With the advent of selective progesterone receptor modulators, what is the place of myoma surgery in current practice?

Jacques Donnez, M.D., Ph.D.,^a Olivier Donnez, M.D., Ph.D.,^{b,c} and Marie-Madeleine Dolmans, M.D., Ph.D.^c

^a Society for Research into Infertility, Brussels; ^b Pôle de Recherche en Gynécologie, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, CHU Mont-Godinne, Gynecology, Yvoir; and ^c Pôle de Recherche en Gynécologie, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Cliniques Universitaires Saint Luc, Brussels, Belgium

Uterine fibroids are the most common benign uterine tumors. This review examines the different management strategies, involving mainly surgery, and evaluates them in the light of new developments with selective progesterone receptor modulators. On the one hand, hysteroscopic and laparoscopic (or minilaparotomic) myomectomy is the treatment of choice in women who wish to preserve their uterus, and hysterectomy has long been considered the standard surgical approach in symptomatic women who no longer wish to conceive. On the other hand, recent studies have demonstrated the efficacy of ulipristal acetate in the medical management of myomas. Analyzing the respective advantages of both medical and surgical therapy, we pro-

pose new guidelines for the management of fibroids that take into account the most important symptoms (bleeding, infertility) and the age of the patients. (Fertil Steril® 2014;102:640–8. ©2014 by American Society for Reproductive Medicine.)

Key Words: Infertility, menorrhagia, myomas, SPRMs, surgery, ulipristal acetate



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terine fibroids (also known as myomas or leiomyomas) are the most common benign uterine tumors in women of reproductive age, occurring in 20%–25% of women (1, 2). Depending on localization, the symptoms vary in frequency and severity, and include pelvic pain, pressure, dysmenorrhea, anemia caused by heavy bleeding, reduced quality of life, and infertility (3).

Current management strategies involve mainly surgical interventions, but the choice of treatment is guided by the patient's age and desire to preserve fertility and avoid "radical" surgery such as hysterectomy (3–5). In the early 1980s, hysterectomy was routinely proposed to women with submucous fibroids who did not wish to conceive. Since then, other surgical and nonsurgical approaches, including myomectomy by laparotomy or laparoscopy, uterine artery embolization (UAE), and other interventions performed under radiologic or ultrasound guidance (3–7), have been proposed.

Medical therapies with progestin, progestin-releasing intrauterine devices, and gonadotropin-releasing hormone

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Reprint requests: Jacques Donnez, M.D., Ph.D., Société de Recherche pour l'Infertilité, Avenue Grandchamp, 143, 1150 Brussels, Belgium (E-mail: jacques.donnez@gmail.com).

Fertility and Sterility® Vol. 102, No. 3, September 2014 0015-0282/\$36.00 Copyright ©2014 American Society for Reproductive Medicine, Published by Elsevier Inc. http://dx.doi.org/10.1016/j.fertnstert.2014.06.041 (GnRH) agonist are also available (8–12), but some small studies have reported that use of oral progestin may cause breakthrough bleeding and promote myoma growth (8). A GnRH agonist can be used as a presurgical treatment (9–12), resulting in reversible reduction of myoma size and correction of anemia. However, because of safety concerns linked to artificially induced menopause (loss of bone mineral density), such treatment is approved only for short-term therapy (9–12).

Progesterone plays an important role in promotion of myoma growth (13, 14). Modulating the progesterone pathway represents one of the possibilities of medical therapy, opening the way to use of selective progesterone receptor modulators (SPRMs) (14). In 2012, two prospective randomized studies concluded that treatment with ulipristal acetate (UPA) for 13 weeks effectively controlled excessive bleeding due to uterine fibroids and reduced their size (15, 16). Very recently, the results of the first study on long-term intermittent (18 months) therapy with 10-mg UPA were published (17), demonstrating that this regimen (four courses of 3 months) maximizes the effect of UPA by inducing a very high rate of amenorrhea and reducing fibroid size. Our review presents a comprehensive overview of the surgical techniques used in cases of myomectomy and hysterectomy and discusses their respective indications in 2014, taking into account recent developments in long-term intermittent therapy with SPRMs (17).

HYSTEROSCOPIC MYOMECTOMY

Over the last 30 years, advances in instruments and techniques have promoted hysteroscopic myomectomy to the rank of a standard minimally invasive surgical procedure for submucous myomas (18). There is some evidence suggesting that fibroids may impede fertility (3, 19, 20) by interfering with sperm migration, ovum transport, and embryo implantation due to focal endometrial inflammation or vascular disturbances (3). Although the absence of randomized studies does not allow any firm conclusions to be drawn (21, 22) in this regard, many investigators have reported an improvement in spontaneous fertility after hysteroscopic myomectomy (3, 18, 20, 23), especially when the uterine cavity was distorted by the presence of submucous myomas.

Numerous classifications of submucous myomas can be found in the literature (24–26). Despite some differences, all of them take into account the degree of intramural extension. The fibroid classification adopted by the European Society for Gynecological Endoscopy (ESGE) is used worldwide and has the advantage of being very simple: G0 is a pedunculated intrauterine myoma, G1 has its largest part (>50%) in the uterine cavity, and G2 has its largest part (>50%) in the myometrium. More recently, the International Federation of Gynecology and Obstetrics (FIGO) classification was published (27) describing eight types of fibroids, including a hybrid class (association of two types of myomas) (Fig. 1). As different types of fibroids are often present at the same time (according to the site), this classification offers a more representative map of fibroid distribution.

Hysteroscopic Techniques

Depending on personal experience and available equipment, the gynecologist has a choice of several alternative procedures (18).

- Cutting the base of pedunculated fibroids with either the resectoscopic loop or laser fiber. The base of the pedicle is cut, and the fibroid is extracted by forceps or may be left in place (28). Office hysteroscopic myomectomy can also be performed. Small fibroids (<2 cm) are now routinely removed in an outpatient setting, according to the technique described by Bettochi et al. (29–31).
- 2. Slicing during resectoscopic myomectomy. The most commonly used technique is the slicing technique. Repeated and progressive passage of the cutting loop allows the surgeon to cut the myoma into small chips. The operation is considered complete when the fasciculate fibers of the myometrium are visualized (19, 32). A recent study by Mazzon et al. (33) found that cold loop hysteroscopic myomectomy appears to be associated with a lower rate of intrauterine adhesions than that documented in other literature reports.
- 3. Excising large fibroids completely by a one-step procedure. Numerous techniques were described in the review by Di Spiezio et al. (18) that use hydromassage or manual massage. The main limitation is the increased risk of operative complications (perforation, bleeding, fluid intravasation) and damage to surrounding healthy myometrium from the use of electrosurgery during dissection of the

Leiomyoma subclassification system	SM - Submucosal	0	Pedunculated intracavitary
		1	<50% intramural
		2	≥50% intramural
	O - Other	3	Contacts endometrium; 100% intramural
25 3 4		4	Intramural
		5	Subserosal ≥50% intramural
		6	Subserosal <50% intramural
		7	Subserosal pedunculated
		8	Other (specify e.g. cervical, parasitic)
	Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below	
		2-5	Submucosal and subserosal, each with less
			than half the diameter in the endometrial
			and peritoneal cavities, respectively.

FIGURE 1

FIGO classification of myomas (Munro et al., 2011 [27]). Donnez. SPRMs in myoma therapy. Fertil Steril 2014.

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