Review of Current Literature for Prostatic Artery Embolization

Hyeon Yu, MD1 Ari J. Isaacson, MD1 Charles T. Burke, MD1

1 Division of Vascular and Interventional Radiology, Department of Radiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina

Address for correspondence Hyeon Yu, MD, Vascular and Interventional Radiology, Department of Radiology, University of North Carolina School of Medicine, 2016 Old Clinic, CB 7510, Chapel Hill, NC 27599-7510 (e-mail: hyeon_yu@med.unc.edu).

Abstract

Prostatic artery embolization (PAE) is an emerging, novel interventional technique in the management of patients with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). BPH is a common clinical condition in middle-aged and elderly men resulting in LUTS, including nocturia, urinary frequency, urgency, decreased urinary flow rates, hesitancy, and incomplete bladder emptying. Traditionally, LUTS have been managed by medical or surgical therapies. Since the initial incidental discovery that selective PAE performed for uncontrolled bleeding secondary to BPH resulted in improved LUTS, the technique has continually evolved with a growing body of evidence supporting its safety and efficacy. However, despite the available data, PAE has yet to be established as a standard-of-care treatment option for patients with LUTS/BPH. In this article, the authors review the history and current state of PAE, including published data from case reports, animal studies, retrospective/prospective cohort studies, and prospective randomized controlled trials.

Keywords

► Benign prostatic hyperplasia
► imaging
► embolization
► interventional radiology
► prostate
► urinary tract

Objectives: Upon completion of this article, the reader will be able to describe the history and current state of prostatic artery embolization (PAE) for the treatment of lower urinary symptoms secondary to benign prostatic hyperplasia. This will include the advantages of PAE compared with traditional surgical therapy, overall clinical outcomes, and future directions of research needed to further validate this technique.

Accreditation: This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Tufts University School of Medicine (TUSM) and Thieme Medical Publishers, New York. TUSM is accredited by the ACCME to provide continuing medical education for physicians.

Credit: Tufts University School of Medicine designates this journal-based CME activity for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Lower urinary tract symptoms (LUTSs) are a common malady in elderly men1 that include storage, voiding, and postmicturition symptoms, and are related to both bladder outlet obstruction and irritation caused by benign prostatic hyperplasia (BPH).2 While mild LUTS can be treated with lifestyle modifications, patients with moderate-to-severe LUTS may benefit from medical therapy, including α-adrenergic blockers, 5-α-reductase inhibitors, muscarinic receptor antagonists, and phosphodiesterase inhibitors.3 Prostate surgery is indicated in patients with medical refractory LUTS secondary to BPH. Transurethral resection of the prostate (TURP) is regarded as the surgical gold standard for men with mild-to-moderate prostatic enlargement. There is an average hospital stay of 2.6 days after TURP and potential complications include TUR syndrome (electrolyte imbalance secondary to saline infusion), acute urinary retention, urinary tract infection, bladder neck stenosis, urethral stricture, retrograde ejaculation, erectile dysfunction, urinary incontinence, and bleeding requiring transfusion.4 Open prostatectomy (OP) is the first-line surgical option for men with very large prostates...
and associated hospital stays average 9.2 days. Complications associated with OP include mortality, blood transfusion, urinary incontinence, and bladder neck stenosis or urethral stricture.

Owing to perioperative complications associated with TURP and OP, less invasive alternative options have been developed. In lieu of TURP photoselective vaporization of the prostate (PVP), transurethral needle ablation (TUNA), transurethral incision of the prostate (TUIP), transurethral microwave therapy (TUMT), and prostatic urethral lift (PUL) all have Food and Drug Administration–approved indications for treatment of BPH. For more severe prostate enlargement, laparoscopic or robot-assisted prostatectomy or transurethral holmium laser enucleation of the prostate (HoLEP) provide less invasive alternatives to OP.

Recently, prostatic artery embolization (PAE) has been proposed as a safe and effective alternative to alleviate LUTS secondary to BPH. In contrast to surgical treatments, PAE has the advantages of being a minimally invasive, outpatient procedure with a short recovery time and a low risk of major complications. However, although available data show promising results, further study will be required for PAE to become part of the standard-of-care treatment algorithm for patients with LUTS secondary to BPH. The aim of this article is to review the history, the technique, the outcomes, and the current state of PAE, summarizing the published data from early case reports, animal studies, retrospective/prospective cohort studies, and recent prospective randomized controlled trials (RCTs).

History: Transcatheter Arterial Embolization for Refractory Hematuria

Since Mitchell et al first reported four cases of transcatheter arterial embolization of bilateral internal iliac arteries for managing severe hematuria, the technique has been widely used as an effective and safe treatment modality for patients with life-threatening intractable bleeding either from the bladder or prostate when all other measures have failed. With the development of microcatheters, the technique has evolved from nonselective embolization of the internal iliac artery to more selective catheterization of its branch arteries.

In 2000, DeMeritt et al first discovered the benefit of PAE for treating LUTS. A 76-year-old man with intractable hematuria secondary to BPH was treated with transcatheter arterial embolization. The authors subselectively embolized the right inferior vesical artery using 150 to 250 µm polyvinyl alcohol until complete devascularization of the prostate. Left-sided branches were not treated due to severe atherosclerosis of the internal iliac artery. At 12-month follow-up, the patient's International Prostate Symptom Score (IPSS), a questionnaire scoring the severity of LUTS, was improved from 24 to 13 with a reduction of prostate volume (PV) from 305 to 190 mL (40%).

Animal Study

The first animal study was conducted in 1980 by Darewicz on five dogs, investigating the changes in the prostate gland after embolization of the internal iliac arteries. The purpose of this experiment was to evaluate the potential role of internal iliac artery embolization as a treatment option for hemorrhage from the prostate gland. Four weeks after transcatheter embolization of the internal iliac arteries using N-butyl-2-cyanoacrylate acid, prostates did not reveal any changes on macroscopic examination. However, under the microscope, infiltrations of lymphocytes, histiocytes, and fibroblasts were observed in the interstitial tissue of the prostate. The authors concluded that embolization of the internal iliac arteries may be useful in the treatment of prostatic hemorrhage in clinical practice, because the technique does not result in any marked gross changes in the prostatic gland.

Later, Sun et al evaluated the technical feasibility and safety of PAE in pigs in 2008. Sixteen pigs were randomly assigned to an embolization or control group. PAE was successful in all eight pigs using microspheres (500–700 µm). Three months after PAE, the mean PV was significantly reduced in the embolization group ($p < 0.001$) without significant difference in sexual function between the two groups ($p = 0.328$). Histologic examination revealed decreased glandular tissue with interdigiting fibrosis. Based on the results, the authors suggested that PAE has potential for treating symptomatic BPH in humans without a compromise in sexual function.

The same group evaluated pathologic responses of the prostate to PAE in seven canine models with hormonally induced BPH in 2011. PAE was performed using 500 to 700 µm microspheres without complications. One month after PAE, prostatic infarction was identified on imaging studies and necropsy. This further supported the notion that evaluation of the procedure in humans was warranted.

Anatomy of Prostatic Arteries

Because of the small size of the prostatic arteries (PAs), its anatomic complexity, and variations, it is often challenging to identify the origins of the PAs, differentiate the PAs from adjacent arterial branches, and detect small arterial anastomoses. To perform successful PAE without nontarget embolization, it is essential to have comprehensive knowledge of the vascular anatomy and its relationship with surrounding structures.

In 1955, PA anatomy was studied by Clegg in a cadaveric study with 21 pelvic halves. He described that the prostate gland was supplied by the prostatovesical artery which was of variable origin. Clegg also noted that terminal branches of the PA continued to the rectum and anal canal to form the middle rectal arteries. He also described a characteristic “corkscrew” pattern of fine branches of PA on the surface of the prostate as they penetrated into the stroma of the gland.

The presence of two independent PAs (cranial and caudal PAs) on each pelvic side was first discovered in 1959 by Bouissou and Talazac. In their cadaveric study with 100 pelvic halves, they compared the PA anatomy in the setting of a normal prostate versus BPH or prostate cancer. They described that the cranial PA (vesicoprostatic artery) ran between the bladder and prostate, supplying the bladder base, and central and cranial prostate. The cranial PA was often enlarged in the setting of BPH. On the other hand, the caudal PA was found to course posteriorly, passing between...
the rectum and the posterior surface of the prostate, supplying the peripheral and caudal prostate.

Bilhim et al. in 2012 studied PA anatomy using computed tomography angiography (CTA) and digital subtraction angiography (DSA) in 75 patients with BPH who underwent PAE. In their study of 150 pelvic halves, a solitary PA and two independent PAs were found in 57 and 43% of pelvic halves, respectively. The PAs had variable origins, including the internal pudendal artery (34%), a common trunk with superior vesical artery (20.2%), the gluteal-pudendal trunk (17.8%), the obturator artery (12.6%), and a common trunk with rectal branches (8.4%). In 57% of pelvic halves, PAs were anastomosed with adjacent pelvic arteries, such as the internal pudendal arteries (43.3%), contralateral PAs (17.6%), ipsilateral PAs (13.4%), rectal arteries (14.4%), vesical arteries (11.3%), and lateral accessory pudendal arteries (20%). They found no significant correlation between PA diameter and patient age, PV, or prostate-specific antigen (PSA) level.

Cone-beam CT (CBCT) can also be used for pelvic vascular mapping with its three-dimensional imaging capability. In 2015, Zhang et al. evaluated PA anatomy using intraprocedural CBCT and DSA in 55 patients (110 pelvic halves) with BPH who underwent PAE. The results were somewhat different from the previous study by Bilhim et al. The incidences of a solitary PA and two independent PAs in this study were 96.4 and 3.6%, respectively. The PAs again were found to originate from various pelvic arteries, including the anterior division of the internal iliac artery (39.5%), the superior vesical artery (32.6%), and the internal pudendal artery (27.9%). The authors also found that the PA often anastomosed with adjacent pelvic arteries outside the prostate (39.1%) as well as with the contralateral PA within the prostate gland (39.1%). In conclusion, they suggested that CBCT can be helpful for identifying the PA anatomy when preprocedural pelvic CTA is not available.

**Techniques and Outcomes of PAE**

Successful PAE in humans with acute urinary retention secondary to BPH was first reported by Carnevale et al in 2010. In two patients, PAE was performed using 300 to 500 μm microspheres and both demonstrated relief of urinary obstruction and reduction of PV at 6-month follow-up. Intravesical prostate protrusion and postvoid residual urine volume (PVR) were also diminished in both patients. Later in 2011, the same group published the midterm follow-up results for the same two patients demonstrating durability of the PV loss and symptomatic improvement to 30 months.

In 2011, a case series evaluating feasibility of PAE in patients with LUTS was published by Pisco et al. PAE was technically successful in 14 of the 15 patients. There was significant IPSS reduction, improved quality of life (QoL), increase in urinary peak flow rate (Qmax), and PV reduction. There was one major complication (bladder ischemia that required surgical resection) and four clinical failures (28.6%).

This small case series was then later expanded to include 89 patients by the same group in 2013. At 1-month follow-up, mean IPSS decreased by 10 points, mean QoL score decreased by 2 points, mean Qmax increased by 38%, mean PV decreased by 20%, mean PVR decreased by 30 mL, and the mean international index erectile function (IIEF) score increased by 0.5 point (all differences at p < 0.01). Besides the bladder ischemia described in their previous paper, no additional major complications were reported.

The same group published again in 2013 on an expanded sample size now numbering 255 patients. Midterm results with a mean follow-up of 10 months were reported. Overall technical success rate of PAE (unilateral embolization) was 97.9%. Cumulative rates of clinical success were 81.9, 80.7, 77.9, 75.2, 72.0, 72.0, and 72.0% at 1, 3, 6, 12, 18, 24, 30, and 36 months, respectively.

In 2013, Antunes et al described the efficacy of PAE in 11 patients with urinary retention due to BPH. Clinical success was 91% with a mean follow-up of 22.3 months. At the first year follow-up, the mean IPSS score was 2.8 points, mean QoL was 0.4 points, mean PSA decreased from 10.1 to 4.3 ng/mL, Qmax improved from 4.2 to 10.8 mL/s, and detrusor pressure decreased from 85.7 to 51.5 cm H₂O. In this study, overall clinical and urodynamic parameters were significantly improved after PAE. Carnevale et al also reported updated results of PAE in 2013. Their technical and clinical success rates were 75 and 91%, respectively, with no major complications. At 1-year follow-up, mean PV reduction was greater than 30%, symptoms were mild (mean IPSS, 2.8 ± 2.1), no erectile dysfunction was observed, and QoL improved significantly (mean, 0.4 ± 0.5).

Bagla et al reported early results from a U.S. trial of PAE in 2014. Bilateral PAE was successful in 18 of 19 patients in their cohort without any complications. One case of unilateral PAE was due to atherosclerotic change of the contralateral PA. Clinical success was found in 19 of 20 patients with significant improvement of the American Urological Association (AUA) symptom score (equivalent to IPSS) and QoL. PV was decreased by 18% at 6 months.

In 2014, Kurbatov et al studied clinical benefits and safety of PAE in patients with PV greater than 80 mL. In this nonrandomized prospective study, PAE was performed in 88 patients affected by clinical benign prostatic obstruction. The mean IPSS (10.40 from 23.98) and the mean Qmax (16.89 from 7.28) at 1 year were significantly improved compared with baseline. PVR, total PV, and PSA level were also significantly improved at 1-year follow-up.

In 2014, the first RCT of PAE versus TURP was reported by Gao et al from China. A total of 114 patients with BPH were randomly assigned to PAE (n = 57) or TURP (n = 57). All the clinical metrics (IPSS, QoL, Qmax, PVR, PSA, and PV) were significantly improved in both groups compared with baseline. However, in the TURP group, improvements of IPSS, QoL, Qmax, and PVR were greater at 1 and 3 months compared with PAE group. Reduction in PSA level and PV were also greater in TURP group at all follow-up time points compared with PAE group. At 2-year follow-up, however, there was no significant difference of any of the clinical metrics between the two groups. Rates of overall adverse events and complications were higher in the PAE group compared with TURP group. It should be noted, however, that postembolization and technical and clinical failures were included as complications. PAE was associated with shorter hospital stay compared with TURP.
In the United Kingdom, preliminary results of PAE in 35 patients with very symptomatic BPH (mean IPSS, 24; mean PV, 94.9 mL) were reported by Somani et al in 2014. A technical success rate was 100% (bilateral PAE, 90%; unilateral PAE, 10%). The mean IPSS and health-related QoL score at 6 months were 12 and 2, respectively. PV was reduced by 42% with an increase of Qmax by 32%. There were no major complications related to PAE.

In 2015, Bagla et al also expanded their previous U.S. trial of PAE to 78 patients. They evaluated AUA symptom index, QoL, and IIEF between three groups with different PV (group 1 with PV < 50 mL, group 2 with PV of 50–80 mL, group 3 with PV < 80 mL). Bilateral PAE was successful in 75 of 78 patients with only two minor complications, including groin hematoma and urinary tract infection. The authors demonstrated a significant reduction in AUA symptom index and QoL in all three groups. There were no statistically significant differences in AUA symptom index, QoL, or IIEF between the groups.

In 2015, de Assis et al published a single-center, single-arm prospective study of PAE for treating LUTS secondary to BPH in 35 patients with PV greater than 90 mL. At 3-month follow-up, PV, IPSS, and QoL were significantly improved compared with baseline values before PAE (p < 0.001). They observed a significant negative correlation between PSA at 24 hours after PAE and IPSS at 3-month follow-up.

Amouyal et al reported their first experience of PAE using proximal embolization first then embolize distal (PErFecTED) technique for treating LUTS in 35 consecutive patients with BPH in 2015. Although the PErFecTED technique was originally introduced by Carnevale et al in 2014, there had been no data reported outside from the Sao Paulo group that initiated this technique. Overall immediate technical success of PAE was 100% and PErFecTED technique was feasible in 68% of patients. There were significant improvements in IPSS, QoL, Qmax, and PV compared with baseline values. There were no major complications. The authors concluded that the PErFecTED technique is feasible, safe, and effective in the management of LUTS related to BPH. In some cases, this technique was not feasible for anatomic reasons.

Later in 2015, Wang et al published midterm follow-up data of PAE in the treatment of BPH with PV greater than 80 mL in 105 Chinese patients with BPH. PAE was performed using particles with combination of 50 and 100 μm in diameter. At 24-month follow-up, IPSS, QoL, Qmax, PVR, and PV were significantly improved compared with baseline. They concluded that a large prostate does not add an increased risk of complications.

In 2016, a RCT of PAE versus TURP was published by Carnevale et al. They compared clinical and urodynamic outcomes of TURP to original PAE and PAE with PErFecTED technique in patients with BPH. Initially, a total of 30 patients were randomly assigned to either TURP (n = 15) or original PAE (n = 15), but later an additional 15 patients who were matched with the TURP patients using urodynamic metrics were enrolled in a separate arm to evaluate PErFecTED PAE technique. In all groups, IPSS, QoL, PV, and Qmax were significantly improved. IPSS was significantly lower in both the TURP group and the PErFecTED PAE group compared with original PAE group. However, there was no significant difference between TURP and PErFecTED PAE groups. Complications resulted from TURP included urinary incontinence (26.7%), rupture of the prostatic capsule (6.7%), retrograde ejaculation (100%), and readmission for temporary bladder irrigation due to hematuria. The authors concluded that TURP and PErFecTED PAE provide similar clinical outcomes with better urodynamic results.

Future Direction in Prostatic Artery Embolization Study

Although there are multiple single-arm studies demonstrating PAE is safe and effective in reducing LUTS, the amount of RCT data are limited. In addition, longer longitudinal data are needed to understand the durability of the urinary improvement that results from PAE. Future study designs should include multicenter, prospective RCTs for comparing PAE and other BPH therapies including OP, TURP, and other transurethral therapies with multiple-year follow-up.

Additional questions that need to be answered include determining the optimal type and size of embolic material, the benefit of a robotic catheter for challenging anatomy, the optimal technique for preventing embolic flow to nontarget organs through PA anastomoses, the potential benefit of a transradial approach, and the optimal pre- and intraprocedural imaging techniques.

Conclusion

Based on the available data, PAE appears to be an effective and safe minimally invasive technique to treat LUTS resulting from BPH. PAE has the advantage of being an outpatient procedure that requires only local anesthesia or moderate sedation. Because PAE can be technically challenging even for experienced interventional radiologists, the mastery of the anatomy and high-quality pre- and intraprocedural imaging is important. To solidify PAE’s place in the BPH treatment algorithm, more RCTs are needed, with more patients and longer follow-up.

Disclosure

Hyoeun Yu: No disclosure
Charles T. Burke: No disclosure

References

3. Oelke M, Bachmann A, Descazeaud A, et al; European Association of Urology. EAU guidelines on the treatment and follow-up of non-

14 Kably I, Pareira K, Chong W, Bhatia S. Prostate artery embolization (PAE) in the management of refractory hematuria of prostatic origin secondary to iatrogenic urological trauma: a safe and effective technique. Urology 2016;88:218–221