

19

Uterine Fibroids

Regine Unkels

INTRODUCTION

Uterine fibroids are the most common benign pelvic tumors in women of reproductive age. They affect 20–40% of those women¹ but are found in 75% of hysterectomy specimens². This is due to the fact that most fibroids are asymptomatic. A true estimate of prevalence would need to be based on ultrasound screening³. From ultrasound-based screening studies in the USA and Europe it is estimated that women have a risk of 50–70% of suffering from fibroids during their lifetime. Onset under the age of 30 years is rare although not impossible³. After menopause (12 months after the last period) fibroids tend to decrease in size or remain stable.

There are known risk factors for developing uterine fibroids but the true etiology is unknown. A genetic pre-condition for developing fibroids seems to exist that differs by ethnicity. From studies in the USA it is known that women of African descent more often have fibroids with an earlier onset, bigger tumors and earlier symptoms than caucasian or Asian women³. Studies imply that this fact is due to different numbers of estrogen, progesterone and aromatase receptors in fibroids and normal uterine muscle according to ethnicity.

Fibroids can cause high morbidity and suffering when they grow and cause symptoms. Fibroid-associated morbidity in the USA results in direct costs of approximately 2 billion US dollar a year and fibroids are the most common indication for hysterectomy, a major operation⁴. As a matter of fact every doctor will encounter patients with fibroid-associated symptoms once in a while depending on his or her workplace and it is worthwhile to sit down and think of how big the problem could be in your area.

DEFINITION

Uterine fibroids or leiomyoma are benign tumors of the uterine muscle, called myometrium. They contain receptors for female reproductive hormones (estrogen and progesterone) and other enzyme receptors related to estrogen production (aromatase receptors). When the receptors are present in the fibroid, the growth of the fibroid will be stimulated by these hormones. The cause of fibroid development is not fully understood. All cells of one fibroid are the same and different to the cells of another fibroid of the same woman (this is called monoclonal cells)². Classification of fibroids is according to their site in the uterine wall:

- *Subserosal fibroids* are found superficially under the outer lining of the uterus, the serosa. They can grow to the interior part of the wall or completely under the serosa and become pedunculated with only a thin bridge to the myometrium (Figure 1).
- *Intramural fibroids* are the most common. They are situated in the middle layer of the uterine muscle (Figure 1).
- *Submucosal fibroids* grow in the myometrium near the inner lining of the uterus, called endometrium. Like the subserous fibroids, they can become pedunculated and protrude into the uterine cavity (Figure 1).
- Uncommon sites are the ligaments of the uterus. These fibroids are difficult to manage surgically as they are often near other structures such as the ureters, vessels and nerves and should only be attempted by experienced surgeons.

This distinction of fibroids is very important as they cause different symptoms and might need a different access during surgery.

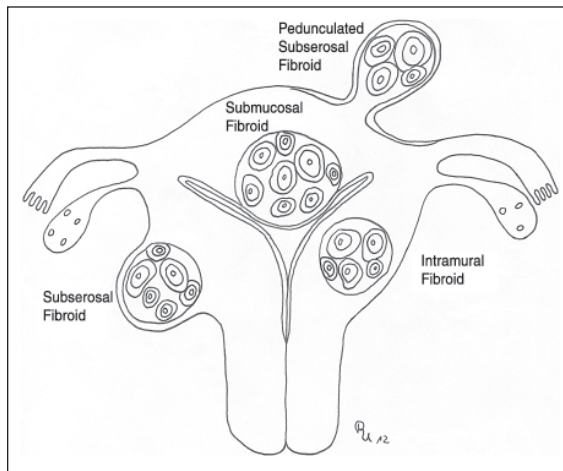


Figure 1 Locations of uterine fibroids

MAGNITUDE OF THE PROBLEM IN LOW-RESOURCE SETTINGS

Not much is known about the true prevalence of fibroids in low-resource settings. First, this is due to the above-mentioned fact that most fibroids are asymptomatic and with decreased availability of ultrasound and preventive gynecological examinations these women never find out that they have them. Second, some women may have symptomatic fibroids but as a result of limited availability of financial resources and healthcare they never reach a healthcare provider for examination. Third, with limited resources of healthcare systems, fibroids are not recognized as a public health problem in comparison to other conditions such as cancer or obstetric problems – they don't kill. Thus you can assume that there is significant under-reporting of patients with fibroids on the care provider side too. A study done in a Nigerian teaching hospital showed that patients with symptomatic fibroids constituted 9.8% of all gynecological admissions⁵. If you consider the results from ultrasound-based prevalence studies mentioned above and compare them to this figure you can appreciate that there may be a significant unmet need for treatment in low-resource settings.

ESTABLISHED RISK FACTORS

Generally, it is very difficult to establish risk factors for a condition that is as common as fibroids because for a good study design to have sound evidence you would need a lot of participants. However, some cohort studies in the USA (groups of participants followed up for several years to see if they

develop a condition or not) on a wide range of diseases dealt with uterine fibroids as well^{3,6}. From ultrasound-based screening studies some risk factors could be established (level of evidence 2):

- Age
- African ancestry
- Early age at menarche (first period)
- Parity.

These risk factors all deal with the already mentioned exposure to female reproductive hormones and the duration of exposure. However, they don't explain why some women with the same risk factors which are fairly common, develop fibroids and others not, and why some fibroids start to grow and others not. Observational studies from environmental health registers (level of evidence 3) have found some interesting new associations or absence of association:

- No association between smoking and fibroids.
- No association between contraceptive pills and fibroids unless used before the age of 17 years.
- Depot-progestins carry a reduced risk for fibroids; so do intrauterine devices (IUD) with or without hormonal coating.
- The association with raised body mass index (BMI) was inconsistent; no association was found for caucasian women, but a slight but significant association was found for African-American women.
- Alcohol and caffeine intake was associated with fibroid development.

SYMPTOMS

When considering Figure 1 it is easy to imagine which fibroid type causes which symptoms. Here is a list of common symptoms associated with uterine fibroids:

- Increase in size and number. A uterine tumor rapidly growing after menopause is unlikely to be a fibroid. Around the last period, however, fibroids can grow due to an increased number of cycles without ovulation and high estrogen levels in the body.
- Menorrhagia (prolonged and heavy bleeding within normal cycle).
- Subfertility.
- Secondary dysmenorrhea (new onset of period pain).

- Pressure symptoms from the bowel and bladder, e.g. constipation, frequency, chronic urinary tract infections (UTIs).
- Chronic pelvic pain, dyspareunia.
- Pregnancy-associated symptoms: spontaneous abortion, recurrent abortion, abdominal pain and pressure signs in pregnancy, premature rupture of membranes, dystocia, post-partum hemorrhage.

Less common symptoms include:

- For submucosal, pedunculated fibroids: protrusion through cervical os with pain and bleeding.
- For subserosal, pedunculated fibroids: torsion with infarction and acute abdominal pain and separation from the uterus.
- Malignant change into leiomyosarcoma (approx. 0.13–0.23%)¹.

The most common complaint is menorrhagia. This is most probably due to an expanded surface of the endometrial lining when a submucosal fibroid bulges into the cavity. But also an increased number of small dilated vessels has been found hinting to other altered growth factors⁷. Menorrhagia can be severe and cause relevant anemia.

The extent to which fibroids alter fertility is not clear and still under discussion. Women with otherwise unexplained infertility showed better reproductive outcome after myomectomy¹. Most likely, submucosal fibroids bulging into the cavity can alter blood circulation in the stretched endometrium above, can distort the uterine cavity or block the tubes if located near their inner orifice or interfere with sperm transportation. Large fibroids can interfere with the ovum pick-up mechanism.

HISTORY TAKING

As always a thorough history should be taken, especially in order to assess how long the symptoms have already lasted. Specific questions you could ask are:

- Age of menarche (as a proxy indicator for a longer exposure to estrogen and progesterone during the reproductive life span).
- Parity.
- History of miscarriages, infertility, present desire for children.
- Actual complaints, duration of symptoms: specifically ask about bleeding pattern, pain, dysmenorrhea and pressure signs.

- History of previous symptoms that might be associated with fibroids.
- History of sexually transmitted infection (STI) symptoms.
- Previous abdominal and vaginal operations.
- Last two menstrual periods with duration and regularity.
- Previous or actual use of contraceptives and type of contraceptives.
- Weight and height.
- Nicotine and alcohol intake.

INVESTIGATIONS

A complete gynecological work-up should be performed. The aim of the investigations is to find out if the patient really has uterine fibroids and if yes, whether they need an operation and if yes, which type of operation and whether it can be performed in your work place. To get the most information out of your work-up you should always explain to the patient what you will do and why. For an exact description of the procedures see Chapter 1 on gynecological examination.

Abdominal palpation

Ask the patient to empty her bladder and lie down on a bed or stretcher with her abdominal muscles relaxed. Palpate the area below the umbilicus softly with your fingertips as deep as the patient allows you. Try to find out if there are any areas where deep palpation is not possible due to pain or if you can feel any hard or soft resistance. If yes, figure out its location and whether it is mobile or not. This can help you to assess the size of the uterus or a single fibroid and can already tell you whether an operation might be difficult in cases where the uterus is not at all mobile. Be aware, however, that sometimes a full bladder could mimic an enlarged uterus by pushing it upwards.

If you find an area with stronger pain, this might hint to peritonism. Deeply palpate at the other side of the abdomen and then briskly let go. If this hurts, the patient has peritoneal signs and might not have a normal fibroid but either something else or a fibroid with torsion, infarction and infection.

Speculum examination

As the onset of fibroid-associated symptoms is rare before 30 years of age, most of the time you do not

need to worry about a patient's virginity when doing the examination. However, you should ask the patient before doing the examination. Now put the patient in the lithotomy position as described in Chapter 1 and perform a speculum examination. Try to find the cervix and assess whether it is in the midline or distorted and whether it seems shortened. If there are uterine fibroids in the lower part of the uterus they can deviate the cervix to one side or shorten it through traction.

Then assess for cervical mucus or discharge and ulcerations. You do not necessarily need this information for your assessment of fibroids but when doing a speculum examination you should always take the opportunity to screen for cervical cancer. In addition, a patient can always have more than one condition, so watch out for other findings too.

Bimanual palpation

Now proceed to bimanual examination as described in Chapter 1. Here as well try to assess the size of the uterus and its mobility. In order to find out whether the uterus is protracted in the small pelvis it is important to try to push it gently upwards. Do this carefully as it can hurt very much if the uterus is fixed in the small pelvis. Try to assess the uterine shape, whether you can feel humps on it and where and whether it is very broad.

Ultrasound

If you have a vaginal and an abdominal ultrasound probe, always start with the vaginal probe to better assess the cervical area, the endometrium and if possible the adnexa. Also you can already diagnose fibroids from the ultrasound picture and this is most often easier vaginally. Uterine fibroids have a clear border to the adjacent myometrium as the latter surrounds them like a capsule. They are mostly darker than the myometrium (Figure 2). Submucosal fibroids are better diagnosed with the vaginal probe.

Do not miss out an abdominal scan as you might underestimate the real size of the uterus if it exceeds the small pelvis as the vaginal probe does not reach that far. By using the vaginal and abdominal probe of the machine, assess the uterine size and, if you can, the number, size and location of the fibroids. This is important to decide about the type of operation (myomectomy or hysterectomy),

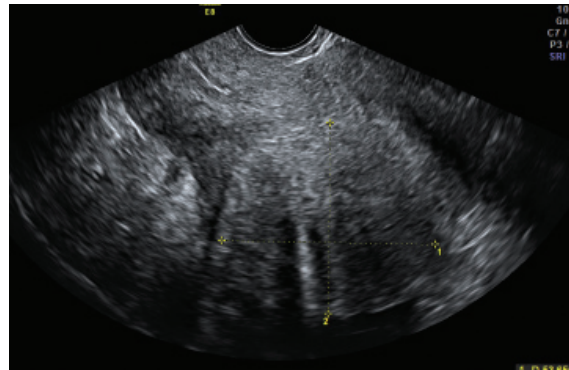


Figure 2 Uterine fibroids on ultrasound. Courtesy of Mirjam Weemhoff

access (horizontal or vertical incision), whether you need more investigations or to prepare for blood transfusion and whether the operation can be done in your facility or not.

Sometimes there are so many fibroids that you cannot assess each of them. At this point a myomectomy will not be possible anymore and it is enough to measure the size of the uterus.

In patients with very large uterine fibroids and those scheduled for operation you must always assess both kidneys for dilatation of the kidney pelvis or ureter. You can do so with the abdominal probe from the right and left upper quadrant or via the patient's back. This is very important as with large fibroids, kidneys can be dilated, which is an indication for operation even if she doesn't have a lot of symptoms. During a hysterectomy, ureters can be damaged or accidentally closed while suturing. Thus you need to assess this prior and postoperatively to exclude this happening (see below).

It is always good to document your findings with a drawing and to write down the measurements of each fibroid (see Chapter 1). If the diagnosis of uterine fibroids was made by coincidence without the patient having any symptoms, you should monitor the woman regularly by ultrasound. By documenting your findings this way you can always compare with your actual findings when you see her again.

If the patient came with fibroid-associated complaints it is important for those colleagues who operate on her to know what you found. In Chapter 1 on gynecological examinations, you will find an example of how to document ultrasound findings, which you can use by either photocopying it or drawing your own sketch.

Laboratory investigations

There might be a routine investigation standards set-up in your laboratory for certain conditions or likely operations. For patients with uterine fibroids make sure they contain at the minimum the following:

- Hb to assess the amount of anemia which will help you to decide whether the patient needs an operation or not and whether you may need a blood transfusion.
- Erythrocyte sedimentation rate (ESR) or white blood cell (WBC) count to know if there is pre-existing infection. Be aware, however, that big fibroids can be necrotic without symptoms which will raise the ESR and maybe even the WBC.
- Blood grouping and cross-matching for operation or to correct anemia prior to operation.
- Urinalysis to detect UTI as a source of post-operative infection prior to operation.

These investigations are only important for you to plan the operation. Your anesthetist might want other additional investigations.

Further investigations***Saline infusion hysterosonography***

In cases where you are not sure if a fibroid is growing submucosally you can perform saline ultrasound (saline infusion hysterosonography, SIHS) as described in Chapter 1. The distention of the uterine cavity will help you to see if the fibroid is pedunculated and entirely growing in the cavity or if parts of it are growing in the uterine wall. If more than 50% of the fibroid is growing in the uterine wall it must be accessed abdominally. So you have to document your assessment during ultrasound.

Hysterosalpingography

Your radiographer might be able to perform a hysterosalpingography (HSG) or you can do it yourself. If you find intramural fibroids close to the right or left fundal area or a big submucosal fibroid distorting the cavity during ultrasound they might be blocking the tubes. With HSG as described in Chapter 18 on subfertility you can assess tubal patency.

Hysteroscopy

Hysteroscopy (HSC) is a very useful investigation but as it needs high-tech equipment it is not gener-

ally available in resource-poor settings. However some clinics in India have already developed ways of doing outreach clinics with hysteroscopic equipment. HSC is very useful for assessing the amount of distortion of the uterine cavity by intramural or submucosal fibroids by introducing a scope with a camera into the uterus. At the same time you can see if the internal os of the tubes is blocked and how the endometrial lining looks. The advantage of HSC is that with advanced scopes you can even remove submucosal fibroids with less than 50% of their mass in the uterine wall vaginally.

Intravenous pyelography

If you found a dilated kidney or ureter on ultrasound you might want to know how far down to the bladder the dilatation of the ureter reaches in order to better plan your operation. If available in your facility, intravenous pyelography can help to evaluate this.

DECISION-MAKING ON THERAPEUTIC APPROACH

We will now consider different possible treatment options with 'pros and cons'. There are basically three treatment options:

- Expectant management
- Medical treatment
- Surgical treatment.

Here are some questions you should think about that will help you to offer the patient a good choice:

- Does the patient still desire fertility? (Age, parity, history of infertility or miscarriage).
- Is the patient near menopause or very young?
- Does the patient desire to preserve the uterus?
- How severe are the symptoms? (Anemia, time off work, subfertility).
- What are the characteristics of the fibroids? (Single/multiple, size, number, site).
- What is the likelihood of malignancy? (Growth after menopause, invasive growth at ultrasound, fast growing 'fibroid').
- Are there any associated medical conditions that might make surgery difficult?
- Is there a higher level health facility available where they are experienced in hysterectomies or myomectomy?

TREATMENT

In this section you will learn about the different treatment options available and how to decide which approach to take. Under surgical treatment, major operation techniques will be explained as well after a short introduction to pelvic anatomy.

With the broad range of symptoms and the fairly numerous treatment options available, it is clear that the approach to treatment should be individualized and be fitted to the patient's perceptions and needs. Especially in Africa, women's burden of disease is probably high but on the other hand many medical treatment options are not (yet) available. But still there are options.

As there have been a lot of new developments in medical treatment options recently it is very important to keep updated concerning the newest study results and also concerning different treatment options becoming available in your country.

In the past, many dedicated and skilled surgeons in low-resource settings tried to preserve the uterus of young women by doing myomectomy as well but many women who might have profited from myomectomy have ended up with a hysterectomy even at a young age because her clinicians didn't know better. Many women, however, could only be treated by hysterectomy as their fibroids were too numerous or too big. Abdominal hysterectomy is likely to be the most frequently needed gynecological operation in resource-limited settings, so it is good to learn how to do it.

Please don't forget though that a hysterectomy is a major debilitating operation and that a uterus is not an appendix but a central organ for female identity and identification. In one study, 64% of women offered medical treatment with a hormone-coated levonorgestrel intrauterine device (LNG-IUD), who were scheduled for hysterectomy, had decided against the operation after 6 months compared to 14% in the control group⁸. In another study done in the USA, 43% of patients asked after hysterectomy expressed regrets about having the operation⁹.

However, after careful patient selection hysterectomy yields satisfaction rates of over 90% as the definite cure for uterine fibroids because the source of their development is removed. The recurrence of fibroids after myomectomy is estimated to be 20.3–22.9%⁹. You can see how important it is to discuss the patient's needs and all available options with her, even if this means referral to another fac-

ility with higher direct and indirect costs associated. The patient and her family will have to decide if they are willing to take the expense for the desired treatment approach. In the decision-making section below we will give you some hints on how to find the best approach for each patient.

Pregnancy-related complications

During pregnancy the uterine tissue is softer and more prone to hemorrhage than outside pregnancy. You should not perform a myomectomy during pregnancy or during a cesarean section as severe hemorrhage is likely to occur and many fibroids regress after delivery anyway. Most complications of fibroids in pregnancy can be treated conservatively.

Complications of fibroids during pregnancy and delivery include:

- Necrosis.
- Torsion of a pedunculated subserous fibroid.
- Mechanical problems impacting the uterus in the pouch of Douglas early in pregnancy or leading to obstructed labor.
- Spontaneous abortion.
- Premature labor and delivery.
- Abruption of placenta.
- Post-partum hemorrhage.

A patient with a necrotic fibroid will usually present with abdominal pain localized on the uterus. There might be slight signs of peritonism but usually no acute abdomen. WBC can be elevated and there can be a slight fever. Through abdominal ultrasound you will be able to locate the pain above a fibroid, often with centrally reduced echogenicity. The therapy consists of bed rest and pain killers (preferably ibuprofen and diclofenac up to 32 weeks of pregnancy, then paracetamol). Important differential diagnoses are abruption of the placenta, acute appendicitis and torsion of an ovarian cyst or tumor and, although very rare torsion of a pedunculated fibroid. Here ultrasound can differentiate between the causes of abdominal pain in pregnancy, and also the clinical picture which is often more acute. Torsion of a pedunculated fibroid is actually the only indication for laparotomy for pregnancy-related fibroid complications. Still you should try to avoid myomectomy during laparotomy. Untwist the fibroid and wait to see if it becomes reddish again. If it is not too big, you can close the abdomen after untwisting the fibroid and observe the patient

closely postoperatively, as circulation will either re-establish itself or not, with the consequence of necrosis which you can try to treat conservatively as above. If the patient still deteriorates you will have to perform a myomectomy or refer the patient. Note that you can't use a mechanical tourniquet or medical hemostatic agents (see below) as your patient is pregnant. Ligate the pedicle of the fibroid with two tight Vicryl-0 sutures and cut it.

Sometimes, because of the fibroids, a pregnant uterus can become impacted in the pelvis. Many patients with an impacted uterus will have urine retention. An impacted retroflected uterus can be pushed out of the pouch of Douglas, vaginally, under a light anesthesia in early pregnancy. If you need to do a cesarean section for obstructed labor, do not attempt to remove the fibroids. If a low cervical fibroid is detected in pregnancy you might consider elective cesarean section or at least a trial of labor in a facility where surgery can be done as there is a risk for obstructed labor in these patients.

Expectant management

At present all experts agree that all women with asymptomatic fibroids should only be monitored (level of evidence 5). However, nobody has ever designed a study to determine if this approach yields a better outcome for most patients with fibroids.

It is important to explain to the patient what she has and the harmlessness of this condition. She should know, however, that uterine fibroids need a regular follow-up by ultrasound to monitor growth in order to remove them in due time when they grow, before they are so big or numerous that only hysterectomy is an option. Intervals between ultrasound scans should be 6 months up to 1 year.

It is important to document your findings, as was explained in the section on investigation, to make them available for comparison with future scans, otherwise your examination will be useless – after 6 months you won't remember. The same accounts for when the patient has lost her records, and she should know this too. Postmenopausal women who present with fibroids for the first time should be examined again after a short period, e.g. 6-weekly intervals, several times in order to establish whether there is really postmenopausal growth.

Fast growing 'fibroids' could be sarcomas of the uterus. When you suspect a sarcoma, the patient needs a hysterectomy (see Chapter 29).

Medical treatment

From what you've learnt by now about fibroids it becomes clear that there could be some form of hormonal treatment to treat symptoms or even decrease fibroid size, as they react to female reproductive hormones. Your patients on medical treatment need to know that you are only treating symptoms and that when the treatment is stopped, these will re-occur.

The hormonal treatment available at present helps to stop or at least decrease menorrhagia. Progestins show several effects in reducing menorrhagia:

- They cause anovulation in the majority of cycles.
- The endometrium becomes flat and inactive, thus reducing the amount of tissue going off during a period.

Depot-progestins (drugs derived from the female reproductive hormone progesterone) such as Depot Provera® (injectables), Implanon® or Norplant® (implants) and Mirena® (LNG-IUD) induce amenorrhea in the majority of women. Studies show a significant decrease of menorrhagia and an increase in hemoglobin levels, especially with the LNG-IUD. Several studies showed for the latter a decrease in size of fibroids and uterine volume. Other studies could not confirm this⁸. It is important to know that this IUD is a special IUD, as it is coated with hormones. Normal IUDs won't do the job. LNG-IUDs are becoming increasingly available in resource-poor countries but you will probably have to look into private pharmacies to find them. They are a bit expensive as well but they last for 5 years, decrease fibroid-associated dysmenorrhea and are a good contraceptive as well. A randomized trial showed equal satisfaction in women using the LNG-IUG for fibroid-associated menorrhagia and for women who had a hysterectomy done 5 years after intervention, but LNG-IUD is a lot cheaper with less serious adverse effects than hysterectomy (level of evidence 1)⁸.

Women with submucosal fibroids, however, have a higher failure rate and the rate of expulsion in women with uterine fibroids is higher compared to women using it for other reasons.

Even those women who still bleed with depot-progestins report a significant decrease in blood loss. The most frequent adverse effect of progestins, however, is intermittent bleeding, which usually stops after 3–4 months, but you must tell your

patient in advance otherwise she will become non-compliant and stop your treatment.

Normal contraceptive pills (COC) and the progesterone-only pill can reduce menorrhagia as well if you tell the patients to use them continuously without a 7-day break for several strips in a row. This will reduce the number of periods and thus menorrhagia. If in your setting, only COC are available which contain iron tablets in the last blister row, tell the patient to start a new packet every time they come to the iron-containing pills. Otherwise they will menstruate. It is likely that the patients will experience a slight bleeding after a couple of months. Tell them to have a 7-day break once they start bleeding and then continue as before.

For more options to treat menorrhagia, such as tranexamic acid or non-steroidal anti-inflammatory drugs, see Chapter 20 on the treatment of abnormal bleeding.

The best candidates for medical treatment are women who are near the menopause or those with underlying medical conditions that forbid operations. Those near menopause might have gone into menopause after 5 years of LNG-IUD or Implanon and won't need any further treatment by then.

However, all women with fibroid-associated menorrhagia who don't suffer from infertility or recurrent miscarriage (as these groups would profit from surgery) should be offered this treatment as a first-line therapy before operation.

Surgical treatment

Indications for surgical treatment are the following:

- Menorrhagia unresponsive to medical treatment with or without anemia.
- Suspected malignancy.
- Infertility of otherwise unexplained origin or recurrent miscarriage.
- Fibroid growth after menopause.
- Other symptoms interfering significantly with daily activities.

Always assess the patient as described above to determine the type of operation and access and be sure you are able to perform the operation in your facility, refer if otherwise. It is important to thoroughly examine women with recurrent pregnancy loss to determine whether the fibroids are really a likely cause of her problem before you decide on an operation. Adverse effects of your

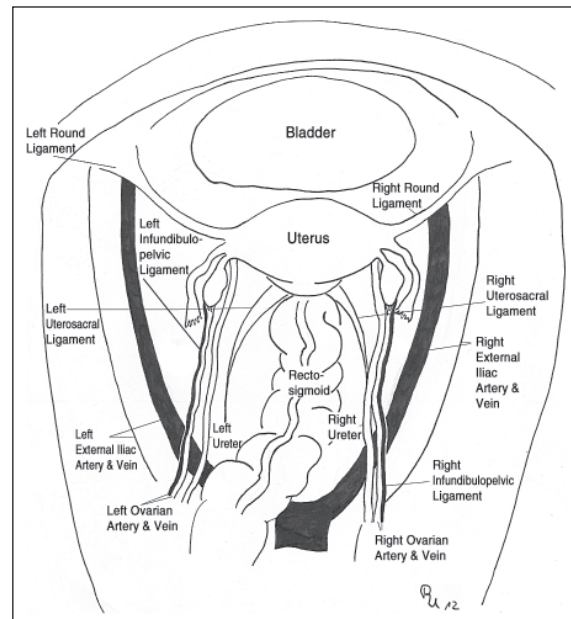


Figure 3 Pelvic anatomy for abdominal hysterectomy and myomectomy

operation might be infection leading to sterility due to tubal blockage or adhesions in a formerly fertile patient. Make sure before you do surgery that the woman does not have cervical cancer, because the surgery can become disastrous if she has!

Pelvic anatomy for abdominal hysterectomy and myomectomy (Figure 3)

Important surrounding structures which are prone to injury and thus have to be identified are:

- Urinary bladder anteriorly.
- Rectum sigmoid posteriorly.
- Ureters and great vessels (external and internal arteries and veins) laterally.

Supporting structures of the uterus are the following. They have to be identified cut and ligated during hysterectomy:

- Blood vessels with peritoneal and connective tissue: uterine veins and arteries, infundibulopelvic ligaments with ovarian arteries, utero-ovarian ligaments with ovarian branch of the uterine arteries.
- Muscular support: round ligaments.
- Connective tissue with vascular and neural tissue: cardinal ligament, uterosacral ligaments.

- Fat and peritoneum: broad ligament, utero-vesical fold, uterorectal fold.

Myomectomy

Definition

Myomectomy means the excision of fibroids from the myometrium without removing the uterus. This can be done by an abdominal incision usually using a subumbilical horizontal incision as for cesarean section called a Pfannenstiel-incision or via mini-laparotomy. Both techniques will be described later. Depending on the site, number and size of the fibroids, a vertical incision might be necessary, as it offers better access to the pelvis, e.g. in very obese patients, but most of the time a horizontal incision is sufficient. If you feel, however, that a vertical incision is necessary due to size and number of fibroids you should consider again whether you have the skills to do the operation as these myomectomies need advanced experience and skills.

Fibroids easily accessible to abdominal myomectomy are subserosal and intramural fibroids. Submucosal fibroids should have a significant intramural part, as otherwise they can't be located abdominally during the operation. Pedunculated submucosal fibroids are sometimes 'born' through the cervical os and can be removed vaginally. The technique is described below.

Indications for myomectomy for symptomatic fibroids (see indications for surgery above) are:

- Desire to preserve fertility.
- Desire to preserve the uterus in symptomatic fibroids.
- History of pregnancy-related complications of fibroids and wishing to conceive again.
- Otherwise unexplained infertility (see Chapter 18 on how to investigate infertility) or recurrent miscarriage (see Chapter 14).

It is very important to consider that for patients with infertility, recurrent miscarriage and desire for future pregnancies, a lot is at risk when undertaking the operation, since you are never sure if you can avoid a hysterectomy beforehand.

Adverse events

Although the uterus is preserved, myomectomy is a major abdominal operation and has as such adverse

effects related to intra- and postoperative complications. The most important ones are listed below:

- Intraoperative blood loss with the need of blood transfusion.
- Postoperative anemia.
- Bladder, bowel or ureter injury.
- Postoperative infection with consecutive tubal blockage.
- Thromboembolism.
- Postoperative adhesions.
- Hysterectomy.
- Uterine rupture in consecutive pregnancies. Although this seems to be a rare event with a low incidence of around 0.9%⁷, it is a calamity and women who desire further pregnancies undergoing myomectomy have to know this. The risk depends on:
 - number, site and size of fibroids
 - surgical technique
 - perioperative infection
 - intraoperative opening of the uterine cavity
 - the capability of healing of the patient's tissue
 - time elapsed since operation.
- Recurrence of fibroids estimated at approx. 20.3–22.9%^{10,11}. These figures, however, are for laparoscopic surgery, a method which will be explained later.

Surgical technique seems to outweigh the time elapsed between surgery and pregnancy. There are only a few studies dealing with uterine rupture after myomectomy and their design doesn't allow an evidence-based risk assessment. Current expert opinion is to allow a period between surgery and pregnancy of 4–6 months (level of evidence 4). This is a difficult subject to discuss with a patient who comes for infertility treatment, as they want to become pregnant as soon as possible, but your patient has to understand that a uterine rupture is dangerous for mother and child. Furthermore, all patients in whom the uterine cavity was opened during surgery should deliver by elective primary cesarean section. All other patients becoming pregnant after myomectomy have to deliver in hospital, with theatre facilities available 24 h, under any circumstances. If a woman is not ready for this prior to surgery, myomectomy is not advisable. Please be aware of the fact that the biggest cause of subfertility in low-resource settings is tubal blockage and you should rule this out before surgery in patients who come with fibroids and a history of infertility (see Chapter 16).

Description of surgical technique

It is always wise to examine the patient yourself as a surgeon, before the operation and again while she is already anesthetized. Depending on size, number and position of the fibroids and the uterine mobility you will have to decide whether you can use a transverse or vertical incision of the abdominal wall for your operation. Here it is important to consider the aim of the operation: most patients for myomectomy undergo the operation in order to become pregnant and deliver safely. Thus, you will need the best access to the fibroids and the uterus to avoid opening of the uterine cavity or harm to the intramural part of the fallopian tubes and to minimize postoperative adhesions. Therefore it is sometimes wise to consider a vertical incision especially if you are not an experienced surgeon. If you are more experienced you can choose a horizontal incision like a Pfannenstiel or Joel Cohen incision. If there are few or a single smaller fibroid which is easily accessible (e.g. in a fundal or anterior position) and you are an experienced surgeon you might consider a mini-lap or an ultra mini-lap⁷: a horizontal incision of 2–4 cm length 2–4 cm above the symphysis with incision of subcutaneous fat and abdominal fascia 2–3 cm above the skin incision. A mini-lap is cheaper and needs a shorter hospital stay with good results concerning complications and pregnancy rates compared to conventional laparotomy⁷.

The most important complication in myomectomy is hemorrhage with consequent anemia. Intraoperatively this may impair your access to the former fibroid capsule and hamper uterine reconstruction resulting in a weak scar. Thus, you must take measures to reduce bleeding. A Cochrane meta-analysis was carried out on several studies dealing with the reduction of hemorrhage during myomectomy (level of evidence 1)¹². Although the sample sizes of these studies were small, the Cochrane collaboration's conclusion was that misoprostol, bupivacaine with epinephrine, tranexamic acid or a triple tourniquet have led to a significant reduction in intraoperative blood loss.

Misoprostol is readily available in most resource-poor settings. Give 400 µg vaginally 1 h before the operation starts. In settings where spinal anesthesia is performed, bupivacaine 0.25% and epinephrine will be available as well. Inject 50 ml of bupivacaine together with 0.5 ml epinephrine in the myo-

metrium above the fibroid before performing the uterine incision¹³.

The intraoperative placement of tourniquets is an effective method but you have to be sure of the pelvic anatomy. This method should only be chosen where misoprostol or bupivacaine/epinephrine are not available¹⁴. The technique for applying tourniquets for reduction of hemorrhage in myomectomy is as follows:

- Incise the anterior part of the peritoneum between the bladder and the uterus and reflect the bladder inferiorly.
- Make a small hole in the avascular part of the posterior part of the broad ligament on either side of the uterine isthmus cranial to the uterine arteries.
- Pass a 20-cm length part of sterile infusion set through the holes and tie it tightly anteriorly around the cervix at the level of the internal cervical os.
- Pass a 20-cm length part of sterile infusion set through the holes in the broad ligament and loop it around the infundibulopelvic ligament laterally to the fallopian tubes and the ovary on both sides. Be careful that you do not damage the tubes!
- Pull the plastic tubes tight and secure them with a small forceps to occlude the ovarian vessels. The plastic tubes should be removed at the end of the operation.

The final approach to the fibroids is not dependent on the choice of skin incision or method for hemorrhage reduction. Here is a stepwise approach:

- Increase access to the uterus by either packing the bowel with damp drapes or by putting the patient in slight Trendelenburg position.
- You may try to deliver the uterus out of the abdominal cavity to increase access.
- Inspect the uterus for size and site of the fibroids in order to determine where to best place your uterine incision:
 - Incise where you will be able to 'harvest' the most fibroids with one incision.
 - Posterior incisions might lead to intestinal adhesions.
 - Aim for a low anterior midline incision. We know that for cesarean section scars a low incision will be stronger and less likely to rupture¹⁵ but there is no stronger evidence for this in myomectomy as studies are lacking.

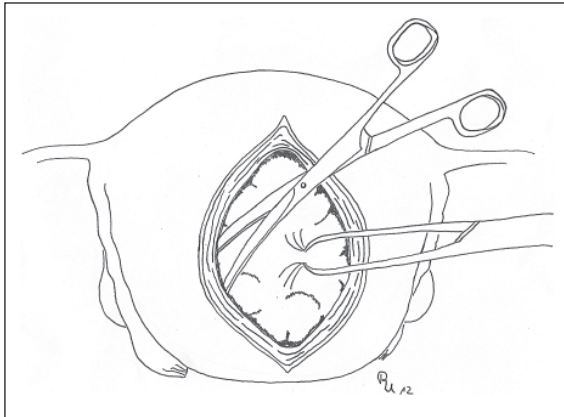


Figure 4 Fibroid dissection from its bed

- If your incision is a low anterior incision, incise the bladder peritoneum and reflect the bladder downwards.
- Incise the uterine serosa and myometrium at the top of the protruding fibroid until you see its particular whitish tissue. You may cut into the fibroid to identify it and make sure you have passed the myometrial layer.
- Grasp the fibroid with a sharp forceps or a vulsellum and apply traction to it.
- Dissect the fibroid carefully bluntly by using your fingers and if necessary sharply with the dissecting scissors or cauterizing forceps (Figure 4).
- Cauterize or ligate the usually stronger fibers and vessels at the bottom of the pseudo-capsule.
- There is no need to trim away excess tissue.
- Uterine reconstruction is important: use several layers of interrupted single Vicryl-0 sutures to close the gap in the myometrium left by the fibroid. There should be as little space left as possible to reduce the possibility of hematoma and further necrosis within the myometrium.
- Close the uterine serosa through running inverted Prolene (if not available: Vicryl-2-0 sutures).

Vaginal myomectomy

Occasionally a submucosal fibroid is 'born' through the cervical os. In this case a vaginal operation can be performed¹⁶:

- Put the patient in lithotomy position and disinfect vulva and vagina with iodine.
- Catheterize the patient and introduce two broad specula into the vagina.

- Grasp the cervix with two toothed forceps at 11 and 1 o'clock and pull it downwards to access the fibroid which should be visible in the external os.
- Grasp the fibroid with a forceps or a tenaculum and put downwards traction on it leaving the two cervical forceps.
- Check digitally if you can access the fibroid's pedicle. If it is visible you can tie it with a 2-0 Vicryl or catgut suture.
- If you cannot visualize the pedicle: simply grasp the fibroid and twist it around its pedicle until it falls off.

Abdominal hysterectomy

Definition

A hysterectomy is the removal of the uterus with or without the ovaries and the tubes. For uterine fibroids this is usually done via an abdominal incision either transverse as the above mentioned Pfannenstiel incision or vertically. If an older lady has been postmenopausal for some years (i.e. she has not had her period for some years) you might consider removing the ovaries but this is not a necessary step of the operation unless you see abnormal growth on their surface during operation. How to remove the ovaries and tubes is described in Chapter 28 on ovarian cancer.

If fibroids are small and the uterus is very mobile and can be pulled downwards easily during anesthesia you might be able to remove the uterus vaginally. The technique is described in Chapter 20 on the treatment of abnormal vaginal bleeding.

Indications for hysterectomy are the above-mentioned indications for surgery in women with a completed family planning history and no desire to preserve the uterus. In the case of high suspicion of malignancy the latter criteria, however, can't be taken into account as the removal of the uterus is life-saving in this situation. When fibroids are too numerous to remove, a hysterectomy can often not be avoided as reconstruction of the uterus will inevitably fail.

Adverse events

- Intraoperative blood loss with the need of blood transfusion.
- Postoperative anemia.
- Bladder, bowel or ureter injury.

- Postoperative infection.
- Thromboembolism.
- Postoperative adhesions.

Description of surgical technique of abdominal hysterectomy

You should always stick to the operation steps described below until you are really experienced in this kind of operation. Like this you will never miss out a step or get lost.

An interesting video clip on how to do an abdominal hysterectomy is available on the internet at: <http://www.medicalvideos.us/videos/239/hysterectomy>.

Examine the patient before the operation to determine your approach, with a vertical or transverse incision. For abdominal hysterectomy this will depend on the size and mobility of the uterus and the location of fibroids as the latter will determine the degree of difficulty you will encounter for your access to the uterine arteries.

An abdominal hysterectomy should be performed by at least two people with the surgeon standing on the left side of the patient. In patients with a big uterus or difficult access you might need a third person to hold additional retractors to improve your view. You can conduct the whole operation using Vicryl or catgut 0, except for suturing the fascia of the rectus muscle in the abdominal wall where you should use Vicryl or catgut 1 or 2. You should always put in a bladder catheter and give the patient a single shot of antibiotics like ampicillin and metronidazole before the operation starts.

After opening of the abdomen and moving the intestines upwards with a wet towel, explore the abdominal cavity. Check the mobility of the uterus by identifying the cervix, putting your fingers around it from abdominally and pushing the uterus upwards out of the true pelvis. In cases where you fail to reach the cervix put a sharp forceps, e.g. a tenaculum, in the uterine fundus (do not do this in cases where you expect malignancies) and pull the uterus upwards and to all sides. Check for adhesions in the Douglas space behind the uterus. If adhesions are present carefully remove them with your fingers or by using scissors if necessary. Insert an abdominal retractor.

Incision and ligation of the round ligaments Put hemostatic clamps on both sides of the uterus on the tubes, the round ligament and the ligamentum

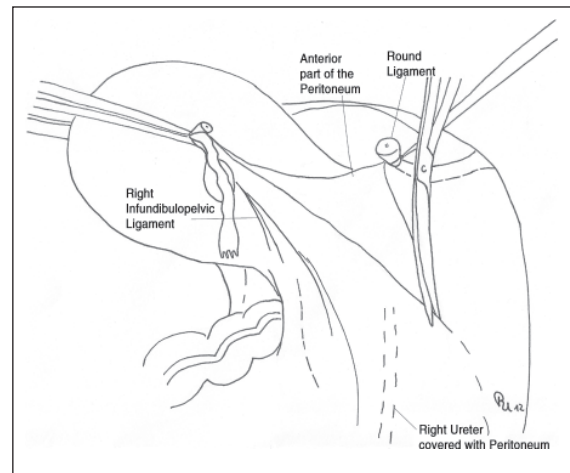


Figure 5 Opening of the posterior peritoneum and identification of the ureters

ovarum proprium. These clamps will stay there the whole operation to facilitate mobilizing the uterus and as hemostatic forceps.

Inspect where the ureter is running by simply touching it with a blunt surgical instrument: it will show peristaltic movements. Identify the round ligaments by asking your assistant to pull the uterus upwards. You will find two folds connecting the uterus to the pelvic brim near the inguinal canal. Put a strong forceps on each around one-third away from the uterus. Cut the ligament on the uterine side and ligate them with a stitch using Vicryl or catgut 0. Leave the suture long after cutting of the needle and secure them with small forceps. These sutures are very helpful as your assistant can intermittently pull them to unfold the peritoneum. Never omit this step as it will provide you with access to the retroperitoneum and will increase mobility of the uterus easily. Now open the anterior part of the peritoneum on each side by asking your assistant to pull on the respective suture. Cut the peritoneum with dissecting scissors along the pelvic rim (Figure 5). This will help you to identify the ureters if you were not able to visualize them before starting the procedure. You can identify the ureters at this stage by putting your thumb in the retroperitoneal space that you just created and your index finger posterior and caudal of the infundibulopelvic ligament. The ureter will snap between your finger and your thumb.

Incision and ligation of the tubes and utero-ovarian ligament or infundibulopelvic ligaments Now put the index finger of your left hand under the uterine side of the

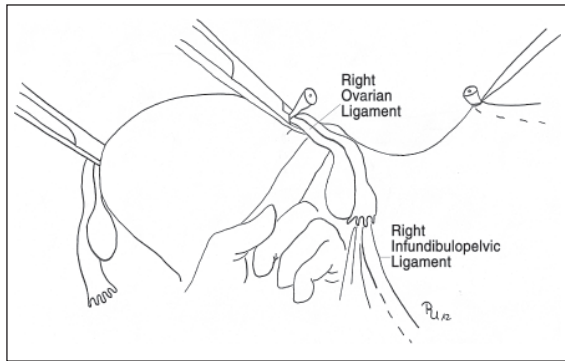


Figure 6 Identification of the infundibulopelvic and ovarian ligament

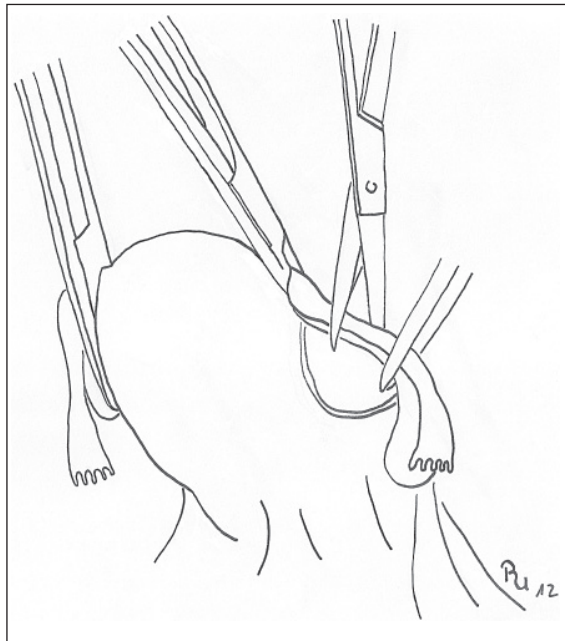


Figure 7 Dissection of the ovarian ligament and the mesosalpinx

round ligament to elevate the ovaries. Like this you can see the infundibulopelvic and the utero-ovarian ligament (Figure 6). If you want to leave the ovaries and fallopian tubes inside, put a strong forceps on the tube and the utero-ovarian ligament and cut them on the uterine side of the forceps. Alternatively you can put a straight forceps on tube and ligament and make a hole with your index fingers in the tissue between the uterus and ovaries where you do not see any vessels, while asking your assistant to pull the forceps gently upwards (Figure 7). Put a strong forceps in the hole and cut in between the

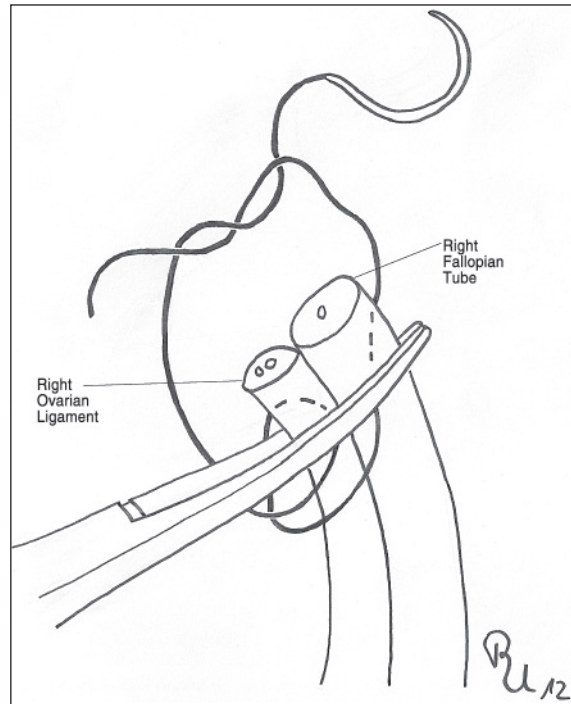


Figure 8 Ligation of the adnexal bundle with a Heaney stitch

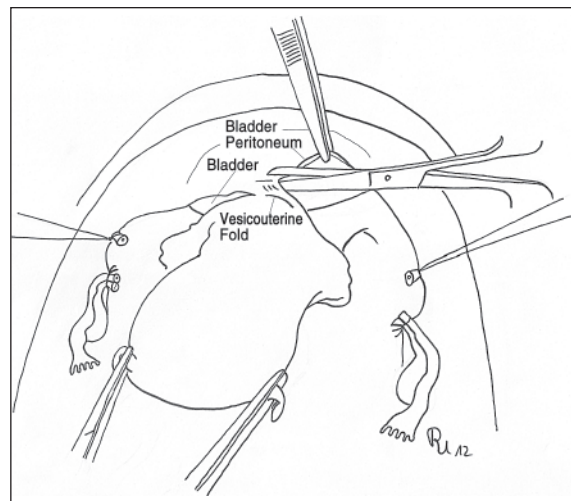


Figure 9 Dissection of the bladder peritoneum

two forceps. Ligate the adnexal bundle under the forceps with a Heaney stitch (Figure 8).

If you need to remove the ovaries, put a clamp on the infundibulopelvic ligaments and simply cut and suture. It is wise to suture the infundibulopelvic ligament twice to prevent bleeding.

Dissection of the bladder peritoneum Now ask your assistant to pull the uterus upwards and the round ligament suture to the side to create tension on the anterior part of the peritoneum. You will see it extends towards the vesico-uterine fold where the bladder is attached to the anterior uterine wall. Incise the anterior part of the peritoneum by gently pushing closed dissecting scissors under it in the direction of the vesico-uterine fold below its reflection onto the uterus separating the peritoneal lining from its underlying tissue and the uterine body. Pull your scissors back, open them and cut the peritoneum where you have just separated it. Do this from both sides in the same way (Figure 9).

Push the bladder gently downwards from the cervix using a sponge on a sponge-holding forceps. Always do this in the midline of the cervix as there are vessels on the sides which will start to bleed once touched with the sponge. Alternatively you can dissect the bladder downwards using scissors. Always be aware not to damage the bladder.

Incision and ligation of the uterine vessels and the broad ligament Ask your assistant to pull the uterus upwards to the opposite side of your area of preparation using the two straight forceps on the adnexal stumps. This will put tension on the respective broad ligament where the ascending branch of the uterine artery and its vein is running. This manoeuvre is very simple but very important. Place two strong forceps with the tips onto the muscular substance of the uterine body/cervix and let them slip down at right angles to the uterus (Figure 10). Cut the broad ligament between the two forceps right down to the tip of the forceps. Ligate it with a Heaney stitch. Do this on both sides of the uterus. This will increase mobility further and reduce bleeding. After you have tied the uterine arteries the uterus will become white.

Incision and ligation of the para-uterine and paracervical tissue Now you will cut the para-uterine and paracervical tissue which are attaching the uterus to the pelvic wall step by step in nearly the same way as you have done for the broad ligament with the important difference that you should place your strong forceps parallel and very close to the uterus (Figure 11). This is because the ureters are running very near to the uterus and your working field now. Make sure at every step that the bladder is deflected down sufficiently. Tie every bit you incised using a Heaney stitch. Once the major

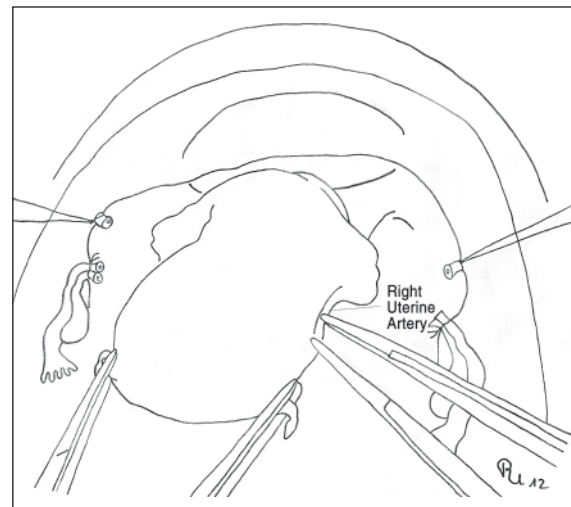


Figure 10 Clamping of the uterine arteries

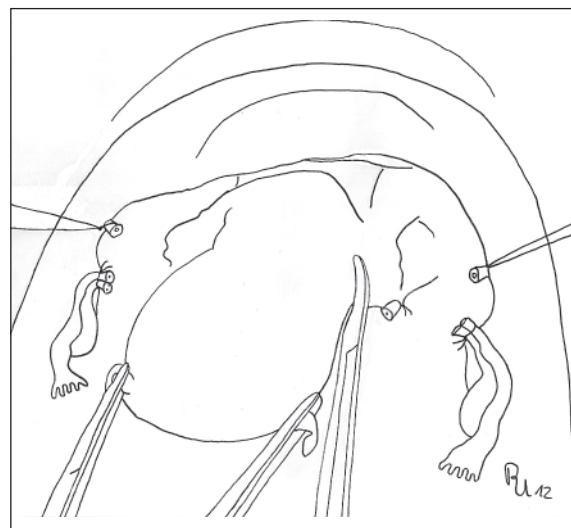


Figure 11 Clamping of the para-uterine tissue

branches of the uterine arteries are ligated on both sides you don't need to place a contra-forceps anymore as there won't be any important bleeding anymore.

Incision and ligation of the uterosacral ligaments This is not a step you will have to do every time you do a hysterectomy. Sometimes the uterosacral ligaments are not easy to identify and they are usually cut with the remaining paracervical tissue and when opening the vagina. So don't worry if you don't have access to the ligaments or can't identify them.

Ask your assistant to pull the uterus upwards and forwards and you will see the uterosacral ligaments on the lower part of the uterine body. Place a strong clamp on each ligament very close to the uterine body as the ureters and the sigmoid are in close proximity. Cut and suture the ligaments leaving the sutures long after cutting the needle.

Opening of the vagina Palpate the cervix between your index finger and your thumb while putting traction on the uterus. You will feel it abdominally well as a hard tumor within the soft vagina. Make sure the bladder is deflected sufficiently. Put curved forceps on the vagina right below the cervix from both sides and let them touch each other in the midline. Cut the vagina and remove the specimen. Inspect if you took the cervix out. It is easier to cut the vaginal tissue around the cervix by using a knife than scissors.

If the uterus is too bulky to reach the cervix you can remove the uterine body after you have safely ligated the branches of the uterine arteries and proceed with the rest of the cardinal ligament or the sacro-uterine ligaments as explained above. To put traction on the cervix you have to grasp it with a tenaculum.

Closing the vagina Simply ligate the tissue under your 'kissing' forceps using a Heaney stitch and if a small hole is present in the midline put a suture there. Make sure the reflected bladder is far enough away from your forceps and that no bowel is included in your stitch. Leave the sutures on the vagina top long and secure them with a small forceps. They mark the lateral margins of the vagina. If the uterosacral ligaments were dissected separately you can tie those sutures with your vaginal sutures.

Now control for bleeding around the vaginal vault, the para-uterine and para-cervical tissues and the infundibulopelvic ligament by putting traction on the vaginal sutures. Cauterize or suture any bleeding vessels and wash the abdominal cavity with warm saline. Visualize both ureters through the peritoneum and see if they move and are not distended. Close the abdominal wall.

Please note, although it might sometimes seem easier, subtotal hysterectomy (the resection of the uterine body only, leaving the cervix in place) is possibly not an option in an environment where regular screening for cervical cancer is not accessible or available. You should then rather consider referring

a patient to a higher level facility; in some resource-limited settings the prevalence of cervical cancer is so high that the likelihood of your patient developing it in her remaining cervical stump outweighs the immediate benefits of being operated in your facility. To perform an operation for cervical cancer after subtotal hysterectomy is very difficult and is associated with a bad prognosis for your patient.

COMMUNITY SENSITIZATION AND PREVENTION

As explained above, at present nobody knows how to prevent the development or growth of fibroids as we don't know how they develop. However, community sensitization should be done to make people aware of this condition, its symptoms and treatment options in order to motivate women to seek help early, to make them profit from the whole range of options that are available to you and to decrease the financial burden on them by not being able to work because of symptoms, and to the health system as well.

If you work in an area where many women suffer from anemia and other problems of fibroids it is good to find out where women go to get advice on their reproductive health problems and include those people in your campaign, such as traditional healers or midwives, women's groups and other civil society organizations. Don't forget that husbands and fathers need to know about reproductive health problems as well as they might get to see symptoms and can serve through their wives as multipliers of information. The same accounts for community or religious leaders, female and male. In addition you should design street campaigns and educate health workers in lower level health facilities about symptoms and therapeutic options of fibroids.

FUTURE OUTLOOK

Currently, a lot of research is done on medical treatment for uterine fibroids. Even if they are not yet available, they will become so in future. Thus it is wise to keep track of new developments. If you have internet access it is good to check on new trial results, e.g. via HINARI, the World Health Organization's (WHO) e-research access, which is free for low-resource countries. You can download free articles from PubMed and the Cochrane library. You should aim for meta-analyses, randomized

controlled trials (RCTs) or systematic reviews as they give the best evidence levels to support your actions.

Other medical and surgical treatment options, already available for industrialized countries may become feasible in your region as well in the future and it is good to know about them even now to incorporate them in your treatment plans as soon as they become available to you. Aromatase inhibitors, for example, are included in breast cancer treatment guidelines of the Breast Health Global Initiative, a non-governmental organization (NGO) for enhanced level facilities in low- and middle-income countries.

The advantage of prolonged waiting is that by the time a drug becomes available in low-resource settings, there is already a lot of evidence through studies in other settings. Below we will explain these treatment options for you to become familiar with them. You can use the names as search terms for your internet query to keep track on their development.

Medical treatment in the future

Treatments change and so do healthcare facilities. In this chapter we describe current developments that may or may not be feasible in your setting in the near future.

Gonadotropin-releasing hormone analogs

Gonadotropin-releasing hormone analogs (GnRHa) are mainly used for *in vitro* fertilization or the treatment of endometriosis and are suitable for the medical treatment of uterine fibroids. They are effective in reducing the size of the fibroids; however, they are too expensive in low-resource settings at the moment.

There are other hormone-based drugs that are currently under investigation for treatment of uterine fibroids:

- Progesterone antagonists (PA)
- Selective prostaglandin receptor modulators (SPRMs)
- Aromatase inhibitors (AI).

Progesterone antagonists

PAs have antiproliferative effects on the endometrium and suppress hormone production via

blockage of late follicle development and mid-cycle luteinizing hormone peak. The only drug currently licensed is mifepristone which is used for medical abortion. A randomized controlled trial on long-term low-dose treatment for fibroids with mifepristone showed significant reduction in uterine size, higher rates of amenorrhea and better quality of life in the mifepristone group compared to placebo¹⁷. A systematic review of mifepristone for fibroid treatment confirmed those findings but found one significant adverse effect, a tendency towards dose-dependent endometrium hyperplasia¹⁸. Other PA are currently under investigation with good safety profiles and phase III trials going on, which means that they have already been tested on humans and will soon be released.

Selective prostaglandin receptor modulators

SPRMs are drugs that change the ability of cellular progesterone receptors to produce genes involved in female reproductive hormone production. Randomized controlled trials on SPRMs showed significant reduction in fibroid size and uterine volume with no serious adverse effects (level of evidence 1)¹⁹. One SPRM called ulipristal acetate, which has been used as an emergency contraceptive for some years now, was recently licensed for preoperative treatment of uterine fibroids in some countries.

Aromatase inhibitors

AIs are currently used in the treatment of hormone receptor-positive breast cancer. The most commonly used drug is called anastrozole. This aromatase is a key enzyme in estrogen production. Anastrozole and other AIs stop aromatase from producing estrogen. Recently, small studies have demonstrated a reduction in fibroid size and associated symptoms under AI therapy^{20,21}.

Surgical treatment in mid- and high-resource settings

Hysteroscopy

Submucosal fibroids and intramural fibroids with more than 50% of their sonographic volume protruding in the uterine cavity can be excised, vaginally, using an operative hysteroscope and a bi- or monopolar power source for excision. As mentioned before this presently needs expensive

high-tech equipment but many low- or less-resourced countries have already introduced hysteroscopic surgery in their fibroid treatment. It is worth inquiring if there are facilities in your reach doing it.

Laparoscopic myomectomy or hysterectomy

The same accounts for laparoscopic surgery which needs even more expensive equipment. But as laparoscopic surgery is an essential part of infertility treatment many high-level services in less- or low-resourced countries are already providing these treatment options such as in India or Mozambique. The advantage of laparoscopic surgery is faster recovery with a shorter hospital stay and fewer complications. In the long run, capital costs for laparoscopic surgery may be recovered and cost-effectiveness can be achieved. But to date this method is not applicable on a regional or district level in low-resource settings due to its vulnerable, expensive material and its dependency on continuous power provision.

REFERENCES

- Duhan N, Sirohiwal D. Uterine myomas revisited. *Eur J Obstet Gynecol Reprod Biol* 2010;152:119–25
- Zaloudek C, Hendrickson MR. Mesenchymal tumors of the uterus. In: Kurman RJ, ed. *Blaustein's Pathology of the Female Genital Tract*, 5th edn. New York, NY: Springer, 2002;561–74
- Laughlin SK, Schroeder JC, Baird DD. New directions in the epidemiology of uterine fibroids. *Semin Reprod Med* 2010;28:204–15
- Ishikiwa H, Reierstad S, Demura M, et al. High aromatase expression in uterine leiomyoma tissues of African-American women. *J Clin Endocrinol Metab* 2009;94:1752–6
- Okezie O, Ezegwui HU. Management of uterine fibroids in Enugu, Nigeria. *J Obstet Gyn* 2006;26:363–5
- Terry KL, De Vivo I, Hankinson SE, Missmer SA. Reproductive characteristics and risk of uterine leiomyomata. *Fertil Steril* 2010;94:2703–7
- Wen KC, Sung PL, Lee WL, et al. Myomectomy for uterine myomas through ultramini-laparotomy. *J Obstet Gynaecol Res* 2011;37:383–92
- Rodriguez MI, Warden M, Darney PD. Intrauterine progestins, progesterone antagonists, and receptor modulators: a review of gynecologic applications. *Am J Obst Gyn* 2010;202:420–8
- Levy BS. Modern management of uterine fibroids. *Acta Obstet Gynecol* 2008;87:812–23
- Seracchioli R, Rossi S, Govoni F, et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. *Hum Reprod* 2000;15:2663–8 (cited in ref. 9)
- Doridot V, Dubuisson JB, Chapron C, et al. Recurrence of leiomyomata after laparoscopic myomectomy. *J Am Assoc Gynecol Laparosc* 2001;8:495–500 (cited in ref. 9)
- Kongnyuy EJ, Wiysonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids (review). *Cochrane Database Syst Rev* 2011;11:CD005355
- Zullo F, Palomba S, Corea D, et al. Bupivacaine plus epinephrine for laparoscopic myomectomy: a randomized placebo-controlled trial. *Obstet Gynecol* 2004;104:243–9
- Taylor A, Sharma M, Tsirkas P, et al. Reducing blood loss at open myomectomy using triple tourniquets: a randomised controlled trial. *BJOG* 2005;112:340–5
- Monaghan JM, Lopes T, Naik R. Myomectomy and the management of fibroids in pregnancy. In: Monaghan JM, Lopes T, Naik R. *Bonney's Gynaecological Surgery*, 10th edn. Oxford: Blackwell Publishing, 2004;87–94
- Baggish MS. Abdominal hysterectomy. In: Baggish MS, Karra MM, eds. *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 3rd edn. St Louis, MO: Elsevier Saunders, 2011;215–41
- Fiscella K, Eisinger SH, Meldrum S, et al. Effect of mifepristone for symptomatic leiomyomata on quality of life and uterine size: a randomized controlled trial. *Obstet Gynecol* 2006;108:1381–7 (cited in ref. 8)
- Steinauer J, Pritts EA, Jackson R, Jacoby AF. Systematic review of mifepristone for the treatment of uterine leiomyomata. *Obstet Gynecol* 2004;103:1331–6 (cited in ref. 8)
- Chwalisz K, Perez MC, Demanno D, et al. Selective progesterone receptor modulator development and use in the treatment of leiomyomata and endometriosis. *Endocr Rev* 2005;26:423–38 (cited in ref. 8)
- Hilario SG, Bozzini N, Borsari R, Baracat EC. Action of aromatase inhibitor for treatment of uterine leiomyoma in perimenopausal patients. *Fertil Steril* 2009;91:240–3 (cited in ref. 4)
- Varelas FK, Papanicolaou AN, Vavatsi-Christaki N, et al. The effect of anastrozole on symptomatic uterine leiomyomata. *Obstet Gynecol* 2007;110:643–9 (cited in ref. 4)