most use historical controls
 - Pregnancy rates of 20-75% mean 45% after TCRM*
 - Pritts metaanalysis PRate RR2 but LBR 2.6 NSD and MC rate RR 0.77 NSD
 - 1 RCT Sokeir et al Korea 2010
 - n=215
 - improved PR TCRM type 0/1 fibroids RR 2.1 63% vs 28%
 - but NSD type 2 fibroids!

Complications (1-3%)

- Uterine perforation
 - Occurs at: dilatation; insertion ; resection
 - Intraop US guidance may help
 - No evidence concomitant laparoscopy reduces this
 - Need to exclude viscus injury
- Excessive fluid overload
 - Stop after 1 hour operating time or >1000ml deficit
 - Fluid management systems or careful monitoring
 - Fluid pressures <MAP (100mmHg)
- Haemorrhage (1-2%)
 - Cytotec and vasopressin
 - Foleys balloon
 - Watch perforation

- Intrauterine adhesions
 - 1-13%
 - avoid excessive trauma/electrosurgery surrounding endometrium
 - mechanical separation eg IUD / foleys
 - oestrogen
 - antiadhesion barriers eg seprafilm
 - FU SSG or hysteroscopy
- Uterine rupture
 - 2 case reports
 - time before attempting conception unknown (3-12 months)

Vaginal myomectomy

Sub mucous fibroids (often prolapsed) and may require cervical dilatation

Posterior colpotomy to perform posterior fibroids

Antibiotics recommended

Selected cases 90% successful with up to 10% requiring further surgery / hysterectomy

Myolysis (thermal and cryo)

Technically easier than myomectomy

Using YAG laser / bipolar needles or freezing probe to destroy fibroid

Preop GnRHa recommended

Reduction fibroid size 30-50%

Can be combined with EA to improve amenorrhoea rates

Concerns

- Leaving dead / necrotic fibroid in situ?
- No histology
- Recurrence
- Adhesions
- Unknown fertility and obstetric outcomes including uterus rupture

Laparoscopic uterine artery ligation

First reported Liu 2000

Methods: bipolar, clips etc

Results from case series with short FU:

- Minimal blood loss
- Reduced volume uterus 25-50%
- Improved symptoms 90%

Problems:

- Fibroid necrosis leading to myomectomy / hysterectomy
- Long term results?
- pregnancy issues ?

Management options for fibroids

Fertility desired

FIGO 0/1/2

- Hysteroscopic surgery ± UPA
- UPA alone?

FIGO 2-5 >3cm with infertility

- myomectomy ± UPA
- UPA alone?
- UAE if poor surgical candidate

FIGO 7/8

- Individualise

Fertility not desired and symptoms

FIGO 0/1/2

- Hysteroscopic surgery ± UPA
- UPA alone or other medical treatment
- Mirena

FIGO 2-8

- UPA cyclical
- Mirena
- UAE <10cm
- Myomectomy or hysterectomy ± UPA

Fibroids in pregnancy

Incidence of 1% -10% of pregnant women have myomas depending on size threshold and when detected. (up to 18% in African American females)

Most fibroids do not grow significantly during pregnancy:

- Stable (<10% change in volume) 60%
- Decrease 15%
- Increase 25%

in general,

- those fibroids that increase in size most growth occur first trimester with little change in 2nd and 3rd trimester
- larger fibroids tend to grow
- mean increase volume 12% with few increase by more than 25%

mechanism

oestrogen receptors down regulated by increase in oestrogens in pregnancy leading to increase in size early but later reduction in size

Degeneration

Pelvic pain in 10-15% women with fibroids

occurs commonly around 20 weeks or post partum (times of rapid changes)

associated with

- large fibroids
- Peduncated fibroids
- superficial fibroids.

diagnosis is clinical i.e. pain, fever, TPL with raised WCC ESR typically lasts 7 to 14 days.

Ultrasound pattern

- complex / coarse
- sonolucent
- calcification.

Management

- analgesia
- NSAIDs (limited to 48 hours at gestations <32 weeks)
- Suppression of TPL
- Surgery is rarely required

Effect of myomas in pregnancy

Depends on

1. Size
2. Location
3. placentation
4. Number

most data from observational studies

Generally smaller fibroids <3cm less significant than large ones.

Complications

- Pre term labour + birth (OR 1.5)
- Fetal malpresentation (OR 3-4) esp larger fibroids in the lower segment
- Increased caesarean section particularly for obstructed labour , malpresentations etc.
- Abruption
- PPH
- IUGR
(If placenta covers the myomas)
- Foetal deformations (rare)

Surgical aspects fibroids during pregnancy

Management of myoma during pregnancy in general observe and avoid surgery although there have been reported cases performed myomectomy during pregnancy

Serial ultrasounds in pregnancy detected growth of fibroid and foetus and presentation

- Preconceptual myomectomy
Individualised depending on patient age, past reproductive history, symptoms, size and location of fibroids etc.
- Antepartum myomectomy
For intractable pain
Some cases series reporting favourable outcomes for myomectomy during pregnancy but generally avoided.
- Intrapartum myomectomy
Uterus at term receives 20% cardiac output
Significant risk PPH and blood Tf and peripartum hysterectomy
Limited to those with significant pain & pedunculated fibroid
- Caesarean section
Consider midline incision
Classical CS or posterior uterine incision to avoid incising fibroids as may be difficult to close incision

References

- 1) A Sardo et al. Hysteroscopic myomectomy: a comprehensive review of surgical techniques. *Hum Rep Update* 2008; 14: 101-119
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