

# Society of Interventional Radiology Position Statement: Prostate Artery Embolization for Treatment of Benign Disease of the Prostate

Justin P. McWilliams, MD, Michael D. Kuo, MD, Steven C. Rose, MD, Sandeep Bagla, MD, Drew M. Caplin, MD, Emil I. Cohen, MD, Salomao Faintuch, MD, MSc, James B. Spies, MD, MPH, Wael E. Saad, MD, and Boris Nikolic, MD, MBA

## ABBREVIATIONS

BPH = benign prostatic hyperplasia, IPSS = International Prostate Symptom Score, LUTS = lower urinary tract symptoms, PAE = prostatic artery embolization, TURP = transurethral resection of the prostate

Prostatic artery embolization (PAE) is a promising new treatment for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). It has therefore garnered much interest in the interventional community. This article will review the scientific background for this therapy, describe the current devices available for treatment, and state the position of the Society of Interventional Radiology (SIR) with regard to the study and potential adoption of this therapy.

## BACKGROUND

BPH is the most common benign neoplasm in men, with more than 50% of men aged 60–69 years and as many as 90% aged 70–89 years having some symptoms of BPH. As life expectancy increases, so does the occurrence of BPH. In 2000, there were 4.5 million visits to physicians for BPH in the United States, with a direct cost of \$1.1 billion (1).

From the Department of Radiology (J.P.M.), University of California, Los Angeles, Ronald Reagan Medical Center, 757 Westwood Plaza, 2nd Floor, Room 2125, Los Angeles, California 90095; Department of Radiology (M.D. K.), University of California, Los Angeles, Medical School, Los Angeles; Section of Interventional Oncology, Department of Radiology (S.C.R.), University of California, San Diego, Medical Center, San Diego, California; Cardiovascular and Interventional Radiology Department (S.B.), Inova Alexandria Hospital, Alexandria, Virginia; Department of Radiology (D.M.C.), Northshore University Hospital, Manhasset; Department of Radiology (B.N.), Stratton Medical Center, Albany, New York; Department of Interventional Radiology (E.I.C.), Medstar Washington Hospital Center; Department of Radiology (J.B.S.), Medstar Georgetown University Hospital, Washington, DC; Department of Radiology (S.F.), Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; and Department of Radiology (W.E.S.), University of Michigan Medical Center, Ann Arbor, Michigan. Received April 23, 2014; final revision received and accepted May 9, 2014. Address correspondence to J.P.M.; E-mail: [jumcwilliams@mednet.ucla.edu](mailto:jumcwilliams@mednet.ucla.edu)

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LUTS are common complaints resulting from BPH, consisting of incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. These symptoms are quantified by using the International Prostate Symptom Score (IPSS), which assigns a severity score of 0 to 5 to each of these seven symptoms. A total score of 0–7 is considered mild, 8–19 is moderate, and 20–35 is severe (2). An eighth question termed the “bother score” pertains to the patient-perceived quality of life related to LUTS, ranging from 0 (delighted) to 6 (terrible).

## EXISTING THERAPIES

Patients with mild LUTS are generally treated with watchful waiting or lifestyle modification. Medical treatment is usually the first-line treatment option, and is indicated for patients with moderate LUTS. The two main categories of medications for management of BPH are  $\alpha$ -blockers and 5 $\alpha$ -reductase inhibitors. Patients who cannot tolerate these drugs, whose disease is refractory to treatment, or who develop complications of BPH while receiving medical therapy are considered for surgical therapy (2).

Transurethral resection of the prostate (TURP) is the gold-standard surgical treatment. It is effective, with IPSS reduced on average by 70%; however, as many as 20% of patients have significant complications, including bleeding, sexual dysfunction, incontinence, and dilutional hyponatremia (3,4). Open prostatectomy is the procedure of choice for prostates larger than 80–100 cm<sup>3</sup>, but it is an invasive surgical procedure with concomitant morbidity and extended hospitalization.

Several other less invasive therapies have been popularized in the past two decades, including photoselective vaporization of the prostate, transurethral needle ablation, transurethral microwave therapy, and holmium laser enucleation of the prostate. The most promising results have been produced with the laser therapies, which achieve similar results to those of TURP, but with fewer complications and side effects (5,6). Data on long-term efficacy of these newer therapies are lacking (7).

## PAE

### Rationale

The prostate receives its blood supply from the prostatic arteries, which arise singly or paired on each pelvic side. Superselection and embolization of the prostatic arteries leads to ischemic necrosis of a large

proportion of the gland (8). Shrinkage of the gland follows, with subsequent reduction of LUTS.

### Feasibility

Embolization of the prostatic arteries has been used since the 1970s to control serious bleeding after biopsy or prostatectomy (9–11) and for refractory hematuria of prostatic origin (12). In 2000, it was first recognized that embolization could have a therapeutic effect on BPH (13). In this case report (13), volume reduction of 40% and improvement in IPSS from 24 to 13 was observed at 12 months after treatment. In 2008, a study of PAE in eight swine demonstrated shrinkage of the prostate and preserved sexual function (14). The same group (15) demonstrated that PAE produced prostatic infarction and no complications in a series of seven dogs with hormonally induced BPH.

### Safety and Efficacy

The first intentional treatment of BPH with PAE in humans was published in 2010, when Carnevale et al (16) demonstrated relief of urinary obstruction and volume reduction in two patients with acute urinary retention. This was followed by a case series by Pisco et al (17), who demonstrated significant IPSS reduction, improved quality of life, increase in urinary peak flow rate, and prostate volume reduction in 15 patients. One major complication was encountered, a small ischemic area of bladder wall requiring partial resection. There were no cases of sexual dysfunction. This case series was then expanded to 89 patients (18). IPSS reduction in this cohort averaged 10 points, peak urinary flow increased by 38%, prostate volume decreased by 20%, and postvoid residual volume decreased by 30 cm<sup>3</sup>. No further major complications were reported, and erectile function was maintained or even improved (18). Most recently, the case series was expanded to 255 patients, with midterm follow-up. Clinical success was achieved in 81.9% of patients at 1 month, 75.2% at 1 year, and 72.0% at 2 and 3 years (19). These three publications (17–19) contained much overlap of patient data, and are best considered as incremental expansions of the same data set, rather than three distinct studies (20). Carnevale et al (21) also reported updated results of their case series, now including 11 patients with acute urinary retention as a result of BPH. Catheter removal and symptom improvement were achieved in 10 of these patients (91%). After 1 year, prostate volume had decreased by 30%, mean IPSS remained a very mild 2.8, there was no erectile dysfunction, and no major complications were observed. Quality of life was significantly improved in both cohorts of patients (19,21).

Preliminary experience in an American cohort was reported by Bagla et al (22) in 2013. In a single-center prospective trial, 17 of 18 men (94%) treated with PAE reported a significant improvement in IPSS and quality of life at 1 and 3 months. There were no minor or major complications (22). They then published their results from 20 patients in the same ongoing United States trial (23), demonstrating similar improvements in symptoms and quality of life to 6 months.

The first randomized controlled trial of PAE versus TURP (24), enrolling 114 patients with moderate to severe LUTS and prostate volumes of less than 100 cm<sup>3</sup>, was recently published. At 12-month and 24-month follow-up, both groups showed similar improvements in IPSS, quality of life, peak flow rate, and postvoid residual volume. Technical failures (5.3% vs 0%) and clinical failures (9.4% vs 3.9%) were more common with PAE, whereas substantial bleeding (3.8%) and transurethral resection syndrome (1.9%) occurred only with TURP. PAE recipients were less likely to require urethral catheterization and required a shorter hospital stay.

### Devices

Three materials have been studied in the published trials of PAE in humans. In the trials of Carnevale et al (16,21), tris-acryl gelatin microspheres (Embosphere microspheres; Merit Medical, South Jordan, Utah) were used. Pisco et al (17–20) used nonspherical polyvinyl alcohol particles. Bagla et al (22,23) used hydrogel microspheres with a

proprietary coating (Embozene microspheres; CeloNova Biosciences, San Antonio, Texas).

### POTENTIAL ADVANTAGES OF PAE

PAE has several potential advantages over traditional surgical therapies. It is minimally invasive, usually performed via a single femoral artery puncture. Conscious sedation rather than general anesthesia is used, and the procedure is well tolerated, without significant pain. Technical success, when defined as embolization of at least one prostatic side, is achieved in greater than 95% of patients (19); bilateral embolization is the preferred definition of technical success, and is achieved in 75%–94% of patients (21,23). Unlike TURP, there does not appear to be an upper limit of prostate size that can be effectively treated. Prolonged Foley catheterization is not necessary, and is sometimes avoided completely. PAE may be performed as an outpatient procedure, with patient discharge typically occurring 4–6 hours after the procedure. Relief begins to occur within days in most cases, and side effects are generally mild. Major complications are rare. Typical complications of urologic surgeries, including blood loss requiring transfusion, bladder incontinence, and erectile dysfunction, have not been reported with PAE. The effect of the treatment is significant, with marked reduction in IPSS and improvement in urinary flow rates, and these results seem durable over at least 1 year of follow-up. Quality of life scores suggest that patients are quite satisfied with their urinary symptoms following the treatment.

### POTENTIAL LIMITATIONS OF PAE

Although PAE is a promising procedure for BPH, it is not likely to be effective for the multitude of other causes of LUTS, including overactive or hyperactive bladder, dysfunction or contracture of the bladder neck, sphincter dyssynergia, prostatitis, urethral strictures, prostate or bladder cancer, and interstitial cystitis (25). Exclusion criteria for PAE have not been fully elucidated, and further research is needed to establish contraindications (26). At this stage of its development, it is clear that PAE for the treatment of BPH should be considered only in patients who are significantly symptomatic. Its relative place in therapy, vis-à-vis medical or other surgical therapies, requires further study.

Occasionally, PAE cannot be technically achieved on at least one side, usually as a result of atherosclerosis, small artery size, tortuosity, or inability to achieve safe position for embolization. Even if PAE is technically successful, not all patients experience significant clinical improvement. As many as 25% of patients may not show a significant reduction in IPSS or improvement in peak flow rate (21). If only unilateral embolization is possible, clinical success is achieved in approximately 50% of patients (27).

PAE is a technically challenging procedure that requires excellent knowledge of pelvic arterial anatomy, advanced microcatheter skills, and precision in achieving the desired endpoint without reflux. The prostatic arteries have highly variable origins and are frequently small and tortuous (28). The prostatic arterial supply is intimately related to that of the other pelvic organs, especially the bladder and rectum, and there is potential for severe complications with nontarget embolization. Collateral circulation may be present, and can be dynamic during the embolization process, with collateral supplies to adjacent arteries opening as resistance within the prostatic bed increases.

Minor side effects are common following PAE, including urinary frequency, dysuria, pelvic pain, hematuria, blood in the stool, hematospermia, and diarrhea (19,21). These are almost always self-limited, but underscore the possibility that nontarget embolization may occur even if not detected during the procedure.

Ionizing radiation and iodinated contrast material are required for procedural guidance. Although older men are less sensitive to stochastic effects of radiation exposure than younger patients, prolonged fluoroscopy times are not uncommon during a PAE procedure, and deterministic effects such as skin burn could potentially occur. The

risk of these deterministic effects is greater in older individuals, and therefore radiation exposure must be carefully monitored. Contrast material can cause allergic reaction or nephropathy.

Midterm PAE efficacy data are emerging (19), but the long-term durability of PAE is unknown. Although the maintenance of the treatment effect at 1 year is promising, it is possible that eventual revascularization or regrowth of the prostate could limit the durability of the treatment. Repeat treatment of patients with recurrent symptoms has been reported and seems effective, but data are limited (19).

## FURTHER STUDY OF PAE

Although there may be emergency indications for PAE for post-operative bleeding or other urgent indications, elective PAE for BPH requires additional investigation before its acceptance into routine therapy. Additional studies, some of which are ongoing, should investigate midterm and long-term efficacy of the procedure, including subjective symptom scores and objective measures such as peak flow rate, prostate volume, and postvoid residual volume. Prospective, randomized comparison versus TURP and other surgical therapies will help delineate the role of PAE among the many treatment options for LUTS. Safety of the procedure should continue to be verified by tracking and reporting of adverse events.

Other topics deserving further study include comparison of different sizes and types of embolic materials for PAE, determination of imaging endpoints that predict good clinical response, and further characterization of the exact mechanisms of PAE success, which may involve more than just reduction of mass effect (29).

For a detailed review of medical and surgical treatments for BPH, as well as further discussion of the emerging role of PAE, its regulatory issues, and future research, readers are directed to the recently published proceedings from a multidisciplinary research consensus panel (30).

## SIR POSITION

PAE for BPH is a novel and promising therapy that appears safe and efficacious based on short-term follow-up. Patient satisfaction is high, and repeat intervention rates are low.

The PAE procedure is technically challenging, with a possibility of complications if it is not performed meticulously. Interventional radiologists, given their knowledge of arterial anatomy, experience with microcatheter techniques, and expertise in other embolization procedures, are the specialists best suited for the performance of PAE.

SIR supports the performance of high-quality clinical research to expand the numbers of patients studied, to extend the duration of follow-up, and to compare the PAE procedure against existing surgical therapies.

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