Radiology

ORIGINAL RESEARCH • VASCULAR AND INTERVENTIONAL RADIOLOGY

Prostatic Artery Embolization for the Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: 10 Years' Experience

Francisco Cesar Carnevale, MD, PhD • *Airton Mota Moreira, MD, PhD* • *Andre Moreira de Assis, MD* • *Alberto Azoubel Antunes, MD, PhD* • *Vanessa Cristina de Paula Rodrigues* • *Miguel Srougi, MD, PhD* • *Giovanni Guido Cerri, MD, PhD*

From the Department of Radiology (F.C.C., A.M.M., A.M.d.A., V.C.d.P.R., G.G.C.) and Division of Urology (A.A.A., M.S.), University of São Paulo Medical School, Av. Dr. Enéas Carvalho de Aguiar, 255, São Paulo, SP 05403-000, Brazil. Received June 12, 2019; revision requested July 16; revision received March 11, 2020; accepted April 14. **Address correspondence to** F.C.C. (e-mail: *francisco.carnevale@criep.com.br*).

Supported in part by Merit Medical Systems.

Conflicts of interest are listed at the end of this article.

Radiology 2020; 00:1–8 • https://doi.org/10.1148/radiol.2020191249 • Content codes: IR VA

Background: Long-term experience with prostatic artery embolization (PAE) for benign prostatic hyperplasia remains limited.

Purpose: To evaluate the efficacy, safety, and long-term results of PAE for benign prostatic hyperplasia.

Materials and Methods: This retrospective single-center study was conducted from June 2008 to June 2018 in patients with moderate to severe benign prostatic hyperplasia–related symptoms. International Prostate Symptom Score (IPSS), quality-of-life score, maximum urinary flow rate, postvoid residual volume, prostate-specific antigen (PSA), and prostate volume were assessed. PAE was performed with 100–500-μm embolic microspheres. Mixed-model analysis of variance and Kaplan-Meyer method was accessed, as appropriate.

Results: A total of 317 consecutive men (mean age ± standard deviation, 65 years ± 8) were treated. Follow-up ranged from 3 months to 96 months (mean, 27 months). Bilateral and unilateral PAE was performed in 298 (94%) and 19 (6%) men, respectively. Early clinical failure occurred in six (1.9%) and symptom recurrence in 72 (23%) men at a median follow-up of 72 months. Mean maximum improvement was as follows: IPSS, 16 points ± 7; quality-of-life score, 4 points ± 1; prostatic volume reduction, 39 cm^3 ± 39 (39% ± 29); maximum urinary flow rate, 6 mL/sec ± 10 (155% ± 293); and postvoid residual volume, 70 mL ± 121 (48% ± 81) ($P < .05$ for all). Unilateral PAE was associated with higher recurrence (42% vs 21%; $P = .04$). Baseline PSA was inversely related with recurrence (hazard ratio, 0.9 per nanograms per milliliter of PSA; 95% confidence interval [CI], 0.8, 0.9; $P < .001$). Embolization with combined particle sizes (100–500 μm) did not relate to symptom recurrence (hazard ratio, 0.4; 95% CI: 0.2, 1.1 for 100–500-μm group vs 300–500-μm group and hazard ratio, 0.4; 95% CI: 0.1, 1.5 for 100–500-μm group vs 100–300-μm group; $P = .19$).None of the patients presented with urinary incontinence or erectile dysfunction.

Conclusion: Prostatic artery embolization was a safe and effective procedure for benign prostatic hyperplasia with good long-term results for lower urinary tract symptoms.

Online supplemental material is available for this article.

Benign prostatic hyperplasia is one of the most common diseases of middle-aged and older men (1). Benign prostatic hyperplasia–associated morbidities affect as many as 75% of men in the United States by age 70 years. Estimated annual costs of treatment for lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia in the United States currently total $3.9 billion dollars (2,3). Medications are the first-line noninvasive treatment to control LUTS. Several minimally invasive treatment alternatives have been developed in recent years, including lasers and lift implants aiming to reduce the adverse effects of traditional surgeries (4,5).

Prostatic artery embolization (PAE) has been widely used by interventional radiologists during the past decades to treat urological bleeding from different prostatic causes (6). DeMeritt et al (7) first reported selective PAE for the treatment of benign prostatic hyperplasia as consequence of the treatment of refractory hematuria in 2000. In 2008, Carnevale et al (8) performed the first intentional treatment of LUTS due to benign prostatic hyperplasia using PAE as a successful minimally invasive endovascular modality of treatment.

A decade after PAE was introduced in clinical practice, there have been multiple reports of symptom reduction, quality-of-life improvement, and reduction of prostate size (9–14). The use of intraprocedural cone-beam CT has improved the accuracy as well as the efficacy of the procedure (15,16).

Long-term follow-up of patients after PAE is needed to understand treatment efficacy and safety. Therefore, the purpose of this study was to evaluate the efficacy, safety, and long-term results of PAE for benign prostatic hyperplasia.

Abbreviations

CI = confidence interval, IPSS = International Prostate Symptom Score, LUTS = lower urinary tract symptoms, PAE = prostatic artery embolization, PSA = prostate-specific antigen

Summary

Prostatic artery embolization was a safe and effective treatment for men with benign prostatic hyperplasia that resulted in long-term improvements for lower urinary tract symptoms and quality of life.

Key Results

- Prostatic artery embolization for lower urinary tract symptoms due to benign prostatic hyperplasia resulted in a 39% reduction of prostate volume at mean follow-up of 27 months, with symptoms recurring in 23% of men at a median follow-up of 72 months.
- After embolization, the International Prostate Symptom Score and quality-of-life score improved by an average of 16 points and 4 points, respectively.
- Men with greater baseline prostate-specific antigen had lower likelihood of symptom recurrence (hazard ratio, 0.9 per nanograms per milliliter of prostate-specific antigen; $P < .001$).

Materials and Methods

Study Participants and Postprocedural Management

The institutional review board approved this single-center retrospective cohort study and all participants signed written informed consent to take part in the study. Merit Medical Systems provided research grant funding to support the first 11 men treated at our institution. Several of the men included in this data set were treated during Merit Medical Systems–funded training courses in support of the BPH-P3–12–01 study (ClinicalTrials.gov identifier, NCT01789840).

Consecutive men included in this review were treated with PAE at the Radiology Institute of the University of São Paulo from June 2008 to June 2018 to treat moderate to severe LUTS with available technical and clinical data (Fig 1). Inclusion criteria comprised men older than 45 years with a diagnosis of moderate to severe LUTS, defined as International Prostate Symptom Score (IPSS) greater than 7 due to benign prostatic hyperplasia refractory to medical treatment (α1-adrenergic receptor antagonist and/or 5-α-reductase inhibitor) for at least 6 months and a prostate volume greater than 30 cm^3 as assessed with MRI. Exclusion criteria for PAE included biopsy-proven prostatic cancer, active prostatitis or urinary tract infection, previous surgical procedure or other invasive treatment for benign prostatic hyperplasia, any disorder impacting bladder function, large bladder diverticula or bladder stones, chronic renal failure, or inability to undergo MRI.

Predictors for outcomes and recurrence were analyzed during long-term follow-up. Of note, of the reported cohort, 155 men have been previously described with a focus on PAE results according to medications, embolic agents, prostate size, and techniques (17–21) (Table E1 [online]).

Embolization Technique

All the men underwent PAE according to previously described methods (22,23). All the men received a single 400-mg intravenous dose of ciprofloxacin before the procedure, followed by 500 mg orally twice per day for 7 days after PAE. If necessary, the men were advised to take nonsteroidal anti-inflammatory medications, opioid analgesics, or both after the procedure. A daily 0.4-mg capsule of tamsulosin was prescribed for 1–4 weeks after PAE to reduce postembolization syndrome and was discontinued afterward.

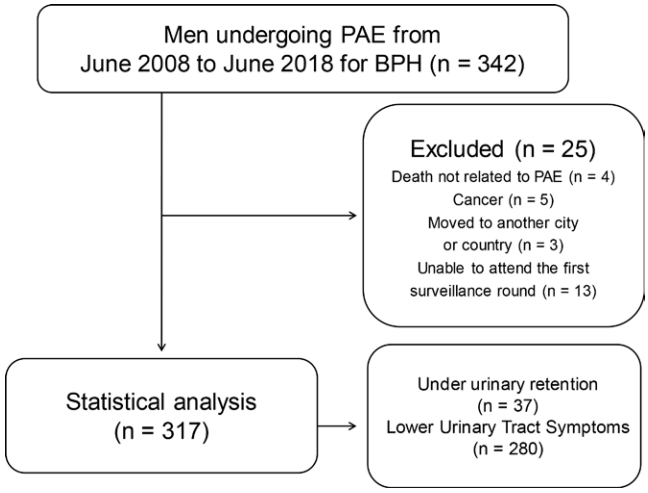

Figure 1: Flow diagram shows inclusion and exclusion criteria. BPH = benign prostatic hyperplasia, PAE = prostatic artery embolization.

Procedures were performed under local anesthesia through unilateral femoral approach, and the prostatic arteries were catheterized by using 2.4-F or smaller microcatheters (Progreat; Terumo, Japan) and cone-beam CT (0.3 mL/sec; 3–5 mL by using power injection with 5-second spin and 10-second delay), when necessary. In most of the men, bilateral PAE was performed with 100–500-μm trisacryl gelatin microspheres (Embosphere Microspheres; Merit Medical Systems, South Jordan, Utah). Whenever possible, the microcatheter was distally inserted into the prostate arterial branches, and then more embolic material was injected according to the Proximal Embolization First, Then Embolize Distal technique (Fig 2) (23). The men were discharged from the hospital on the same day as PAE and were followed by both the urologist and the interventional radiologist. In men with urinary retention, the first attempt to remove the Foley catheter was performed 1–2 weeks after PAE.

Outcome Evaluation

Primary end point was improvement in the mean IPSS and quality-of-life score. Secondary end points were changes in maximum urinary flow rate, postvoid residual volume assessed with US, prostate-specific antigen (PSA) level, and prostatic volume according to MRI at 3 months and 12 months after the procedure, and every 12 months thereafter. PSA level was assessed before PAE and at 24 hours, 3 months, 12 months, and every 12 months after the procedure. Baseline data were obtained before PAE (Table 1).

Technical success was defined as bilateral PAE, and the overall results of embolization were evaluated at 3 months, 12 months, and annually after PAE. Reduction of IPSS, postvoid residual volume, and PSA level were analyzed as well as improvement of the quality-of-life score and maximum urinary flow rate.

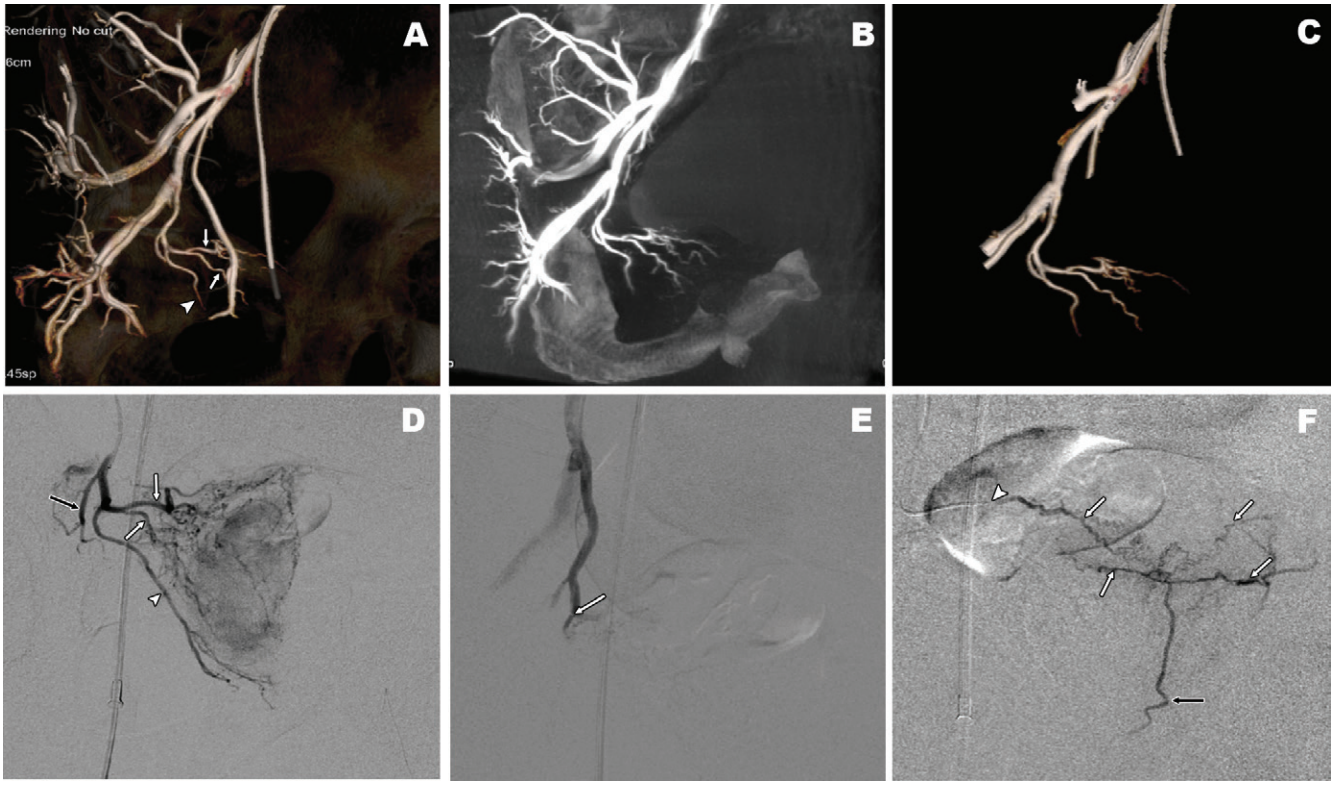

Figure 2: *A,* Three-dimensional rotational angiography reconstruction using cone-beam CT software shows right prostatic posterolateral (arrowhead) and anteromedial branches (arrows), as well as other right-sided pelvic arteries. *B,* Reconstruction, including soft tissues, confirms right-lobe prostatic vascular anatomy. *C,* Arterial segmentation reconstruction shows best oblique angulation to be used as road-map guide, avoiding use of additional digital subtraction arteriogram (DSA). *D,* Selective ipsilateral oblique DSA shows right posterolateral (arrowhead) and anteromedial (white arrows) prostatic branches, right seminal vesical artery (black arrow), and right-lobe intraprostatic branches. *E,* DSA after embolization with tip of microcatheter at main trunk of prostatic artery (arrow) shows occlusion of distal intraprostatic branches, and reflux to origin of right prostatic artery. *F,* After distal navigation of microcatheter (arrowhead) for Proximal Embolization First, Then Embolize Distal technique, DSA shows intraprostatic branches still patent (white arrows) and opened collateral shunt (black arrow).

Clinical success was considered improvement of LUTS assessed by using IPSS and quality-of-life questionnaires (scores <8 and <3, respectively), or removal of indwelling catheters in men with urinary retention prior to PAE (17).

Clinical failure was divided into early and late recurrence. Early clinical failure was defined as the impossibility of indwelling catheter removal in men with urinary retention, the need for LUTS medication, or the need of any other additional treatment during the first 3 months after PAE. Recurrence was defined as the need for any additional LUTS retreatment (medication, surgical procedure, or prostatic artery re-embolization) after 3 months of follow-up. Follow-up time was divided into short term (<12 months), medium term (from 12–36 months), and long term (after 36 months). A modified Clavien-Dindo grading system (grades I–IV) for classification of surgical complications adapted to PAE was used to report adverse events and complications. Regarding the intensity of the event, grades I and II are reported as minor and grades III and IV, as major (24).

Statistical Analysis

All statistical tests were performed by using SAS (version 9.4; SAS Institute, Cary, NC). Baseline and follow-up values for IPSS, quality-of-life score, maximum urinary flow rate, prostatic volume, postvoid residual volume, and PSA level entered the model as parametric variables, described as means or medians as appropriate with standard deviations. Values were compared between time points by using a mixed-model analysis of variance and Tukey multiple comparison tests.

Outcomes assessment regarding laterality (unilateral vs bilateral embolization) was performed by using the nonparametric Wilcoxon and the Pearson Chi-square tests. Overall recurrence-free survival was obtained by using the Kaplan-Meier method to account for incomplete follow-up time points. Comparison of the sizes of particles was assessed with the log-rank test. The analysis of outcomes regarding microsphere sizes was performed comparing three groups: 100–300 μm, 300–500 μm, and a combination of 100–300 μm with 300–500 μm (100–500 μm). Predictors of recurrence-free survival were assessed by using Cox proportional hazards for both univariable and multivariable analysis. Once the cohort was a single-center study, all available data were assessed without sample power evaluation. The significance level for all statistical tests was defined as a two-sided *P* value of .05 or less.

Results

A total of 342 men met the inclusion criteria and were treated with PAE, of whom 317 had complete data for statistical evaluation. Twenty-five men were excluded due to reasons not related to PAE or difficulties following the clinical and imaging

Table 1: Baseline Characteristics of 317 Men Included in the Study

Variable	Mean and Standard Deviation	Range	No. of Men
Age (y)	65 ± 8	46–91	317
IPSS	19.7 ± 6.3	2–35	279
Quality-of-life score	4.8 ± 0.9	0–6	316
Prostatic volume (cm^3)	93 ± 49	30–330	316
PVR (mL)	108 ± 118	0–790	244
PSA level (ng/mL)	5.4 ± 5.4	0.2–37.5	317
Q_{max} (mL/sec)	6.8 ± 4.1	0–25	289

Note.—IPSS = International Prostate Symptom Score, PSA = prostate-specific antigen, PVR = postvoid residual volume, Q_{max} = maximum urinary flow rate.

protocol (Fig 1). Patients' baseline characteristics are summarized in Table 1 and variables with numbers of men at risk at several time points are shown in Table 2.

Thirty-seven of 317 men (12%) had indwelling catheters due to urinary retention at the time of study inclusion. The indwelling catheter was removed in 34 of 37 (92%), in a mean of 13.3 days ± 10.4 (standard deviation) after PAE (range, 1–60 days). Early clinical failure occurred in six of 317 (2%) men, of whom three were unable to have the indwelling catheter removed (three of 37, 8%). The other three men (three of 280, 1%) did not present LUTS improvement within the 3-month follow-up period.

Technical success (bilateral PAE) was achieved in 298 of 317 men (94%). Unilateral PAE was achieved in 19 men (6%). The PAE procedure lasted 67–379 minutes (mean, 160 minutes ± 46), and the fluoroscopy time was 20–181 minutes (mean, 49 minutes ± 18). The PAE particle size for treatment changed over time (Table E2 [online]).

Follow-up data ranged 3–96 months (mean, 27 months) and are presented in Figure 3 with the point estimates and 95% confidence intervals (CIs) of the change from baseline in the effectiveness variables after PAE. Mean baseline PSA level (5.4 ng/mL ± 5.4) increased to 130 ng/mL ± 173 (range, 0.3–761 ng/mL; $P < .001$) 24 hours after PAE. However, at 3-month follow-up, mean PSA level was lower than at baseline (by 2.3 ng/mL ± 1.9; $P < .001$). Mean maximum improvement was as follows: IPSS, 16 points ± 7; quality-of-life score, 4 points ± 1; prostatic volume reduction, 39 cm^3 ± 39 (39% ± 29); maximum urinary flow rate, 6 mL/sec ± 10 (155% ± 293); and postvoid residual volume, 70 mL ± 121 (48% ± 81) ($P < .05$ for all).

Kaplan-Meier estimates of recurrence-free survival were 89% ($n = 242$; 95% CI: 85%, 93%) at 12-month follow-up, 80% ($n = 121$; 95% CI: 74%, 85%) at 30-month follow-up, and 35% ($n = 7$; 95% CI: 20%, 54%) at 78-month follow-up.

LUTS Recurrence

Symptom recurrence occurred in 72 of 317 men (23%). The mean and median time for recurrence was 67.4 months and 72 months, respectively. Men with LUTS recurrence were treated with α1-adrenergic receptor antagonist (34 of 72, 47%), transurethral resection of the prostate (26 of 72, 36%), or repeat PAE (12 of 72, 17%). Figure 4 demonstrates LUTS recurrence-free survival during follow-up.

Table 3 shows data comparing bilateral with unilateral PAE. Men treated with unilateral PAE were older than those treated with bilateral PAE (aged 71 years vs 65 years, respectively; $P < .001$). LUTS recurrence was more common when unilateral PAE was performed ($P = .04$), occurring in eight of 19 men (42%) treated with unilateral PAE and in 64 of 298 (21%) of men treated with bilateral PAE. Nevertheless, the log-rank analysis comparing unilateral and bilateral PAE groups showed no statistically significant difference in the median time to recurrence between them during follow-up (48 months and 72 months, respectively) ($P = .19$) (Fig 5).

Log-rank analysis comparing microsphere sizes demonstrated that the three groups of men (100–300-μm group, 300–500-μm group, and 100–500-μm group) had no difference in the median time to recurrence among them during follow-up ($P = .16$). The univariable Cox proportional hazards analysis did not show difference between microsphere sizes (hazard ratio, 0.4; 95% CI: 0.2, 1.1 for 100–500-μm group vs 300–500-μm group and hazard ratio, 0.4; 95% CI: 0.1, 1.5 for 100–500-μm group vs 100–300-μm group; $P = .19$). However, LUTS recurrence occurred less in patients treated with 100–500-μm (five of 87, 6%) than 100–300-μm (five of 17, 29%) or 300–500-μm (62 of 213, 29%) microspheres ($P < .01$, Fisher exact test).

Baseline PSA level was inversely related to LUTS recurrence. In multivariable analysis adjusted for age, unilateral and bilateral PAE, and embolic agent, the baseline PSA level was an independent predictor of recurrence outcomes after PAE (hazard ratio, 0.9 per nanograms per milliliter of PSA; 95% CI: 0.8, 0.9; $P < .001$).

Adverse Events and Complications

Adverse events after PAE according to the Clavien-Dindo grading system adapted to PAE (24) are shown in Table 4. All men had at least mild dysuria, frequency, burning during voiding, and some episodes of urgency or urinary incontinence. Most frequent major complications were urinary tract infection and collapsed asymmetric median lobe (0.6% each). None of the men presented with urinary incontinence or erectile dysfunction during short-, medium-, and long-term follow-up.

Discussion

We addressed the safety, effectiveness, and long-term outcomes of prostatic artery embolization in men with lower urinary tract symptoms (LUTS), complicated or not with urinary retention due to benign prostatic hyperplasia–enlarged prostates. PAE resulted in an average reduction of prostate volume of 39% and improved International Prostate Symptom Score and quality-of-life score by a mean of 16 points and 4 points, respectively. Men with greater baseline prostate-specific antigen (PSA) level had less likelihood of symptom recurrence (hazard ratio, 0.9 per nanograms per milliliter of PSA; $P < .001$), and LUTS recurrence was observed in 23% of men at a median follow-up of 72 months. Similar to previously described data (10–12,25,26), we observed a considerable improvement in LUTS at short-, medium-, and long-term follow-up. Improve-

Table 2: Numbers of Men at Risk

Months of Follow-up	PSA	IPSS	Quality-of-Life Score	Q_{max}	Prostatic Volume	PVR
Before PAE	317	279	316	289	316	244
3	260	283	284	210	251	144
12	182	241	241	149	170	134
24	93	173	173	78	84	60
36	53	121	121	46	57	32
48	27	75	78	13	21	13
60	7	26	26	5	7	2
72	7	10	10	7	6	2
84	4	1	1	1	2	2
96	1	1	1	0	0	0

Note.—IPSS = International Prostate Symptom Score, PAE = prostatic artery embolization, PSA = prostate-specific antigen, PVR = postvoid residual volume, Q_{max} = maximum urinary flow rate.

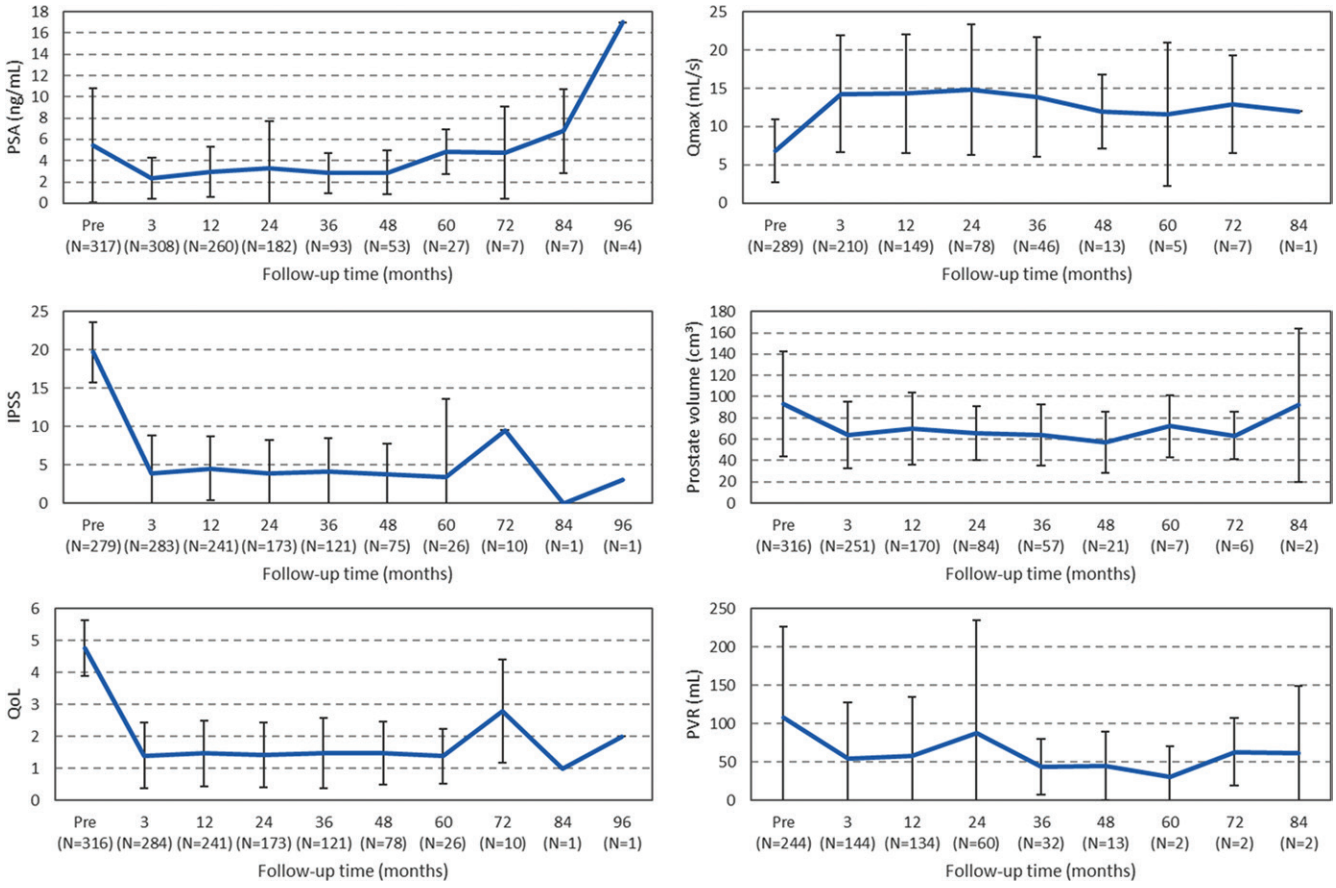

Figure 3: Graphs with line chart show changes in prostate-specific antigen (PSA) level, International Prostate Symptom Score (IPSS), quality-of-life (QoL) score, maximum urinary flow rate (Q_{max}), prostate volume, and postvoid residual volume (PVR) over time after prostatic artery embolization (PAE). Vertical bars indicate point estimates and 95% confidence intervals. Pre = before PAE.

ments were also obtained in the urinary flow as reductions in PSA level and postvoid residual volume.

One of the most common questions raised about PAE is about its durability. Although 63% of the men were free of LUTS recurrence at 60-month follow-up, our study reports a high rate of long-term recurrence, especially after 72 months. In our cohort, LUTS recurrence was defined as IPSS greater than 7 points, quality-of-life score greater than 2 points, and the need for any additional treatment after PAE, including medications, surgical procedures, or repeat PAE. LUTS recurrence occurred in 72 of 317 men (23%) at a mean follow-up of 27 months. Overall, the mean and median time for LUTS recurrence was 67.4 months and 72 months (range, 3–96 months), respectively. None of the men with recurrent symptoms presented urinary retention after PAE. Among men with LUTS recurrence, 47% were retreated with α-1-adrenergic receptor antagonist. This group of men still has the opportunity for a repeat PAE in the future, if necessary. Repeat PAE was performed in 12 of 72 men (17%), with good

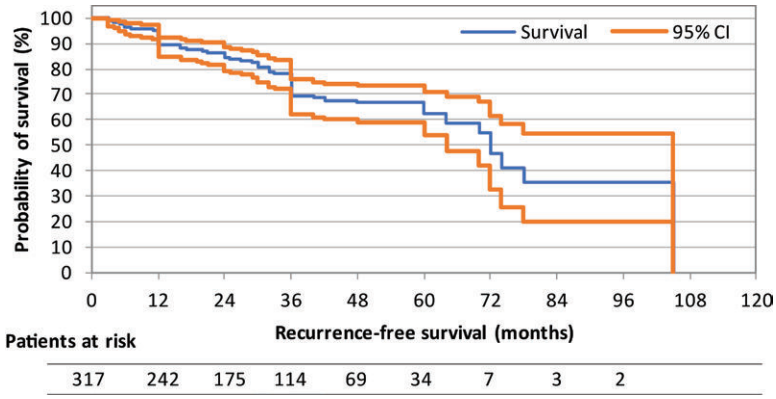

Figure 4: Kaplan-Meier curve shows recurrence-free survival from lower urinary tract symptoms following prostatic artery embolization for benign prostatic hyperplasia. CI = confidence interval.

Table 3: Baseline Characteristics for the 317 Men Divided into Unilateral and Bilateral Prostatic Artery Embolization Groups

Variable	Unilateral (n = 19)	Bilateral (n = 298)	P Value
Age (y)			< .001
Mean	71 ± 8	65 ± 8	
Median*	71 (67–77)	65 (59–70)	
PSA (ng/mL)			.73
Mean	6.7 ± 7.3	5.3 ± 5.2	
Median*	4.9 (1.9–7.7)	3.9 (2.2–6.6)	
IPSS			.83
Mean	20 ± 6	20 ± 6	
Median*	20 (15–22)	20 (15–25)	
Quality-of-life score			.05
Mean	5 ± 1	5 ± 1	
Median*	5 (5–6)	5 (4–5)	
Q_{max} (mL/sec)			.83
Mean	6.5 ± 2.7	6.8 ± 4.2	
Median*	6 (5–10)	6 (4–9)	
Prostatic volume (cm^3)			.22
Mean	87 ± 56	94 ± 49	
Median*	64 (62–120)	82 (30–112)	
PVR (mL)			.24
Mean	112 ± 61	108 ± 121	
Median*	118 (56–164)	74 (30–140)	
Embolic agent†			
100–300 μm	0	17	.23
100–300 and 300–500 μm	3	84	
300–500 μm	16	197	
Recurrence‡	8 (42)	64 (21)	.04

Note.—Unless otherwise specified, data are means ± standard deviation. IPSS = International Prostate Symptom Score, PSA = prostate-specific antigen, PVR = postvoid residual volume, Q_{max} = maximum urinary flow rate.

* Data in parentheses are interquartile ranges.

† Data are the number of patients treated with embolic agent for unilateral and bilateral prostatic artery embolization.

‡ Data are the number of patients, with percentages in parentheses.

clinical results, showing another advantage of PAE. The other 26 of 72 (36.1%) men preferred to be treated with transurethral resection of the prostate. Among these men, some presented prostate downsizing after PAE and were treated with transurethral resection of the prostate instead of open surgery. LUTS recurrence occurred twice more in unilateral than bilateral PAE (42% vs 21%; P = .04). However, the mean time for recurrence was not different at the same follow-up period (P = .19). Men treated with unilateral PAE were older than were those treated with bilateral PAE (aged 71 years vs 65 years, respectively; P < .001). Our data are in accordance with others when comparing unilateral and bilateral PAE (27). In another publication, unilateral PAE was associated with a smaller mean IPSS reduction when compared with bilateral PAE (32.9% vs 54.4%; P = .03) (28). In general, unilateral PAE improves LUTS—however, with worse long-term outcomes.

Because of the subjectivity of the IPSS and quality-of-life questionnaires, we considered that the best criteria for the analysis of clinical failure would be the need for retreatment during any follow-up period. Higher early clinical failure was observed in men with urinary retention compared with LUTS (8% vs 1%, respectively). This fact could be related not only to prostate enlargement itself, but also due to severe bladder impairment.

Twenty-four hours after PAE, the mean value of PSA level increased 24 times compared to baseline (P < .001), decreasing to 50% when compared with baseline at 3-month follow-up. This fact could support the rationale between prostate ischemia after embolization with 24-hour PSA level elevation and clinical success. PSA level returned to pre-PAE levels 5 years after PAE due to prostate regrowth resulting from revascularization and/or recanalization.

In multivariable analysis, baseline PSA and LUTS recurrence (P < .001) were inversely related. Because there is a direct correlation between PSA level and prostate size, this fact suggests that men with larger prostates could be considered as the best candidates for PAE. This information has been recently observed in the UK Register of Prostate Embolization, or UK-ROPE, study (28), when men with larger prostates had a greater IPSS reduction (median of 65%) compared with those with smaller prostates (median of 46%).

Most adverse events related to PAE were transient and linked to postembolization syndrome due to prostate infarct. Most common symptoms such as dysuria, burning during voiding, frequency, urgency, and incontinency are related to prostate ischemia and inflammatory processes. Symptoms are transient (lasting 1 week). Anti-inflammatory drugs and analgesics are usually enough to control pain. Periprostatic organs and structures such as the bladder, rectum, penis, seminal vesicle, pelvis, bones, and skin may be damaged by nontargeted embolization, especially due to the

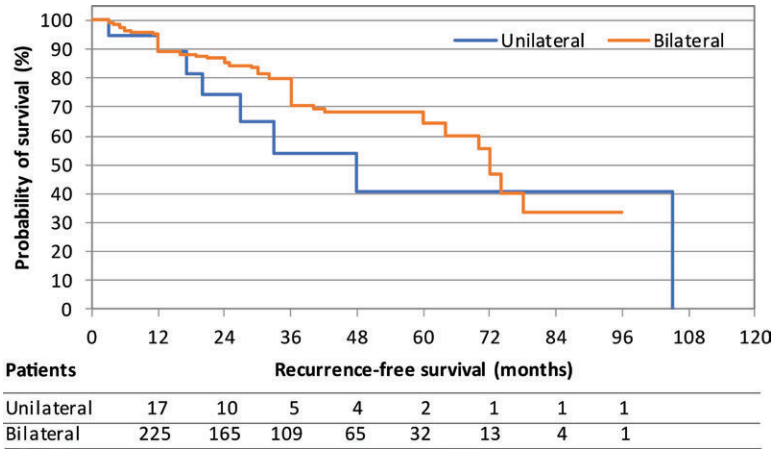

Figure 5: Kaplan-Meier curve shows estimated cumulative probability of recurrence of lower urinary tract symptoms after unilateral and bilateral prostatic artery embolization.

Table 4: Prostatic Artery Embolization–related Adverse Events and Complications

Adverse Events and Complications	No. of Men (n = 317)
Minor	
Self-limiting hematuria	18 (6)
Ejaculatory volume reduction	16 (5)
Self-limiting hematospermia	15 (5)
Inguinal bruise	13 (4)
Low fever	12 (4)
Self-limiting hematochezia	11 (4)
Urinary tract infection	9 (3)
Prostatic tissue elimination	5 (2)
Penile ulcer	4 (1)
Diarrhea	3 (1)
Pubic bone infarct	2 (1)
Transient bladder ischemia	2 (1)
Urethral trauma (Foley placement)	1 (0)
Major	
Persistent urinary tract infection	2 (1)
Collapsed asymmetric median lobe	2 (1)
Bladder urothelium ischemia	1 (0)

Note.—Data in parentheses are percentages.

misidentification of the normal vascular anatomy and variants, or due to inadvertent embolic reflux (24). Two men (two of 317, 1%) who were candidates for open prostatectomy due to large glands and greater than 1.5-cm intravesical protrusion presented with hematuria during the first months after PAE. US and MRI showed bladder ischemia. One of the men was treated conservatively and the other underwent a transurethral resection of the bladder confirming urothelial ischemia. Four men treated with smaller microspheres presented transient penile ulcer. Ulcers were healed after 1 month and were related to nontargeted embolization during embolic reflux or intraprostatic shunt opening during embolization. Two men (two of 317, 1%) had to be referred for transurethral resection of the prostate during the first month after PAE due to collapsed infarcted asymmetric median lobe that was flopping over the internal urethra orifice. In our opinion, big median lobes with asymmetric intravesical protrusion should be a concern when performing PAE.

Our study also showed that LUTS recurrence was less common with 100–500-μm microspheres (five of 87, 6%) compared with 100–300-μm (five of 17, 29%) and 300–500-μm (62 of 213, 29%) microspheres (hazard ratio, 2.4; 95% confidence interval: 0.94, 5.94; P = .06). The role of combining different sizes of embolic agents (trisacryl gelatin microspheres, 100–300 μm and 300–500 μm) could achieve better outcomes when compared with 300–500-μm microspheres alone. Two recent studies addressing this aspect showed controversial results. A study (29) using 50-μm and 100-μm polyvinylalcohol particles resulted in greater improvement in clinical and imaging outcomes and no significant differences in adverse events compared with 100-μm polyvinylalcohol particles alone. Another study (30) comparing three groups (100–300-μm vs 300–500-μm vs 100–300-μm with 300–500-μm trisacryl gelatin microspheres) did not find a significant difference in the outcomes, but the short period of follow-up presented (18 months) is considered to be an important limitation, because LUTS recurrence increases in medium- and long-term follow-up (30). However, most instances of nontargeted embolization occurred when smaller microspheres were used. Recently, we have started to use the combination of smaller and larger microspheres in an attempt to achieve better long-term outcomes. The rationale to use smaller microspheres before the larger ones is based on the fact that the smaller would navigate deeper and cause more ischemia, and the larger would occlude the trunk of the prostatic artery and reduce the chance of recanalization. This rationale could be supported by a recent publication (31) showing that the mean sizes of the intraprostatic arteries in cadavers ranged from 56 μm (24–104 μm) inside the prostatic hyperplastic nodules to 317 μm (155–555 μm) outside of them.

Our study had some limitations. The first one-third of PAE procedures was carried out without cone-beam CT. Also, baseline IPSS was unavailable for men with an indwelling catheter. In addition, to achieve better results, different PAE techniques and embolic agents have been used during the past 10 years. Even with long-term results, only a few men presented more than 5 years of follow-up data. To improve these results and to achieve more prostate ischemia with additional intraprostatic particles injection, in 2013–2014 we decided to use the Proximal Embolization First, Then Embolize Distal technique with different sizes of microspheres. After 10 years, we changed the technical protocol and now use CT angiography with three-dimensional reconstruction from the internal iliac artery, instead of the aortoiliac and internal iliac arteriograms. With cone-beam CT, both the procedure and radiation time have been reduced, and we have a better understanding of the pelvic anatomy.

Although long-term results for prostatic artery embolization (PAE) are promising, further investigations regarding optimal technical aspects of the procedure and patient selection are still required. Our data indicate that PAE is a safe and effective procedure with the potential to become an alternative treatment in the management of benign prostatic enlargement due to benign prostatic hyperplasia.

Author contributions: Guarantors of integrity of entire study, F.C.C., A.M.M., A.M.d.A., V.C.d.P.R., G.G.C.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, F.C.C., A.M.M., A.M.d.A., A.A.A.; clinical studies, F.C.C., A.M.M., A.M.d.A., V.C.d.P.R., M.S., G.G.C.; statistical analysis, A.M.d.A.; and manuscript editing, F.C.C., A.M.M., A.M.d.A., G.G.C.

Disclosures of Conflicts of Interest: F.C.C. Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed no relevant relationships. Other relationships: author receives patent royalties from Merit Medical Systems. **A.M.M.** disclosed no relevant relationships. **A.M.d.A.** disclosed no relevant relationships. **A.A.A.** disclosed no relevant relationships. **V.C.d.P.R.** disclosed no relevant relationships. M.S. disclosed no relevant relationships. **G.G.C.** disclosed no relevant relationships.

References

1. Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. J Urol 1984;132(3):474–479.
2. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. J Urol 2005;173(4):1256–1261.
3. Saigal CS, Joyce G. Economic costs of benign prostatic hyperplasia in the private sector. J Urol 2005;173(4):1309–1313.
4. Cornu JN, Ahyai S, Bachmann A, et al. A Systematic Review and Meta-analysis of Functional Outcomes and Complications Following Transurethral Procedures for Lower Urinary Tract Symptoms Resulting from Benign Prostatic Obstruction: An Update. Eur Urol 2015;67(6):1066–1096.
5. Gratzke C, Barber N, Speakman MJ, et al. Prostatic urethral lift vs transurethral resection of the prostate: 2-year results of the BPH6 prospective, multicentre, randomized study. BJU Int 2017;119(5):767–775.
6. Rastinehad AR, Caplin DM, Ost MC, et al. Selective arterial prostatic embolization (SAPE) for refractory hematuria of prostatic origin. Urology 2008;71(2):181–184.
7. DeMeritt JS, Elmasri FF, Esposito MP, Rosenberg GS. Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolization. J Vasc Interv Radiol 2000;11(6):767–770.
8. Carnevale FC, Antunes AA, da Motta Leal Filho JM, et al. Prostatic artery embolization as a primary treatment for benign prostatic hyperplasia: preliminary results in two patients. Cardiovasc Intervent Radiol 2010;33(2):355–361.
9. Carnevale FC, da Motta-Leal-Filho JM, Antunes AA, et al. Quality of life and clinical symptom improvement support prostatic artery embolization for patients with acute urinary retention caused by benign prostatic hyperplasia. J Vasc Interv Radiol 2013;24(4):535–542.
10. Gao YA, Huang Y, Zhang R, et al. Benign prostatic hyperplasia: prostatic arterial embolization versus transurethral resection of the prostate--a prospective, randomized, and controlled clinical trial. Radiology 2014;270(3):920–928.
11. Pisco JM, Bilhim T, Pinheiro LC, et al. Medium- and Long-Term Outcome of Prostate Artery Embolization for Patients with Benign Prostatic Hyperplasia: Results in 630 Patients. J Vasc Interv Radiol 2016;27(8):1115–1122.
12. Rampoldi A, Barbosa F, Secco S, et al. Prostatic Artery Embolization as an Alternative to Indwelling Bladder Catheterization to Manage Benign Prostatic Hyperplasia in Poor Surgical Candidates. Cardiovasc Intervent Radiol 2017;40(4):530–536.
13. Bhatia S, Harward SH, Sinha VK, Narayanan G. Prostate Artery Embolization via Transradial or Transulnar versus Transfemoral Arterial Access: Technical Results. J Vasc Interv Radiol 2017;28(6):898–905.
14. Ray AF, Powell J, Speakman MJ, et al. Efficacy and safety of prostate artery embolization for benign prostatic hyperplasia: an observational study and propensity-matched comparison with transurethral resection of the prostate (the UK-ROPE study). BJU Int 2018;122(2):270–282.
15. Bagla S, Smirniotopoulos JB, Orlando JC, van Breda A, Vadlamudi V. Comparative analysis of prostate volume as a predictor of outcome in prostate artery embolization. J Vasc Interv Radiol 2015;26(12):1832–1838.
16. Desai H, Yu H, Ohana E, Gunnell ET, Kim J, Isaacson A. Comparative Analysis of Cone-Beam CT Angiogram and Conventional CT Angiogram for Prostatic Artery Identification Prior to Embolization. J Vasc Interv Radiol 2018;29(2):229–232.
17. de Assis AM, Moreira AM, de Paula Rodrigues VC, et al. Prostatic artery embolization for treatment of benign prostatic hyperplasia in patients with prostates > 90 g: a prospective single-center study. J Vasc Interv Radiol 2015;26(1):87–93.
18. Gonçalves OM, Carnevale FC, Moreira AM, Antunes AA, Rodrigues VC, Srougi M. Comparative Study Using 100-300 Versus 300-500 μm Microspheres for Symptomatic Patients Due to Enlarged-BPH Prostates. Cardiovasc Intervent Radiol 2016;39(10):1372–1378.
19. Carnevale FC, Iscaife A, Yoshinaga EM, Moreira AM, Antunes AA, Srougi M. Transurethral resection of the prostate (TURP) versus original and PErFecTED prostate artery embolization (PAE) due to benign prostatic hyperplasia (BPH): preliminary results of a single center, prospective, urodynamic-controlled analysis. Cardiovasc Intervent Radiol 2016;39(1):44–52.
20. Carnevale FC, Moreira AM, Harward SH, et al. Recurrence of lower urinary tract symptoms following prostate artery embolization for benign hyperplasia: single center experience comparing two techniques. Cardiovasc Intervent Radiol 2017;40(3):366–374.
21. Cardarelli-Leite L, de Assis AM, Moreira AM, et al. Impact of 5-Alpha-Reductase Inhibitors Use at the Time of Prostatic Artery Embolization for Treatment of Benign Prostatic Obstruction. J Vasc Interv Radiol 2019;30(2):228–232.
22. Carnevale FC, Antunes AA. Prostatic artery embolization for enlarged prostates due to benign prostatic hyperplasia. How I do it. Cardiovasc Intervent Radiol 2013;36(6):1452–1463.
23. Carnevale FC, Moreira AM, Antunes AA. The "PErFecTED technique": proximal embolization first, then embolize distal for benign prostatic hyperplasia. Cardiovasc Intervent Radiol 2014;37(6):1602–1605.
24. Moreira AM, de Assis AM, Carnevale FC, Antunes AA, Srougi M, Cerri GG. A Review of Adverse Events Related to Prostatic Artery Embolization for Treatment of Bladder Outlet Obstruction Due to BPH. Cardiovasc Intervent Radiol 2017;40(10):1490–1500.
25. Pisco J, Campos Pinheiro L, Bilhim T, et al. Prostatic arterial embolization for benign prostatic hyperplasia: short- and intermediate-term results. Radiology 2013;266(2):668–677.
26. Ahyai SA, Gilling P, Kaplan SA, et al. Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. Eur Urol 2010;58(3):384–397.
27. Bilhim T, Pisco J, Rio Tinto H, et al. Unilateral versus bilateral prostatic arterial embolization for lower urinary tract symptoms in patients with prostate enlargement. Cardiovasc Intervent Radiol 2013;36(2):403–411.
28. Hacking N, Vigneswaran G, Maclean D, et al. Technical and Imaging Outcomes from the UK Registry of Prostate Artery Embolization (UK-ROPE) Study: Focusing on Predictors of Clinical Success. Cardiovasc Intervent Radiol 2019;42(5):666–676.
29. Wang MQ, Zhang JL, Xin HN, et al. Comparison of Clinical Outcomes of Prostatic Artery Embolization with 50-μm Plus 100-μm Polyvinyl Alcohol (PVA) Particles versus 100-μm PVA Particles Alone: A Prospective Randomized Trial. J Vasc Interv Radiol 2018;29(12):1694–1702.
30. Torres D, Costa NV, Pisco J, Pinheiro LC, Oliveira AG, Bilhim T. Prostatic Artery Embolization for Benign Prostatic Hyperplasia: Prospective Randomized Trial of 100-300 μm versus 300-500 μm versus 100- to 300-μm + 300- to 500-μm Embospheres. J Vasc Interv Radiol 2019;30(5):638–644.
31. Garcia-Monaco RD, Garategui LG, Onorati MV, Rosasco NM, Peralta OA. Cadaveric Specimen Study of Prostate Microvasculature: Implications for Arterial Embolization. J Vasc Interv Radiol 2019;30(9):1471–1479.e3.