Prostatic Artery Embolization for Benign Prostatic Hyperplasia—A Primer for Interventional Radiologists

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Abstract

Male patients over 50 years with lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH) are potential candidates for prostatic artery embolization (PAE). PAE is not a perfect fit for all BPH patients. Careful pre- and postprocedural evaluation/consultation with correct selection of patients should be tailored on an individual basis. Evaluated parameters include the following: LUTS severity quantification with validated questionnaires as the international prostate symptom score (IPSS) and quality of life (QoL), erectile and ejaculatory evaluation with validated questionnaires, blood tests including full blood count, coagulation profile, renal function and total/free prostate-specific antigen (PSA), prostate volume measured by multiparametric magnetic resonance (mpMR) of the prostate and/or transrectal ultrasound, uroflowmetry measuring the peak urinary flowrate (Qmax), and postvoid residual urine (PVR). Correct arterial anatomy identification with either computed tomography (CT) angiography, MR angiography, or intraprocedural cone-beam CT (CBCT) are suggested for a confident procedure and avoiding potential complications. The minimally invasive nature of PAE with a faster recovery, preserving the sexual function, and comparable results to standard prostatic surgery make the procedure an attractive choice for many male patients suffering with this condition. Patients should be informed about the potential for higher retreatment rates and shorter duration of treatment effect when compared with standard prostatic surgery. In this comprehensive review, we provide an updated toolbox for all interventional radiologists interested in the PAE practice for patients with BPH. We explain how to evaluate patients during consultation before and after PAE, describe the preprocedural imaging required, explain the technique, and narrate how to optimize outcomes. Finally, we review the level of evidence of PAE for BPH.

Keywords

► prostatic artery embolization
► prostate embolization
► benign prostatic hyperplasia
► lower urinary tract symptoms

Preprocedural Patient Consultation

Male patients over 50 years of age, presenting for consultation before prostatic artery embolization (PAE), usually have bothersome lower urinary tract symptoms (LUTS) and an enlarged prostate gland. Less frequently they can present with acute urinary retention (AUR) requiring a bladder catheter or gross hematuria.¹ The most frequent cause for

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LUTS and AUR in male patients over 50 years of age is benign prostatic hyperplasia (BPH) or benign prostatic enlargement (BPE). However, other causes may be present such as bladder dysfunction, urethral stricture, bladder stones or diverticula, prostate, and bladder cancer.\textsuperscript{2,3} Thus, preprocedural patient evaluation is essential to make sure that the correct diagnosis is made to optimize the treatment approach. For patients with gross hematuria, it is essential to perform a renal ultrasound to exclude renal cancer and a bladder ultrasound and/or cystoscopy to rule out a bladder tumor. Only, after excluding these causes, a prostatic origin can be assumed.\textsuperscript{3}

The international prostate symptom score (IPSS) is a validated questionnaire that allows for confident quantification on the severity of LUTS before and after a prostatic intervention. The IPSS consists of seven questions, four for obstructive/voiding LUTS (hesitancy, weak stream, poor emptying, straining, prolonged micturition, and dribbling) and three for irritative/storage LUTS (frequency, urgency, urge incontinence, and nocturia) with a final question pertaining the overall quality of life (QoL) related to the LUTS. These seven questions are rated on a scale of 1 to 5, providing and overall score of 0 to 35 points. The QoL question is graded on a scale of 0 to 6 (0 being delighted and 6 as terrible). Based on the overall IPSS score, LUTS are divided into mild (0–7 points), moderate (8–19 points), and severe (20–35 points). However, it is the QoL question that often dictates management. When the QoL is equal or greater than 4, the patient is dissatisfied with the LUTS, and frequently requires an invasive treatment approach.\textsuperscript{1,3}

It is important to stress that the IPSS/QoL allows for quantification of LUTS, but it does not allow for a confident diagnosis on the causes of LUTS. So, laboratory and imaging studies are needed to exclude other causes than BPH. Before PAE, to exclude prostatic malignancy, a digital rectal examination, blood tests with measurement of the prostate-specific antigen (PSA), and prostate multiparametric magnetic resonance (mpMR) might be useful tools.\textsuperscript{1}

Another relevant point to consider is the severity of bladder outlet obstruction (BOO). Patients frequently are not bothered by BOO because it does not have an immediate impact on the QoL. However, BOO is critical when assessing the potential for complications from the progression of BPH, such as AUR, bladder stones, or diverticula and obstructive uropathy. Postvoid residual urine (PVR) is an easy test using ultrasound of the bladder after urination that allows for confident screening of severe BOO. It should be included in the evaluation of all male patients with LUTS. Uroflowmetry is another easy and accessible noninvasive tool to assess BOO. It provides the peak urinary flowrate (Qmax) that should be quantified before and after a prostatic intervention, as it provides an indirect measure on the severity of BOO caused by BPH. A normal Qmax is \( > \) 15 mL/s with values under 12 mL/s suggestive of BOO or underactive bladder. Invasive urodynamic studies can be used when BOO due to BPH is doubtful such as in young patients (<50 years of age) with small prostate volumes (<30 cm\(^3\)), predominately irritative LUTS, high Qmax (>15 mL/s), very high PVR (>300 cm\(^3\)), or when a clinical suspicion of neurogenic bladder (diabetic patients and neurological diseases) exists. These invasive urodynamic studies can be very helpful as they differentiate LUTS from prostatic obstruction from LUTS due to bladder under- or hyperactivity. Bladder underactivity can be suspected when the Qmax is less than 12 mL/s in diabetic patients or patients suffering from neurological diseases, when the PVR is \( > \) 300 cm\(^3\), when multiple large bladder diverticula are present, or when bilateral hydronephrosis is seen. Bladder hyperactivity can be suspected in young patients with Qmax \( > \) 15 mL/s and predominately irritative LUTS. It should be stressed; however, that bladder hyperactivity typically coexists with BOO due to BPH.\textsuperscript{2,3}

When dealing with LUTS patients in consultation prior to PAE, one of the key aspects is managing expectations. Patients will enquire about mostly three main things as follows: (1) it is painful/complications, (2) recovery period, and/or (3) effectiveness. Regarding the procedure, it is very well tolerated. PAE is a painless procedure that is performed under 2 hours and can be performed under an outpatient setting. Adverse events are present in less than 3% of patients, even though frequency and a burning sensation during urination might be felt by up to 50% of treated patients in the first 1 or 2 days. The recovery is almost immediate, as patients can return to normal daily activities after 2 or 3 days. The effectiveness is around 80%, which means that 80% of patients will have their LUTS significantly improved after PAE for the following 3 to 5 years. Data are still scarce to inform on longer follow-up above 5 years. This also means that up to 20% of treated patients may not improve or do not improve as much the LUTS as they wanted. This might mean that these patients may require prostatic medication or surgery soon. When dealing with AUR patients, we usually inform a 90% chance of success on spontaneous urination and freedom from bladder catheter within 2 weeks and 1 month after PAE.\textsuperscript{3}

Finally, when dealing with male patients with LUTS, erectile and ejaculatory function are also discussed. One of the main advantages of PAE when compared with prostatic surgery is the fact that it allows a painless, almost immediate recovery preserving both erectile and ejaculatory functions. It should be stressed, however, that PAE is not a procedure to improve erectile and ejaculatory functions. Prostatic medication is another topic to debate. Most patients presenting to consultation have already been treated with \( \alpha \)-blockers and/or 5-\( \alpha \)-reductase inhibitors. The \( \alpha \)-blockers have an immediate effect and washout and significantly improve LUTS, whereas 5-\( \alpha \)-reductase inhibitors reduce prostate volume (25–30%) and PSA (up to 50%) with minimal effect on LUTS, with a longer time to reach effect and washout (3–6 months). These \( \alpha \)-blockers are first-line therapy in virtually all LUTS patients, whereas 5-\( \alpha \)-reductase inhibitors might be recommended in high-risk patients (prostate volume \( > \) 40 cm\(^3\)) to prevent disease progression. Also, \( \alpha \)-blockers may cause orthostatic hypotension or retrograde ejaculation, whereas 5-\( \alpha \)-reductase inhibitors may lead to gynecomastia, reduced libido, and erectile dysfunction. Most patients treated with PAE can discontinue all prostatic medication after the embolization. Anticholinergic medication is also
used when irritative LUTS are predominant, and a hyperactive bladder is suspected, provided that Qmax > 12 mL/s.1–3
To summarize, when consulting patients before PAE the followings can be considered: LUTS versus AUR versus gross hematuria, for LUTS patients evaluate if voiding versus storage symptoms predominate, inquire about prostatic medication, and erectile/ejaculatory expectations. At this point, validated questionnaires are very useful such as IPSS/QoL, international index of erectile function (IIEF-5 questions version), and ejaculatory function questionnaire. Blood tests including full blood count, coagulation profile, renal function, and total/free PSA values should be obtained. We recommend mpMR of the prostate before PAE. Uroflowmetry measuring the Qmax and PVR should also be used. Renal and bladder ultrasound are also frequently performed. Follow-up after PAE should be at 1 month, 6 months, and then yearly with IPSS/QoL, IIEF-5, PSA, prostate volume measured by transrectal ultrasound, Qmax, and PVR. Cystoscopy might be needed when hematuria is present, when the prostatic obstruction is doubtful, or when bladder cancer is suspected. Invasive urodynamic studies are required in specific situations as outlined above.

**Imaging Planning for Prostatic Artery Embolization**

As discussed above, some imaging studies are usually required before PAE. Bladder ultrasound to measure the PVR and study the bladder should be used routinely.3 Prostate volume measurement and zonal anatomy of the prostate could be done with transrectal ultrasound or mpMR of the prostate.4 mpMR has advantages over ultrasound, as it allows for confident identification of prostate cancer, better zonal volumetry and estimation of the intravesical prostatic protrusion, detailed study of the bladder wall, and lumen and can also be used for vascular assessment of the pelvic arteries. However, mpMR is more expensive, time consuming, and less available than prostatic ultrasound. As such, mpMR of the prostate can be used at baseline, whereas transrectal ultrasound can be used after PAE to assess prostate volume.4 Another aspect relevant for PAE planning relies on the vascular mapping of the pelvic and prostatic arteries. One approach has been using computed tomography angiography (CTA) prior to PAE to study the anatomy of the pelvic and prostatic arteries.5 CTA prior to PAE allows confident identification of the prostatic arteries and helps plan the procedure.5,6 CTA can also be used to predict the level of difficulty of the PAE procedure and predict technical outcomes.5 To achieve predictable and confident identification of the prostatic arteries, the CTA protocols should be adjusted: contrast used should have concentrations 350 to 400 mg I/mL with a volume of 100 to 120 mL, flowrate of 4 mL/s, saline flushing (40 mL) at the same rate; acquisition times for the pelvis should be 10 to 15 seconds (too fast or too slow can affect correct prostatic artery opacification); delay usually 16 to 20 seconds based on bolus tracking in the aorta (200 Hounsfield’s Units level of threshold), leading to approximately 30 to 35 seconds from contrast injection until the end of acquisition.5 The use of 0.5 mg sublingual nitroglycerin has also shown to be useful to improve prostatic artery opacification.5,6

Modern angiography machines have flat panel detectors that allow the use of rotational three-dimensional (3D) cone-beam CT (CBCT) scans besides the two-dimensional (2D) conventional digital subtraction angiographies (DSA). The use of CBCT is very important for PAE and can be used in following two scenarios: (1) to map the pelvic arteries and identify the prostatic arteries, and (2) to certify correct microcatheter position within the prostatic arteries and prostatic coverage and exclude anastomoses. CBCT has shown to have similar accuracy to CTA in identifying the prostatic arteries with lower radiation exposure and contrast volume used.6 However, CBCT can only be performed with the patient already in the angiosuite during PAE; CBCT does not allow for preprocedural vascular assessment. CBCT allows for the acquisition of 3D datasets that can be used with dedicated software’s, with automatic feeder detection. These software’s automatically identify the arteries feeding the prostate and provide an overlay with 2D fluoroscopy and the 3D roadmaps allowing direct guidance into the prostate, obviating extensive knowledge of the pelvic arterial anatomy.5 More recently, CBCT has shown to be superior to DSA in detecting the prostatic arteries, allowing for a reduced number of DSA runs with an overall decrease in radiation exposure.10

CBCT injection protocols should be adjusted according to rotational scan time and catheter position. Injection of contrast should cover the whole scanning time plus 3 to 5 seconds. The injection should start before CBCT start (scan delay). Diluted contrast media/saline (50%/50%) can be used for CBCT. Some examples of CBCT injection protocols with a rotational scan of 10 seconds are as follows: with the catheter in the aorta: 35 mL, 3 mL/s, and scan delay for 4 seconds; with the catheter in the internal iliac artery: 20 mL, 1.5 mL/s, and scan delay for 4 seconds; and with the microcatheter in the prostatic artery: 8 mL, 0.5 mL/s, and scan delay for 3 seconds. CBCT with the catheter in the distal aorta allows roadmapping of the whole pelvic arteries, whereas in the internal iliac arteries only one pelvic side is studied. Both injections are used to map the pelvic arteries and identify the prostatic arteries. On the other hand, selective CBCT injections in the prostatic arteries are used to certify correct microcatheter position, exclude relevant anastomoses that could lead to nontarget embolization, and certify if more than one prostatic artery is present in each pelvic side.8–11 It has been shown that in up to 20% of patients, more than one prostatic artery feeding the central gland may be present on either pelvic side.5,11

Recently, MR angiography protocols with 3-Tesla scanners have shown high accuracy (>90%) for detecting the prostatic arteries.12 This has a huge advantage of assessing the prostate with mpMR and the pelvic arteries with MR within a single examination. This has led to a shift from preprocedural CTA towards MRA (→ Fig. 1). With preprocedural MRA, procedural times, radiation exposure, and contrast volume used are significantly reduced during PAE.12 The MR
scanners need to be 3 Tesla to be able to have acquisition times like CTA with the same image resolution, using surface phase array coils to scan the whole pelvis (including the distal aorta). It is possible to have voxels of 1 to 2 mm and perform volumetric scanning of the whole pelvis in 10 to 20 seconds. With MRA, the pelvis can be analyzed with and without subtraction. Injection protocols usually use 0.1 to 0.2 mL per kg of body weight, with a total of 16 to 25 mL of intravenous gadolinium, at a flow rate of 3 mL/s, followed by saline flushing (2 mL/s). We adjusted a previously published protocol\textsuperscript{12} to identify the prostatic arteries during MRA; after the administration of 0.2 mL/kg of Dotarem (gadoteric acid; Guerbet, Roissy CdG, France) injected at 3 mL/s using a power injector followed by 20 mL saline flush at the rate of 2 mL/s. MRA using 3D volumetric interpolated spoiled gradient echo was obtained with the following parameters: field of view extending from the iliac bifurcation to the common femoral arteries with 1.3-mm slice thickness; matrix: $256 \times 100$ (voxel of 1.3 mm $\times 0.9$ mm $\times 0.9$ mm); repetition time (TR): 7.9; echo time (TE): 3.6; and acquisition time of 22 seconds of a total of five phases (\textit{Video 1} and 2).

Video 1


Video 2


Technique

PAE is all about anatomy, having the right tools and knowing how/when to use them. Starting with anatomy, it is important to have a clear idea on all major pelvic side branches, including the superior and inferior gluteal arteries, the internal pudendal, and the obturator arteries. With ipsilateral anterior oblique views, it is relatively easy to identify all these major pelvic vessels and thus identify the smaller side branches. The ipsilateral anterior oblique views help to separate all the major internal iliac artery side branches and correctly identify the vesical, prostatic, and rectal arteries.\textsuperscript{13,14} Most bladder arteries arise from the superior vesical artery that is always the first side branch of the anterior division of the internal iliac artery. The superior vesical artery should not be confused with the prostatic artery. The superior vesical artery has a straight trajectory forward and medially into the bladder, whereas the prostatic artery has a trajectory first caudally and only after that it runs medially (in a C or L trajectory), underneath the bladder. The prostatic artery frequently has a parallel trajectory to the internal pudendal artery and is usually the most tortuous pelvic vessel. After prostatic artery catheterization, the prostatic arteries are seen overlying the pubic bone as seen on 2D fluoroscopic imaging, usually with horizontal branches. Vertical branches above the pubic bone should alert to the

Fig. 1 (A) MRA 3D-oblique view of a maximum intensity projection reformat of the right internal iliac artery, depicting the prostatic artery (arrow) arising from the internal pudendal artery (dashed arrow). (B) DSA with ipsilateral anterior oblique view (35 degrees) of the right internal iliac artery, depicting the prostatic artery (arrow) arising from the internal pudendal artery (dashed arrow). (C) MRA 3D-oblique view of a maximum intensity projection reformat of the left internal iliac artery, depicting the prostatic artery (arrow) arising from the superior vesical artery (dashed arrow). (D) DSA with ipsilateral anterior oblique view (35 degrees) of the left internal iliac artery, depicting the prostatic artery (arrow) arising from the superior vesical artery (dashed arrow). Note how closely the MRA and DSA images match, certifying the accuracy of preprocedural MRA to identify the prostatic arteries. (E) CBCT after selective prostatic artery catheterization with a microcatheter (arrows), in both pelvic sides, confirming correct location and excluding anastomoses that could lead to nontarget embolization. 3D, three dimensional; CBCT, cone-beam computed tomography; DSA, digital subtraction angiographies; MRA, magnetic resonance angiography.
prospective study for PAE, catheters, microcatheters, and microwire preferences vary among interventional radiologists. Most would agree that 2.0- to 2.4-F microcatheters with preshaped swan-neck curves at the tip (Progreat Lambda, Terumo, Tokyo, Japan), Maestro or Pursue, Merit Medical Systems, Inc. (South Jordan, UT, USA); Direxion, Boston Scientific Corporation [Marlborough, MA, USA]) are the first-line option for PAE. Having these angulations at the microcatheter tip allows for navigation with torque capability, even without the need for microwires. In up to 60% of PAE procedures, we can only use microcatheters without microwires. It is also important to have multiple choices when it comes to microwire selection; most frequently used ones include 0.014- to 0.016-inch Glidewire GT (double-angled or 90-degree angled, Terumo, Tokyo, Japan), Fathom (shapeable, Boston Scientific Corporation [Marlborough, MA, USA], Asahi Meister (shapeable, Asahi Intecc USA, Inc.), Hi-Torque BMW wire (Abbott, Chicago, IL, USA), and Synchro (Stryker, Kalamazoo, MI, USA). With the most challenging PAE procedures, in older patients, with severe arterial tortuosity and atherosclerosis and prostatic arteries arising from the superior vesical artery, having steerable microcatheters can be very useful (SwiftNinja, Merit Medical Systems, Inc., South Jordan, UT, USA).

Optimizing Outcomes

Outcomes can be optimized through technique and patient selection. It is already proven that bilateral PAE provides better outcomes than unilateral PAE. Thus, physician expertise is needed, as it has a direct impact on technical outcomes. Coil protection during PAE might be required in up to 25% of patients before embolization to exclude anastomoses that could lead to complications from nontarget embolization. The use of protective coils prior to embolization increases the radiation exposure but allows for a safe and effective PAE. The paradox as to the best embolic agent and size for PAE remains, with conflicting evidence from existing literature. Currently used embolic agents include 100- to 300-µm polyvinyl alcohol (PVA) particles (Bearing nPVA, Merit Medical Systems, Inc.; Contour, Boston Scientific Corporation) and anastomoses that could lead to nontarget embolization. CBCT, cone-beam computed tomography. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0041-1739302.
spherical embolic agents such as spherical PVA (300–500µm Bead Block, Boston Scientific Corporation), 100- to 300-µm and/or 300- to 500-µm triacryl gelatin microspheres (Embosphere, Merit Medical Systems, Inc.), 250-µm and/or 400-µm polyzene-coated hydrogel microspheres (Embocene, Varian Medical Systems), and 250-µm and/or 400-µm polyethylene glycol microspheres (HydroPearl, Terumo Interventional). There is conflicting evidence regarding the use of smaller particles and the potential to have better outcomes or longer treatment effects. It has been proven that smaller spherical embolic agents may lead to more adverse events, even though the safety profile is the same for PVA particles regardless of the size. As such, one could recommend using 100 to 300µm PVA particles or 400-µm or 300- to 500-µm spherical embolic agents.

As for optimizing patient selection, there is conflicting evidence regarding baseline patient factors that may predict a good or bad clinical outcome. Patients under AUR seem to respond very well to PAE. Younger patients seem to perform better than older patients and the potential for larger prostates to have better outcomes is highly controversial, even though the ratio of transitional prostate volume/whole prostate volume >50% and the presence of large (>1 cm) central gland adenomas predict better outcomes. The presence of pedunculated median lobes has proven to lead to worse clinical outcomes after PAE. Post-PAE identified predictors of clinical outcome include blood tests with 24-hour post-PAE PSA and C-reactive protein levels, MR detected prostate infarction, and prostate volume reduction within the first month post-PAE.

Level of Evidence

The safety and efficacy of PAE has been shown in multiple phase-II trials. In a recent meta-analysis including 1,046 patients from 10 studies with a mean follow-up of 12 months, PAE induced a mean IPSS improvement of 16.2 points, a mean QoL improvement of 3.0 points, and a mean prostate volume reduction of 20.3 cm³ (25%). These improvements remained statistically significant throughout 3 years. Minor adverse events, including the postembolization syndrome with transient dysuria in 10% and increased urinary frequency in 16% of patients were reported. Major adverse events were reported in three patients (0.3%): one bladder ischemia, one urinary tract infection, and one persistent perineal pain.

More recently, a systematic review analyzed six trials comparing PAE with transurethral resection of the prostate (TURP) in 598 patients. TURP provided a significantly higher increase of the Qmax (mean difference of 5.02 mL/s), greater prostate volume reduction (mean difference = 15.59 mL) and greater PSA reduction (mean difference = 1.02 ng/mL). No significant differences between PAE and TURP were noted for the IPSS/QoL scores, IIEF-5 scores and PVR. There were significantly less adverse events with PAE (39.0% vs. 77.7%) and shorter hospitalization times with PAE (mean difference = −1.94 days). PAE had significantly longer procedural times (mean difference = 51.43 minutes). Another recent meta-analysis of comparative studies including PAE, analyzed six randomized clinical trials against TURP and two nonrandomized comparative trials against prostate surgery and one comparative trial against a sham procedure. Little to no difference in IPSS and QoL improvements when PAE is compared with prostate surgery. However, PAE may increase retreatment rates (risk ratio = 3.64 in short-term and risk-ratio of 1.51 in long-term). PAE may reduce the occurrence of ejaculatory disorders (risk ratio of 0.51). The need for more studies reporting long-term data after PAE was highlighted. Long-term data after PAE have shown the potential for a 20% retreatment rate at 2 years, with clinical success rates of approximately 75% after 3 years. Repeat PAE may be an option especially for those patients who initially improved after embolization but had relapsing symptoms. Most interventional radiology guidelines recommend PAE as a valid treatment option for BPH patients, as well as national guidelines and European urology guidelines.

Conclusion

PAE is a minimally invasive treatment option for BPH patients with symptomatic improvements comparable to standard prostatic surgery. The key aspects for the preprocedural patient consultation and evaluation, imaging planning for PAE, technique, and optimizing outcomes are revised. The minimally invasive nature of PAE with a faster recovery, preserving the sexual function is very attractive to patients. However, patients should be informed about the potential risks of higher retreatment rates with PAE and shorter duration of treatment effect when compared with standard prostatic surgery.

Conflicts of Interest

T.C.A.F.B.: Speaker fees for Terumo, Merit, Philips, Cook, stockholder for EmbolX. N.V.C.: Speaker fees for Terumo, Merit, and Bial. All the other authors report no conflict of interest.

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