

## Selected Summaries

### Symptomatic uterine fibroids: Is uterine artery embolization better than surgery?

Edwards RD, Moss JG, Lumsden MA, Wu O, Murray LS, Twaddle S, Murray GD; Committee of the Randomized Trial of Embolization versus Surgical Treatment for Fibroids. (Gartnavel Hospital; University of Glasgow, Glasgow, Scotland; Scottish Intercollegiate Guidelines Network; University of Edinburgh Medical School, Edinburgh, UK.) Uterine-artery embolization versus surgery for symptomatic uterine fibroids. *N Engl J Med* 2007;**356**:360–70.

#### SUMMARY

This randomized trial, conducted in 27 hospitals in the UK, compared uterine artery embolization and surgery in 157 women with symptomatic uterine fibroids. The original target for number of patients was 200 but had to be revised to 150 because of difficulty in recruitment. Women of at least 18 years of age were eligible if they had 1 or more fibroids, >2 cm in diameter that could be adequately visualized by magnetic resonance imaging (MRI), caused symptoms (such as menorrhagia or pelvic pain and pressure) and were considered by the patient's physician to require surgical treatment. The exclusion criteria included contraindication to MRI, severe allergy to iodinated contrast media, subserosal pedunculated fibroids, recent or ongoing pelvic inflammatory disease, pregnancy and any contraindication to surgery. There was no upper limit on the size or number of fibroids.

A total of 157 eligible women were randomized in a ratio of 2:1, with 106 being assigned to the embolization group and 51 assigned to the surgical group (43 hysterectomies and 8 myomectomies). The primary outcome measure was quality-of-life (QOL), as assessed at 12 months on the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36). Scores ranged from 0 to 100, with higher scores indicating better function. Secondary outcomes included assessment of findings on the EuroQol-5D questionnaire to measure preferences for certain health outcomes, including hysterectomy. An 11-point symptom score, ranging from -5 (markedly worse) to +5 (markedly better), measured time until resumption of usual activities, satisfaction score measuring whether patients would recommend the procedure to a friend, linear-analogue pain score at 24 hours; presence or absence of complications, and treatment failure defined as the need for subsequent intervention for symptom control including hysterectomy or repeated embolization. Complications were graded according to the classification system of the Society of Interventional Radiology, as follows:

- Grade 1: No therapy required or no consequence;
- Grade 2: Nominal therapy required or no consequence, including overnight admission for observation only;
- Grade 3: Therapy required, including minor hospitalization of <48 hours;

Grade 4: Major therapy required, including an unplanned increase in the level of care or hospitalization for >48 hours; and

Grade 5: Permanent adverse sequelae.

Grades 1 and 2 were considered to be minor; grades 3 through 5 were considered to be major. Two investigators (a gynaecologist and a radiologist) independently categorized the grade of complications. In 56% of cases, the investigators were in complete agreement; in 91% of cases, they were in agreement to within one grade of complication. In discordant cases, the worse grade was used. Major adverse events included any major complication, a life-threatening event, initial or prolonged hospitalization, an intervention required to prevent permanent impairment or damage, and death. Treatment failures requiring subsequent intervention were considered separately. Outcome measures (with the exception of the 24-hour pain score) were recorded at 1, 6, 12 and 21 months and annually thereafter. An independent data and safety monitoring committee reviewed the results and serious adverse events every 12 months. The data were assessed using 2-sided Student *t*-test and the Mann-Whitney test for continuous data and the Chi-square test for categorical data. The original power calculation required the enrolment of 200 patients to give a power of 90% at 0.05 significance level. However, because of slower than expected recruitment, it was decided to enrol only 150 patients, giving a power of 80%.

There were no significant differences between groups in any of the 8 components of the SF-36 scores at 1 year. The embolization group had a shorter median duration of hospitalization than the surgical group (1 day *v.* 5 days,  $p < 0.001$ ) and a shorter time before returning to work ( $p < 0.001$ ). At 1 year, symptom scores were better in the surgical group ( $p = 0.03$ ). Minor complications were reported by 34% in the embolization and 20% in the surgical group, mainly post-embolization syndrome in the first group and minor infections in the latter. Major complications were encountered by 12% in the embolization and 20% in the surgical group. Ten patients in the embolization group (9%) required repeated embolization or hysterectomy for inadequate symptom control. After 1 year of follow up, 14 women in the embolization group (13%) required hospitalization, 3 of them for major adverse events and 11 for re-intervention for treatment failure. The study concluded that to treat women with symptomatic fibroids the faster recovery after embolization must be weighed against the need for further treatment in a minority of patients.

#### COMMENT

Uterine fibroid is the commonest tumour of the female reproductive tract. Fifty per cent of patients with uterine fibroids are symptomatic with abnormal bleeding, pressure symptoms, pain, abdominal distension or pregnancy-associated problems including infertility.<sup>1</sup> Treatment is necessary once fibroids become symptomatic or for asymptomatic fibroids if they are large or show rapid growth.<sup>2</sup> Much of the data describing the relationship between the presence of fibroids and symptoms are based on uncontrolled studies that assessed the effect of myomectomy on presenting symptoms.<sup>3</sup>

Traditionally, the only options available were hysterectomy or myomectomy. In recent years, medical management has been tried in those who desire to retain future fertility and in perimenopausal women who wish to preserve their uterus.<sup>4</sup> Therapeutic alternatives to hysterectomy include treatment with gonadotrophin-releasing agonists, alone or in combination with other conservative procedures such as myomectomy or myolysis.<sup>5</sup> Gonadotrophin-releasing agonists have a temporary effect, as do other medical methods such as mifepristone or danazol.<sup>6</sup> With the current trend of minimally invasive therapy, uterine artery embolization is gaining popularity.<sup>7</sup>

Uterine artery embolization was first introduced in 1995.<sup>8</sup> This procedure can obviate the need for surgical procedures such as myomectomy in patients who have symptomatic leiomyomas. Fertility rates post-embolization appear similar to patients undergoing myomectomy although it has been hypothesized that uterine artery embolization-induced myoma necrosis can be associated with compromise of the vascular supply to the uterus or ovaries, which could lead to decreased fertility.<sup>9</sup> It has also been suggested that in a subsequent pregnancy there could be placental insufficiency resulting from inadequate blood flow through the uterus. Uterine rupture during pregnancy has also been postulated. However, there is no such published report.<sup>9</sup>

Three randomized controlled trials have been done to ascertain the better option—embolization or surgery. The first trial comparing uterine artery embolization and hysterectomy was published by Pinto *et al.* in 2002. This was a small prospective study enrolling only 57 women. However, the consent methodology was controversial in which one group had the option to choose between embolization and hysterectomy while the other group underwent embolization without being told of the alternative treatment. Also, at the end of 2 years of follow up, the study concluded that for the treatment of bleeding fibroids, embolization was a safer alternative to hysterectomy, and had a shorter hospital stay and fewer major complications.<sup>10</sup>

The second study was the EMMY trial, published in 2005 which enrolled 177 women.<sup>11</sup> This study showed a significantly shorter mean hospital stay but a higher rate of minor complications and re-admission with embolization. Their final conclusions, which were published in 2006, were that the procedural failure rate for embolization was higher than previously reported, mainly as a result of difficult anatomy and absence of uterine artery visualization in some cases.<sup>12</sup> The risk of procedural failure increased for patients with a single fibroid and/or small uterine volume. A clear dose–effect response was seen between the amount of embolization material used and the risk for post-procedural fever, major complications and severe pain.

The present study (REST trial) was adequate in number and the groups were well matched at baseline. The power of the study was reduced to 80% from the originally planned 90% because less women were recruited ( $n=150$ ) than targeted ( $n=200$ ). The randomization was in a ratio of 2:1. Another drawback was that the majority of women in the surgical group underwent hysterectomy and only 8 underwent myomectomy.

The 95% confidence intervals for the differences between the groups indicate that there could be as much as a 10-point difference between groups in some components of the SF-36. However, there is no suggestion of clinically important differences. The use of ‘time until resumption of usual activities’ as a secondary outcome must be viewed cautiously since such an interval could be biased by the patient’s expectation (or the

caregiver’s guidance) regarding the time to recovery.

A direct comparison of myomectomy and embolization would be difficult to perform unless recruitment involves a very large population base. The results of this study make it clear that the choice between surgery and embolization for symptomatic uterine fibroids involves trade-offs. The advantages of embolization, including a significant reduction in the length of the hospital stay and 24-hour pain level and a more rapid return to usual activities, need to be weighed against the risk of treatment failure requiring a second intervention and the possibility, although infrequent, of major late adverse events. Longer follow up is necessary, with attention to the need for repeat intervention, to inform future decision-making.

The Cochrane Review (2006) concluded that the only advantages of embolization were shorter hospital stay and quicker return to routine activities.<sup>13</sup> There is no evidence of benefit of embolization over surgery (hysterectomy/myomectomy) with regard to patient satisfaction. There is a higher minor complication rate after discharge, as well as unscheduled visits and re-admission rates in embolization group, which has also been our experience. Longer follow up trials are required to comment on the effectiveness and safety profile of uterine artery embolization as a therapeutic alternative to surgery in women with uterine fibroids.

## REFERENCES

- 1 Breech LL, Rock JA. Leiomyomata uteri and myomectomy. In: Rock JA, Jones HW III (eds). *Te Linde's Operative Gynecology*. 9th ed. Philadelphia: Lippincott Williams and Wilkins; 2003:753–92.
- 2 Lethaby A, Vollenhoven B. Fibroids (uterine myomatosis, leiomyomas). *Am Fam Physician* 2005;**71**:1753–6.
- 3 Lumsden MA, Wallace EM. Clinical presentation of uterine fibroids. *Baillieres Clin Obstet Gynaecol* 1998;**12**:177–95.
- 4 Smith SJ. Uterine fibroid embolisation. *Am Fam Physician* 2000;**61**:3601–7, 3611–12. Erratum in: *Am Fam Physician* 2000;**62**:1786.
- 5 Lefebvre G, Vilos G, Allaire C, Jeffrey J, Arneja J, Birch C, *et al*; Clinical Practice Gynaecology Committee, Society for Obstetricians and Gynaecologists of Canada. The management of uterine leiomyomas. *J Obstet Gynaecol Can* 2003;**25**:396–418; quiz 419–22.
- 6 Freidman A. Use of gonadotropin-releasing hormone agonists before myomectomy. *Clin Obstet Gynecol* 1993;**36**:650–9.
- 7 Lyon SM, Cavanagh K. Uterine artery embolisation—a treatment alternative for women with fibroids. *Aust Fam Physician* 2006;**35**:300–3.
- 8 Goodwin SC, Vedantham S, McLucas B, Forno AE, Perrella R. Preliminary experience with uterine artery embolization for uterine fibroids. *J Vasc Interv Radiol* 1997;**8**:517–26. Erratum in *J Vasc Interv Radiol* 1999;**10**:991.
- 9 Mc Lucas B, Goodwin S, Adler L, Rappaport L, Reed R, Perrella R. Pregnancy following uterine artery embolisation. *Int J Gynecol Obstet* 2001;**74**:1–7.
- 10 Pinto I, Chimento P, Romo A, Paul L, Haya J, de la Cal MA, *et al*. Uterine fibroids: Uterine artery embolization versus abdominal hysterectomy for treatment—a prospective, randomized, and controlled clinical trial. *Radiology* 2003;**226**:425–31.
- 11 Hehenkamp WJ, Volkers NA, Donderwinkel PF, de Blok S, Birnie E, Ankum WM, *et al*. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): Peri- and postprocedural results from a randomized controlled trial. *Am J Obstet Gynecol* 2005;**193**:1618–29.
- 12 Volkers NA, Hehenkamp WJ, Birnie E, de Vries C, Holt C, Ankum WM, *et al*. Uterine artery embolization in the treatment of symptomatic uterine fibroid tumors (EMMY trial): Peri-procedural results and complications. *J Vasc Interv Radiol* 2006;**17**:471–80.
- 13 Gupta J, Sinha AS, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. *Cochrane Database Syst Rev* 2006;**1**:CD005073.

NEERJABHATLA

SHILPA SINGLA

Department of Obstetrics and Gynaecology  
All India Institute of Medical Sciences

Ansari Nagar

New Delhi

neerjabhatla@rediffmail.com