Prostatic Artery Embolization for Benign Prostatic Hyperplasia: A 10-Year Update

A review of technical tips, available devices, and embolic agents used in PAE for benign prostatic hyperplasia.

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It has been 10 years since the first two prospective observational studies have shown that prostatic artery embolization (PAE) is safe and effective to treat lower urinary tract symptoms (LUTS) and acute urinary retention associated with benign prostatic hyperplasia (BPH).[1,2] Since then, many single-arm prospective studies and randomized controlled studies have been published showing that PAE is safe and effective to treat LUTS, with comparable results to surgery.[1-19] Even though functional outcomes such as prostate volume reduction and relief of bladder outlet obstruction may be superior with surgery when compared with PAE, clinical improvement is similar between the two techniques.[4,6,9,14-16] The lower adverse event profile and faster recovery favor PAE over surgery, making PAE a very attractive treatment alternative for patients refractory to, not responding to, or who cannot tolerate medical therapy for bothersome LUTS.[4,6,9,14-16]

PAE may be useful for very large prostates, for patients under acute urinary retention, or patients with hematuria of prostatic origin due to BPH and prostatic cancer.[1-23] From a cost-analysis point of view, PAE may be more favorable than prostatic surgery.[24] The cumulative evidence from the past 10 years has led to PAE being endorsed by interventional radiology societies around the world as an acceptable minimally invasive treatment option for appropriately selected men with BPH and moderate to severe LUTS.[25,26] The United Kingdom guidelines propose PAE as an acceptable treatment option for men with LUTS and BPH,[27,28] although the urology guidelines only advise the use of PAE for BPH in clinical trials.[29,30] This is mostly due to the absence of sham-controlled trials or long-term evidence of treatment efficacy. Recently, a sham-controlled trial has established the safety and efficacy of PAE, eliminating all claims that the PAE outcomes could be explained by a placebo effect.[31] Growing evidence on long-term outcomes after PAE is starting to appear as PAE awaits impending acceptance in the urology guidelines.[20,32]

OVERVIEW OF APPLICABLE MEDICAL DEVICES FOR PAE

Types of Embolic Material(s)

Materials, characteristics, and approaches for use. Currently used embolic agents for PAE include polyvinyl alcohol (PVA) particles (Bearing nsPVA, Merit Medical Systems, Inc.; Contour, Boston Scientific Corporation) and spherical embolic agents such as spherical PVA (Bead Block, Boston Scientific Corporation), trisacryl gelatin microspheres (Embosphere, Merit Medical Systems, Inc.), polyzene-coated hydrogel microspheres (Embozene, Varian Medical Systems), and polyethylene glycol microspheres (HydroPearl, Terumo Interventional).[1-24,33-35] There are limited comparative studies between the different commonly used embolic agents for PAE and no clear benefit of one over another.[34,36,37] Basic knowledge of how to use and prepare these embolic agents for PAE is required because prostatic arteries are small, and premature stasis may be obtained after only 1 or 2 mL of the embolic solution have been injected, leading to suboptimal results.

To avoid premature stasis during PAE, the operator has four options: (1) place the microcatheter distally inside the prostatic arteries to avoid clumping of the embolic material proximally inside the main prostatic artery trunk; (2) use

very diluted embolic solutions; (3) flush the microcatheter with saline with every 1 to 3 mL of embolic solution injected; and (4) downsize the embolic materials.

Although the tendency for clumping is usually linked to PVA particles, it is also often seen with spherical embolic agents during PAE. The operator should be aware of the volume of embolic material that comes with each vial. Many embolization packages provide vials with 2 mL of embolic material; however, other vials only contain 1 mL of embolic material. Some distributors may provide embolic vials with either 1 or 2 mL of embolic material. Each 2 mL of embolic material should be diluted into 20 to 40 mL of embolic solution (high dilution) with a mixture of saline and contrast so that the embolic material stays in suspension. If the embolic material drops, contrast is added. If the embolic material goes up, saline is added. This addition of saline and contrast should be made until 20 to 40 mL of embolic solution in a homogeneous suspension is achieved with PVA particles and microspheres. By positioning the microcatheter distally inside the prostatic arteries, either inside the prostate or near the prostatic capsule, higher amounts of embolic solutions can be injected.[9,38]

Specific applicable sizes. Regarding embolic sizes used for PAE, PVA particles are different from microspheres. With PVA particles, results may be improved with the combined use of smaller (100 µm) followed by larger (200 µm) PVA particles.[33,39] The use of smaller (100 µm) PVA particles alone may lead to greater revascularization and relapsing symptoms.[33] Smaller (100 µm) PVA particles have shown greater prostate volume reduction and bladder outlet obstruction relief, which may be due to the deeper penetration, and more prostatic ischemia and destruction.[33,39] Both PVA particle sizes are equally safe, with no increase in the rate of adverse events with downsizing.[33,39] Thus, when using PVA particles, the recommendation would be to start with 2 to 5 mL of embolic solution with smaller (100 µm) particles, followed by larger (200 µm) PVA particles. Using PVA particles < 100 µm is not feasible in most countries, as they are not readily available. Using only PVA particles > 200 µm is not recommended because it may lead to proximal embolization with lower penetration inside the prostate and suboptimal outcomes.

For microspheres available for PAE, one should value the different characteristics among them. Embospheres are more rigid and penetrate less distally than Bead Block, Embozene, or HydroPearl. Bead Block, Embozene, and HydroPearl are more compressible with a higher in vivo deformation, which leads to a more distal occlusion within the vascular network, and are more unpredictable and less correlated with the actual particle size being used.[40,41] The size paradox of microspheres for PAE has its threshold at 300 µm. Because one vial is enough for virtually all PAE procedures, the question remains whether to use microspheres ≥ 300 µm or ≤ 300 µm.[42] Standard use sizes for PAE include Embosphere 100–300 µm and/or 300–500 µm, Bead Block 300–500 µm (100–300 µm is discouraged due to the potential of nontarget embolization associated with deep penetration due to compressibility), and Embozene and HydroPearl 250 µm and/or 400 µm. Some studies have shown that using < 300-µm microspheres could be safe and effective for PAE[11,15,35,43] and that PAE with smaller (< 300 µm) microspheres could lead to better results.[44,45] However, prospective comparative studies using smaller (< 300 µm) microspheres versus larger (> 300 µm) microspheres have failed to show any added clinical benefit and a potential for increasing adverse events after PAE, bringing into question the role of < 300-µm microspheres for PAE.[46,47] Use of microspheres > 400 µm is not recommended due to the potential for proximal embolization with lower penetration inside the prostate and suboptimal outcomes.

Catheters and Wires

Even though most commonly performed from a transfemoral approach (TFA),[1-23] PAE can also be performed using a transradial approach (TRA).[48,49] Dedicated radial sheaths and longer 5-F Berenstein catheters (ie, 125- to 135-cm-long, Performa, Merit Medical Systems, Inc.) should be used for PAE from TRA, and longer microcatheters are needed (150-cm long instead of 135-cm long). When using TFA, 5-F catheter preference varies within institutions and operators. Some commonly used 5-F catheters include uterine artery catheters (Impress hydrophilic diagnostic UAC2, Merit Medical Systems, Inc.; Beacon Tip, Cook Medical), Cobra catheters, Berenstein catheters, Simmons catheters, and Rösch inferior mesenteric catheters. In our practice, we use the PPC2 catheter (Performa) that was redesigned similarly to the uterine catheters but with a stiffer body, allowing better torqueability. These catheters have a preshaped Waltman loop 20 to 30 cm proximally to the tip, allowing bilateral internal iliac artery catheterization from a single femoral puncture. Common 0.035-inch hydrophilic wires used with these catheters include the Laureate (Merit Medical Systems, Inc.), Radifocus (Terumo Interventional Systems), and Glidewire (Terumo Interventional Systems). Radifocus and Glidewire are 0.035-inch shapeable hydrophilic wires that can be very useful.

Commonly used microcatheters range in size from 2 to 2.4 F. We tend to prefer microcatheters with preshaped swan-neck curves at the tip (Maestro or Pursue, Merit Medical Systems, Inc.; Direxion, Boston Scientific Corporation). These tip angulations provide the microcatheter with torque capability, which allows for selective prostatic artery catheterizations even without a microguidewire in some procedures.[38] Preferred microwires include 0.014- to 0.016-inch Glidewire GT (double-angled or 90°-angled), Fathom (shapeable, Boston Scientific Corporation), Asahi

Meister (shapeable, Asahi Intecc USA, Inc.), Hi-Torque BMW wire (Abbott), and Synchro (Stryker). For very challenging prostatic arteries with tight, angulated origins from the superior vesical artery, steerable microcatheters (SwiftNinja, Merit Medical Systems, Inc.) may be very useful.

Next-Generation Developments

Although the steerable and preshaped swan-neck curved microcatheters have been helpful for many previously impossible PAE procedures, there are still some technical failures of selective prostatic artery catheterization. Iliac artery tortuosity, atheroma, and prostatic arteries arising from the superior vesical artery with angulated origins are known risk factors for the failure of prostatic artery catheterization.[44,50,51] Existing guidewires still fail to achieve selective catheterization in many of these situations, and unilateral PAE is reported in up to 16%, 22%, and 37% of patients with mild, moderate, or severe tortuosity of pelvic arteries, respectively.[51] Better supporting 5-F catheters with torqueability, steerable 5-F catheters, and steerable wires would be interesting future technologic developments to improve PAE success. The steerable microcatheters work within the large-space vascular lumen (> 2 mm); however, they lose steering capabilities within smaller lumens (< 2 mm). Redesigned technology to increase the steering capabilities with greater resistance to maneuvers (some still break the steering wires after multiple uses) would be important points for improvement. Also, many available microwires do not have torque response when used within smaller lumens (< 3 mm); thus, they cannot be used for selective catheterizations.

TECHNICAL TIPS

Imaging Tips/Techniques

We are strong advocates of preprocedural imaging planning. We introduced the concept of using CTA before PAE in 2011 and still use it today.[52] Preprocedural MRA has also been shown to be reliable for pre-PAE planning, but its use is less generalized as compared with CTA.[53,54] Preprocedural imaging planning is essential because PAE may be a procedure associated with high radiation exposure for patients and medical staff.[55] Cone-beam CT (CBCT) can also be used during the procedure to map the pelvic arteries, identify all feeders to the prostate, assure correct microcatheter location before selective PAE, and exclude nontarget embolization.[56,57] CBCT can also provide accurate information about central gland coverage during PAE and if there is any missing artery that should be embolized.[58] With CBCT, duplicate feeders to the central gland can be identified, allowing a more complete embolization of the whole central gland (Figure 1). Our digital subtraction angiography (DSA) protocols are 6 mL at 3 mL/second in the internal iliac arteries and 5 mL at 2 mL/second in the prostatic arteries. For CBCT, our protocols are diluted contrast 350 mg I/mL (50%/50% with saline), 10-second rotational scan of 180° at 18° rotation per second, image acquisition every 0.5°, source power of 125 kVp, and 316 matrix images (512 X 512 voxels). Injection volume and rate of injection should be adjusted to cover the whole acquisition time plus some more time to start injection 2 to 5 seconds before the start of acquisition (arrival time). Therefore, with a 10-second acquisition time, our protocols are CBCT in the aorta, 45 mL, 3 mL/second, arrival time of 5 seconds; CBCT in the internal iliac artery, 28 mL, 2 mL/second, arrival time of 4 seconds; and CBCT in the prostatic arteries, 7 mL, 0.5 mL/second, arrival time of 4 seconds.

Technical Advice

We use TRA as the first-line approach if the patient is aged < 75 years; has a radial artery diameter > 2 mm; has a Barbeau test result of A, B, or C; and is < 1.85 m (< 6 ft). TRA is only performed using the left arm to exclude any neurologic event from passing over the supra-aortic trunks. As such, our practice has shifted to 70% radial versus 30% femoral access for PAE. With radial access, we use the 5-F Berenstein catheter (125- to 135-cm-long) and the 150-cm swan-neck curved-tip 2.4-F Maestro. With TFA, we use the PPC2 catheter, which allows bilateral pelvic catheterization with a single femoral puncture and the 135-cm–long swan-neck curved-tip 2.4-F Maestro. Balloon occlusion microcatheters (2.4-F Sniper, Emblx, Inc.) are available options to minimize nontarget embolization[38,59] and may prevent the need for protective coil placement before PAE.[60,61] Our preferred microguidewires include the 0.016-inch Glidewire GT (double-angled), Fathom (shapeable), or Asahi Meister (shapeable).

Because we use preprocedural CTA, the anatomy of the pelvic arteries is identified before the procedure so that we do not routinely use intraprocedural DSA, which is responsible for 75% of the radiation exposure during PAE and may reach problematic levels because of the frequently used magnified steep oblique views.[55] Limiting the use of DSA allows for significant reduction in radiation exposure. Acquisitions acquired with CBCT cut the amount of radiation exposure in half when compared with DSA. The 35° to 40° ipsilateral anterior oblique view with caudal-cranial angulation (-10°) is essential to help separate the internal iliac branches and identify the anatomy of the prostatic arteries. Also, magnified views are recommended because the prostatic arteries may be very small (1 to 2 mm in size).[62]

After identifying the prostatic arteries, road map imaging is recommended to help guide selective catheterization attempts. With preprocedural imaging guidance, there is no need for DSA or CBCT runs from the aorta or internal iliac arteries to study the vascular anatomy of the pelvis. After selective catheterization of the prostatic arteries,

we routinely use CBCT (and not DSA) due to lower radiation exposure and because it can detect potential arteries leading to nontarget embolization. CBCT also allows for confident targeting of the prostate, whereas DSA findings after prostatic artery catheterization are nonpathognomonic and may resemble the bladder, seminal vesicles, rectum, or penis.[52,55-58,62] The certification of correct targeting of the prostate with CBCT without nontarget embolization to the rectum, penis, or bladder is fundamental, as serious adverse events from nontarget embolization have been described.[63,64]

When large anastomoses are present between the prostate and the bladder, rectum, or penis, protective coils may be placed to exclude these anastomoses and redirect flow into the prostate and away from the surrounding organs.[38,59-61] Because these anastomoses tend to be very small in size (2–3 mm), short (2–3-cm long) pushable (Tornado, Cook Medical) or detachable (Retracta, Cook Medical; Interlock, Boston Scientific Corporation; Concerto, Medtronic) 0.018-inch microcoils are most frequently used. Sometimes, 3- to 6-mm microcoils can be used in larger collateral branches to redirect flow into the prostate.

After ensuring correct prostatic location without nontarget embolization, we proceed with embolization using smaller (100 µm) PVA particles, followed by larger (200 µm) PVA particles or 300–500-µm Embosphere, 300–500-µm Bead Block, or 400-µm Embozene. We give 100 to 200 µg of intra-arterial nitroglycerin inside the prostatic arteries and flush with saline just before starting embolization. We try to position the microcatheter deep inside the prostatic arteries from the start of embolization[38] to allow reflux of the embolic material along the main prostatic artery trunk without the need for control DSA after embolization.

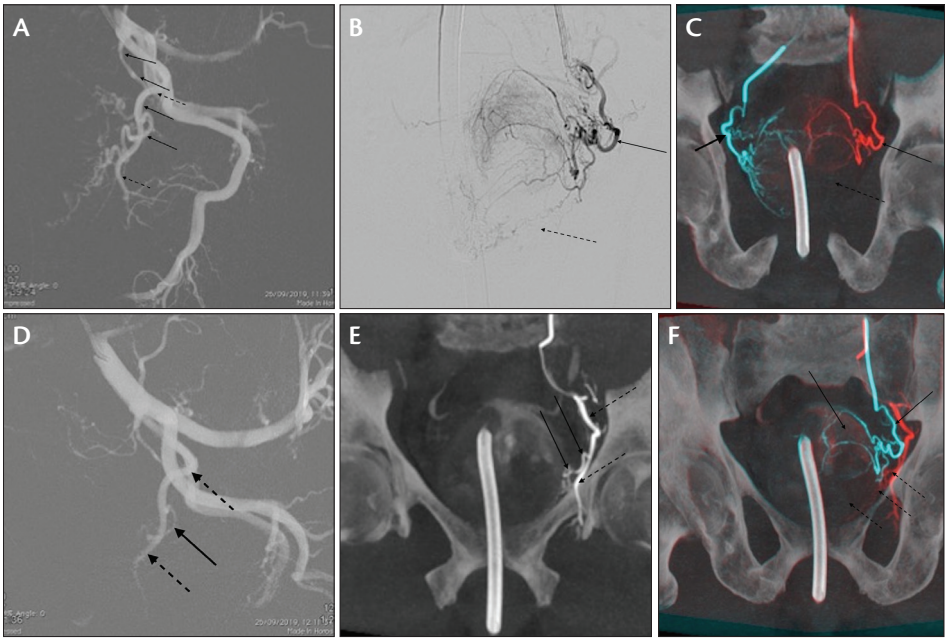

Figure 1. Left anterior oblique view (35° with caudal-cranial angulation -10°) road map of the left internal iliac artery depicting the left prostatic artery (arrows) overlapping with the obturator artery (dashed arrows; A). Posteroanterior DSA after selective catheterization of the left prostatic artery (arrow) denoting lack of vascularization of the inferior third of the left central gland of the prostate (dashed arrow; B). CBCT coronal reformat overlaid imaging after selective catheterization of the left prostatic artery (arrow) and right prostatic artery (solid arrow), denoting the asymmetric lack of vascularization of the inferior third of the left central gland of the prostate (dashed arrow; C). Left anterior oblique view (35° with caudal-cranial angulation -10°) road map of the left obturator artery (dashed arrows) depicting a second left prostatic artery (arrow; D). CBCT coronal reformat confirming a second left prostatic artery (arrows) vascularizing the lower third of the central gland arising from the obturator artery (dashed arrows; E). CBCT coronal reformat overlaid imaging after selective catheterization of the left prostatic artery vascularizing the upper two-thirds of the central gland (arrows) and the left prostatic artery vascularizing the lower third of the central gland (dashed arrows; F).

Embolization is considered finished when complete stasis of embolic material is seen with reflux almost up to the prostatic artery origin. As a final tip, we always try to work with the "double torque" provided by the 5-F catheter and the microcatheter, positioning the 5-F catheter tip as close as possible to the prostatic artery origin, guiding the prostatic artery catheterization with the microcatheter and providing more support.

CONCLUSION

PAE has come a long way since it was introduced 10 years ago. At present, the level of evidence in favor of PAE is unanimous within interventional radiology societies around the globe and within certain national health care systems. However, acceptance within the urology guidelines as an alternative treatment option to surgery or medical therapy for men with BPH is still on hold. ■

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