CardioVascular and Interventional Radiology


Published Online: 15 December 2005

Cardiovasc Intervent Radiol (2006) 29:1–3
DOI: 10.1007/s00270-005-0243-5

EDITORIAL/OPINION

# Higher Rate of Partial Devascularization and Clinical Failure After Uterine Artery Embolization for Fibroids with Spherical Polyvinyl Alcohol

Jafar Golzarian,[1] Elvira Lang,[2] David Hovsepian,[3] Thomas Kroncke,[4] Leo Lampmann,[5] Paul Lohle,[5] Jean-Pierre Pelage,[6] Richard Shlansky-Goldberg,[7] David Valenti,[8] Dierk Vorwerk,[9] James Spies[10]

[1]Department of Radiology, 200 Hawkins Drive, 3957 JPP, University of Iowa, Iowa City, Iowa 52242, USA
[2]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA
[3]Mallinckrodt Institute, St. Louis, MO 63110, USA
[4]Department of Radiology, University Clinic Charité, Berlin 10117, Germany
[5]Department of Radiology, St. Elisabeth Hospital, AN Tilburg 5032, The Netherlands
[6]Department of Radiology, Hôpital Ambroise Pare, Boulogne 92104 cedex, France
[7]University of Pennsylvania Medical Center, Philadelphia, PA 19104, USA
[8]Royal Victoria Hospital, McGill University, Montreal, H3A 1A1 Quebec, Canada
[9]Department of Diagnosis and Imaging, Klinikum Ingolstadt, Ingolstadt 85049, Germany
[10]Georgetown University Medical Center, Washington, DC 20007, USA

Ten years after Ravina and coworkers first introduced the concept of embolization as a definitive therapy for symptomatic fibroids, uterine fibroid embolization (UFE) is accepted as a safe alternative to surgical treatment of fibroid tumors. Much progress has been made in our understanding of fibroid vasculature, management of postoperative pain and complications, and causes of treatment failure. Technique and materials have been greatly refined. To ensure clinical success, most authors agree that complete devascularization of all fibroids is mandatory [1, 2]. Although partial devascularization of fibroids can result in clinical improvement and volume reduction initially, it has been associated with higher recurrence rates in the long term [2]. Thus, persistent contrast enhancement in fibroid(s) after UFE should be considered no better than a partial success.

Several causes of failure have been identified. These include the inability to cannulate uterine arteries, arterial spasm, flow restriction, variation of vascular anatomy, and/or misdiagnosis of fibroids as a cause of symptoms. Another important cause of failure is insufficient embolization, with recanalization of the fibroid vasculature minutes to hours after completion of the procedure [3].

The first embolic materials used for UFE were nonspherical polyvinyl alcohol (nPVA) particles, which were familiar to most interventional radiologists, readily available, inexpensive, and has a long history of being well tolerated. Variation in the size of the particles and the tendency for them to aggregate is thought to provoke a proximal vessel occlusion or unpredictable level of occlusion [4]. The aggregation of the particles may also cause microcatheter occlusion. However, dilution and slow infusion of nPVA particles during the embolization procedures can reduce the tendency for particulate aggregation, which may subsequently lead to a more distal embolization [3, 5]. Diluted PVA solution is also associated with much less clumping and microcatheter occlusion [6, 7]. The accepted endpoint with nPVA has been complete stasis in the uterine artery as evidenced by a standing column of contrast.

Other newer agents have been introduced for use in UFE. Gelatin-coated trisacryl microspheres (Embospheres, Biosphere Medical, Rockland, MA) were the first spherical

*Correspondence to:* Jafar Golzarian; 200 Hawkins Drive, JPP 3957, Iowa City, IA 52242, USA; *email:* jafar-golzarian@uiowa.edu

agent and offered the theoretical advantage of a more uniform and targeted embolization of the perifibroid plexus [8]. Their compressibility also made microcatheter clogging less likely. A new endpoint was proposed with Embospheres: a limited embolization of uterine arteries resulting in a ''pruned-tree'' appearance of the vasculature [8].

In a prospective, randomized study, Spies et al. [7] compared nPVA and Embospheres. There was a significantly higher rate of microcatheter clogging in the nPVA group, but no difference in success rates, by either imaging criteria (nonenhancement of all fibroids) or clinical outcome. Moreover, the intensity of pain and the complication rates were similar. In choosing between embolic agents with identical clinical outcomes, one needs to weigh the ease of handling, the total volume of particles required, the time for reaching the expected endpoint (with longer times being associated with higher radiation doses), and the cost of the agents.

In response to the rapid adoption of Embospheres for UFE, although not affecting the clinical outcome in patients after UFE, many companies have introduced spherical PVA (sPVA). Preliminary animal studies demonstrate that sPVA is safe [9, 10]. A recent animal study has shown that the sPVA particles are more compressible and can result in a more distal penetration than Embospheres [11]. Interestingly, in clinical usage, the embolization endpoint is achieved much faster and with a lower embolic volume than with Embospheres and nPVA, suggesting a more proximal occlusion. In the authors' experience the total volume of particles to achieve the same endpoint as with nPVA was at least 2 times less [12]. This proximal occlusion of the uterine artery causes an insufficient embolization. In line with this, there have been an increasing number of reports of clinical and imaging failures after UFE using sPVA, prompting many centers such as ours to discontinue its use as early as September 2004 [12]. A recently published randomized study compared tris-acryl gelatin microspheres versus sPVA particles (Contour, Boston Scientific) in patients undergoing UFE. This study has demonstrated that patients treated with sPVA were much more likely to have incomplete fibroid infarction than those treated with tris-acryl gelatin microspheres [13]. While this may not clinically make a difference in the short run, Pelage's work suggests that these patients are more likely to suffer a recurrence [2]. Shlansky-Goldberg et al. [14] retrospectively compared two groups of 23 patients treated with either sPVA (Contour SE, Boston Scientific, Rockland, MA) or nPVA (Contour, Boston Scientific). Contrast-enhanced MRI (CEMRI) follow-up demonstrated a significantly higher rate of residual fibroid perfusion in the sPVA group (3.7 times more). Shrinkage of the uterine volume at 3 months was 16% in the sPVA group and 28% in the nPVA group. In an almost identical study, Mujoomdar et al. [15] found a higher clinical failure rate in the sPVA group (17%) than in the nPVA group (8%).

In a single-arm study Siskin [16] studied 69 UFE patients with CEMRI following UFE. Only 51% of them had total devascularization of all fibroids. Similarly, using a hydrogel form of sPVA (BeadBlock, Terumo Medical, Somerset, NJ), Kroencke et al. [17] treated 42 patients and found a clinical satisfaction rate of 77%. On CEMRI, complete fibroid devascularization was observed in only 47% of patients. Pelage [18] noted complete devascularization of the dominant fibroid in 8% (1/13) of their patients using sPVA (Contour SE). They were able to achieve 83% devascularization by changing their embolization technique to use of larger (700–900 μm) particles and extensive embolization to complete occlusion of uterine arteries. Boston Scientific is now recommending use of this so-called refined protocol. While this technique may be effective, it has not yet been tested in a comparative study with any other accepted embolic agent. We believe that sPVA must be used with great caution and patients should be carefully followed to ensure an acceptable outcome.

In summary, acceptance of UFE among gynecologists requires a reliably high level of clinical success and safety. We strongly advocate that future studies of new embolic agents and techniques rely on CEMRI to provide objective evidence of fibroid infarction in order to ensure durable, high-quality outcomes. The use of any new material, especially at this stage of development of the technique, has to be strongly supported by solid clinical studies. Failure to do so may cause permanent harm to the future of this promising minimally invasive technique.

## References


1. Marret H, Le Brun Keris Y, Acker O, Cottier JP, Herbreteau D (2004) Late leiomyoma expulsion after uterine artery embolization. J Vasc Interv Radiol 15:1483–1485
2. Pelage JP, Guaou-Guaou N, Jha RC, Ascher SM, Spies JB (2004) Uterine fibroid tumors: Long-term MR imaging outcome after embolization. Radiology 230:803–809
3. Spies JB (2003) Uterine artery embolization for fibroids: Understanding the technical causes of failure. J Vasc Interv Radiol 14:11–14
4. Derdeyn C, Moran C, Cross D, Dietrich H, Dacey R (1995) Polyvinyl alcohol particle size and suspension characteristics. AJNR Am J Neuroradiol 16:1335–1343
5. Choe DH, Moon HH, Gyeong HK, et al. (1997) An experimental study of embolic effect according to infusion rate and concentration of suspension in transarterial particulate embolization. Invest Radiol 32:260–267
6. Golzarian J, Torres C, Sun S, Valenti D (2004) Comparison of two different angiographic endpoints for uterine fibroid embolization with PVA. A multicentre study (abstract). J Vasc Interv Radiol 15:S173
7. Spies JB, Allison S, Flick P, et al. (2004) Polyvinyl alcohol particles and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: Results of a randomized comparative study. J Vasc Interv Radiol 15:793–800
8. Pelage JP, LeDref O, Beregi JP, et al. (2003) Limited uterine artery embolization with tris-acryl gelatin microspheres for uterine fibroids. J Vasc Interv Radiol 14:15–20
9. Redd D, Chaouk H, Shengelaia G, et al. (2002) Comparative study of PVA particles, embospheres and gelspheres in a rabbit renal artery embolization model (abstract). J Vasc Interv Radiol 13:S57
10. Siskin GP, Dowling K, Virmani R, Jones R, Todd D (2003) Pathologic evaluation of a spherical polyvinyl alcohol embolic agent in porcine renal model. J Vasc Interv Radiol 14:89–98

11. Laurent A, Wassef M, Pelage JP, et al. (2005) In vitro and in vivo deformation of TGMS and PVA microsphere in relation with their arterial location (abstract). J Vasc Interv Radiol 16:S77
12. Golzarian J, Sabri S, Small S, Stolpen A, Vibhakar J, Sun S (2005) High rate of partial devascularization demonstrated by MR after uterine artery embolization for fibroids with Spherical PVA. Annual Meeting and Postgraduate Course of the Cardiovascular and Interventional Radiological Society of Europe, Nice, September 10–14, 2005
13. Spies JB, Allison S, Flick PF, Cramp M, Bruno J, Jha RC, Ascher SA (2005) Spherical polyvinyl alcohol versus tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: Results of a limited randomized comparative study. J Vasc Intervent Radiol 16:1431–1437
14. Shlansky-Goldberg RD, Levin DA, Rosen M, et al. (2005) PVA boulders or spheres for UFE: Is there a difference? Late Breaking Abstracts, 30th Annual Meeting of the Society of Interventional Radiology, New Orleans, April 2, 2005
15. Mujoomdar A, Rafat Zand R, Torres CI, et al. (2005) Initial experience with spherical PVA in comparison with irregular PVA in UFE (abstract). J Vasc Interv Radiol 16:S65
16. Siskin GP (2005) Late Breaking Abstracts, 30th Annual Meeting of the Society of Interventional Radiology, New Orleans, April 2, 2005
17. Kroencke TJ, Lampmann L, Boekkooi F, et al. (2005) Initial experience with use of PVA microspheres for UFE: Results of a prospective two-center registry (abstract). J Vasc Interv Radiol 15:S79
18. Pelage JP (2005) Late Breaking Abstracts, 30th Annual Meeting of the Society of Interventional Radiology, New Orleans, April 2, 2005