

# Embolization of Prostate Gland as Treatment for Benign Prostatic Hyperplasia (Bph): Review and Update

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## Abstract:

Prostatic artery embolization has been emerging as an effective and safe treatment option of symptomatic benign prostatic hyperplasia. Symptomatic benign prostatic hyperplasia is a common condition which afflicts the aging population which is ensued by the development of bothersome lower urinary tract symptoms and decreased quality of life and at times urinary retention as well as haematuria. Patients who are afflicted by BPH often are treated with medication and offered surgery for persistent symptoms. Transurethral resection of the prostate is regarded as the traditional standard of care, and in cases of extremely large prostate glands prostatectomy tend to be undertaken either as retropubic or trans-vesical prostatectomy but several minimally invasive surgical treatments also are offered. Prostatic artery embolization (PAE) has emerging as an effective treatment option with few reported adverse effects, minimal blood loss, and infrequent overnight hospitalization. The procedure is offered to patients who have moderate to severe lower urinary tract symptoms and depressed urinary flow due to bladder outlet obstruction. Proper patient selection and meticulous embolization are pivotal for optimization of the outcome of PAE. In order to undertake PAE safely and to avoid non-target embolization, interventional radiologists need to be very well trained they should have a detailed understanding of the pelvic arterial anatomy. Even though the prostatic arteries often arise from the internal pudendal arteries, many anatomical variants and pelvic anastomoses are encountered. Prospective cohort studies, small randomized controlled trials, and meta-analyses had demonstrated improved symptoms after PAE treatment, with serious adverse effects occurring rarely. This article has been written to provide an update on PAE which must be understood in order to develop a thriving PAE practice. These principles include careful assessment of patients, review of surgical therapies, details of the anatomy of the arteries of the pelvis including the prostate artery including its origin and branches, basic principles of embolization, and an overview of published results.

**keywords:** prostate artery embolization; prostatic artery embolization; angiography; interventional radiologist; benign prostate hyperplasia; urinary retention; lower urinary tract symptoms; haematuria

## Introduction

Prostate artery embolization (PAE) has emerged as a new treatment option for patients who have symptomatic benign prostatic hyperplasia with lower urinary tract symptoms or urinary retention. The main challenges related to this procedure include the navigation of arteries with atherosclerosis and anatomical variations, and the potential risk of non-target embolization to pelvic structures related to the presence of collateral shunts and reflux of microparticles. Understanding of the classical vascular anatomy and the most common variations of the vasculature of the pelvis is pivotal for the undertaking of a safe embolization, good clinical practice, and optimal outcomes. The undertaking of PAE requires availability of a well-trained interventional

radiologist as well as availability of good radiology imaging facilities. Unfortunately, there are not many interventional radiologists in various health care establishments in the world especially within the developing countries. Considering that a number of patients who have benign prostate hyperplasia may have comorbidities that would render them unfit to undergo surgical operations for their BPH problems, availability of facilities and well-trained interventional radiologist who can undertake PAE in most urology establishments in the world would be of great help to many patients globally. Considering that PAE is now developing in the world, it would be envisaged that some clinicians in the world may not be

familiar with the PAE procedure. The ensuing article has been written to provide an update on PAE for BPH.

## Aim

- To provide an update on embolization of the prostate artery in the treatment of benign prostatic hyperplasia.

## Methods

- Internet databases were searched including: Google; Google Scholar; Yahoo; and PUBMED. The search words that were used included: Prostate artery embolization, and prostatic artery embolization. Thirty-four articles were identified which were used to write the article which has been divided into two parts: (A) Overview, and (B) miscellaneous narrations and discussions from some case reports, case series, and studies related to prostate artery embolization in the treatment of problems emanating from benign prostatic hyperplasia (BPH).

## Results

### [A] Overview

#### General statements / definition

Benign prostatic hyperplasia (BPH), also known as benign prostatic hypertrophy, is a histological diagnosis which is characterized by proliferation of the cellular elements of the prostate, leading to an enlarged prostate gland. Chronic bladder outlet obstruction (BOO) secondary to BPH may lead to urinary retention, impaired kidney function, recurrent urinary tract infections, visible hematuria, and bladder calculi.

- It has been iterated that nodular hyperplasia of the prostate gland, is also referred to as benign prostatic hyperplasia, which is abbreviated (BPH), is a common benign pathology of the prostate gland. [1]
- It has also been pointed out that nodular hyperplasia of the prostate gland is also referred to as prostatic nodular hyperplasia. [1]
- It has also been iterated that nodular hyperplasia of the prostate gland occasionally, is referred to as benign prostatic hypertrophy, which is a misnomer, in that nodular hyperplasia of the prostate gland is not a hypertrophy of the prostate gland. hypertrophy.
- It has been pointed out that BPH is very common. [1]
- It has also been iterated that BPH does increase with age.

#### Clinical Features

A number of individuals who have BPH, may be asymptomatic but others may manifest with symptoms some which include the ensuing:

- Lower urinary tract symptoms including:
  - Poor flow of urine
  - Hesitancy
  - Intermittent flow of urine
  - Incomplete emptying of bladder post voiding
  - Post-micturition dribbling
  - Straining to void
- Irritative voiding symptoms including:
  - Urinary urgency

- Urinary urge incontinence
- Visible haematuria
- Urinary retention

#### Assessment / Diagnosis

- Clinical examination upon digital rectal examination may reveal an enlarged benign feeling prostate gland, the size would tend to be dependent upon how big the prostate is at the time of manifestation and this varies from individual to individual.
- Pre-micturition and post micturition urinary bladder scan would demonstrate the extent of emptying of the urinary bladder by enabling the urologist know how much urine is left after voiding.
- Assessment of the urine flow rate would enable the clinician know the rate of flow of the urine.
- Taking a full history and assessment of the IPSS questionnaire by the clinician to ascertain the severity of the symptoms.

#### Laboratory tests

##### Urine

- Urinalysis, urine microscopy and culture and general assessment tests that tend to be undertaken of each patient and in the majority of patients, the results would tend to be normal but if there is any evidence of urinary tract infection, based upon the sensitivity pattern of the cultured organism, the patient would be treated with the appropriate antibiotics based upon the antibiotic sensitivity pattern of the cultured organism.

##### Haematology blood tests

- Full blood count, and coagulation screen tend to be undertaken in the initial assessment of all patients who are afflicted by BPH, and most often the results would be normal, but if there is any evidence of anaemia or impairment in any of the haematology blood test results, it would be investigated and treated accordingly to improve the general state of the patient.

##### Biochemistry blood tests

- Serum urea, creatinine, and electrolytes levels tend to be assessed during the initial assessment of each patient and the results would tend to be normal in majority of cases, but in cases of retention, sometimes there may be evidence of impaired renal function which the clinician would have to treat appropriately.
- Serum prostate-specific antigen is a test that is generally undertaken in the initial assessment of any individual who manifests with BPH symptoms and this would establish a base line level of the serum PSA level. In the majority of cases, the results would tend to be normal, but in some cases, the serum PSA level, may be raised for which the clinician would have investigate to confirm whether or not the individual could have prostate cancer even if upon digital rectal examination, the prostate gland feels benign regarding its consistency. The age of the individual in relation to his serum PSA level and subsequent PSA velocity also provide information to the clinician whether or not to assess the individual to ascertain if he has adenocarcinoma of prostate gland.

## Radiology image assessments

### Ultrasound scan

- During the outpatient clinic assessment, basic information regarding pre-micturition urinary bladder volume of urine and post-micturition measurement of residual urine volume helps the clinician to decide if the commence medical treatment of the BPH or not. If the clinician doing the ultrasound scan in the clinic can interpret the ultrasound features reasonably, the clinician could also measure the volume of the prostate gland as well as ascertain if there are any abnormal areas with the prostate gland as well as if there is any evidence of hydroureter.
- Subsequent ultrasound scan of the prostate gland that is undertaken in the radiology department would be reported including the size, the regularity, and symmetry of the prostate gland as well as if there are any abnormal areas within the prostate gland including the site of the abnormal area. The ultrasound scan would also report the features of the urinary bladder and the upper urinary tract.
- In some centres, if there is any suspicion or possibility of a prostate cancer then ultrasound-guided biopsy of the prostate gland is undertaken for pathology examination.

### Computed Tomography (CT) scan.

- If there is any abnormality felt in the prostate upon digital rectal examination, depending upon the radiology imaging facilities that are available, CT scan of the prostate gland tends to be undertaken to assess the prostate gland further.
- CT-scan-guided biopsy of the prostate gland tends to be undertaken in some centres to exclude prostate cancer in the scenario of suspicion of prostate cancer.

### Magnetic Resonance Imaging (MRI) scan.

- If there is any abnormality felt in the prostate upon digital rectal examination, depending upon the radiology imaging facilities that are available, MRI scan of the prostate gland tends to be undertaken to assess the prostate gland further.
- MRI-scan-guided biopsy of the prostate gland tends to be undertaken in some centres to exclude prostate cancer in the scenario of suspicion of prostate cancer.

### Urodynamics

- In some patients with lower urinary tract symptoms on medical management who still have symptoms, flow cytometry / urodynamics may be undertaken to further assess the patients.
- Flexible urethroscopy
- In the scenario where an individual has previously had pelvic injury or sexually transmitted urethritis that was treated, cystoscopy tends to be undertaken to exclude urethral stenosis, urethral stricture, a urethral diverticulum or any other lesion within the urethra, that could be treated to improve the voiding of the patient

### Treatment:

Many treatments are made available for BPH, including medications such as  $\alpha$ -blockers and 5 $\alpha$ -reductase inhibitors and surgical options of treatment including transurethral resection of the prostate and prostatectomy which had been summated as follows:

- Urethral catheterisation – individuals who have urinary retention are catheterised to ensure the bladder is emptied and the catheter is connected to a leg bag.
- Medications
  - Tamsulosin is one type of medication that tends to be prescribed for some individuals to improve the flow of urine.
  - Alfuzosin also tends to be prescribed if the prostate is large
- Operations
  - Some individuals may undergo trans-urethral resection of the prostate gland or (TURP) or bladder neck incision or another type of operation to improve the flow of urine including Rezum, and laser treatment.
  - In some parts of the world, open prostatectomy by either trans-vesical prostatectomy or retropubic prostatectomy may be undertaken
- Associated problems of prostatectomy
  - Some individuals may have co-morbidities and may not be adjudged to be fit to under operation under general anaesthesia or spinal anaesthesia.
  - Some individuals would prefer a minimally invasive procedure and one of which in selected centres if there is a well-trained interventional radiologist, embolization of the prostatic artery.

### Differential diagnoses

Some of the differential diagnoses of BPH include:

- Urothelial carcinoma
- Low-grade adenocarcinoma of the prostate gland.
- Prostatic stromal tumour of uncertain malignant potential

### [B] Miscellaneous Narrations and Discussions from Some Case Reports, Case Series, And Studies Related to Embolization of Prostate Gland

Uflacker et al. [2] undertook a meta-analysis of available data on prostatic artery embolization (PAE). Uflacker et al. [2] undertook a meta-analysis on articles which had been published between November 2009 and December 2015. Uflacker et al. [2] included peer-reviewed studies with > 5 patients and standard deviations and/or individual-level data on one or more of the following outcomes: prostate volume (PV), peak flow rate (Qmax), postvoid residual (PVR), International Prostate Symptom Score (IPSS), quality of life (QOL) score, International Index of Erectile Function (IIEF) score, and prostate-specific antigen (PSA) level. They undertook a random-effects meta-analysis on the outcomes at 1 month, 3 months, 6 months, and 12 months after PAE compared with baseline values, with a  $P < .05$  decision rule as the null hypothesis rejection criterion. Uflacker et al. [2] summated the results as follows:

- They had included nineteen of 268 studies in the data collection, with 6 included in the meta-analysis.
- At 12 months, PV had decreased by 31.31 cm<sup>3</sup> ( $P < .001$ ), serum PSA level had remained unchanged ( $P = .248$ ), PVR had decreased by 85.54 mL ( $P < .001$ ), Qmax had increased by 5.39 mL/s ( $P < .001$ ), IPSS had improved by 20.39 points ( $P < .001$ ), QOL score had improved by -2.49 points ( $P < .001$ ), and IIEF was unchanged ( $P = 1.0$ ).

- There were, a total of 218 adverse events (AEs) among 662 patients (32.93%), with 216 being Society of Interventional Radiology class A/B (99%).
- The most common complications were rectalgia/dysuria (n = 60; 9.0%) and acute urinary retention (n = 52; 7.8%). No class D/E complications were reported.
- Uflacker et al. [2] made the ensuing conclusion:
- PAE provided improvement in Qmax, PVR, IPSS, and QOL endpoints at 12 months, with a low incidence of serious AEs (0.3%), although minor AEs were common (32.93%).
- There was no adverse effect on erectile function.

#### Carnevale et al. [3] made the ensuing iterations:

- Prostatic artery embolization (PAE) has emerged as an alternative to surgical treatments for benign prostatic hyperplasia (BPH).
- Patient selection and refined technique are essential to achieve good results.
- Urodynamic assessment and magnetic resonance imaging are very important and technical limitations are related to elderly patients with tortuous and atherosclerotic vessels, anatomical variations, difficulty visualizing and catheterizing small diameter arteries feeding the prostate, and the potential risk of bladder and rectum ischemia.
- Utilisation of small-diameter hydrophilic microcatheters is mandatory.
- Patients could be treated safely by PAE with low rates of side effects, reducing prostate volume with clinical symptoms and quality of life improvement without urinary incontinence, ejaculatory disorders, or erectile dysfunction.
- A multidisciplinary approach with urologists and interventional radiologists is essential to achieve better results.

Pisco et al. [4] evaluated whether prostatic arterial embolization (PAE) might be a feasible procedure to treat lower urinary tract symptoms associated with benign prostatic hyperplasia (BPH). Pisco et al. [4] selected fifteen patients, whose ages had ranged between 62 years and 82 years and whose mean age, was 74.1 years and who had symptomatic BPH after failure of medical treatment for PAE with non-spherical 200- $\mu$ m polyvinyl alcohol particles. The procedure was undertaken by a single femoral approach. Technical success was considered when selective prostatic arterial catheterization and embolization was achieved on at least one pelvic side. Pisco et al. [4] summated the results as follows:

- PAE was technically successful in 14 of the 15 patients which amounted to in 93.3% of the cases.
- There was a mean follow-up of 7.9 months and the follow-up had ranged between 3 months and 12 months.
- International Prostate Symptom Score had decreased by a mean of 6.5 points (P = .005), quality of life had improved 1.14 points (P = .065), International Index of Erectile Function had increased 1.7 points (P = .063), and peak urinary flow had increased 3.85 mL/sec (P = .015).
- There was a mean serum prostate-specific antigen reduction of 2.27 ng/mL (P = .072) and a mean prostate volume decrease of 26.5 mL (P = .0001) by ultrasound scan and 28.9 mL (P = .008) by magnetic resonance imaging.
- There was one major complication (a 1.5-cm<sup>2</sup> ischemic area of the bladder wall) and four clinical failures (28.6%).

- Pisco et al. [4] concluded that:
- In their small group of patients, PAE was a feasible procedure, with preliminary results and short-term follow-up indicating good symptom control without sexual dysfunction in suitable candidates, associated with a reduction in prostate volume.

#### Picel et al. [5] made the ensuing iterations:

- Prostatic artery embolization is emerging as an effective and safe treatment of symptomatic option for benign prostatic hyperplasia.
- Symptomatic benign prostatic hyperplasia is a common condition in the aging population which results in bothersome lower urinary tract symptoms and decreased quality of life.
- Patients who are afflicted by BPH often are treated with medication and offered surgery for persistent symptoms.
- Transurethral resection of the prostate gland is considered to be the traditional standard of care, but many minimally invasive surgical treatments also are offered.
- Prostatic artery embolization (PAE) has been emerging as an effective treatment option with few reported adverse effects, minimal blood loss, and infrequent overnight hospitalization.
- The procedure is offered to patients who have moderate to severe lower urinary tract symptoms and depressed urinary flow due to bladder outlet obstruction.
- Proper patient selection and meticulous embolization are critical so as to optimize results.
- In other to undertake PAE safely and avoid non-target embolization, interventional radiologists should have a detailed understanding of the pelvic arterial anatomy.
- Even though the prostatic arteries often arise from the internal pudendal arteries, many anatomic variants and pelvic anastomoses tend to be encountered.
- Prospective cohort studies, small randomized controlled trials, and meta-analyses had demonstrated improved symptoms after treatment, with serious adverse effects occurring rarely.

de Assis et al. [6] described the safety and efficacy of prostatic artery embolization (PAE) with spherical microparticles to treat lower urinary tract symptoms associated with benign prostatic hyperplasia in patients whose prostate volume was greater than 90 grams. de Assis et al. [6] undertook a prospective, single-centre, single-arm study in 35 patients with prostate volumes ranging from 90 grams to 252 grams. The mean age of the patients was 64.8 years and the ages of the patients had ranged between 53 years and 77 years. Magnetic resonance imaging, uroflometry, and the International Prostate Symptom Score (IPSS) were used to assess clinical and functional outcomes. de Assis et al. [6] summated the results as follows:

- The mean prostate size had decreased significantly from 135.1 grams before PAE to 91.9 grams at 3 months of follow-up (P < .0001).
- The mean IPSS and quality-of-life index had improved from 18.3 to 2.7 and 4.8 to 0.9 (P < .0001 for both), respectively.
- A significant negative correlation was identified between serum prostate-specific antigen at 24 hours after PAE and IPSS 3 months after PAE (P = .0057).
- de Assis et al. [6] made the ensuing conclusions:

- PAE is a safe and effective treatment for lower urinary tract symptoms secondary to benign prostatic hyperplasia in patients whose prostate volume is greater than 90 grams.
- Excessively elevated serum prostate-specific antigen within 24 hours of PAE is associated with lower symptom burden in short-term follow-up.

#### Carnevale et al. [7] made the ensuing iterations:

- Symptomatic benign prostatic hyperplasia (BPH) typically occurs within the sixth and seventh decades, and the most frequent obstructive urinary symptoms are hesitancy, decreased urinary stream, sensation of incomplete emptying, nocturia, frequency, and urgency.
- Many medicaments, specifically 5- $\alpha$ -reductase inhibitors and selective  $\alpha$ -blockers, could decrease the severity of the symptoms secondary to BPH, but prostatectomy is still considered to be the traditional method of management.

Carnevale et al. [7] reported the preliminary results for two patients with acute urinary retention due to BPH, who were successfully treated by prostatic artery embolization (PAE). The patients were investigated utilising the International Prostate Symptom Score, by digital rectal examination, urodynamic testing, prostate biopsy, transrectal ultrasound (US), and magnetic resonance imaging (MRI). Uroflowmetry and post-void residual urine volume complemented the investigation at 30, 90, and 180 days after PAE. The procedure was undertaken under local anaesthesia; embolization of the prostate arteries was undertaken with a microcatheter and 300- to 500- $\mu$ m microspheres utilising complete stasis as the end point. One patient was subjected to bilateral PAE and the other to unilateral PAE; they voided spontaneously pursuant to the removal of the urethral catheter, 15 days and 10 days after the procedure, respectively. At 6-month follow-up, US and MRI scan had revealed a prostate reduction of 39.7% and 47.8%, respectively, for the bilateral PAE and 25.5 and 27.8%, respectively, for the patient submitted to unilateral PAE. Carnevale et al. [7] concluded that:

- The early results, at 6-month follow-up, for the two patients with BPH had demonstrated a promising potential alternative for treatment with PAE.

Gao et al. [8] stated that prostatic arterial embolization is an effective treatment in patients with lower urinary tract symptoms due to benign prostatic hyperplasia, especially in those with benign prostatic hyperplasia with predominant prostatic arteries and a rich vasculature. Gao et al. [8] compared prostatic arterial embolization (PAE) and transurethral resection of the prostate (TURP) in the care of patients with benign prostatic hyperplasia (BPH). Gao et al. [8] undertook a prospective randomized clinical trial which was approved by the institutional review board. A total of 114 patients had provided written informed consent and were randomly assigned to undergo PAE (n = 57) or TURP (n = 57). The groups were compared regarding relevant adverse events and complications. Functional results—including improvement of International Prostate Symptom Score (IPSS), quality of life (QOL), peak urinary flow, postvoiding residual urine volume, prostate-specific antigen (PSA) level, and prostate volume—were assessed at 1 month, 3 months, 6 months, 12 months, and 24 months follow-ups between January 20, 2007, and January 31, 2012. Student t test,  $\chi^2$  test, Fisher exact test, and repeated measures analysis of variance were utilised, as appropriate. Gao et al. [8] summated the results as follows:

- The overall technical success rates for TURP and PAE were 100% and 94.7%, respectively; the clinical failure rates were 3.9% and 9.4%, respectively.
- The six functional results had demonstrated improvements after TURP and PAE at all follow-up time points when compared with preoperative values (P = .001).
- Nevertheless, the TURP group had demonstrated greater degrees of improvement in the IPSS, QOL, peak urinary flow, and postvoiding residual urine volume at 1 month and 3 months, as well as greater reductions in the serum PSA level and prostate volume at all follow-up time points, when compared with the PAE group (P < .05).
- The PAE group showed more overall adverse events and complications (P = .029), which were mostly related to acute urinary retention (25.9%), post-embolization syndrome (11.1%), and treatment failures (5.3% technical; 9.4% clinical).

#### Gao et al. [8] made the ensuing conclusions:

- Both procedures had resulted in significant clinical improvements in the treatment of BPH.
- However, the advantages of the PAE procedure must be weighed against the potential for technical and clinical failures in a minority of patients.

Pisco et al. [9] undertook a study to confirm that prostatic artery embolization (PAE) has a positive medium- and long-term effect in symptomatic benign prostatic hyperplasia (BPH). Pisco et al. [9] reported that between March 2009 and October 2014, 630 consecutive patients with BPH and moderate-to-severe lower urinary tract symptoms refractory to medical therapy for at least 6 months or who refused any medical therapy had undergone PAE. Pisco et al. [9] evaluated outcome parameters of the patients at baseline; 1 month, 3 months, and 6 months; every 6 months between 1 year and 3 years; and yearly thereafter up to 6.5 years. Pisco et al. [9] summated the results as follows:

- The mean age of the patients was 65.1 years  $\pm$  8.0 and the ages of the patients had ranged between 40 years and 89 years.
- There were 12 (1.9%) technical failures.
- Bilateral PAE was undertaken in 572 (92.6%) patients and unilateral PAE was undertaken in 46 (7.4%) patients.
- The cumulative clinical success rates at medium- and long-term follow-up were 81.9% (95% confidence interval [CI], 78.3%–84.9%) and 76.3% (95% CI, 68.6%–82.4%).
- There was a statistically significant (P < .0001) change from baseline to last observed value in all clinical parameters: International Prostate Symptom Score (IPSS), quality-of-life (QOL), prostate volume, prostate-specific antigen, urinary maximal flow rate, postvoid residual, and International Index of Erectile Function.
- There were 2 major complications without sequelae.

#### Pisco et al. [9] made the ensuing conclusions:

- PAE had a positive effect on IPSS, QOL, and all objective outcomes in symptomatic BPH.
- The medium- (1 year to 3 years) and long-term (> 3–6.5 y) clinical success rates were 81.9% and 76.3%, with no urinary incontinence or sexual dysfunction reported.

Kurbatov et al. [10] investigated the clinical benefits and safety of prostatic artery embolization (PAE) in patients with prostate volume  $\geq 80$  cm<sup>3</sup> and Charlson comorbidity index (CCI)  $\geq 2$  and affected by benign prostatic obstruction (BPO). Kurbatov et al. [10] reported that from January 2009 to January 2012, PAE was undertaken in 88 consecutive patients who were affected by clinical BPO. The inclusion criteria were symptomatic BPO refractory to medical treatment, International Prostate Symptom Score (IPSS)  $\geq 12$ , total prostate volume (TPV)  $\geq 80$  cm<sup>3</sup>, Qmax  $< 15$  mL/s, and CCI  $\geq 2$ . Primary end points were the reduction of 7 points of the IPSS and the increase of Qmax. Secondary end points were the reduction of TPV, postvoid residue (PVR), prostate-specific antigen (PSA), International Index of Erectile Function 5 score, and IPSS-quality of life (QoL). Follow-up was addressed at 3 months, 6 months, and at 1 year. Kurbatov et al. [10] summated the results as follows:

- The mean IPSS (10.40 vs 23.98;  $P < .05$ ) and the mean Qmax (16.89 vs 7.28;  $P < .05$ ) at 1 year were significantly different with respect to baseline.
- When considering secondary end points, they had observed significant variation in terms of PVR (18.38 vs 75.25;  $P < .05$ ), TPV (71.20 vs 129.31;  $P < .05$ ), and PSA level (2.12 vs 3.67;  $P < .05$ ) at 1 year compared with baseline.
- Finally, the mean IPSS-QoL significantly had changed from baseline to 1 year after PAE (5.10 vs 2.20;  $P < .05$ ).
- No minor or major complications had been documented.

#### **Kurbatov et al. [10] concluded that:**

They had demonstrated the clinical benefits of PAE for the treatment of lower urinary tract symptoms and/or BPO by reducing IPSS, TPV, PSA, PVR, and improvement in urinary flow and QoL after 1 year in patients with prostate volume  $\geq 80$  cm<sup>3</sup> and CCI  $\geq 2$ .

Carnevale et al. [11] stated that long-term experience with prostatic artery embolization (PAE) for benign prostatic hyperplasia had remained limited. Carnevale et al. [11] evaluated the efficacy, safety, and long-term results of PAE for benign prostatic hyperplasia. Carnevale et al. [11] undertook a retrospective single-centre study from June 2008 to June 2018 in patients with moderate to severe benign prostatic hyperplasia-related symptoms. International Prostate Symptom Score (IPSS), quality-of-life score, maximum urinary flow rate, postvoid residual volume, prostate-specific antigen (PSA), and prostate volume were assessed. PAE was performed with 100–500- $\mu$ m embolic microspheres. Mixed-model analysis of variance and Kaplan-Meier method was accessed, as appropriate. Carnevale et al. [11] summated the results as follows:

- A total of 317 consecutive men (mean age  $\pm$  standard deviation, 65 years  $\pm$  8) had undergone treatment.
- The follow-up had ranged from 3 months to 96 months (mean, 27 months).
- Bilateral and unilateral PAE was undertaken in 298 (94%) and 19 (6%) men, respectively.
- Early clinical failure had occurred in six (1.9%) and symptom recurrence in 72 (23%) men at a median follow-up of 72 months.
- The mean maximum improvement was as follows: IPSS, 16 points  $\pm$  7; quality-of-life score, 4 points  $\pm$  1; prostatic volume reduction, 39 cm<sup>3</sup>  $\pm$  39 (39%  $\pm$  29); maximum urinary flow rate, 6 mL/sec  $\pm$  10 (155%  $\pm$  293); and postvoid residual volume, 70 mL  $\pm$  121 (48%  $\pm$  81) ( $P < .05$  for all).

- Unilateral PAE was found to be associated with higher recurrence (42% versus 21%;  $P = .04$ ).
- The baseline serum PSA level was found to be inversely related with recurrence (hazard ratio, 0.9 per nanograms per millilitre of serum PSA; 95% confidence interval [CI], 0.8, 0.9;  $P < .001$ ).
- Embolization with combined particle sizes (100–500  $\mu$ m) did not relate to symptom recurrence (hazard ratio, 0.4; 95% CI: 0.2, 1.1 for 100–500- $\mu$ m group vs 300–500- $\mu$ m group and hazard ratio, 0.4; 95% CI: 0.1, 1.5 for 100–500- $\mu$ m group vs 100–300- $\mu$ m group;  $P = .19$ ).
- None of the patients had manifested with urinary incontinence or erectile dysfunction.

#### **Carnevale et al. [11] concluded that:**

Prostatic artery embolization was found to be a safe and effective procedure for benign prostatic hyperplasia with good long-term results for lower urinary tract symptoms.

Bagla et al. [12] rereported early findings from a prospective United States clinical trial to evaluate the efficacy and safety of prostatic artery embolization (PAE) for benign prostatic hyperplasia (BPH). Bagla et al. [12] reported that from January 2012 to March 2013, 72 patients were screened and 20 patients had undergone treatment. The patients were evaluated at baseline and selected intervals (1 month, 3 months, and 6 months) for the following efficacy variables: American Urological Association (AUA) symptom score, quality of life (QOL)-related symptoms, International Index of Erectile Function score, peak urine flow rate, and prostate volume (on magnetic resonance imaging at 6 months). The complications were monitored and reported per Society of Interventional Radiology guidelines. Bagla et al. [12] summated the results as follows:

- Embolization was technically successful in 18 out of 20 patients which amounted to in 90% of the patients; bilateral PAE was successful in 18 out of 19 patients which amounted to in 95% of the patients.
- Unsuccessful embolization procedures were found to be secondary to atherosclerotic occlusion of prostatic arteries.
- Clinical success was noted in 95% of patients (in 19 of 20 patients) at 1 month, with average AUA symptom score improvements of 10.8 points at 1 month ( $P < .0001$ ), 12.1 points at 3 months ( $P = .0003$ ), and 9.8 points at 6 months ( $P = .06$ ). QOL improved at 1 month (1.9 points;  $P = .0002$ ), 3 months (1.9 points;  $P = .003$ ), and 6 months (2.6 points;  $P = .007$ ).
- Sexual function had improved by 34% at 1 month ( $P = .11$ ), 5% at 3 months ( $P = .72$ ), and 16% at 6 months ( $P = .19$ ).
- The prostate volume at 6 months had decreased 18% ( $n = 5$ ;  $P = .05$ ).
- No minor or major complications had been reported.

#### **Bagla et al. [12] concluded that:**

- Early results from the clinical trial had indicated that PAE offers a safe and efficacious treatment option for men with BPH.

Grosso et al. [13] reported the clinical outcome after prostatic artery embolization (PAE) in 13 consecutive patients with benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS). Grosso et al. [13] reported that from May 2012 to October 2013, they had undertaken PAE in 13 consecutive patients, whose mean age was 75.9

years, and who had with BPH and LUTS and refractory to medical therapy; seven patients had an indwelling urinary bladder catheter. Clinical follow-up (mean follow-up time 244 days) was undertaken using the international prostate symptoms score (IPSS), quality of life (QoL), the international index of erectile function (IIEF), blood prostatic specific antigen (PSA) testing and transrectal prostatic ultrasound (US) scan with volume and weight calculation at 3, 6 and 12 months. Pre-procedural CT angiography (CTA) was undertaken for vascular mapping. Embolization was undertaken utilising Embosphere (300–500 micron). Technical success was defined when the selective prostatic arterial embolization was completed in at least one pelvic side. Clinical success was defined when symptoms and quality of life were improved. Grosso et al. [13] summated the results as follows:

- PAE was adjudged to be technically successful in 12 out of 13 patients, which amounted to in 92 % of the patients.
- In one patient, PAE was not undertaken because of tortuosity and atherosclerosis of iliac arteries.
- PAE was completed bilaterally in 9 out of 13 patients which amounted to in 75 % of the patients and unilaterally in three patients which amounted to in 27 % of the patients.
- All patients had their catheters removed the urinary bladder from 4 days to 4 weeks after PAE.
- They had obtained a reduction in IPSS (mean, 17.1 points), an increase in IIEF (mean, 2.6 points), an improvement in QoL (mean, 2.6 points) and a volume reduction (mean, 28 %) at 12 months.

#### Grosso et al. [13] made the ensuing conclusions:

- Consistent with the literature, their experience had demonstrated the feasibility, safety and efficacy of PAE in the management of patients with LUTS related to BPH.
- PAE may play a pivotal role in patients in whom medical therapy has failed, who are not candidates for surgery or transurethral prostatic resection (TURP) or refuse any surgical treatment.
- Larger case series and comparative studies with standard TURP could confirm the validity of the technique.

Bilhim et al. [14] undertook a study which was designed to compare baseline data and clinical outcome between patients with prostate enlargement/benign prostatic hyperplasia (PE/BPH) who underwent unilateral and bilateral prostatic arterial embolization (PAE) for the relief of lower urinary tract symptoms (LUTS). Bilhim et al. [14] reported that their single-centre, ambispective cohort study had compared 122 consecutive patients whose mean age was 66.7 years, with unilateral versus bilateral PAE undertaken from March 2009 to December 2011. Selective PAE was undertaken with 100- and 200- $\mu$ m nonspherical polyvinyl alcohol (PVA) particles by a unilateral femoral approach. Bilhim et al. [14] summated the results as follows:

- Bilateral PAE was undertaken in 103 patients which amounted to in 84.4 % of the patients (group A).
- The remaining 19 (15.6 %) patients had undergone unilateral PAE (group B).
- The mean follow-up time was 6.7 months in group A and 7.3 months in group B.
- The mean prostate volume, PSA, International prostate symptom score/quality of life (IPSS/QoL) and post-void

residual volume (PVR) reduction, and peak flow rate (Q<sub>max</sub>) improvement were 19.4 mL, 1.68 ng/mL, 11.8/2.0 points, 32.9 mL, and 3.9 mL/s in group A and 11.5 mL, 1.98 ng/mL, 8.9/1.4 points, 53.8 mL, and 4.58 mL/s in group B.

- Poor clinical outcome was observed in 24.3 % of patients from group A and 47.4 % from group B ( $p = 0.04$ ).

#### Bilhim et al. [14] made the ensuing conclusions:

- PAE is a safe and effective technique which could induce 48 % improvement in the IPSS score and a prostate volume reduction of 19 %, with good clinical outcome in up to 75 % of treated patients.
- Bilateral PAE seemed to lead to better clinical results; nevertheless, up to 50 % of patients after unilateral PAE might have a good clinical outcome.

Bhatia et al. [15] determined if coil embolization is a safe adjunctive measure to prevent nontarget embolization during prostatic artery embolization (PAE). Bhatia et al. [15] undertook a retrospective analysis of patients who had undergone PAE with coil embolization (cPAE) or without coil embolization (nPAE) between January 2014 and June 2016. They compared adverse events, identified in accordance with SIR guidelines, and procedural variables between the 2 cohorts. Bhatia et al. [15] summated the results as follows:

- Out of 122 patients, 32 which amounted to 26.2% of the patients, underwent coil embolization in 39 arteries, with coils placed to prevent nontarget embolization ( $n = 36$ ), treat prostatic artery extravasation ( $n = 2$ ), and occlude an intraprostatic arteriovenous fistula ( $n = 1$ ).
- Compared with nPAE, cPAE had a non-significant increase in dose area product (64,516  $\mu$ Gy·m<sup>2</sup> vs 52,100  $\mu$ Gy·m<sup>2</sup>,  $P = .053$ ) but significantly longer procedure (160.1 min vs 137.1 min,  $P = .022$ ) and fluoroscopy (62.9 min vs 46.1 min,  $P = .023$ ) times.
- One major complication (urosepsis) had occurred in each group (cPAE, 1/32 [3.1%]; nPAE, 1/80 [1.3%]). Both cases had resolved after 2 weeks of intravenous antibiotics.
- A minor ischemic complication (1/32 [3.1%]) had occurred in a patient with coil embolization, which manifested as white discoloration of the glans penis and resolved with topical therapy.
- There were no statistically significant differences noted in major and minor complications between cohorts at 1-month and 3-month follow-up visits.

Bhatia et al. [15] made the ensuing conclusion:

- Even though coil embolization does lead to increases in procedure and fluoroscopy times, it is a safe adjunctive technique to occlude communications between the prostatic artery and pelvic vasculature to potentially prevent nontarget embolization.

#### Sun et al. [16] made the ensuing iterations:

- Rationale of prostatic artery embolization (PAE) in the treatment of symptomatic benign prostatic hyperplasia is conventionally understood to include two parts: shrinkage of the enlarged prostate gland as a result of PAE-induced ischemic infarction and potential effects to relax the increased prostatic

smooth muscle tone by reducing the number and density of  $\alpha$ 1-adrenergic receptor in the prostate stroma.

- They had found in a review of the literature which had described new insights into the likely mechanisms behind PAE, such as ischemia-induced apoptosis, apoptosis enhanced by blockage of androgens circulation to the embolized prostate, secondary denervation following PAE, and potential effect of nitric oxide pathway immediately after embolization. Studies on therapeutic mechanisms in PAE may shed light on potentially new treatment strategies and development of novel techniques.

Kuang et al. [17] summarized current evidence on outcomes and complications of prostatic artery embolization as a treatment for patients with lower urinary tract symptoms secondary to benign prostatic hyperplasia. Kuang et al. [17] undertook a database search of MEDLINE, Embase, Web of Science, and Cochrane Library for published literature up to August 2015 concerning PAE in the treatment of BPH. Inclusion and exclusion criteria were applied by two independent reviewers, and disagreements were resolved by consensus. Peer-reviewed studies concerning PAE with BPH with a sample size >10 and at least one measured parameter were included. Kuang et al. [17] summated the results as follows:

- The search had yielded 193 articles, of which ten studies representing 788 patients, with a mean age of 66.97 years, were included.
- The patients had LUTS which had ranged from moderate to severe.
- At 6 months following the procedure, PV, PVR, Qmax, IPSS, and QoL were found to be significantly improved ( $P < 0.05$ ), while for serum PSA there was no significant change.
- At 12 months and 24 months, PV, PSA, PVR, Qmax, IPSS, and QoL were noted to be significantly improved ( $P < 0.05$ ). IIEF was unchanged at 6 months and 12 months but was significantly reduced at 24 months.

#### **Kuang et al. [17] concluded that:**

- Their findings had suggested that PAE is effective in treating LUTS in the short and intermediate term.

#### **Abt et al. [18] made the ensuing iterations:**

- Prostatic artery embolization (PAE) had emerged as a truly minimally invasive treatment option for patients with lower urinary tract symptoms presumed secondary to benign prostatic obstruction (LUTS/BPO) over the last few years and is now supported by evidence-based international guidelines.
- They had provided an overview on the profile of PAE based upon the most relevant and recent literature.
- Abt et al. [18] undertook a comprehensive review of the literature on PAE on PubMed–Medline. They narratively summarized the most relevant literature. Abt et al. [18] summated the results as follows:
- While there has still been a lack of long-term data, efficacy and safety data had been published for the short to mid-term.
- As with any minimally invasive technique, relief of bladder outlet obstruction is less pronounced after PAE compared to more invasive resective techniques.

- This is likely to be associated with higher re-intervention rates during the longer term.
- Nevertheless, due to its beneficial safety profile, PAE represents an interesting option for many patients and could fill a niche between pharmacotherapy and formal surgical intervention.
- Given its unique treatment approach, for example. endovascular instead of transurethral, PAE has a clearly different profile compared to other minimally invasive treatments.
- Performance under local anaesthesia with possible continuation of anticoagulant drugs and no upper prostate size limit are the most important advantages of PAE.

#### **Abt et al. [18] concluded that:**

- PAE represents a valuable supplement in the treatment armamentarium of LUTS/BPH if patients are selected appropriately.

#### **Moreira et al. [19] made the ensuing iterations:**

- Minimally invasive procedures had gained great importance among the treatments for benign prostate hyperplasia (BPH) due to their low morbidity.
- Prostate artery embolization had emerged as a safe and effective alternative for patients with large volume BPH, not suited for surgery.

Moreira et al. [19] undertook a review of adverse events related to prostatic artery embolization to treat urinary bladder outflow obstruction and they iterated that low adverse events rates had been reported following prostate artery embolization and which may include dysuria, urinary infection, haematuria, hematospermia, acute urinary retention and rectal bleeding. They pointed out that even though most complaints had been reported as side effects, complications could also be superimposed. They made the ensuing summing educative discussions:

- The prostate gland is the most common source of complaints following PAE, where the inflammatory process could create a large variety of localized symptoms.
- Periprostatic organs and structures such as urinary bladder, rectum, penis, seminal vesicle, pelvis, bones and skin might be damaged by non-target embolization, especially due to the misidentification of the normal vascular anatomy and variants or due to inadvertent embolic reflux.
- Radiodermatitis might also happen in case of small vessel size, atherosclerosis, the learning curve and long procedure or fluoroscopy times.

#### **Dias et al. [20] made the ensuing iterations:**

- Benign prostatic hyperplasia (BPH) is a non-cancerous growth of the transitional zone of the prostate, which surrounds the prostatic urethra.
- Consequently, it could cause lower urinary tract symptoms (LUTS) and bladder outlet obstruction symptoms which may substantially reduce a patient's quality of life.
- Many treatments are available for BPH, including medications such as  $\alpha$ -blockers and 5 $\alpha$ -reductase inhibitors and surgical options including transurethral resection of the prostate and prostatectomy.

- Recently, prostatic artery embolization (PAE) has emerged as a minimally invasive treatment option for selected men with BPH and moderate to severe LUTS. Adequate pre- and postprocedural evaluations with clinical examinations and questionnaires, laboratory tests, and urodynamic and imaging examinations (particularly US, MRI, and CT) are of key importance to achieve successful treatment. Considering that the use of PAE has been increasing in tertiary hospital facilities, radiologists and interventional radiologists should be aware of the main technical concepts of PAE and the key features to address in imaging reports in pre- and postprocedural settings.

- They had undertaken a review to assess the safety and efficacy of PAE as a new treatment in BPO and had explored risks surrounding its performance.

Christidis et al. [22] undertook a review of the literature. Christidis et al. [22] searched medical databases which included PubMed, EMBASE, and Cochrane databases, that were limited to English, peer-reviewed articles. Their search terms included prostatic artery embolization, lower urinary tracts symptoms, minimally invasive therapies, interventional radiology prostate, and benign prostatic hyperplasia. Articles were screened by two independent reviewers for content on development, methods, outcomes, and complications of PAE. Christidis et al. [22] summarized the results as follows:

- Suitability of patients to undergo PAE had depended upon review of patient history, pre-procedure visualisation of appropriate vascular anatomy and clinical parameters.
- Despite this selection of candidates favourable for procedural success, PAE is not without risk of complications, some of which could significantly affect patient quality of life.

#### **Christidis et al. [22] made the ensuing conclusions:**

- Even though initial findings had demonstrated promise regarding safety and efficacy of PAE in improving symptom and quality-of-life scores, further investigation is needed to establish durability of effect and the appropriate use of this experimental modality.
- There had been at the time of publication of their article limited robust evidence for the beneficial outcomes of PAE.
- Long-term follow-up studies would add to the evidence base to help further assess the feasibility of this procedure as an alternative to TURP.

Zhang et al. [23] described the prostatic arterial supply using Cone-beam computed tomography (CT) and digital subtraction angiography (DSA) before prostatic arterial embolization (PAE) for benign prostatic hyperplasia (BPH). Zhang et al. [23] undertook a retrospective study from January 2012 to January 2014, 55 male patients (110 hemipelvises) with BPH who underwent PAE were evaluated by Cone-beam CT in addition to pelvic DSA during embolization planning. Each hemipelvis was evaluated regarding the number of prostatic arteries (PA) and their origins, diameters, territorial perfusion, and anastomoses with adjacent arteries.

#### **Zhang et al. [23] summarized the results as follows:**

- A total of 114 PAs were identified in 110 hemipelvises.
- There was one PA in 96.4% of the hemipelvises (n=106), and two independent PAs in the other 3.6% (n=4).
- The PA was found to originate from the anterior trunk of the internal iliac artery in 39.5% of cases (n=45), from the superior vesical artery in 32.6% (n=37), and from the internal pudendal artery in 27.9% of cases (n=32).
- Extra-prostatic anastomoses between PA and adjacent arteries were identified in 39.1% of hemipelvises (n=43).
- Intra-prostatic anastomoses between PAs and contra-lateral prostatic branches were identified in 61.8% of hemipelvises (n=68). In 67.3% of our study population (n=37), the prostate was dominantly supplied via a unilateral PA.
- Zhang et al. [23] made the ensuing conclusions

Amouyal et al. [21] stated that prostatic artery embolization (PAE) had been undertaken for a few years, but there had not been any report on PAE before 2016, using the PERFecTED technique outside from the team that initiated this approach. Amouyal et al. [21] reported their single-centre retrospective open label study reports of their experience and clinical results on patients who were suffering from symptomatic BPH, who had undergone PAE aiming at utilising the PERFecTED technique. Amouyal et al. [21] reported that they had treated 32 consecutive patients, whose mean age was 65 years and whose ages had ranged between 52 years and 84 years of age between December 2013 and January 2015. The patients were referred for PAE after failure of medical treatment and refusal or contra-indication to surgery. They were treated utilising the PERFecTED technique, when feasible, with 300–500 µm calibrated microspheres (two-night hospital stay or outpatient procedure). Follow-up assessment was undertaken at 3 months, 6 months, and 12 months. Amouyal et al. [21] summarized the results as follows:

- They had a 100 % immediate technical success of embolization (68 % of feasibility of the PERFecTED technique) with no immediate complications.
- After a mean follow-up of 7.7 months, they had observed a 78 % rate of clinical success.
- The mean IPSS had decreased from 15.3 to 4.2 (p = .03), mean QoL had decreased from 5.4 to 2 (p = .03), the mean Qmax had increased from 9.2 to 19.2 (p = .25), the mean prostatic volume had decreased from 91 to 62 (p = .009) mL.
- There was no retrograde ejaculation and no major complication reported.

#### **Amouyal et al. [21] made the ensuing conclusions:**

- The undertaking of PAE utilising the PERFecTED technique is a safe and efficient technique to treat bothersome LUTS related to BPH.
- It is of interest to realise that the PERFecTED technique cannot be undertaken in some cases for anatomical reasons.

#### **Christidis et al. [22] made the ensuing iterations:**

- Prostatic artery embolization (PAE) had seen a recent increase in interest as a treatment option for men with benign prostatic obstruction (BPO).
- The appeal of this intervention lies in the reported reduction in morbidity and its minimally invasive nature.

- The prostatic vascularization is complex with frequent anatomical variations.
- Knowledge of the vascular anatomy of the prostate might provide indications for the planning of PAE and avoiding non-target embolization.

Frenk et al. [24] assessed and described the MRI findings after prostatic artery embolization for the treatment of benign prostatic hyperplasia. Frenk et al. [24] retrospectively evaluated 17 patients who had undergone prostatic artery embolization as part of different prospective studies to evaluate this alternative treatment of benign prostatic hyperplasia. Frenk et al. [24] evaluated the clinical results by assessment of urinary catheterization and International Prostate Symptom Score (IPSS). Frenk et al. [24] performed serial MRI examinations, and they also evaluated the prostatic central gland and peripheral zone for signal intensity changes and the presence and characteristics of infarcted areas. Frenk et al. [24] undertook statistical analysis with ANOVA for repeated measures and Student t test. Frenk et al. [24] summarized the results as follows:

- All of the patients had clinical success, as defined by the removal of indwelling urinary catheter or decreased IPSS after embolization.
- Infarcts were identified in 70.6% of the subjects, exclusively in the central gland, were almost always characterized by hyperintensity on T1-weighted images and predominant hypointensity on T2-weighted images, and became smaller (mean reduction,  $p < 0.001$ ) and isointense to the remaining of the central gland over time.
- Volume reduction of the prostate after embolization was found to be significant (averaging 32.0% after 12–18 months;  $p < 0.001$ ) only in patients with infarcts.
- No statistically significant association was demonstrated between the development of infarcts and IPSS.

#### **Frenk et al. [24] concluded that:**

- MRI could be utilised for assessing the development of infarcts and volume reduction in the prostate after embolization.
- Further studies are required to correlate these findings to clinical outcome.

Enderlein et al. [25] undertook a study to ascertain if cone-beam CT and digital subtraction angiography analysis of pelvic arterial anatomy has predictive value for radiation exposure and technical success of prostatic artery embolization (PAE). Enderlein et al. [25] undertook a prospective, non-randomized, single-centre study which included 104 consecutive patients with lower urinary tract symptoms secondary to benign prostatic hyperplasia. Cone-beam CT was undertaken in 160 out of 208 (76.9%) hemipelvises to determine prostatic artery (PA) origin. Enderlein et al. [25] stated that classification of pelvic arterial tortuosity was possible in 73/104 (70.2%) patients and that learning curves of 2 interventionalists who had undertaken 86.5% of PAEs were analysed. Enderlein et al. [25] summarized the results as follows:

- Tortuosity of pelvic arteries was classified as mild in 25 (34.2%) patients whose median age was 64 years, moderate in 40 (54.8%) patients whose median age was 69 years, and severe in 8 (11.0%) patients whose median age was 70 years (mild vs moderate,  $P = .002$ ; mild versus severe,  $P = .019$ ); median fluoroscopy times were 24, 36, and 46 minutes ( $P = .008$ ,  $P = .023$ ); median contrast volumes were 105, 122.5, and 142 mL

( $P = .029$ ,  $P = .064$ ); and bilateral PAE rates were 84.0%, 77.5%, and 62.5% ( $P = .437$ ), respectively.

- PA origin from superior vesical artery was the most frequent finding (27.5%) and showed higher dose area product (median 402.4 versus 218 Gy · cm<sup>2</sup>,  $P = .033$ ) and fluoroscopy time (median 42.5 vs 27 min,  $P = .01$ ) compared with PA origin from obturator artery, which was least frequent. Interventionalist experience revealed significant impact on procedure times (median 159 vs 130 min,  $P = .006$ ).

#### **Enderlein et al. [25] made the ensuing conclusions:**

- Tortuosity of pelvic arteries was found to be more frequent in older patients and had predicted worse technical outcomes of PAE.
- PA origin from obturator artery was found to be associated with lower dose area product and fluoroscopy time, especially compared with PA origin from superior vesical artery.
- Interventionalist experience had demonstrated significant influence on technical outcome.

Insausti et al. [26] compared clinical and functional outcomes of prostatic artery embolization (PAE) with those of transurethral resection of the prostate (TURP) for the treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH). Insausti et al. [26] undertook a noninferiority randomized trial which involved men over 60 years of age with LUTS secondary to BPH. They reported that from November 2014 to January 2017, 45 patients were randomized to PAE ( $n = 23$ ) or to TURP ( $n = 22$ ). PAE was undertaken with 300- to 500- $\mu$ m microspheres with the patient under local anaesthesia, whereas bipolar TURP was undertaken with the patients under spinal or general anaesthesia. Primary outcomes were changes in peak urinary flow (Q<sub>max</sub>) and international prostate symptoms score (IPSS) from baseline to 12 months. Quality of life (QoL), and prostate volume (PV) changes from baseline to 12 months were secondary outcomes. Insausti et al. [26] compared the adverse events using the Clavien classification. Insausti et al. [26] summarized the results as follows:

- The mean Q<sub>max</sub> had increased from 6.1 mL/s in the PAE group and from 9.6 mL/s in the TURP patients ( $P = .862$  for noninferiority), and mean IPSS reduction was 21.0 points for PAE and 18.2 points for TURP subjects ( $P = .080$ ) at 12 months.
- A greater QoL improvement had been reported in the PAE group (3.78 points for PAE and 3.09 points for TURP;  $P = .002$ ). Mean PV reduction was 20.5 cm<sup>3</sup> (34.2%) for PAE subjects and 44.7 cm<sup>3</sup> (71.2%) for TURP subjects ( $P < .001$ ).
- There were fewer adverse events that were reported in the PAE group than in the TURP group ( $n = 15$  vs  $n = 47$ ;  $P < .001$ ).

#### **Insausti et al. [26] made the ensuing conclusions:**

- Reduction of LUTS in the PAE group was similar to that obtained in the TURP group at 12 months, with fewer complications secondary to PAE.
- Long-term follow-up is required to compare the durability of the symptomatic improvement from each procedure.

#### **Pereira et al. [27] made the ensuing iterations:**

- Prostatic haematuria is among the most common genitourinary complaints of emergency room visits, distressing and

troublesome to men and a challenging clinical problem to the treating physician.

- The most common aetiologies of prostatic haematuria include benign prostatic hyperplasia and prostate cancer.
- Prostatic haematuria usually resolves with conservative and medical methods; failure of these interventions results in refractory haematuria of prostatic origin (RHPO), a potentially life-threatening scenario.
- Many different treatments had been described, with varying degrees of success.
- Patients with RHPO are often elderly and not fit to undergo radical surgery.
- Prostate artery embolization (PAE) had evolved as a safe and effective technique in the management of RHPO.
- Utilisation of a super-selective approach optimizes clinical success while minimizing complications.
- This minimally invasive approach improves patients with haemodynamic instability, serves as a bridge to elective surgery, and is a highly effective treatment for RHPO.
- PAE may obviate the need for more invasive and morbid surgical therapies.

Bilhim et al. [28] assessed long-term outcomes of prostatic artery embolization (PAE) for patients with benign prostatic hyperplasia (BPH). Bilhim et al. [28] undertook a single centre retrospective study from 2009–2019 including 1072 patients who had undergone PAE and had available follow-up. The patients were evaluated yearly at 1 year to 10 years post PAE using the International Prostate Symptom Score (IPSS) and quality of life (QoL), prostate volume (PV), prostate-specific antigen (PSA), peak urinary flow rate (Qmax) and postvoid residual (PVR) volume. The need for prostatic medication, re-intervention rates, repeat PAE and prostatectomy rates were assessed with Kaplan–Meier survival analysis and compared between different embolic agents using Cox regression analysis. Bilhim et al. [28] summated the results as follows:

- The mean follow-up time was  $4.39 \pm 2.37$  years.
- At the last follow-up visit, the mean IPSS and QoL improvements were  $-10.14 \pm 8.34$  ( $p < .0001$ ) and  $-1.87 \pm 1.48$  ( $p < .0001$ ) points, mean PV reduction was  $-6.82 \pm 41.11$  cm<sup>3</sup> ( $p = 0.7779$ ), mean PSA reduction was  $-1.12 \pm 4.60$  ng/mL ( $p = 0.9713$ ), mean Qmax increase was  $2.72 \pm 6.38$  mL/s ( $p = 0.0005$ ), mean PVR reduction was  $-8.35 \pm 135.75$  mL ( $p = 0.6786$ ).
- There were 335 patients (31.3%) who needed prostatic medication after PAE.
- The re-intervention rates were 3.4% at 1 year, 21.1% at 5 years and 58.1% at 10 years.
- The repeat-PAE rates were 2.3% at 1 year, 9.5% at 5 years and 23.1% at 10 years. Prostatectomy rates were 1.1% at 1 year, 11.6% at 5 years and 35.0% at 10 years.
- No significant differences were identified between polyvinyl alcohol particles, Bead Block, Embospheres and Embozenes.

#### **Bilhim et al. [28] concluded that:**

- PAE induces durable long-term LUTS relief, with re-intervention rates of 20% in the first 5 years and 30%–60% > 5 years post-PAE.

Wang et al. [29] compared the outcomes of prostatic arterial embolization (PAE) in treating large (>80 mL) in comparison with medium-sized prostate glands (50–80 mL) to determine whether size affects the outcome of PAE. Wang et al. [28] reported that a total of 115 patients (mean age 71.5 years) who were diagnosed with lower urinary tract symptoms (LUTS) attributable to benign prostatic hyperplasia (BPH) refractory to medical treatment had undergone PAE. Group A ( $n = 64$ ) included patients with a mean prostate volume of 129 mL; group B ( $n = 51$ ) included patients with a mean prostate volume of 64 mL. PAE was undertaken utilising 100- $\mu$ m particles. Follow-up was undertaken using the International Prostate Symptom Score (IPSS), quality of life (QoL), peak urinary flow rate (Qmax), post-void residual urine volume (PVR), the International Index of Erectile Function short form (IIEF-5), prostate-specific antigen (PSA) and prostate volume measured by magnetic resonance imaging at 1, 3 and 6 months, and every 6 months thereafter. Wang et al. [28] summated the results as follows:

- There were no significant differences found between groups in baseline IPSS, QoL, Qmax, PVR, PSA level or IIEF-5 score.
- The technical success rate was documented to be 93.8% in group A and 96.8% in group B ( $P = 0.7$ ).
- A total of 101 patients (55 patients in group A and 46 patients in group B) had completed the mean (range) follow-up of 17 (12–33) months.
- When compared with baseline, there were significant improvements in IPSS, QoL, Qmax, prostate volume and PVR in both groups after PAE.
- The outcomes in group A were found to be significantly better than in group B with regard to mean  $\pm$  sd IPSS ( $-14 \pm 6.5$  versus  $-10.5 \pm 5.5$ , respectively), Qmax ( $6.0 \pm 1.5$  vs  $4.5 \pm 1.0$  mL/s, respectively), PVR ( $-80.0 \pm 25.0$  versus  $-60.0 \pm 20.0$  mL, respectively), prostate volume ( $-54.5 \pm 18.0$  mL [ $-42.3\%$ ] vs  $-18.5 \pm 5.0$  mL [ $-28.9\%$ ], respectively), and QoL score ( $-3.0 \pm 1.5$  versus  $-2.0 \pm 1.0$ ) with  $P$  values  $< 0.05$ .
- The mean IIEF-5 score was not to be significantly different from baseline in both groups. No major complications were noted.

#### **Wang et al. [29] made the ensuing conclusions:**

- They had found that PAE is a safe and effective treatment method for patients with LUTS attributable to BPH.
- The clinical and radiology imaging outcomes of PAE were better in patients with larger prostate glands than medium-sized ones.

#### **Naidu et al. [30] made the ensuing iterations:**

- Lower urinary tract symptoms (LUTS) due to benign prostatic hypertrophy (BPH) are a very common problem in men ranging from mild urinary symptoms to recurrent urinary tract infections or renal failure.
- Many treatment options are available that range from conservative medical therapies to more invasive surgical options.
- Prostate artery embolization (PAE) had emerged as a novel treatment option for this common problem with clinical efficacy comparable to the current surgical gold standard, transurethral resection of the prostate (TURP).

- PAE does offer fewer complications and side effects without a need for general anaesthesia or hospitalization.

#### Jung et al. [31] made the ensuing iterations:

- A variety of minimally invasive surgical approaches are available as an alternative treatment option to transurethral resection of the prostate (TURP) for management of lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH).
- Prostatic arterial embolization (PAE) is a relatively new, minimally invasive treatment approach.

Jung et al. [31] assessed the effects of PAE compared to other procedures for treatment of LUTS in men with BPH. Jung et al. [31] undertook a comprehensive search the Cochrane Library, MEDLINE, Embase, three other databases, trials registries, other sources of grey literature, and conference proceedings with no restrictions on language of publication or publication status, up to 8 November 2021. Jung et al. [31] included parallel-group randomized controlled trials (RCTs), as well as non-randomized studies (NRS, limited to prospective cohort studies with concurrent comparison groups) enrolling men over the age of 40 years with LUTS attributed to BPH undergoing PAE versus TURP or other surgical interventions. Jung et al. [31] reported that two review authors had independently classified studies for inclusion or exclusion and abstracted data from the included studies. Jung et al. [31] undertook statistical analyses by using a random-effects model and interpreted them according to the Cochrane Handbook for Systematic Reviews of Interventions. Jung et al. [31] used GRADE guidance to rate the certainty of evidence of RCTs and NRSs. Jung et al. [31] summated the min results as follows:

- They had found data to inform two comparisons: PAE versus TURP (six RCTs and two NRSs), and PAE versus sham (one RCT).
- The mean age was 66 years, International Prostate Symptom Score (IPSS) was 22.8, and prostate volume of participants was 72.8 mL.
- Jung et al. [31] included six RCTs and two NRSs with short-term (up to 12 months) follow-up, and two RCTs and one NRS with long-term follow-up (13 to 24 months). Jung et al. [31] summated their findings as follows:
- Short-term follow-up
  - Based on RCT evidence, there might be little to no difference in urologic symptom score improvement measured by the International Prostatic Symptom Score (IPSS) on a scale from 0 to 35, with higher scores indicating worse symptoms (mean difference [MD] 1.72, 95% confidence interval [CI] -0.37 to 3.81; 6 RCTs, 360 participants;  $I^2 = 78\%$ ; low-certainty evidence).
  - There might be little to no difference in quality of life as measured by the IPSS-quality of life question on a scale from 0 to 6, with higher scores indicating worse quality of life between PAE and TURP, respectively (MD 0.28, 95% CI -0.28 to 0.84; 5 RCTs, 300 participants;  $I^2 = 63\%$ ; low-certainty evidence).
  - While they were very uncertain about the effects of PAE on major adverse events (risk ratio [RR] 0.75, 95% CI 0.19 to 2.97; 4 RCTs, 250 participants;  $I^2 =$

24%; very low-certainty evidence), PAE likely increases retreatments (RR 3.20, 95% CI 1.41 to 7.27; 4 RCTs, 303 participants;  $I^2 = 0\%$ ; moderate-certainty evidence).

- PAE might make little to no difference in erectile function measured by the International Index of Erectile
- Function-5 on a scale from 1 to 25, with higher scores indicating better function (MD 0.50 points, 95% CI -5.88 to 4.88; 2 RCTs, 120 participants;  $I^2 = 68\%$ ; low-certainty evidence).
- Based upon NRS evidence, PAE may reduce the occurrence of ejaculatory disorders (RR 0.51, 95% CI 0.35 to 0.73; 1 NRS, 260 participants; low-certainty evidence).
- Long-term follow-up:
  - Based on RCT evidence, PAE might result in little to no difference in urological symptom scores (MD 2.58 points, 95% CI -1.54 to 6.71; 2 RCTs, 176 participants;  $I^2 = 73\%$ ; low-certainty evidence) and quality of life (MD 0.50 points, 95% CI -0.03 to 1.04; 2 RCTs, 176 participants;  $I^2 = 29\%$ ; low-certainty evidence).
  - They were very uncertain about major adverse events (RR 0.91, 95% CI 0.20 to 4.05; 2 RCTs, 206 participants;  $I^2 = 72\%$ ; very low-certainty evidence).
  - PAE likely increases retreatments (RR 3.80, 95% CI 1.32 to 10.93; 1 RCT, 81 participants; moderate-certainty evidence).
  - While PAE might result in little to no difference in erectile function (MD 3.09 points, 95% CI -0.76 to 6.94; 1 RCT, 81 participants; low-certainty evidence), PAE might reduce the occurrence of ejaculatory disorders (RR 0.67, 95% CI 0.45 to 0.98; 1 RCT, 50 participants; low-certainty evidence).

#### Authors' conclusions

- Compared to TURP, PAE might provide similar improvement in urologic symptom scores and quality of life.
- While they were very uncertain about major adverse events, PAE likely increases retreatment rates.
- While erectile function might be similar, PAE may reduce ejaculatory disorders.
- Certainty of evidence for the outcomes of this review was low or very low except for retreatment (moderate-certainty evidence), signalling that their confidence in the reported effect size was limited or very limited, and that this topic should be better informed by future research.

Wang et al. [32] evaluated the safety and efficacy of prostatic artery embolization (PAE) using the combination of 50- $\mu$ m and 100- $\mu$ m polyvinyl alcohol (PVA) particles versus 100- $\mu$ m PVA particles alone in the treatment of patients with symptomatic benign prostatic hyperplasia (BPH). Wang et al. [32] reported that over a 5-year period, 120 patients who were treated with PAE for lower urinary tract symptoms (LUTS) secondary to BPH were randomized to undergo embolization with 50- $\mu$ m

plus 100- $\mu$ m PVA particles (group A) or 100- $\mu$ m PVA particles alone (group B). The mean follow-up time was 34 months and the follow-up had ranged between 12 months and 57 months. There were no differences between the groups regarding baseline data. The primary outcome measurements included change in International Prostate Symptom Score (IPSS) and incidence of adverse events. Three secondary outcome measurements included procedure-associated pain, prostate ischemia measured on magnetic resonance (MR) imaging 1 week after PAE, and changes over time in quality of life (QOL) questionnaire, peak urinary flow rate (Qmax), postvoid residual (PVR) volume, prostate volume (PV), prostate-specific antigen (PSA) level, and International Index of Erectile Function (IIEF) were evaluated. Recurrence of LUTS following PAE was defined as relief of LUTS temporally but increased IPSS  $\geq$  8 or QOL score  $\geq$  3 or decrease in Qmax to  $<$  7 mL/s. Wang et al. [32] summarized the results as follows:

- The mean follow-up periods were 35 months  $\pm$  22 in group A and 33 months  $\pm$  25 in group B ( $P = .629$ ).
- No differences were found between groups regarding procedural details, pain scores, or adverse events were noted ( $P > .05$ ).
- At 24 months of follow-up, patients in group A were found to have a greater decrease in mean IPSS ( $18.7 \pm 12.5$  vs  $14.8 \pm 13.5$ ), QOL score ( $3.7 \pm 1.5$  vs  $2.4 \pm 1.8$ ), Qmax ( $10.5 \text{ mL} \pm 9.5$  vs  $6.8 \text{ mL} \pm 5.0$ ), PVR ( $92.0 \text{ mL} \pm 75.0$  vs  $60.0 \text{ mL} \pm 55.0$ ), and PV ( $37.0 \text{ mL} \pm 19.5$  vs  $25.5 \text{ mL} \pm 15.0$ ) compared with patients in group B ( $P < .05$  for all).
- The mean ratios of prostate ischemic volume at 1 week after PAE were  $70\% \pm 20$  in group A and  $41\% \pm 25$  in group B ( $P = .021$ ); mean PSA levels at 24 hour after PAE were  $92.5 \text{ ng/mL} \pm 55.0$  in group A and  $77.5 \text{ ng/mL} \pm 45.0$  in group B ( $P = .031$ ); LUTS recurrence rates were 3.6% in group A and 14.6% in group B ( $P = .024$ ). The mean IIEF-5 was not significantly different from baseline in either group.

#### Wang et al. [32] concluded that

PAE with 50- $\mu$ m plus 100- $\mu$ m PVA particles had resulted in greater improvement in clinical and imaging outcomes and no significant differences in adverse events compared with 100- $\mu$ m PVA particles alone.

Ray et al. [33] assessed the efficacy and safety of prostate artery embolization (PAE) for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and to conduct an indirect comparison of PAE with transurethral resection of the prostate (TURP). Ray et al. [33] reported that as a joint initiative between the British Society of Interventional Radiologists, the British Association of Urological Surgeons and the National Institute for Health and Care Excellence, they had conducted the UK Register of Prostate Embolization (UK-ROPE) study, which recruited 305 patients across 17 UK urological/interventional radiology centres, 216 of whom underwent PAE and 89 of whom underwent TURP. The primary outcomes were International Prostate Symptom Score (IPSS) improvement in the PAE group at 12 months post-procedure, and complication data post-PAE. We also aimed to compare IPSS score improvements between the PAE and TURP groups, using non-inferiority analysis on propensity-score-matched patient pairs. The clinical results and urological measurements were performed at clinical sites. IPSS and other questionnaire-based results were mailed by patients directly to the trial unit managing the

study. All data were uploaded centrally to the UK-ROPE study database. Ray et al. [33] summarized the results as follows:

- The results had demonstrated that PAE was clinically effective, producing a median 10-point IPSS improvement from baseline at 12 months post-procedure.
- PAE did not appear to be as effective as TURP, which produced a median 15-point IPSS score improvement at 12 months post-procedure.
- The aforementioned findings were further supported by the propensity score analysis, in which we formed 65 closely matched pairs of patients who underwent PAE and patients who underwent TURP.
- In terms of IPSS and quality-of-life (QoL) improvement, there was no evidence of PAE being non-inferior to TURP.
- Patients in the PAE group had a statistically significant improvement in maximum urinary flow rate and prostate volume reduction at 12 months post-procedure.
- PAE had a reoperation rate of 5% before 12 months and 15% after 12 months (20% total rate), and a low complication rate. Of 216 patients, one had sepsis, one required a blood transfusion, four had local arterial dissection and four had a groin haematoma.
- Two patients had non-target embolization that manifested as self-limiting penile ulcers.
- Additional patient-reported outcomes, pain levels and return to normal activities were very encouraging for PAE.
- Seventy-one percent of PAE cases were undertaken as outpatient procedures or day cases. In contrast, 80% of TURP cases required at least 1 night of hospital stay, and the majority required 2 nights.

#### Ray et al. [33] made the ensuing conclusions:

- Their results had indicated that PAE provides a clinically and statistically significant improvement in symptoms and QoL, even though some of these improvements were greater in the TURP arm.
- The safety profile and quicker return to normal activities might be seen as highly beneficial by patients considering PAE as an alternative treatment to TURP, with the concomitant advantages of reduced length of hospital stay and need for admission after PAE.
- PAE is an advanced embolization technique which demands a high level of expertise, and should be undertaken by experienced interventional radiologists who have been trained and proctored appropriately.
- Utilisation of cone-beam computed tomography is encouraged to improve operator confidence and minimize non-target embolization.
- The place of PAE in the care pathway is between that of medications and surgery, allowing the clinician to tailor treatment to individual patients' symptoms, requirements and anatomical variation

#### Jung et al. [34] made the ensuing iterations:

- Various minimally invasive surgical approaches are available as an alternative to transurethral resection of the prostate

(TURP) for management of lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH).

- Prostatic arterial embolization (PAE) is a relatively new, minimally invasive treatment option.

Jung et al. [34] assessed the effects of PAE compared to other procedures for treatment of LUTS in men with BPH. Jung et al. [34] undertook a comprehensive search the Cochrane Library, MEDLINE, Embase, three other databases, trials registries, other sources of grey literature, and conference proceedings with no restrictions on language of publication or publication status, up to 8 November 2021. Jung et al. [34] included parallel-group randomized controlled trials (RCTs), as well as non-randomized studies (NRS, limited to prospective cohort studies with concurrent comparison groups) enrolling men over the age of 40 years with LUTS attributed to BPH undergoing PAE versus TURP or other surgical interventions.

Jung et al. [34] reported that two review authors had independently classified studies for inclusion or exclusion and abstracted data from the included studies. Jung et al. [34] undertook statistical analyses by using a random-effects model and interpreted them according to the Cochrane Handbook for Systematic Reviews of Interventions. Jung et al. [34] used GRADE guidance to rate the certainty of evidence of RCTs and NRSs. Jung et al. [34] summated the results as follows:

- They found data to inform two comparisons: PAE versus TURP (six RCTs and two NRSs), and PAE versus sham (one RCT).
- The mean age was 66 years, International Prostate Symptom Score (IPSS) was 22.8, and prostate volume of participants was 72.8 mL. The abstract had focused on the comparison of PAE versus TURP as the primary topic of interest. Prostatic arterial embolization versus transurethral resection of the prostate
- They included six RCTs and two NRSs with short-term (up to 12 months) follow-up, and two RCTs and one NRS with long-term follow-up (13 to 24 months).
- The short-term follow-up:
  - Based on RCT evidence, there might be little to no difference in urological symptom score improvement measured by the International Prostatic Symptom Score (IPSS) on a scale from 0 to 35, with higher scores indicating worse symptoms (mean difference [MD] 1.72, 95% confidence interval [CI] -0.37 to 3.81; 6 RCTs, 360 participants;  $I^2 = 78\%$ ; low-certainty evidence).
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#### Long-term follow-up:

- Based upon RCT evidence, PAE may result in little to no difference in urologic symptom scores (MD 2.58 points, 95% CI -1.54 to 6.71; 2 RCTs, 176 participants;  $I^2 = 73\%$ ; low-certainty evidence) and quality of life (MD 0.50 points, 95% CI -0.03 to 1.04; 2 RCTs, 176 participants;  $I^2 = 29\%$ ; low-certainty evidence). They were very uncertain about major adverse events (RR 0.91, 95% CI 0.20 to 4.05; 2 RCTs, 206 participants;  $I^2 = 72\%$ ; very low-certainty evidence). PAE likely increases retreatments (RR 3.80, 95% CI 1.32 to 10.93; 1 RCT, 81 participants; moderate-certainty evidence). While PAE might result in little to no difference in erectile function (MD 3.09 points, 95% CI -0.76 to 6.94; 1 RCT, 81 participants; low-certainty evidence), PAE may reduce the occurrence of ejaculatory disorders (RR 0.67, 95% CI 0.45 to 0.98; 1 RCT, 50 participants; low-certainty evidence).

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#### Conclusions

- Prostatic artery embolization had been undertaken in a number of patients who had BPH with lower urinary tract symptoms or retention of urine which had demonstrated improved voiding in a number of patients in the short-term and medium term.
- For individuals who are not fit to undergo TURP or prostatectomy or individuals who refuse to undergo surgical operations, prostatic artery embolization may be offered and undertaken by well-trained and experienced interventional radiologists.
- It needs to be pointed out that some patient who undergo prostate artery embolization for BPH, may in due course require re-embolization.

- Selective prostate artery angiography, and super-selective embolization of a branch of the prostate artery supplying an intractable bleeding from the prostate artery which has not settled by conservative management may be undertaken to stop the haematuria.
- The anatomy of the prostatic artery in some instances may not enable the interventional radiologist to undertake the embolization procedure.
- Quite often, prostate artery embolization could be undertaken under local anaesthesia.

### Conflict Of Interest - Nil

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