

UFE:

State of the Evidence

A look at what the literature says about uterine fibroid embolization as an alternative treatment to surgery.

BY JAFAR GOLZARIAN, MD

The first cases of uterine artery embolization for fibroids (UFE) were performed almost 20 years ago by Merlan et al in France in patients with intractable bleeding related to uterine fibroids who had contraindications to surgery. In 1995, Dr. Ravina from the same institution published the first report in *The Lancet* on the role of uterine artery embolization in treating menorrhagia related to fibroids.¹ Since then, hundreds of articles have demonstrated the efficacy of UFE in the management of fibroid-related symptoms. Although the majority of those articles were case series and retrospective studies, they have clearly demonstrated several important points. First, we learned that UFE is effective in controlling fibroid symptoms in 85% to 95% of patients. We have also learned about the postprocedure pain and major complications after UFE and how to manage and minimize them. The indications and contraindications have been defined. Finally, the technique of UFE was further refined with new endpoints and new materials that also modified the way most interventional radiologists perform other embolization procedures.

UFE is one of the few procedures in the interventional and endovascular field that has been subject to many randomized trials providing strong level I/level A evidence. In this article, we review the state of evidence on UFE based on major prospective randomized trials.

UFE VERSUS HYSTERECTOMY

Pinto et al randomized UFE versus hysterectomy (2:1 ratio) with 38 UFE and 19 hysterectomy patients. They demonstrated a shorter hospitalization stay for UFE over hysterectomy (1.7 vs 5.8 days, respectively; $P < .001$) and faster return to routine activities for UFE patients than those who underwent hysterectomy (9.5 vs 36.2

days, respectively; $P < .001$) with no difference in complication rates (25% [UFE] vs 20% [hysterectomy]; $P = .8$). Menorrhagia improved in 86% of UFE patients at 6-month follow-up.²

The EMMY trial from the Netherlands was the next trial comparing hysterectomy to UFE in 34 centers (28 active).³ They included 177 patients (88 UFE, 89 hysterectomy) with menorrhagia from a group of patients that had previously agreed to hysterectomy. The EMMY trial was a noninferiority trial that considered UFE not inferior to hysterectomy if it was successful in at least 75% of patients. Short-term results showed no difference in SIR major complications (4.9% vs 2.7%; $P = .68$); however, more frequent minor complications were seen in UFE patients (58% vs 40%; $P = .024$). They reported a higher readmission rate for UFE (11.1% vs 0%; $P = .003$) but shorter hospital stay and faster recovery. The EMMY trial was associated with a higher failure rate than previously reported for UFE, with a technical failure rate of 5.3% and procedural failure rate of 17.3% (failed on one or both sides). This failure rate was significantly higher than any other published series. The UFE success rate in treating menorrhagia was 76.5% in this study.

The EMMY trial was subject to many critics because of some major limitations and drawbacks, including inexperience of some of the operators performing UFE, no follow-up by an interventional radiologist, inadequate pain control protocol, and misvaluation of surgical complications such as transfusion.

The latest randomized multicenter study in the United Kingdom (REST trial) was published in the *New England Journal of Medicine* in 2007.⁴ This 2:1 ratio randomized study compared UFE to surgery (UFE, 106

patients; surgery, 51 [hysterectomy 43, myomectomy 8]). Short-term results showed that UFE was less painful at 24 hours compared to surgery. UFE was associated with a shorter hospital stay (1 vs 5 days; $P < .001$) and faster return to work (20 vs 62 days; $P < .001$). There was no difference in adverse events between the two procedures (major events, 15% UFE vs 20% surgery; $P = .22$; minor events, 34 UFE vs 20% surgery; $P = .47$). At 1 month, the quality of life was significantly superior in the UFE arm; however, at a median follow-up of 32 months, both groups were equally satisfied. UFE patients were more likely to need reintervention (21 for UFE vs 1 for surgery; $P < .001$): 10 in the first year and 11 in subsequent follow-up. UFE was more cost effective than surgery.

UFE VERSUS MYOMECTOMY

A level II-2 evidence, multicenter, prospective cohort, controlled study compared UFE to myomectomy in 209 patients (149/60) in 16 centers in the United States. This study demonstrated similar clinical outcomes in both groups in controlling the symptoms. However, hospital stay was 2.5 times less for UFE patients, and the time to recovery was also shorter in this group (15 vs 44 days). UFE was associated with significantly lower morbidity rates. The patients' quality of life significantly improved in both groups.⁵

The first level I evidence study was published by Mara et al.⁶ They compared 30 UFE to 33 myomectomy (15 laparoscopic, 18 open) patients with a mean follow-up of 17 months. Again, UFE patients had shorter hospital stays (3.7 vs 5.3 days; $P < .001$) and faster recovery (13.6 vs 30 days; $P < .0001$). There was no difference in major complications (UFE 10% vs myomectomy 3%) and in basal follicle-stimulating hormone concentration after treatment (UFE, 7.6 international units vs myomectomy, 6.8 international units). Symptoms were resolved in 87.5% of UFE patients compared to 93.3% of patients who underwent myomectomy. Mara et al have confirmed the previous data showing higher reintervention rates in the UFE group (36% vs 6.1%; $P = .01$).

The same group published an update of this study including more patients (58 UFE, 63 myomectomy) with a mean follow-up of 25 months.⁷ They have confirmed the same outcome reported in their preliminary study. However, they have also demonstrated that the rate of pregnancy after myomectomy was significantly higher than after UFE. The investigators concluded that UFE was less invasive and had an identical clinical success rate than myomectomy. Myomectomy remained superior to UFE in terms of reproductive outcome.

Laparoscopic UA Occlusion Versus UFE

Based on the success of the UFE, some investigators have decided to compare this technique to the laparoscopic occlusion of the uterine artery (LUAO). The first prospective randomized trial by Hald et al included 28 patients in each arm.⁸ The preliminary results showed that UFE was more painful than LUAO; however, UFE was associated with significantly better outcomes and fewer complications. The same authors published the update of the study with 66 patients and a median follow-up of 48 months (range, 8–73 months).⁹ Clinical failure and symptom recurrence occurred in 14 patients after laparoscopy (48%) and in five after UAE (17%; $P = .02$, log-rank test). Hysterectomy was performed in two patients after UAE (7%) and in eight patients after laparoscopy (28%; $P = .041$). Magnetic resonance imaging results of complete leiomyoma infarction were even more impressive in favor of UFE.

These investigators have concluded that the recurrence rate was significantly lower after UFE than after laparoscopic treatment. Larger volume reduction and more complete devascularization of leiomyomas were found after UAE treatment and among patients with no recurrence. These findings are not surprising because LUAO is similar to a proximal occlusion of the uterine arteries by coils that is well-known in interventional radiology literature to be ineffective in controlling the bleeding or symptoms related to the fibroids.

EMBOLIZATION MATERIALS

Excellent prospective randomized studies have been published comparing different embolization materials. These studies have shown that not all embolization materials are equal. Spies et al have compared the classic polyvinyl alcohol (PVA) particles to Embospheres (BioSphere Medical, Inc., Rockland, MA). This prospective randomized trial has shown that although there was more clogging with PVA particles, the clinical outcomes were the same in both groups. The volume of Embospheres used was three times superior to the PVA volume.¹⁰

In 2005, Spies et al compared a newly commercialized spherical PVA (SPVA) to Embosphere particles. The authors have stopped the trial due to a high clinical and imaging failure rate in the SPVA group.¹¹

Siskin et al have compared the same materials in another level I study with a new endpoint for the SPVA group (total stasis instead of limited endpoint).¹² They have found a significantly higher failure rate in SPVA than in the Embosphere group (29.6% vs 3.8%). These trials confirm that the results of embolization will

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depend on the type of materials and technique of embolization. Therefore, any new particles for embolization should be tested in a clinical trial before being adopted.

Based on this evidence, the American College of Obstetricians and Gynecologists has recognized UFE to be a level A treatment category. Specifically, the College states: "Based on long- and short-term outcomes, uterine artery embolization is a safe and effective option for appropriately selected women who wish to retain their uteri."

CONCLUSION

Evidence shows that UFE is a safe and reliable alternative treatment to surgery and should be offered as an option to symptomatic patients with uterine fibroids. ■

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1. Ravina JH, Herbreteau D, Ciraru-Vigneron N. Arterial embolisation to treat uterine myomata. *Lancet*. 1995;346:671-672.
2. Pinto I, Chimeno P, Romo A, et al. Uterine Fibroids: Uterine artery embolization versus abdominal hysterectomy for treatment—a prospective, randomized, and controlled clinical trial. *Radiology*. 2003;226:425-431.
3. Volkers NA, Hehenkamp WJ, Smit P. Economic evaluation of uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: results from the randomized EMMY trial. *J Vasc Interv Radiol*. 2008;19:1007-1016; quiz 1017.
4. The REST Investigators Uterine-Artery Embolization versus Surgery for Symptomatic Uterine Fibroids. *NEJM*. 2007;356:360-370.
5. Goodwin SC, Bradley LD, Lipman JC, et al; UAE versus Myomectomy Study Group. Uterine artery embolization versus myomectomy: a multicenter comparative study. *Fertil Steril*. 2006;85:14-21.
6. Mara M, Fucikova Z, Maskova J, et al. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. *Eur J Obstet Gynecol Reprod Biol*. 2006;126:226-233.
7. Mara M, Maskova J, Fucikova Z, et al. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. *Cardiovasc Intervent Radiol*. 2008;31:73-85.
8. Hald K, Kløw NE, Qvigstad E, et al. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. *Obstet Gynecol*. 2007;109:20-27.
9. Hald K, Noreng HJ, Istre O, et al. Uterine artery embolization versus laparoscopic occlusion of uterine arteries for leiomyomas: long-term results of a randomized comparative trial. *J Vasc Interv Radiol*. 2009;20:1303-1310; quiz 1311. Published online ahead of print August 26, 2009.
10. Spies JB, Allison S, Flick P, et al. Polyvinyl alcohol particles and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a randomized comparative study. *J Vasc Interv Radiol*. 2004;15:793-800.
11. Spies JB, Allison S, Flick P, et al. Spherical polyvinyl alcohol versus tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a limited randomized comparative study. *Vasc Interv Radiol*. 2005;16:1431-1437.
12. Siskin GP, Shlansky-Goldberg RD, Goodwin SC, et al; UAE versus Myomectomy Study Group. A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: long-term clinical outcomes in patients with symptomatic uterine fibroids. *J Vasc Interv Radiol*. 2006;17:1287-1295.