

# Comparison of the Efficacy of the Embolic Agents Acrylamido Polyvinyl Alcohol Microspheres and Tris-Acryl Gelatin Microspheres for Uterine Artery Embolization for Leiomyomas: A Prospective Randomized Controlled Trial

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## Abstract

**Objective** To evaluate the efficacy of acrylamido polyvinyl alcohol microspheres (a-PVAM) as an embolic agent for uterine artery embolization (UAE) compared with Tris-acryl gelatin microspheres (TAGM).

**Design, Setting, Participants** Prospective randomized double-blind noninferiority trial. Conducted at two sites both with regional UAE practices. Forty-six women with symptomatic leiomyomas.

**Intervention** UAE procedure was performed with either of the two embolic agents. Either 700–900- $\mu\text{m}$  a-PVAM or 500–700- $\mu\text{m}$  TAGM was used.

**Main Outcome Measures** Changes in leiomyoma perfusion, overall uterine volume, and dominant leiomyomas volume measured by contrast-enhanced magnetic resonance imaging at 1 week, 3 months, and 6 months after UAE by a reader blinded to the embolic agent used. Changes in Uterine Fibroid Symptoms and Quality of Life questionnaire scores were measured at 3, 6, and 12 months after UAE.

**Results** Forty-six patients were randomized and treated under the study protocol (a-PVAM  $n = 22$ , TAGM  $n = 24$ ). There were no procedure-related complications.

Two patients were excluded from analysis (one technical failure of the procedure, one withdrawal from study). Successful (>90%) leiomyoma devascularization was observed in 81% of subjects at 1 week after UAE, 97% at 3 months after UAE, and 95% at 6 months after UAE. No significant differences were observed in 14 of 15 outcome measurements, consistent with noninferiority. TAGM was slightly superior to a-PVAM on one comparison (overall quality of life at 3 months after UAE).

**Keywords** Clinical practice · Embolization · Uterine artery embolization · Uterine fibroid embolization · Urogenital · Uterine fibroid

## Introduction

In recent years, the process of selecting an embolic agent for uterine artery embolization (UAE) has been made easier by the results from several randomized trials evaluating the use of different agents [1–4]. These studies have concluded that either Tris-acryl gelatin microspheres (TAGM) (Embosphere; Biosphere Medical, Rockland, MA) or nonspherical polyvinyl alcohol particles are the preferred agents for UAE in light of both clinical and imaging outcomes after this procedure.

The clinical goal of UAE is symptom relief. The U.S. Food and Drug Administration (FDA) considers symptom relief to be the most important measure of success [5]. Leiomyoma infarction on contrast-enhanced magnetic resonance imaging (MRI) has been cited as an important outcome measure because it indicates that the leiomyomas present within the uterus have been treated definitively [6]. Infarction seems to be linked to clinical outcome and may well be a predictor of long-term durability of symptom

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control [6]. This outcome measure was largely responsible for highlighting differences between existing embolic agents and demonstrating that Contour SE Microspheres (Boston Scientific, Natick, MA) are not an effective agent for UAE [2–4]. Technically successful UAE performed with TAGM consistently yields high rates of complete or near-complete leiomyoma infarction [1, 3, 4].

Given that not all embolic agents lead to equivalent clinical and imaging outcomes after UAE, it has become apparent that many interventionalists were quick to adopt new technology for this procedure with relatively little scrutiny [7]. As a result of this, Spies has called for standardization in how future studies are designed to evaluate the use of different embolic agents for UAE. Importantly, he has called for these studies to be prospectively randomized with clinical outcomes measured using the Uterine Fibroid Symptoms and Quality of Life (UFS-QOL) questionnaire [8] and imaging outcomes assessed using contrast-enhanced MRI with blinded interpretations [7]. If future investigators follow these recommendations, the standardized approach will enable accurate and consistent comparisons between agents.

Acrylamido polyvinyl alcohol hydrogel microspheres (a-PVAM) (Bead Block; Biocompatibles UK, Farnham, Surrey, UK) have been shown to be a clinically effective and safe embolic agent for UAE [9]. a-PVAM has been cleared by the U.S. FDA for general and neurologic embolic use. This agent is in many ways similar to TAGM. It is an elastic hydrogel microsphere that maintains the manufactured size and shape within the vessel wall and causes a complete mechanical occlusion. Given the similarities of these two materials, it is believed that the use of a-PVAM will yield the same degree of clinical improvement and leiomyoma infarction as after UAE with TAGM. a-PVAM particles are somewhat softer than TAGM [10] and do seem to act as a smaller-size particle than TAGM of the same nominal size. The present study was therefore designed to compare the degree of clinical improvement and leiomyoma infarction after UAE performed with either a-PVAM or TAGM, taking into account the difference in elasticity to determine particle size choice.

## Methods

This was a prospective randomized study that received approval from the institutional review boards at the study sites before study initiation. The study was designed with two treatment arms, one with a-PVAM used as the embolic agent for UAE and one with TAGM used as the embolic agent for UAE. The study was funded by an unrestricted research grant provided by Terumo Interventional Systems

USA (Somerset, NJ) and Biocompatibles UK (Farnham, Surrey, UK).

A total of 46 patients were enrolled and treated, 22 at site 1 and 24 at site 2. All patients signed institutional review board-approved informed consent for the study before treatment. All patients were evaluated in consultation in an established outpatient office to determine the appropriateness of performing the UAE procedure and their eligibility for participation in this trial. The inclusion and exclusion criteria are listed in Table 1. All patients for whom UAE was considered appropriate underwent a preprocedure contrast-enhanced MRI. At each site, a specific MRI facility was designated as the study MRI facility. The preprocedure and follow-up MRI studies were performed at this designated facility to maintain consistency in the imaging.

Before the procedure, all patients completed a UFS-QOL questionnaire [8]. Each UFS-QOL questionnaire was graded with the Excel grading spreadsheet provided by the SIR Foundation. The UFS-QOL is a validated instrument for evaluation of leiomyoma-related symptoms. It provides scores for both leiomyoma-related symptom severity and leiomyoma-related quality of life (QOL). The QOL portion contains six subscales (Concern, Activities, Energy/Mood, Control, Self-Conscious, Sexual Function) and an overall QOL score. Both the overall symptom severity and QOL scores were recorded, as well as the QOL subscales. All scores are reported on a scale of 0–100. The symptom severity scale is set so that worsening symptoms result in higher scores. The overall QOL and QOL subscales are set so that worsening symptoms result in lower scores. The worst score possible is a symptom severity score of 100 and a QOL score of 0, and the best score possible is a symptom severity score of 0 and a QOL score of 100.

On the day of the embolization procedure, patients were randomly assigned to treatment with either a-PVAM or TAGM using a lottery-type system managed by the independent clinical research organization. Patients were not informed which embolic material was used for their procedure either at the time of the procedure or until the completion of data collection.

All patients were treated according to the standard current protocols at each site. Before UAE, all patients had i.v. access placed and received a single dose of antibiotics (cefazolin, 1 g i.v., or clindamycin, 300 mg i.v., if allergic to penicillin). At arrival to the angio suite, electrocardiogram, blood pressure, and pulse oximetry monitors were placed and baseline values established. Oxygen was administered by nasal cannula throughout the procedure.

Patients were given the option of i.v. conscious sedation or intrathecal (spinal) analgesia, depending on institutional protocols and patient preference. After skin preparation, local anesthesia, and puncture of the right common femoral

**Table 1** Study inclusion and exclusion criteria

<i>Inclusion criteria</i>	
Age	30–50 years
MRI-proven leiomyomas	
Bleeding and/or bulk-related symptoms	
Normal renal function	
Willing and able to undergo follow-up studies	
Participation chosen and informed consent signed	
<i>Exclusion criteria</i>	
Desire for future fertility	
History of gynecologic malignancy	
Pelvic pain as primary symptom	
Known endometrial hyperplasia, adenomyosis, or pelvic inflammatory disease	
Previous invasive treatment for leiomyomas (except for D&C) or GnRH agonist in last 6 months	
Pedunculated subserosal or submucosal fibroidleiomyomas with stalk diameter 50% of leiomyoma diameter	
Uterine volume <250 ml or >24 weeks	

artery, a 5F catheter such as a Levin-1 catheter (Cook Medical, Bloomington, IN) or Cobra Glidecatheter (Terumo Interventional Systems USA) was used to selectively catheterize the left internal iliac artery. An angiogram was then performed to assess the internal iliac artery and its branches, including the uterine artery. The left uterine artery was then selectively catheterized, and a microcatheter such as a Progreat Omega (Terumo Interventional Systems USA) or Renegade Hi-Flo (Boston Scientific) was passed into the transverse segment of the uterine artery, distal to the origin of the cervicovaginal branch when possible, and was used for embolization. Before embolization, a control angiogram was performed through the microcatheter to verify catheter tip position and evaluate the flow in the uterine artery and perileiomyoma vessels.

In both arms of the study, the desired end point for embolization was angiographic demonstration of one of the following: filling of cross-uterine collaterals that were not filled on initial injection of the uterine artery, cessation of visible flow into the ascending ramus of the uterine artery, with “staining” of the lower uterine segment, transient dilation of the uterine artery with injection of embolic particle slurry or contrast, or retrograde flow of contrast from the catheter tip [11]. Once the end point was reached, contrast was again injected through the microcatheter after a 5-min waiting period to determine whether additional embolic material was needed. If additional material was needed, embolization was performed until the previously described end point was reached again.

For patients in the TAGM arm of the study, embolization was started with 500–700- $\mu\text{m}$  particles, unless there was significant reflux across the utero-ovarian collateral on

the pre-embolization injection. In that case, embolization was started with 700–900- $\mu\text{m}$  particles. A total of 6–8 ml of 500–700- $\mu\text{m}$  particles were administered into a uterine artery. If reflux across the utero-ovarian collateral developed before this volume was used, or if this volume was used and the end point had not been reached, then the embolic was upsized to 700–900- $\mu\text{m}$  particles with the next syringe. If the end point had not been reached after 6–8 ml of 700–900- $\mu\text{m}$  particles, then the particle size could again be increased to 900–1,200  $\mu\text{m}$ , with additional particles provided until the end point was reached.

For patients in the a-PVAM arm of the study, embolization was started with 700–900- $\mu\text{m}$  particles. A total of 6–8 ml of 700–900- $\mu\text{m}$  particles was provided into a uterine artery. If the target end point has not been reached, then the particle size was increased to 900–1,200  $\mu\text{m}$ , with additional particles provided until the end point was reached.

After the left uterine artery was embolized, the loop technique of Waltman et al. [12] was used to move the 5F catheter from the left uterine artery into the right uterine artery. The right uterine artery was then catheterized and embolized in the same manner as the left uterine artery. Flush aortography was performed at the completion of the procedure at the discretion of the interventional radiologist performing the procedure. In addition, closure devices were used at the discretion of the treating interventional radiologist. Technical success was defined as successful embolization of one vessel on each side of the uterus, whether both uterine arteries or one uterine artery and one ovarian artery.

Patients were managed postoperatively according to the standard protocols at each site. All patients received medications to address the expected pain and nausea after UAE. Patients were discharged from the hospital when they no longer required i.v. pain medications and were tolerating fluids by mouth.

After the procedure, patients were assessed at 1 week, 3 months, 6 months, and 12 months. Contrast-enhanced MRI examinations of the pelvis were obtained 3–7 days, 3 months, and 6 months after UAE. Patients completed UFS-QOL questionnaires at office visits, by mail, or by telephone interview with the independent clinical research organization 3, 6, and 12 months after the procedure. Beyond this point, study participation was completed, and patients were followed according to each site’s standard clinical protocol.

The images for all MRI examinations were interpreted by an independent reader who was blinded regarding which embolic agent was used. The MRI grader is a board-certified diagnostic radiologist with over 20 years’ experience in body imaging. Pelage et al. [6] have reported that interobserver reliability for this type of scoring is very reliable. The overall perfusion of the entire visible leiomyoma burden was graded. The extent of perfusion

demonstrated on the pre-UAE study was evaluated and used as a basis of comparison for the follow-up imaging. At each follow-up study, the perfusion was scored 1 if there was complete absence of enhancement of all visible leiomyomas, 2 if there was 1–10% residual perfusion, 3 if there was 11–20% residual perfusion, 4 if there was 21–30% residual perfusion, and so on. A score of 1 or 2 ( $\geq 90\%$  leiomyoma devascularization) was considered success, 3 or 4 (70–89% leiomyoma devascularization) was considered a partial success, and  $\geq 5$  ( $< 70\%$  leiomyoma devascularization) was considered a failure.

In addition, measurements of the maximal dimensions (anterior–posterior, right–left, and cephalad–caudad) of the entire uterus and the dominant leiomyoma were obtained and the volume calculated by using the formula for a prolate ellipse ( $L \times D \times W \times 0.52$ ). Given the wide disparity of initial uterine and leiomyoma volumes, the proportional changes in volumes were charted for each MRI follow-up point.

The primary outcome measure for the study was the change in perfusion of the entire fibroid burden demonstrated at contrast-enhanced MRI. The secondary outcome measure was clinical outcome, as indicated by the scores on the UFS-QOL. The tertiary outcome measure was change in the volume of the uterus and dominant fibroid demonstrated at contrast-enhanced MRI. Our hypothesis was that none of these outcomes would differ between the control and study arms by  $> 10\%$ . A target of 44 patients was set for enrollment onto this study (22 patients in each group). Biostat International (Tampa, FL) performed the sample size calculations. The study was designed to detect a difference of 10% at 90% power by two-sided Student's *t*-test (equivalent to 95% power by one-sided Student's *t*-test).

All data were monitored and collated by an independent clinical research organization. All data were entered into spreadsheets in Microsoft Excel. Summary statistics included averages, standard deviations, and 95% confidence intervals. Analysis was performed on an intent-to-treat basis. Charts of results were generated in Excel. All results are reported at a level of two significant figures. Study statistics (tests of hypotheses, *t*-scores, and *P*-values) were calculated by InStat, Prism 3D software (GraphPad Software, San Diego, CA). Results were considered statistically significant at the 95% level ( $P < 0.05$ ). Unless otherwise noted, *P*-values were determined by the two-sided Student's *t*-test.

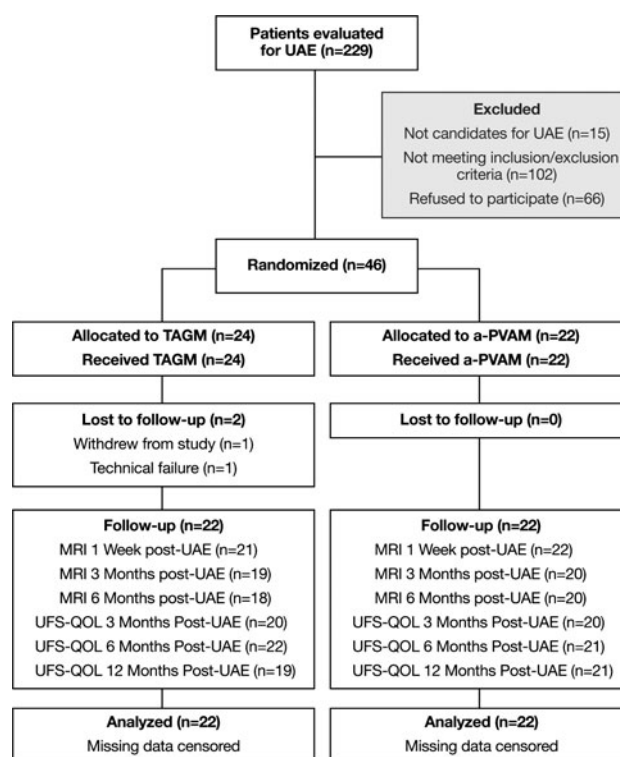
## Results

Site 1 is a 145-bed community hospital with a regional UAE practice. At this site, enrollment onto the study was

open from July 17, 2006, through April 25, 2007. Site 2 is a 651-bed tertiary-care facility with a regional UAE practice. At site 2, enrollment onto the study was open from June 5, 2008, through March 31, 2009. Enrollment and follow-up flow are presented in Chart 1.

The two study groups were similar in age, race, leiomyoma-related symptom severity and overall health-related QOL, QOL subscores, distribution of dominant leiomyomas, and overall volumes of both the uterus as a whole and dominant leiomyomas (Table 2). When compared to the general U.S. population, the study groups had markedly higher proportions of African American women. This is not unusual, given that leiomyomas are significantly more common in African American women than in Caucasians [13, 14].

There was no significant difference between the two study groups in fluoroscopy time, contrast dose, or embolic dose (Table 2). Of the 46 procedures, there was one technical failure, resulting in a technical success rate of 98%. The technical failure occurred in a patient who had an anatomic variant, with the entire uterus supplied by the left uterine artery. There was no right uterine artery and no flow to the right side of the uterus from the right ovarian artery. This patient did have successful embolization of all demonstrated arterial supply to the uterus, but the procedure was considered a technical failure because a bilateral embolization was not performed.



**Chart 1** Study subject flow

**Table 2** Patient demographic and procedural data

Characteristic	a-PVAM	TAGM	P
Age (years)	45 ± 2.2, 33–51	44 ± 2.8, 22–52	0.83 (NS)
Race (n)			0.5 (NS)
African American	16	20	
Caucasian	7	3	
Initial symptom severity	70 ± 7.9, 47–100	68 ± 8.8, 9–100	0.71 (NS)
Initial overall QOL	41 ± 9.6, 7–89	42 ± 19.6, 0–82	0.91 (NS)
Location of dominant leiomyoma (n)			0.77 (NS) ( $\chi^2$ test)
Submucosal	5	3	
Intramural	7	6	
Transmural	8	9	
Subserosal	3	5	
Overall uterine volume (ml)	540 ± 90, 120–940	650 ± 180, 160–1800	0.29 (NS)
Volume of dominant leiomyoma	130 ± 69, 13–740	96 ± 50, 8.3–540	0.42 (NS)
Fluoroscopy time (min)	13 ± 3.6, 5.0–46	11 ± 1.5, 4.9–18	0.25 (NS)
Contrast dose (ml)	110 ± 13, 50–150	97 ± 14, 30–160	0.17 (NS)
Embolic dose (ml)	8.8 ± 2.1, 3–21	9.2 ± 2.3, 3–18	0.78 (NS)

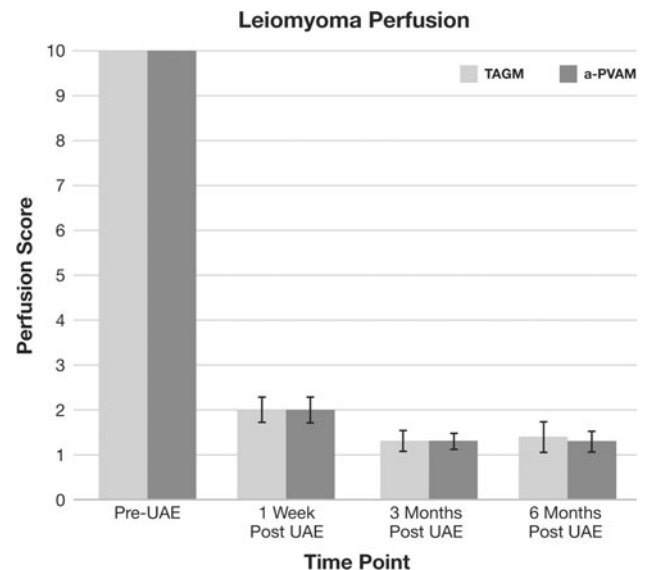
Comparison shows no difference between the two study groups in terms of demographics, clinical presentation, or procedural data. Values provided as mean ± 95% confidence interval, range, unless otherwise indicated

At site 1, a flush aortogram was performed only on the patient whose UAE was a technical failure. At site 2, all patients underwent flush aortography at completion of the UAE. No patient underwent embolization of an ovarian artery or any other anomalous supply to the uterus.

All patients were discharged within 24 h of the procedure. There were no procedural or periprocedural complications in any of the study patients. In the 30-day follow-up period after UAE, one patient sought medical attention for an episode of gastroenteritis, which was diagnosed as viral and seemed to be unrelated to the UAE procedure. Another patient saw her primary care physician with complaints of fatigue and was noted to have mild anemia, although her hemoglobin level was unchanged from before the UAE procedure. This patient received a transfusion of packed red blood cells without incident as treatment for her anemia.

The follow-up data for the patient in whom there was a technical failure are not included in the analysis. In addition, there was one patient who withdrew from the study after her UAE was completed but before any follow-up data were collected. The first of these patients was treated at site 1, and the second at site 2. Both were in the TAGM treatment group. Two more patients were subsequently recruited and treated to bring the study groups for follow-up to 22 in each group. The baseline and procedural data for all 46 patients are listed in Table 2.

Follow-up data were obtained for 86–97% of patients at the various follow-up points, with no significant differences between the two study groups (Chart 1). The missing data points were censored during the statistical analysis to ensure validity of that analysis.

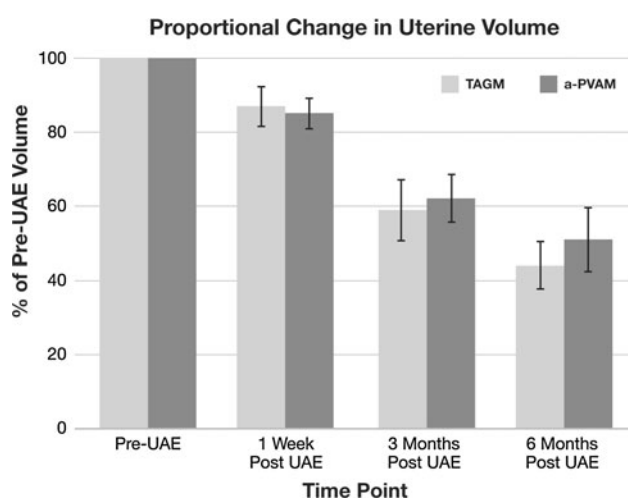


**Fig. 1** Perfusion scores for entire leiomyoma burden (mean, 95% confidence interval)

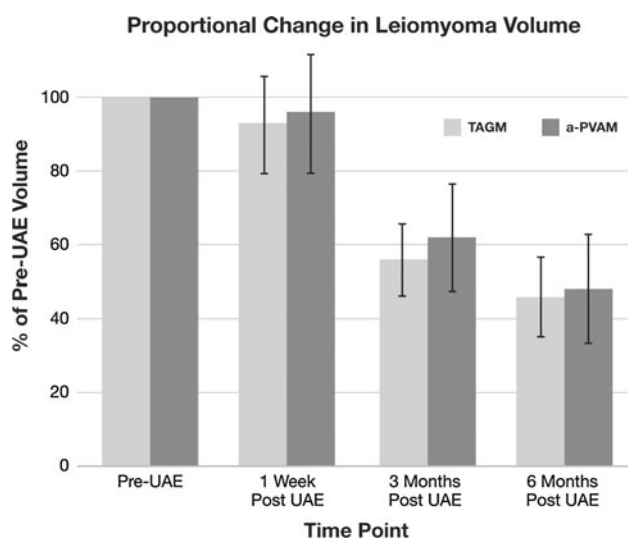
Perfusion of the entire visible leiomyoma burden was graded on the basis of MRIs obtained on the scheduled outlined previously. Thirty-five of 43 (81%) evaluable patients at 1 week after UAE, 38 of 39 (97%) evaluable patients at 3 months after UAE, and 36 of 38 (95%) evaluable patients at 6 months after UAE had successful devascularization ( $\leq 10\%$  residual perfusion) of all visible leiomyomas (Fig. 1). The remaining evaluable patients all showed partially successful embolization (11–30% residual perfusion). There were no failures of embolization by imaging criteria. For each patient, the initial volume of the uterus was set to 100%, and subsequent measurements

converted to proportions of the pre-embolization measure (Fig. 2). *P*-values at all three post-UAE time points ( $P = 0.61$  for 1 week after UAE,  $P = 0.31$  for 3 months after UAE, and  $P = 0.31$  for 6 months after UAE) indicate no significant difference between the two study groups. Measurements of the dominant leiomyoma for each patient were obtained and analyzed in a similar fashion (Fig. 3). *P*-values at all three post-UAE time points ( $P = 0.77$  for 1 week after UAE,  $P = 0.56$  for 3 months after UAE, and  $P = 0.84$  for 6 months after UAE) indicate no significant difference between the two study groups.

The 95% confidence interval was calculated for the mean difference of change in both fibroid devascularization and uterine volume as observed at contrast-enhanced MRI



**Fig. 2** Proportional changes in uterine volume (mean, 95% confidence interval)



**Fig. 3** Proportional changes in volume of the dominant leiomyoma (mean, 95% confidence interval)

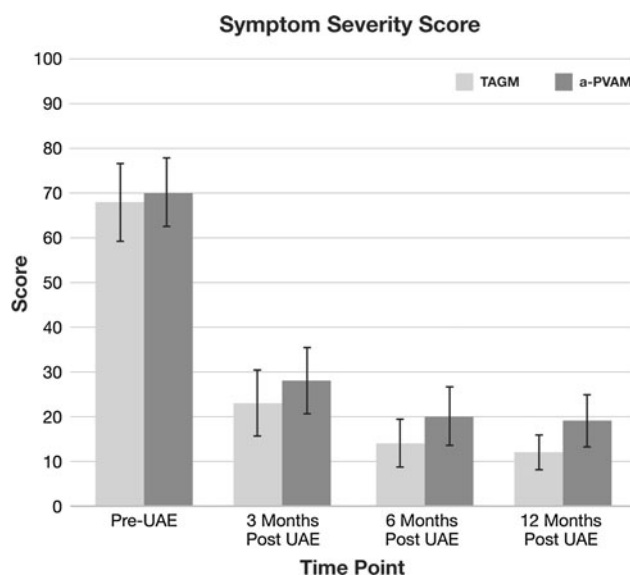
from baseline to several days after UAE, 3 months, and 6 months after UAE between the two study arms. No statistically significant differences were found. Overall, non-inferiority (no statistical differences) was demonstrated between the study groups.

As stated above, the two study groups were similar in pre-UAE symptom severity and QOL scores on the UFS-QOL. The UFS-QOL was administered again at 3, 6, and 12 months after UAE. There was no significant difference in the symptom severity scores between the two groups at any time after UAE (Fig. 4).

The data for overall QOL are presented in Fig. 5. At 3 months after UAE, the TAGM group had a significantly higher QOL score than the a-PVAM group. There was no other significant difference in QOL scores between the two study groups before UAE or at 6 or 12 months after UAE. At 3 months after UAE, four of the six subscales (Concern, Activity, Energy/Mood, and Control) showed the TAGM group with a statistically significant better score than the a-PVAM group. There was no statistically significant difference between the two groups regarding the other two subscales (Self-Conscious and Sexuality). The QOL subscale comparisons are presented in Fig. 6.

With the single exception of the QOL score at 3 months after UAE, noninferiority (no statistical differences) was demonstrated between the study groups.

There were two patients (one in each group) who showed evidence of leiomyoma reperfusion during follow-up. Both of these patients had a good clinical response at 3 and 6 months. The patient from the TAGM group was also doing well at 12 months. The patient from the a-PVAM group had significant (>10-point change) worsening of her scores on the UFS-QOL between 6 and 12 months after



**Fig. 4** Symptom severity scores (mean, 95% confidence interval)

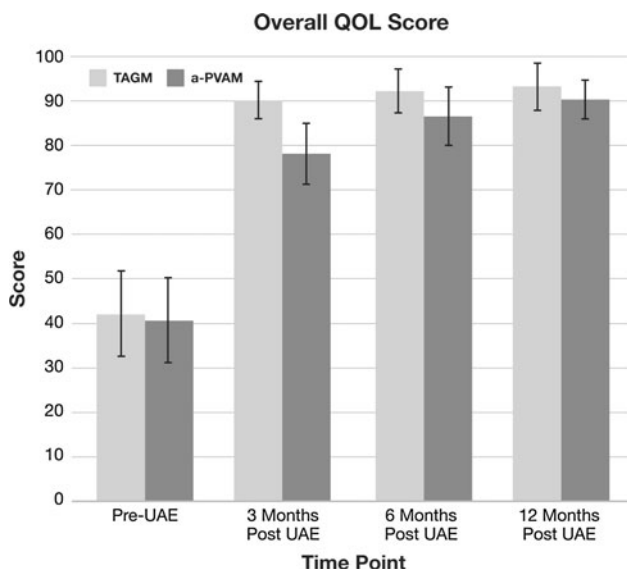


Fig. 5 Overall QOL scores (mean, 95% confidence interval)

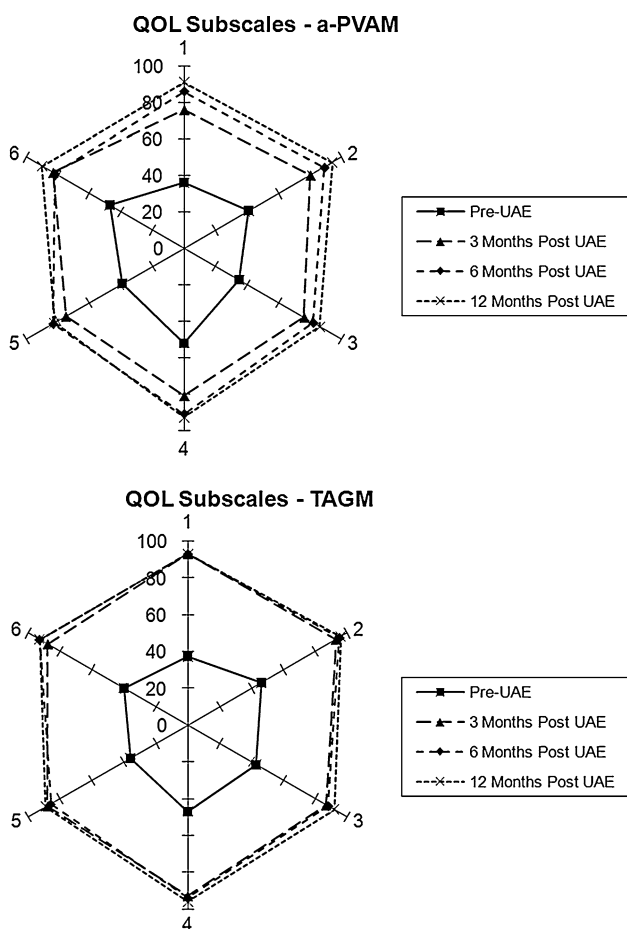


Fig. 6 UFS-QOL quality-of-life subscales. Each axis represents a different subscale. 1 = Concern; 2 = Activities; 3 = Energy/Mood; 4 = Control; 5 = Self-Conscious; 6 = Sexuality

UAE. This suggests that she experienced recurrence of leiomyoma symptoms.

Two patients, one from each group, demonstrated discordance of UFS-QOL results over time. One patient from the TAGM group showed durable improvement in her symptom severity score, but she had significant worsening of her overall QOL score between 6 and 12 months. One patient from the a-PVAM group showed durable improvement in her overall QOL score, but she had significant worsening in her symptom severity score between 6 and 12 months. Both of these patients had successful fibroid devascularization by the study imaging criteria.

### Discussion

Recently, Spies emphasized the need for caution in how interventional radiologists approach technical innovation to the UAE procedure [7]. One of the concerns he raises lies in the potential differences between available embolic agents and how these differences may in turn lead to differences in the clinical outcomes experienced by patients after UAE. In an effort to suggest how best to evaluate the inevitable evolution of the materials used for UAE, Spies suggested that future studies need to be performed with very specific criteria. These studies should be prospective, randomized, blinded (when possible), and performed in well-defined study populations with a sample size determined by an appropriate statistical analysis. End points should include an assessment of symptom severity and QOL using the UFS-QOL questionnaire and an assessment of leiomyoma perfusion using contrast-enhanced MRI. The present study was designed with these requirements in mind in order to determine whether a-PVAM was noninferior to TAGM in both clinical and imaging outcomes after UAE.

Other studies have compared the performance of various embolic agents for UAE. However, most of these studies have not been prospective randomized, controlled trials, which limits their conclusions. Several studies have compared TAGM to spherical non-hydrogel polyvinyl acetate (PVA)-based microspheres (Contour SE Microspheres; Boston Scientific); they demonstrated that this agent does not perform satisfactorily for UAE [2, 3]. The a-PVAM used in this study is quite different from the non-hydrogel PVA-based microspheres that have been deemed unacceptable for use in UAE procedures. As a hydrogel microsphere, a-PVAM are much more similar in performance to TAGM than to nonhydrogel preparations of PVA.

In the present study, 15 different comparisons were made between the two study groups, evaluating residual leiomyoma perfusion, volume changes, symptom severity, and overall QOL after UAE. Fourteen of these 15

comparisons showed no significant differences between the two study groups. These findings support the hypothesis that a-PVAM are noninferior to TAGM as an embolic agent for UAE.

A major caveat to this assertion is that the embolic particle size has to be appropriately chosen. a-PVAM particles are softer and more compressible than TAGM particles [10] and thus have the potential to penetrate further into the vascular bed than do TAGM [15, 16]. On the basis of these previous studies, a-PVAM of any specific size range seems to perform similarly to TAGM of the next smaller size range. Because the target vessels for UAE are the vessels of the perileiomyoma vascular plexus [17], standard protocol has been to use 500–700- $\mu\text{m}$  TAGM [1, 3, 18, 19]. The 500–700- $\mu\text{m}$  a-PVAM are effectively smaller than is desirable for UAE [9, 20]. This is why the protocol specified the use of 700–900- $\mu\text{m}$  a-PVAM, which are similar in embolic performance to 500–700- $\mu\text{m}$  TAGM. The U.S. FDA requested this approach while reviewing the investigational device exemption application.

This thought process was important for this study and for all future studies evaluating new embolic agents for UAE. The compressibility, elasticity, and depth of penetration of any new embolic particle should be evaluated before it is put into clinical use so that the appropriate size can be chosen for this and any other indication.

This difference might help to explain the recent findings of Abramowitz et al. [21]. In a retrospective study comparing the performance of four embolic agents (TAGM, “traditional” nonspherical PVA, nonhydrogel PVAM, and a-PVAM) in UAE, they concluded that a-PVAM did not perform adequately for UAE. However, in the study of Abramowitz et al., UAE was performed with both 500–700- $\mu\text{m}$  and 700–900- $\mu\text{m}$  particles. The small microspheres used were likely not appropriate for use in UAE procedures.

In the present study, 42 of 44 patients (95.5%) demonstrated durable leiomyoma devascularization after UAE, with no significant differences observed between the two embolic agents used. There were also two other patients who had suboptimal clinical outcomes over time, despite durable fibroid devascularization. It is generally accepted that the clinical success rate for UAE is approximately 90% for control of bleeding-related symptoms and approximately 80–85% for control of bulk-related symptoms [22, 23]. These four cases were still well within these expectations.

This study could be improved in a number of areas. The study was powered at 90%, and the results obtained are statistically significant at a power of 95%. A larger study might possibly resolve the issue of the difference in QOL at 3 months after UAE, which may be a statistical anomaly within the current study. A larger sample size would also

allow for a more extensive statistical examination. However, to significantly increase the power of the study would require a much larger sample size, on the order of 75–100 patients per arm. Because of losses to follow-up, the analyzed data are less than expected in the original study design. Increasing enrollment might have provided a data set that more fully met the study design. There were a total of eight protocol deviations regarding inclusion and exclusion criteria. Two patients older than 50 were enrolled, one in each treatment group. Both were clearly premenopausal. Six patients were enrolled whose uteri were at or below the lower size limit of 250 ml. These patients were fairly evenly distributed between the treatment groups, with four in the a-PVAM group and two in the TAGM group. We think that these deviations do not significantly affect the study results.

In conclusion, this study demonstrates that a-PVAM are not inferior to TAGM as an embolic agent for UAE. Of particular importance, however, is particle size selection based on the compressibility, elasticity, and depth of penetration of the agents that were evaluated in this study. Therefore, it is important to note that it was the 700–900- $\mu\text{m}$ -size a-PVAM that was found to be noninferior to TAGM for UAE.

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