
به نام خداوند بخشنده و مهربان

Uterine leiomyoma

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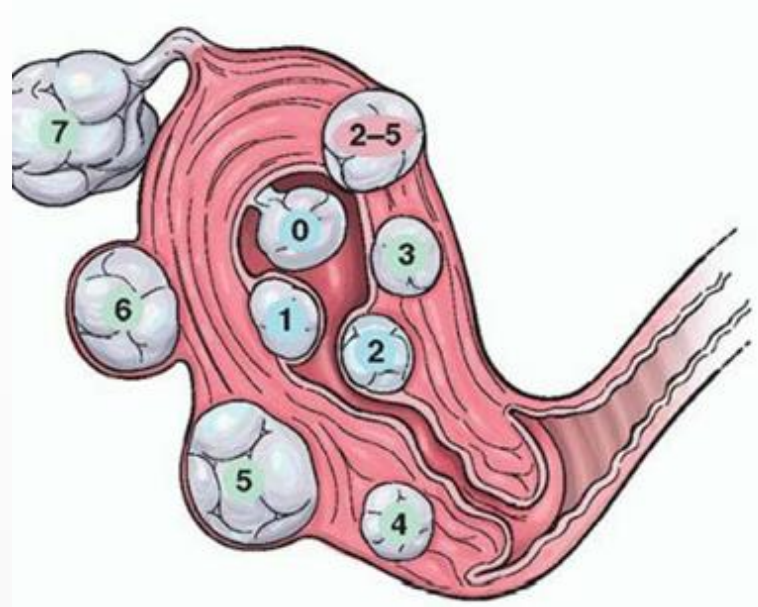
they are noncancerous monoclonal tumors arising from the smooth muscle cells and fibroblasts of the myometrium

Submucosal	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50 intramural
	6	Subserosal <50 intramural
	7	Subserosal pedunculated
	8	Other (specify, e.g., cervical, parasitic)
Hybrid Leimyomas	2–5	Submucosal and subserosal



RISK FACTORS

- **Reproductive and endocrine factors** , Although the growth of fibroids is responsive to gonadal steroids, these hormones are not necessarily responsible for the genesis of the tumors

- **Parity** decreases the chance of fibroid formation

- **Early menarche** , (<10 years old) is associated with an increased risk of developing fibroids in Black patients

  In White patients, a specific polymorphism in the transcription

  factor *HMGA2* appears to be linked to both uterine **leiomyomas**

  and **shorter adult height**,

  suggesting that early menarche may be a key influence

- **Race** , African American or Black
- **Age** , Increasing incidence with age

  By 50 years of age, **70% of white women** and **80% of African American** women will develop a uterine leiomyoma

clinically apparent in approximately **12 to 25** percent of reproductive-age women

- **ovulation induction**

  There are **no** credible cases of uterine enlargement with ovulation induction .

  A nationwide cohort study of patients undergoing in **IVF** reported a **decrease in risk** of fibroids for patients with a higher response to ovarian stimulation than those with a normal response

- **Genetic factors** , Germ-line mutations associated with fumarate hydratase deficiency; somatic chromosomal rearrangements

Hormonal contraception

- **OCP** does not appear to cause fibroids to grow

  administration of these drugs is **not contraindicated** in patients with fibroids.

  One possible exception , use of OC was associated with an increased risk of leiomyoma in patients with **early exposure** to OCs (**13 to 16 years old**) .

- **Long-acting progestin-only contraceptives** (eg, depot medroxyprogesterone) appear to **protect** against development of leiomyoma

  DMPA may **inhibit fibroid regression** when used in the **postpartum period** .

  Studies investigating the symptomatic control of bleeding by **progestin IUD** have shown small **decreases** in fibroid or uterine size

Diet

- Significant consumption of **beef** and **other reds meats** is associated with an increased relative risk of fibroids and consumption of **green vegetables** and **fruit** (especially citrus fruit) with a decreased risk

- consumption of **dairy products**, but not soy products, is inversely related to fibroid risk in Black patients

- Increases in dietary **glycemic index** : a small increase in fibroid risk
- **fat intake** does not appear to be related, dietary consumption of marine **omega-3 fatty acids** may be associated with an increase in fibroid risk in some patients

Lifestyle

- Dietary consumption of **carotenoids** has no effect
- Dietary **vitamin A** from animal sources may also be associated with decreased fibroid risk
- **vitamin D deficiency** or insufficiency, which is more prevalent among Black patients, increase fibroid risk

- **Caffeine consumption** is generally not a risk factor for fibroids, except for weak associations in patients under age 35 with high consumption of coffee or caffeine intake

  The maximum intake of caffeine for adults over the age of 18 years old is up to 400 milligrams, which is about the equivalent of 4 cups of coffee

- **Alcohol ,** associated with an increased risk of developing fibroids
- **Smoking** , Early studies showed that smoking decreased the risk of having fibroids, possibly through the inhibition of aromatase . Subsequent studies have not found an association with fibroids

Medical history

- **Hypertension** is associated with an increased leiomyoma risk.

  The risk is related to increased duration or severity of hypertension

- **type 2 diabetes ,** a decreased leiomyoma risk

  which appears to have a stronger association among European Americans

  than African Americans

- **Uterine infection** was previously associated with an increased risk of leiomyomas, but a subsequent study not find an association

  and one study found an **inverse relationship** with **chlamydia exposure**

- Factors associated with cervical neoplasia are associated with a decreased risk of leiomyoma

clinical features

- **Heavy or prolonged menstrual bleeding**
- **Bulk-related symptoms**, such as pelvic pressure and pain

  Urinary tract or bowel issues , Venous compression

  (4 percent with an enlarged fibroid uterus)

- **Reproductive dysfunction** (ie, infertility or obstetric complications)
- **Endocrine effects** , Rare symptoms of fibroid tumors where fibroids can secrete ectopic hormones include:
  - **Polycythemia** from autonomous production of erythropoietin
  - **Hypercalcemia** from autonomous production of parathyroid hormone-related protein
  - **Hyperprolactinemia**

Isolated heavy menstrual bleeding

HMB is a common presenting symptom in patients with fibroids.

- **First tier** : Hysteroscopic resection of submucosal fibroids if there is a submucosal fibroid (FIGO type 0, type 1, or type 2) because of the safety and efficacy of hysteroscopic myomectomy as a treatment
  there is a lower risk of complete resection of FIGO type 2 greater than
  5 cm in diameter and
  >50 percent extension into the myometrium

- Submucosal leiomyomas,
  which derive from myometrial cells
  just below the endometrium, account
  for approximately **15 to 20** percent of fibroids

Indications

- intracavitary fibroids with

  Abnormal uterine bleeding , Recurrent pregnancy loss , Infertility .

  Dysmenorrhea

  And

- Leukorrhea
- Necrotic leiomyoma following uterine fibroid embolization, MRI-focused ultrasound,or transcervical ultrasound therapy
- History of preterm delivery
- Postpartum hemorrhage
- Puerperal infection arising in or exacerbated by a submucosal fibroid
- Postmenopausal bleeding

It is important that:

- For leiomyomas that are **multiple or are >3 cm or deep in myometrium**, it is prudent to include in the informed consent the possibility of a **two-stage hysteroscopy** procedure

- Patients with **abnormal uterine bleeding** or **dysmenorrhea** may have **adenomyosis** in addition to intracavitary fibroids and hysteroscopic myomectomy is unlikely to provide complete symptomatic relief.

  These patients can also benefit from **medical therapy** or insertion of a **levonorgestrel-containing IUD** in combination with hysteroscopic myomectomy.

- **evaluation** of the endometrium

  in patient with abnormal uterine bleeding at risk for **endometrial hyperplasia** or cancer , **prior to hysteroscopic** myomectomy

PERIOPERATIVE MEDICATIONS

Agents to decrease bleeding

- **GnRH agonists,**
  - decrease the size of large fibroids; however
  - more difficult to dissect fibroids from the surrounding capsule.
  - incomplete resection possible for large fibroids
  - no reduce intraoperative blood loss or distention fluid absorption .
  - they result in vasomotor symptoms and may lead to cervical stenosis

indication for use of GNRHa include:

patients with severe anemia that may preclude surgery,

those in whom intravenous iron therapy is contraindicated,

or those who refuse blood products.

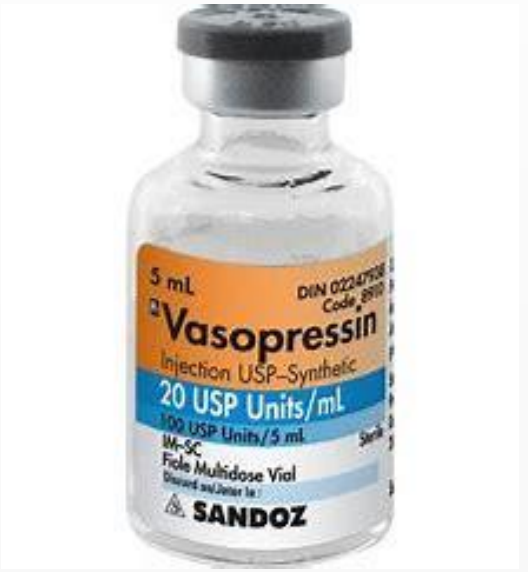
Vasopressin

Injection of 10 units in 100 mL of normal saline into the cervical stroma in 5 mL aliquots at the 10, 2, 5, and 8 o'clock positions around the ectocervix.

This dose can be repeated every 30 to 45 minutes if bleeding is encountered or the procedure is prolonged.

An additional benefit of vasopressin is that it

facilitates cervical dilation



- **Use of uterine contractions**

  Deflation of the uterine cavity refers to removing the operative hysteroscope and waiting for several minutes to permit myometrial contractions to cause extrusion of the myoma.

  When the hysteroscope is replaced, the surgeon will commonly see more of the myoma extruding into the cavity.

- **prostaglandin**

  profound diarrhea and difficult uterine distention may be associated with carboprost.

- **Uterine massage** via bimanual examination

Medical therapy

- **Estrogen-progestin contraceptives**

  oral contraceptive pills, vaginal ring, or transdermal patch are the most common medical therapy utilized by patients with HMB and fibroids especially those who desire contraception

- **Progestin-releasing intrauterine devices (IUDs)**

  supporting data are mainly observational and less strong than for its use with generic HMB

  Nonetheless, most guidelines support the use of LNG IUDs as a first-line agent for fibroid-related HMB

  First, identifying patients with significant submucosal fibroids is important since the risk of expulsion of the IUD is greater in patients with fibroids that distort the endometrial cavity.

Tranexamic acid is a nonhormonal oral medication

it can be preferred by patients who cannot or do not wish to use hormonal contraceptives or by those who desire a treatment that is used only when symptoms are present.

- A systematic review reported that it can be more effective than oral progestin

Dose: 1300 mg (two 650 mg tablets) orally three times a day (3900 mg/day)

during monthly menstruation

Duration: Maximum of 5 days

Progestin-only contraceptives

Oral progestin-only contraceptives, progestin implants, and progestin injections do not appear to be effective for fibroid-related HMB

GnRH antagonists

- Elagolix, in combination with estradiol and norethindrone acetate, was approved by the US Food and Drug Administration (FDA) in May 2020 for the treatment of fibroid-related HMB for **up to 24 months of use**

commercial name **Oriahnn**

is available as two co-packaged capsules:

one contains elagolix 300 mg plus estradiol 1 mg plus norethindrone 0.5 mg to be taken in the morning,

the other contains elagolix 300 mg alone to be taken in the evening.

During treatment with elagolix plus add-back, **side effects**

were modest, including

- **hot flushes** (7 percent), **night sweats** (3 percent), **headache** (5.5 percent), and **nausea** (4 percent).
- **Reduce of Bone mineral density** at the end of 12 months of treatment, (1.5 percent)

- The benefit of add-back therapy is that it mitigates many of the hypoestrogenic side effects of elagolix; however, the effect on fibroid volume reduction is also attenuated.
- As ovulation suppression with elagolix plus add-back is variable,

it should not be considered a contraceptive

Relugolix, in combination with estradiol and norethindrone acetate,

- was approved by the US FDA in May 2021 for the treatment of fibroid-related HMB for **up to 24 months**
- is available as one copackaged capsule containing relugolix 40 mg plus estradiol 1 mg plus norethindrone acetate 0.5 mg in a single daily dose.
- An advantage of relugolix is its once daily dosing and potential for greater reduction of pain and bulk symptoms

Myfembree®
(relugolix, estradiol, and norethindrone acetate) tablets
40 mg, 1 mg, 0.5 mg

GnRH agonists

are primarily used as either

- as transitional therapy for patients in late perimenopause as they move to menopause.
- For patients with fibroids and anemia who are planning surgery for fibroids but have not responded adequately to iron-only therapy,

  (typically three to six months in duration)

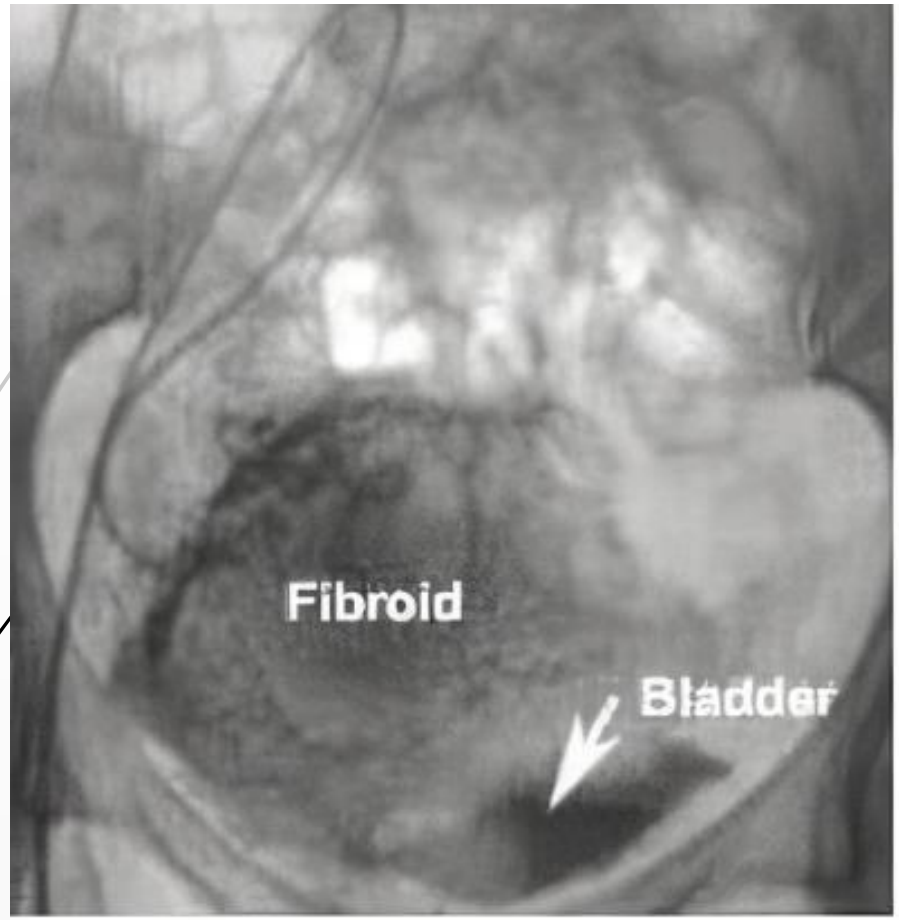
Uterine artery embolization

- minimally invasive option
- Up to 90 percent of patients will report improved or resolved HMB symptoms after treatment.

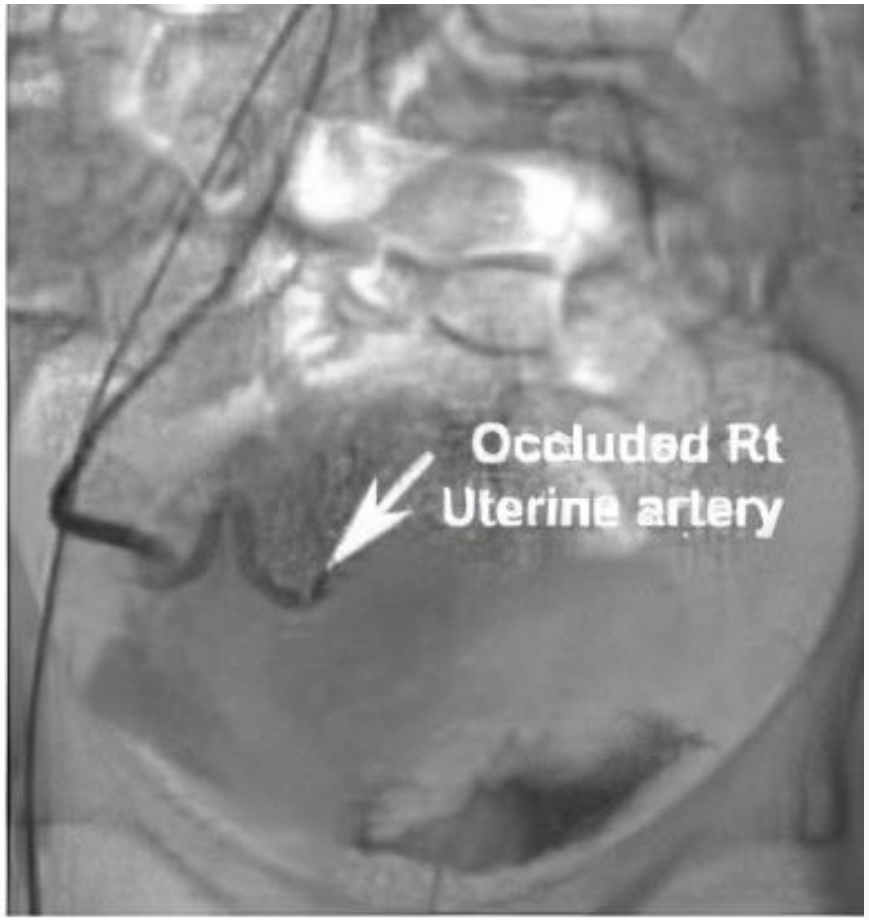
Advantages

- When compared with hysterectomy or myomectomy, patients undergoing UAE have a substantially decreased risk of transfusion, a shortened hospital stay, less pain, and a quicker return to work. patients have more short-term complications

- UAE is not limited by number of fibroids or presence of intra abdominal adhesions.



Pre-embolization



Post-embolization

Limitations of UAE

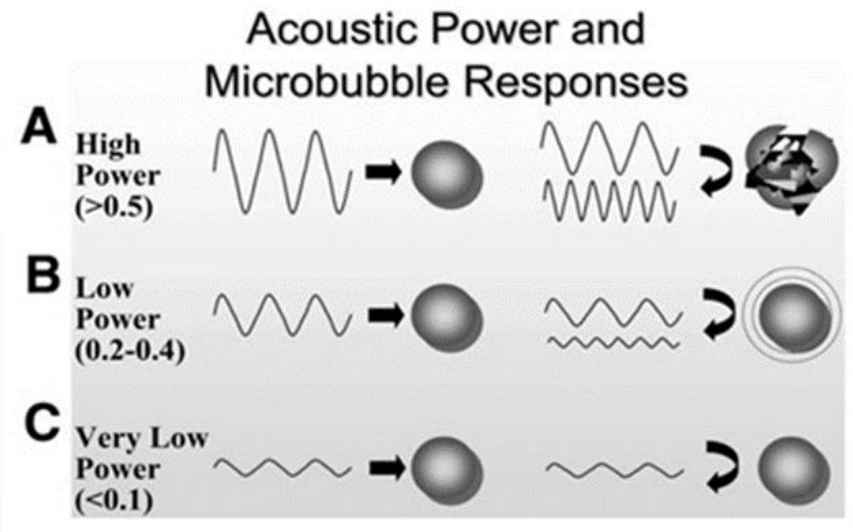
- **Hysterectomy risk** –25 percent risk of subsequently undergoing hysterectomy larger uteri and/or more fibroids at baseline are at greater risk of failure, and failure may represent other concomitant disease, such as adenomyosis and endometriosis

- **Premenopause only**
- **Anatomy** – UAE is not able to treat fibroids that are supplied by the cervical or ovarian arteries and is not generally indicated for uteri greater than 20 gestational weeks in size
- **Fibroid expulsion** – If submucosal fibroids are present, they can be passed vaginally in an unpredictable fashion
- **Menopause risk**
- **Pregnancy** – UAE is not intended for use in patients who desire optimization of future childbearing.

Focused ultrasound surgery

high intensity ultrasound energy to induce coagulative necrosis of fibroids

- high intensity focused ultrasound (HIFU)
- MRI Guided Focused Ultrasound (MRgFUS)



- **outpatient** procedure with sedation
- each fibroid is targeted individually,

- size, vascularity, heterogeneity, calcifications, and abdominal scars through which the ultrasound energy passes can all affect treatment.
- **Ideal treatment candidates** have three or fewer fibroids, size less than 10 centimeters in maximal dimension, homogenous and well-vascularized without calcification

- **Outcomes** – Symptomatic improvement is observed within the **first three months post procedure**, and has been maintained at least through 24 to 36 months of follow-up, with more complete ablation leading to better outcomes

- **Post procedure pregnancy**

The case series of MRgFUS described 54 pregnancies in 51 patients with mean birth weight of 3.3 kg and a 64 percent vaginal delivery rate. complications; 9 percent of patients had placentation problems

The HIFU series described 80 pregnancies in 78 patients who delivered at a mean of 38.1±2.2 weeks

Impact of fibroids on fertility

- Generally, the literature has concluded that fibroids that distort the cavity FIGO types 0 to 3 have more of an impact on fertility, and surgical treatment can be effective in reversing that impairment

- for patients with a uterus 16 weeks in size or larger, shortening the interval for trying for pregnancy

  six months for patients <35 years old and after

  three months for patients ≥35 years old.

Fertil Steril. 2018 May;109(5):817-822.e2. doi: 10.1016/j.fertnstert.2018.01.007. Epub 2018 Mar 28.

Effect of type 3 intramural fibroids on in vitro fertilization–intracytoplasmic sperm injection outcomes: a retrospective cohort study

- **Conclusion(s):** Our results suggest that **type 3 fibroids** exert a **negative impact** on the **rates of implantation**, **clinical pregnancy**, and live birth in patients undergoing IVF-ICSI, but do not significantly increase the clinical miscarriage rate.
- The deleterious impact of type 3 fibroids was remarkable in women with type 3 fibroids with single fibroid diameter (SD) or total reported fibroid diameter (TD) >2.0 cm.

Abdominal myomectomy

Indications — The most common indications for open abdominal myomectomy are:

- Abnormal uterine bleeding
- Bulk-related symptoms – pelvic/abdominal pain or pressure; pressure on the urinary or gastrointestinal tract resulting in urinary or bowel symptoms
- Dysmenorrhea is more commonly associated with conditions (eg, endometriosis) other than with myomas.

  Myomectomy or other fibroid-specific treatment for the indication of dysmenorrhea should be performed only when other therapies for dysmenorrhea have failed
- **Infertility**

Myomectomy versus hysterectomy

Some factors that may affect a patient's decision include

- **blood loss** is not more in myomectomy
- Prevention of future cervical or uterine pathology is not a relevant indication for hysterectomy in current practice

- Hysterectomy offers the advantage of definitive treatment but studies show a higher risk of injury to ureters, bladder and bowel with hysterectomy and a risk of subsequent pelvic organ prolapse surgery and decrease of AMH

EXPECTANT MANAGEMENT

Candidates

- Asymptomatic
- Attempting pregnancy
- With lesions that are stable in size as demonstrated by serial imaging studies for one year
- Peri- or postmenopausal
- With uteri less than 12 weeks in size (not palpable abdominally)

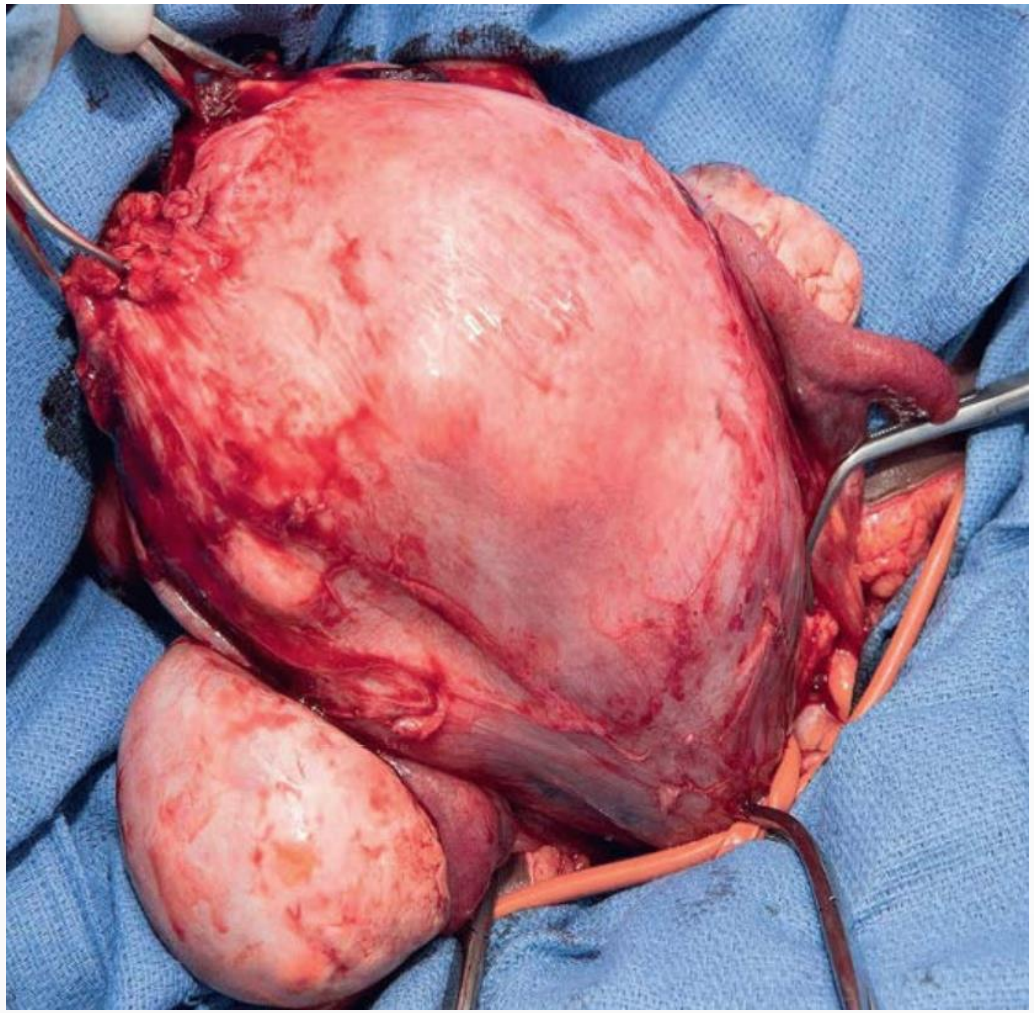
Components of expectant management

periodic evaluation of the patient for new symptoms by **history** and **physical examination** or may require **imaging** or laboratory studies

yearly evaluation is reasonable.

Risk factors for Sarcoma

- **Increasing age and postmenopausal status**
- **Tamoxifen** — Long-term use of tamoxifen (five years or more) is associated with an increase in risk of developing uterine sarcoma
- pelvic irradiation, a history of childhood retinoblastoma, and hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome.
- Data are inconclusive regarding parity and time of menarche and menopause as risk factors for sarcoma.



A catheter is placed around the lower uterine segment in order to occlude the uterine vessels

A vascular clamp is placed across the ovarian vessels

Use of misoprostol in myomectomy: a systematic review and meta-analysis

- The mechanisms of action include **uterine contraction** which leads to contraction of vascular structures and blood flow reduction as well as **vasoconstrictive** effect on uterine arteries
- misoprostol reaches its peak in almost 1 h
- Rectal route has a longer half-life than oral route

- reduces significantly intraoperative blood loss, but there was not statistical significant difference in the need for blood transfusion

Conclusion: Easy to use, minor or no side effects, and

good clinical outcomes

Vasopressin

- Vasopressin acts by constricting the smooth muscle in the walls of capillaries, small arterioles, and venules.
- Randomized trial data show that **blood loss** during myomectomy with vasopressin is **significantly less than with placebo** (299 mL less)

- **Safety ,** bradycardia, cardiovascular collapse, and death (in rare cases)

  Vasopressin use may be contraindicated in patients with medical comorbidities

  (eg, cardiovascular, vascular, or renal disease).

  has not been approved by the FDA for this purpose

- 20 units of vasopressin in 100 mL of saline; 4 to 6 units of vasopressin equals 20 to 30 mL of this solution. The half-life of intramuscular vasopressin is 10 to 20 minutes and the duration of action is two to eight hours.

Tranexamic acid

10 mg/kg intravenously [IV] infused over 10 minutes

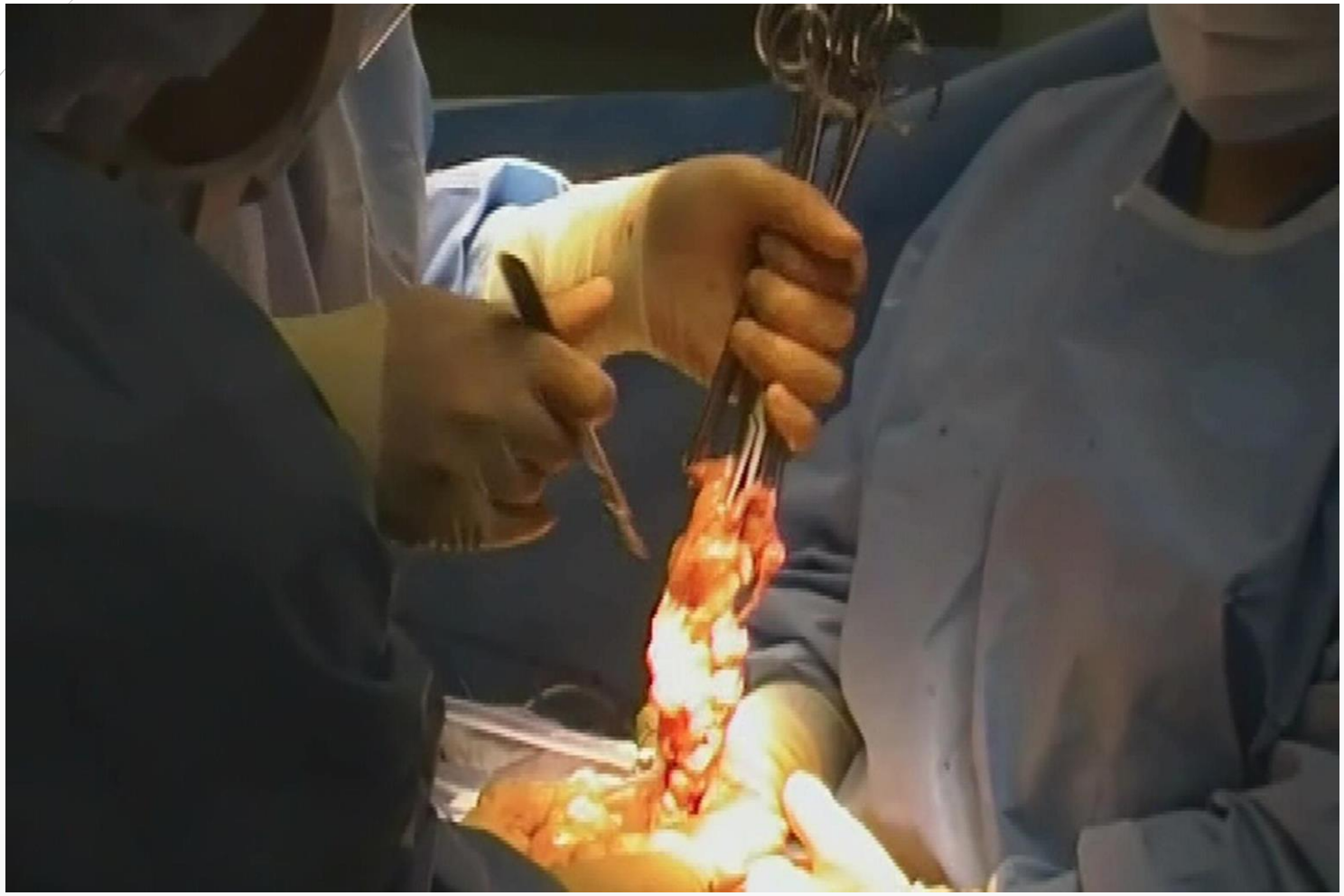
20 minutes prior to surgical incision; larger doses have been described

- Tranexamic acid is contraindicated in patients with a history of thrombotic events
- the efficacy of tranexamic acid on blood loss at time of myomectomy have yielded mixed results

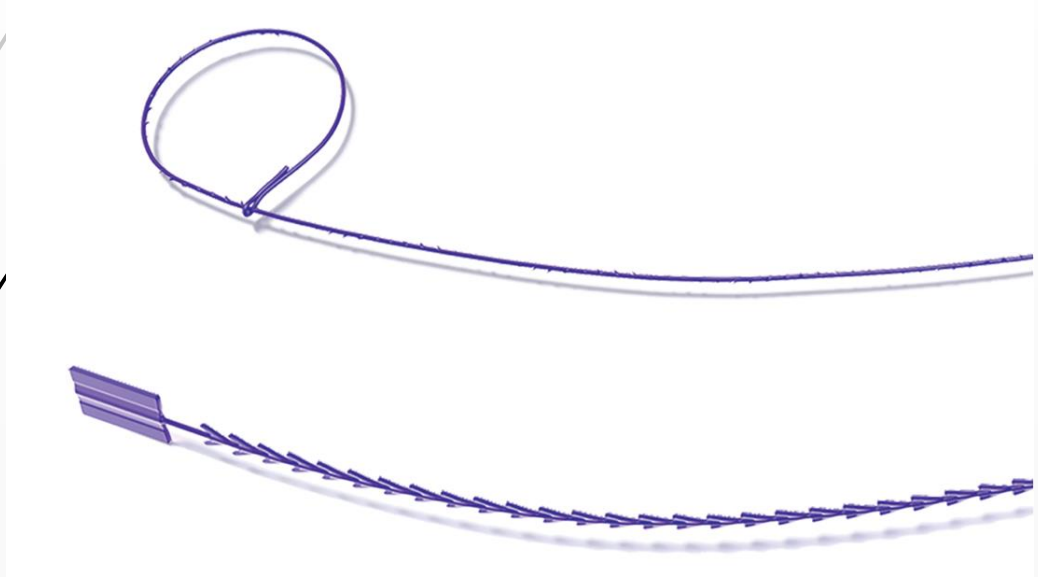
TABLE 18.3 Perioperative Medical Measures to Reduce Intraoperative Blood Loss

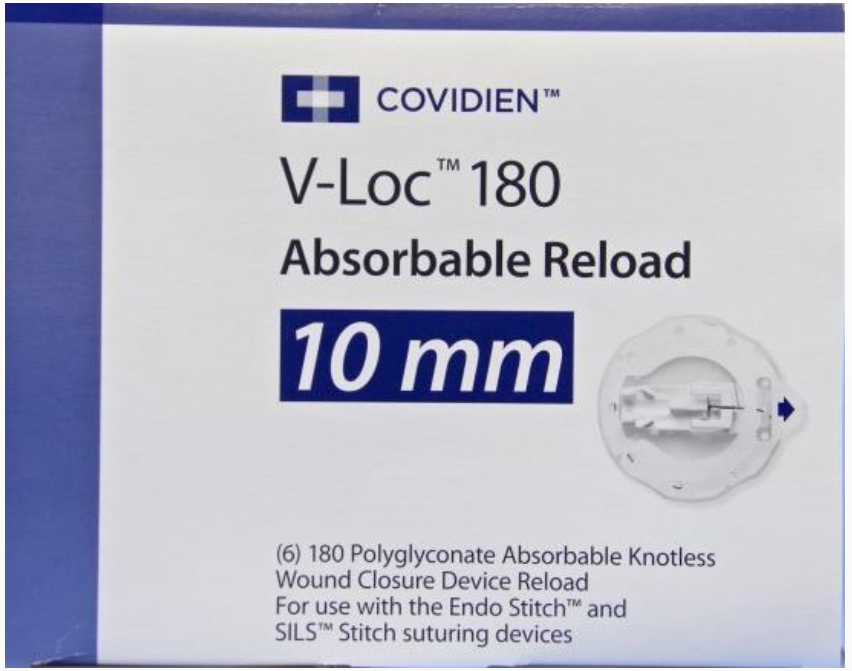
AGENT	MEAN DIFFERENCE IN BLOOD LOSS VERSUS PLACEBO	NEED FOR BLOOD TRANSFUSION
Intramyometrial vasopressin[b]	245 mL	Decrease need
Intramyometrial bupivacaine and epinephrine[a]	68 mL	No effect
Vaginal misoprostol[b]	97 mL	No effect
Fibrin sealant patch[a]	26 mL	No effect
Intravenous ascorbic acid[a]	411 mL	No effect
Intravenous tranexamic acid[a]	243 mL	No effect

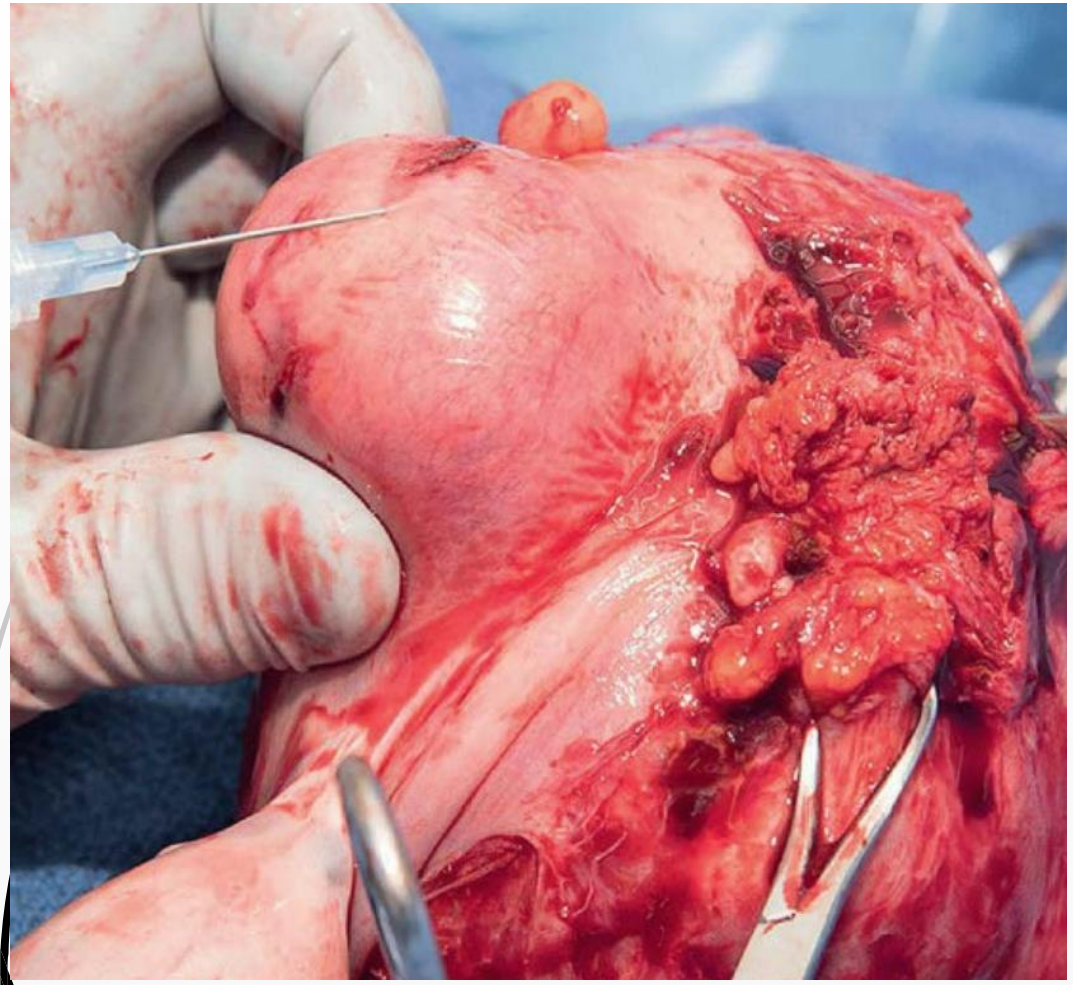
Scalpel morcellation

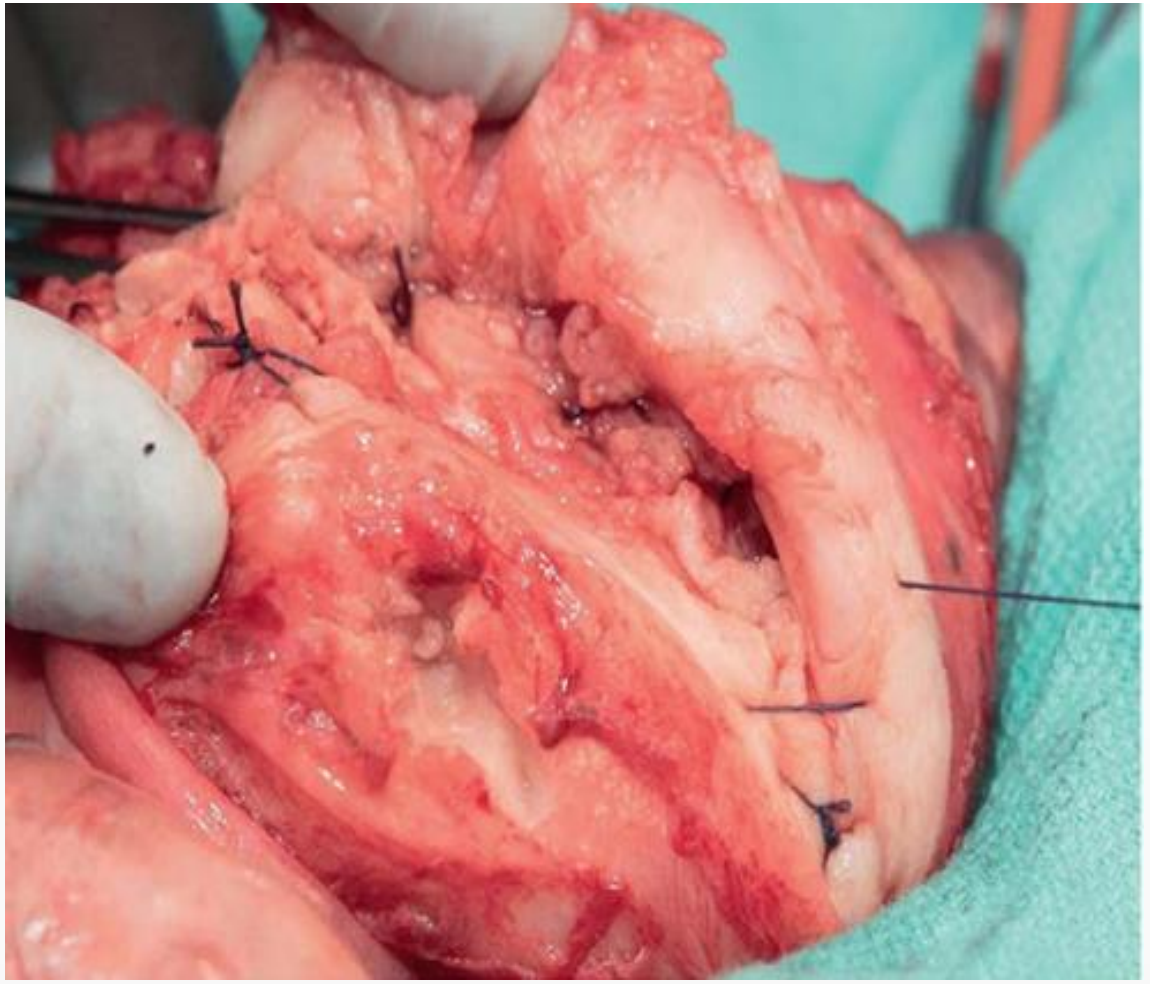


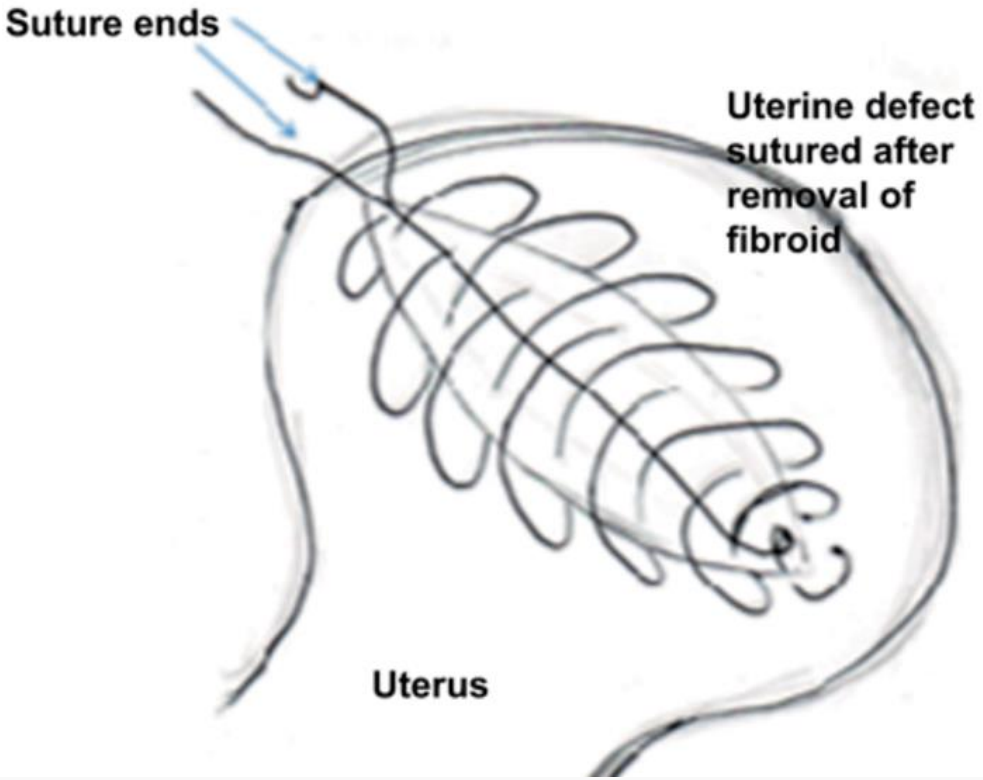
Barbed Sutures

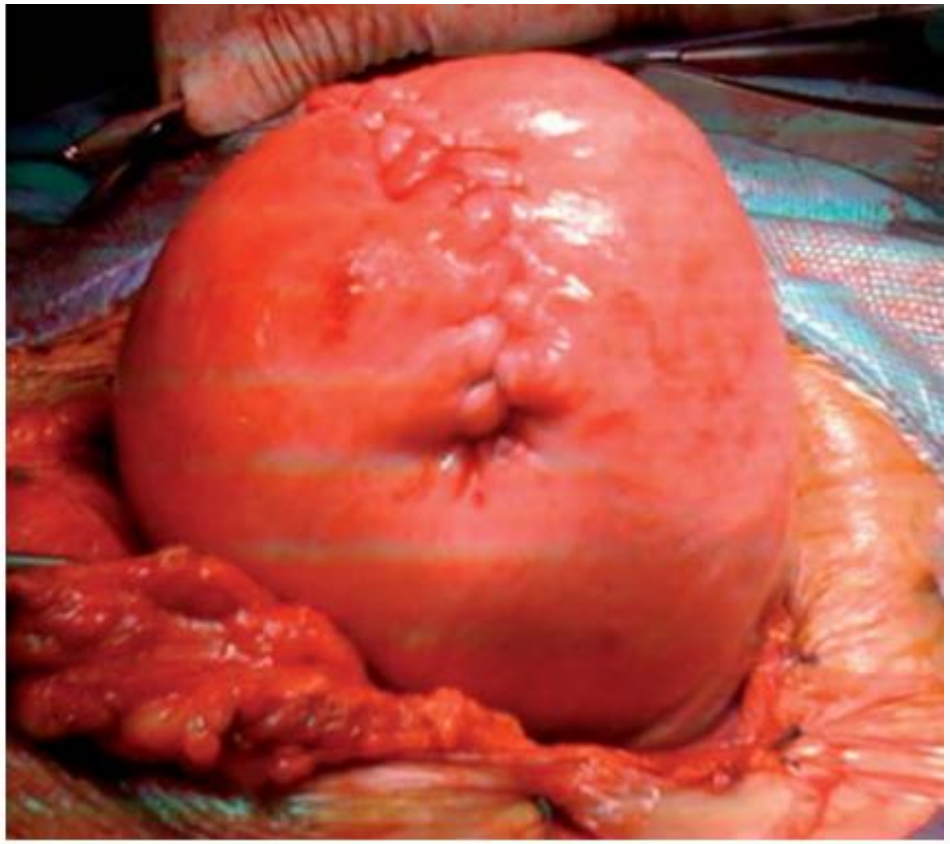









Suture ends
Uterine defect sutured after removal of fibroid
Uterus



Arch Gynecol Obstet. 2011 Feb;283(2):311-5. doi: 10.1007/s00404-010-1355-y. Epub 2010 Jan 23.

Uterine fibroids: risk of recurrence after myomectomy in a Nigerian population

Jesse Y Obed [1], Babagana Bako, Joshua D Usman, Joel Y Moruppa, Saidu Kadas

- **Methods:** Two hundred and thirty-two women who had open myomectomy were followed up for 3-10 years, Age : 29.3 ± 3.8 years
- **Results:** The overall recurrence rate during the follow-up period was **20.7%** (48/232) at 10 years and this increases with time.

  Positive family history of uterine fibroids,

  multiple uterine fibroids, and

  persistence or recurrence of three or more of the pre-myomectomy symptoms

  were significantly associated with the recurrence of uterine fibroids
- Pregnancy and use of OCP are protective

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Obstetrics and Gynaecology Research
doi:10.1111/jog.13519
J. Obstet. Gynaecol. Res. Vol. 44, No. 2: 298–302, February 2018

Recurrence of uterine myoma after myomectomy: Open myomectomy versus laparoscopic myomectomy

Results

- The cumulative recurrence rates between the two groups were

  76.2% (LM) vs. **63.4% (OM)** at **eight years** postoperatively.

- **LM**, **a larger number of enucleated myoma** masses and the **absence of postoperative gestation** and **vitamin D deficiency** significantly contributed to the postoperative recurrence rate.
- **high physical activity** and **OCP** are protective