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UROGENITAL

Prostate artery embolisation for benign prostatic hyperplasia: a systematic review and meta-analysis

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Abstract

Objectives Prostate artery embolisation (PAE) is a new minimally invasive treatment for lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH). The purpose of this study was to review the efficacy and safety of PAE in the treatment of BPH with LUTS.

Methods A systematic review performed according to the PRISMA guidelines with a pre-specified search strategy for PubMed, Web of Science, Cochrane Library and Embase databases protocol (PROSPERO ID: CRD42017059196). Trials studying the efficacy of prostate artery embolisation to treat LUTS with more than ten participants and follow-up longer than 6 months were included by two independent authors. Outcomes investigated were International Prostate Symptom Score (IPSS), quality of life (QoL), International Index of Erectile Function (IIEF-5), prostate volume (PV), prostate-specific antigen (PSA), peak void flow (Qmax), post-void residual (PVR) and complications. To summarise mean change from baseline, a meta-analysis was done using the random-effects model.

Results The search returned 210 references, of which 13 studies met the inclusion criteria, representing 1,254 patients. Patients in the included studies with data available for meta-analysis had moderate to severe LUTS and a mean IPSS of 23.5. Statistically significant (p value < 0.05) improvements of all investigated outcomes were seen at 12-month follow-up. Major complications were reported in 0.3% of the cases.

Conclusions Our findings suggest that PAE can reduce moderate to severe LUTS in men with BPH with a low risk of complications.

Key Points

- *Prostate artery embolisation (PAE) improved International Prostate Symptom Score (IPSS) by 67%.*
- *Major complications after PAE are very rare.*
- *Use of cone-beam CT may reduce risk of non-target embolisation.*

Keywords Male · Lower urinary tract symptoms · Prostatic hyperplasia · Embolisation, therapeutic

Abbreviations

AUR	Acute urinary retention
BPH	Benign prostatic hyperplasia
IPSS	International Prostate Symptom Score
IIEF-5	International Index of Erectile Function
LUTS	Lower urinary tract symptoms
NTE	Non-target embolisation
PAE	Prostate artery embolisation
PES	Post-embolisation syndrome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PSA	Prostate-specific antigen
PV	Prostate volume
PVR	Post-void residual
Qmax	Peak urinary flow
QoL	Quality of life
SIR	Society of Interventional Radiology
TURP	Transurethral resection of the prostate
UTI	Urinary tract infection

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Introduction

The estimated prevalence of benign prostatic hyperplasia (BPH) is up to 80% of men older than 70 years [1]. Of these, about 25% experience moderate to severe lower urinary tract symptoms (LUTS) impairing their quality of life (QoL) [2, 3].

Randomised controlled trials have demonstrated that both medical and surgical treatment can improve urinary function and reduce LUTS compared to observation/placebo in men with LUTS [4, 5]. Surgery is recommended for management of recurrent episodes of urinary tract infections (UTIs) or acute urinary retention (AUR), bladder calculi, gross haematuria and renal insufficiency caused by bladder outlet obstruction [6].

Transurethral resection of the prostate (TURP) remains the "gold standard" surgical management of BPH with LUTS and can reduce the International Prostate Symptom Score (IPSS) by 70% [4]. Recent multicentre studies showed that TURP is associated with a short-term morbidity of 11%, including the need for blood transfusion, surgical revision, UTI and urinary retention [7]. Bladder neck contracture and urethral stricture are late complications reported in up to 9.8% and 9.2%, respectively [7, 8]. Some men hesitate to accept TURP because of the risk of retrograde ejaculation and erectile dysfunction associated with the procedure [8]. The higher rate of complications in patients with pre-existing comorbidity, increasing age and large prostate volume may limit eligibility for TURP [9, 10]. A number of surgical alternatives to TURP have been proposed in the past decades to address these issues [11].

Prostate artery embolisation (PAE) is a new endovascular technique that can serve as an alternative to more invasive procedures in the management of LUTS. In 2000, the first case report described the potential of PAE to reduce voiding symptoms and prostate volume [12]. In this systematic *review* and meta-analysis, we focused on *efficacy and safety* of PAE in the treatment of LUTS.

Methods

Search strategy

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [13]. A published protocol (PROSPERO ID: CRD42017059196) with pre-specified outcomes, inclusion criteria and search strategy can be accessed online [14]. The search sources were PubMed, Web of Science, Cochrane Library and Embase. The following search terms were applied: prostatic OR prostate, artery OR arterial, embolisation OR embolisation AND benign, hyperplasia OR hypertrophy OR obstruction. The MESH terms were: embolisation, therapeutic and benign prostatic hyperplasia. The search terms were combined and conducted in appropriate combinations on 22 March 2017.

Two authors (M.A.R. and B.M.) reviewed abstracts. Trials studying the efficacy of PAE to treat BPH were included. Trials with less than ten participants, short follow-up (<6 months) or indications for PAE other than BPH were excluded. Conference papers, case reports and abstracts were excluded. We applied no restrictions on language or publication date. Full-text of all included articles was obtained and read by the same two authors. Agreement was reached through consensus using Covidence Systematic Review software [15].

Studies with overlapping recruitment period or data were excluded in favour of the publication with the longest follow-up or highest number of patients when the former did not vary.

To evaluate the risk of bias of randomised controlled trials (RCTs), the revised Cochrane Risk of Bias tool with three categories—high, low or some concern—was applied [16]. Two authors (M.T. and B.M.) evaluated the risk of bias.

First author, publication year, study design, number of patients, embolic agent, clinical and technical success rates, complications, and outcome measures for all included articles were collected.

Outcomes measures

The primary outcome measure was mean change in IPSS, a commonly used and validated questionnaire for evaluation of LUTS [17]. Secondary outcome measures were QoL, prostate volume (PV), prostate-specific antigen (PSA), post-void residual (PVR), peak urinary flow (Qmax), International Index of Erectile function (IIEF-5), complications, and technical and clinical success rates. Mean values and standard deviations were extracted for each outcome at baseline and all reported follow-up times. Complications were grouped into major or minor according to the Society of Interventional Radiology (SIR) classification [18].

Statistical considerations

Meta-analysis was performed to summarise mean values at baseline and changes from the baseline value at every follow-up. Only studies with samples at the relevant time of follow-up were included in the meta-analysis of changes from baseline. If standard errors of mean changes over time were not provided these were expressed as:

$$SE(change)^2 = SE(baseline)^2 + SE(follow\text{–}up)^2 - 2r \times SE(baseline)^2 \times SE(follow\text{–}up)^2$$

Where r is the correlation between the baseline and follow-up measurement. Since the correlation a priori is positive, the

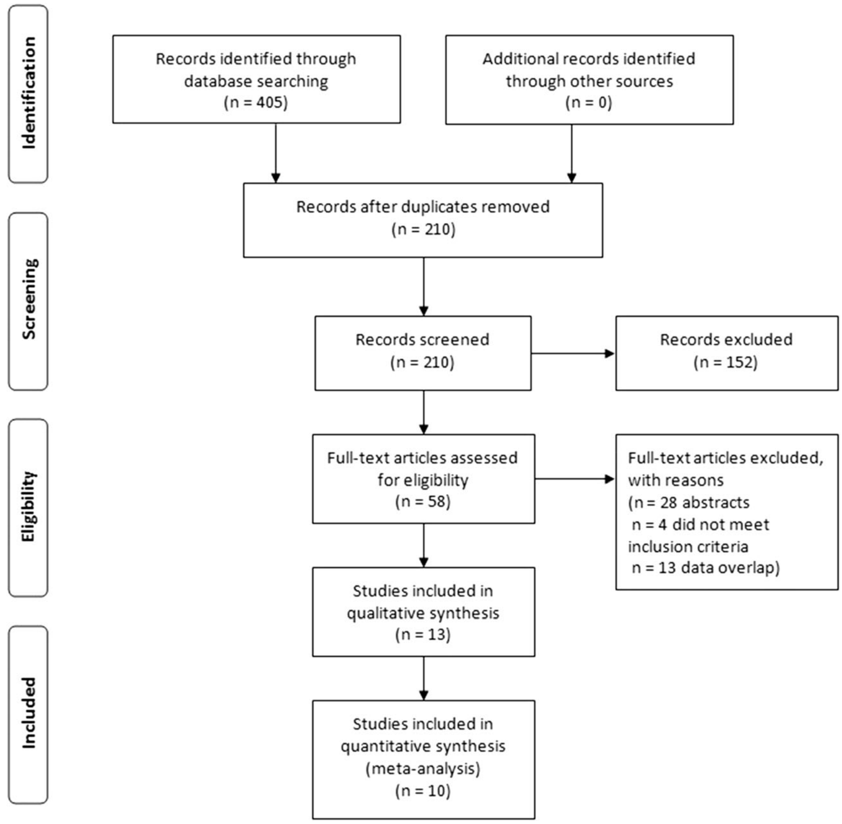

Fig. 1 PRISMA flow diagram

standard errors for mean changes can be estimated conservatively by

$$\sqrt{SE(baseline)^2 + SE(follow\text{-}up)^2}$$

The random-effects model used due to the clinical heterogeneity of the different study cohorts has previously been described in detail [19]. Heterogeneity should a priori be anticipated due to differences in study design and study populations. Therefore, test of heterogeneity was not performed since these may have low power [19]. The analysis was performed using R statistical software version 3.4.1 and the rmeta package version 2.16 [20, 21]. A p value of <0.05 was considered statistically significant.

Corresponding authors of publications not reporting standard deviations were contacted by e-mail. If data could not be retrieved, they were excluded from the meta-analysis.

Results

Study selection and overview

The search returned 210 references after removing duplicates. A total of 152 articles were excluded after reading the abstract. Of the remaining 58 studies assessed for full-text eligibility, we included 13 studies with 1,254 patients for data extraction [22–34].

Three studies did not report standard deviations of mean values [22, 29, 31]. One study did not report changes in prostate volume [24]. All four corresponding authors were e-mailed to retrieve missing data but had not responded by the time of submission.

The number of participants in each study ranged from 22 to 630. Assis et al [31] excluded one patient from analysis because of unsuccessful embolisation on both sites. After excluding studies with missing data, a total of 1,046 patients with a mean age of 68.6 years and up to 6.5 years of follow-up were available for meta-analysis.

A PRISMA flow diagram depicts the process of evidence synthesis (Fig. 1). Prior to submission and according to the pre-specified protocol, we searched for newly published studies eligible for inclusion. No further studies were included as of 3 November 2017.

Two of the included studies were RCTs [22, 34]. Study characteristics and assessment of risk of bias are summarised in Tables 1 and 2, respectively.

Outcome measures

All investigated outcomes were reported by nine studies, while the remaining did not. Bagla et al [24] did not study changes in Qmax, PSA, PV or PVR. Gonçalves et al [25] did

Table 1 Study characteristics

Study (year)	Country of origin	Data collection	No. of patients in PAE group	Mean age	Inclusion criteria	Exclusion criteria	Embolic material
Amouyal (2016)	France	Retrospective	32	65	IPSS ≥8 and/or QoL ≥3 Refused surgery or contra-indication to surgery after failure of medical therapy	Other causes of LUTS and complicated BPH (bladder wall insufficiency vesical diverticula or stones chronic obstructive renal failure) Active urinary infection Neoplasia PV <40 mL If PSA >4.0 ng/mL, then prostate biopsy was performed to rule out cancer	Embosphere 300-500 μm
Assis (2015)	Brazil	Prospective	35	64.8	Age ≥50 years LUTS secondary to BPH refractory to medical treatment for ≥30 days Prostate volume >90 g on MRI Confirmed infravesical obstruction in invasive urodynamic testing	Histological diagnosis of PCa Hypocontractile bladder/other neurogenic bladder disorders Cr >2.0 mg/dL Other indication for surgery (bladder stones or diverticula) If PSA >4.0 ng/mL or abnormal DRE, underwent TRUS guided prostate biopsy to exclude PCa	Embosphere 300-500 μm
Carnevale (2016)	Brazil	Prospective -RCT (*n* = 15) -PErFecTED arm (*n* = 15)	30	Group: Original PAE63.5 PErFecTED 60.4	On waiting list for TURP Age >45 IPSS >19 Symptoms refractory to medical treatment for ≥6 months Negative PCa screening Prostate volume 30-90 cm^3 on MRI BOO confirmed by urodynamic examinations	Renal failure Bladder calculi or diverticula Suspected Pac Urethral stenosis Neurogenic bladder disorders	Embosphere 300-500 μm
Bagla (2015)	USA	Retrospective	78	By volume: Small 62.7 Medium 65.5 Large 66.1	Moderate or severe-grade symptoms from BPH	If PSA >4 ng/mL prostate biopsy was performed to exclude prostate cancer	Embozene 100-400 μm
Gabr (2016)	Kingdom of Saudi Arabia	Prospective	22	72.5	Age >50 years LUTS/BPH refractory to medical treatment or indwelling catheter due to refractory urine retention Ineligible to standard BPH surgical treatment ASA 3	IPSS <8 Prostate size <60 g Suspicious cancer findings (DRE, US, PSA) Previous lower urinary tract surgery Urethral stricture Bladder stones Neurogenic bladder Large bladder diverticulum Other urethral/bladder abnormalities Contraindications for use of iodine CM Advanced atherosclerosis and tortuosity	Biosphere 300-500 μm
Gao (2014)	China	Prospective RCT	57	67.7	IPSS >7 after failed medical therapy with a washout period of ≥2 weeks PV 20-100 mL on TRUS or MRI Qmax <15 mL/s Patient understanding and written informed consent	Detrusor hyperactivity or hypocontractility at urodynamic study Urethral stricture Prostate cancer Diabetes mellitus Previous prostate, bladder neck or urethral surgery If PSA >4 ng/mL or abnormal finding at DRE underwent US-guided prostate biopsy	PVA 355-500 μm

Table 1 (continued)

Study (year)	Country of origin	Data collection	No. of patients in PAE group	Mean age	Inclusion criteria	Exclusion criteria	Embolic material
Goncalves (2016)	Brazil	Prospective	30	NR	Age >45 IPSS >19 QoL ≥3 Symptoms refractory to medical treatment for at least 6 months Negative screening for prostate cancer PV 30-90 cm^3 on MRI BOO confirmed by urodynamic studies	Renal failure Bladder calculi or diverticula Suspected prostate cancer Urethral stenosis Neurogenic bladder	Group A Embospheres 100-300 μm Group B Embospheres 300-500 μm
Kurbatov (2014)	Russia	Prospective	88	66.38	Symptomatic LUTS or BPO IPSS ≥12 PSA <4 ng/mL or PSA 4-10 ng/mL and negative biopsy PV >80 cm3 Qmax <15 mL/s Charlson comorbidity index ≥2	Neurogenic bladder dysfunction Sphincter decompensation Coagulation disorders and/or antiplatelet or anticoagulant therapy Chronic kidney disease Previous surgical treatment for LUTS or BPO or therapy with 5a-reductase inhibitors Life expectancy <2 years Bladder stones Catheter AUR in the last 4 weeks	Embosphere 300-500 μm
Li (2015)	China	Prospective	24	74.5	Symptomatic LUTS due to BPH IPSS ≥12 PSA <4 ng/ml or PSA 4-10 ng/ml but negative prostate biopsy PV ≥80 cm^3 Qmax <15 ml/s	Malignancy Neurogenic bladder dysfunction and/or sphincter decompensation Unregulated coagulation disorders Large bladder diverticula (>5 cm) Large bladder stones (>2 cm) Chronic renal failure (serum Cr >1.2 mg/dL) Active UTI previous surgical treatment for LUTS or BPH Current diagnosis of bladder stones Patients with catheter or with AUR in the last 4 weeks	PVA 50-100 μm
Pisco (2016)	Portugal	Retrospective	630	65.1	Age >40 IPSS ≥18 and QoL ≥3 Qmax ≤12 mL/s or AUR Refractoriness to medical or other treatment for at least 6 months PV > 30 mL PV < 30 mL if urodynamic study showed infravesical obstruction	Malignancy Advanced atherosclerosis Tortuosity on CT angiography Secondary renal insufficiency Large bladder diverticula or stones Neurogenic bladder Detrusor failure Active UTI Unregulated and uncontrollable coagulation parameters	418 patients: PVA 100-200 μm 167 patients PVA 300-500 μm 33 patients Embozene 400 μm
Rampoldi (2017)	Italy	Prospective	43	77.9	≥1 month Indwelling bladder catheter for management of urinary retention secondary to BOO	Eligibility for surgery Active bladder cancer or known PCa	Embosphere 300-500 μm
Shaker (2016)	Egypt	Prospective	28	68.5	Age >45 years with a diagnosis of BPH with significant LUTS refractory to medical treatment for at least 6 months Adverse reactions from medical treatment Unfit for surgery or refusing surgery IPSS ≥20 QoL ≥3 Qmax <12 mL/s PV >40cc^3	Prostate cancer Uncorrectable coagulation profile Renal insufficiency Active UTI Neurogenic bladder	PVA 150-250 μm

Table 1 (continued)

Study (year)	Country of origin	Data collection	No. of patients in PAE group	Mean age	Inclusion criteria	Exclusion criteria	Embolic material
Wang (2016)	China	Prospective	157	Group A 82.5 Group B 67.5	Age >50 years IPSS ≥18 QoL > 3 Qmax<12 mL/s and/or urinary retention Refractory to medical treatment for at least 6 months PV >40 mL	Pelvic malignancy Large bladder diverticula (>5 cm) Large bladder stones (>2 cm) Chronic renal failure Active UTI Neurogenic bladder and detrusor failure Urethral stricture Unregulated coagulation parameters Allergy to intravenous contrast media	PVA 100 μm

ASA American Society of Anesthesiologists score, *AUR* acute urinary retention, *BOO* bladder outlet obstruction, *BPO* benign prostatic obstruction, *BPH* benign prostatic hyperplasia, *Cr* creatinine, *CT* computed tomography, *DRE* digital rectal examination, *LUTS* lower urinary tract symptoms, *IPSS* International Prostate Symptom Score, *MRI* magnetic resonance imaging, *PCa* prostate cancer, *PErFecTED* proximal embolisation first then embolise distal, *PSA* prostate-specific antigen, *PV* prostate volume, *PVA* polyvinyl alcohol, *Qmax* peak urinary flow, *QoL* quality of life, *RCT* randomised controlled trial, *TRUS* transrectal ultrasound, *TURP* transurethral resection of the prostate, *UTI* urinary tract infection

not report on changes in IEFF and PVR. Baseline values of PSA, IEFF, Qmax, and PVR were not reported by Rampoldi et al [28] Finally, IEFF was not assessed by Shaker et al [33].

The severity of LUTS at baseline ranged from moderate to severe with a mean IPSS of 23.5 and a QoL score of 4.7. Pre-embolisation mean prostate volume was 77.3 cm^3.

Since only one study had longer than 1 year of follow-up, we report values at the 12-month follow-up where all investigated outcomes had significantly improved. Relief of symptoms after PAE was demonstrated by a 16.2-point (95% CI, -18.3, -14.0) IPSS mean reduction and improved QoL of 3.0 points (95% CI, -3.7, -2.3). Mean PV was significantly reduced by 20.3 cm^3 (95% CI, -25.8, -14.8) one year after PAE. IPSS, QoL, PV, PVR and IIEF remained statistically significantly improved after 3 years. Baseline values and changes from baseline are summarised in Fig. 2 and Table 3. Changes from baseline in each individual study at 12-month follow-up are shown in Fig. 3.

Complications

SIR classification [18] of complications was used by six studies, Clavien-Dindo [35] or a modification in three studies, National Cancer Institute Common Terminology Criteria for Adverse Events [36] in two studies, and the remaining two studies did not specify the classification.

The most frequent minor post-operative complications were transient dysuria and increased urinary frequency reported in 10% and 16%, respectively. The occurrence of post-embolisation syndrome (PES) was reported in 3.6%. One study with 22 participants reported no complications at all [32].

Major post-operative complications were reported in three cases (0.3%). One incidence of bladder ischaemia was treated by surgery. One was treated with intravenous antibiotics for a persistent UTI. Finally, one patient reported persistent perineal pain for 3 months. All observed complications have been summarised according to the SIR classification in Table 4.

Discussion

This systematic review and meta-analysis investigated the efficacy and safety of PAE in the treatment of LUTS. At 12-month follow-up, significant improvements of all investigated outcomes were reported with a low risk of complications. These results indicate that PAE may have a role in the management of LUTS associated with BPH, especially in men with high risk of complications due to pre-existing medical conditions.

Rates of clinical and technical success were reported between 76.3 to 100% and 76.7 to 100%, respectively. In the included studies, both bilateral and unilateral embolisations

Table 2 Risk of bias

Cochrane risk of bias tool	Randomisation process	Deviation from intended intervention	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Randomised controlled trials						
Carnevale 2015	-	+	+	?	+	?
Gao 2014	+	+	+	?	+	?
Non-randomised studies						
Amouyal 2016	Study design with an inherent risk of bias					
Assis 2015	Study design with an inherent risk of bias					
Bagla 2015	Study design with an inherent risk of bias					
Gabr 2016	Study design with an inherent risk of bias					
Goncalves 2016	Study design with an inherent risk of bias					
Kurbatov 2014	Study design with an inherent risk of bias					
Li 2015	Study design with an inherent risk of bias					
Pisco 2016	Study design with an inherent risk of bias					
Rampoldi 2017	Study design with an inherent risk of bias					
Shaker 2016	Study design with an inherent risk of bias					
Wang 2016	Study design with an inherent risk of bias					

\+ low risk, - high risk, *?* some concern

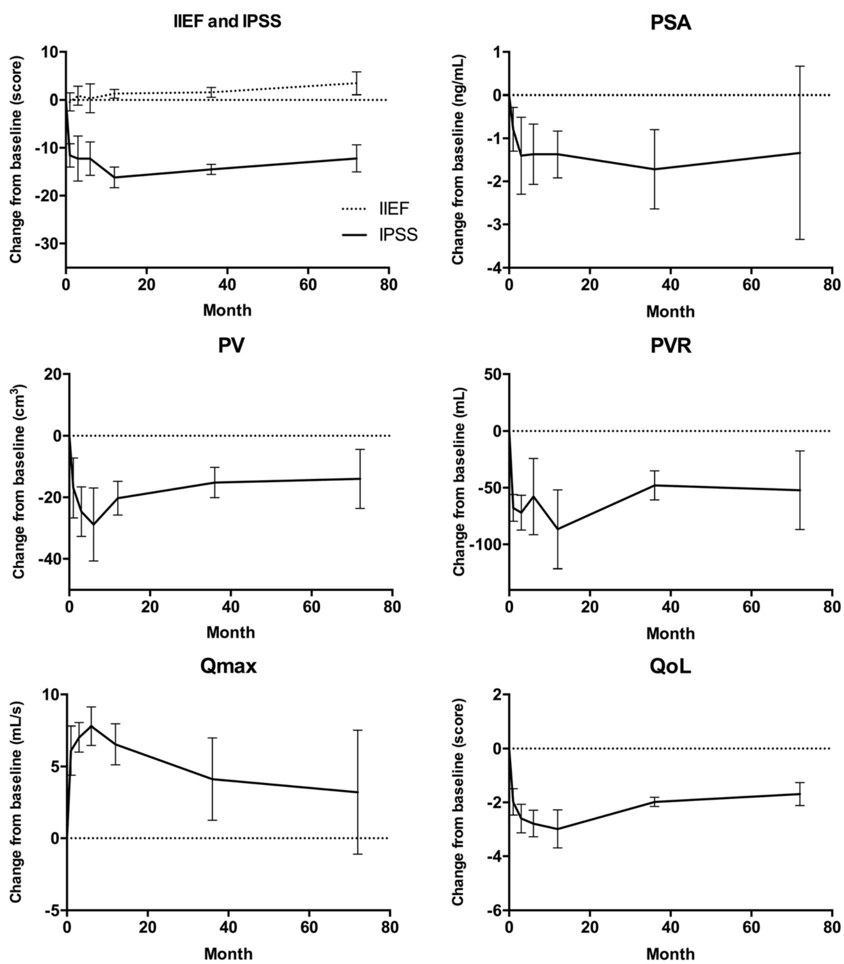

Fig. 2 Mean changes from baseline with confidence interval bars. *IIEF* International Index of Erectile Function, *IPSS* International Prostate Symptom Score, *PSA* prostate-specific antigen, *PV* prostate volume, *PVR* post-void residual, *Qmax* peak urinary flow, *QoL* quality of life

Table 3 Baseline and changes from baseline

Variable	Baseline		1-month follow-up			3-month follow-up			6-month follow-up			12-month follow-up			1-3 years' follow-up			3-6.5 years' follow-up		
	n	mean [95% CI]	*n*	change [95% CI]	*p* value	*n*	change [95% CI]	*p* value	*n*	change [95% CI]	*p* value	*n*	change [95% CI]	*p* value	*n*	change [95% CI]	*p* value	*n*	change [95% CI]	*p* value
Age	1,046	68.6 [65.0, 72.2]																		
IIEF	895	15.2 [11.8, 18.6]	84	-0.4 [-2.3, 1.4]	0.65	76	0.9 [-1.1, 2.8]	0.39	42	0.3 [-2.6, 3.3]	0.83	594	1.3 [0.4, 2.2]	0.005	227	1.6 [0.6, 2.5]	0.002	32	3.4 [1.1, 5.8]	0.005
IPSS	1,033	23.5 [21.8, 25.2]	108	-11.6 [-14.0, -9.1]	<0.001	162	-12.2 [-17.0, -7.5]	<0.001	177	-12.3 [-15.8, -8.8]	<0.001	716	-16.2 [-18.3, -14.0]	<0.001	237	-14.5 [-15.6, -13.4]	<0.001	36	-12.2 [-15.1, -9.3]	<0.001
PSA (ng/mL)	870	4.6 [3.9, 5.2]	42	-0.8 [-1.3, -0.3]	0.004	261	-1.4 [-2.3, -0.5]	0.002	209	-1.4 [-2.1, -0.7]	<0.001	664	-1.4 [-1.9, -0.8]	<0.001	234	-1.7 [-2.6, -0.8]	<0.001	35	-1.3 [-3.4, 0.7]	0.19
PV (cm^3)	995	77.3 [71.4, 83.2]	42	-17.0 [-26.7, -7.2]	0.001	104	-24.6 [-32.7, -16.6]	<0.001	118	-28.8 [-40.7, -16.9]	<0.001	667	-20.3 [-25.8, -14.8]	<0.001	232	-15.2 [-20.1, -10.3]	<0.001	35	-14.0 [-23.6, -4.4]	0.004
PVR (mL)	865	111.9 [96.5, 127.3]	42	-67.8 [-79.5, -56.0]	<0.001	74	-72.0 [-87.3, -56.7]	<0.001	75	-57.8 [-91.4, -24.2]	0.001	588	-86.6 [-121.3, -51.9]	<0.001	210	-47.9 [-60.8, -35.0]	<0.001	30	-52.2 [-86.8, -17.5]	0.003
Qmax (mL/s)	901	7.3 [7.3, 8.3]	42	6.1 [4.4, 7.8]	<0.001	104	7.0 [6.0, 8.0]	<0.001	75	7.8 [6.5, 9.1]	<0.001	617	6.5 [5.1, 8.0]	<0.001	211	4.1 [1.3, 7.0]	0.005	32	3.2 [-1.1, 7.5]	0.15
QoL	1,035	4.7 [4.5, 5.0]	106	-2.0 [-2.5, -1.5]	<0.001	161	-2.6 [-3.1, -2.1]	<0.001	157	-2.8 [-3.3, -2.3]	<0.001	720	-3.0 [-3.7, -2.3]	<0.001	236	-2.0 [-2.1, -1.8]	<0.001	38	-1.7 [-2.1, -1.3]	<0.001

CI confidence interval, *IIEF* International Index of Erectile Function, *IPSS* International Prostate Symptom Score, *PSA*, prostate-specific antigen, *PV* prostate volume, *PVR* post-void residual, *Qmax* peak urinary flow, *QoL* quality of life

were considered technical successes, despite evidence suggesting a better clinical result after bilateral embolisation [37]. However, more than 50% of patients treated with unilateral embolisation can achieve improvement in IPSS, QoL, Qmax and become independent of prostatic medication [37]. Additionally, the definition of clinical success also varied. One study specified clinical success as the ability void with less than 80 mL PVR after removing the indwelling bladder catheter [28]. Most studies considered improvement in IPSS, QoL and Qmax clinical success, although threshold values varied.

Some studies performed a pre-intervention computed tomography angiography (CTA) as proposed by several authors [38, 39]. The CTA can be used to plan the procedure and exclude patients with advanced atherosclerosis or tortuous arteries. This selection may increase rates of bilateral embolisation and better clinical outcomes. PV is a valuable outcome since the primary mechanism of action of conventional therapies such as 5a-reductase inhibitors and TURP is to reduce the size of the prostate and consequently the urethral pressure to relieve obstruction. The reduction of PV after PAE peaked at 6-month follow-up at almost 29 cm^3. At long-term follow-up (up to 6.5 years) the reduction of PV from baseline was only 14 cm^3 and PSA (as an indirect measure of PV) had a similar increasing trend over time. Interestingly, IPSS remained improved by 12 points despite this apparent partial regrowth of the prostate. Regrowth of the prostate is a known phenomenon after surgery and may explain the rate of re-intervention after TURP, which can be as high as 15.5% within 8 years [40].

Both IPSS and QoL scores are important patient-reported outcomes that subjectively grade the severity of LUTS and patients undergoing PAE experienced significant symptomatic improvements at every follow-up. The meta-analysis showed a 67% reduction of IPSS 1 year after embolisation. The findings are comparable to the 61% improvement reported by Kuang et al [41]. In comparison, a meta-analysis of 20 RCTS representing 954 patients undergoing TURP observed a 70% improvement of IPSS after TURP [42]. Further, a RCT involving 3,047 men found a 41% reduction of IPSS following a combined medical therapy of doxazosin and finasteride [43]. Our meta-analysis showed a comparable symptomatic effect of PAE compared to TURP. This was in agreement with the RCT by Gao et al [22]. Likewise, in the study by Carnevale et al [34], patients treated in the non-randomised arm with "proximal embolisation first, then embolise distal" (PErFecTED) technique experienced similar rates of symptomatic relief as patients treated with TURP.

The different effect sizes reported by studies included in our analysis may be explained by the inhomogeneity in respect to patient selection, embolisation technique and timing of follow-up. For instance, the biggest cohort by Pisco et al [39] found a reduction of 13.7 points and 20.3 cm^3 of IPSS and PV, respectively, within the first year of follow-up. Meanwhile, the

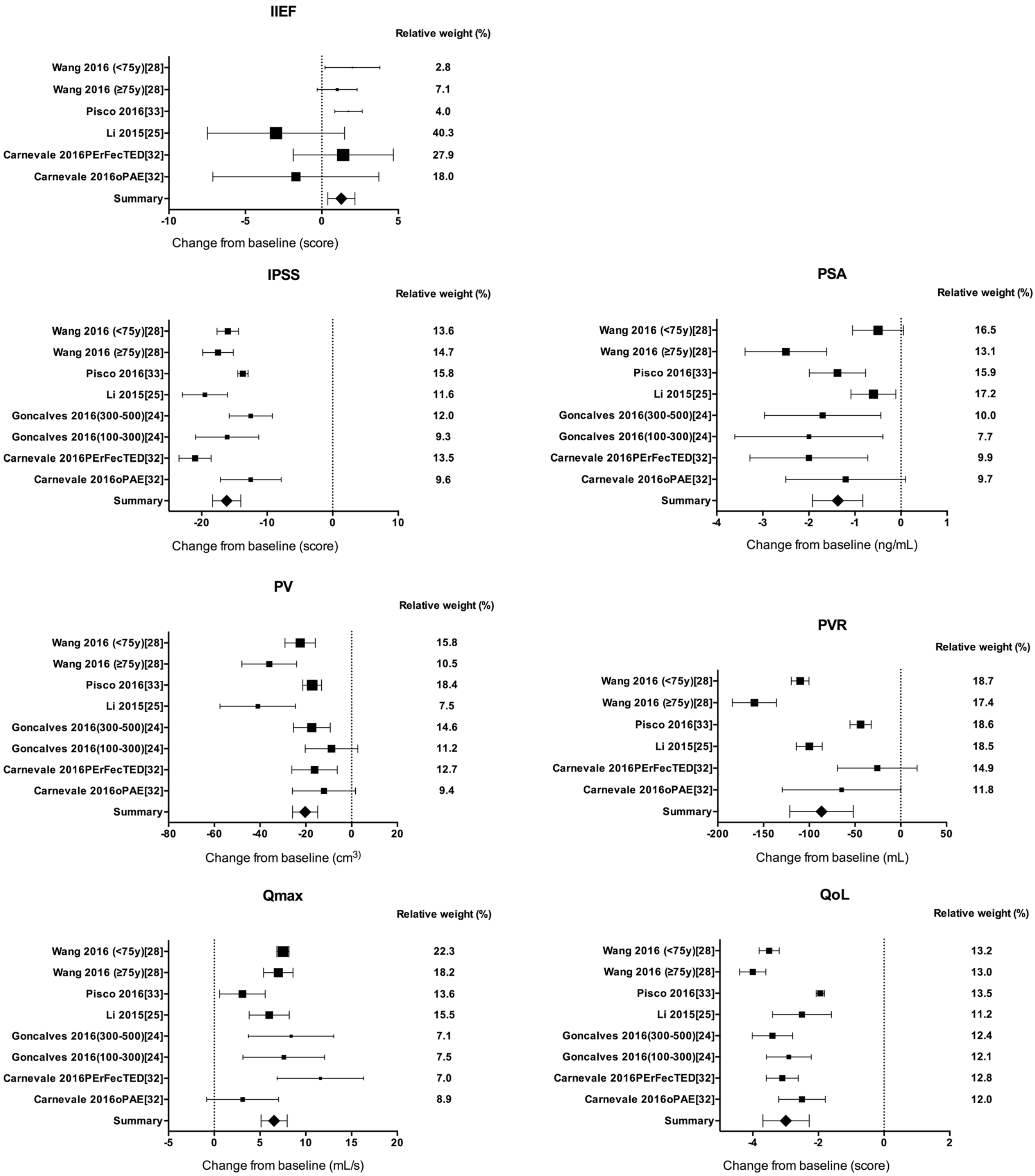

Fig. 3 Forest plot showing mean changes from baseline at 12-month follow-up with confidence interval bars. *IIEF* International Index of Erectile Function, *oPAE* original prostate artery embolisation technique, *PErFecTED* proximal embolisation first, then embolise distal, *IPSS* International Prostate Symptom Score, *PSA* prostate-specific antigen, *PV* prostate volume, *PVR* post-void residual, *Qmax* peak urinary flow, *QoL* quality of life, *≥75y* men aged 75 or older, *<75* men aged younger than 75, *100-300* group treated using 100-300 μm particles, *300-500* group treated using 300-500 μm particles

second largest cohort included in this systematic review followed by Wang and colleagues [30] observed an 18 points reduction in IPSS and a PV reduction of 29 cm^3.

The degree of obstruction was routinely assessed by PVR and Qmax and was significantly improved at 12-month follow-up. PVR was reduced by 52.2 ml and Qmax improved by

Table 4 Complications reported in all studies during follow-up

Total incidence of complications		Number of incidents (%)
No. of patients = 1,253		
SIR Classification		
Major		
	Urinary tract infection requiring IV antibiotics	1 (0.08)
	Bladder wall ischaemia	1 (0.08)
	Persistent perineal pain	1 (0.08)
Minor		
	Dysuria	212 (16.92)
	Frequency	145 (11.57)
	Obstipation	76 (6.07)
	Haematospermia	69 (5.51)
	Haematuria	69 (5.51)
	Urinary retention	57 (4.55)
	Transient rectal bleeding	57 (4.55)
	Post-embolisation syndrome	47 (3.75)
	Urinary tract infection treated with oral antibiotics	33 (2.63)
	Groin haematoma	19 (1.52)
	Reduction in ejaculate volume	9 (0.72)
	Balanitis	4 (0.32)
	Rectorrhagia	3 (0.24)
	Diarrhoea	2 (0.16)
	Hyperthermia	1 (0.08)
	Severe pelvic pain	1 (0.08)
	Transient pubic bone ischaemia	1 (0.08)

6.5 ml/s, indicating a relief of obstruction. The improved peak flow is less than the 9.7 ml/s reported after TURP, but higher than the 3.7 ml/s observed after medical treatment [43, 44]. This superiority of TURP on uroflowmetry is in agreement with the results from the RCTs included in this review.

Erectile dysfunction impacts QoL. Following PAE, erectile function assessed by IIEF-5 significantly improved by 3.4 points. Despite the controversy of TURP and impaired erectile function, it is a major concern that may guide the choice of therapy in favour of PAE.

A strong argument for minimally invasive techniques is the expected mild side-effects and lower rate of complications compared to surgery. PES is a side-effect commonly reported after therapeutic embolisation. The syndrome consists of fever, nausea, pain and transient worsening of LUTS in particular, dysuria and frequency. The most commonly observed complication in this review was self-limited dysuria (16%), followed by frequency (11%). According to Moreira et al [45], both symptoms should instead be considered expected side-effects of the treatment and a part of the PES. Lack of consensus to distinguish complications from side-effects may explain why some authors observed no complications and others reported minor complications in 100%.

Few major complications were reported and only one incidence of non-target embolisation (NTE) of the bladder wall required surgical intervention. NTE is a recognised risk associated with trans-arterial embolisation and likely to be caused by failure to correctly identify the prostate artery and its anastomoses or by reflux of embolic material due to high pressure administration [46, 47]. Utilisation of cone-beam computed tomography (CBCT) has been proposed to reduce the occurrence of NTE and assist in the identification of the prostate arteries [48].

Limitations

This systematic review is limited by the diversity in patient selection between studies as well as the use of different embolic material and embolisation techniques. The consequence was an inhomogeneous group of studies for meta-analysis. Being an emerging technique, long-term follow-up data is warranted but only one study in the meta-analysis had more than 12-month follow-up. Thus, long-term results are based on limited samples. Additionally, only two authors participated in the initial screening and full-text inclusion.

Conclusions

This systematic review and meta-analysis showed that PAE was feasible and reduced moderate to severe LUTS with a low risk of major complications. More randomised controlled trials and long-term follow-ups are needed.

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Compliance with ethical standards

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Informed consent Written informed consent was not required for this study because this was a systematic review and meta-analysis.

Ethical approval Institutional Review Board approval was not required because this was a systematic review and meta-analysis.

Methodology
• prospective
• systematic review and meta-analysis

References

1. Roehrborn CG (2005) Benign prostatic hyperplasia: an overview. Rev Urol 7:S3–S14
2. Thorpe A, Neal D (2003) Benign prostatic hyperplasia. Lancet 361: 1359–1367. https://doi.org/10.1016/S0140-6736(03)13073-5
3. Girman CJ, Epstein RS, Jacobsen SJ et al (1994) Natural history of prostatism: impact of urinary symptoms on quality of life in 2115 randomly selected community men. Urology 44:825–831
4. Oelke M, Bachmann A, Descazeaud A et al (2013) EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. Eur Urol 64:118–140. https://doi.org/10.1016/j.eururo.2013.03.004
5. McVary KT, Roehrborn CG, Avins AL et al (2011) Update on AUA guideline on the management of benign prostatic hyperplasia. J Urol 185:1793–1803. https://doi.org/10.1016/j.juro.2011.01.074
6. Chua ME, Mendoza J, See M et al (2015) A critical review of recent clinical practice guidelines on the diagnosis and treatment of non-neurogenic male lower urinary tract symptoms. Can Urol Assoc J 9: E463–E470. https://doi.org/10.5489/cuaj.2424
7. Reich O, Gratzke C, Bachmann A et al (2008) Morbidity, mortality and early outcome of transurethral resection of the prostate: a prospective multicenter evaluation of 10,654 patients. J Urol 180:246–249. https://doi.org/10.1016/j.juro.2008.03.058
8. Rassweiler J, Teber D, Kuntz R, Hofmann R (2006) Complications of transurethral resection of the prostate (TURP)—incidence, management, and prevention. Eur Urol 50:969–979; discussion 980. https://doi.org/10.1016/j.eururo.2005.12.042
9. Guo R, Yu W, Meng Y et al (2016) Correlation of ASA Grade and the Charlson Comorbidity Index with complications in patients after transurethral resection of prostate. Urology 98:120–125. https://doi.org/10.1016/j.urology.2016.07.025
10. Muzzonigro G, Milanese G, Minardi D et al (2004) Safety and efficacy of transurethral resection of prostate glands up to 150 ml: a prospective comparative study with 1 year of follow up. J Urol 172:611–615. https://doi.org/10.1097/01.ju.0000131258.36966.d1
11. Smith C, Craig P, Taleb S et al (2017) Comparison of traditional and emerging surgical therapies for lower urinary tract symptoms in men: a review. Cardiovasc Intervent Radiol 40:1176–1184. https://doi.org/10.1007/s00270-017-1575-7
12. DeMeritt JS, Elmasri FF, Esposito MP, Rosenberg GS (2000) Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolisation. J Vasc Interv Radiol JVIR 11:767–770
13. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339:b2535. https://doi.org/10.1136/bmj.b2535
14. Malling B (2016) Prostatic artery embolisation for benign prostatic hyperplasia: a systematic review. PROSPERO: International prospective register of systematic reviews. Available from: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=59196
15. Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org
16. Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S (2016) A revised tool for assessing risk of bias in randomized trials. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD201601
17. Gratzke C, Bachmann A, Descazeaud A et al (2015) EAU Guidelines on the assessment of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. Eur Urol 67:1099–1109. https://doi.org/10.1016/j.eururo.2014.12.038
18. Angle JF, Siddiqi NH, Wallace MJ et al (2010) Quality improvement guidelines for percutaneous transcatheter embolisation: Society of Interventional Radiology Standards of Practice Committee. J Vasc Interv Radiol JVIR 21:1479–1486. https://doi.org/10.1016/j.jvir.2010.06.014
19. Borenstein M (2009) Introduction to meta-analysis, 1st edn. Wiley, New York
20. R Development Core Team (2008) R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0. URL http://www.R-project.org
21. Lumley T (2012) rmeta: meta-analysis. R package version 2.16. https://CRAN.R-project.org/package=rmeta
22. Gao Y, Huang Y, Zhang R et al (2014) Benign prostatic hyperplasia: prostatic arterial embolisation versus transurethral resection of the prostate—a prospective, randomized, and controlled clinical trial. Radiology 270:920–928. https://doi.org/10.1148/radiol.13122803
23. Amouyal G, Thiounn N, Pellerin O et al (2016) Clinical results after prostatic artery embolisation using the PErFecTED technique: a single-center study. Cardiovasc Intervent Radiol 39:367–375. https://doi.org/10.1007/s00270-015-1267-0
24. Bagla S, Smirniotopoulos JB, Orlando JC et al (2015) Comparative analysis of prostate volume as a predictor of outcome in prostate artery embolisation. J Vasc Interv Radiol JVIR 26:1832–1838. https://doi.org/10.1016/j.jvir.2015.08.018
25. Gonçalves OM, Carnevale FC, Moreira AM et al (2016) Comparative study using 100-300 versus 300-500 μm microspheres for symptomatic patients due to enlarged-BPH prostates. Cardiovasc Intervent Radiol 39:1372–1378. https://doi.org/10.1007/s00270-016-1443-x
26. Pisco JM, Bilhim T, Pinheiro LC et al (2016) Medium- and long-term outcome of prostate artery embolisation for patients with benign prostatic hyperplasia: results in 630 patients. J Vasc Interv

Radiol JVIR 27:1115–1122. https://doi.org/10.1016/j.jvir.2016.04.001

27. Li Q, Duan F, Wang M-Q et al (2015) Prostatic arterial embolisation with small sized particles for the treatment of lower urinary tract symptoms due to large benign prostatic hyperplasia: preliminary results. Chin Med J (Engl) 128:2072–2077. https://doi.org/10.4103/0366-6999.161370
28. Rampoldi A, Barbosa F, Secco S et al (2017) Prostatic artery embolisation as an alternative to indwelling bladder catheterization to manage benign prostatic hyperplasia in poor surgical candidates. Cardiovasc Intervent Radiol 40:530–536. https://doi.org/10.1007/s00270-017-1582-8
29. Kurbatov D, Russo GI, Lepetukhin A et al (2014) Prostatic artery embolisation for prostate volume greater than 80 cm^3: results from a single-center prospective study. Urology 84:400–404. https://doi.org/10.1016/j.urology.2014.04.028
30. Wang MQ, Wang Y, Yan JY et al (2016) Prostatic artery embolisation for the treatment of symptomatic benign prostatic hyperplasia in men ≥75 years: a prospective single-center study. World J Urol 34:1275–1283. https://doi.org/10.1007/s00345-016-1771-0
31. de Assis AM, Moreira AM, de Paula Rodrigues VC et al (2015) Prostatic artery embolisation for treatment of benign prostatic hyperplasia in patients with prostates > 90 g: a prospective single-center study. J Vasc Interv Radiol JVIR 26:87–93. https://doi.org/10.1016/j.jvir.2014.10.012
32. Gabr AH, Gabr MF, Elmohamady BN, Ahmed A-F (2016) Prostatic artery embolisation: a promising technique in the treatment of high-risk patients with benign prostatic hyperplasia. Urol Int 97:320–324. https://doi.org/10.1159/000447360
33. Shaker M, Abd El Tawab KA, Abd El Tawab KH, El-Gharib M (2016) Role of prostatic artery embolisation in management of symptomatic benign prostatic hyperplasia. Egypt J Radiol Nucl Med 47:839–845. https://doi.org/10.1016/j.ejrnm.2016.04.012
34. Carnevale FC, Iscaife A, Yoshinaga EM et al (2016) Transurethral resection of the prostate (TURP) versus original and PErFecTED prostate artery embolisation (PAE) due to benign prostatic hyperplasia (BPH): preliminary results of a single center, prospective, urodynamic-controlled analysis. Cardiovasc Intervent Radiol 39:44–52. https://doi.org/10.1007/s00270-015-1202-4
35. Dindo D, Demartines N, Clavien P-A (2004) Classification of surgical complications. Ann Surg 240:205–213. https://doi.org/10.1097/01.sla.0000133083.54934.ae
36. National Cancer Institute Common Terminology Criteria for Adverse Events v4.0 NCI, NIH, DHHS (2009) NIH publication no. 09-7473. National Institutes of Health, Bethesda
37. Bilhim T, Pisco J, Tinto HR et al (2013) Unilateral versus bilateral prostatic arterial embolisation for lower urinary tract symptoms in patients with prostate enlargement. Cardiovasc Intervent Radiol 36:403–411. https://doi.org/10.1007/s00270-012-0528-4
38. Bilhim T, Pisco JM, Furtado A et al (2011) Prostatic arterial supply: demonstration by multirow detector angio CT and catheter angiography. Eur Radiol 21:1119–1126. https://doi.org/10.1007/s00330-010-2015-0
39. Pisco JM, Tinto HR, Pinheiro LC et al (2013) Embolisation of prostatic arteries as treatment of moderate to severe lower urinary symptoms (LUTS) secondary to benign hyperplasia: results of short- and mid-term follow-up. Eur Radiol 23:2561–2572. https://doi.org/10.1007/s00330-012-2714-9
40. Roos NP, Wennberg JE, Malenka DJ et al (1989) Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. N Engl J Med 320:1120–1124. https://doi.org/10.1056/NEJM198904273201705
41. Kuang M, Vu A, Athreya S (2017) A systematic review of prostatic artery embolisation in the treatment of symptomatic benign prostatic hyperplasia. Cardiovasc Intervent Radiol 40:655–663. https://doi.org/10.1007/s00270-016-1539-3
42. Ahyai SA, Gilling P, Kaplan SA et al (2010) Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. Eur Urol 58:384–397. https://doi.org/10.1016/j.eururo.2010.06.005
43. McConnell JD, Roehrborn CG, Bautista OM et al (2003) The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 349:2387–2398. https://doi.org/10.1056/NEJMoa030656
44. Madersbacher S, Marberger M (1999) Is transurethral resection of the prostate still justified? BJU Int 83:227–237
45. Moreira AM, de Assis AM, Carnevale FC et al (2017) A review of adverse events related to prostatic artery embolisation for treatment of bladder outlet obstruction due to BPH. Cardiovasc Intervent Radiol 40:1490–1500. https://doi.org/10.1007/s00270-017-1765-3
46. Ingraham CR, Johnson GE, Nair AV, Padia SA (2011) Nontarget embolisation complicating transarterial chemoembolisation in a patient with hepatocellular carcinoma. Semin Intervent Radiol 28:202–206. https://doi.org/10.1055/s-0031-1280665
47. López-Benítez R, Radeleff BA, Barragán-Campos HM et al (2007) Acute pancreatitis after embolisation of liver tumors: frequency and associated risk factors. Pancreatology 7:53–62. https://doi.org/10.1159/000101878
48. Wang MQ, Duan F, Yuan K et al (2017) Benign prostatic hyperplasia: cone-beam CT in conjunction with DSA for identifying prostatic arterial anatomy. Radiology 282:271–280. https://doi.org/10.1148/radiol.2016152415