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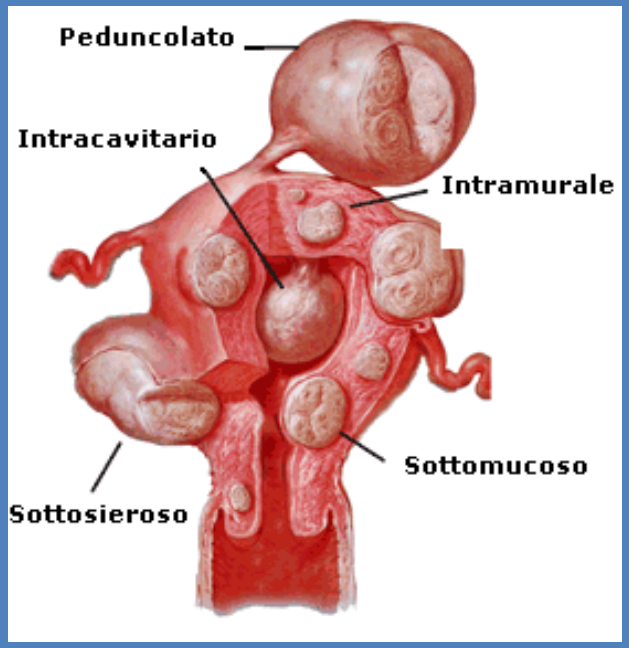
Fibromatosi uterina: Definizione

Il fibromioma o fibroma o mioma uterino è **il più comune tumore benigno dell'utero** ed è caratterizzato da tessuto muscolare uterino circondato da una pseudocapsula di tessuto connettivo lasso.



EPIDEMIOLOGI

- Razza caucasica: 20-35%
- Razza afro-americana: 50%

Manifestazione: 35-50 anni,
mai prima della pubertà

Key risk factors associated with leiomyomas

Race and ethnic groups

Hypertension

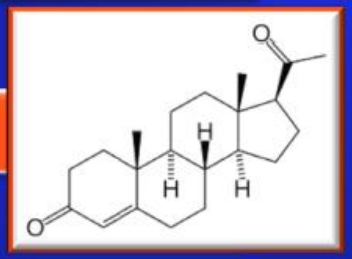
Genetic predisposition

Age

Infections

Tobacco, alcohol and caffeine

Hormones



BMI ≥ 30

Nulliparity

Diet

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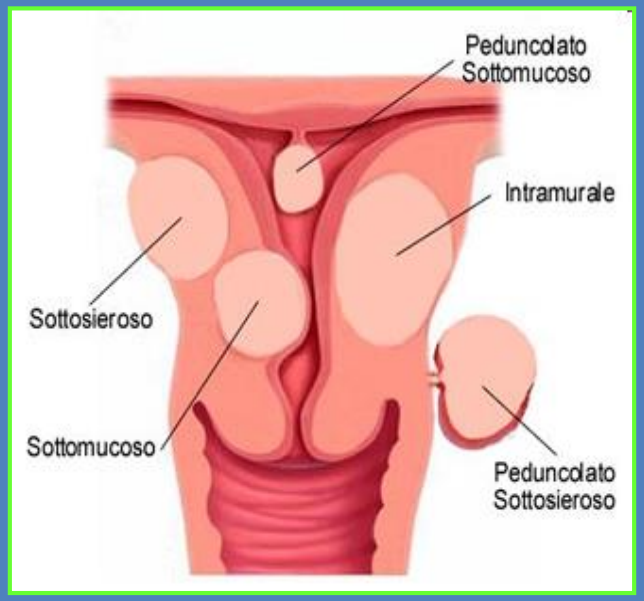
Classificazione dei fibromi uterini

SEDE UTERINA INTERESSATA

- Corpo 90% (parete anteriore e/o posteriore)
- Istmo
- Collo
- Legamento largo



STRATO UTERINO INTERESSATO

- Sottosieroso
- Intralegamentario
- Intramurale
- Sottomucoso

70%

20%

10%

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Sintomatologia

- Sanguinamento uterino anomalo — 40%
- Anemia
- Dolore e senso di peso pelvico
- Dismenorrea
- Dispareunia
- Sterilità o infertilità
- Patologia ostetrica

- Asintomatico — 20%

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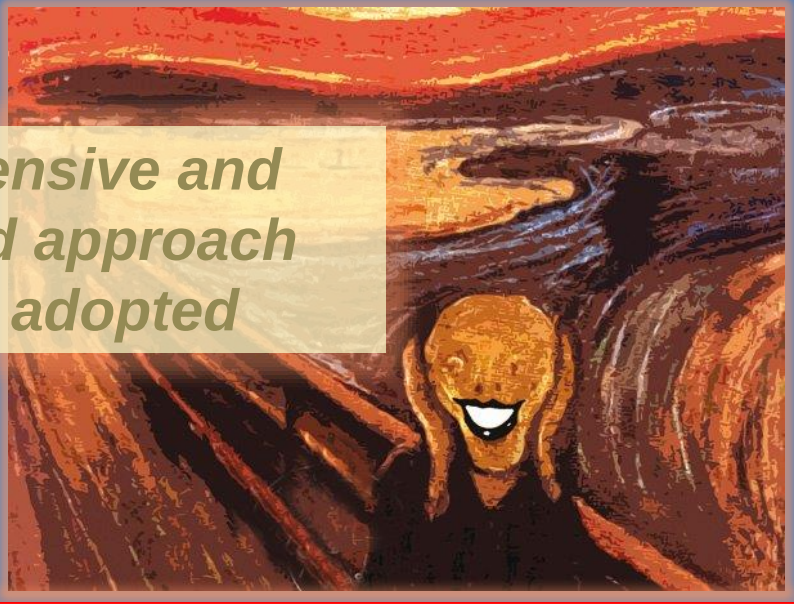
A comprehensive and personalized approach should be adopted



The most important variables to be considered are:

- ✓ age
- ✓symptoms
- ✓fibroids localization
- ✓infertility

Somigliana E et al, Curr Opin Obstet Gynecol. 2008

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Approccio terapeutico

Surgery

Non surgical alternatives

Medical treatment

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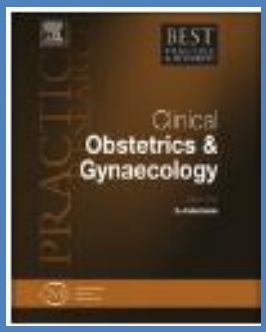
Nonsurgical Alternatives for Uterine Fibroids

Errico Zupi [b,*], Gabriele Centini [a], Lorenzo Sabbioni [a], Lucia Lazzeri [a], István Máté Argay [c], Felice Petraglia [a]



2015

Uterine artery embolization

Magnetic Resonance Guided Focused Ultrasound

Cryomyolysis

Vaginal occlusion of uterine arteries

Laparoscopic occlusion of uterine arteries

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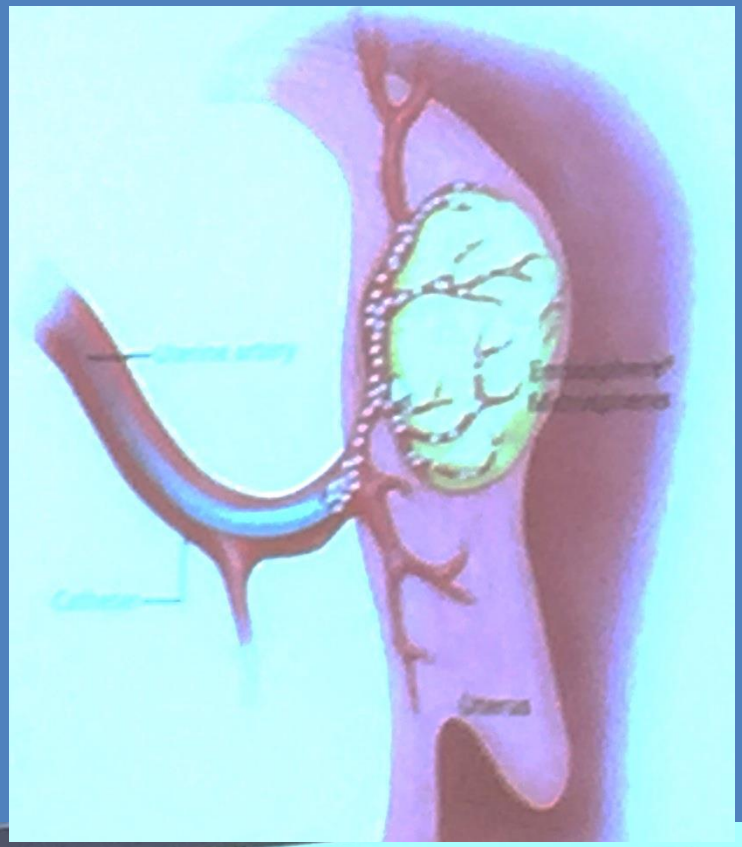
Uterine artery embolization

FIBROID (Fibroid Registry for Outcomes Data) registry based on a 3-year study of 2112 patients who underwent uterine artery embolization for symptomatic leiomyomas

- ***improvement in quality of life***
- ***need for hysterectomy in 9.79%***
- ***need for myomectomy in 2,82%***
- ***need for repeated UAE in 1,83%***

- ***Persistent ischemic pain,***
- ***postembolization fever***
- ***severe postembolization syndrome***
- ***Pyometra***
- ***sepsis***

Goodwin SC et al. Obstet Gynecol. 2008



- **UAE leads to a decrease in fibroid volume**
  - Impact due to cell damage and death as demonstr by DWI
  - Pre –treatment perfusion determines outcome
- **UAE leads to a decrease in menstrual blood loss**
  - Mechanism still unclear.
  - Possible modification of endometrial function

The goal of the technique is the occlusion or marked reduction in blood flow to the fibroids causing selective ischemic necrosis acting at arteriolar level minimizing the uterine damage

UAE is usually performed by an interventional radiologist where the arterial access is obtained at the level of the femoral artery. The access can be ether mono- or bilateral; the monolateral approach reduces complications due to arterial puncture but exposes the patient to a fluoroscope for a longer duration

A 4-5F catheter or microcatheter is inserted into the uterine artery, and then the embolic agent is released.

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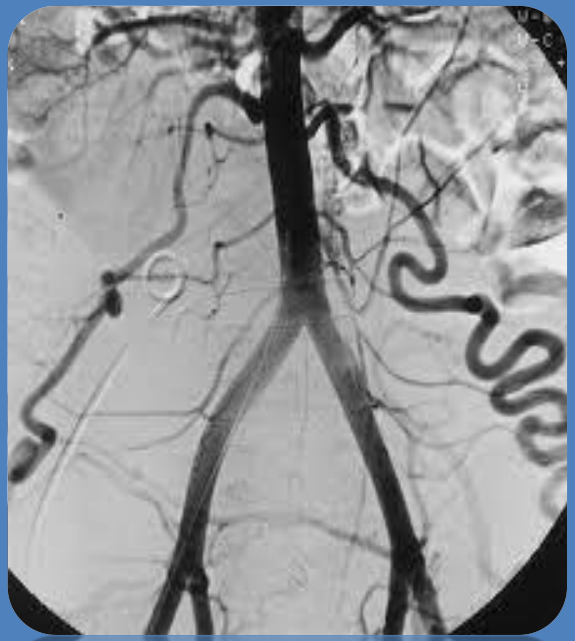
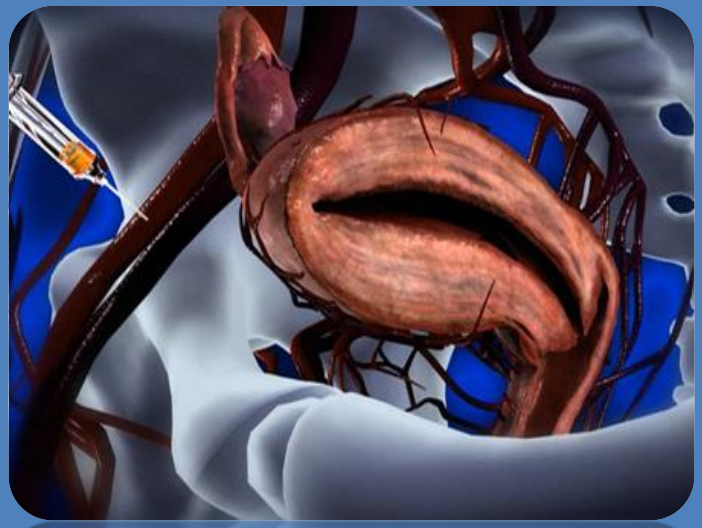
Uterine artery embolization

Contraindications: costs, pain and desire of pregnancy





patient selection and counselling are fundamental to the much higher risk of requiring further surgical intervention

Gupta et al. Cochrane Database Syst Rev. 2014

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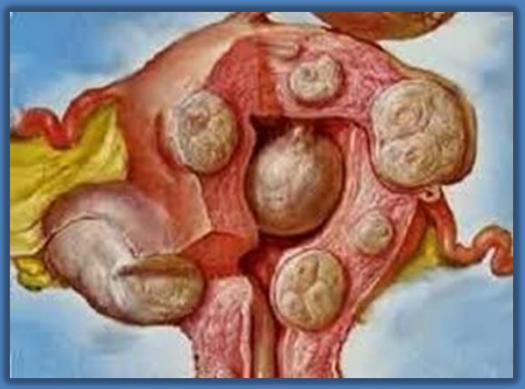
Magnetic Resonance Guided Focused Ultrasound

non-invasive procedure which uses high doses of focused ultrasound waves to destroy uterine fibroids, without affecting any of the other tissues around the fibroid



- ✓ not require general anesthesia
- ✓ outpatient procedure or day hospital

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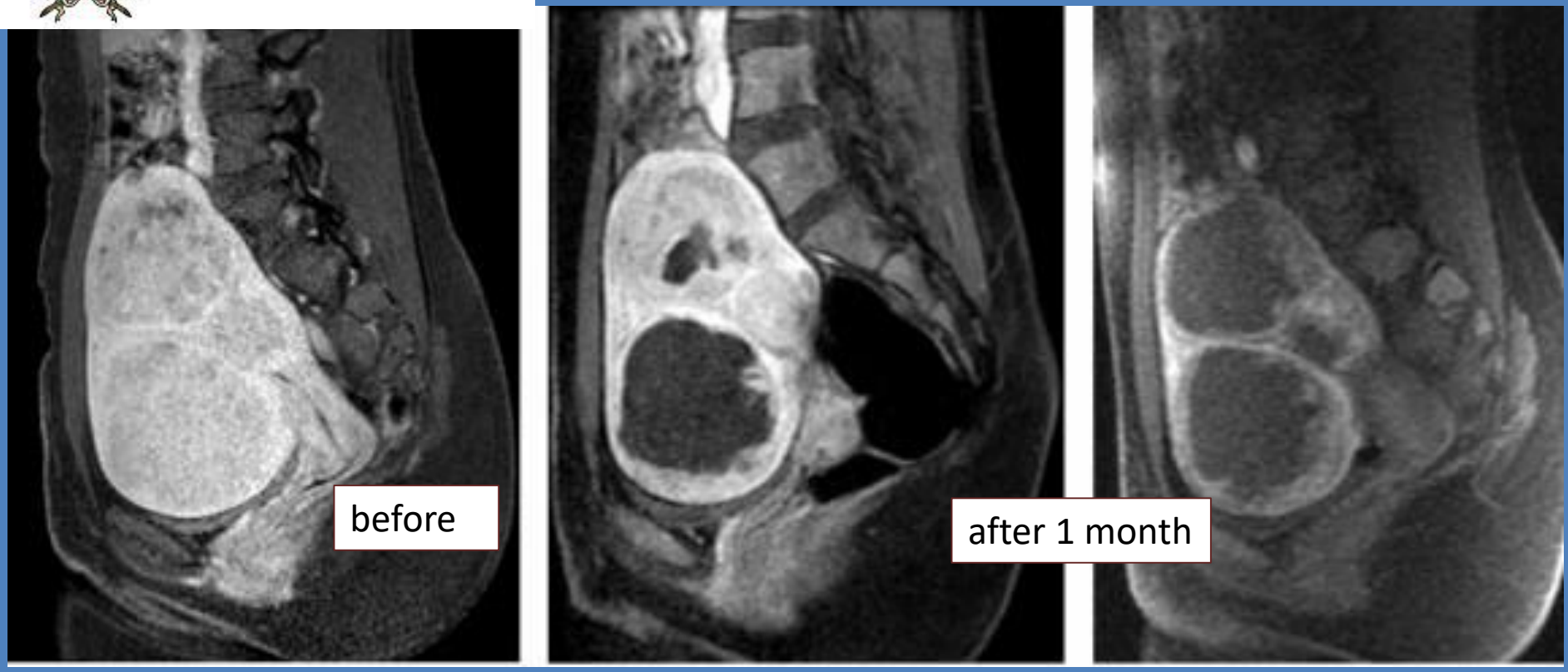
Magnetic Resonance Guided Focused Ultrasound



- **fibroid volume reduction**
- **symptoms improvement**
- **restricted selective criteria**
- **costs**

Rueff et al 2013

Ultrasound-assisted laparoscopic cryomyolysis: two- and three-dimensional findings before, during and after treatment

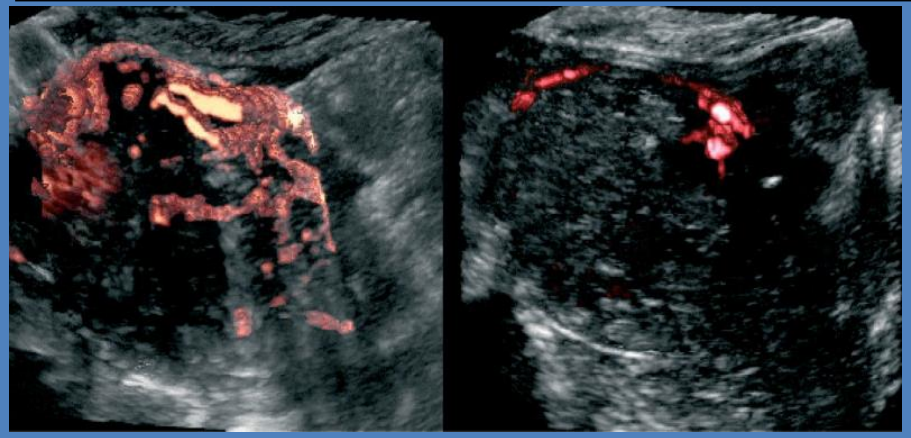
C. EXACOUSTOS, E. ZUPI, D. MARCONI, M. E. ROMANINI, B. SZABOLCS, A. PIREDDA and D. ARDUINI

Obstetrics and Gynecology Department, Università degli Studi di Roma 'Tor Vergata' Italy, Rome, Italy

2005

Cryomyolysis is a conservative surgical option for uterine fibroids, which involves a probe with a cooling agent that is applied directly to the myoma followed by vessel coagulation.

Variable	*Preoperative*	*Postoperative*			P
		1 month	*3 months*	*6 months*	
Maximum diameter (mm, mean ± SD)	62.6 ± 11.4	57.1 ± 12.6	52.1 ± 13.1	47.1 ± 11.7	0.045*
Volume (cm^3, mean ± SD)	97.5 ± 61.3	75.9 ± 47.9	63.8 ± 44.3	49.4 ± 38.1	< 0.001†
Volume reduction (%, mean ± SD)		22.2 ± 15.6	37.5 ± 24.7	52.6 ± 12.4	



cryomyolysis permits treatment of uterine myomata in a relatively short time, without blood loss, with no relevant pain post-surgery, with significant reduction in size of the myoma (more than 50%) within 6 months, and with complete relief of symptoms.

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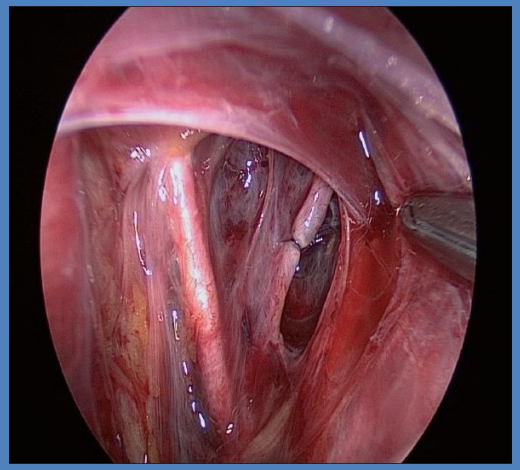
Laparoscopic occlusion of uterine arteries

Surgical and postoperative parameters following LUVO and LM.

	LUVO ($n = 52$)	LM ($n = 43$)	p
Surgical time (min) (95% CI)	36.9 ± 4.9 (35.0–38.7)	86.7 ± 17.0 (79.2–94.2)	0.0001
Blood loss (mL) (95% CI)	24.7 ± 5.8 (22.9–26.5)	143.7 ± 81.7 (102.8–184.7)	0.0001
Complications (95% CI)	1.9% ($n = 1$) (0–5.6)	11.6% ($n = 5$) (2.0–21.2)	0.069
Max fever (°C) (95% CI)	37.4 ± 0.2 (37.3–37.4)	37.7 ± 0.5 (37.5–37.9)	0.0001
VAS (95% CI)	3.1 ± 0.5 (2.9–3.2)	3.6 ± 0.3 (3.5–3.7)	0.0001
Tolerance to food intake (h) (95% CI)	4.7 ± 3.1 (3.7–5.6)	16.6 ± 7.3 (13.9–19.2)	0.0001
Satisfaction rate (95% CI)	100% (52/52)	97.7% (42/43) (93.2–100)	0.323

The effectiveness of both procedures is similar, but the LUVO group experienced less surgical and postoperative suffering



Wang et al 2012

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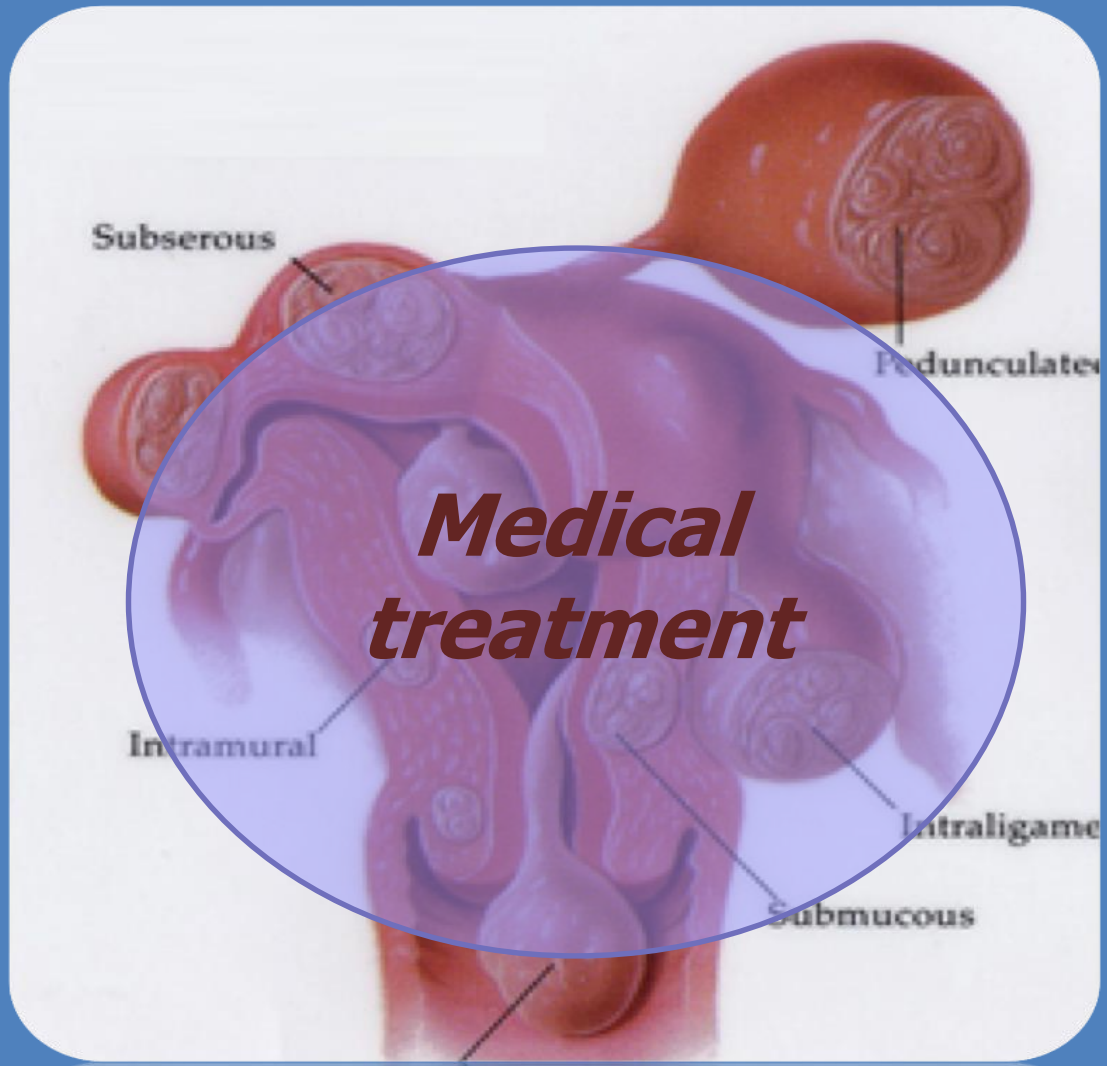
Medical treatments for uterine fibroids



- COCs
- Progestins
- LNG-IUS
- Danazol
- GnRH agonists

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Official guidelines

NHS
National Institute for Health and Clinical Excellence

Pharmaceutical treatments for HMB

should be considered where no structural or histological abnormality is present, or for fibroids less than 3 cm in diameter which are causing no distortion of the uterine cavity

Either hormonal or non-hormonal treatments are acceptable, treatments should be considered in the following order:

- **LNG-IUS provided long-term (at least 12 months)**
- **Tranexamic acid or NSAIDs or COCs**
- **Norethisterone (15 mg) daily from days 5 to 26 of the menstrual cycle, or injected long-acting progestogens**

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Official guidelines

Oral progestogens

- ✓ Given during the luteal phase only, it should not be used for the treatment of HMB

Danazol

- ✓ Should not be routinely used for the treatment of HMB

GnRH agonists

- ✓ Prior to surgery or when all other treatment options for uterine fibroids, including surgery, are contraindicated
- ✓ If this treatment is used for more than 6 months ‘add-back’ therapy is recommended

NICE guidelines 2007

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Official guidelines

Review

Therapeutic management of uterine fibroid tumors: updated French guidelines

Updated from previous College National des Gynecologues et Obstetriciens Francais (CNGOF) guidelines (1999)

No currently validated medical treatment is capable of making fibroid tumors disappear (LE1)

In cases of symptomatic fibroids (pain or bleeding), the only objective of medical treatment is to treat the symptoms associated with them (grade C)

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COCs

Because of unpredictable effects of progestins on leiomyoma growth, it doesn't recommend either progestins or combination COCs for leiomyoma-related symptoms

ASRM Fertil Steril. 2004

The benefit of a COCs on menstrual bleeding patterns is instrumental in encouraging consistent and long-term use

eshre
Science Moving People Moving Science

ESHRE Hum Reprod 2005

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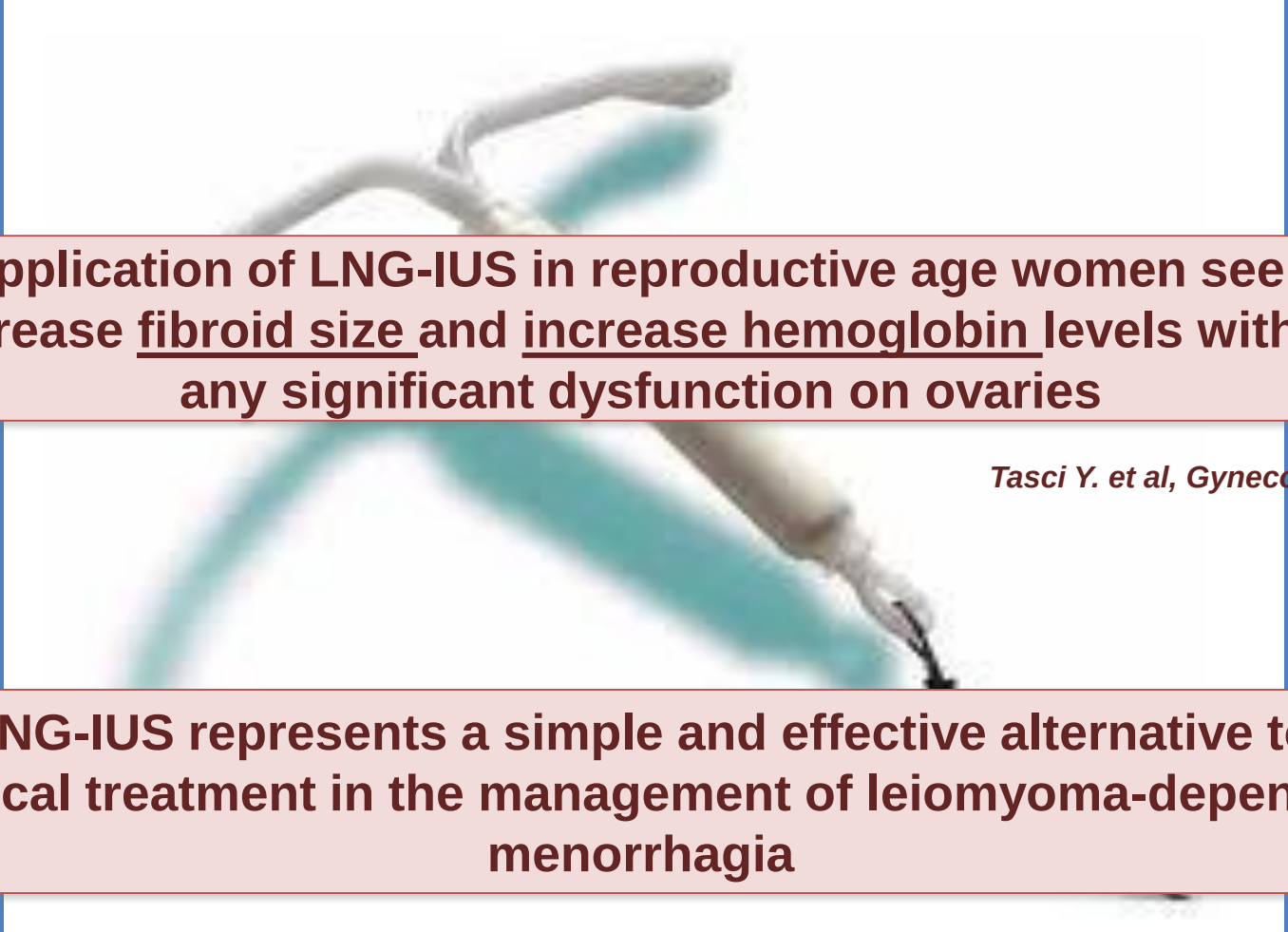
LNG-IUS



The application of LNG-IUS in reproductive age women seems to decrease fibroid size and increase hemoglobin levels without any significant dysfunction on ovaries

Tasci Y. et al, Gynecol Obst 2009

LNG-IUS represents a simple and effective alternative to surgical treatment in the management of leiomyoma-dependent menorrhagia

Murat Naki M. et al Fertil Steril 2009

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Uterine fibroids: Levonorgestrel IUS

LNG-IUS is an effective therapeutic option conservative type also in selected cases of menometrorragie associated with uterine fibromatosis

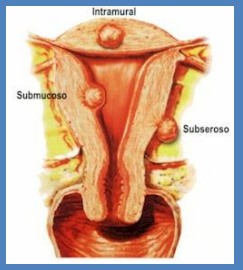


Figura 2. Riduzione della perdita ematica mestruale 3, 6 e 12 mesi dopo l'inserimento di MIRENA® in donne affette da menorragia.[4]

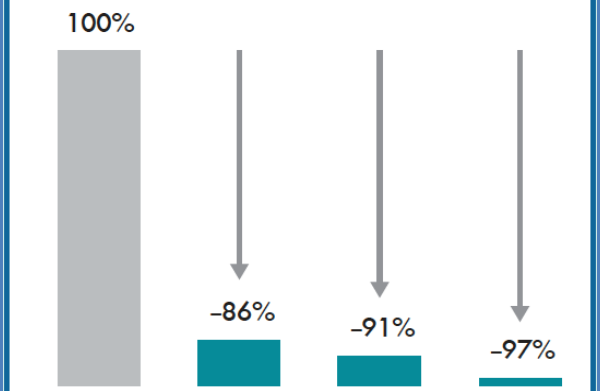
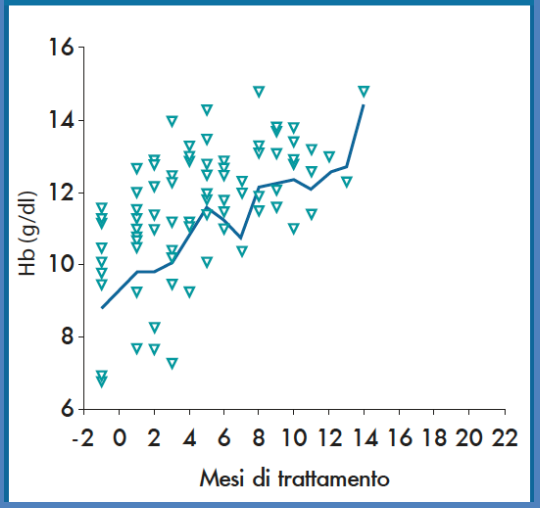


Figura 1. Valori di emoglobina dopo l'inserimento di MIRENA®. La linea continua rappresenta i valori mediani.[6]



Rosa e Silva JC et al. J Reprod Med 200

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Mechanisms of action SPRMs on HMB

antiproliferative

proapoptotic

antifibrotic

reduction uterine artery blood flow

reduction of bleeding

reduction of volume

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Mechanisms of action SPRMs on HMB

The apparent importance of progesterone for the growth and development of uterine leiomyoma suggests that SPRMs may be a promising treatment for leiomyomas

The greatest challenge is to identify a SPRMs compound with exquisite progesterone receptor selectivity to:

- act as a progestin in the endometrium
- act as an anti-progestin within the leiomyoma

Ohara N. et al, Clin Exp Obstet Gynecol 2005
Spitz IM, Curr Opin Obstet Gynecol. 2009

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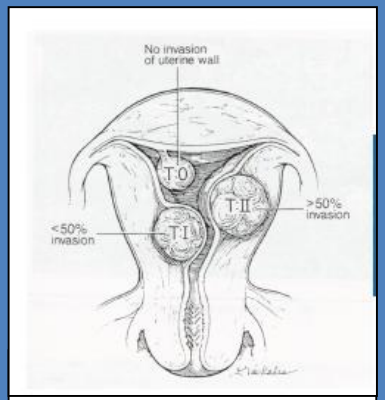
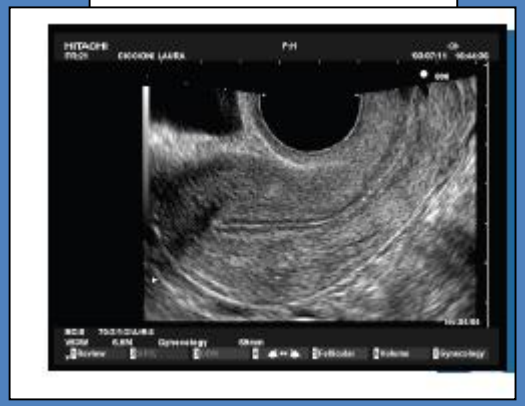
Ulipristal acetato: meccanismo d'azione





Effetto diretto sui fibromi, riducendone le dimensioni

Effetto sull'ipofisi, inducendo amenorrea

Effetto diretto sull'endometrio, bloccando il sanguinamento uterino

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When is necessary the surgical treatment ?

ACOG The American College of Obstetricians and Gynecologists
Women's Health Care Physicians

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE 19 44

- Abnormal uterine bleeding not responsive to conservative treatments
- High level of suspicion of malignancy
- Growth after menopause
- Pain or pressure that interfere with quality of life
- Urinary tract frequency or obstruction, or iron deficiency anemia related to abnormal uterine bleeding
- Infertile patients with leiomyomata of sufficient size or specific location to be a probable factor, and/or in absence of other explanation
- At the time of diagnostic laparoscopy in infertile patients for the concern of increase in size, complications in pregnancy and as adjuvant for subsequent IVF

ASRM Practice Committee, 2001
ACOG Practice Bulletin, Obstet Gynecol 2004

Why should we perform myomectomy by laparoscopy?

- ✓ lower postoperative pain
- ✓ shorter hospital stay (Ribeiro '99: 9 hours!!)
- ✓ faster postoperative recovery
- ✓ lower morbidity
- ✓ lower blood loss
- ✓ lower risk of adhesions
- ✓ no identificable trend to increasing hospital cost (probably related to the reduced need for inpatient care)

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Laparoscopic myomectomy

Which are the limits?

- **Dimension**

6 cm	7 cm	8 cm	10 cm
Parker '95	*Darai '97*	*Dubuisson '96* *Mais '96*	*Stringer '96*

- **Number**

< 2	< 5	< 3

- **Site** — **No myomas near the uterine artery or tubal cornua**
- **Deep** — **At least 50 % subserosal** ***(Miller 1996)***

Operative time!

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Laparoscopic myomectomy

Which are the limits?

- **Sutura**
- **Morcellazione**
- **Dimensioni numero e sede del mioma\i**
- **Esperienza del chirurgo**
- **Tempi operatori**
- **Costi***
- **Perdita della sensazione tattile**