Rewriting the script: time to rethink the indications for myoma surgery

Uterine fibroids, the most frequently encountered benign uterine tumors, have a profound impact on the quality of life (QOL) of patients. Moreover, they are associated with a considerable societal burden due to the direct costs of treatment and the indirect costs linked to work absenteeism. Around 30% of women with leiomyomas will request treatment because of severe heavy menstrual bleeding, abdominal pain, bulk symptoms, and/or infertility.

Current therapy is mainly surgical: hysterectomy or laparoscopic or hysteroscopic myomectomy. Hysterectomy is an effective surgical option, but is considered a radical approach when increasing numbers of women are opting to preserve their uterus (1). Among the 600,000 hysterectomies performed each year in the United States, 200,000 are for fibroids, a highly significant proportion. Health care costs for leiomyoma management have been estimated at over $2 billion a year.

There are many areas of uncertainty surrounding the management of myomas, as only a few randomized trials have compared different surgical therapies, data on long-term outcomes relating to posthysterectomy QOL, recurrence of symptoms (bleeding, pain, bulk sensation), fertility, and complication rates (1, 2).

FROM HYSTERECTOMY TO MYOMECTOMY … AND BEYOND

The first steps toward a less radical surgical approach came about as a natural consequence of advances made in instrumentation and techniques over the last 30 years. Hysteroscopic myomectomy is known to be effective for control of bleeding, but requires skill and experience. Failures are often related to growth of fibroids in other sites, association with adenomyosis, and incomplete resection. Laparoscopic myomectomy is perceived by many endoscopists to be more difficult than myomectomy by laparotomy, but the advantages are real. However, the Food and Drug Administration's warning about the risk of inadvertently morcellating undiagnosed uterine leiomyosarcomas has probably served to curtail the number of laparoscopic procedures carried out for myomas.

In our opinion, as voiced in a recent review (1), the argument against the use of electric morcellation has been somewhat overstated, not only because of the fear of medicolegal issues, but also due to a heated emotional response to a particular case. What we really need to ask ourselves is should we change our surgical habits, which bring relief in more than 99.5% of cases, for a disease that occurs in less than 0.5% of women with myomas?

The introduction of uterine artery embolization and high-frequency magnetic resonance–guided focused ultrasound surgery has varied widely across the globe. Although both techniques are effective for treating symptoms, the risk of reoperation is a legitimate concern, with rates ranging from 15% to 30%. It should also be emphasized that a desire for future pregnancy is a relative contraindication.

WHY DO WE NEED NEW OPTIONS?

There is no doubt that fibroids have a significant economic impact, but the cost of therapy both to sufferers and to the health care system must be balanced against the cost of untreated disease conditions, as well as against the expense of ongoing or repeated investigations and treatment modalities (1).

There is a lack of relevant medicoeconomic data on the different available strategies, but it is reasonable to assume that reducing the number of hysterectomies and other surgical procedures will cut costs and morbidity. Moreover, it is essential to evaluate new approaches and alternatives to surgical and nonsurgical interventions, especially when fertility preservation is the goal (1, 2).

This point is particularly pertinent for African-American women, as well as women of African descent living in Europe, who have a greater chance of being affected by uterine fibroids, especially at an earlier age. Indeed, these women are known to experience more severe symptoms at a younger age and often require surgery.

MEDICAL THERAPY: WHERE ARE WE AND WHAT DO WE KNOW SO FAR?

Estrogen was previously considered to be the major growth factor involved in myoma development, but P has now emerged as the key player in uterine fibroid growth, implicated in the regulation of genes associated with proliferation and apoptosis.

By modulating the P pathway, selective P receptor modulators (SPRMs) have been found to have a significant impact on myoma growth (1, 3, 4). Their mechanism of action on P receptors (PRs) depends on how they alter the PR conformation, resulting in either exposure or inactivation of specific binding domains. They exert a sustained effect, decreasing myoma volume thanks to their crucial role in collagen degradation induced by MMP-2 (1). The efficacy and safety of repeated use of ulipristal acetate (5 mg/day) for uterine fibroids were indeed recently demonstrated (4). It should be noted that these drugs may induce PR modulator-associated endometrial changes, but these changes are benign and reversible, and their incidence is not increased by repeated courses, even as many as eight courses.

SPECIAL EMPHASIS ON INFERTILITY: WHAT IS THE BEST THERAPY TO ADOPT?

There is clearly an urgent need for alternatives to surgery, especially when fertility preservation is the goal. Too many surgical procedures are performed for intramural myomas distorting the uterine cavity. Gynecologists need to be aware of the fact that multiple myomectomies do not exclude the risk of recurrence and will surely impact future pregnancy outcomes (need for cesarean section, risk of placental anomalies, scar tissue formation, etc.). There is no doubt that surgery remains indicated in some instances, but we should

bear in mind that SPRMs may allow less invasive surgery, or even its complete avoidance (1, 4).

To determine the most appropriate approach, patient age, severity of symptoms, wish to preserve the uterus and/or fertility, and myoma volume and localization must be taken into account according to the International Federation of Gynecology and Obstetrics (FIGO) classification (1).

In infertile women with large myomas distorting the uterine cavity, medical therapy (UPA 5 mg/day) can be given in two courses of 3 months, as we know that a second course maximizes the effects of the first (4). Depending on the response in terms of myoma regression and restoration of the uterine cavity, the patient may attempt pregnancy either by sexual intercourse or IVF (if required) after the second bleed. A meta-analysis by Pritts et al. (5) evaluating 23 studies reported a significant drop in implantation and pregnancy rates in the presence of myomas, especially submucous and/or intramural myomas that distort the uterine cavity. Therefore, if two courses of SPRMs are able to reduce the size of myomas and 'push' them back into the myometrium, implantation rates could easily be improved, leading to more pregnancies with favorable outcomes.

In some cases, if the uterine cavity remains distorted or the myomas do not shrink enough, having been very large at screening, surgery is of course indicated. This also holds true if the response is deemed inadequate. Because it reduces the need for surgery in approximately 40% of cases, medical therapy should be considered a first-line approach before myomectomy is contemplated.

Women of African descent have a greater chance of developing symptomatic myomas at an earlier age than Caucasian women. For this reason, if there is no immediate wish to conceive, medical therapy with SPRMs may well prove adequate. Indeed, there is no pressing need for surgery if the symptoms abate satisfactorily. The role of medical therapy in this particular group of young women with symptomatic myomas is very clear—to postpone or avoid surgery—in the knowledge that recurrence rates after myomectomy can reach almost 60% after an interval of 4–5 years and that repeated surgery increases the risk of pelvic adhesions (1).

In conclusion, we must be open to new therapeutic avenues in a rapidly changing world. The message is clear: it is time to rethink and redefine the true indications for myomectomy in infertile women.

Jacques Donnez, M.D., Ph.D.[a]
Olivier Donnez, M.D., Ph.D.[b]
Marie-Madeleine Dolmans, M.D., Ph.D.[c,d]

[a] Société de Recherche pour l'Infertilité, Brussels, Belgium; [b] Institut du Sein et de Chirurgie Gynécologique d'Avignon, Polyclinique Urbain V (ELSAN Group), Avignon, France; [c] Pôle de Gynécologie, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Brussels, Belgium; and [d] Gynecology Department, Cliniques Universitaires Saint Luc, Brussels, Belgium

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