

PAE: Factors That Will Influence Widespread Acceptance

A look at the current position of PAE and the opportunities and challenges of establishing its role in the treatment pathway for symptomatic benign prostatic hyperplasia.

BY TIMOTHY J.C. BRYANT, BMedSci, BMBS, MRCP, FRCR

Prostate artery embolization (PAE) has been established as a viable option for treatment of lower urinary tract symptoms (LUTS) caused by obstruction secondary to benign prostatic hyperplasia (BPH). It was recognized as an appropriate treatment for BPH by the Brazilian Federal Council of Medicine in March 2016 and the National Institute for Health and Care Excellence (NICE) in the United Kingdom in 2018.^{1,2} Results from randomized controlled trials in Brazil, China, Switzerland, and, more recently, Spain have been presented but not yet published and have been supported by the results of comparative cohort studies (eg, UK-ROPE) and large-volume data.³⁻⁸ All of these studies have demonstrated similar outcomes across operators and embolic choice and have found that PAE is a safe and reproducible procedure with minimal side effects. The procedure allows same-day discharge, without the need for urinary catheterization in the majority of patients, and a rapid return to normal activity. However, PAE has not yet been recognized by the European Association of Urology (EAU) or American Urological Association (AUA).^{9,10}

Outcome data have not shown PAE to be noninferior to transurethral resection of the prostate (TURP), but they have demonstrated a significant improvement in symptoms in those treated. Clinical improvement has been reproducibly demonstrated in over 80% of patients. There appears to be an early cohort of nonresponders (10%–20%), despite good technical success. The reason for this is not yet clear, but retrospective analysis of this patient cohort may help preemptively identify those who are unlikely to benefit and, in turn, define the likely

responders. Current evidence suggests symptom recurrence in responders of up to 10% over 5 years.⁸

LONG-TERM OUTCOME DATA

Within the published literature on PAE, there are limited long-term outcome data. In the largest cohort study from Portugal that included 630 patients, most clinical failures occurred during the short term (< 1 month in nonresponders), with a decrease in the incidence of symptom recurrence at medium- and long-term follow-up.⁸ The overall clinical success rate was 85.1% at short-term, 81.9% at medium-term, and 76.3% at long-term follow-up (232 patients were followed to 36 months, 103 out to 48 months, 36 out to 60 months, and 8 out to 78 months). This mirrors outcomes from the Southampton cohort presented at CIRSE 2018, in which 48 patients were followed to 3 years, with the majority of clinical failures occurring within the first 15 months and a small reduction in clinical success from 81% to 71.4% between 1 and 3 years.¹¹ Data from a Chinese study using smaller embolic agents demonstrated even better rates of success, with clinical success in 91.7% at 24 months.¹²

Many of the initial cohort studies and randomized controlled trials are now at the stage where longer-term data should be available, which would help to define the expected longevity of clinical outcomes. More long-term outcome data are required if PAE is to be considered a lasting and economical treatment option.

SAFETY

All evidence so far points to the safety of PAE. In general, complications are not clinically significant. Although

there is a risk of acute urinary retention requiring catheterization postprocedure, in most studies, this rate was < 2%. When nontarget embolization has occurred, it has been generally self-limiting and has resolved with conservative management.

A major selling point of PAE is the low morbidity and avoidance of side effects associated with long-term medication, such as aspermia and reduced libido, as well as the risks involved with surgery, including retrograde ejaculation and incontinence. Results from the Swiss randomized controlled trial and UK-ROPE have noted an incidence of ejaculatory dysfunction post-PAE,^{5,7} but this is less than with TURP. Retrograde ejaculation was reported in 24% of patients post-PAE versus 48% post-TURP. However, on further questioning, most patients reported that the problem had existed prior to embolization, most commonly secondary to medication. In the Swiss trial, 56% of the PAE arm reported ejaculatory dysfunction compared with 84% in the TURP arm. In the literature, TURP causes retrograde ejaculation in between 48% to 84% of cases.¹³

Radiation is a perceived risk from PAE, although radiation doses have been within acceptable limits with no significant clinical implications. In the UK-ROPE cohort, the median screening time was 38 minutes with a median dose area product of 17,892 cGy·cm² and median skin dose of 1,368 mGy.⁷ This equates to

44 mSv with a 0.17% additional lifetime cancer risk in a 50- to 59-year-old man compared with the estimated lifetime risk of a cancer diagnosis of 1 in 2 (50%) for men in the general population.¹⁴⁻¹⁶

PATIENT SELECTION

Patient selection rightly depends on collaboration with urologists. Educated patients are often driven to seek alternative and new therapies directly; however, interventional radiology is not able to take on the holistic care of this subgroup of patients. Some patients may have underlying prostate cancer, and others may have symptoms unrelated to bladder outflow obstruction. Moving forward, as with uterine artery embolization for fibroids, it is vital that patients are adequately informed of all available treatment options so that they can make an informed decision. In this respect, interventional radiology should not be seen as a threat but rather as a partner. UK-ROPE has shown how well collaboration can work with engagement from the British Association of Urological Surgeons, British Society of Interventional Radiology, and NICE. Further trials using this collaborative approach would be hugely beneficial. It is essential to work together to provide patients with evidence to support or refute each treatment option and enable them to choose that which suits them best.

At present, the ideal patient for PAE has not yet been identified. There is still a tendency for PAE to only be offered to patients who are not candidates for surgery, such as elderly and infirm patients and those on anti-coagulation, who are more likely to have severe arterial tortuosity and atheromatous disease, the incidence of which increases with age and comorbidity. Although many of these patients benefit from PAE, difficult anatomy can result in longer screening times and higher radiation doses both to patient and operator.

The natural position of PAE on the treatment pathway is in a younger patient cohort that has significant symptoms, has tried medication and either not tolerated the side effects or not seen a benefit, and would not consider surgery due to its inherent risks. This patient subgroup now has several options to choose from in terms of minimally invasive therapies. These include PAE, transurethral water vapor ablation (Rezüm, NxThera, Inc.), and UroLift (NeoTract, Inc.), which are all recognized and approved by NICE.

Treatment options depend on gland size and morphology. UroLift is only suitable for treating smaller glands (< 70 mL in most studies) and has no proven benefit in individuals with a large median lobe.¹⁷ Rezüm is only beneficial in treating glands < 120 mL, and there are limited long-term outcome data.¹⁸ PAE is technically

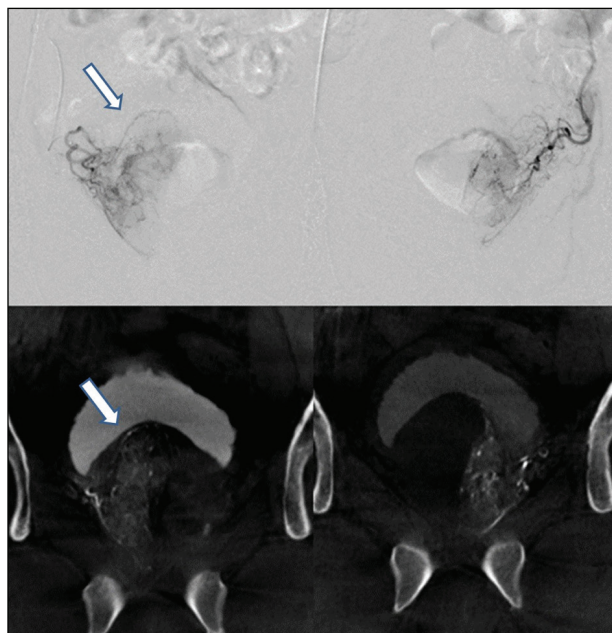


Figure 1. Bilateral prostate artery angiograms in an antero-posterior projection with matching coronal cone-beam CT reformatted demonstrating supply to the median lobe arising from the right prostatic artery (arrow).

easier with larger, more vascular prostates. There is no concrete evidence to support improved outcomes in larger prostates, although some studies have shown a linear association between prostate size and the magnitude of symptom relief, and there is evidence that percentage volume reduction at 3 months is a strong predictor of symptomatic improvement at 12 months.¹⁹ There remains the question of efficacy of PAE in patients with large median lobes. At present, the only available treatments with proven benefit for patients with glands > 120 mL are PAE and surgery with holmium laser enucleation or Millin prostatectomy.

Symptoms also play a role in patient selection for PAE. Storage symptoms including frequency, urgency, and nocturia often represent the most significant symptoms for patients and have the most impact on quality-of-life score. Initial evidence suggests that embolization has a proportionally greater effect on these symptoms than surgical therapies.²⁰ The underlying mechanism behind this is not yet fully understood, and it should be noted that storage symptoms in the absence of voiding symptoms can be multifactorial and not related to bladder outflow obstruction. In questionable cases, urodynamic testing can be important to identify bladder outflow obstruction.

Urodynamic testing is also useful for catheter-dependent patients to assess bladder function to ensure a potential for response post-PAE. PAE has been shown to be beneficial in the management of patients with acute urinary retention and repeated failure of trial without catheter. In this subgroup, success rates are > 90%.^{21,22}

An understanding of the ideal candidate for PAE would help with recognition of the procedure by the national urologic societies and allow formal positioning on the LUTS treatment pathway.

PROCEDURAL STANDARDIZATION, TRAINING, AND PROCTORING

PAE is a complex procedure involving highly variable anatomy and a high incidence of nontarget anastomoses. It is essential that interventional radiologists who perform this procedure are experienced with embolization. Specifically, they need to have an in-depth knowledge and understanding of pelvic arterial anatomy,²³ have attended a training course or been an observer at a high-volume center, and have been properly trained and proctored for at least the first six cases. PAE courses are available around the world, and proctoring is well supported such that dissemination of the technique should be safe and sustainable.

Use of appropriate modern angiographic equipment is essential. Modern equipment with improved image quality and low-dose algorithms significantly reduces pro-

cedural dose and is important for patient and operator safety. Cone-beam CT has significantly improved visualization of the target territory (Figure 1) and appreciation of potential nontarget vessels; therefore, the capability to perform cone-beam CT should be mandatory in centers performing PAE even if it is not used in every case. This is particularly true for low-volume centers and those early within the learning curve.

There is still debate regarding the optimal embolic agent, both in terms of size and type. For instance, both conventional polyvinyl alcohol (PVA) and spherical embolic agents are widely used. Size ranges from 50–500 μ m for PVA in different trials to 100–500 μ m for spherical embolic agents. Each spherical agent has different properties, with some being more compressible than others and subsequently having different endpoints. At present, there is no evidence to support any one embolic type or size.²⁴ The short-term outcomes are similar irrespective of embolic size; however, it remains to be seen whether long-term outcome is affected.

Evolution of embolization technique has also occurred since the initial studies, culminating in the PErFecTED technique pioneered in Brazil.²⁵ This relies on flow-directed embolization followed by wedge injections into the arteries supplying the transitional zone. The published results with PErFecTED are better than those of the original PAE studies. Qmax and postvoid residual results are not as good as those observed with TURP, but other parameters are similar. The caveat is that the PErFecTED technique requires more time, an increased radiation dose, and a theoretical increased risk of nontarget embolization.

HEALTH ECONOMICS

Symptomatic BPH is a significant economic burden on health care systems. Bothersome LUTS affect up to 30% of men > 65 years and increase with age.

Health economic data suggest that the procedural costs for PAE are lower than with surgical alternatives. Although equipment costs are higher for PAE, overall costs including anesthetic/nursing and theatre time, in addition to inpatient stay, are greater for TURP.²⁶

It is vital that PAE is adequately reimbursed to make it an economically viable option. This relies on a robust tariff structure that covers costs and does not penalize purchasers or providers. At present, although PAE is recognized by NICE in the United Kingdom, there is still some resistance to funding the treatment pending a formal tariff, as well as resistance from the EAU and AUA, and this is proving a stumbling block to widespread acceptance and availability.

CONCLUSION

All patients with BPH fall under the urology investigation and treatment pathway. Treatment options are either provided by urologists (TURP, laser treatments, water vapor ablation, water jet ablation, UroLift) or interventional radiologists (PAE). All treatments should be of interest to urologists, as each show benefits in different settings. None are mutually exclusive, and all can be used in the treatment of LUTS secondary to BPH, thus offering patient choice.

More comprehensive studies evaluating comparative safety, efficacy, cost, and long-term outcome would be beneficial for this large patient population. These should include randomized controlled trials comparing minimally invasive therapies with pharmacologic therapy in addition to surgical options. Each treatment will likely have an optimal patient cohort, and identifying appropriate patients would facilitate treatment planning and help with patient decision-making. Identification of real-world procedural costs will help to optimize reimbursement, benefitting both purchasers and providers. In addition, the secondary costs of managing complications and retreatment can be assessed if an appropriate patient population and areas where morbidity is lowest can be established. In general, early treatment may reduce the morbidity of intervention later in the patient pathway, where there is an increased risk with surgery and the secondary effects of long-term chronic retention have developed.

Interventional radiologists should grasp the opportunity to build on the excellent and innovative work already carried out and should continue to collect robust data and work collaboratively with urologists to establish the position of PAE in the treatment pathway for LUTS. ■

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Timothy J.C. Bryant, BMedSci, BMBS, MRCP, FRCR

Consultant Interventional Radiologist

University Hospital Southampton

NHS Foundation Trust

Southampton, Hampshire, United Kingdom

timothy.bryant@uhs.nhs.uk

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