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The Role of Prostatic Arterial Embolization in Patients with Benign Prostatic Hyperplasia: A Systematic Review

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Abstract
Purpose This study was designed to summarize the evidence on clinical outcomes and complications of prostatic arterial embolization (PAE) in patients with benign prostatic hyperplasia (BPH).
Methods We searched Medline and Embase for PAE trials of patients with BPH upto November 2013. Two reviewers independently checked the inclusion and exclusion criteria and performed data extraction of study characteristics, quantitative and qualitative outcomes, and complications.
Results The search yielded 562 studies, of which 9 articles with 706 patients were included. In these 9 articles, there was a possible overlap of data and the quality of 8 studies was assessed as poor. All patients had moderate-to-severe, lower urinary tract symptoms (LUTS). The mean age ranged from 63.4–74.1 years. After embolization, a decrease of the prostate volume (PV) and post void residual (PVR) was seen mainly in the first month with a further decrease up to 12 months, increasing afterwards. The prostate specific antigen (PSA) decreased up to 3 months after PAE, increasing afterwards. The peak urinary flow (Qmax) increased mainly the first month and decreased after 30 months. The international prostate symptom score (IPSS) and quality of life-related symptoms (QOL) improved mainly during the first month, with a further improvement up to 30 months. No deterioration of the international index of erectile function (IIEF) was seen after PAE. The PAE procedure seems safe.
Conclusions Although the number of studies was small, qualitatively poor, and with overlap of patients, the initial clinical outcomes as reported up to 12 months seem positive and the procedure seems safe.

Keywords Prostate · BPH · Embolization · Symptoms · Quality of life · Complications

Introduction

Benign prostatic hyperplasia (BPH) is common in middle-aged and elderly men [1]. The enlarged gland is an important cause of lower urinary tract symptoms (LUTS), such as a weak urinary stream, higher urinary frequency, intermittent voiding, nocturia, and urinary urgency [2, 3]. The prevalence and severity of LUTS in aging men can be progressive. Approximately 25 % of men in their 50s, 33 % of men in their 60s, and circa 50 % of men at 80 years of age suffer from moderate to severe LUTS [1]. LUTS caused by BPH can have a significant impact on the quality of life (QOL), and when severe, BPH can even lead to acute urinary retention. The severity of LUTS and effect on QOL are important considerations for deciding when treatment is indicated [3–5]. Treatment options include watchful waiting, medical treatment, minimally invasive, or surgical therapies [6]. Medical therapy is usually the first-line treatment option for patients with mild-to-moderate LUTS [7, 8]. In patients with moderate-to-severe

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LUTS, transurethral resection of the prostate (TURP) is still the "gold standard" surgical treatment for BPH to improve symptoms and decrease progression. However, it is associated with substantial morbidity, such as bleeding, irritative voiding symptoms postoperative, long-term ejaculatory dysfunction, and bladder neck contractures [9].

Prostatic arterial embolization (PAE) gained special attention in the past years as a potential minimally invasive technique for patients with moderate-to-severe LUTS due to BPH. Previous animal studies have shown that PAE can induce prostatic volume reduction and is safe, with no procedure-related sexual dysfunction [10, 11]. In this review, we systematically summarized all evidence on PAE in humans to assess the quantitative clinical outcomes [prostate volume (PV), prostate-specific antigen (PSA), peak urinary flow (Qmax), post void residual (PVR)], qualitative clinical outcomes [International Prostate Symptom Score (IPSS), QOL, and International Index of Erectile Function (IIEF)], and complications related to the procedure.

Materials and Methods

This review was conducted according to the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines [12]. The review protocol was not published or registered in advance.

Search Strategy

Search was performed in Medline and Embase until the end of November 2013. The Medline search included: (Embolisation [MeSH Terms/Title/Abstract] OR Embolization [MeSH Terms/Title/Abstract]) AND (Prostate [Title/Abstract] OR Prostatic [Title/Abstract] OR Prostatic diseases [MeSH Terms] OR Prostate [MeSH Terms]).

The Embase search included: (Artificial Embolism [MeSH Terms] OR Embolization [All field] OR Embolisation [All field])) AND (Prostate [MeSH Terms] OR Prostate disease [MeSH Terms] OR Prostate [All field] OR Prostatic [All field]).

Study Selection

Two independent reviewers (S.M.S. and A.E.S.) selected all potentially relevant studies. Based on titles and abstract, studies were excluded if they were duplicates, reviews, comments, letters, case reports (<5 patients), studies not concerning prostatic hyperplasia, animal studies, conference abstracts, and nonhuman studies. All other studies were considered as potentially relevant and full texts were retrieved. Inclusion and exclusion criteria were checked by two independent reviewers (S.M.S. and A.E.S.), and a third reviewer was consulted (S.B.) in case of disagreement. Studies were included if they contained information about more than five cases of PAE in patients with BPH and if one or more of the following clinical outcomes were evaluated: PV, PSA, Qmax, PVR, IPSS, QOL, and IIEF.

Data Extraction

Data extraction was performed in a standardized manner by using a data extraction form. Two authors (S.M.S. and A.E.S.) extracted the data independently from the included studies. A third reviewer performed the consensus (S.B.).

Study Design Characteristics

The following data on study design characteristics were extracted: (1) Study type (cohort, RCT or other); (2) Data collection (prospective, retrospective, or other); (3) Study design (multicenter/single center); (4) Institutions involved (academic, non-academic); (5) Departments involved (radiology, urology); (6) Period of recruitment; (7) METC approval; and (8) Funding and potential role of funders in study.

Patient Characteristics

The following data on patient characteristics were extracted: (1) Patient population inclusion (consecutive or non-consecutive); (2) Inclusion and exclusion criteria; (3) Number of patients included; (4) Number of patients analysed; (5) Age of patients; (6) Medication at baseline. Based on all items mentioned above, we defined whether the spectrum of patients was representative for the patients who would receive the embolization in practice.

Embolization Procedure

The following data on the embolization procedures were assessed: (1) Performing physician; (2) Unilateral or bilateral; (3) Embolization material; (4) Procedure time total; (5) Procedure time fluoroscopy, (6) Previous treatment other than medication; (7) Drop outs reported. Based on items 1–5, we defined whether the procedure was described in sufficient detail to permit its replication.

Risk of Bias (Quality Assessment)

For the risk of bias (quality assessment), several items of the study design characteristics, patient population, and embolization procedure were used based on the QUADAS2 tool [13]: study design characteristics: (1) study type (cohort, RCT or other); (2) data collection (prospective, retrospective, or other); (3) study design (multicenter/

single-center); (4) METC approval (yes, no, or unclear); and (5) funding and potential role of funders in study (yes, no, or unclear).

Patient characteristics: (1) patient population inclusion (consecutive or nonconsecutive); (2) inclusion and exclusion criteria; (3) whether the spectrum of patients was representative for the patients who would receive the embolization in practice (yes or no).

Embolization procedure: (1) dropouts in study (yes, no, or unclear); and (2) whether the procedure was described in sufficient detail to permit its replication (yes or no).

Sample size: we checked whether sample size calculation was performed (yes or no).

Quality was judged based as follows: study type (0 = cohort or other vs. 1 = RCT), data collection (0 = retrospective or other vs. 1 = prospective), design (0 = single-center vs. 1 = multicenter), METC approval (0 = no or unclear vs. 1 = yes), funding or conflict of interest (0 = yes or unclear vs. 1 = no), inclusion/exclusion criteria defined (0 = no vs. 1 = yes), patients spectrum generalizable (0 = no vs. 1 = yes), dropouts in study (0 = yes or unclear vs. 1 = no), procedure description sufficient (0 = no vs. 1 = yes) and sample size calculation (0 = no vs. 1 = yes). Finally, all points were summed to reach a quality assessment. More than eight points was considered good quality.

Baseline and Follow-Up and Data Extraction on Outcomes

Baseline and follow-up (time, number of patients, dropout description) were recorded, and the following data on outcomes were extracted per given follow-up: (1) Quantitative clinical outcomes (PV, PSA, Qmax, PVR, others): (2) Qualitative clinical outcomes (IPSS, QOL, IIEF, Others); (3) Complications related to the procedure; (4) Other outcomes related to the procedure (technical success, clinical failures, hospitalization, others). All outcomes were continuous data.

The baseline data were presented as means and standard deviation, because these were always reported in the published studies. For the follow-up, we also aimed to present the means and standard deviations; however, these were not always reported.

Data-Analysis

For the comparison of follow-up with the baseline, we present means. If means were not presented, we calculated means first by using the available mean changes (decrease or increase) or second by using the available % change (decrease or increase). Because standard deviation was not available in all datasets, we were not able to pool the results for a meta-analysis approach. Therefore, we calculated pooled weighted mean, taking into account the number of patients and the mean per study to present an overview of the results at baseline and follow-up.

Results

Search Strategy and Study Selection

The search yielded 562 studies: 170 in Medline and 392 in Embase. After removing studies not concerning BPH or studies evaluating animals (415), conference papers/letters/comments (51), duplicates (41), reviews/case reports (44), and one article of which the full article was not found, ten studies were selected for full-text review, checking on inclusion and exclusion criteria (Supplement 1). After checking the inclusion and exclusion criteria, one study was excluded based on Chinese language. All data were extracted from the nine studies eligible for the systematic review (Supplement 1) [14–22]. These nine studies were all published by three research groups, with probably an overlap of patients. However, there was no complete duplication of patients (based on inclusion/exclusion criteria, inclusion period, patients' characteristics), and each study showed differences in outcomes; therefore, all studies were included in this review.

Study Design Characteristics

All studies were performed between June 2008 and March 2013. Of the nine studies, eight were cohort studies [14–17, 19–22]. Only one study, comparing two different sizes of PVA particles, was a randomized, controlled trial [18]. All studies were initiated by a department of radiology, and the majority was supported by a department of urology. There was a variation in prospective and retrospective data collection. In Table 1, all study design characteristics are described.

Funding

No conflict of interest was stated in four studies [15, 16, 21, 22]. Potential conflict of interest was unclear in four studies [14, 17, 18, 20]. In one study, the authors stated a potential conflict of interest (Cook Medical; speaker/honoraria; consultant/advisory board) [19].

Patient Population Characteristics

In total, 706 patients were included. The mean age ranged from 63.4–74.1 years (mean of means is 68.1 years). As stated before, there is probably an overlap in patients. All included patients were diagnosed with BPH and moderate-

Table 1 Study design characteristics

Study	Study type	Data collection	Design[a]	Authors from involved institutions	Departments[b]	Recruitment period	Informed consent
Pisco [14]	Cohort	Prospective	Multicenter	Academic and nonacademic	Radiology and urology	March 2009–April 2010	Yes
Pisco [15]	Cohort	Prospective	Multicenter*	Academic and nonacademic	Radiology and urology	March 2009–April 2012	Yes
Pisco [16]	Cohort	Prospective	Multicenter	Academic and nonacademic	Radiology and urology	March 2009–April 2011	Yes
Rio Tinto [17]	Cohort	Retrospective	Multicenter	Academic and nonacademic	Radiology and urology	March 2009–June 2011	Unclear
Bilhim [18]	RCT (comparing different PVA particle size)	Prospective	Single center	Academic	Radiology and urology	May 2011–December 2011	Yes
Bilhim [19]	Cohort (comparing unilateral vs bilateral embolization)	Ambispective[c]	Multicenter*	Academic and nonacademic	Radiology and urology	March 2009–December 2011	Yes
Carnevale [20]	Cohort	Prospective	Single center	Academic	Radiology and urology	June 2008–November 2011	Yes
Antunes [21]	Cohort	Prospective	Single center	Academic	Radiology and urology	June 2008–November 2011	Yes
Bagla [22]	Cohort	Prospective	Single center	Nonacademic	Radiology	January 2012–March 2013	Yes

[a] Design: authors from more than one center involved in study were considered multicenter

[b] Departments: radiology and/or urology. Other departments were not assessed

[c] Both prospective and retrospective component

* We considered these studies as multicenter, although the text states single-center

to-severe LUTS. Malignancy was an exclusion criterion in all studies. Table 2 provides detailed information on patient population.

Embolization Procedure Description

In two studies [18, 22], the authors explicitly stated that the embolization procedure was performed by an interventional radiologist. However, we presume that interventional radiologists also performed the procedure in the other studies. The embolization procedure was performed using 90–180 or 180–300 μm nonspherical polyvinyl alcohol (PVA) particles [14–19], 300–500 μm microspheres [20, 21], or 100–400 μm spherical embolic agents [22]. Mean total procedure time varied from 70.4 to 96.3 min (mean of the means 80.1 min), and the mean fluoroscopy time varied from 18 to 85.9 min (mean of the means 36.5 min). Most studies had the intention to perform the embolization bilaterally; however, in some cases only unilateral embolization was performed due to atherosclerosis. One cohort study compared bilateral versus unilateral embolization [19]. In total, 564 patients underwent a bilateral embolization, 91 a unilateral embolization, and for 22 patients it was unclear if one or both sides were treated [20, 21]. In 13 patients, embolization could not be performed due to tortuosity of vessels. In Table 3, an overview of the embolization procedures are described.

Risk of Bias (Quality Assessment)

Only one study fulfilled our criteria of quality assessment (16). All other studies, including the RCT (18), were rated below 8 points, mainly due to the type of study (mostly cohort, $n = 8$), unclear inclusion of patients ($n = 6$), unclear or conflict of interest ($n = 5$), dropouts ($n = 8$), and missing sample size calculation ($n = 9$). Details are given in Table 4.

Follow-up and Data Presentation

Follow-up Intentional follow-up varied between 6 and 24 months. All patients had at least 1 month of follow-up. Detailed data of the number of patients at various times of follow-up is presented in the tables with outcomes.

Quantitative clinical data All data for PV, PSA, Qmax, PVR are presented in Tables 5, 6, 7, 8.

Table 2 Patient population

Study	Consecutive patients	Inclusion criteria	Exclusion criteria	Number of patients included for PAE	Number of patients for analysis (technical success)	Age of patients (mean +SD, median, range)	Medication at baseline	Patients spectrum generalizable
Pisco [14]	Unclear	≥60 years Diagnosis of BPH Moderate-severe LUTS (IPSS > 18) Refractory to medical treatment ≥6 months Sexual dysfunction (or accepting risk) And/or Qmax < 12 ml/s And/or acute urinary retention	Malignancy Advanced atherosclerosis/ tortuosity of iliac arteries	$n = 15$	$n = 14$ (technical failure)	74.1 (62–82)	Yes Stopped 1 week before PAE, after PAE all prostatic medication was abandoned	Yes
Pisco [15]	Unclear	≥45 years and diagnosis of BPH Moderate–severe LUTS and/or QOL ≥ 3 Refractory to medical treatment ≥6 months and/or Qmax < 12 ml/s or acute urinary retention and PV > 40 with sexual dysfunction or accepting the risk of developing sexual dysfunction after treatment Detrusor failure	Malignancy Advanced atherosclerosis or tortuosity of the iliac arteries Secondary renal insufficiency Bladder diverticula or stones Neurogenic bladder	$n = 255$ (for PAE)	$n = 250$	65.5 ± 7.4 (45–85)	Yes	Yes
Pisco [16]	Yes	≥50 years Diagnosis of BPH Moderate-severe LUTS Refractory to medical treatment ≥6 months IPSS > 18 and/or QOL ≥ 3 And/or Qmax < 12 ml/s And/or acute urinary retention. >40 g prostate Sexual dysfunction (or accepting risk)	Malignancy Advanced atherosclerosis or tortuosity of iliac arteries	$n = 89$ included for PAE	$n = 86$	74.1 (52–85)	Yes Stopped 1 week before PAE, restarted after PAE	Yes

Table 2 continued

Study	Consecutive patients	Inclusion criteria	Exclusion criteria	Number of patients included for PAE	Number of patients for analysis (technical success)	Age of patients (mean +SD, median, range)	Medication at baseline	Patients spectrum generalizable
Rio Tinto [17]	Unclear	≥50 years Symptomatic BPH Refractory to medical treatment ≥6 months IPSS > 18 and/or QOL ≥ 3 And/or Qmax < 12 ml/s And/or acute urinary retention Baseline PV > 40 with sexual dysfunction or accepting the risk of developing sexual dysfunction after treatment.	Malignancy Advanced atherosclerosis or tortuosity of the aortic bifurcation or iliac arteries Detrusor failure Neurogenic bladder Urethral stenosis Bladder diverticula or stones	$n = 103$	$n = 100$	66.8 (50–85)	Yes	Yes
Bilhim [18]	Yes	≥40 years BPH with refractory to medical treatment ≥6 months or acute urinary retention PV ≥ 30 cm^3 IPSS > 18 and/or QOL > 3	<40 years Prostate or bladder Malignancy PV < 30 cm^3 IPSS ≤ 18 and QOL ≤ 3 Bladder diverticula >5 cm or stones >2 cm Chronic renal failure Active urinary tract infection Extensive atherosclerosis	Total: $n = 80$ Group A: $n = 40$ 90–180 μm Group B: $n = 40$ 180–300 μm	Total: $n = 64$ (loss to FU 16, not due to technical failure) Group A: $n = 34$ Group B: $n = 30$	Group A: 64.4 ± 6.9 Group B: 63.4 ± 6.8	Yes Stopped 1 week before PAE	Yes

Table 2 continued

Study	Consecutive patients	Inclusion criteria	Exclusion criteria	Number of patients included for PAE	Number of patients for analysis (technical success)	Age of patients (mean +SD, median, range)	Medication at baseline	Patients spectrum generalizable
Bilhim [19]	Yes	≥40 years PV > 30 cc PE/BPH with moderate-to-severe LUTS (IPSS > 18 and/or QOL > 3) Refractory to medical treatment ≥6 months or acute urinary retention.	Malignancy Bladder diverticula >5 cm or stones >2 cm Chronic renal failure Tortuosity and advanced atherosclerosis of iliac and/or prostatic arteries Active urinary tract infection Unregulated coagulation parameters	Total: $n = 122$ Group A: $n = 103$ Group B: $n = 19$	$n = 122$	Total: 66.7 ± 7.2 Group A: 65.8 ± 6.9 Group B: 71.3 ± 1.7	Yes α blockers, stopped 1 week before PAE	Yes
Carnevale [20]	Unclear	CAD caused by BPH No effect medication	Malignancy Any other cause of voiding dysfunction	$n = 11$ patients $n = 12$ procedures	$n = 10$ (1 lost to FU)	68.5 ± 5.2 (59–78)	Yes α-blockers, Stopped 1 month before PAE	No (only patients with CAD).
Antunes [21]	Unclear	≥50 years Acute urinary retention due to BPH Refractory to medical treatment ≥30 days PV 30–90 g Infravesical obstruction	Prostate Malignancy Hypocontractile bladder Neurogenic bladder Renal failure	$n = 11$	$n = 10$ (1 loss to FU)	68.5 ± 5.2 (59–78)	Yes α blockers, stopped directly after PAE	No (Only acute urinary retention)
Bagla [22]	Unclear	>50 years LUTS secondary to BOO from BPH AUA symptom score ≥8 Ability to give informed consent	Bleeding diathesis Renal insufficiency Neurologic disease that is believed to affect bladder or neurogenic bladder Known prostate cancer Active bladder cancer PSA > 4 (unless biopsy negative or declined) Acute urinary retention	$n = 20$	$n = 19$ (1 FU)	66.5 (57–81)	Unclear	Yes

Table 3 Details on embolization procedure

Study	Performing physician	Unilateral or bilateral	Embolization material	Procedure time total	Procedure time fluoroscopy	Previous treatment other than medication	Dropouts reported	Procedure description sufficient
Pisco [14]	Probably Interventional Radiology	Bilateral (13 bilateral, 1 unilateral)	200 µm nonspherical PVA particles	25–135 min (mean 85 min)	15–45 min (mean 35)	None	Yes: 1 patient with atherosclerosis	Yes
Pisco [15]	Probably interventional radiology	205 bilateral (82 %) 45 unilateral (18 %)	100 or 200 µm PVA particles	20–185 min (mean 73 min)	7–64 min (mean 18 min)	8 patients with TURP	Yes: 5 patients tortuosity of vessels / atherosclerosis (technical failure)	Yes
Pisco [16]	Probably interventional radiology	79 bilateral 7 unilateral	180–300 ($n = 14$) or 80–180 ($n = 74$) nonspherical PVA particles	20–185 min (mean 86 min)	7–63 min (mean 27 min)	1 patient with 2 TURPs and prostatectomy 3 patients with TURP	Yes: 3 patients with tortuosity of vessels (technical failure)	Yes
Rio Tinto [17]	Probably interventional radiology	93 bilateral 7 unilateral	100 or 200 µm PVA particles	25–185 min (mean 83 min)	7–63 min (mean 24 min)	3 patients with prostatic resection	Yes: 3 patients with tortuosity vessels / atherosclerosis (technical failure)	No
Bilhim [18]	Interventional radiologist	Group A: 28 bilateral 6 unilateral Group B: 25 bilateral 5 unilateral	Group A: 80–180 µm PVA particles Group B: 180–300 µm PVA particles	Group A: 79.3 ± 42.3 ($n = 40$) Group B: 70.4 ± 26.0 ($n = 40$)	Group A: 23.4 ± 17.2 ($n = 40$) Group B: 20.0 ± 10.9 ($n = 40$)	NA	Yes: 16 patients loss to FU	Yes
Bilhim [19]	Probably interventional radiology	Group A: 103 bilateral Group B: 19 unilateral	100 and 200 µm nonspherical PVA particles	83.7 (26–182) Group A: 67.3 ± 30.9 Group B: 96.3 ± 26.4	27.8 (8–61) Group A: 18.1 ± 12.9 Group B: 34.0 ± 10.3	4 patients with TURP	Yes: all included	Yes
Carnevale [20]	Probably interventional radiology	Unclear	300–500 µm microspheres	197.5 ± 84.5	85.9 ± 49.3	None	Yes: 1 patient loss to follow-up	Yes
Antunes [21]	Probably interventional radiology	Unclear	300–500 µm microspheres	197.5 ± 84.5	85.9 ± 49.3	None	Yes: 1 patient loss to follow-up	Yes
Bagla [22]	Interventional Radiology	Bilateral approach (18 bilateral, 1 unilateral)	100–400 µm spherical embolic agents	72 min (range 41–177)	30.2 min (range 11.5–63.9)	None	Yes: 1 patient with atherosclerosis	Yes

Table 4 Risk of bias

Study	Study type	Data collection	Design[a]	Informed consent	Consecutive patients	Funding (conflict of interest)	Inclusion criteria/ exclusion criteria	Patients spectrum generalizable	Dropouts in study	Procedure description sufficient	Sample size	Quality
Pisco [14]	Cohort	Prospective	Multicenter	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	No	6
Pisco [15]	Cohort	Prospective	Multicenter*	Yes	Unclear	No	Yes	Yes	Yes	Yes	No	7
Pisco [16]	Cohort	Prospective	Multicenter	Yes	Yes	No	Yes	Yes	Yes	Yes	No	8
Rio Tinto [17]	Cohort	Retrospective	Multicenter	Unclear	Unclear	Unclear	Yes	Yes	Yes	No	No	3
Bilhim [18]	RCT	Prospective	Single center	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	7
Bilhim [19]	Cohort	Ambispective[b]	Multicenter*	Yes	Yes	Yes	Yes	Yes	No	Yes	No	7
Carnevale [20]	Cohort	Prospective	Single center	Yes	Unclear	Unclear	Yes	No	Yes	Yes	No	4
Antunes [21]	Cohort	Prospective	Single center	Yes	Unclear	No	Yes	No	Yes	Yes	No	4
Bagla [22]	Cohort	Prospective	Single center	Yes	Unclear	No	Yes	Yes	Yes	Yes	No	5

Quality was judged based as follows: study type (0 = cohort or other vs. 1 = RCT), data collection (0 = retrospective or other vs. 1 = prospective), design (0 = single center vs. 1 = multicenter, METC approval (0 = no or unclear vs. 1 = yes), funding or conflict of interest (0 = yes or unclear vs. 1 = no), inclusion/exclusion criteria defined: (0 = no vs. 1 = yes), patients spectrum generalizable (0 = no vs. 1 = yes), dropouts in study (0 = yes or unclear vs. 1 = no), procedure description sufficient (0 = no vs. 1 = yes), sample size calculation (0 = no vs. 1 = yes)

* We considered these studies as multicenter, although the text states single center

[a] Design: authors from more than one center involved in study were considered multicenter

[b] Both prospective and retrospective component

Table 5 PV by either rectal examination or transrectal ultrasound (US) or magnetic resonance imaging (MRI)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* value
Pisco [14]	$n = 9$*		$n = 9$*						$P = 0.008$: Last FU compared with baseline
PV by MRI	Mean: 104.9 ml		Mean: 76.0 ml						
Pisco [14]	$n = 14$		$n = 14$						$P = 0.0001$: Last FU compared with baseline
PV by US	Mean: 97.4 ml		Mean: 70.9 ml						
Pisco [14]	*Calculated mean: 100.3 ml*		*Calculated mean: 72.9 ml*						
mean MRI and US									
Pisco [15]	$n = 283$	$n = 183$	$n = 147$	$n = 111$	$n = 63$	$n = 29$	$n = 14$	$n = 4$	$P < 0.0001$: Changes over time
	Mean: 83.5 ml	Mean: 66.8 ml	Mean: 68.3 ml	Mean: 66.6 ml	Mean: 69.9 ml	Mean: 72.0 ml	Mean: 90.9 ml	Mean: 72.0 ml	
Pisco [16]	$n = 86$	$n = 81$	$n = 69$	$n = 55$	$n = 29$	$n = 13$	$n = 7$		$P < 0.0001$: Changes over time
	Mean: 85.3 ml	*Calculated mean: 67.7 ml*	*Calculated mean: 64.8 ml*	*Calculated mean: 63.9 ml*	*Calculated mean: 66.1 ml*	*Calculated mean: 69.6 ml*	*Calculated mean: 75.9 ml*		
Rio Tinto [17]	$n = 100$	$n = 100$	$n = 83$	$n = 62$	$n = 29$	$n = 13$	$n = 6$		
	Mean: 88.0 ml	Mean: 68.7 ml	Mean: 67.0 ml	Mean: 67.8 ml	Mean: 68.0 ml	Mean: 72.5 ml	Mean: 76.0 ml		
Bilhim [18]	Group A: $n = 40$			Group A: $n = 34$					$P = 0.5$: Comparison groups at baseline
Comparing 2 particles	(80–180 μm PVA)			*Calculated mean: 67.0 cm^3*					$P = 0.127$: Comparison changes between groups
	Mean: 78.6 cm^3								
	Group B: $n = 40$			Group B: $n = 30$					
	(180–300 μm PVA)			*Calculated mean: 80.0 cm^3*					
	Mean: 83.6 cm^3								
Bilhim [19]	Group A: $n = 103$ (bilateral)	Group A: $n = 103$							$P = 0.38$: Comparison groups as baseline.
Comparing bilateral vs. unilateral embolization	Mean: 84.1 ml	*Calculated mean: 64.7 ml*							$P = 0.21$: Comparison changes between groups.
	Group B: $n = 19$ (unilateral)	Group B: $n = 19$							$P < 0.0001$: Last FU compared with baseline.
	Mean: 75.8 ml	*Calculated mean: 64.3 ml*							
Carnevale [20]	$n = 10$	$n = 10$	$n = 10$	$n = 10$	$n = 10$				$P = 0.002$: 12 months FU compared with baseline
PV by MRI	Mean: 69.7 g	Mean: 51.5 g	Mean: 48.2 g	Mean: 45.1 g	Mean: 46.3 g				

Table 5 continued

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* value
Carnevale [20]	$n = 10$	$n = 10$	$n = 10$	$n = 10$	$n = 10$				$P = 0.004$: 12 months FU compared with baseline
PV by US	Mean: 62.0 g	Mean: 44.4 g	Mean: 39.4 g	Mean: 39.4 g	Mean: 40.8 g				
Carnavale [20] mean MRI and US	*Calculated mean: 65.9 g*	*Calculated mean: 48.0 g*	*Calculated mean: 43.8 g*	*Calculated mean: 42.3 g*	*Calculated mean: 43.6 g*				
Antunes [21]	$n = 11$		$n = 10$						
PV by MRI	Mean: 69.7 g		*Calculated mean: 49.0 g*						
Antunes [21]	$n = 11$		$n = 10$						
PV by US	Mean: 62.0 g		*Calculated mean: 40.7 g*						
Antunes [21] mean MRI and US	*Calculated mean: 65.9 g*		*Calculated mean: 44.9 g*						
Bagla [22]	$n = 5$* Mean: 56.7 ml			$n = 5$ *Calculated mean: 48.0 ml*					
Pooled weighted mean	83.6 ml	66.4 ml	65.6 ml	66.3 ml	65.7 ml	71.6 ml	83.7 ml	72.0 ml	

Calculated mean indicates that these were calculated based on the data given in studies

* No comparison with complete cohort was available

Table 6 Prostate-specific antigen (PSA)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* value
Pisco [14]	$n = 14$ Mean: 8.76 ng/ml		$n = 14$ Mean: 6.49 ng/ml						$P = 0.072$: Last FU compared with baseline
Pisco [15]	$n = 238$ Mean: 5.68 ng/ml	$n = 195$ Mean: 4.23 ng/ml	$n = 150$ Mean: 3.64 ng/ml	$n = 111$ Mean: 4.30 ng/ml	$n = 62$ Mean: 5.08 ng/ml	$n = 28$ Mean: 6.08 ng/ml	$n = 13$ Mean: 6.10 ng/ml	$n = 3$ Mean: 7.41 ng/ml	$P < 0.0001$: Changes over time
Pisco [16]	$n = 86$ Mean: 6.37 µg/L	$n = 78$ *Calculated mean: 4.51 µg/L*	$n = 69$ *Calculated mean: 3.91 µg/L*	$n = 53$ *Calculated mean: 4.33 µg/L*	$n = 28$ *Calculated mean: 4.66 µg/L*	$n = 12$ *Calculated mean: 4.75 µg/L*	$n = 4$ *Calculated mean: 5.08 µg/L*		$P < 0.0001$: Changes over time
RioTinto [17]	$n = 100$ Mean: 6.4 ng/ml	$n = 100$ Mean: 4.52 ng/ml	$n = 83$ Mean: 4.04 ng/ml	$n = 62$ Mean: 4.71 ng/ml	$n = 29$ Mean: 5.24 ng/ml	$n = 13$ Mean: 5.53 ng/ml	$n = 6$ Mean: 6.24 ng/ml		
Bilhim [18] *Comparing 2 particles*	Group A: $n = 40$ (80–180 µm PVA) Mean: 5.62 ng/ml			Group A: $n = 34$ *Calculated mean: 3.28 ng/ml*					$P = 0.47$: Comparison groups at baseline $P = 0.001$: Comparison changes between groups
	Group B: $n = 40$ (180–300 µm PVA) Mean: 8.37 ng/ml			Group B: $n = 30$ *Calculated mean: 8.12 ng/ml*					
Bilhim [19] *Comparing bilateral vs unilateral embolization*	Group A: $n = 103$ (Bilateral) Mean: 5.6 ng/ml	Group A: $n = 103$ *Calculated mean: 3.9 ng/ml*							$P = 0.22$: Comparison groups at baseline $P = 0.33$: Comparison changes between groups $P < 0.0001$: Last FU compared with baseline
	Group B: $n = 19$ (Unilateral) Mean: 7.5 ng/ml	Group B: $n = 19$ *Calculated mean: 5.5 ng/ml*							

Table 6 continued

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* value
Carnevale [20]	$n = 10$	$n = 10$	$n = 10$	$n = 10$	$n = 10$				$P = 0.003$: 12-month FU compared with baseline
	Mean: 10.1 ng/ml	Mean: 3.5 ng/ml	Mean: 3.7 ng/ml	Mean: 3.5 ng/ml	Mean: 4.3 ng/ml				
Antunes [21]	$n = 10$	$n = 10$	$n = 10$	$n = 10$	$n = 10$				$P = 0.003$: Compared with baseline
	Mean: 10.1 ng/ml	Mean: 3.5 ng/ml	Mean: 3.7 ng/ml	Mean: 3.5 ng/ml	Mean: 4.3 ng/ml				
Pooled weighted mean	6.28 ng/ml	4.28 ng/ml	3.98 ng/ml	4.53 ng/ml	4.56 ng/ml	5.64 ng/ml	5.96 ng/ml	7.41 ng/ml	

Calculated mean indicates that these were calculated based on the data given in studies

PV The pooled weighted mean PV at baseline was 83.6 ml (range of the means 56.7–104.9). In the first month after embolization, PV decreased to a pooled weighted mean of 66.4 ml (range of the means 44.4–68.7). This decrease persisted up to 12 months after treatment. At further follow-up, PV showed an increase to a pooled weighted mean of 83.7 ml (range of the means 75.9–90.9) at 24 months in 27 patients and 72.0 ml at 30 months in 4 patients. There was no significant effect on PV in patients who underwent unilateral versus bilateral embolization, nor in patients who underwent embolization with 90–180 or 180–300 μm PVA particles [18, 19].

PSA The pooled weighted mean PSA at baseline was 6.28 ng/ml (range of the means 5.6–10.1). The first 3 months after treatment, PSA decreased to a pooled weighted mean of 3.98 ng/ml (range of the means 3.7–6.49). After 6 months follow-up, PSA started to increase to a pooled weighted mean of 5.96 ng/ml (range of the means 5.08–6.24) at 24 months and 7.41 ng/ml at 30 months. A significant greater reduction of PSA was seen in PAE with 90–180 μm PVA particles compared with PAE with 180–300 μm PVA particles ($P = 0.001$) [18]. Unilateral versus bilateral treatment showed no significant differences [19].

Qmax The pooled weighted mean Qmax at baseline was 8.69 ml/s (range of the means 4.2–9.94). The Qmax increased mainly in the first month after PAE to a pooled weighted mean of 12.00 ml/s (range of the means 11.6–13). This increase persisted up to 18 months, whereas at 30 months the Qmax decreased to 10.80 ml/s in two patients. There was no significant effect on Qmax in patients who underwent unilateral versus bilateral embolization, nor in patients who underwent embolization with 90–180 or 180–300 μm PVA particles [18, 19].

PVR The pooled weighted mean PVR at baseline was 103.15 ml (range of the means 93.9–160.5). After embolization, the residual decreased mainly in the first month to a pooled weighted mean of 66.56 ml (range of the means 61–72.3). The PVR decreased further to 57.88 ml at 12 months (range of the means 51.7–60.6). After 18 months follow-up, PVR started to increase to 88.0 ml (ranges of the means 74–93.54) at 24 months and 95.3 ml at 30 months in three patients. There was no significant effect on PVR in patients who underwent unilateral versus bilateral embolization, nor in patients who underwent embolization with 90–180 or 180–300 μm PVA particles [18, 19].

Qualitative clinical data All data on the IPSS, QOL, and international index of erectile dysfunction (IIEF) are presented in Tables 9, 10, 11.

IPSS The pooled weighted mean IPSS score at baseline was 23.31 (range of the means 21–24.7). After PAE, the IPSS decreased mainly in the first month to a score of 11.92

Table 7 Peak urinary flow (Qmax)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	P value
Pisco [14]	$n = 8$*		$n = 8$*						$P = 0.015$: Last FU compared to baseline
	Mean: 7.06 ml/s		Mean: 10.91 ml/s						
Pisco [15]	$n = 208$	$n = 185$	$n = 146$	$n = 105$	$n = 60$	$n = 25$	$n = 12$	$n = 2$	$P < 0.0001$: Changes over time
	Mean: 9.2 ml/s	Mean: 11.9 ml/s	Mean: 12.4 ml/s	Mean: 12.0 ml/s	Mean: 12.8 ml/s	Mean: 13.0 ml/s	Mean: 13.9 ml/s	Mean: 10.8 ml/s	
Pisco [16]	$n = 86$	$n = 79$	$n = 69$	$n = 49$	$n = 24$	$n = 11$	$n = 3$		$P < 0.0001$: Changes over time
	Mean: 8.68 ml/s	*Calculated mean:*	*Calculated mean:*	*Calculated mean:*	*Calculated mean:*	*Calculated mean:*	*Calculated mean:*		
		11.99 ml/s	*12.79 ml/s*	*12.71 ml/s*	*12.77 ml/s*	*11.81 ml/s*	*12.40 ml/s*		
Rio Tinto [17]	$n = 100$	$n = 100$	$n = 83$	$n = 62$	$n = 29$	$n = 13$	$n = 6$		
	Mean: 8.7 ml/s	Mean: 11.6 ml/s	Mean: 12.68 ml/s	Mean: 12.63 ml/s	Mean: 12.9 ml/s	Mean: 13.73 ml/s	Mean: 14.42 ml/s		
Bilhim [18]	Group A: $n = 40$			Group A: $n = 34$					$P = 0.07$: Comparison groups at baseline
Comparing 2 particles	(80–180 µm PVA)								
	Mean: 7.91 ml/s			*Calculated mean:*					$P = 0.904$: Comparison changes between groups
				10.27 ml/s					
	Group B: $n = 40$			Group B: $n = 30$					
	(180–300 µm PVA)								
	Mean: 9.94 ml/s			*Calculated mean:*					
				11.58 ml/s					
Bilhim [19] *Comparing bilateral vs unilateral embolization*	Group A: $n = 103$	Group A: $n = 103$							$P = 0.9$: Comparison groups at baseline
	Mean ± SD:	*Calculated mean: 12.4 ml/s*							
	8.5 ml/s ± 4.2								$P = 0.66$: Comparison changes between groups
	Group B: $n = 19$	Group B: $n = 19$							
	Mean: 8.4 ml/s	*Calculated mean: 13.0 ml/s*							$P < 0.0001$: Last FU compared with baseline
Carnevale [20]	$n = 10$ (→ difficult to measure)				$n = 10$				$P = 0.009$: 12 months FU compared to baseline
	Mean: 4.2 ml/s				Mean: 10.8 ml/s				
Antunes [21]	$n = 10$				$n = 10$				$P = 0.009$: Compared with baseline
	Mean: 4.2 ml/s				Mean: 10.8 ml/s				
Pooled weighted mean	8.69 ml/s	12.0 ml/s	12.52 ml/s	12.13 ml/s	12.51 ml/s	12.93 ml/s	13.83 ml/s	10.8 ml/s	

Calculated means indicates that these were calculated based on the data given in studies

* No comparison with complete cohort was available

Table 8 Post void residual (PVR)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* values
Pisco [14]	$n = 8$*		$n = 8$*						$P = 0.0004$: Last FU compared with baseline
	Mean: 130.8 ml		Mean: 51.3 ml						
Pisco [15]	$n = 210$	$n = 175$	$n = 134$	$n = 99$	$n = 58$	$n = 23$	$n = 13$	$n = 3$	$P < 0.0001$: Change s over time
	Mean: 102.9 ml	Mean: 65.6 ml	Mean: 59.2 ml	Mean: 62.8 ml	Mean: 51.7 ml	Mean: 75.4 ml	Mean: 91.9 ml	Mean: 95.3 ml	
Pisco [16]	$n = 86$	$n = 76$	$n = 60$	$n = 48$	$n = 22$	$n = 12$	$n = 6$		$P = 0.002$: Changes over time
	Mean: 102.2 ml	*Calculated mean: 72.3 ml*	*Calculated mean: 62.5 ml*	*Calculated mean: 62.5 ml*	*Calculated mean: 60.6 ml*	*Calculated mean: 70.6 ml*	*Calculated mean: 74.0 ml*		
Rio Tinto [17]	$n = 100$	$n = 100$	$n = 83$	$n = 62$	$n = 29$	$n = 13$	$n = 6$		
	Mean: 104.9 ml	Mean: 70.38 ml	Mean: 60.85 ml	Mean: 61.1 ml	Mean: 53.38 ml	Mean: 77.5 ml	Mean: 93.54 ml		
Bilhim [18]	Group A: $n = 40$			Group A: $n = 34$					$P = 0.83$: Comparison groups at baseline
Comparing 2 particles	(80–180 µm PVA)			*Calculated mean: 55.9 ml*					$P = 0.752$: Comparison changes between groups
	Mean: 103.8 ml								
	Group B: $n = 40$			Group B: $n = 30$					
	(180–300 µm PVA)			*Calculated mean: 59.1 ml*					
	Mean: 99.3 ml								
Bilhim [19]	Group A: $n = 103$	Group A: $n = 103$							$P = 0.37$: Comparison groups at baseline
Comparing bilateral vs unilateral embolization	(bilateral)	*Calculated mean: 61.0 ml*							$P = 0.9$: Comparison changes between groups
	Mean: 93.9 ml								
	Group B: $n = 19$	Group B: $n = 19$							$P = 0.002$: Last FU compared with baseline
	(unilateral)	*Calculated mean: 62.4 ml*							
	Mean: 116.2 ml								
Carnevale [20]	$n = 10$				$n = 10$				$P = 0.04$: 12 months FU compared with baseline
	Mean: 160.5 ml				Mean: 60.0 ml				
Pooled weighted mean	103.15 ml	66.56 ml	60.47 ml	60.94 ml	57.88 ml	74.77 ml	88.0 ml	95.3 ml	

Calculated means indicates that these were calculated based on the data given in studies

* No comparison with complete cohort was available

Table 9 International prostate symptom score (IPSS)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	Eighth FU 36 months	*P* value
Pisco [14]	$n = 8$*		$n = 8$*							$P = 0.005$: Compared with baseline
	Mean: 21.0		Mean: 14.5							
Pisco [15]	$n = 238$	$n = 236$	$n = 224$	$n = 167$	$n = 101$	$n = 58$	$n = 25$	$n = 14$	$n = 9$	$P < 0.0001$: Changes over time
	Mean: 24.0	Mean: 12.2	Mean: 11.0	Mean: 11.5	Mean: 10.4	Mean: 10.1	Mean: 9.0	Mean: 8.1	Mean: 9.1	
Pisco [16]	$n = 86$	$n = 79$	$n = 70$	$n = 50$	$n = 28$	$n = 12$	$n = 4$			$P < 0.0001$: Changes over time
	Mean: 23.0	*Calculated mean: 12.6*	*Calculated mean: 11.0*	*Calculated mean: 10.8*	*Calculated mean: 9.9*	*Calculated mean: 10.9*	*Calculated mean: 10.1*			
Rio Tinto [17]	$n = 100$	$n = 100$	$n = 83$	$n = 62$	$n = 29$	$n = 13$	$n = 6$			
	Mean: 22.8	Mean: 11.73	Mean: 10.29	Mean: 10.85	Mean: 11.22	Mean: 10.3	Mean: 9.3			
Bilhim [18]	Group A: $n = 40$			Group A: $n = 34$						$P = 0.96$: Comparison groups at baseline
Comparing 2 particles	(80–180 µm PVA)			*Calculated mean: 15.7*						$P = 0.052$: Comparison changes between groups
	Mean: 22.8									
	Group B: $n = 40$			Group B: $n = 30$						
	(180–300 µm PVA)			*Calculated mean: 11.9*						
	Mean: 22.7									
Bilhim [19]	Group A: $n = 103$	Group A: N = 103								$P = 0.54$: Comparison groups at baseline
Comparing bilateral vs unilateral embolization	(bilateral)	*Calculated mean: 11.3*								$P = 0.29$: Comparison changes between groups
	Mean: 23.1									$P < 0.0001$: Last FU compared with baseline
	Group B: $n = 19$	Group B: N = 19								
	(unilateral)	*Calculated mean: 13.0*								
	Mean: 21.9									
Carnevale [20]	Not stated	$n = 10$	$n = 10$	$n = 10$	$n = 10$					$P = 0.04$: Compared with baseline
		Mean: 7.1	Mean: 2.7	Mean: 2.2	Mean: 2.8					
Antunes [21]	Not applicable (catheter in situ)	$n = 10$			$n = 10$					$P = 0.04$: Compared with baseline
		Mean: 7.1			Mean: 2.8					

Table 9 continued

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	Eighth FU 36 months	*P* value
Bagla [22]	$n = 19$ Mean: 24.7	$n = 19$ Mean: 13.9	$n = 13$ Mean: 13.6	$n = 5$ *Calculated mean: 12*						$P < 0.0001$: FU 1 month compared with baseline (19 patients) $P = 0.0002$: FU 3 months compared with baseline in 13 paired patients $P = 0.06$: FU 6 months compared with baseline in 5 paired patients
Pooled weighted mean	23.31	11.92	11.01	11.54	10.37	10.25	9.18	8.1	9.1	

Lower IPSS scores indicate fewer symptoms [24, 25]

Calculated means indicates that these were calculated based on the data given in studies

* No comparison with complete cohort was available

(range of the means 7.1–13.9). After the first month, the IPSS showed a further decrease to 8.1 at 30 months. The pooled weighted mean score at 36 months showed a slight increase to 9.1. There was no significant effect on IPSS score in patients who underwent unilateral versus bilateral embolization, nor in patients who underwent embolization with 90–180 or 180–300 μm PVA particles [18, 19].

QOL The pooled weighted mean QOL score at baseline was 4.34 (range of the means 3.86–6). After embolization, the QOL decreased mainly in the first month to a pooled weighted mean of 2.4 (range of the means 1.1–3.89). In the following months, the QOL showed a further decrease to 1.67 at 36 months. No significant effect on QOL score was stated in patients who underwent unilateral versus bilateral embolization or in patients who underwent embolization with 90–180 or 180–300 μm PVA particles [18, 19].

IIEF After PAE, no deterioration of erectile function was seen. After PAE, the IIEF score showed a maximum score of 20.58 at 6 months (range of the means 19.38–23.9); at baseline the pooled weighted mean IIEF score was 19.1 (range of the means 16.2–21.8). There was a significant greater score of IIEF when using 180–300 μm PVA particles compared with 90–180 μm particles ($P = 0.043$) [18].

Complications and other outcomes All complications are listed in detail per study in Supplement 2. Correct identification of the prostatic arteries is necessary to avoid untargeted ischemia to the bladder, rectum, anus, or corpus cavernosum [23]. Six cases of bladder ischemia were reported; of which two were transient, and four needed minor surgery, such as resection of a small area of necrosis. Transient rectal bleeding was reported in 20 cases, although no cases of intestinal wall ischemia were reported. No cases of ischemia of the corpus cavernosum were reported.

Most patients experienced no or mild pain. Only four patients experienced a lot of pain (VAS 9 or 10), related to four reported cases of bladder wall ischemia. A total of 21 patients experienced acute urinary retention after PAE, of which most were transient. Minor complications, such as hematoma on puncture site ($n = 26$), hematuria ($n = 59$), hematospermia ($n = 38$), urinary tract infection ($n = 67$), and prostatitis and balanitis ($n = 10$) were reported more frequently. However, these were transient or could be treated with antibiotics. No cases of impotence or retrograde ejaculation were reported. Most patients were discharged from the hospital on the day of the procedure (89 %). A minority was discharged the day after treatment (11 %) or 3 days after treatment (<1 %). Clinical failures after the first PAE were reported in a total of 131 patients, based on IPSS, QOL, and Qmax. Some of these patients underwent a second embolization procedure or a TURP.

Table 10 QOL-related symptoms

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	Eighth FU 36 months	*P* value
Pisco [14]	$n = 7$*		$n = 7$*							$P = 0.065$: Compared with baseline
	Mean: 3.86		Mean: 2.71							
Pisco [15]	$n = 238$	$n = 236$	$n = 221$	$n = 167$	$n = 102$	$n = 54$	$n = 25$	$n = 13$	$n = 9$	$P < 0.0001$:
	Mean: 4.40	Mean: 2.48	Mean: 2.23	Mean: 2.27	Mean: 1.96	Mean: 1.83	Mean: 1.76	Mean: 1.85	Mean: 1.67	Changes over time
Pisco [16]	$n = 86$	$n = 79$	$n = 70$	$n = 51$	$n = 28$	$n = 12$	$n = 4$			$P < 0.0001$:
	Mean: 4.07	*Calculated mean: 2.36*	*Calculated mean: 2.12*	*Calculated mean: 2.02*	*Calculated mean: 1.93*	*Calculated mean: 2.07*	*Calculated mean: 1.94*			Changes over time
Rio Tinto [17]	$n = 100$	$n = 100$	$n = 83$	$n = 62$	$n = 29$	$n = 13$	$n = 6$			
	Mean: 4.11	Mean: 2.26	Mean: 2.04	Mean: 1.96	Mean: 2.01	Mean: 2.0	Mean: 2.0			
Bilhim [18]	Group A: $n = 40$			Group A: $n = 34$						$P = 0.92$: Comparison groups at baseline
Comparing 2 particles	(80–180 μm PVA)			*Calculated mean: 2.98*						$P = 0.073$: Comparison changes between groups
	Mean: 4.33									
	Group B: $n = 40$			Group B: $n = 30$						
	(180–300 μm PVA)			*Calculated mean: 2.39*						
	Mean: 4.32									
Bilhim [19]	Group A: $n = 103$	Group A: $n = 103$								$P = 0.16$: Comparison groups at baseline
Comparing bilateral vs unilateral embolization	(bilateral)	*Calculated mean: 2.2*								$P = 0.34$: Comparison changes between groups
	Mean: 4.2									
	Group B: $n = 19$	Group B: $n = 19$								$P < 0.0001$: Last FU compared with baseline
	(unilateral)	*Calculated mean: 2.5*								
	Mean: 3.9									
Carnevale [20]	$n = 10$	$n = 10$	$n = 10$	$n = 10$	$n = 10$					$P = 0.001$: Compared with baseline
	Mean: 6	Mean: 1.1	Mean: 0.6	Mean: 0.1	Mean: 0.4					
Antunes [21]	$n = 10$				$n = 10$					$P = 0.001$: Compared with baseline
	Mean: 6				Mean: 0.4					

Table 10 continued

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	Eighth FU 36 months	*P* value
Bagla [22]	$n = 19$ Mean: 5.79	$n = 19$ Mean: 3.89	$n = 13$ Mean: 4.00	$n = 5$ *Calculated mean: 3.2*						$P = 0.0002$: FU 1 months compared with baseline in 19 patients $P = 0.02$: FU 3 months compared with baseline in 13 paired patients $P = 0.007$: FU 6 months compared with baseline in 5 paired patients
Pooled weighted mean	4.34	2.40	2.21	2.23	1.97	1.89	1.82	1.85	1.67	

Lower scores indicate better QOL [25]

Calculated means indicates that these were calculated based on the data given in studies

* No comparison with complete cohort was available

Discussion

This review summarizes all the available evidence on PAE and all clinical outcomes were stated. The primary clinical outcomes seem positive. After PAE, a decrease of the PV and PVR was reported mainly in the first month with a further decrease up to 12 months, increasing afterwards. The PSA also decreased up to 3 months after PAE, increasing afterwards. The Qmax increased mainly the first month and decreased after 30 months. The IPSS and QOL improved mainly during the first month, with further improvement up to 30 months. No deterioration of IIEF was seen.

The PAE procedure seems safe. Only six patients had a transient or small area of bladder wall necrosis. These patients with bladder wall necrosis were presented in six different studies of two study groups [14–17, 20, 21]. There is probably an overlap in reported patients, but even than the complication rate is low. Although 20 cases of transient rectal bleeding were stated, no cases of intestinal ischemia were reported.

A major limitation of this review is that only a small number of studies ($n = 9$) are available and were published by only three different research groups; all are pioneers in the field of prostate embolization. The extent to which patients in different series overlap is unclear, but we assume that there is an overlap in patients and complications. Based on inclusion and exclusion criteria, inclusion period, and patients' characteristics, we are certain that there were no full duplicates, because all presented data showed some differences in outcomes. Therefore, we decided to include all relevant papers.

The second limitation was the poor quality of studies, mainly based on the type of study (cohort), unclear patient selection, and dropouts. In the trials with more than 50 patients, a large dropout was already seen within 3 months, ranging from 6 to 48 % [15–17]. A follow-up of 18–36 months was only seen in three studies, representing a minority of patients [15–17]. In this small group of patients, a possible deterioration of parameters is seen. A relatively large number of clinical failures were described with persisting symptoms (131 patients; 19 %). Moreover, in none of the studies sample size calculations were given.

As for the methodological part of this systematic review, we did not perform a search in the Cochrane Library. However based on previous experience with at least 25 systematic reviews, we know that this database contains the same trials as Medline. As described earlier, different studies were reported by the same research group. Because we could not exclude duplication with certainty, we included all studies; our goal was to summarize the complete evidence on this topic. We therefore made several calculations to obtain means of mean values. We could not

Table 11 International Index of Erectile Function (IIEF)

Study	Baseline	First FU 1 month	Second FU 3 months	Third FU 6 months	Fourth FU 12 months	Fifth FU 18 months	Sixth FU 24 months	Seventh FU 30 months	*P* value
Pisco [14]	$n = 14$ Mean: 16.2		$n = 14$ Mean: 17.9						$P = 0.063$: Compared with baseline
Pisco [15]	$n = 230$ Mean: 18.9	$n = 197$ Mean: 20.6	$n = 152$ Mean: 20.9	$n = 110$ Mean: 20.5	$n = 65$ Mean: 20.1	$n = 25$ Mean: 20.4	$n = 12$ Mean: 18.7	$n = 3$ Mean: 20.0	$P = 0.0002$: Changes over time
Pisco [16]	$n = 86$ Mean: 18.3	$n = 77$ *Calculated mean: 18.79*	$n = 67$ *Calculated mean: 19.25*	$n = 49$ *Calculated mean: 19.38*	$n = 23$ *Calculated mean: 21.57*	$n = 11$ *Calculated mean: 22.25*	$n = 4$ *Calculated mean: 26.6** *Adjustment: 25*		$P = 0.003$: Changes over time
Rio Tinto [17]	$n = 100$ Mean: 18.47	$n = 100$ Mean: 19.61	$n = 83$ Mean: 20.07	$n = 62$ Mean: 20.20	$n = 29$ Mean: 19.76	$n = 13$ Mean: 20.41	$n = 6$ Mean: 17.1		
Bilhim [18] *Comparing 2 particles*	Group A: $n = 40$ (80–180 µm PVA) Mean: 21.8 Group B: $n = 40$ (180–300 µm PVA) Mean: 21.8			Group A: $n = 34$ *Calculated mean: 21.45* Group B: $n = 30$ *Calculated mean: 23.9*					$P = 0.99$: Comparison groups at baseline $P = 0.043$: Comparison changes between groups
Pooled weighted mean	19.1	19.96	20.2	20.58	20.3	20.82	19.41	20.0	

Higher IIEF scores indicate better function [26]

Calculated means indicates that these were calculated based on the data given in studies

* Calculated mean based on baseline and change was 26.6; however, a maximum score of this questionnaire is 25. Therefore, we adjusted this value to 25

determine risk of bias across studies, in terms of whether good quality studies had other outcomes than poor quality studies, due to the low number of studies and overlap of data. This also is the reason that we did not perform a meta-analysis but downstaged this paper to a systematic review.

In the different studies, variations on embolization technique were described, using unilateral or bilateral embolization and using different embolization material. One study showed no significant differences in the quantitative or qualitative outcomes comparing unilateral versus bilateral PAE. However, they state a significantly greater chance of poor clinical outcome in the unilateral group (47.4 vs. 24.3 % in the bilateral group) [19]. Another study of the same research group compared PAE using 90–180 μm PVA particles with PAE using 180-300 μm PVA particles [18].

This study showed a significant lower PSA using the smaller particles. However, the IIEF score was significantly higher using larger particles. This is contradictory, because different particle sizes showed different benefits. However, the intention of the procedure is not to improve the IIEF score but to avoid deterioration. The ideal embolization technique should be explored in larger studies.

In conclusion, we state that the initial reported results of PAE seem promising, mainly during the first 12 months after treatment. However, no comparison was made to medical therapy or surgical therapies. Overlapping patient data and reporting bias could not be excluded. None of the included studies performed a power analysis. Also, a relatively small number of patients are treated with a short follow-up period. Therefore, more studies are needed with more patients and longer periods of follow-up, compared with standard medical and surgical therapies, to assess whether PAE is an effective and safe alternative treatment for BPH.

Conflict of interest Sanne M. Schreuder, Alexander E. Scholtens, Jim A. Reekers, and Shandra Bipat have no conflict of interest.

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