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Prostatic arterial embolization for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (Review)

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[Intervention Review]

Prostatic arterial embolization for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia

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ABSTRACT

Background

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

Objectives

To assess the effects of PAE compared to other procedures for treatment of LUTS in men with BPH.

Search methods

We performed a comprehensive search using multiple databases (The Cochrane Library, MEDLINE, Embase, LILACS, Scopus, Web of Science, and Google Scholar), trials registries, other sources of grey literature, and conference proceedings with no restrictions on language of publication or publication status, up until 25 September 2020.

Selection criteria

We included parallel-group randomized controlled trials (RCTs), as well as non-randomized studies (NRS, limited to prospective cohort studies with concurrent comparison groups) enrolling men over the age of 40 with LUTS attributed to BPH undergoing PAE versus TURP or other surgical interventions.

Data collection and analysis

Two review authors independently classified studies for inclusion or exclusion and abstracted data from the included studies. We performed statistical analyses by using a random-effects model and interpreted them according to the *Cochrane Handbook for Systematic Reviews of Interventions.* We used GRADE guidance to rate the certainty of evidence of RCTs and NRSs.

Main results

We found data to inform two comparisons: PAE versus TURP (six RCTs and two NRSs), and PAE versus sham (one RCT). Mean age, IPSS, and prostate volume of participants were 66 years, 22.8, and 72.8 mL, respectively. This abstract focuses on the comparison of PAE versus TURP as the primary topic of interest.

PAE versus TURP

We included six RCTs and two NRSs with short-term (up to 12 months) follow-up and one RCT with long-term follow-up (13 to 24 months).

Short-term follow-up: based on RCT evidence, there may be little to no difference in urologic symptom score improvement (mean difference [MD] 1.55, 95% confidence interval [CI] -0.40 to 3.50; 369 participants; 6 RCTs; I^2 = 75%; low-certainty evidence) measured by the International Prostatic Symptom Score (IPSS) on a scale from 0 to 35, with higher scores indicating worse symptoms. There may be little to no difference in quality of life (MD 0.16, 95% CI -0.37 to 0.68; 309 participants; 5 RCTs; I^2 = 56%; low-certainty evidence) as measured by the IPSS quality of life question on a scale from 0 to 6, with higher scores indicating worse quality of life between PAE and TURP, respectively. While we are very uncertain about the effects of PAE on major adverse events (risk ratio [RR] 0.71, 95% CI 0.16 to 3.10; 250 participants; 4 RCTs; I^2 = 26%; very low-certainty evidence), PAE may increase re-treatments (RR 3.64, 95% CI 1.02 to 12.98; 204 participants; 3 RCTs; I^2 = 0%; low-certainty evidence). Based on 18 re-treatments per 1000 men in the TURP group, this corresponds to 47 more (0 more to 214 more) per 1000 men undergoing PAE.

We are very uncertain about the effects on erectile function (MD -0.03, 95% CI -6.35 to 6.29; 129 participants; 2 RCTs; I^2 = 78%; very low-certainty evidence) measured by the International Index of Erectile Function at 5 on a scale from 1 to 25, with higher scores indicating better function. NRS evidence when available yielded similar results. Based on evidence from NRS, PAE may reduce the occurrence of ejaculatory disorders (RR 0.51, 95% CI 0.35 to 0.73; 260 participants; 1 NRS; low-certainty evidence).

Longer-term follow-up: based on RCT evidence, we are very uncertain about the effects of PAE on urologic symptom scores (MD 0.30, 95% CI -3.17 to 3.77; 95 participants; very low-certainty evidence) compared to TURP. Quality of life may be similar (MD 0.20, 95% CI -0.49 to 0.89; 95 participants; low-certainty evidence). We are also very uncertain about major adverse events (RR 1.96, 95% CI 0.63 to 6.13; 107 participants; very low-certainty evidence). We did not find evidence on erectile function and ejaculatory disorders. Based on evidence from NRS, PAE may increase re-treatment rates (RR 1.51, 95% CI 0.43 to 5.29; 305 participants; low-certainty evidence); based on 56 re-treatments per 1000 men in the TURP group. this corresponds to 143 more (25 more to 430 more) per 1000 men in the PAE group.

Authors' conclusions

Compared to TURP up to 12 months (short-term follow-up), PAE may provide similar improvement in urologic symptom scores and quality of life. While we are very uncertain about major adverse events, PAE may increase re-treatment rates. We are uncertain about erectile function, but PAE may reduce ejaculatory disorders. Longer term (follow-up of 13 to 24 months), we are very uncertain as to how both procedures compare with regard to urologic symptom scores, but quality of life appears to be similar. We are very uncertain about major adverse events but PAE may increase re-treatments. We did not find longer term evidence on erectile function and ejaculatory disorders. Certainty of evidence for the main outcomes of this review was low or very low, signalling that our confidence in the reported effect size is limited or very limited, and that this topic should be better informed by future research.

PLAIN LANGUAGE SUMMARY

Prostatic arterial embolization for treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia

Review question

What are the effects of a procedure that reduces blood flow to the prostate (called prostatic arterial embolization) in men with symptoms caused by an enlarged prostate?

Background

An enlarged prostate may cause difficulty with urination such as a weak stream or the need to urinate often during the day or at night. This can be treated by medications or by different types of surgery. One main type of surgery is called transurethral resection of the prostate. This involves going inside the urethra through the penis and removing prostate tissue. Prostatic arterial embolization is another form of treatment that works by stopping blood flow to parts of the prostate. We did this study to compare how prostatic arterial embolization compares to transurethral resection of the prostate and other procedures used in men with an enlarged prostate.

Study characteristics

We found eight studies that compared prostatic arterial embolization to transurethral resection of the prostate. In six of eight studies, so-called randomized trials, chance decided which group people were in. In the other two studies, the men themselves and their doctors decided. We also included one study that compared prostatic arterial embolization to a sham procedure (men were made to believe that

they received treatment, but in reality, they did not). We found no evidence comparing prostatic arterial embolization to other treatments than TURP.

Key results

Prostatic arterial embolization compared to transurethral resection of the prostate

Based on up to 12 months' follow-up (short term), prostatic arterial embolization and transurethral resection of the prostate may work similarly well in helping to relieve symptoms. Men's quality of life may also improve similarly. We are very uncertain about differences in major unwanted effects. Prostatic arterial embolization may increase the need for being treated again for the same problem. We are very uncertain as to any differences with regard to the need for an erection problem, but prostatic arterial embolization may reduce problems with ejaculation.

Based on 13 to 24 months' follow-up (longer term), we are very uncertain about the effects of prostatic arterial embolization on urinary symptoms compared to transurethral resection of the prostate. Quality of life may be similar. We are also very uncertain about the effects of prostatic arterial embolization on major unwanted effects. Prostatic arterial embolization may increase the need for another treatment. We found no data on erection or ejaculation problems.

Certainty of evidence

The certainty of evidence for all main outcomes was low or very low. This means that the true effect can be very different from what this review shows. Better, larger studies with longer follow-up are needed to better answer the question of how prostatic arterial embolization compares to other treatments.

Summary of findings 1. PAE compared to TURP for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (short term)

Patient or population: treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia
Setting: RCTs (likely single center) and NRSs (including multicenter registry-based study)/China, Brazil, Egypt and Europe
Intervention: PAE
Comparison: TURP

Outcomes	No. of participants (studies) Follow-up	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		What happens?
				Risk with TURP (short term)	Risk difference with PAE	
Urologic symptom scores[a] assessed with International Prostate Symptom Score Scale from 0 (best; not at all) to 35 (worst; almost always) Follow-up: range 12 weeks to 12 months MCID: 3 points	369 (6 RCTs)	⊕⊕⊖⊖ Low[b,c,d]	-	Urologic symptom scores of RCTs ranged from 6.1 to 10.2	MD 1.55 higher (0.40 lower to 3.50 higher)	There may be little to no difference in urologic symptom score improvement between PAE and TURP
Quality of life[a] assessed with International Prostate Symptom Score-Quality of Life Scale from 0 (best; delighted) to 6 (worst; terrible) Follow-up: range 12 weeks to 12 months MCID: 0.5 points	309 (5 RCTs)	⊕⊕⊖⊖ Low[b,c,d]	-	Quality of life of RCTs ranged from 0.9 to 2.91	MD 0.16 higher (0.37 lower to 0.68 higher)	There may be little to no difference in quality of life improvement between PAE and TURP
Major adverse events Follow-up: range 12 weeks to 12 months MCID: relative risk reduction/increase of 0.25	250 (4 RCTs)	⊕⊖⊖⊖ Very low[b,e]	RR 0.71 (0.16 to 3.10)	Study population		We are very uncertain whether PAE results in more or fewer major adverse events than TURP
				51 per 1000	15 fewer per 1000 (43 fewer to 108 more)	
	305 (1 NRS)	⊕⊖⊖⊖ Very low[b,f]	Not estimable[g]	Study population		
				-	-	

Re-treatment[a] Follow-up: range 6 months to 12 months MCID: relative risk reduction/increase of 0.25	204 (3 RCTs)	⊕⊕⊖⊖ Low[b,h]	RR 3.64 (1.02 to 12.98)	Study population		PAE may increase re-treatment rates
				18 per 1000	47 more per 1000 (0 fewer to 214 more)	
Erectile function assessed with International Index of Erectile Function-5 Scale from 1 (worst; severe) to 25 (best; normal) Follow-up: range 12 weeks to 12 months MCID: 5 points	129 (2 RCTs)	⊕⊖⊖⊖ Very low[b,c,e]	-	Erectile function in RCTs ranged from 11.67 to 16.1	MD 0.03 lower (6.35 lower to 6.29 higher)	We are very uncertain- whether PAE results in better or worse erectile function than TURP
	122 (1 NRS)	⊕⊖⊖⊖ Very low[b,h]	-	Erectile function in observational study was 14.8	MD 1.5 higher (2.01 lower to 5.01 higher)	
Ejaculatory disorders[i] Follow-up: range 12 weeks to 12 months MCID: relative risk reduction/increase of 0.25	260 (1 NRS)	⊕⊕⊖⊖ Low[b]	RR 0.51 (0.35 to 0.73)	Study population		PAE may reduce ejaculatory disorder compared to TURP
				475 per 1000	233 fewer per 1000 (309 fewer to 128 fewer)	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; MCID: minimal clinically important difference; MD: mean difference; NRS: non-randomized study; PAE: prostatic arterial embolization; RCT: randomized controlled trial; RR: risk ratio; TURP: transurethral resection of prostate.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Certainty evidence of RCTs was higher than NRSs (Appendix 1).
[b]Downgraded for study limitations: RCTs, unclear or high risk of bias in half or more domains in the included studies (-1)/NRS, overall serious or critical risk of bias according to risk of bias tool to assess non-randomized studies of interventions (-2).
[c]Downgraded by one level for inconsistency due to clinical important heterogeneity with high I-square values.
[d]Not downgraded further for imprecision; wide confidence intervals attributed to observed inconsistency (for which we rated down).
[e]Downgraded by two levels for imprecision: wide confidence interval crosses assumed threshold of clinically important difference and/or large risk difference in absolute effects.
[f]Downgraded by two levels for imprecision: very rare event.
[g]No event in group.

[h]Downgraded by one level for imprecision: confidence interval crosses assumed threshold of clinically important difference and/or large risk difference in absolute effects.
[i]Certainty of evidence of NRSs was higher than RCTs (Appendix 1).

Summary of findings 2. PAE compared to TURP for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (long term)

Participants: men with lower urinary tract symptoms suggesting benign prostatic hyperplasia

Setting: RCT (likely single center) and NRS (multicenter registry-based study)/China and Europe

Intervention: PAE

Comparator: TURP

Outcomes	No. of participants (studies) Follow-up	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		What happens?
				Risk with TURP (long term)	Risk difference with PAE	
Urologic symptom scores assessed with International Prostate Symptom Score Scale from 0 (best; not at all) to 35 (worst; almost always) Follow-up: 24 months MCID: 3 points	95 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	-	Urologic symptom score was 8.4	MD 0.3 higher (3.17 lower to 3.77 higher)	We are very uncertain how PAE symptom score improvement compares to TURP
Quality of life assessed with International Prostate Symptom Score-Quality of Life Scale from 0 (best; delighted) to 6 (worst; terrible) Follow-up: 24 months MCID: relative risk reduction/increase of 0.5	95 (1 RCT)	⊕⊕⊖⊖ Low[a,c]	-	Quality of life was 1.4	MD 0.2 higher (0.49 lower to 0.89 higher)	There may be little to no difference in quality of life from PAE compared to TURP
Major adverse events Follow-up: 24 months MCID: relative risk reduction/increase of 0.25	107 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	RR 1.96 (0.63 to 6.13)	Study population		We are very uncertain whether PAE results in more or fewer major adverse events than TURP
				75 per 1000	72 more per 1000 (28 fewer to 387 more)	

Re-treatment Follow-up: after 12 months (not specified) MCID: relative risk reduction/increase of 0.25	305 (1 NRS)	⊕⊕⊖⊖ Low[a]	RR 3.54 (1.45 to 8.65)	Study population		PAE may increase re-treatment rates
				56 per 1000	143 more per 1000 (25 more to 430 more)	
Erectile function - not reported	-	-	-	-	-	We found no studies and therefore do not know
Ejaculatory disorders - not reported	-	-	-	-	-	We found no studies and therefore do not know

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; MCID: minimal clinically important difference; MD: mean difference; NRS: non-randomized study; PAE: prostatic arterial embolization; RCT: randomized controlled trial; RR: risk ratio; TURP: transurethral resection of prostate.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded by one level for study limitations: RCT, unclear risk of selection and reporting bias/high risk of performance or detection bias (-1) /NRS, overall serious or critical risk of bias according to risk of bias tool to assess non-randomized studies of interventions (-2).
[b]Downgraded by two levels for imprecision: wide confidence interval crosses assumed threshold of clinically important difference.
[c]Downgraded by one level for imprecision: confidence interval crosses assumed threshold of clinically important difference.

Summary of findings 3. PAE compared to sham for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (short term)

Patient or population: men with lower urinary tract symptoms suggesting benign prostatic hyperplasia
Setting: RCT/single center/Portugal
Intervention: PAE
Comparison: sham

Outcomes	No. of participants (studies) Follow-up	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	What happens?

				Risk with sham	Risk difference with PAE	
Urologic symptom scores assessed with International Prostate Symptom Score Scale from 0 (best; not at all) to 35 (worst; almost always) Follow-up: 6 months MCID: 3 points	80 (1 RCT)	⊕⊕⊕⊖ Moderate[a]	-	Change in urologic symptom scores was -5.03	MD 12.07 lower (15.45 lower to 8.69 lower)	PAE likely improves urologic symptom scores compared to sham
Quality of life assessed with International Prostate Symptom Score-Quality of Life Scale from 0 (best; delighted) to 6 (worst; terrible) Follow-up: 6 months MCID: relative risk reduction/increase of 0.5	80 (1 RCT)	⊕⊕⊕⊖ Moderate[a]	-	Change in quality of life was -1.03	MD 1.97 lower (2.48 lower to 1.46 lower)	PAE likely improves quality of life compared to sham
Major adverse events Follow-up: 6 months MCID: relative risk reduction/increase of 0.25	80 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	Not estimable[c]	Study population -	- -	We are very uncertain about the effects of PAE on major adverse events
Re-treatment Follow-up: 6 months MCID: relative risk reduction/increase of 0.25	80 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	Not estimable[c]	Study population -	- -	We are very uncertain about effects of PAE on re-treatment
Erectile function - not reported	-	-	-	-	-	We do not know
Ejaculatory disorders Follow-up: 6 months MCID: relative risk reduction/increase of 0.25	80 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	Not estimable[c]	Study population -	- -	We are very uncertain about effects of PAE on major adverse events

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; MCID: minimal clinically important difference; MD: mean difference; PAE: prostatic arterial embolization; RCT: randomized controlled trial.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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[a]Downgraded by one level for study limitations: high risk of performance and detection bias.
[b]Downgraded by two levels for imprecision: very rare event.
[c]No event in both groups.

BACKGROUND

Description of the condition

Benign prostatic hyperplasia (BPH) is histologically defined as an increased number of epithelial and stromal cells in the periurethral area of the prostate, which may cause prostate enlargement (Roehrborn 2008). Prostate enlargement may constrict urine flow and cause lower urinary tract symptoms (LUTS) (Dunphy 2015). The development of LUTS resulting from BPH is associated with increasing age, and is most commonly encountered in men over the age of 45 years (Barry 1997; Dunphy 2015; Egan 2016). LUTS consist of storage symptoms (such as urinary frequency, urgency, and nocturia) and voiding symptoms (such as urinary hesitancy, weak urinary stream, straining to void, and prolonged voiding). LUTS severity was positively correlated with men's overall distress based on patient perception of bladder condition, which can be measured by a single-item global question (ranging from 1 [no problems at all] to 6 [causes severe problems]) (Chapple 2017). However, LUTS are relatively non-specific and may also be associated with bladder disorders, such as detrusor overactivity. This review specifically considers the term BPH as prostatic enlargement with LUTS by which to define the disease condition and the potential need for intervention (Dunphy 2015; Roehrborn 2008).

The histological prevalence of BPH is reported to be 8% in the fourth decade of life, and up to 40% and 70% in the sixth and eighth decades of life, respectively (Barry 1995; Roehrborn 2008; Yoo 2012). Aside from LUTS, untreated BPH can result in other serious medical consequences, such as acute urinary retention, urinary tract infection, and upper urinary tract deterioration. Subsequently, BPH results in a negative impact on public health and reduction in a person's quality of life (Martin 2014; Yoo 2012). BPH results in a significant economic burden as well, with an estimated cost to the USA of USD 4 billion annually (Taub 2006). It is reasonable to assume that the cost will escalate further in the future with increasing life expectancy in men over the age of 65 years (Centers for Disease Control and Prevention 2003).

Treatment decisions for patients with BPH are typically based on severity of symptoms and subjectively perceived bother, presence of complications such as acute urinary retention, risk of progression, and treatment-related morbidity. Self-administered questionnaires, namely, the International Prostate Symptom Score (IPSS), which consists of eight questions (seven symptom questions + one quality of life question) to evaluate symptom severity and relative degree of bother, have been used to guide management of LUTS (Barry 1995). Watchful waiting and behavioral management is an appropriate first-line option in patients with mild or non-bothersome symptoms. Additional medical treatment options in patients with more bothersome symptoms consist of alpha-blockers, 5-alpha reductase inhibitors, or a combination of the two (EAU 2020; McVary 2011). If symptoms progress despite medical therapy, or if BPH-related complications such as acute urinary retention, recurrent urinary tract infection, bladder stones, hematuria, or renal insufficiency occur, surgical options are considered (EAU 2020; McVary 2019; McVary 2011).

A wide variety of surgical options are available for treatment of BPH, from open simple prostatectomy to minimally invasive surgeries, such as transurethral resection of the prostate (TURP), laser ablation, or enucleation of the prostate. According to current guidelines, TURP remains the "gold standard" surgical procedure for men over 40 years of age with various forms of non-neurogenic benign LUTS. Although TURP resulted in a mean decrease in LUTS of 70% and a mean increase in maximum flow rate (Qmax) of 162%, considerable rates of perioperative and long-term complications, such as bleeding requiring blood transfusion (2%), transurethral resection syndrome (0.8%), acute urinary retention (4.5%), clot retention (4.9%), urinary tract infection (4.1%), bladder neck stenosis (4.7%), urethral stricture (3.8%), retrograde ejaculation (65.4%), and erectile dysfunction (6.5%), have been reported (Ahyai 2010). TURP also commonly requires a period of temporary catheterization or hospital admission, or both. Reducing treatment-related morbidity and patient burden has therefore motivated the development of new, minimally invasive alternatives. Minimally invasive surgeries, such as those using electrode, laser, transurethral thermal ablation of prostate (needle ablation, microwave therapy, and radiofrequency ablative techniques), and mechanical stents, have been introduced and are widely recognized as alternatives to TURP in select patients (EAU 2020; McVary 2019). Prostatic arterial embolization (PAE) represents a relatively new, minimally invasive treatment option that is particularly suitable for men who are at high risk to undergo anesthesia (Wang 2015).

Description of the intervention

Embolization of the prostatic arteries has been used historically to control persistent or massive prostatic bleeding not otherwise amenable to treatment, with typical causes of BPH or locally advanced prostate cancer, or occurring after transurethral prostatectomy (Mitchell 1976). DeMeritt 2000 reported a case of PAE performed with polyvinyl alcohol particles for BPH-induced hematuria, in which hematuria was immediately stopped and the patient reported symptomatic improvement of his BPH symptoms. These researchers also found that prostate size was reduced by 52% and 62% of the initial size at five-month and 12-month follow-up, respectively. Carnevale 2010 reported positive preliminary results of PAE procedures with microspheres as a primary treatment in two patients with acute urinary retention due to BPH. For elderly patients with symptomatic BPH, PAE can be an alternative treatment, which is performed by a femoral artery puncture and use of conscious sedation instead of general anesthesia. The procedure is typically performed on an outpatient basis and usually does not require catheterization, unless the patient is experiencing urinary retention (Wang 2015).

In preparation for PAE, preoperative computed tomography or magnetic resonance angiography is typically performed to evaluate the pelvic artery anatomy. Digital subtraction angiography of the right and left internal iliac arteries is performed to assess the prostatic blood supply (Martins Pisco 2012). Super-selective micro catheterization and embolization are then performed on the prostatic arteries. Embolization is typically performed to complete stasis (Carnevale 2010; Martins Pisco 2012; Wang 2015). Particle embolics are used almost exclusively, with wide variation in the type and size of particles (Carnevale 2010; DeMeritt 2000). Vasodilators to mitigate vasospasm once the prostatic artery is catheterized are recommended by some authors to avoid premature stasis (Martins Pisco 2012).

Adverse effects of the intervention

Although major complications were low (less than 1%) (Pisco 2016), perineal pain (9.4%), hematuria (9%), and acute urinary retention

(7%) were commonly reported as complications of PAE (Feng 2017). The highest prevalence of acute urinary retention was 28.4% amongst the included studies (Wang 2015). Minor complications, such as hematospermia, rectal bleeding, urinary tract infection, inguinal hematoma, and transient urinary frequency, were also reported (Feng 2017; Kuang 2017; Pyo 2017; Shim 2017). However, there was inconsistency in reporting or classifying the adverse events.

How the intervention might work

The underlying mechanism of PAE is ischemia or hypoxia that induces apoptosis, necrosis, sclerosis, and prostatic shrinkage with cystic transformation of part, or all, of the gland, resulting in a softer gland with reduced compression of the urethra (DeMeritt 2000; Sun 2008). In addition, PAE may decrease the plasma concentration of free testosterone that enters prostate cells, thereby lowering dihydrotestosterone levels in the prostate. This may result in secondary inhibition of prostate growth (Sun 2008). Furthermore, ischemia or hypoxia may induce prostate cell death and necrosis with decreased numbers of some receptors, such as alpha-adrenergic receptors. Therefore, the neuromuscular tone may be decreased, resulting in improvement in clinical symptoms associated with the dynamic pathologic component of BPH (Zlotta 1997).

Why it is important to do this review

Despite reported relative advantages of PAE, it remains unclear how this procedure compares to the numerous surgical alternatives that are available. Although existing systematic reviews have compared PAE to other therapies used to treat BPH (Feng 2017; Kuang 2017; Pyo 2017; Shim 2017), none so far has used the same rigorous methods as Cochrane Reviews, which include application of the GRADE approach with focus on patient-important outcomes (Guyatt 2008). In this era, with the availability of numerous minimally invasive procedures to treat LUTS suggestive of BPH, the findings of this Cochrane Review will be relevant to policymakers, healthcare providers, and patients alike.

OBJECTIVES

To assess the effects of PAE compared to other procedures for treatment of LUTS in men with BPH.

METHODS

Criteria for considering studies for this review

Types of studies

We considered parallel-group randomized controlled trials (RCTs) and cluster-RCTs for inclusion. We excluded cross-over studies as not applicable. We also included non-randomized studies (NRSs), limited to prospective cohort studies with concurrent comparison groups, which is similar to relevant randomized controlled trials, as a source of complementary, sequential, or replacement evidence for RCTs if RCTs provided low-certainty evidence for a given outcome and comparison (e.g. limited information about adverse events and long-term effects) (Schunemann 2013). We did not include single-armed studies. We included studies regardless of their publication status or language of publication.

Types of participants

We defined the eligible patient population as men over the age of 40 with a minimum prostate volume of 20 mL or greater (as assessed by ultrasound or cross-sectional imaging), with LUTS as determined by an IPSS of 8 or over, and with Qmax less than 15 mL/s, as measured by non-invasive uroflowmetry, invasive pressure flow studies, or both (EAU 2020; McVary 2011). The age limitation is based on the observation that the prevalence of BPH increases among middle-aged and older men, and that BPH is infrequent in younger men (Barry 1997; EAU 2020; Egan 2016).

We excluded trials including men with chronic renal failure, untreated bladder calculi or large diverticula, a diagnosis of prostate cancer, urethral stricture disease, or prior prostate, bladder neck, or urethral surgery. We also excluded studies including patients with other conditions that affect urinary symptoms, such as neurogenic bladder due to spinal cord injury, multiple sclerosis, or central nervous system disease.

Types of interventions

We compared experimental and comparator interventions for the following outcomes. Concomitant interventions had to be the same in experimental and comparator groups to establish fair comparisons.

Experimental interventions

- PAE

Comparator interventions

- Sham control (or no intervention)
- TURP (monopolar or bipolar)
- Laser ablation of the prostate (e.g. photoselective vaporization of the prostate [PVP])
- Laser enucleation of the prostate (e.g. holmium laser enucleation of the prostate)
- Other minimally invasive therapies (e.g. transurethral incision of the prostate, transurethral thermal ablation of the prostate [needle ablation, microwave therapy, and radiofrequency ablative techniques], prostate stent, and prostatic urethral lift [PUL])

Comparisons

- PAE versus sham control (or no intervention)
- PAE versus TURP
- PAE versus laser ablation of the prostate
- PAE versus laser enucleation of the prostate
- PAE versus other minimally invasive therapies

Types of outcome measures

We did not use measurement of the outcomes assessed in this review as an eligibility criterion.

Primary outcomes

- Urologic symptom scores
- Quality of life
- Major adverse events

Secondary outcomes

- Re-treatment
- Erectile function
- Ejaculatory disorders
- Minor adverse events
- Acute urinary retention
- Indwelling urinary catheter
- Hospital stay

Method and timing of outcome measurement

We considered clinically important differences for review outcomes to rate certainty of the evidence for imprecision in the "Summary of findings" tables (Johnston 2010).

Urologic symptom scores

- Final value or change from baseline measured as IPSS
- We considered improvement in the IPSS score of 3 points as a minimal clinically important difference (MCID) to assess efficacy and comparative effectiveness (Barry 1995)

Quality of life

- Final value or change from baseline measured as IPSS-quality of life
- No threshold was established for IPSS-quality of life. We used an MCID of 0.5 to assess efficacy and comparative effectiveness (Brasure 2016; Rees 2015)

Major adverse events

- For example, postoperative hemorrhage requiring admission or intervention
- We used the Clavien-Dindo Classification System to assess surgical complications (Dindo 2004), and we categorized grade III, IV, and V complications as major
- We judged the adverse events by severity using the available information described in the studies

Re-treatment

- Participants undergoing the same or other surgical treatment modalities due to insufficient treatment response

Erectile function

- Final value or change from baseline measured by International Index of Erectile Function-5 questionnaire (IIEF-5) (Rosen 1997)
- We considered improvement in IIEF-5 over 5 points as an MCID (Spaliviero 2010)

Ejaculatory disorders

- We intended to measure the outcome of ejaculatory function based on the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD; Rosen 2007)
- Due to lack of data based on the questionnaire, we used the incidence rate of ejaculatory disorders such as postoperative retrograde ejaculation or reduction in ejaculation volume as summarized under the outcome ejaculatory disorder

Minor adverse events

- For example, postoperative fever or pain requiring medication
- We used the Clavien-Dindo Classification System to assess surgical complications (Dindo 2004), and we categorized grade I and II complications as minor
- We judged the adverse events by severity using the available information described in the studies

Acute urinary retention

- Events requiring catheterization after intervention

Indwelling urinary catheter

- Measured in days from intervention to urinary catheter removal

Hospital stay

- Measured in days from admission to discharge

There is no reported threshold for adverse events, re-treatment, ejaculatory function (based on the questionnaire), acute urinary retention, indwelling urinary catheter, or hospital stay. We considered the clinically important difference for adverse events, re-treatment, acute urinary retention, and ejaculatory disorders (based on the events) as a relative risk reduction of at least 25% (Guyatt 2011a). We used an MCID of 25% improvement from baseline on the MSHQ-EjD for ejaculatory function (Nickel 2015). We used a clinically important difference of one day to assess efficacy and comparative effectiveness for indwelling urinary catheter and hospital stay; this was informed by the clinical expertise of urologists on the review author team. We did not seek other stakeholder feedback.

We considered outcomes measured up to and including 12 months after randomization as short term, and beyond 12 months as long term, for urologic symptom scores, quality of life, major adverse events, re-treatment, erectile function, ejaculatory disorders, minor adverse events, and acute urinary retention. We assessed indwelling urinary catheter and hospital stay only at short term.

Main outcomes for "Summary of findings" tables

We present "Summary of findings" tables reporting the following outcomes listed according to priority.

- Urologic symptom scores.
- Quality of life.
- Major adverse events.
- Re-treatment.
- Erectile function.
- Ejaculatory disorders.

Search methods for identification of studies

We searched the following sources from inception of each database to 22 May 2017. The date of last search of all databases was 25 September 2020 (Appendix 2).

Electronic searches

We searched the following sources from inception of each database.

- Cochrane Library via Wiley (from 1991)
  - *Cochrane Database of Systematic Reviews* (CDSR).
  - Cochrane Central Register of Controlled Trials (CENTRAL).
  - Database of Abstracts of Reviews of Effects (DARE).
  - Health Technology Assessment Database (HTA).
- MEDLINE via Ovid (from 1946).
- Embase via Ovid (from 1947).
- Latin American and Caribbean Health Sciences Literature (LILACS; www.bireme.br/; from 1982).
- Scopus (from 1966).
- Web of Science (from 1900).
- Google Scholar.

We also searched the following.

- ClinicalTrials.gov (www.clinicaltrials.gov/).
- World Health Organization (WHO) International Clinical Trials Registry Platform search portal (apps.who.int/trialsearch/).
- Grey literature repository from the current Grey Literature Report (www.greylit.org/).

Searching other resources

We tried to identify other potentially eligible trials or ancillary publications by searching the reference lists of retrieved included trials, reviews, meta-analyses, and health technology assessment reports. We also contacted study authors of included trials to identify any further studies that we may have missed. We searched for unpublished studies by handsearching abstract proceedings of annual meetings of the American Urological Association, the European Association of Urology, and the Radiological Society of North America.

Data collection and analysis

Selection of studies

We used reference management software to identify and remove potentially duplicate records (EndNote 2016). Two review authors (JHJ, BR, or KAM) independently scanned the abstract, the title, or both, of remaining records retrieved, to determine which studies should be assessed further through Covidence 2017. Two review authors (JHJ, BR, or KAM) investigated all potentially relevant records as full text, mapped records to studies, and classified studies as included studies, excluded studies, studies awaiting classification, or ongoing studies, in accordance with the criteria for each provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019). We resolved any discrepancies through consensus or recourse to a third review author (PD). We documented reasons for exclusion of studies that may have reasonably been expected to be included in the review in a Characteristics of excluded studies table. We present an adapted PRISMA flow diagram showing the process of study selection (Liberati 2009).

Data extraction and management

We developed a dedicated data abstraction form that we pilot-tested ahead of time.

For studies that fulfilled our inclusion criteria, two review authors (JHJ and BR) independently abstracted the following information, which we have provided in the Characteristics of included studies table.

- Study design.
- Study dates.
- Study settings and countries.
- Participant inclusion and exclusion criteria.
- Participant details, baseline demographics (age, prostate volume, prostate-specific antigen, IPSS, and Qmax) including confounders listed in Assessment of risk of bias in included studies.
- Numbers of participants by study and by study arm.
- Details of relevant experimental and comparator interventions, such as embolization, catheterization approach (unilateral or bilateral), and characteristics of the embolization agent used (polyvinyl alcohol particle size) including co-intervention listed in Assessment of risk of bias in included studies.
- Definitions of relevant outcomes and methods (type of instrument, such as IPSS) and timing of outcome measurement (in months).
- Study funding sources.
- Declarations of conflicts of interest by primary investigators.

We extracted outcome data relevant to this Cochrane Review as needed for calculation of summary statistics and measures of variance. For dichotomous outcomes, we obtained numbers of events and totals for populations in a 2 × 2 table, as well as summary statistics with corresponding measures of variance. For continuous outcomes, we obtained means and standard deviations (SDs) or data necessary to calculate this information.

We resolved any disagreements by discussion or, if required, by consultation with a third review author (PD).

We provided information, including trial identifier, about potentially relevant ongoing studies in the table Characteristics of ongoing studies.

We contacted authors of included studies to obtain key missing data as needed.

Dealing with duplicate and companion publications

In the event of duplicate publications, companion documents, or multiple reports of a primary study, we maximized the yield of information by mapping all publications to unique studies and collating all available data. We used the most complete data set aggregated across all known publications. In case of doubt, we gave priority to the publication reporting the longest follow-up associated with our primary or secondary outcomes.

Assessment of risk of bias in included studies

Two review authors (JHJ and BR) assessed the risk of bias of each included study independently. We resolved disagreements by consensus, or by consultation with a third review author (PD). We present a "Risk of bias" summary figure to illustrate these findings. We further summarized risk of bias across domains for each outcome in each included study, as well as across studies and domains for each outcome, in accordance with the approach for summary assessments of risk of bias as presented in the *Cochrane*

Handbook for Systematic Reviews of Interventions (Higgins 2011; Sterne 2016a).

Assessment of risk of bias in RCTs

We assessed risk of bias using Cochrane's "Risk of bias" assessment tool (Higgins 2011). We assessed the following domains.

- Random sequence generation (selection bias).
- Allocation concealment (selection bias).
- Blinding of participants and personnel (performance bias).
- Blinding of outcome assessment (detection bias).
- Incomplete outcome data (attrition bias).
- Selective reporting (reporting bias).
- Other sources of bias.

We judged risk of bias domains as "low risk," "high risk," or "unclear risk," and we evaluated individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

For selection bias (random sequence generation and allocation concealment), we evaluated risk of bias at a trial level.

For performance bias (blinding of participants and personnel), we considered all outcomes similarly susceptible to performance bias.

For detection bias (blinding of outcome assessment), we grouped outcomes as susceptible to detection bias (subjective outcomes) or not susceptible to detection bias (objective outcomes).

We defined the following endpoints as subjective outcomes.

- Urologic symptom scores.
- Quality of life.
- Major adverse events.
- Erectile function.
- Minor adverse events.

We defined the following endpoints as objective outcomes.

- Re-treatment.
- Acute urinary retention.
- Indwelling urinary catheter.
- Hospital stay.

We assessed attrition bias (incomplete outcome data) on an outcome-specific basis, and we presented the judgment for each outcome separately when reporting our findings in the "Risk of bias" tables. We collapsed reporting for identical judgments.

For reporting bias (selective reporting), we evaluated risk of bias at a trial level. We assessed the risk as low if an a priori protocol was identified, and if outcome reporting and planned analyses actually performed matched.

We further summarized risk of bias across domains for each outcome in each included study, as well as across studies and domains for each outcome, in accordance with the approach for summary assessments of risk of bias as presented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of risk of bias in NRS

We assessed risk of bias in NRS with a risk of bias tool to assess non-randomized studies of interventions (ROBINS-I): a tool for assessing risk of bias in non-randomized studies of interventions (Sterne 2016a). We assessed the following domains on outcome-specific basis for each study and

- Bias due to confounding.
- Bias in selection of participants into the study.
- Bias in classification of interventions.
- Bias due to deviations from intended interventions.
- Bias due to missing data.
- Bias in measurement of outcomes.
- Bias in selection of the reported result.

We judged risk of bias domains as "low risk," "moderate risk," "serious risk," "critical risk," or "no information," and we evaluated individual bias items as described in Sterne 2016a.

Based on a particular level of risk of bias for an individual domain, we made an overall judgement about risk of bias.

- Low risk of bias (the study is comparable to a well-performed randomized trial).
- Moderate risk of bias (the study provides sound evidence for a non-randomized study but cannot be considered comparable to a well-performed randomized trial).
- Serious risk of bias (the study has some important problems).
- Critical risk of bias (the study is too problematic to provide any useful evidence and should not be included in any synthesis).
- No information on which to base a judgement about risk of bias.

The effect of interest in the NRS was that of assigning intervention at baseline (start of follow-up), regardless of the extent to which the intervention was received during follow-up (sometimes referred to as the “intention-to-treat” effect in the context of randomized trials).

List of confounding factors and co-interventions

We considered the following as baseline confounding factors and co-interventions.

Confounding factors

- Age.
- Co-morbidities such as hypertension and diabetes mellitus.
- Prostate volume.
- Severity of LUTS based on baseline questionnaire score (such as IPSS, IPSS-quality of life, IIEF-5, MSHQ-EjD).

We did not consider time-varying confounding, as these instances of confounding were not relevant in this setting (Sterne 2016b).

Co-interventions

- Medications such as alpha-blockers, 5-alpha reductase inhibitors, or anticholinergics

The listed confounding factors and co-interventions can affect a participant's preference for each surgical intervention (both experimental and control) based on the recent guideline (EAU 2020; McVary 2019).

Measures of treatment effect

We expressed dichotomous data as risk ratios (RRs) with 95% confidence interval (CIs). We expressed continuous data as mean differences (MDs) with 95% CIs. If we find the studies use different measures to assess the same outcome, in which case we will express data as standardized MDs with 95% CIs.

Unit of analysis issues

The unit of analysis was the individual participant. Should we identify cluster-randomized trials, or trials with more than two intervention groups for inclusion in next update, we will handle these in accordance with guidance provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019).

Dealing with missing data

We obtained missing data from study authors and performed intention-to-treat analyses if data were available. We investigated attrition rates (e.g. dropouts, losses to follow-up, withdrawals), and we critically appraised issues of missing data. We did not impute missing data.

Assessment of heterogeneity

We identified heterogeneity (inconsistency) through visual inspection of forest plots to assess the amount of overlap of CIs and the I^2 statistic, which quantified inconsistency across studies, to assess the impact of heterogeneity on the meta-analysis (Higgins 2002; Higgins 2003); we interpreted the I^2 statistic as follows (Deeks 2011).

- 0% to 40%: may not be important.
- 30% to 60%: may indicate moderate heterogeneity.
- 50% to 90%: may indicate substantial heterogeneity.
- 75% to 100%: considerable heterogeneity.

When we found heterogeneity, we determined possible reasons for it by examining individual study and subgroup characteristics.

Assessment of reporting biases

We obtained study protocols to assess for selective outcome reporting. Given the fact that we included only seven studies, we could not use funnel plots to assess small-study effects.

Data synthesis

We summarized data using a random-effects model in accordance with Cochrane Urology Editorial as likely to provide the more conservative effect size estimate (in most cases). We performed statistical analyses according to the statistical guidelines contained in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019). For dichotomous outcomes, we used the Mantel-Haenszel method; for continuous outcomes, we used the inverse variance method. We reported effect estimates for RCTs and NRSs separately when both were included in the review. We used Review Manager 5 software to perform analyses by pooling studies only when appropriate (Review Manager 2014).

Subgroup analysis and investigation of heterogeneity

We expected the following characteristics to introduce clinical heterogeneity. We planned to carry out subgroup analyses with investigation of interactions, but did not find any studies reported relevant data. If we have sufficient data, we will perform subgroup analysis accordingly.

- Patient age (younger than 65 years versus older than 65 or 65 years of age).
- Prostate volume (less than or equal to 40 mL versus greater than 40 mL).
- Severity of LUTS based on IPSS (score less than or equal to 19 [moderately symptomatic] versus score greater than 19 [severely symptomatic]).

These planned subgroup analyses were based on the following observations.

- Age is a well-known risk factor for BPH surgery. Elderly patients have a higher rate of postoperative complications compared with younger patients (Bhojani 2014; Pariser 2015). The age cut-off is based on the WHO definition of old age (WHO 2002).
- Outcomes and complications of ablative procedures, such as TURP, correlate with prostate volume (Reich 2008). The prostate volume cut-off > 40 cc is based on this being the most commonly used threshold to distinguish "small" from "large" for the indication of treatment with a 5-alpha reductase inhibitor (EAU 2020).
- The relationship between changes in IPSS scores and patient global ratings of improvement is influenced by baseline scores (Barry 1995).

Sensitivity analysis

We planned to perform sensitivity analyses only for RCTs (not non-RCTs) and limited to primary outcomes to explore the influence of the following factor (when applicable) on effect sizes.

- Restricting the analysis by taking into account risk of bias, by excluding studies at "high risk" or "unclear risk"

"Summary of findings" (SoF) tables

We presented the certainty of evidence for each outcome according to the GRADE approach (Guyatt 2008). For each comparison, two review authors (JHJ and BR) independently rated the certainty of evidence for each outcome as "high," "moderate," "low," or "very low" using GRADEpro GDT 2015 (Guyatt 2011a; Guyatt 2011b). We resolved any discrepancies by consensus or, if needed, by arbitration by a third review author (PD).

For RCTs, we took into account criteria related not only to internal validity (risk of bias, inconsistency, imprecision, and publication bias) but also to external validity, such as directness of results, when downgrading the certainty of evidence for a specific outcome (Schünemann 2011a; Schünemann 2011b). For NRS, we additionally considered three criteria for upgrading the certainty of evidence (large magnitude of effects, all plausible confounding that would reduce a demonstrated effect or suggest a spurious effect when results show no effect, and the dose-response gradient) (Schünemann 2011a; Schünemann 2011b). Based on recent guidance to rate the certainty of evidence of NRS in the context of GRADE, we noted that an initial rating of "high" was used, with appropriate consideration of the impact of lack of randomization leading to rating down for risk of bias according to the ROBINS-I tool (Schünemann 2018).

When RCTs and NRSs were considered together, we followed current GRADE guidance; if certainty of evidence differed in a body of RCTs and a body of NRSs, we presented SoF tables only with higher-certainty evidence; If certainty ratings were the same, we presented results from the two bodies of evidence separately. In addition, if results were consistent, then the overall certainty assessment was that of the two bodies of evidence. If results were inconsistent, and we believed both bodies of evidence should be taken into consideration, then we rated down further for this inconsistency (Schünemann 2018). We did not pool across bodies of evidence from RCTs and NRSs.

RESULTS

Description of studies

Details of included studies are presented elsewhere (Characteristics of included studies; Table 1; Table 2; Table 3).

Results of the search

We identified 2418 records through electronic database searching, including 87 records in trials registers. We found no records in the grey literature repository. We further identified one record through other sources by searching the reference lists of included study (protocol of Abt 2018 published in BMC Urology). After removing duplicates, we screened the titles and abstracts of 1028 records, and we excluded 989 records. We screened 39 full-text articles and excluded seven studies (10 records) that did not meet the inclusion criteria or were not relevant to the question under trial. Six studies (six records) are ongoing. We included a total of nine studies (seven RCTs: 17 records; two NRSs: six records) in the review. The flow of literature through the assessment process is shown in the PRISMA flowchart (Figure 1).

Figure 1. Flow diagram.

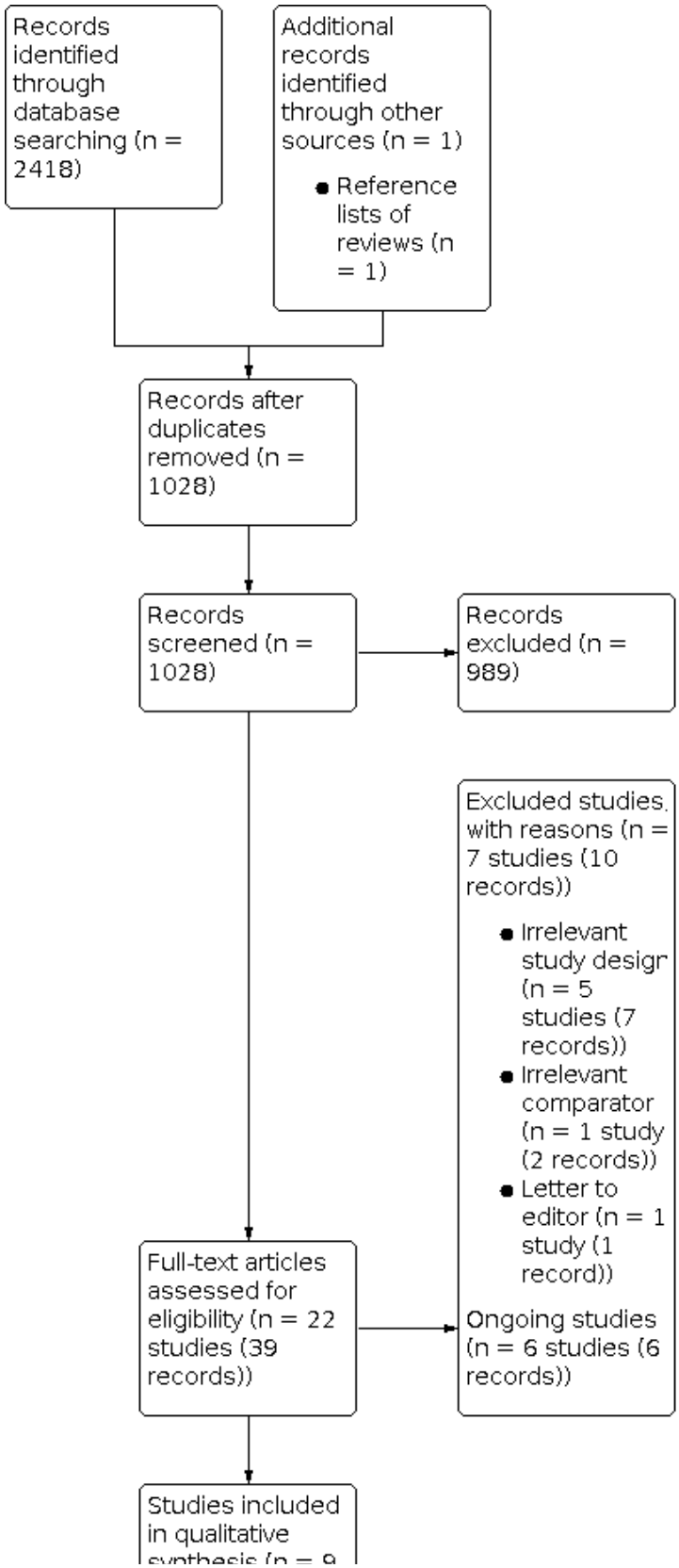
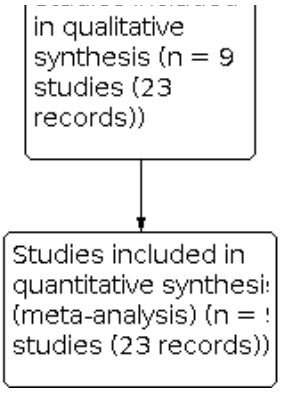


Figure 1. (Continued)



Included studies

1. RCTs

Sources of data

We identified the seven published full-text studies (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020; Pisco 2020; Radwan 2020; Zhu 2018). Six trials were published in English, and Zhu 2018 was published in Chinese. We attempted to contact all corresponding authors of included trials to obtain additional information on study methods and results, and we received replies from three (Abt 2018; Pisco 2020; Radwan 2020; see Appendix 3).

Study design and settings

All trials were likely single-center parallel randomized controlled trials that were conducted in various countries, namely, Brazil (Carnevale 2016), China (Gao 2014; Zhu 2018), Egypt (Radwan 2020), Portugal (Pisco 2020), Spain (Insausti 2020), and Switzerland (Abt 2018). Abt 2018 and Insausti 2020 were reported as "open label." Four studies did not provide information regarding blinding (Carnevale 2016; Gao 2014; Radwan 2020; Zhu 2018). Pisco 2020 blinded study participants only. The included studies were performed between the years 2007 and 2018.

Participants

The seven studies included 488 randomized participants (PAE 234, TURP 214, sham 40). Mean age, IPSS, and maximum flow rate (Qmax) were 65 years, 23.8, and 7.89 mL/s, respectively. Mean prostate volume was 62.6 mL.

Most studies included participants with LUTS as defined by an IPSS score greater than 7 despite medical treatment, and prostate volume between 20 and 100 mL. Five trials used uroflowmetry as an inclusion criterion (Qmax less than 15 mL/s: Abt 2018; Gao 2014; Insausti 2020; Pisco 2020; average flow less than 10 mL/s: Radwan 2020). Carnevale 2016 included participants based on bladder outlet obstruction confirmed by urodynamic evaluation (Bladder Outlet Obstruction Index > 40).

Major exclusion criteria relevant to all trials included urethral (e.g. urethral stricture) or bladder disorders (e.g. neurogenic bladder, bladder calculi, diverticula); renal failure; history of prostate, bladder neck, or urethral surgery; and suspected prostate cancer.

Intervention(s) and comparator(s)

All PAE procedures were conducted via a femoral approach under local anesthesia. In the included studies, an initial pelvic arteriogram was obtained to evaluate the iliac vessels and the prostatic arteries. Selective angiography of the internal iliac arteries was performed to better assess the blood supply to the prostate. After super-selective catheterization of the inferior vesicle arteries was performed to ensure that the tip of the microcatheter was inside or at the ostium of the prostatic arteries, embolization using microspheres (Abt 2018: 250 to 400 µm microspheres [Embozene, Boston Scientific, USA]; Carnevale 2016 and Zhu 2018: calibrated 300 to 500 µm tris-acryl gelatin microspheres [Embosphere Microspheres, Merit Medical, USA]; Gao 2014: 355 to 500 µm polyvinyl alcohol microspheres [Ivalon, Cook, USA]; Insausti 2020 and Pisco 2020: 300 to 500 µm poly(vinyl alcohol) microspheres [Bead Block BTG plc, Boston Scientific, USA]; Radwan 2020: not specified) was performed. Embolization was terminated when complete stasis was achieved, without reflux of the mixture to undesired arteries.

Six studies used TURP as a comparator. Monopolar or bipolar TURP (Abt 2018; Carnevale 2016: monopolar TURP; Gao 2014; Insausti 2020: bipolar TURP; Radwan 2020: both TURP techniques; Zhu 2018: not specified) was performed under spinal or general anesthesia.

One study used a sham procedure as a comparator (Pisco 2020). In the sham group, no embolization particles were injected after catheterization of the prostatic arteries.

Comparisons

Six studies included RCTs comparing PAE to TURP (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020; Radwan 2020; Zhu 2018); one study compared PAE to sham (Pisco 2020); no study compared PAE to laser ablation or enucleation of the prostate, or other minimally invasive therapies.

Outcomes

We identified reporting of all primary and secondary outcomes in each of the included studies. All included studies reported urologic symptom scores and quality of life outcomes except Radwan 2020 (only reported urologic symptom scores). Urologic symptom scores and quality of life were reported by IPSS (scale 0 to 35; higher scores indicating worse urologic symptoms) and IPSS-quality of life (scale 0 to 6; higher scores indicating worse

quality of life), respectively. Adverse events were classified by National Cancer Institute Common Toxicity Criteria for Adverse Events, version 4.0 (Carnevale 2016), or by the Clavien-Dindo Classification System (Abt 2018; Gao 2014; Insausti 2020; Pisco 2020). Adverse events classification system was not specified in the remaining studies. Abt 2018 reported all primary and secondary outcomes except re-treatment, which was assessed during follow-up. The Erectile function was reported by IIEF-5 (scale 1 to 25; higher scores indicating better erectile function) in two studies (Abt 2018; Carnevale 2016). Although we did not find any studies using a questionnaire to assess ejaculatory function, all studies except Gao 2014 (outcome not measured) reported data on ejaculatory disorders as reduction in ejaculate volume or retrograde ejaculation. Abt 2018 reported the duration (days) of indwelling catheter, and Gao 2014 provided the proportion of participants with indwelling catheter after intervention. Four studies reported hospital stay (days) (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020), but only two studies reported the data, which we were able to use for meta-analysis (Abt 2018; Gao 2014).

Gao 2014 reported both short-term and long-term follow-up outcomes (up to 24 months), and the remaining studies reported only short-term follow-up outcomes (Abt 2018; Carnevale 2016; Insausti 2020; Pisco 2020; Radwan 2020; Zhu 2018: up to 12 months).

Funding sources and conflicts of interest

Abt 2018 was supported by a grant from the research committee of St. Gallen Cantonal Hospital. Two studies were supported by device manufacturers (Insausti 2020; Pisco 2020). One study reported no external funding (Carnevale 2016), and the others did not report the funding source (Gao 2014; Radwan 2020; Zhu 2018).

Study authors of five included studies reported that they had no relevant conflicts of interest (Abt 2018; Carnevale 2016; Gao 2014; Pisco 2020; Radwan 2020). One study reported conflicts of interest of members of the investigative team with the device manufacturer (Insausti 2020), and the other study did not report the funding source (Zhu 2018).

2. NRSs (prospective comparative studies)

Sources of data

We identified two published studies (Ray 2018; Soluyanov 2018). Ray 2018 and Soluyanov 2018 were published in English and Russian, respectively. We attempted to contact all corresponding authors of included trials to obtain additional information on study methods and results, and we received replies from Ray 2018 (see Appendix 3).

Study design and settings

Ray 2018 was a multicenter registry-based NRS (UK-ROPE) with a propensity-matched pair analysis as a joint initiative between the British Society of Interventional Radiologists, the British Association of Urological Surgeons, and the National Institute for Health and Care Excellence. Soluyanov 2018 was a single center–based prospective NRS conducted in Russia.

Participants

We included 332 participants (PAE 224, TURP 108) who were analyzed in the included studies (Ray 2018; Soluyanov 2018). Mean age was 67 years. Mean prostate volume and IPSS were 87.1 mL and 21.4, respectively. Baseline characteristics of participants who underwent PAE versus TURP were significantly different in age, prostate volume, and postvoid residual in UK-ROPE (Ray 2018). Neither study reported its inclusion and exclusion criteria in detail (Ray 2018; Soluyanov 2018).

Intervention(s) and comparator(s)

Ray 2018 did not report its PAE technique in any detail, and Soluyanov 2018 performed PAE using 300 to 500 µm microspheres (product manufacturer: not described) under local anesthesia.

Both studies used TURP as a comparator (Ray 2018: monopolar or bipolar TURP; Soluyanov 2018: bipolar TURP). Ray 2018 did not provide information with regard to anesthesia, and Soluyanov 2018 performed TURP under spinal anesthesia.

Comparisons

Both studies compared PAE to TURP (Ray 2018; Soluyanov 2018). Soluyanov 2018 included more than two intervention groups - PAE, TURP, and transvesical adenectomy.

We found no study that compared PAE to sham (no treatment), laser ablation or enucleation of the prostate, or other minimally invasive therapies. UK-ROPE planned to report multiple comparisons with PAE and holmium laser enucleation of the prostate, but these data are not available.

Outcomes

We identified reporting of all review outcomes except indwelling urinary catheter outcomes in each of the included studies for comparisons with TURP (Ray 2018; Soluyanov 2018).

Urologic symptom scores and quality of life were reported using IPSS and IPSS-quality of life, respectively. Ray 2018 used Clavien-Dindo Classification to report adverse events, and Soluyanov 2018 did not provide details on measuring this outcome. Ray 2018 reported re-treatment, erectile function by IIEF-5 and the event of retrograde ejaculation during the follow-up period.

All NRSs reported short-term outcomes only except re-treatment (Ray 2018reported the outcome after 12 months [long term]).

Funding sources and conflicts of interest

UK-ROPE was supported by a medical device company, the British Society of Interventional Radiologists, and the British Association of Urological Surgeons. The National Institute for Health and Care Excellence funded an independent academic unit to run the registry through a competitive tender (Ray 2018). The other study did not mention a funding source (Soluyanov 2018).

Ray 2018 reported having relationships with medical device companies, and Soluyanov 2018 did not indicate any conflicts of interest.

Excluded studies

We excluded seven studies (10 records) out of 22 studies (39 records) after evaluating the full-text publications. Five studies used the wrong study design (Bagla 2017; Brown 2018; NCT01835860; Pereira 2018; Qiu 2017). Russo 2015 compared PAE to simple prostatectomy, which was outside the scope of this review (wrong comparator). One study was reported as a letter to the

editor (Bilhim 2015). Further details of the excluded studies are presented elsewhere (see Characteristics of excluded studies).

Studies awaiting classification and ongoing trials

We found no studies awaiting classification. Six studies including four RCTs - ACTRN12617001235392, NCT02006303, NCT02566551 and NCT04236687 - and two NRS - ChiCTR1800014818 and NCT01789840 - are ongoing. Details of these trials are presented elsewhere (see Characteristics of ongoing studies).

Risk of bias in included studies

1. RCTs

We found seven RCTs compared PAE to TURP (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020; Radwan 2020; Zhu 2018) or Sham (Pisco 2020). Only Gao 2014 reported anything beyond short term outcomes. Details are reported below; see also Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for randomised controlled studies. Categories: green point (+) = low risk of bias; yellow point (?) = unclear risk of bias; red point (-) = high risk of bias.

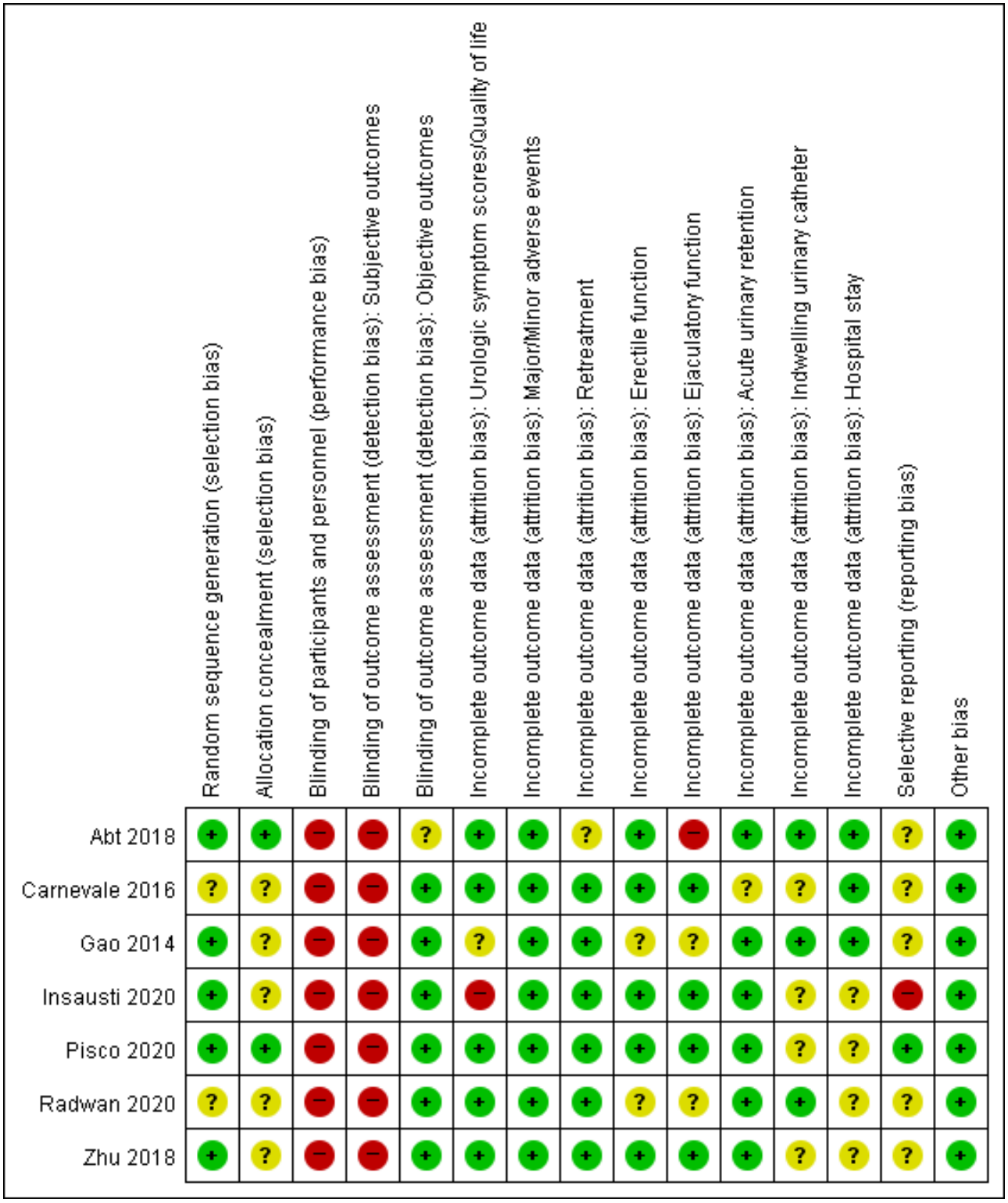
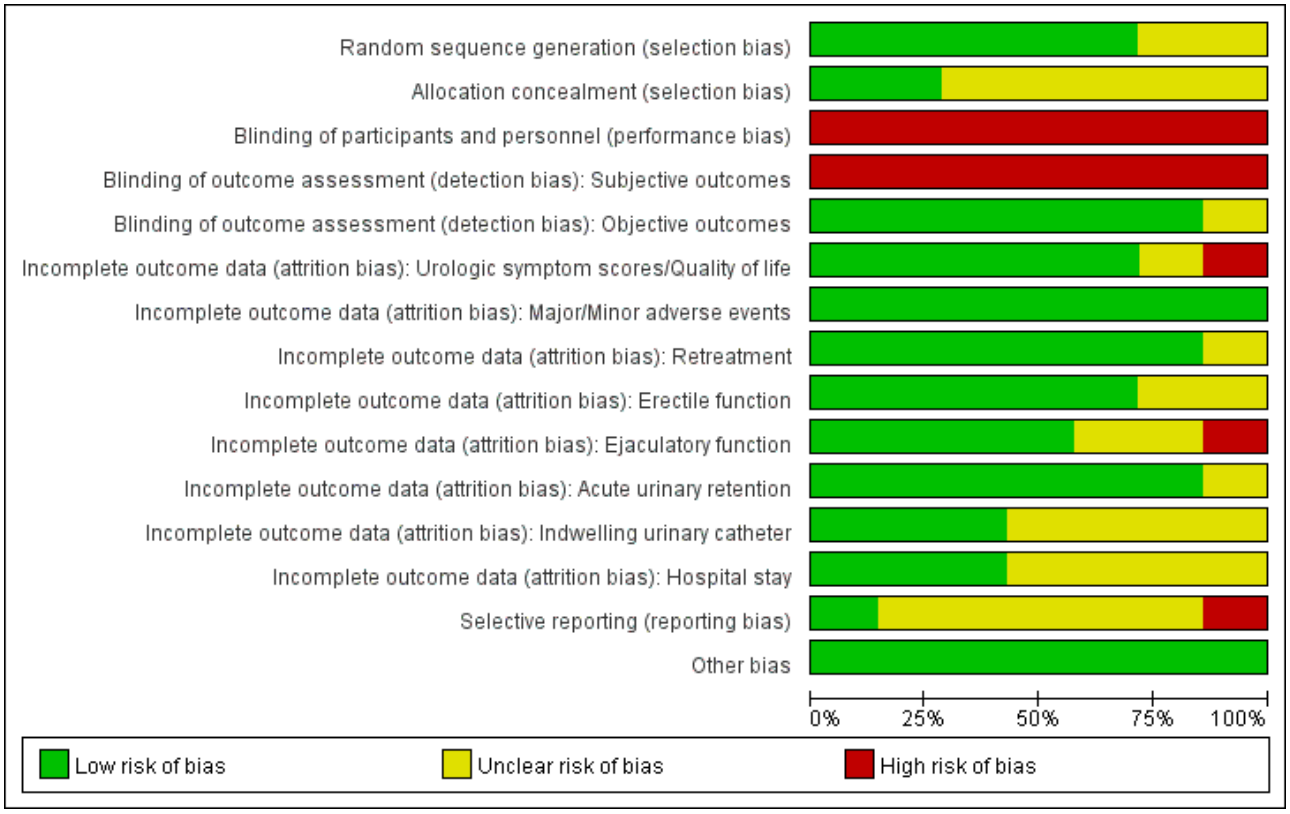


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included randomised controlled studies.



Allocation

Random sequence generation

We rated five studies as having low risk of bias (Abt 2018; Gao 2014; Insausti 2020; Pisco 2020; Zhu 2018), and we rated two study as having unclear risk of bias (Carnevale 2016; Radwan 2020).

Allocation concealment

We rated two studies as having low risk of bias (Abt 2018; Pisco 2020), and we rated the remaining studies as having unclear risk of bias due to lack of information on the allocation method (Carnevale 2016; Gao 2014; Insausti 2020; Radwan 2020; Zhu 2018).

Blinding

Blinding of participants and personnel

We rated all studies as having high risk of bias. Abt 2018 and Insausti 2020 were open-label studies. Pisco 2020 was a single-blind study. Although Carnevale 2016, Radwan 2020 and Zhu 2018 did not report any information on blinding, blinding appeared highly unlikely to have taken place in a surgical trial without specific measures, which would have found mention. In Gao 2014, study authors included participants after informing them about details of the procedure, thereby indicating lack of blinding.

Blinding of outcome assessment

- Subjective outcomes (urologic symptom scores, quality of life, major adverse events, erectile function, ejaculatory disorders, and minor adverse events): we judged all studies as having high risk of bias given lack of assurance of appropriate methods of blinding
- Objective outcomes (re-treatment, acute urinary retention, indwelling urinary catheter, and hospital stay): we rated all studies as having low risk of bias for these outcomes as they were unlikely to be affected by lack of blinding (ascertaining this does not involve judgment)

Incomplete outcome data

Gao 2014 reported both short-term and long-term (longer than 12 months' follow-up) outcome data, but the remaining studies reported only short-term outcomes (up to 12 months' follow-up). We rated the risk of bias separately for all outcomes in Gao 2014 according to the timing of outcome measurement (short-term or long-term), but judgments were the same for all outcomes; therefore, reporting was collapsed.

- Urologic symptom scores and quality of life: we rated five studies as having low risk of bias (Abt 2018; Carnevale 2016; Pisco 2020; Radwan 2020; Zhu 2018); we judged Gao 2014 and Insausti 2020 as having unclear and high risk of bias, respectively.
- Major and minor adverse events: we rated all studies as having low risk of bias.
- Re-treatment: we rated six studies as having low risk of bias (Carnevale 2016; Gao 2014; Insausti 2020; Pisco 2020; Radwan 2020; Zhu 2018); we judged one study as having unclear risk of bias (Abt 2018).
- Erectile function: we rated five studies as having low risk of bias (Abt 2018; Carnevale 2016; Insausti 2020; Pisco 2020; Zhu 2018);

we judged the remaining studies as having unclear risk of bias (Gao 2014; Radwan 2020)

- Ejaculatory disorders: we rated four studies as having low risk of bias (Carnevale 2016; Insausti 2020; Pisco 2020; Zhu 2018); we judged the others as having unclear - Gao 2014 and Radwan 2020 - or high - Abt 2018 - risk of bias.
- Acute urinary retention: we rated six studies as having low risk of bias (Abt 2018; Gao 2014; Insausti 2020; Pisco 2020; Radwan 2020; Zhu 2018); we judged Carnevale 2016 as having unclear risk of bias.
- Indwelling urinary catheter: we rated only three studies as having low risk of bias (Abt 2018; Gao 2014; Radwan 2020); we judged four studies as having unclear risk of bias (Carnevale 2016; Insausti 2020; Pisco 2020; Zhu 2018).
- Hospital stay: we rated three studies as having low risk of bias (Abt 2018; Carnevale 2016; Gao 2014); we judged the remaining studies as having unclear risk of bias (Insausti 2020; Pisco 2020; Radwan 2020; Zhu 2018).

Selective reporting

We rated only one study as having low risk of bias (Pisco 2020). We rated four studies as having unclear risk of bias given lack of available protocols - Carnevale 2016, Gao 2014, Radwan 2020 and Zhu 2018 - or reporting of study outcomes that were not predefined in the protocol - Abt 2018. We judged one study as having high risk of bias due to deviation in study outcomes from the protocol (Insausti 2020).

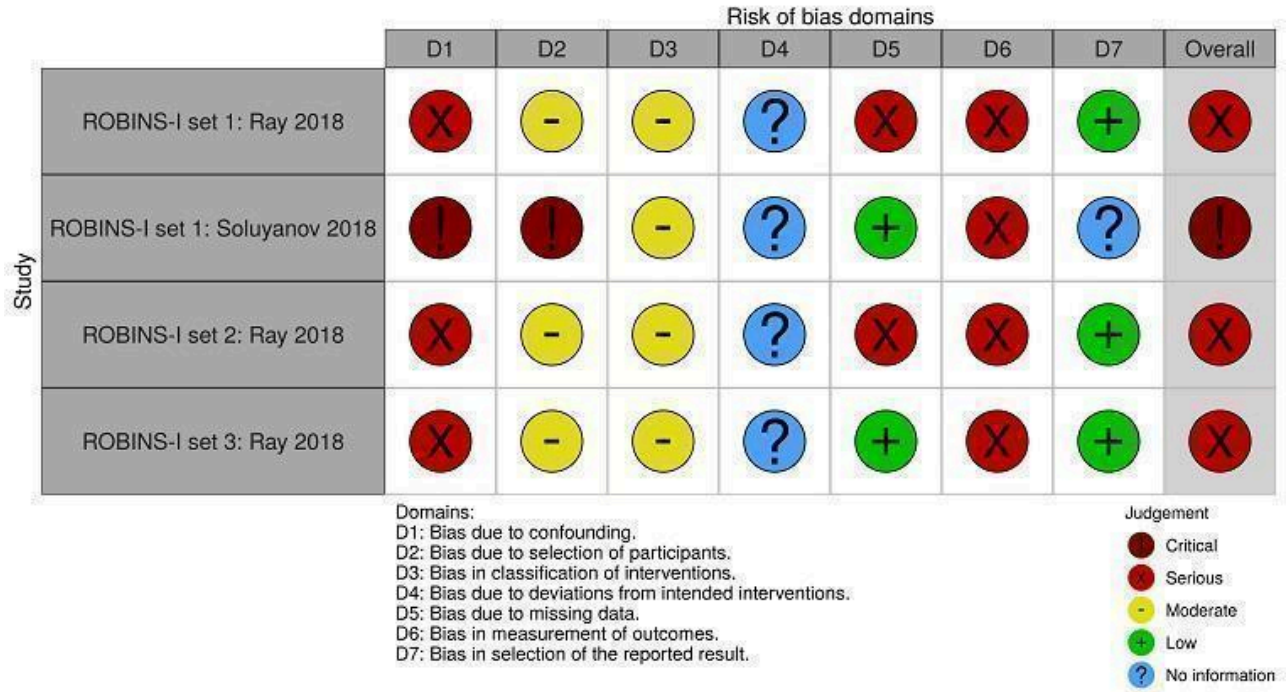
Other potential sources of bias

We rated all studies as having low risk of bias; we identified no other sources of bias.

2. NRSs (prospective comparative studies)

We found two prospective comparative studies (Ray 2018; Soluyanov 2018) comparing PAE to TURP for short-term only. For reporting purposes, we have split the risk of bias assessments for the outcomes into 3 sets. Within each set of outcomes the risk of bias assessments were the same across all domains. Set 1: urologic symptom scores; Set 2: quality of life, erectile function, ejaculatory disorders, and hospital stay; Set 3: major adverse events, re-treatment, minor adverse events, and acute urinary retention. No study reported indwelling catheter (no information). Overall, we judged outcomes in set 1 (Urologic symptom scores) to be at critical risk of bias for Soluyanov 2018 and serious risk of bias overall for Ray 2018 (Figure 4, Table 4). Outcome sets 2 and 3 were reported only by Ray 2018 and these we judged to be at serious risk of bias (Figure 4, Table 5). Details of risk of bias from NRSs using ROBINS-I are presented in Figure 4, Table 4, Table 5, and Appendix 4.

Figure 4. Risk of bias summary: ROBINS-I set 1 includes outcome: urologic symptom scores; ROBINS-I set 2 includes outcomes: quality of life, erectile function, ejaculatory disorders, hospital stay; ROBINS-I set 3 includes outcomes: adverse events, re-treatment, acute urinary retention; ROBINS-I set 4 includes outcome (not reported in both studies): indwelling catheter measured at up to 12 months (short term). Figure created using robvis: https://www.riskofbias.info/welcome/robvis-visualization-tool.



Effects of interventions

See: **Summary of findings 1** PAE compared to TURP for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (short term); **Summary of findings 2** PAE compared to TURP for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (long term); **Summary of findings 3** PAE compared to sham for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (short term)

Details are presented elsewhere (see Summary of findings 1; Summary of findings 2; Summary of findings 3).

PAE versus TURP (short term)

Primary outcomes

1. Urologic symptom scores

We included six RCTs with 369 participants (PAE 173, TURP 196) in the analysis for urologic symptom scores (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020; Radwan 2020; Zhu 2018). There may be little to no difference between PAE and TURP in improvement of IPSS (mean difference [MD] 1.55, 95% confidence interval [CI] -0.40 to 3.50; I^2 = 75%; low-certainty evidence). We downgraded the certainty of evidence for serious study limitations (-1) and for serious inconsistency (-1); we did not downgrade further for imprecision, since we attributed the wide confidence intervals to the observed inconsistency.

We included one prospective NRS with 161 participants (PAE 132, TURP 29) (Ray 2018). We are very uncertain about the effect on urologic symptom scores (MD 2.80, 95% CI 0.04 to 5.56; very low-certainty evidence). We downgraded the certainty of evidence for very serious study limitations (-2) and for serious imprecision (-1).

Based on evidence from RCTs that provided evidence of higher certainty, there may be little to no difference between these procedures in the improvement of urologic symptom scores (low-certainty evidence; Analysis 1.1).

2. Quality of life

We included five RCTs with 309 participants (PAE 153, TURP 156) in the analysis for quality of life (Abt 2018; Carnevale 2016; Gao 2014; Insausti 2020; Zhu 2018). There may be little to no difference between PAE and TURP in quality of life improvement (MD 0.16, 95% CI -0.37 to 0.68; I^2 = 56%; low-certainty evidence). We downgraded the certainty of evidence for serious study limitations (-1) and for serious inconsistency (-1); we did not downgrade further for imprecision, since we attributed the wide confidence intervals to the observed inconsistency.

We included one prospective NRS with 164 participants (PAE 133, TURP 31) (Ray 2018). We are very uncertain about the effect on quality of life (MD 0.50, 95% CI -0.03 to 1.03; very low-certainty evidence). We downgraded the certainty of evidence for very serious study limitations (-2) and for serious imprecision (-1).

Based on the evidence from RCTs that provided evidence of higher certainty, there may be little to no difference between PAE and TURP in quality of life (low-certainty evidence; Analysis 1.2).

3. Major adverse events

Based on the findings of four RCTs with 250 participants (PAE 114, TURP 136) (Abt 2018; Carnevale 2016; Insausti 2020; Radwan 2020), we are very uncertain about the effects of PAE on major adverse events (risk ratio [RR] 0.71, 95% CI 0.16 to 3.10; I^2 = 26%; very low-certainty evidence); this corresponds to 15 fewer (95% CI 43 fewer to 108 more) major adverse events per 1000 participants. We rated the certainty of evidence as very low, downgrading for serious study limitations (-1) and for very serious imprecision (-2).

Based on one prospective NRS with 305 participants (PAE 216, TURP 89) (Ray 2018), no major adverse events were reported in either study group (very low-certainty evidence). We rated the certainty of evidence as very low, after downgrading for very serious study limitations (-2) and for very serious imprecision (-2).

Based on the entire body of evidence that included both RCTs and non NRS, we are very uncertain whether PAE results in fewer or more major adverse events than TURP (very low-certainty evidence; Analysis 1.3).

Secondary outcomes

1. Re-treatment

Based on three RCTs with 204 participants (PAE 92, TURP 112) (Carnevale 2016; Gao 2014; Radwan 2020), PAE may increase re-treatment rates (RR 3.64, 95% CI 1.02 to 12.98; I^2 = 0%; low-certainty evidence); this corresponds to 47 more (95% CI 0 fewer to 214 more) major adverse events per 1000 participants. We downgraded the certainty of evidence for serious study limitations (-1) and for very serious imprecision (-1).

We are very uncertain about the effects of PAE on re-treatment based on one prospective NRS (RR 1.51, 95% CI 0.43 to 5.29; very low-certainty evidence); this corresponds to 17 more (95% CI 19 fewer to 145 more) major adverse events per 1000 participants (Ray 2018). We downgraded the certainty of evidence for very serious study limitations (-2) and very serious imprecision (-2).

Based on evidence from RCTs that provided evidence of higher certainty, PAE may increase re-treatment rate (low-certainty evidence; Analysis 1.4).

2. Erectile function

Based on two RCTs with 129 participants (PAE 63, TURP 66) (Abt 2018; Carnevale 2016), we are very uncertain about the effects of PAE on erectile function (MD -0.03, 95% CI -6.35 to 6.29; I^2 = 78%; very low-certainty evidence). We downgraded the certainty of evidence for serious study limitations (-1), serious inconsistency (-1), and for very serious imprecision (-2).

Based on one prospective NRS with 122 participants (PAE 102, TURP 20) (Ray 2018), we are very uncertain about the effects of PAE on erectile function (MD 1.50, 95% CI -2.01 to 5.01; very low-certainty evidence). We downgraded the certainty of evidence for very serious study limitations (-2) and for serious imprecision (-1).

Based on the entire body of evidence that included RCTs and non NRS, we are very uncertain about effects on erectile function of these two procedures (very low-certainty evidence; Analysis 1.5).

3. Ejaculatory disorders

We included three RCTs with 141 participants (PAE 71, TURP 70) in the analysis for ejaculatory disorders (Abt 2018; Carnevale 2016; Insausti 2020). We are uncertain how PAE effects this outcome (RR 0.26, 95% CI 0.06 to 1.19; I^2 = 83%; very low-certainty evidence); this would correspond to 476 fewer ejaculatory disorders per 1000 men (95% CI 604 fewer to 122 more). We rated the certainty of evidence as very low, downgrading for serious study limitations (-1) and for very serious imprecision (-2).

We included one prospective NRS with 260 participants (PAE 199, TURP 61) in the analysis for ejaculatory disorders (Ray 2018). PAE may reduce ejaculatory disorders (RR 0.51, 95% CI 0.35 to 0.73; low-certainty evidence); this would correspond to 233 fewer ejaculatory disorders per 1000 men (95% CI 309 fewer to 128 fewer). We rated the certainty of evidence as low, downgrading for very serious study limitations (-2).

Based on the body of evidence from NRS that provided evidence of higher certainty, PAE may reduce ejaculatory disorders (low-certainty evidence; Analysis 1.6).

4. Minor adverse events

We included three RCTs with 189 participants (PAE 83, TURP 106) in the analysis for minor adverse events (Abt 2018; Carnevale 2016; Radwan 2020). We are very uncertain about the effects of PAE on minor adverse events (RR 0.83, 95% CI 0.41 to 1.69; I^2 = 73%; very low-certainty evidence); this would correspond to 77 fewer minor adverse events per 1000 men (95% CI 267 fewer to 312 more). We downgraded the certainty of evidence for serious study limitations (-1), serious inconsistency (-1), and for very serious imprecision (-2).

We included one prospective NRS with 305 participants (PAE 216, TURP 89) in the analysis for minor adverse events (Ray 2018). We are very uncertain about the effects of PAE on minor adverse events (RR 2.27, 95% CI 0.51 to 10.02; very low-certainty evidence); this would correspond to 74 fewer minor adverse events per 1000 men (95% CI 180 more to 115 fewer). We downgraded the certainty of evidence for very serious study limitations (-2) and for very serious imprecision (-2).

Based on the entire body of evidence, we are very uncertain about the effects of PAE on minor adverse events (very low-certainty evidence; Analysis 1.7).

5. Acute urinary retention

We included five RCTs with 367 participants (PAE 173, TURP 194) in the analysis for acute urinary retention (Abt 2018; Gao 2014; Insausti 2020; Radwan 2020; Zhu 2018). We are very uncertain about the effects of PAE on acute urinary retention (RR 1.65, 95% CI 0.54 to 5.07; I^2 = 44%; very low-certainty evidence). PAE may result in 37 more acute urinary retention events per 1000 men (95% CI 26 fewer to 231 more). We downgraded the certainty of evidence for serious study limitations (-1) and for very serious imprecision (-2).

We included one prospective NRS with 305 participants (PAE 216, TURP 89) in the analysis for acute urinary retention (Ray 2018). No acute urinary retention episodes were reported in either group (very low-certainty evidence). We downgraded the certainty of evidence for very serious study limitations (-2) and for very serious imprecision (-2).

Based on the entire body of evidence, we are very uncertain about effects of these procedures on acute urinary retention (very low-certainty evidence; Analysis 1.8).

6. Indwelling urinary catheter

Based on only one RCT with 99 participants (PAE 48, TURP 51) (Abt 2018), PAE likely reduces time with an indwelling urinary catheter (MD -2.00, 95% CI -2.55 to -1.45; moderate-certainty evidence) (Analysis 1.9). We rated the certainty of evidence as moderate, after downgrading for study limitations (-1). No NRS reported this outcome.

7. Hospital stay

Based on only two RCTs with 206 participants (PAE 102, TURP 104) (Abt 2018; Gao 2014), PAE likely reduces hospital stay (MD -1.96, 95% CI -2.36 to -1.57; I^2 = 0%; moderate-certainty evidence) (Analysis 1.10). We rated the certainty of evidence as moderate, after downgrading for study limitations (-1). No NRS reported this outcome.

Subgroup and sensitivity analyses

We were unable to perform any predefined secondary analyses because there were no relevant data and the included studies had a similar risk of bias.

PAE versus TURP (long term)

The analysis for primary outcomes was informed by a single RCT (Gao 2014). We included 95 participants (PAE 47, TURP 48) in the analysis for urologic symptom scores and quality of life and 107 participants (PAE 54, TURP 53) in the analysis for major adverse events.

We included one NRS with 305 participants (PAE 216, TURP 89) in the analysis for re-treatment and one RCT with 107 participants (PAE 54, TURP 53) in the analysis for minor adverse events.

Primary outcomes

1. Urologic symptom scores

We are very uncertain about the effects of PAE on urologic symptom scores compared to TURP (MD 0.30, 95% CI -3.17 to 3.77; very low-certainty evidence). We rated the certainty of evidence as very low, downgrading for serious study limitations (-1) and very serious imprecision (-2) (Analysis 2.1).

2. Quality of life

PAE may result in little to no difference in quality of life (MD 0.20, 95% CI -0.49 to 0.89; low-certainty evidence). We rated the certainty of evidence as low, downgrading for serious study limitations (-1) and for serious imprecision (-1) (Analysis 2.2).

3. Major adverse events

We are very uncertain about the effects of PAE on major adverse events (RR 1.96, 95% CI 0.63 to 6.13; very low-certainty evidence). PAE would result in 72 more major adverse events per 1000 men (95% CI 28 fewer to 387 more). We downgraded the certainty of evidence to very low due to serious study limitations (-1) and very serious imprecision (-2) (Analysis 2.3).

Secondary outcomes

1. Re-treatment

PAE may increase re-treatment rates (RR 3.54, 95% CI 1.45 to 8.65; low-certainty evidence); this corresponds to 47 more (95% CI 0 fewer to 214 more) major adverse events per 1000 participants. We downgraded the certainty of evidence for serious study limitations (-2) (Analysis 2.4).

2. Erectile function

This outcome was not reported by the included study.

3. Ejaculatory disorders

This outcome was not reported by the included study.

4. Minor adverse events

We are very uncertain about the effects of PAE on minor adverse events (RR 1.66, 95% CI 0.94 to 2.94; very low-certainty evidence). PAE would result in 162 more minor adverse events per 1000 men (95% CI 15 fewer to 476 fewer). We rated the quality of evidence as very low, after downgrading for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 2.5).

5. Acute urinary retention

This outcome was not reported by the included study.

6. Indwelling urinary catheter

This outcome was not reported by the included study.

7. Hospital stay

This outcome was not reported by the included study.

Subgroup and sensitivity analyses

We were unable to perform any predefined secondary analyses because there were no relevant data and the included studies had a similar risk of bias.

PAE versus sham (short term)

This analysis was informed by a single RCT (Pisco 2020). We included 80 participants (PAE 40, TURP 40) in the analysis for all review outcomes.

Primary outcomes

1. Urologic symptom scores

PAE likely improves urologic symptom scores (MD -12.07, 95% CI -15.45 to -8.69; moderate-certainty evidence). We rated the certainty of evidence as moderate, after downgrading for serious study limitations (-1) (Analysis 3.1).

2. Quality of life

PAE likely improves quality of life (MD -1.97, 95% CI -2.48 to -1.46; moderate-certainty evidence). We rated the certainty of evidence as moderate, after downgrading for serious study limitations (-1) (Analysis 3.2).

3. Major adverse events

No major adverse events were reported in either study group (very low-certainty evidence). We rated the certainty of evidence as very low, after downgrading for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 3.3).

Secondary outcomes

1. Re-treatment

No re-treatment was reported in either study group (very low-certainty evidence). We rated the certainty of evidence as very low, after downgrading for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 3.4).

2. Erectile function

This outcome was not reported by the included study.

3. Ejaculatory disorders

We are very uncertain about the effects of PAE versus Sham on ejaculatory disorders; given no events in either group no effect size could be calculated (very low-certainty evidence). We rated down for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 3.5).

4. Minor adverse events

We are very uncertain about effects of PAE on minor adverse events (RR 1.08, 95% CI 0.58 to 1.99; very low-certainty evidence). PAE would result in 26 more minor adverse events per 1000 men (95% CI 137 fewer to 322 fewer). We rated down for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 3.6).

5. Acute urinary retention

We are very uncertain about the effects of PAE versus Sham on acute urinary retention; given no events in either group no effect size could be calculated (very low-certainty evidence). We rated down for serious study limitations (-1) and for very serious imprecision (-2) (Analysis 3.7).

6. Indwelling urinary catheter

This outcome was not reported by the included study.

7. Hospital stay

This outcome was not reported by the included study.

Subgroup and sensitivity analyses

We were unable to perform any predefined secondary analyses because there were no relevant data and the included studies had a similar risk of bias.

DISCUSSION

Summary of main results

We found evidence to inform two comparisons, namely, prostatic arterial embolization (PAE) versus transurethral resection of the prostate (TURP) and PAE versus a sham procedure. Mean age, International Prostate Symptom Score (IPSS), and prostate volume of participants were 66 years, 22.8, and 72.8 mL, respectively.

PAE versus TURP

Based on short-term data (up to 12 months' follow-up) from both randomized controlled trials (RCTs) and prospective comparative non-randomized studies (NRSs), PAE may result in a somewhat lesser but overall similar improvement in urologic symptom score

and in quality of life. While we are very uncertain as to whether PAE results in more or fewer major adverse events, PAE may increase re-treatment rates. Although there was uncertainty about its effects on erectile function, PAE may reduce ejaculatory disorders.

As to longer-term outcomes (greater than 12 months' follow-up), we are very uncertain about how PAE affects symptom score compared to TURP, but we found that quality of life may be similarly improved. We are very uncertain as to whether PAE results in more or fewer major adverse events. While PAE may increase re-treatment rates, we found no evidence to inform the outcomes of erectile dysfunction, and ejaculatory disorders.

PAE versus sham

PAE likely improves urologic symptom scores and quality of life. No major adverse events or re-treatment was reported in either study group. We found no evidence to inform the outcomes of erectile function, and no ejaculatory disorders were reported in either study group.

We were unable to perform any of the predefined secondary analyses for both comparisons based on patient age, prostate volume, or severity of lower urinary tract symptoms (LUTS).

Overall completeness and applicability of evidence

The studies included in this review have important limitations.

- Although the included studies were performed across the world (Asia, Europe, and Latin America), these studies were likely each conducted at single-center locations. Given our focus on comparative effectiveness versus other treatment modalities, and in accordance with our published protocol, we excluded single-armed NRSs and included only comparative studies. This forms a fairly narrow evidence base. Several prospective trials appear ongoing (Characteristics of ongoing studies); their findings may be highly valuable in improving our understanding of the role of PAE in the armamentarium to treat male LUTS secondary to benign prostatic hyperplasia (BPH).
- We found additional retrospective case-control studies (not included, in accordance with our protocol) to inform the two comparisons of PAE versus prostatic urethral lift (PUL) and PAE versus photoselective vaporization of the prostate (PVP); however as expected, these studies provided only evidence of very low certainty, mainly due to very serious study limitations. An ongoing trials compared PAE to PVP, may help inform this particular comparison (NCT02006303). Given the rapid pace of change in the surgical treatment of BPH (e.g. continuing decline of TURP, increased use of laser vaporization and other techniques) in routine clinical practice, more studies comparing PAE to other modalities are needed (Malaeb 2012).
- We were unable to conduct any of our predefined subgroup analyses for factors such as patient age, prostate volume, or LUTS severity, which may be important effect modifiers.
- Although the studies in this review included men with a large prostate (ranging from 80 to 100 mL) as a subset, most participants had smaller prostate volumes - less than 80 mL. Currently, simple prostatectomy and laser enucleation procedures remain the standard treatments for men with gland size greater than 80 to 100 mL; PAE may have a potential role in treating men with a very large prostate (> 80 mL) (Bhatia 2018; Wang 2015). Therefore, studies about effects of PAE in this population would be of particular interest.
- More than half the PAE studies did not report on the technical success rate of PAE (Abt 2018; Insausti 2020; Pisco 2020; Radwan 2020; Ray 2018; Zhu 2018). Given that the technical success of PAE depends on the expertise of intervention radiologists, this would be a topic of interest. Widespread adoption of PAE (as for any other newer surgical treatment modality) would likely require specialized training and quality assurance.
- Each included study used a different TURP method (monopolar or bipolar) as a comparator. Given the reported lower rate of adverse events with bipolar TURP (Omar 2014), studies comparing monopolar TURP versus bipolar TURP may overestimate the risk of adverse events.
- Three studies did not report how they categorized the severity of adverse events (Carnevale 2016; Soluyanov 2018; Zhu 2018), and Young 2017 has expressed concerns that the classified numbers of participants with adverse events used in Gao 2014 were not accurate. Although Gao 2014 chose to label technical and clinical failures as major complications in the PAE group, these researchers did not consider hemorrhage requiring blood transfusion as a major complication in the TURP group.
- The existing body of evidence is limited to relatively short-term outcomes (up to 12 months' follow-up); only one study provided outcomes up to of 24 months in duration (Gao 2014). This appears insufficient to provide assurance of long-term effectiveness, namely, with regard to comparative re-treatment rates. However, the same is unfortunately true for many other surgical techniques to treat BPH. More high-quality studies with long-term follow-up are needed to address these limitations.
- In accordance with our published and peer-reviewed protocol (Jung 2017), this review focuses on outcomes of direct patient importance; therefore, it does not provide information on maximum urinary flow nor on postvoid residuals.

Quality of the evidence

For evidence from RCTs, we downgraded the certainty of evidence for study limitations and imprecision.

- Study limitations: we downgraded for unclear risk of selection bias and high risk of blinding of participants, personnel, and outcome assessors.
- Imprecision: confidence intervals were wide and crossed the assumed threshold of a clinically important difference.

For evidence from NRSs, we also downgraded the certainty of evidence for study limitations and imprecision.

- Study limitations: We judged studies to be at critical risk of bias due to known or unknown of confounding variables even though Ray 2018 made some attempt to (incompletely) adjust for these using statistical methods. In addition, we had major concerns about detection bias in the absence of any efforts to blind outcome assessors.
- Imprecision: confidence intervals were wide and crossed the assumed threshold of a clinically important difference.

Potential biases in the review process

Despite a comprehensive search strategy with no publication or language restrictions, we may have missed additional RCTs that

may be unpublished and/or were published in languages other than English. The small number of studies included in this review was insufficient to generate funnel plots; therefore, the risk of publication bias may have been underestimated.

Agreements and disagreements with other studies or reviews

A recent systematic review (by the authors of an included trial [Abt 2018]) found that PAE may not be as effective as TURP in improving urologic symptom score but may have a more favorable side effect profile (Zumstein 2018). Study authors called for additional high-quality trials with longer-term follow-up, and we concur.

A more recent review that included nine studies including RCTs and comparative NRSs also reported similar results (Xu 2020). The review authors found that the IPSS (mean difference [MD] 2.50, 95% confidence interval [CI] 0.78 to 4.21) and quality of life (MD 0.40, 95% CI 0.09 to 0.71) were better more improved after TURP than PAE but did not take minimal clinical important differences in consideration in their interpretation. They also found that PAE was associated with a lower sexual dysfunction rate (odd ratio [OR] 0.24, 95% CI 0.15 to 0.39) and less complications (OR 0.57, 95% CI 0.21 to 1.55) compared with TURP. A systematic review by Malling 2019 based their conclusions on indiscriminate pooling of RCTs and NRSs including comparative and non-comparative studies. Other systematic reviews and meta-analyses based on single-arm studies have also consistently reported significant improvement in urologic symptom scores and in quality of life after PAE (Kuang 2017; Pyo 2017). However, we would caution against taking these reported findings, which included all study designs including case series, at face value, given their major risk of bias.

Shim 2017, which is another systematic review that included comparative and non-comparative studies, was criticized by Narayan 2017 for considerable shortcomings in its assessment of risk of bias and data synthesis, thus questioning the validity of its findings. These review authors found that PAE improved International Prostate Symptom Score (IPSS) (MD -12.77, 95% CI -15.04 to -10.50) and quality of life (MD -2.34, 95% CI -2.72 to -1.97). This review also reported that PAE had inferior effectiveness with regard to IPSS (standardized mean difference [SMD] 0.88, 95% CI 0.10 to 1.66) yet a similar effect on quality of life (SMD 0.25, 95% CI -0.28 to 0.77) when compared to control (TURP or simple prostatectomy) based on three comparative studies (Carnevale 2016; Gao 2014; Russo 2015). The incidence rate of adverse events was higher for PAE (41.6%) when compared to control (30.4%).

In terms of individual studies other than RCTs and NRSs, single-armed cohort studies should have a limited role in informing comparative effectiveness in settings such as this, where several effective treatment modalities exist and define the standard of care. Pisco 2016 reported a single-armed cohort study with 630 consecutive men with BPH and moderate to severe LUTS refractory to medical therapy who were followed for a median of 2 years. Participants reported a large reduction in IPSS (long term: mean change -16.94, standard deviation [SD] 8.70) and quality of life (long term: mean change -1.74, SD 1.45). A cumulative clinical success rate, defined as improved symptoms (IPSS ≤ 15 points and a decrease ≥ 25% from the baseline score), improved quality of life (quality of life score ≤ 3 points or a decrease of at least 1 point from baseline), and no need for any medical or other therapy after PAE at long-term follow-up, was met by 76.3% (95% CI 68.6% to 82.4%) of participants. This study reported two major complications - bladder wall ischemia and persistent perineal pain - in addition to a total of 555 minor adverse events (Pisco 2016).

We found one study comparing PAE to open simple prostatectomy (Russo 2015). PAE was inferior to open simple prostatectomy in terms of symptoms (IPSS: 10.4 vs 4.31) and maximum flow rate (Qmax) (16.89 vs 23.82) one year after the procedures. PAE had a lower rate of adverse events compared to open surgery (8.25% versus 32.25%). We excluded this trial from the present review comparing PAE to open simple prostatectomy as open surgery, as we did not consider open simple prostatectomy as a comparator of relevance given its considerable morbidity and fading appeal compared to less invasive surgical alternatives (Parsons 2015).

Guideline recommendations based on this evidence base are currently contradictory and potentially in flux, thereby emphasizing the importance of this up-to-date review. Specifically, current American Urological Association guideline recommends against the use of PAE outside of clinical trials (McVary 2019). Meanwhile, guidance provided by the National Institute for Health and Care Excellence (NICE) indicates that PAE is a treatment option for LUTS caused by BPH (NICE 2018). This guidance was in part informed by the UK-ROPE study, which was run by UK interventional radiologists and urologic surgeons (Ray 2018). More recent guideline of European Association of Urology recommends that PAE can be offered to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal objective outcomes (e.g. urological symptoms and urodynamic parameters such as flow rate) when compared to TURP (EAU 2020).

AUTHORS' CONCLUSIONS

Implications for practice

The main implications for clinical practice can be drawn from the comparison to TURP that has long been considered the treatment reference standard. Compared to TURP and based on short-term follow-up, the impact on urologic symptoms and quality of life improvement as perceived by patients appears to be similar. This review did reveal major uncertainty as to how major adverse events compare. PAE may increase re-treatment rates and have an uncertain effects on erectile function.

This review found that PAE may reduce the incidence of ejaculatory disorders over the short term compared to TURP, which is an important consideration for some men. The rate of ejaculatory disorders in the largest, non-randomized study by Ray 2018, which is also known as the UK-ROPE study, was 24.1% (48/199). A Cochrane Review on convective radiofrequency water vapor thermal therapy (REZUM) found that it may not adversely impact ejaculatory function compared to sham at three months (Kang 2020), but no longer-term studies with an active control exist, which represents a major limitation. A Cochrane Review on the prostatic urethral lift procedure (Urolift) found that it probably preserved ejaculatory function better at both short-term (up to 12 months) and long-term assessment (up to 24 months) (Jung 2019).

For longer-term follow-up of PAE versus TURP beyond 12 months, we found only evidence of very low certainty and therefore are very uncertain about the effects on urologic symptom scores, major

adverse events, and minor adverse events. While quality of life appear to be similar, PAE may increase the need of re-treatment.

Compared to a sham procedure with short-term follow-up, PAE likely improves urologic symptom score and quality of life. No major adverse events or re-treatments were reported in either study group. Although we found no evidence to inform the outcome of erectile function, no ejaculatory problems were reported in either study group. This analysis was based on a single study (Pisco 2020), in which these outcomes were compared with those for convective radiofrequency water vapor thermal therapy (Kang 2020), as well as the prostatic urethral lift procedure (Jung 2019), and it should be noted that enrolled patients with severe LUTS (median IPSS 25.5) and quite a large prostate (median 63.5 mL) limit comparability.

Implications for research

A variety of minimally invasive surgeries such as PULand convective radiofrequency water vapor thermal therapy have recently become available (McVary 2018; Roehrborn 2017). In addition, less invasive techniques than open simple prostatectomy for very large prostates, such as robotic assisted laparoscopic prostatectomy and laser enucleation of the prostate, are increasingly accepted as appropriate treatment approaches by current evidence-based guidelines (EAU 2020; McVary 2019). Given the low and very low certainty of evidence found for PAE, additional research studies of better quality comparing PAE to TURP and newer evolving treatment alternatives appear essential. Future trials should be conducted according to higher methodological standards with regard to allocation concealment and blinding to minimize concerns about selection, performance, and detection bias. These studies also need to provide long-term data across treatment modalities.

Given that PAE outcomes are hampered by technical issues related to variations in arterial anatomy, PAE techniques should be standardized for indication, preoperative evaluation, approach method (e.g. transfemoral, transbrachial), and type of embolization material.

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We have based parts of the Assessment of risk of bias in included studies, Risk of bias in included studies as well as Figure 4, Table 4 Table 5, and Appendix 4 with regard to non-randomized study on a guidance under the Cochrane Methods. We used the robvis app (https://www.riskofbias.info/welcome/robvis-visualization-tool: free, online and recommended by the ROBINS-I team) to create Figure 4 as Cochrane Methods recommended.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abt 2018

Study characteristics	
Methods	**Study design:** open-label, randomised controlled trial (non-inferiority trial)

Abt 2018 *(Continued)*

	Setting/Country: single center/Switzerland **Dates when study was conducted:** February 2014 to May 2017
Participants	**Inclusion criteria:** men aged at least 40 years, TURP indicated, refractory to medical treatment or not willing to undergo or continue medical treatment, with prostate size 25 to 80 mL as measured by transabdominal ultrasound, with IPSS of at least 8, with IPSS-related QoL of at least 3 points, with a maximum urinary flow rate less than 12 mL/s or urinary retention, and who provided written informed consent **Exclusion criteria:** men with severe atherosclerosis, aneurysmatic changes or severe tortuosity in the aortic bifurcation or internal iliac arteries, acontractile detrusor, neurogenic lower urinary tract dysfunction, urethral stenosis, bladder diverticulum, bladder stone, allergy to intravenous contrast media, contraindication for magnetic resonance imaging, pre-interventionally proven carcinoma of the prostate, and renal failure (glomerular filtration rate < 60 mL/min) **Total number of participants randomly assigned:** 103 **Group A** (PAE) • Number of all participants randomly assigned: 51 • Age (years): 65.7 ± 9.3 • Prostate volume (mL): 52.8 ± 32.0 • PSA (ng/mL): 4.2 ± 5.4 • IPSS: 19.38 ± 6.37 • Qmax (mL/s): 7.47 ± 4.14 **Group B** (TURP) • Number of all participants randomly assigned: 52 • Age (years): 66.1 ± 9.8 • Prostate volume (mL): 56.5 ± 31.1 • PSA (ng/mL): 4.5 ± 5.6 • IPSS: 17.59 ± 6.17 • Qmax (mL/s): 7.25 ± 4.46
Interventions	**Group A:** PAE **Group B:** monopolar TURP **Follow-up:** 12 weeks
Outcomes	**Primary outcome** • IPSS How measured: IPSS questionnaire Time points measured: at baseline, and at 1, 6, and 12 weeks Time points reported: at baseline, and at 1, 6, and 12 weeks **Secondary outcomes** • Free uroflowmetry/PVR/QoL/Chronic Prostatitis Symptoms Index/IIEF-5 How measured: uroflowmetry/transabdominal ultrasound/IPSS questionnaire/Chronic Prostatitis Symptoms Index questionnaire/IIEF-5 questionnaire Time points measured: data were collected before intervention (baseline), during participants' stay in hospital, and at 3 scheduled follow-up visits at 1, 6, and 12 weeks after surgery but did not describe the details per each outcome

Abt 2018 *(Continued)*

Time points reported: at baseline, and at 1, 6, and 12 weeks

- Hemoglobin/PSA/inflammatory blood parameters (e.g. cytokines)

How measured: blood test

Time points measured: data were collected before intervention (baseline), during participants' stay in hospital, and at 3 scheduled follow-up visits at 1, 6, and 12 weeks after surgery but did not describe the details

Time points reported: at preop and postop/at baseline, at postop, and at 1, 6, and 12 weeks/not reported

- Bladder diaries/prostate volume/Pdet Qmax and urodynamic obstruction

How measured: bladder diaries/magnetic resonance imaging/pressure flow studies

Time points measured: data were collected before intervention (baseline), during participants' stay in hospital, and at 3 scheduled follow-up visits at 1, 6, and 12 weeks after surgery but did not describe the details/at baseline and at 12 weeks/not reported

Time points reported: at baseline and at 12 weeks

- Postoperative pain/procedural parameters/indwelling bladder catheters/tissue vascularization after PAE

How measured: visual analogue scale (ranging from 0 [no pain] to 10 [maximum pain])/operation time, weight of resected tissue (for TURP), success of embolization (monolateral or bilateral), and radiation dose (for PAE)/history-taking/magnetic resonance imaging

Time points measured: during hospital stay/perioperative/at baseline/not reported

Time points reported: during hospital stay/perioperative/before IPSS assessment/not reported

Safety outcomes: adverse events

How measured: modified Clavien system and common terminology criteria for adverse events

Time points measured: before intervention (baseline), during participants' stay in hospital, and at 3 scheduled follow-up visits at 1, 6, and 12 weeks after surgery

Time points reported: likely cumulative incidence

Subgroup: none

Funding sources	Grant from the research committee of St. Gallen Cantonal Hospital
Declarations of interest	None
Notes	**Protocol:** NCT02054013 **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using the data management software SecuTrial, stratifying for patient age (< 70 or ≥ 70 years) and prostate volume (< 50 or ≥ 50 mL) through minimisation. SecuTrial was programmed by the clinical trials unit's data manager, and automatic treatment allocation by SecuTrial was determined for individual patients without a predefined sequence after inclusion and entry of baseline characteristics by the investigators"

Abt 2018 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "using the data management software SecuTrial, stratifying for patient age (< 70 or ≥ 70 years) and prostate volume (< 50 or ≥ 50 mL) through minimisation. SecuTrial was programmed by the clinical trials unit's data manager, and automatic treatment allocation by SecuTrial was determined for individual patients without a predefined sequence after inclusion and entry of baseline characteristics by the investigators"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "masking: none (open label)" in protocol
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Quote: "masking: none (open label)" in protocol
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Judgment: objective outcomes are likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Retreatment	Unclear risk	Judgment: no information (not reported): author reply - the data are not yet controlled, validated, and analyzed
Incomplete outcome data (attrition bias) Erectile function	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Ejaculatory function	High risk	Judgment: 25/51 (49.0%) and 25/52 (48.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Hospital stay	Low risk	Judgment: 48/51 (92.3%) and 51/52 (98.0%) participants randomized in PAE and TURP were included in the analysis, respectively (short term)
Selective reporting (reporting bias)	Unclear risk	Judgment: protocol was published and study author shared the data (not shown in the article). But results that were not predefined in the protocol were

Abt 2018 *(Continued)*

		reported. Data from bladder diary were not described in the methods section but they were described in the protocol
Other bias	Low risk	Judgment: not detected

Carnevale 2016

Study characteristics	
Methods	**Study design:** prospective, randomized, controlled study **Setting/Country:** single center/Brazil **Dates when study was conducted:** November 2010 to December 2012
Participants	**Inclusion criteria:** men aged > 45 years; IPSS > 19; symptoms refractory to medical treatment for at least 6 months; negative screening for prostate cancer; prostate volume between 30 and 90 mL on magnetic resonance imaging; and bladder outlet obstruction confirmed by urodynamic examination **Exclusion criteria:** men with renal failure, bladder calculi or diverticula, suspected prostate cancer, urethral stenosis, or neurogenic bladder disorders **Total number of participants randomly assigned:** 30 **Group A** (PAE) • Number of all participants randomly assigned: 15 • Age (years): 63.5 ± 8.7 • Prostate volume (mL): 63.0 ± 17.8 • PSA (ng/mL): 3.4 ± 2.2 • IPSS: 25.3 ± 3.6 • Qmax (mL/s): 7.0 ± 3.6 **Group B** (TURP) • Number of all participants randomly assigned: 15 • Age (years): 66.4 ± 5.6 • Prostate volume (mL): 56.6 ± 21.5 • PSA (ng/mL): 3.2 ± 2.5 • IPSS: 27.6 ± 3.2 • Qmax (mL/s): 9.7 ± 3.8
Interventions	**Group A:** PAE **Group B:** monopolar TURP **Follow-up:** 12 months
Outcomes	• IPSS, IIEF-5/Qmax, PVR/PSA/prostate volume How measured: IPSS and IIEF questionnaires/non-invasive uroflowmetry/not reported/magnetic resonance imaging Time points measured: at baseline and at 1 year Time points reported: at baseline and at 1 year • Urodynamics (Bladder Contractility Index, Bladder Outlet Obstruction Index)

Carnevale 2016 *(Continued)*

	How measured: invasive pressure flow study Time points measured: at baseline Time points reported: at baseline **Safety outcomes:** adverse events How measured: National Cancer Institute Common Toxicity Criteria for Adverse Events, version 4.0 Time points measured: not reported Time points reported: not reported **Subgroup:** none
Funding sources	No financial disclosure
Declarations of interest	None
Notes	**Protocol:** not available **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgment: not described
Allocation concealment (selection bias)	Unclear risk	Judgment: not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes are likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: all randomized participants were included in the analysis (short term)

Carnevale 2016 *(Continued)*

Incomplete outcome data (attrition bias) Erectile function	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Ejaculatory function	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Acute urinary retention	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Hospital stay	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Selective reporting (reporting bias)	Unclear risk	Judgment: study outcomes were well predefined and described, but protocol was not found
Other bias	Low risk	Judgment: statistical differences in baseline IIEF and Qmax, but those likely underestimate the effect size of PAE (more conservative)

Gao 2014

Study characteristics	
Methods	**Study design:** prospective parallel randomized controlled study **Setting/Country:** not defined/China **Dates when study was conducted:** January 2007 to January 2012
Participants	**Inclusion criteria:** men with IPSS greater than 7 after failed medical therapy with a washout period of 2 or more weeks, prostate volume 20 to 100 mL on transrectal ultrasonographic or magnetic resonance imaging, Qmax less than 15 mL/s, and negative prostate biopsy if PSA > 4 ng/mL or abnormal digital rectal examination **Exclusion criteria:** men with detrusor hyperactivity or hypocontractility at urodynamic study, urethral stricture, prostate cancer, diabetes mellitus, and previous prostate, bladder neck, or urethral surgery, or positive prostate biopsy **Total number of participants randomly assigned:** 114 **Group A** (PAE) • Number of all participants randomly assigned: 57 • Age (years): 67.7 ± 8.7 • Prostate volume (mL): 64.7 ± 19.7 • PSA (ng/mL): 3.7 ± 2.0 • IPSS: 22.8 ± 5.9 • Qmax (mL/s): 7.8 ± 2.5

Gao 2014 *(Continued)*

	Group B (TURP) • Number of all participants randomly assigned: 57 • Age (years): 66.4 ± 7.8 • Prostate volume (mL): 63.5 ± 18.6 • PSA (ng/mL): 3.6 ± 1.9 • IPSS: 23.1 ± 5.8 • Qmax (mL/s): 7.3 ± 2.3
Interventions	**Group A:** PAE **Group B:** bipolar TURP **Follow-up:** 24 months
Outcomes	• IPSS and QoL/Qmax/PVR How measured: IPSS questionnaire/uroflowmetry/transabdominal US Time points measured: at baseline, 1 month, 3 months, 6 months, 1 year, and 2 years Time points reported: at baseline, 1 month, 3 months, 6 months, 1 year, and 2 years • Urinary retention (catheter requirements)/re-treatment, hospital stay/hospital stay How measured: intraoperative, perioperative, and postoperative study data Time points measured: not reported Time points reported: early (< 30 days), late (≤ 2 years) **Safety outcomes:** adverse events How measured: modified Clavien Classification System Time points measured: not reported Time points reported: early (< 30 days), late (≤ 2 years) **Subgroup:** none
Funding sources	Not reported
Declarations of interest	None
Notes	**Protocol:** not available **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated simple random tables"
Allocation concealment (selection bias)	Unclear risk	Judgment: not described
Blinding of participants and personnel (performance bias)	High risk	Judgment: not described; blinding highly unlikely to have taken place

Gao 2014 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Unclear risk	Judgment: 47/57 (82.5%) and 48/57 (84.3%) randomized participants in PAE and TURP were included in the analysis, respectively (short and long term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: 54/57 (94.8%) and 53/57 (93.0%) randomized participants in PAE and TURP were included in the analysis, respectively (short and long term)
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Erectile function	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Ejaculatory function	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: 54/57 (94.8%) and 53/57 (93.0%) randomized participants in PAE and TURP were included in the analysis, respectively (long term)
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Low risk	Judgment: 54/57 (94.8%) and 53/57 (93.0%) randomized participants in PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Hospital stay	Low risk	Judgment: 54/57 (94.8%) and 53/57 (93.0%) randomized participants in PAE and TURP were included in the analysis, respectively (short term)
Selective reporting (reporting bias)	Unclear risk	Judgment: study outcomes were well predefined and described, but protocol was not found
Other bias	Low risk	Judgment: not detected

Insausti 2020

Study characteristics	
Methods	**Study design:** prospective randomized non-inferiority clinical trial
	Setting/Country: single center/Spain

Insausti 2020 *(Continued)*

	Dates when study was conducted: November 2014 and January 2017
Participants	**Inclusion criteria:** men over 60 years of age; BPH-related LUTS refractory to medical treatment for at least 6 months, or the patient could not tolerate medical treatment; TURP was indicated; IPSS was ≥ 8; QoL related to LUTS was ≥ 3; Qmax was ≤ 10 mL/s or urinary retention **Exclusion criteria:** men with advanced atherosclerosis and tortuosity of the iliac arteries, non-visualization of the prostatic artery or other accessory arteries supplying the prostate on computed tomography angiography, urethral stenosis, detrusor failure or neurogenic bladder, glomerular filtration rate less than 30 mL/min, and the presence of prostate cancer **Total number of participants randomly assigned:** 61 **Group A** (PAE) • Number of all participants randomly assigned: 31 • Age (years): 72.4 ± 6.2 • Prostate volume (mL): 60.0 ± 21.6 • PSA (ng/mL): 3.5 ± 2.8 • IPSS: 25.8 ± 4.64 • Qmax (mL/s): 7.7 ± 2.0 **Group B** (TURP) • Number of all participants randomly assigned: 30 • Age (years): 71.8 ± 5.5 • Prostate volume (mL): 62.8 ± 23.8 • PSA (ng/mL): 4.4 ± 8.7 • IPSS: 26.0 ± 7.29 • Qmax (mL/s): 7.0 ± 2.5
Interventions	**Group A:** PAE **Group B:** bipolar TURP **Follow-up:** 12 months
Outcomes	**Primary outcomes** • Qmax/IPSS How measured: uroflowmetry/IPSS questionnaire Time points measured: at baseline, and at 3, 6, and 12 months Time points reported: at baseline, and at 3, 6, and 12 months **Secondary outcomes** • QoL/prostate volume/PVR/IIEF-5 How measured: IPSS questionnaire/transabdominal US/transabdominal US/IIEF-5 questionnaire Time points measured: at baseline, and at 3, 6, and 12 months Time points reported: at baseline, and at 3, 6, and 12 months • PSA How measured: blood test Time points measured: at baseline, and at 3 and 12 months

Insausti 2020 *(Continued)*

	Time points reported: at baseline, and at 3 and 12 months **Safety outcomes:** adverse events How measured: modified Clavien Classification System Time points measured: at all follow-up visits Time points reported: likely cumulative incidence **Subgroup:** none
Funding sources	Biocompatibles UK Ltd
Declarations of interest	Biocompatibles UK Ltd
Notes	**Protocol:** NCT01963312 **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "principal Investigator randomly selected a number from a table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Quote: "the individual enrolling participants were unaware of the allocation of the next participants" Judgment: the method was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "there was no blinding of clinicians or patients due to the nature of the trial"
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Quote: "there was no blinding of clinicians or patients due to the nature of the trial"
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	High risk	Judgment: 23/31 (74.1%) and 22/30 (73.3%) participants randomized to PAE and TURP were included in the analysis, respectively (short term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: all randomized participants were included in the analysis

Insausti 2020 *(Continued)*

Incomplete outcome data (attrition bias) Erectile function	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Ejaculatory function	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	Judgment: reported, but no information provided about the number of participants
Selective reporting (reporting bias)	High risk	Judgment: protocol was published, but study outcomes were not identical to the outcomes prespecified in the protocol
Other bias	Low risk	Judgment: BPH medication was prescribed longer for the PAE group; however it seems this did not affect results 12 months after treatment

Pisco 2020

Study characteristics	
Methods	**Study design:** parallel randomized controlled study **Setting/Country:** single center/Portugal **Dates when study was conducted:** September 2014 to March 2018
Participants	**Inclusion criteria:** men over 45 years old; diagnosis of LUTS/BPH based on clinical history, digital rectal examination, urinalysis, transrectal ultrasound, and PSA; severe LUTS defined, at screening and at a baseline visit 2 weeks apart, by IPSS of 20 and QoL score of 3 after a minimum of 6 months' treatment with alpha-blockers for LUTS/BPH; Qmax < 12 mL/s; prostate volume 40 mL **Exclusion criteria:** men with computed tomography angiography showing that prostatic arteries were not feasible for PAE; previous surgical or invasive prostate treatments such as TURP, transurethral microwave therapy, transurethral needle ablation, laser, or any other minimally invasive treatment; acute or chronic prostatitis or suspected prostatitis including chronic pain, intermittent pain, or abnormal sensation in the penis, testis, or anal or pelvic area in the previous 12 months; history of prostate or bladder cancer or pelvic irradiation; active or recurrent urinary tract infections (more than 1 episode in the previous 12 months); history of neurogenic bladder or LUTS secondary to neurologic disease; advanced atherosclerosis and tortuosity of iliac and prostatic arteries; secondary renal insufficiency (due to prostatic obstruction); large bladder diverticula or stones; detrusor failure; previous history of acute urinary retention; current severe, significant, or uncontrolled disease; bleeding disorder such as hemophilia, clotting factor deficiency, anticoagulation, or bleeding diathesis; hypersensitivity or contraindication to tamsulosin use; mental condition or disorder that would interfere with the patient's ability to provide informed consent; participation in a study of any investigational drug or device in the previous 3 months; and administration of the 5-alpha reductase inhibitors finasteride and dutasteride in the previous 6 and 3 months, respectively. The latter criterion was changed by a protocol amendment to

Pisco 2020 *(Continued)*

	administration of the 5-alpha reductase inhibitors finasteride and dutasteride in the previous 2 weeks and 4 months, respectively (these patients may be included if they stop those medications and replace them for tamsulosin, alfuzosin, or silodosin for at least 2 weeks and 4 months, respectively) **Total number of participants randomly assigned:** 80 **Group A** (PAE) • Number of all participants randomly assigned: 40 • Age (years): median 64 (IQR 59 to 67.5) • Prostate volume (mL): median 63.5 (IQR 55.5 to 100) • PSA (ng/mL): median 3.04 (IQR 1.54 to 5.15) • IPSS: median 25.5 (IQR 22.5 to 29) • Qmax (mL/s): median 7.9 (IQR 5.55 to 10.2) **Group B** (sham) • Number of all participants randomly assigned: 40 • Age (years): median 64 (IQR 60 to 68.5) • Prostate volume (mL): median 66 (IQR 55.5 to 94.5) • PSA (ng/mL): median 3.10 (IQR 1.59 to 3.71) • IPSS: median 27.5 (IQR 24 to 30.5) • Qmax (mL/s): median 7.30 (IQR 4.90 to 9.40)
Interventions	**Group A:** PAE **Group B:** sham (after catheterization of 1 prostatic artery, the catheter was removed and no particles were injected) **Follow-up:** 6 months
Outcomes	**Primary outcome** • IPSS and QoL How measured: IPSS questionnaires Time points measured: at baseline, and at 1, 3, and 6 months Time points reported: at baseline, and at 1, 3, and 6 months **Secondary outcomes** • BPH Impact Index/IIEF-15/prostate volume/Qmax/PVR/PSA How measured: BPH Impact Index/IIEF-15/TRUS/not reported/not reported/not reported Time points measured: at baseline, and at 1, 3, and 6 months Time points reported: at baseline, and at 1, 3, and 6 months • Procedure variable: fluoroscopy times/radiation dose/pain How measured: not reported/not reported/visual analogue scale Time points measured: during procedure, at discharge, and the next morning Time points reported: during procedure, at discharge, and the next morning **Safety outcomes:** adverse events How measured: Clavien-Dindo Classification

Pisco 2020 *(Continued)*

	Time points measured: at baseline, and at 1, 3, and 6 months Time points reported: likely cumulative incidence **Subgroup:** none
Funding sources	Partially funded by an unrestricted grant from BTG plc (London, UK)
Declarations of interest	None
Notes	**Protocol:** NCT02074644 **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a randomisation list consisting of permuted blocks of size varying between 4 and 8 was prepared by the trial biostatistician"
Allocation concealment (selection bias)	Low risk	Quote: "the allocation sequence was concealed using opaque envelopes numbered sequentially"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients were blinded to the intervention received until end of single-blind period" Judgment: single-blind study (participants)
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Judgment: single-blind study (participants)
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: no information given (not reported): author reply - all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Erectile function	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Ejaculatory function	Low risk	Judgment: all randomized participants were included in the analysis (short term)

Pisco 2020 *(Continued)*

Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	Judgment: no information given (not measured)
Selective reporting (reporting bias)	Low risk	Judgment: protocol was published and study outcomes were well predefined and described
Other bias	Low risk	Judgment: tamsulosin was prescribed longer for the sham group. However, it made the difference between groups much smaller (more conservative)

Radwan 2020

Study characteristics	
Methods	**Study design:** parallel randomized controlled study **Setting/Country:** single center/Egypt **Dates when study was conducted:** January 2016 to January 2018
Participants	**Inclusion criteria:** men complained of LUTS with an IPSS score of 8 to 35 (8 being moderate and 35 being severe), uroflowmetry with an average flow ≤ 10 mL/s, and a prostate volume less than 100 mL by TRUS **Exclusion criteria:** men with elevated kidney functions (1.5 mg/dL), with allergy to intravenous contrast media, unfit for surgery, with prostatic adenocarcinoma, with previous history of prostatic or urethral operations, with signs of the decompensated bladder (e.g., bladder diverticulum), with signs of upper urinary tract infection revealed by pelvic abdominal ultrasound were excluded **Total number of participants randomly assigned:** 60 **Group A** (PAE) • Number of all participants randomly assigned: 20 • Age (years): 63.0 ± 7.2 • Prostate volume (mL): 58.7 ± 23.4 • PSA (ng/mL): not reported • IPSS: 27.0 ± 5.0 • Qmax (mL/s): 9.2 ± 4.8 **Group B** (TURP) • Number of all participants randomly assigned: 40 • Age (years): 62.0 ± 9.0 • Prostate volume (mL): 60.1 ± 21.5 • PSA (ng/mL): not reported • IPSS: 26.5 ± 4.0

Radwan 2020 *(Continued)*

	• Qmax (mL/s): 8.3 ± 5.7
Interventions	**Group A:** PAE **Group B:** TURP (monopolar or bipolar) **Follow-up:** 6 months
Outcomes	• IPSS How measured: IPSS questionnaire/uroflowmetry/TRUS/not reported Time points measured: at baseline, 1 month, and 6 months Time points reported: at baseline, 1 month, and 6 months • Qmax, prostate volume, PVR How measured: uroflowmetry/TRUS/NR Time points measured: at baseline, 1 month, and 6 months Time points reported: at baseline and postoperatively (not defined) **Safety outcomes:** How measured: TUR syndrome, acute urinary retention, post-embolization syndrome Time points measured: not reported Time points reported: likely cumulative incidence **Subgroup:** none
Funding sources	Not reported
Declarations of interest	None
Notes	**Protocol:** not available **Language of publication:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgment: not described
Allocation concealment (selection bias)	Unclear risk	Judgment: not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place

Radwan 2020 *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Erectile function	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Ejaculatory function	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: all randomized participants were included in the analysis
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Low risk	Judgement: all randomized participants were included in the analysis (catheter removal time: TURP [third postoperative day], PAE [fifth postoperative day])
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	Judgment: no information given (not measured)
Selective reporting (reporting bias)	Unclear risk	Judgment: protocol was not found, the outcomes at prespecified time point (likely 1 month) were omitted
Other bias	Low risk	Judgment: not detected

Ray 2018

Study characteristics	
Methods	**Study design:** prospective cohort study (United Kingdom Register of Prostate Embolization) **Setting/Country:** multicenter/United Kingdom **Dates when study was conducted:** July 2014 to January 2016
Participants	**Inclusion criteria:** men with LUTS who had consented to undergo PAE, TURP, open prostatectomy, or holmium enucleation of the prostate at one of the United Kingdom Register of Prostate Embolization

Ray 2018 *(Continued)*

collaborating centres; were able to read, write, and understand English; and were capable of giving informed written consent

Exclusion criteria: men who were not able to read, write, or understand English; not able/willing to provide informed written consent

Total number of participants analyzed: 305

Group A (PAE)

- Number of all participants analyzed: 216
- Age (years): 66 ± 7.4
- Prostate volume (mL): 101.2 ± 57.1
- PSA (ng/mL): not reported
- IPSS: 21.3 ± 6.7
- Qmax (mL/s): 8.8 ± 4.718

Group B (TURP)

- Number of all participants analyzed: 89 (45 monopolar, 44 bipolar)
- Age (years): 70 ± 7.5
- Prostate volume (mL): 68.7 ±9.2
- PSA (ng/mL): not reported
- IPSS: 21.63 ± 5.8
- Qmax (mL/s): 10.36 ± 6.3

Interventions

Group A: PAE

Group B: monopolar and bipolar TURP

Follow-up: 12 months

Outcomes

Primary outcome

- IPSS changes at 12 months

How measured: IPSS questionnaire

Time points measured: at baseline, and at 1, 3, 6, and 12 months

Time points reported: at baseline, and at 1, 3, 6, and 12 months

Secondary outcomes

- IPSS changes at 12 months (non-inferiority)/IIEF

How measured: IPSS questionnaire/IIEF questionnaire

Time points measured: at baseline, and at 1, 3, 6, and 12 months

Time points reported: at baseline, and at 3 and 12 months

- Prostate volume/urinary flow studies (only for PAE group)

How measured: not reported/flow study

Time points measured: at baseline, and at 3 and 12 months

Time points reported: at baseline, and at 3 and 12 months

Safety outcomes: adverse events

Ray 2018 *(Continued)*

	How measured: Clavien Dindo Classification (by patients and clinicians) and re-treatment (not defined in the methods section) Time points measured: at baseline, and at 1, 3, 6, and 12 months (by mail)/ within 12 months and after 12 months Time points reported: likely cumulative incidence **Subgroup:** none
Funding sources	Cook Medical, British Society of Interventional Radiologists, and British Association of Urological Surgeons. National Institute for Health and Care Excellence funded an independent academic unit (the Cardiff and Vale UHB/Cardiff University-based unit, Cedar) to run the registry through a competitive tender
Declarations of interest	Prof. Powell works part-time as a Consultant Clinical Advisor to the Interventional Procedures Programme at NICE. Mr. Speakman was President of BAUS 2014–2016. Dr. Hacking holds a Consultant Contract with Boston Scientific and has held contracts over the last 2 years with Terumo, Cook Medical, and Celonova
Notes	**Protocol:** NCT02434575 **Language of publication:** English

Soluyanov 2018

Study characteristics	
Methods	**Study design:** prospective comparative study **Setting/Country:** not reported/Russia **Dates when study was conducted:** 2016
Participants	**Inclusion criteria:** BPH with 2 to 3 stages (stage was not defined) **Exclusion criteria:** not reported **Total number of participants analyzed:** 27 **Group A** (PAE) • Number of all participants analyzed: 8 • Age (years): median 68 (IQR 63 to 75) • Prostate volume (mL): median 53 (IQR 37.5 to 56.5) • PSA (ng/mL): median 1.6 (IQR 1.1 to 2) • IPSS: median 23 (IQR 22 to 24) • Qmax (mL/s): not available **Group B** (TURP) • Number of all participants analyzed: 19 • Age (years): median 67 (IQR 62 to 75) • Prostate volume (mL): median 43.1 (IQR 36.5 to 50) • PSA (ng/mL): median 3.3 (IQR 1.7 to 5.2) • IPSS: median 22 (IQR 21 to 24) • Qmax (mL/s): not available

Soluyanov 2018 *(Continued)*

Interventions	**Group A:** PAE **Group B:** bipolar TURP **Follow-up:** 6 months
Outcomes	• IPSS/PVR/prostate volume How measured: IPSS questionnaire/not reported/TRUS Time points measured: at baseline, and at 3 and 6 months Time points reported: at baseline, and at 3 and 6 months **Safety outcomes:** not reported **Subgroup:** none
Funding sources	Not reported
Declarations of interest	None
Notes	**Protocol:** not available **Language of publication:** Russian

Zhu 2018

Study characteristics	
Methods	**Study design:** parallel randomised controlled study **Setting/Country:** single center/China **Dates when study was conducted:** January to October 2016
Participants	**Inclusion criteria:** Men with • Comprehensive diagnosis of BPH through ultrasound prostate examination, digital rectal examination, IPSS, etc. • No absolute contraindication for surgery • No previous history of surgery; not taking 5-alpha reductase inhibitors **Exclusion criteria:** Men with • Severe liver and kidney disorders, severe urethral strictures • Prostate tumors, bladder neck stenosis, urinary infections, and neurogenic bladder • Severe heart and brain diseases, coagulopathy, systemic organ low functionality **Total number of participants randomly assigned:** 40 **Group A** (PAE) • Number of all participants randomly assigned: 20 • Age (years): 61.1 ± 4.4 • Prostate volume (mL): 81.21 ± 6.34

Zhu 2018 *(Continued)*

- PSA (ng/mL): 8.97 ± 3.04
- IPSS: median 25.63 ± 4.28
- Qmax (mL/s): 8.25 ± 2.36

Group B (sham)

- Number of all participants randomly assigned: 20
- Age (years): 62.4 ± 4.9
- Prostate volume (mL): 82.09 ± 6.47
- PSA (ng/mL): 8.95 ± 2.86
- IPSS: median 26.22 ± 4.35
- Qmax (mL/s): 8.47 ± 2.39

Interventions	**Group A:** PAE **Group B:** TURP (not defined) **Follow-up:** 12 months
Outcomes	• IPSS/QoL/prostate volume/PVR/Qmax/PSA How measured: IPSS questionnaires/IPSS questionnaires/TRUS/US/JDNL-II urine flow rate detector/blood sampling Time points measured: at baseline, and at 3, 6, and 12 months Time points reported: at baseline, and at 3, 6, and 12 months • Sexual dysfunction How measured: follow-up by telephone (erectile dysfunction and retrograde ejaculation) Time points measured: at baseline, and at 3 and 12 months Time points reported: at baseline, and at 3 and 12 months **Safety outcomes:** adverse events How measured: not reported Time points measured: within 12 months Time points reported: likely cumulative incidence **Subgroup:** none
Funding sources	Not reported
Declarations of interest	Not reported
Notes	**Protocol:** not available **Language of publication:** Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgment: random numbers table method

Zhu 2018 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Judgment: not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Judgment: not described; blinding highly unlikely to have taken place
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Judgment: objective outcomes likely not affected by lack of blinding
Incomplete outcome data (attrition bias) Urologic symptom scores/ Quality of life	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Major/Minor adverse events	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Retreatment	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Erectile function	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Ejaculatory function	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Acute urinary retention	Low risk	Judgment: all randomized participants were included in the analysis (short term)
Incomplete outcome data (attrition bias) Indwelling urinary catheter	Unclear risk	Judgment: no information given (not measured)
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	Judgment: no information given (not measured)
Selective reporting (reporting bias)	Unclear risk	Judgment: study outcomes were well predefined and described, but protocol was not found
Other bias	Low risk	Judgment: not detected

BPH: benign prostatic hyperplasia; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; IQR: interquartile range; LUTS: lower urinary tract symptoms; PAE: prostatic arterial embolization; PSA: prostate-specific antigen; PVR: postvoid

residual; Qmax: maximum flow rate; QoL: quality of life; TRUS: transrectal ultrasound; TURP: transurethral resection of prostate; US: ultrasound.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bagla 2017	Irrelevant study design (retrospective chart review for cost analysis)
Bilhim 2015	Letter to editor
Brown 2018	Irrelevant study design (retrospective comparative study)
NCT01835860	Irrelevant study design (single group assignment)
Pereira 2018	Irrelevant study design (retrospective comparative study)
Qiu 2017	Irrelevant study design (retrospective comparative study)
Russo 2015	Irrelevant comparator (open simple prostatectomy). We focused on effects of prostatic arterial embolization compared to minimal invasive therapies (Jung 2017)

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12617001235392

Study name	PAE for patients with LUTS due to BPH
Methods	**Study design:** parallel randomized controlled trial (open label) **Setting/Country:** single center/New Zealand
Participants	**Inclusion criteria** • Men were willing, able and mentally competent to provide written consent • Men aged 40 years or older • Men with LUTS (IPSS > 8, QoL >3) • Men with prostate gland > 40mL on transabdominal ultrasound • Men with vascular anatomy that in the opinion of the Interventional radiologist is amenable to PAE as assessed on CTA • Men with adequate laboratory parameters: platelets > 100, INR < 1.5, bilirubin < 2, albumin > 2.5, estimated glomerular filtration rate > 60
Interventions	**Group A:** PAE **Group B:** TURP
Outcomes	**Primary outcome** • Change in IPSS • Successful trial of voiding after removal catheter **Secondary outcomes** • Patient satisfaction evaluations as assessed by the IPSS

ACTRN12617001235392 *(Continued)*

Starting date	August 2017
Contact information	martin.krauss@cdhb.health.nz
Notes	**Sponsor:** Christchurch hospital

ChiCTR1800014818

Study name	PAE as a primary treatment for BPH
Methods	**Study design:** prospective non-randomized study (cohort study) **Setting/Country:** single center/China
Participants	**Inclusion criteria** • Men were diagnosed as BPH by the 2014 Chinese urological disease diagnosis and treatment guideline
Interventions	**Group A:** PAE **Group B:** TURP
Outcomes	• Prostate volume • Qmax • Operation time • Blood loss • Complication
Starting date	February 2018
Contact information	wjh9877@163.com
Notes	**Sponsor:** Tianjin First Center Hospital

NCT01789840

Study name	PAE with embosphere microspheres compared to TURP for BPH
Methods	**Study design:** prospective non-randomized study **Setting/Country:** multicenter/USA
Participants	**Inclusion criteria** • Patient ages 50 to 79, inclusive • Patient has signed informed consent • Patient has had LUTS secondary to BPH for at least 6 months before study treatment • Patient has a baseline IPSS score > 13 at baseline • Patient has a prostate size of at least 50 grams and not more than 90 grams, measured by MRI • Patient has BPH symptoms refractory to medical treatment or for whom medication is contraindicated, not tolerated, or refused • Patient must be a candidate for TURP

NCT01789840 *(Continued)*

	• Patient must meet 1 of the following criteria: baseline PSA < 2.5 ng/mL (no prostate biopsy required), baseline PSA > 2.5 ng/mL and ≤ 10 ng/mL and free PSA > 25% of total PSA (no prostate biopsy required), baseline PSA > 2.5 ng/mL and ≤ 10 ng/mL and free PSA < 25% of total PSA and a negative prostate biopsy result (minimum 12-core biopsy), baseline PSA >10 ng/mL, and a negative prostate biopsy (minimum 12-core biopsy)
Interventions	**Group A:** PAE **Group B:** TURP
Outcomes	**Primary outcome** • IPSS score **Secondary outcomes** • Duration of hospitalization post procedure • Duration of postprocedure catheterization • Overall and procedure-related adverse events • Safety by assessing adverse events, as well as changes in laboratory values and findings on physical examination **Other outcomes** • Change from baseline in Qmax • Change from baseline in erectile function using the IIEF • Change from baseline in mean prostate volume, as determined by MRI • Change from baseline in PVR • Change in baseline from PSA
Starting date	July 2013
Contact information	Not provided but we reached out to Dr. Francisco C. Carnevale (who is listed as PI) using f-carnevale@uol.com.br on 8/31/2020.
Notes	Study was completed in December 2017 **Sponsor:** Merit Medical Systems, Inc.

NCT02006303

Study name	PAE versus 532 nm green light PVP for catheterized patients
Methods	**Study design:** parallel randomized controlled trial (open label) **Setting/Country:** multicenter/Canada
Participants	**Inclusion criteria** • Male subjects, over 50 years of age at the time of enrollment • Subjects referred to urology for BPH leading to permanent indwelling bladder catheter, and considered poor surgical candidates • Written informed consent to participate in the study • Ability to comply with requirements of the study procedures
Interventions	**Group A:** PAE

NCT02006303 *(Continued)*

	Group B: Green light PVP
Outcomes	**Primary outcome** • Ability of the patient to void after removal of the urethral catheter **Secondary outcomes** • Patient subjective satisfaction evaluated by the IPSS • Degree of prostatic size reduction evaluated by MRI • Change in Qmax • Change in PVR • Change in PSA
Starting date	December 2013
Contact information	mostafa.elhilali@muhc.mcgill.ca (deceased); melkoushy@yahoo.com
Notes	Recruitment status of this study is unknown. The completion date has passed and the status has not been verified in more than 2 years. We learnt that the PI died in April 4/2017; we reached out to Dr. Elkoushy on 8/30/2020 and were informed that the study was aborted and that no results are available. **Sponsor:** Royal Victoria Hospital, Canada

NCT02566551

Study name	Prospective controlled randomized study of PAE vs TURP for BPH treatment
Methods	**Study design:** single (outcome assessor) blinded parallel randomized controlled trial **Setting/Country:** single center/Spain
Participants	**Inclusion criteria** Patients evaluated in the Urology Service because of BPH, candidates for TURP • Signed informed consent • LUTS secondary to BPH for at least 6 months before study and/or baseline IPSS score > 13 and/or acute urinary retention with impossibility to remove urinary catheter and/or BPH symptoms refractory to medical treatment or for whom medication is contraindicated, not tolerated, or refused; prostate size of at least 50 grams measured by MRI • Patient must meet 1 of the following criteria: baseline PSA < 4 ng/mL (no prostate biopsy required), baseline PSA > 4 ng/mL and ≤ 10 ng/mL and free PSA > 15% of total PSA (no prostate biopsy required), baseline PSA > 4 ng/mL and ≤ 10 ng/mL and free PSA < 15% of total PSA and a negative prostate biopsy result (minimum 12-core biopsy), baseline PSA > 10 ng/mL and a negative prostate biopsy (minimum 12-core biopsy)
Interventions	**Group A:** PAE **Group B:** TURP
Outcomes	**Primary outcome** • Improved symptoms assessed by IPSS score **Secondary outcomes**

NCT02566551 *(Continued)*

	• Improved QoL • Duration of hospitalization post procedure • Preservation of erectile function using the IIEF **Other outcomes** • Change from baseline in Qmax • Change from baseline in PVR • Change from baseline in detrusor pressure • Change from baseline in mean prostate volume, as determined by transrectal ultrasound • Structural and morphologic changes on MRI • Change from baseline in PSA • Overall adverse events • Procedure-related adverse events
Starting date	October 2015
Contact information	mgregori@unizar.es
Notes	The trial registration notes that the study was closed without recruiting any participants. **Sponsor:** Group of Research in Minimally Invasive Techniques Hospital Clínico Universitario Lozano Blesa Universidad de Zaragoza

NCT04236687

Study name	PAE compared to Holmium laser enucleation of the prostate for BPH
Methods	**Study design:** parallel randomized controlled trial (open label) **Setting/Country:** single center/Spain
Participants	**Inclusion criteria** Patients evaluated in the urology department and candidates to surgical treatment • Age > 45 years • IPSS ≥ 10 • Qmax < 12 mL/s • PVR < 300mL • Prostatic volume between 20mL and 250mL assessed by ultrasound • Signed informed consent
Interventions	**Group A:** PAE **Group B:** Holmium laser enucleation of the prostate
Outcomes	**Primary outcome** • Improvement of symptoms assessed by IPSS **Secondary outcomes**

NCT04236687 *(Continued)*	• Qmax • PVR • PSA • Procedure related adverse events assessed by Clavien-Dindo modified score • Procedure related effects on sexual function assessed by IIEF • Procedure related effects on urinary continence assessed by the International Consultation on Continence Questionnaire Short Form
Starting date	February 2020
Contact information	fagreda.germanstrias@gencat.cat
Notes	**Sponsor:** Hospital Universitari Germans Trias i Pujol

BPH: benign prostatic hyperplasia; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; LUTS: lower urinary tract symptoms; MRI: magnetic resonance imaging; PAE: prostatic arterial embolization; PSA: prostate-specific antigen; PVR: postvoid residual; Qmax: maximum flow rate; QoL: quality of life; TURP: transurethral resection of prostate.

DATA AND ANALYSES

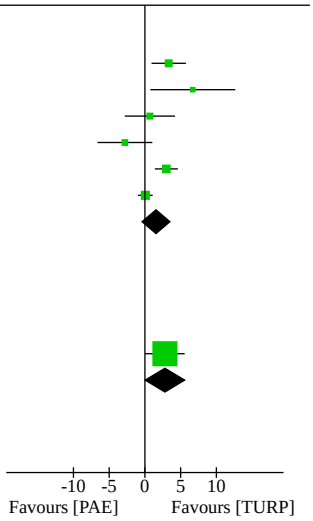
Comparison 1. PAE vs TURP (short term)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Urologic symptom scores	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 RCTs	6	369	Mean Difference (IV, Random, 95% CI)	1.55 [-0.40, 3.50]
1.1.2 NRSs	1	161	Mean Difference (IV, Random, 95% CI)	2.80 [0.04, 5.56]
1.2 Quality of life	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.2.1 RCTs	5	309	Mean Difference (IV, Random, 95% CI)	0.16 [-0.37, 0.68]
1.2.2 NRSs	1	164	Mean Difference (IV, Random, 95% CI)	0.50 [-0.03, 1.03]
1.3 Major adverse events	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.3.1 RCTs	4	250	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.16, 3.10]
1.3.2 NRSs	1	305	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.4 Re-treatment	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.4.1 RCTs	3	204	Risk Ratio (M-H, Random, 95% CI)	3.64 [1.02, 12.98]
1.4.2 NRSs	1	305	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.43, 5.29]
1.5 Erectile function	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.5.1 RCTs	2	129	Mean Difference (IV, Random, 95% CI)	-0.03 [-6.35, 6.29]
1.5.2 NRSs	1	122	Mean Difference (IV, Random, 95% CI)	1.50 [-2.01, 5.01]
1.6 Ejaculatory disorder	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.6.1 RCTs	3	141	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.06, 1.19]
1.6.2 NRSs	1	260	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.35, 0.73]
1.7 Minor adverse events	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.7.1 RCTs	3	189	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.41, 1.69]
1.7.2 NRSs	1	305	Risk Ratio (M-H, Random, 95% CI)	2.27 [0.51, 10.02]
1.8 Acute urinary retention	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.8.1 RCTs	5	367	Risk Ratio (M-H, Random, 95% CI)	1.65 [0.54, 5.07]
1.8.2 NRSs	1	305	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.9 Indwelling urinary catheter	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.9.1 RCTs	1	99	Mean Difference (IV, Random, 95% CI)	-2.00 [-2.55, -1.45]
1.10 Hospital stay	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.10.1 RCTs	2	206	Mean Difference (IV, Random, 95% CI)	-1.96 [-2.36, -1.57]

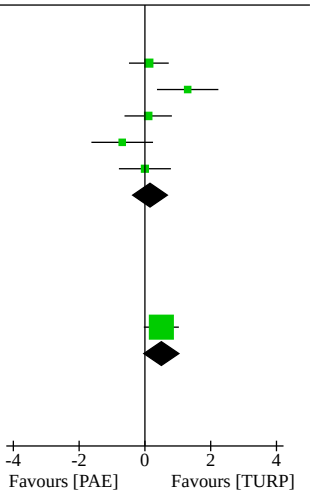
Analysis 1.1. Comparison 1: PAE vs TURP (short term), Outcome 1: Urologic symptom scores

Study or Subgroup	PAE Mean	PAE SD	PAE Total	TURP Mean	TURP SD	TURP Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 RCTs								
Abt 2018	10.15	6.79	48	6.82	5.27	51	18.7%	3.33 [0.93 , 5.73]
Carnevale 2016	12.8	8	15	6.1	8.6	15	7.6%	6.70 [0.76 , 12.64]
Gao 2014	10.9	8.5	47	10.2	9	48	14.1%	0.70 [-2.82 , 4.22]
Insausti 2020	-21	6.24	23	-18.2	6.87	22	13.0%	-2.80 [-6.64 , 1.04]
Radwan 2020	12	3	20	9	3	40	22.2%	3.00 [1.39 , 4.61]
Zhu 2018	7.28	1.73	20	7.22	1.57	20	24.4%	0.06 [-0.96 , 1.08]
Subtotal (95% CI)			**173**			**196**	**100.0%**	**1.55 [-0.40 , 3.50]**
Heterogeneity: Tau² = 3.77; Chi² = 20.04, df = 5 (P = 0.001); I² = 75%								
Test for overall effect: Z = 1.56 (P = 0.12)								
1.1.2 NRSs								
Ray 2018	10	6.7	132	7.2	6.9	29	100.0%	2.80 [0.04 , 5.56]
Subtotal (95% CI)			**132**			**29**	**100.0%**	**2.80 [0.04 , 5.56]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.99 (P = 0.05)								
Test for subgroup differences: Chi² = 0.53, df = 1 (P = 0.47), I² = 0%								



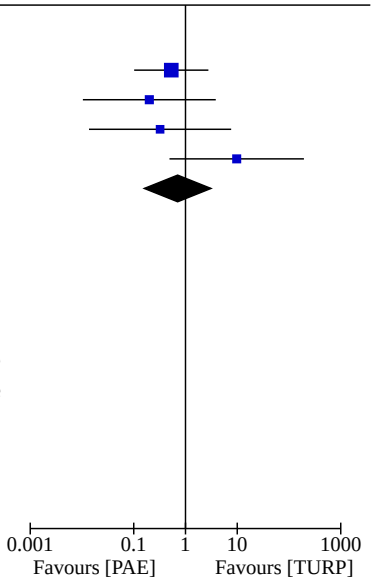
Analysis 1.2. Comparison 1: PAE vs TURP (short term), Outcome 2: Quality of life

Study or Subgroup	PAE Mean	PAE SD	PAE Total	TURP Mean	TURP SD	TURP Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 RCTs								
Abt 2018	1.67	1.59	48	1.55	1.47	51	24.5%	0.12 [-0.48 , 0.72]
Carnevale 2016	2.2	1.2	15	0.9	1.4	15	17.0%	1.30 [0.37 , 2.23]
Gao 2014	1.9	1.79	47	1.8	1.79	48	21.6%	0.10 [-0.62 , 0.82]
Insausti 2020	-3.78	1.79	23	-3.09	1.4	22	16.9%	-0.69 [-1.63 , 0.25]
Zhu 2018	2.91	1.28	20	2.91	1.27	20	20.0%	0.00 [-0.79 , 0.79]
Subtotal (95% CI)			**153**			**156**	**100.0%**	**0.16 [-0.37 , 0.68]**
Heterogeneity: Tau² = 0.20; Chi² = 9.09, df = 4 (P = 0.06); I² = 56%								
Test for overall effect: Z = 0.58 (P = 0.56)								
1.2.2 NRSs								
Ray 2018	2	1.6	133	1.5	1.3	31	100.0%	0.50 [-0.03 , 1.03]
Subtotal (95% CI)			**133**			**31**	**100.0%**	**0.50 [-0.03 , 1.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.84 (P = 0.07)								
Test for subgroup differences: Chi² = 0.81, df = 1 (P = 0.37), I² = 0%								



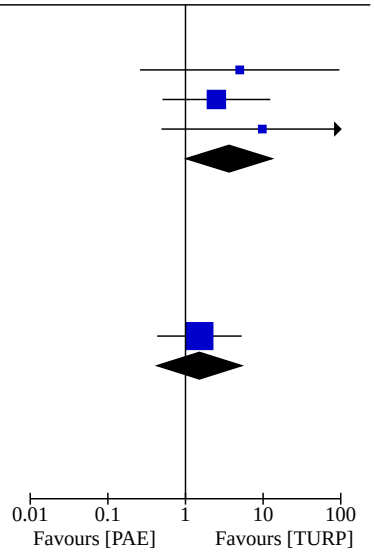
Analysis 1.3. Comparison 1: PAE vs TURP (short term), Outcome 3: Major adverse events

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 RCTs						
Abt 2018	2	48	4	51	43.1%	0.53 [0.10 , 2.77]
Carnevale 2016	0	15	2	15	19.8%	0.20 [0.01 , 3.85]
Insausti 2020	0	31	1	30	17.7%	0.32 [0.01 , 7.63]
Radwan 2020	2	20	0	40	19.4%	9.76 [0.49 , 194.21]
Subtotal (95% CI)		**114**		**136**	**100.0%**	**0.71 [0.16 , 3.10]**
Total events:	4		7			
Heterogeneity: Tau² = 0.61; Chi² = 4.06, df = 3 (P = 0.26); I² = 26%						
Test for overall effect: Z = 0.46 (P = 0.64)						
1.3.2 NRSs						
Ray 2018	0	216	0	89		Not estimable
Subtotal (95% CI)		**216**		**89**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



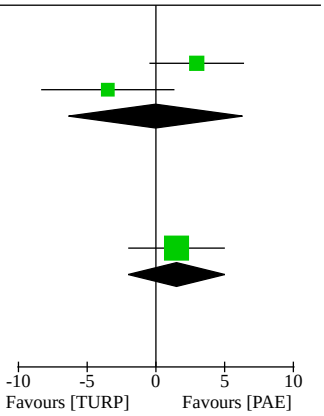
Analysis 1.4. Comparison 1: PAE vs TURP (short term), Outcome 4: Re-treatment

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 RCTs						
Carnevale 2016	2	15	0	15	18.5%	5.00 [0.26 , 96.13]
Gao 2014	5	57	2	57	63.4%	2.50 [0.51 , 12.36]
Radwan 2020	2	20	0	40	18.1%	9.76 [0.49 , 194.21]
Subtotal (95% CI)		**92**		**112**	**100.0%**	**3.64 [1.02 , 12.98]**
Total events:	9		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 2 (P = 0.71); I² = 0%						
Test for overall effect: Z = 1.99 (P = 0.05)						
1.4.2 NRSs						
Ray 2018	11	216	3	89	100.0%	1.51 [0.43 , 5.29]
Subtotal (95% CI)		**216**		**89**	**100.0%**	**1.51 [0.43 , 5.29]**
Total events:	11		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						
Test for subgroup differences: Chi² = 0.93, df = 1 (P = 0.33), I² = 0%						



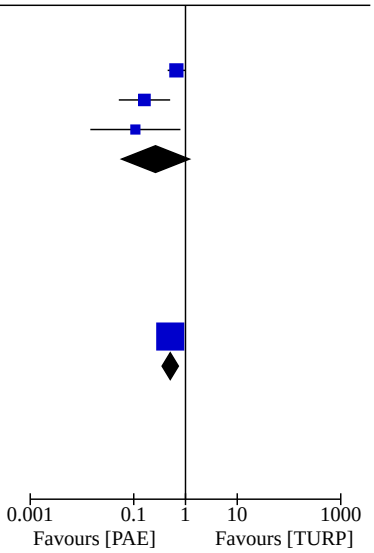
Analysis 1.5. Comparison 1: PAE vs TURP (short term), Outcome 5: Erectile function

Study or Subgroup	PAE Mean	PAE SD	PAE Total	TURP Mean	TURP SD	TURP Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 RCTs								
Abt 2018	14.64	8.58	48	11.67	8.89	51	53.6%	2.97 [-0.47 , 6.41]
Carnevale 2016	12.6	7.7	15	16.1	5.7	15	46.4%	-3.50 [-8.35 , 1.35]
Subtotal (95% CI)			**63**			**66**	**100.0%**	**-0.03 [-6.35 , 6.29]**
Heterogeneity: Tau² = 16.33; Chi² = 4.55, df = 1 (P = 0.03); I² = 78%								
Test for overall effect: Z = 0.01 (P = 0.99)								
1.5.2 NRSs								
Ray 2018	16.3	7.5	102	14.8	7.3	20	100.0%	1.50 [-2.01 , 5.01]
Subtotal (95% CI)			**102**			**20**	**100.0%**	**1.50 [-2.01 , 5.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.84 (P = 0.40)								
Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%								



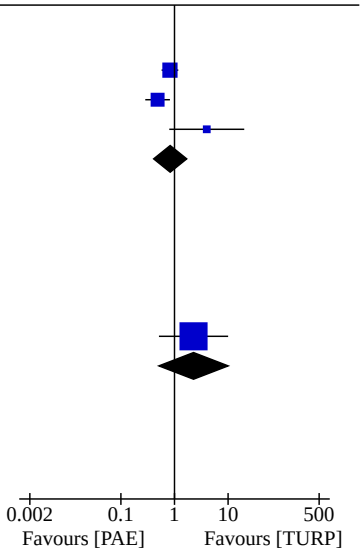
Analysis 1.6. Comparison 1: PAE vs TURP (short term), Outcome 6: Ejaculatory disorder

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 RCTs						
Abt 2018	14	25	21	25	41.5%	0.67 [0.45 , 0.98]
Carnevale 2016	2	15	15	15	34.2%	0.16 [0.05 , 0.51]
Insausti 2020	1	31	9	30	24.3%	0.11 [0.01 , 0.80]
Subtotal (95% CI)		**71**		**70**	**100.0%**	**0.26 [0.06 , 1.19]**
Total events:	17		45			
Heterogeneity: Tau² = 1.38; Chi² = 11.61, df = 2 (P = 0.003); I² = 83%						
Test for overall effect: Z = 1.74 (P = 0.08)						
1.6.2 NRSs						
Ray 2018	48	199	29	61	100.0%	0.51 [0.35 , 0.73]
Subtotal (95% CI)		**199**		**61**	**100.0%**	**0.51 [0.35 , 0.73]**
Total events:	48		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.69 (P = 0.0002)						
Test for subgroup differences: Chi² = 0.69, df = 1 (P = 0.41), I² = 0%						



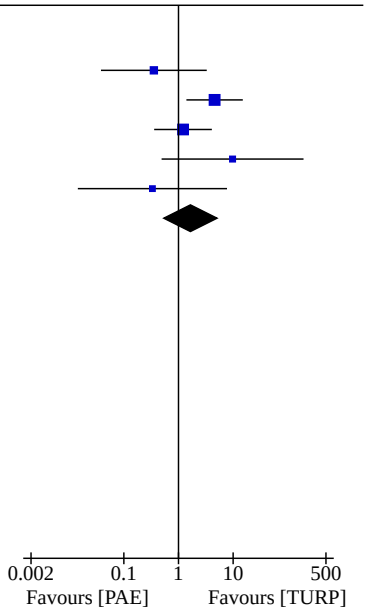
Analysis 1.7. Comparison 1: PAE vs TURP (short term), Outcome 7: Minor adverse events

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 RCTs						
Abt 2018	24	48	31	51	45.7%	0.82 [0.57 , 1.18]
Carnevale 2016	7	15	15	15	40.2%	0.48 [0.29 , 0.82]
Radwan 2020	4	20	2	40	14.1%	4.00 [0.80 , 20.02]
Subtotal (95% CI)		**83**		**106**	**100.0%**	**0.83 [0.41 , 1.69]**
Total events:	35		48			
Heterogeneity: Tau² = 0.25; Chi² = 7.34, df = 2 (P = 0.03); I² = 73%						
Test for overall effect: Z = 0.51 (P = 0.61)						
1.7.2 NRSs						
Ray 2018	11	216	2	89	100.0%	2.27 [0.51 , 10.02]
Subtotal (95% CI)		**216**		**89**	**100.0%**	**2.27 [0.51 , 10.02]**
Total events:	11		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.08 (P = 0.28)						
Test for subgroup differences: Chi² = 1.43, df = 1 (P = 0.23), I² = 29.8%						

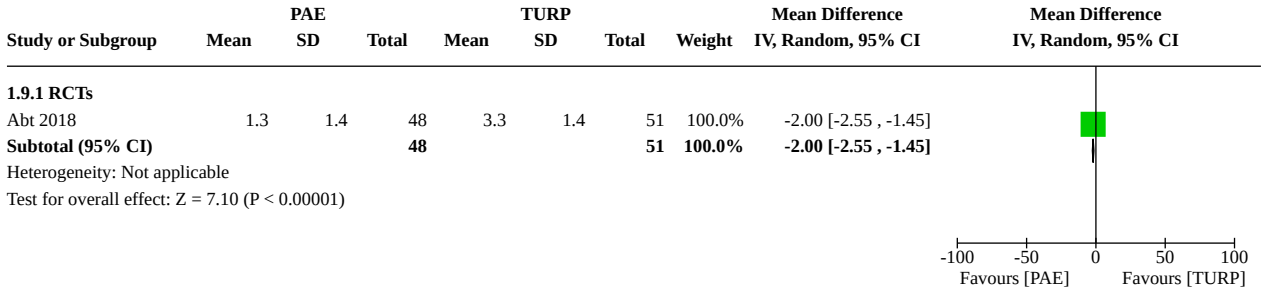


Analysis 1.8. Comparison 1: PAE vs TURP (short term), Outcome 8: Acute urinary retention

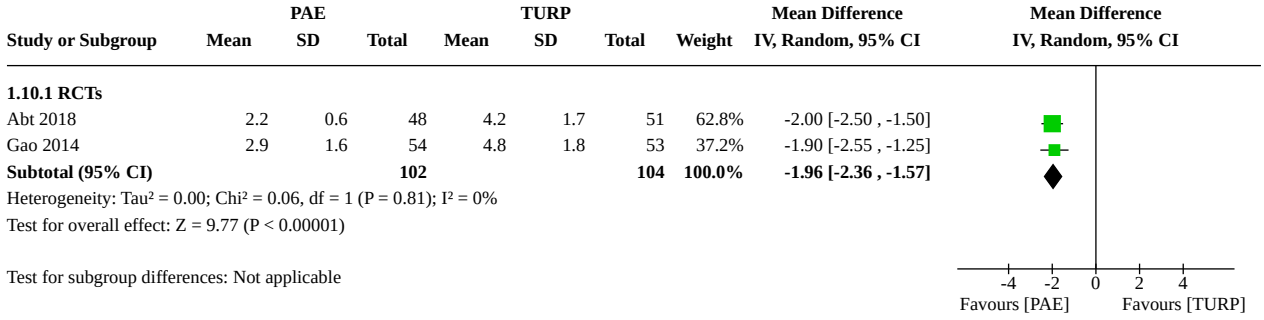
Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 RCTs						
Abt 2018	1	48	3	51	16.6%	0.35 [0.04 , 3.29]
Gao 2014	14	54	3	53	31.5%	4.58 [1.40 , 15.03]
Insausti 2020	5	31	4	30	31.0%	1.21 [0.36 , 4.08]
Radwan 2020	2	20	0	40	10.9%	9.76 [0.49 , 194.21]
Zhu 2018	0	20	1	20	10.1%	0.33 [0.01 , 7.72]
Subtotal (95% CI)		**173**		**194**	**100.0%**	**1.65 [0.54 , 5.07]**
Total events:	22		11			
Heterogeneity: Tau² = 0.67; Chi² = 7.17, df = 4 (P = 0.13); I² = 44%						
Test for overall effect: Z = 0.88 (P = 0.38)						
1.8.2 NRSs						
Ray 2018	0	216	0	89		Not estimable
Subtotal (95% CI)		**216**		**89**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 1.9. Comparison 1: PAE vs TURP (short term), Outcome 9: Indwelling urinary catheter



Analysis 1.10. Comparison 1: PAE vs TURP (short term), Outcome 10: Hospital stay

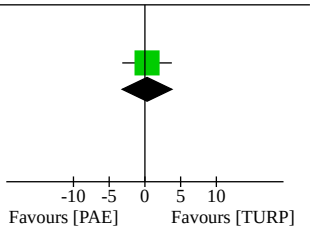


Comparison 2. PAE vs TURP (long term)

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
2.1 Urologic symptom scores	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1.1 RCTs	1	95	Mean Difference (IV, Random, 95% CI)	0.30 [-3.17, 3.77]
2.2 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.2.1 RCTs	1	95	Mean Difference (IV, Random, 95% CI)	0.20 [-0.49, 0.89]
2.3 Major adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.3.1 RCTs	1	107	Risk Ratio (M-H, Random, 95% CI)	1.96 [0.63, 6.13]
2.4 Re-treatment	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.4.1 NRSs	1	305	Risk Ratio (M-H, Random, 95% CI)	3.54 [1.45, 8.65]
2.5 Minor adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.5.1 RCTs	1	107	Risk Ratio (M-H, Random, 95% CI)	1.66 [0.94, 2.94]

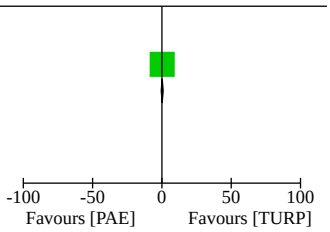
Analysis 2.1. Comparison 2: PAE vs TURP (long term), Outcome 1: Urologic symptom scores

Study or Subgroup	PAE Mean	PAE SD	PAE Total	TURP Mean	TURP SD	TURP Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 RCTs								
Gao 2014	8.7	8.5	47	8.4	8.75	48	100.0%	0.30 [-3.17 , 3.77]
Subtotal (95% CI)			**47**			**48**	**100.0%**	**0.30 [-3.17 , 3.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.17 (P = 0.87)								



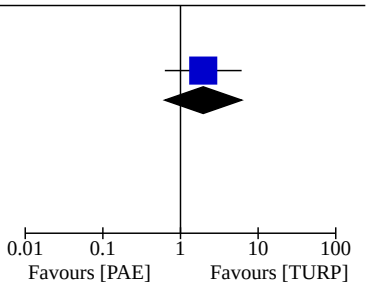
Analysis 2.2. Comparison 2: PAE vs TURP (long term), Outcome 2: Quality of life

Study or Subgroup	PAE Mean	PAE SD	PAE Total	TURP Mean	TURP SD	TURP Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 RCTs								
Gao 2014	1.6	1.83	47	1.4	1.58	48	100.0%	0.20 [-0.49 , 0.89]
Subtotal (95% CI)			**47**			**48**	**100.0%**	**0.20 [-0.49 , 0.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.57 (P = 0.57)								



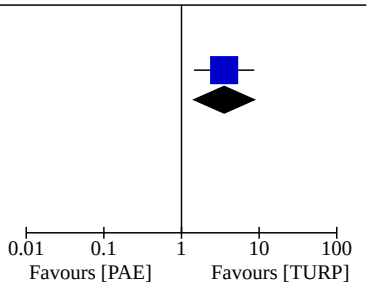
Analysis 2.3. Comparison 2: PAE vs TURP (long term), Outcome 3: Major adverse events

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 RCTs						
Gao 2014	8	54	4	53	100.0%	1.96 [0.63 , 6.13]
Subtotal (95% CI)		**54**		**53**	**100.0%**	**1.96 [0.63 , 6.13]**
Total events:	8		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						



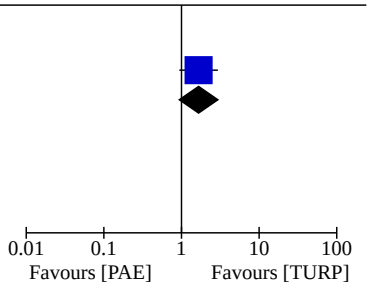
Analysis 2.4. Comparison 2: PAE vs TURP (long term), Outcome 4: Re-treatment

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
2.4.1 NRSs						
Ray 2018	43	216	5	89	100.0%	3.54 [1.45 , 8.65]
Subtotal (95% CI)		**216**		**89**	**100.0%**	**3.54 [1.45 , 8.65]**
Total events:	43		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.78 (P = 0.005)						
Test for subgroup differences: Not applicable						



Analysis 2.5. Comparison 2: PAE vs TURP (long term), Outcome 5: Minor adverse events

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 RCTs						
Gao 2014	22	54	13	53	100.0%	1.66 [0.94 , 2.94]
Subtotal (95% CI)		**54**		**53**	**100.0%**	**1.66 [0.94 , 2.94]**
Total events:	22		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.74 (P = 0.08)						



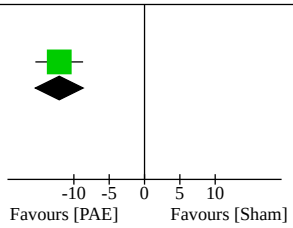
Comparison 3. PAE vs sham (short term)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Urologic symptom scores	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1.1 RCTs	1	80	Mean Difference (IV, Random, 95% CI)	-12.07 [-15.45, -8.69]
3.2 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.2.1 RCTs	1	80	Mean Difference (IV, Random, 95% CI)	-1.97 [-2.48, -1.46]
3.3 Major adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.3.1 RCTs	1	80	Risk Ratio (M-H, Random, 95% CI)	Not estimable
3.4 Re-treatment	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.4.1 RCTs	1	80	Risk Ratio (M-H, Random, 95% CI)	Not estimable
3.5 Ejaculatory disorder	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.5.1 RCTs	1	80	Risk Ratio (M-H, Random, 95% CI)	Not estimable
3.6 Minor adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.6.1 RCTs	1	80	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.58, 1.99]
3.7 Acute urinary retention	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.7.1 RCTs	1	80	Risk Ratio (M-H, Random, 95% CI)	Not estimable

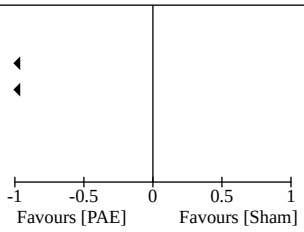
Analysis 3.1. Comparison 3: PAE vs sham (short term), Outcome 1: Urologic symptom scores

Study or Subgroup	PAE Mean	PAE SD	PAE Total	Sham Mean	Sham SD	Sham Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 RCTs								
Pisco 2020	-17.1	7.25	40	-5.03	8.13	40	100.0%	-12.07 [-15.45 , -8.69]
Subtotal (95% CI)			**40**			**40**	**100.0%**	**-12.07 [-15.45 , -8.69]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.01 (P < 0.00001)								



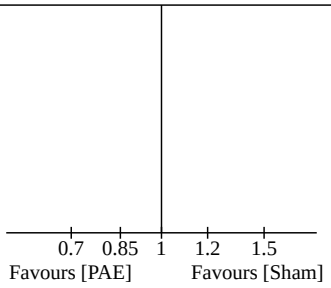
Analysis 3.2. Comparison 3: PAE vs sham (short term), Outcome 2: Quality of life

Study or Subgroup	PAE Mean	PAE SD	PAE Total	Sham Mean	Sham SD	Sham Total	Weight	Mean Difference IV, Random, 95% CI
3.2.1 RCTs								
Pisco 2020	-3	1.13	40	-1.03	1.19	40	100.0%	-1.97 [-2.48 , -1.46]
Subtotal (95% CI)			**40**			**40**	**100.0%**	**-1.97 [-2.48 , -1.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.59 (P < 0.00001)								



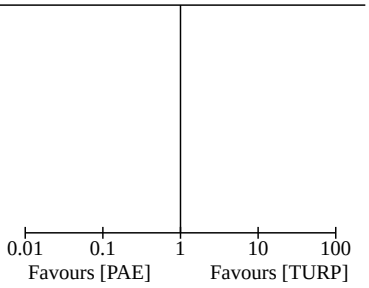
Analysis 3.3. Comparison 3: PAE vs sham (short term), Outcome 3: Major adverse events

Study or Subgroup	PAE Events	PAE Total	Sham Events	Sham Total	Weight	Risk Ratio M-H, Random, 95% CI
3.3.1 RCTs						
Pisco 2020	0	40	0	40		Not estimable
Subtotal (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



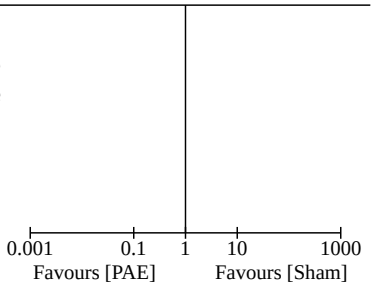
Analysis 3.4. Comparison 3: PAE vs sham (short term), Outcome 4: Re-treatment

Study or Subgroup	PAE Events	PAE Total	TURP Events	TURP Total	Weight	Risk Ratio M-H, Random, 95% CI
3.4.1 RCTs						
Pisco 2020	0	40	0	40		Not estimable
Subtotal (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



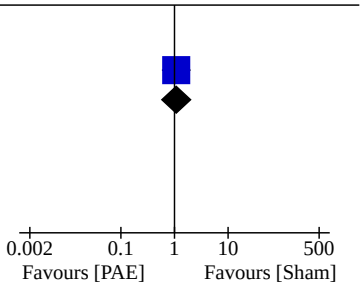
Analysis 3.5. Comparison 3: PAE vs sham (short term), Outcome 5: Ejaculatory disorder

Study or Subgroup	PAE Events	PAE Total	Sham Events	Sham Total	Weight	Risk Ratio M-H, Random, 95% CI
3.5.1 RCTs						
Pisco 2020	0	40	0	40		Not estimable
Subtotal (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



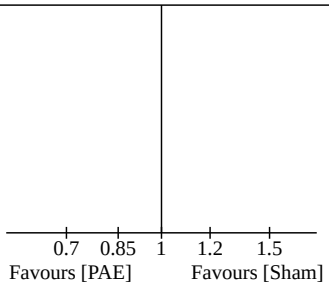
Analysis 3.6. Comparison 3: PAE vs sham (short term), Outcome 6: Minor adverse events

Study or Subgroup	PAE Events	PAE Total	Sham Events	Sham Total	Weight	Risk Ratio M-H, Random, 95% CI
3.6.1 RCTs						
Pisco 2020	14	40	13	40	100.0%	1.08 [0.58 , 1.99]
Subtotal (95% CI)		**40**		**40**	**100.0%**	**1.08 [0.58 , 1.99]**
Total events:	14		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						



Analysis 3.7. Comparison 3: PAE vs sham (short term), Outcome 7: Acute urinary retention

Study or Subgroup	PAE Events	PAE Total	Sham Events	Sham Total	Weight	Risk Ratio M-H, Random, 95% CI
3.7.1 RCTs						
Pisco 2020	0	40	0	40		Not estimable
Subtotal (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



ADDITIONAL TABLES

Table 1. Baseline characteristics of included studies

Study name	Trial period (year to year)	Study design/Setting/Country	Description of participants	Intervention(s) and comparator(s)	Duration of follow-up	Age	IPSS	Prostate volume
Abt 2018	2014 to 2017	RCT/single center/Switzerland	Men aged at least 40 years, TURP indicated, refractory to medical treatment or not willing to undergo or continue medical treatment, with prostate size 25 to 80 mL as measured by transabdominal ultrasound, with IPSS of at least 8, with IPSS-related quality of life of at least 3, with Qmax less than 12 mL/s or urinary retention, and who provided written informed consent	PAE	12 weeks	65.7 ± 9.3	19.38 ± 6.37	52.8 ± 32.0
				TURP		66.1 ± 9.8	17.59 ± 6.17	56.5 ± 31.1
Carnevale 2016	2010 to 2012	RCT/single center/Brazil	Men aged > 45 years; IPSS > 19; symptoms refractory to medical treatment for at least 6 months; negative screening for prostate cancer; prostate volume between 30 and 90 mL on magnetic resonance imaging; and bladder outlet obstruction confirmed by urodynamic examination	PAE	12 months	63.5 ± 8.7	25.3 ± 3.6	63.0 ± 17.8
				TURP		66.4 ± 5.6	27.6 ± 3.2	56.6 ± 21.5
Gao 2014	2007 to 2012	RCT/not defined/China	Men with IPSS greater than 7 after failed medical therapy with a washout period of 2 or more weeks, prostate volume 20 to 100 mL on transrectal ultrasonographic or magnetic resonance imaging, Qmax less than 15 mL/sec, and negative prostate biopsy if PSA > 4 ng/mL or abnormal digital rectal examination	PAE	24 months	67.7 ± 8.7	22.8 ± 5.9	64.7 ± 19.7
				TURP		66.4 ± 7.8	23.1 ± 5.8	63.5 ± 18.6
Insausti 2020	2014 to 2017	RCT/single center/Spain	Men aged > 60 years; BPH-related LUTS refractory to medical treatment for at least 6 months or the patient could not tolerate medical treatment; TURP was indicated; IPSS ≥ 8; quality of life related to LUTS ≥ 3; Qmax ≤ 10 mL/s or urinary retention	PAE	12 months	72.4 ± 6.2	25.8 ± 4.64	60.0 ± 21.6
				TURP		71.8 ± 5.5	26.0 ± 7.29	62.8 ± 23.8
Pisco 2020	2014 to 2018	RCT/single center/Portugal	Men over 45 year old; diagnosis of LUTS/BPH based on clinical history, digital rectal examination, urinalysis, transrectal ultrasound, and PSA; severe LUTS defined, at screening and at a baseline visit 2 weeks apart, by IPSS of 20	PAE	6 months	Median 64 (IQR 59 to 67.5)	Median 25.5 (IQR 22.5 to 29)	Median 63.5 (IQR 55.5 to 100)

Table 1. Baseline characteristics of included studies *(Continued)*

			and quality of life score of 3 after a minimum of 6 months' treatment with alpha-blockers for LUTS/BPH; Qmax < 12 mL/s; prostate volume 40 mL	Sham		Median 64 (IQR 60 to 68.5)	Median 27.5 (IQR 24 to 30.5)	Median 66 (IQR 55.5 to 94.5)
Radwan 2020	2016 to 2018	RCT/single center/Egypt	Men complained of LUTS with an IPSS score of 8 to 35 (8 being moderate and 35 being severe), uroflowmetry with an average flow ≤ 10 mL/s, and a prostate volume less than 100 mL by TRUS	PAE	6 months	63.0 ± 7.2	27.0 ± 5.0	58.7 ± 23.4
				TURP		62.0 ± 9.0	26.5 ± 4.0	60.1 ± 21.5
Ray 2018	2014 to 2016	NRS/multicenter/United Kingdom	Men with LUTS who had consented to undergo PAE, TURP, open prostatectomy, or holmium enucleation of the prostate at 1 of the United Kingdom Register of Prostate Embolization collaborating centers; were able to read, write, and understand English; and were capable of giving informed written consent	PAE	12 months	66 ± 7.4	21.3 ± 6.7	101.2 ± 57.1
				TURP		70 ± 7.5	21.63 ± 5.8	68.7 ± 9.2
Soluyanov 2018	2016	NRS/not reported/Russia	BPH with 2 to 3 stages (stage was not defined).	PAE	6 months	Median 68 (IQR 63 to 75)	Median 23 (IQR 22 to 24)	Median 53 (IQR 37.5 to 56.5)
				TURP		Median 67 (IQR 62 to 75)	Median 22 (IQR 21 to 24)	Median 43.1 (IQR 36.5 to 50)
Zhu 2018	2016	RCT/single center/China	Men with comprehensive diagnosis of BPH through ultrasound prostate examination, digital rectal examination, IPSS, etc.; no absolute contraindication for surgery; no previous history of surgery; not taking 5-alpha reductase inhibitors	PAE	12 months	61.1 ± 4.4	25.63 ± 4.28	81.21 ± 6.34
				TURP		62.4 ± 4.9	26.22 ± 4.35	82.09 ± 6.47

BPH: benign prostatic hyperplasia; IPSS: International Prostate Symptom Score; IQR: interquartile range; LUTS: lower urinary tract symptoms; NRS: non-randomized study; PAE: prostatic arterial embolization; PSA: prostate-specific antigen; Qmax: maximum flow rate; RCT: randomized controlled trial; TURP: transurethral resection of prostate.

Table 2. Participants in included randomized controlled trials

Study name	Intervention(s) and comparator(s)	Screened/ eligible, N	Randomized, N	Analyzed, N: efficacy[a]	Analyzed, N: safety[b]	Finishing trial, N (%)
Abt 2018	PAE	144/103	51	48	48	48 (94.1)
	TURP		52	51	51	51 (98.0)
	Total		103	99	99	99 (96.1)
Carnevale 2016	PAE	NR/30	15	15	15	15 (100.0)
	TURP		15	15	15	15 (100.0)
	Total		30	30	30	30 (100.0)
Gao 2014	PAE	120/114	57	47	54	47 (82.4)
	TURP		57	48	53	48 (84.2)
	Total		114	95	107	95 (83.3)
Insausti 2020	PAE	81/61	31	23	31	23 (74.1)
	TURP		30	22	30	22 (73.3)
	Total		61	45	61	45 (73.7)
Pisco 2020	PAE	677/80	40	40	40	39 (97.5)
	Sham		40	40	40	38 (95.0)
	Total		80	80	80	77 (96.2)
Zhu 2018	PAE	NR/40	20	20	20	20 (100.0)
	TURP		20	20	20	20 (100.0)
	Total		40	40	40	40 (100.0)
Radwan 2020	PAE	NR/60	20	20	20	20 (100.0)
	TURP		40	40	40	40 (100.0)
	Total		60	60	60	60 (100.0)
Grand total	Intervention: PAE		234	213	228	212 (90.5)
	Comparator: TURP		214	196	209	196 (91.5)
	Comparator: sham		40	40	40	38 (95.0)
	Overall		488	449	477	446 (91.3)

NR: not reported; PAE: prostatic arterial embolization; TURP: transurethral resection of prostate.

[a]Number of participants analyzed for urologic symptom scores.
[b]Number of participants with adverse events.

Table 3. Participants in included non-randomized studies

Study name	Intervention(s) and comparator(s)	eligible, N	Analyzed, N: efficacy[a]	Analyzed, N: safety[b]	Finishing study, N (%)
Ray 2018	PAE	216	132	216	189 (87.5)
	TURP	89	29	89	65 (73.0)
	Total		161	305	254 (83.2)
Soluyanov 2018	PAE	8	8	NR	8 (100.0)
	TURP	19	19	NR	19 (100.0)
	Total		27	NR	27 (100.0)
Grand total	Intervention: PAE	224	140	216	197 (87.9)
	Comparator: TURP	108	48	89	84 (82.4)
	Overall		188	305	281 (84.6)

NR: not reported; PAE: prostatic arterial embolization; TURP: transurethral resection of prostate.
[a]Number of participants analyzed for urologic symptom scores.
[b]Number of participants with adverse events.

Table 4. ROBINS-I assessment by study: Ray 2018

Study name: Ray 2018

Risk of bias domain	Assessments by outcome	Support for judgment	Conclusion
Bias due to confounding	All outcomes[a]	Quote: "multivariate analysis was performed in R version 3.3.2 (2016-10-31). We applied a combination of multiple imputation and propensity-matched pairing in the comparative between-group analysis. Propensity matching was based on a logistic regression model and yielded 65 matched pairs. Background variables used for matching were age at procedure; length of time with LUTS; baseline IPSS; IPSS QoL; IIEF; Qmax; and PVR" Judgment: although authors likely used an appropriate analysis method to control confounding factors, concerns for confounding may remain. In addition, multivariate analysis including propensity-matched paring was reported only for IPSS and IPSS QoL. For all other outcomes in the review, risk of bias due to confounding could be considerable.	Serious
Bias in selection of participants into the study		Judgment: selection of participants into the study was not based on participant characteristics observed after the start of the intervention and the start of follow-up and the start of the intervention likely coincided for most participants. As inclusion criteria were not reported in detail in protocol as well as in pub-	Moderate

Table 4. ROBINS-I assessment by study: Ray 2018 *(Continued)*

		lication, there are concerns for postintervention variables that influenced selection likely to be associated with intervention (e.g. prostate volume)	
Bias in classification of interventions		Quote: "the British Society of Interventional Radiologists and the British Association of Urological Surgeons co-funded the online UK Register of Prostate Embolization (UK-ROPE), which was built and hosted by Dendrite Clinical Systems Ltd" Judgment: this study was based on the ongoing authorized registry (UK-ROPE) that predefined the interventions	Moderate
Bias due to deviations from intended interventions		Judgment: although this study was based on the prospective enrolled registry (UK-ROPE), no information was provided with regard to co-intervention	No information
Bias due to missing data	Urological symptom scores, QoL, erectile function, ejaculatory disorders, and hospital stay	Judgment: although the proportion of participants for missing data was similar across interventions, about 2/3 participants in each group were included in the analysis	Serious
	Major adverse events, re-treatment, minor adverse events, and AUR	Judgment: all participants were included in the analysis	Low
Bias in measurement of outcomes	Subjective outcomes[b]	Quote: "there was no blinding (either clinician or participant) in this single-arm observational study" Judgment: given that study outcomes were subjective, outcome measures were likely influenced by knowledge of the intervention received	Serious
	Objective outcomes[c]	Judgment: although objective outcomes are unlikely influenced by knowledge of the intervention received in outcome assessment, participants and personnel were not blinded	Serious
Bias in selection of the reported result	All outcomes[a]	Judgment: protocol was published and study outcomes were well predefined and described. In addition, study author provided unreported data via email	Low
Overall	-	Judgment: serious risk of bias in at least 1 domain, but not at critical risk of bias in any domain	Serious

AUR: acute urinary retention; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; LUTS: lower urinary tract symptoms; PVR: postvoid residual; Qmax: maximum flow rate; QoL: quality of life; ROBINS-I: risk of bias tool to assess non-randomized studies of interventions.

[a]All review outcomes reported in study: urological symptom scores, QoL, major adverse events, re-treatment, minor adverse events, erectile function, AUR, ejaculatory disorders, and hospital stay

[b]Urological symptom scores, QoL, major adverse events, erectile function, ejaculatory disorders, and minor adverse events

[c]Re-treatment, AUR, and hospital stay

Table 5. ROBINS-I assessment by study: Soluyanov 2018

Study name: Soluyanov 2018

Table 5. ROBINS-I assessment by study: Soluyanov 2018 *(Continued)*

Risk of bias domain	Assessments by outcome	Support for judgement	Conclusion
Bias due to confounding	Urologic symptom scores[a]	Quote: "patients were assigned to one of three groups (i.e., planning one of three operations) taking into account the volume of the prostate gland and the presence of concomitant chronic diseases" Judgment: participants were selected based on participant characteristics and post intervention and study author did not use an appropriate analysis method that controlled for confounding	Critical
Bias in selection of participants into the study		Quote: "patients were assigned to one of three groups (i.e., planning one of three operations) taking into account the volume of the prostate gland and the presence of concomitant chronic diseases" Judgment: participants were selected based on prostate volume related to the results of outcomes	Critical
Bias in classification of interventions		Judgment: likely prospective comparative trial with predefined criteria for the intervention	Moderate
Bias due to deviations from intended interventions		Judgment: no information with regard to co-intervention and analysis used to estimate the effects of starting and adhering to the intervention	No information
Bias due to missing data		Judgment: all participants were included in the analysis	Low
Bias in measurement of outcomes		Judgment: given that study outcomes were subjective, outcome measures were likely influenced by knowledge of the intervention received	Serious
Bias in selection of the reported result		Judgment: study outcomes were not well predefined and described, and the protocol was not found	No information
Overall[b]	-	Judgment: critical risk of bias in at least 1 domain	Critical

ROBINS-I: risk of bias tool to assess non-randomized studies of interventions.
[a]The review outcome reported in study

APPENDICES

Appendix 1. Certainty of evidence decisions (PAE versus TURP [short term])

Outcomes	Study design	Certainty of evidence (GRADE)
Urologic symptom scores[a]	RCT	Low

(Continued)

	NRS	Very low
Quality of life[a]	RCT	Low
	NRS	Very low
Major adverse events	RCT	Very low
	NRS	Very low
Re-treatment[a]	RCT	Low
	NRS	Very low
Erectile function	RCT	Very low
	NRS	Very low
Ejaculatory disorder[a]	RCT	Very low
	NRS	Low

Footnotes

NRS: non-randomized study; PAE: prostatic arterial embolization; RCT: randomized controlled trial; TURP: transurethral resection of prostate.

[a]Higher Certainty of evidence only shown in Summary of findings 1 due to the difference in a body of RCTs and a body of non-RCTs.

Appendix 2. Search strategy

Cochrane Library (via Wiley)
1 MeSH descriptor: [Prostatic Hyperplasia] explode all trees
2 (prostat* near/3 hyperplasia*):ti,ab,kw (Word variations have been searched)
3 (prostat* near/3 hypertroph*):ti,ab,kw (Word variations have been searched)
4 (prostat* near/3 adenoma*):ti,ab,kw (Word variations have been searched)
5 (BPH or BPO or BPE):ti,ab,kw (Word variations have been searched)
6 (prostat* near/3 enlarg*):ti,ab,kw (Word variations have been searched)
7 MeSH descriptor: [Prostatism] explode all trees
8 prostatism:ti,ab,kw (Word variations have been searched)
9 MeSH descriptor: [Urinary Bladder Neck Obstruction] explode all trees
10 ("bladder outlet obstruction" or BOO):ti,ab,kw (Word variations have been searched)
11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
12 MeSH descriptor: [Embolization, Therapeutic] this term only
13 emboli?ation*:ti,ab,kw (Word variations have been searched)

(Continued)

14 Embolotherap*:ti,ab,kw (Word variations have been searched)

15 #12 or #13 or #14

16 #11 and #15

MEDLINE (via Ovid)

1 exp Prostatic Hyperplasia/

2 (Prostat* adj3 hyperplasia*).tw.

3 (Prostat* adj3 hypertroph*).tw.

4 (Prostat* adj3 adenoma*).tw.

5 (BPH or BPO or BPE).tw.

6 (prostat* adj3 enlarg*).tw.

7 exp Prostatism/

8 Prostatism.tw.

9 exp Urinary Bladder Neck Obstruction/

10 (Bladder* adj3 obstruct*).tw.

11 BOO.tw.

12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

13 Embolization, Therapeutic/

14 emboli#ation$.tw.

15 Embolotherap*.tw.

16 13 or 14 or 15

17 12 and 16

18 (animals not (humans and animals)).sh.

19 17 not 18

Embase (via Elsevier**)**

1 'prostate hypertrophy'/exp

2 (Prostat* NEAR/3 hyperplasia*):ab,ti

3 (Prostat* NEAR/3 hypertroph*):ab,ti

4 (Prostat* NEAR/3 adenoma*):ab,ti

5 'bph':ab,ti OR 'bpo':ab,ti OR 'bpe':ab,ti

6 (prostat* NEAR/3 enlarg*):ab,ti

7 'prostatism'/exp

8 'prostatism':ab,ti

9 'bladder obstruction'/exp

(Continued)

10 (bladder* NEAR/3 obstruct*):ab,ti

11 'BOO':ab,ti

12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

13 'artificial embolization'/de

14 embolisation*:ab,ti

15 embolization*:ab,ti

16 Embolotherap*:ab,ti

17 #13 OR #14 OR #15 OR #16

18 #12 AND #17

19 ('animals'/exp) NOT ('humans'/exp and 'animals'/exp)

20 #18 NOT #19

LILACS

1 (mh:("Prostatic Hyperplasia" or Prostatism or "Urinary Bladder Neck Obstruction"))

2 (tw:("Prostatic Hyperplasia" or "Prostatic Adenoma" or "Prostatic Hypertrophy" or "Prostatic Enlargement" or BPH or BPO or BPE or Prostatism or "Bladder Neck Obstruction" or "Bladder Outlet Obstruction" or BOO))

3 1 OR 2

4 tw:(embolisation$ OR embolization$ OR embolotherap$)

5 3 AND 4

Scopus

1 TITLE-ABS-KEY((hyperplasia* W/3 prostat*) OR (hypertroph* W/3 prostat*) OR (adenoma* W/3 prostat*) OR (prostat* W/3 enlarg*) OR (bph OR bpo OR bpe OR boo) OR prostatism OR (bladder* W/3 obstruct*))

2 TITLE-ABS-KEY(embolisation* OR embolization* OR Embolotherap*)

3 1 AND 2

Web of Science

1 TS= ((hyperplasia* NEAR/3 prostat*) OR (hypertroph* NEAR/3 prostat*) OR (adenoma* NEAR/3 prostat*) OR (prostat* NEAR/3 enlarg*) OR (bph OR bpo OR bpe OR boo) OR prostatism OR (bladder* NEAR/3 obstruct*))

2 TS= (embolisation* OR embolization* OR Embolotherap*)

3 1 AND 2

Google Scholar

1 allintitle: ("Prostatic Hyperplasia" OR "prostatic hypertrophy" OR prostatism OR "bladder obstruction" OR "bladder outlet obstruction" OR bph OR bpo OR bpe OR boo) AND (embolisation OR embolisations OR embolization OR embolizations OR embolotherapy OR embolotherapies))

ClinicalTrials.gov

1 ("Prostatic Hyperplasia" OR "Prostatic Hypertrophy" OR "Prostatic Adenoma" OR BPH OR BPO OR BPE OR Prostatism OR "Bladder Neck Obstruction" OR "Bladder Outlet Obstruction" or BOO)

(Continued)

2 (embolisation OR embolisations OR embolization OR embolizations OR embolotherapy OR embolotherapies)
3 1 AND 2

World Health Organization International Clinical Trials Registry Platform search portal
1 In the title = ("Prostatic Hyperplasia" OR "Prostatic Hypertrophy" OR "Prostatic Adenoma" OR BPH or BPO or BPE OR Prostatism OR "Bladder Neck Obstruction" or "Bladder Outlet Obstruction" or BOO) AND In the intervention= (embolisation OR embolisations OR embolization OR embolizations OR embolotherapy OR embolotherapies)

Grey Literature (Open Grey)
1 ("Prostatic Hyperplasia" OR "Prostatic Hypertrophy" OR "Prostatic Adenoma" OR BPH or BPO or BPE OR Prostatism OR "Bladder Neck Obstruction" or "Bladder Outlet Obstruction" or BOO)
2 (embolisation OR embolisations OR embolization OR embolizations OR embolotherapy OR embolotherapies)
3 1 AND 2

Appendix 3. Survey of trial investigators providing information on included trials

Study name	Date trial author contacted (first)	Date trial author provided data (latest)	Data trial author provided short summary
Abt 2018	13 October 2018	25 October 2018	Standard deviations of IPSS, QoL, IIEF, Qmax, and PVR at baseline and 12 weeks/number of participants with AEs and re-treatment
Ray 2018	19 October 2018	1 November 2018	Standard deviations at endpoint and changes from baseline in IPSS, QoL, and IIEF/number of participants with AEs, acute urinary retention, and re-operation/mean length of hospital stay
Pisco 2020	28 March 2020	3 April 2020	Number of participants with major and minor AEs, and reoperation rate at 6 month (blinded period)
Radwan 2020	7 October 2020	15 October 2020	Baseline characteristics (age, IPSS, QoL, prostate volume, Qmax, PVR)/number of participants analyzed at 6 months (study endpoint)/means and standard deviations for IPSS, AEs, re-treatment, and acute urinary retention

Footnotes

AEs: adverse events; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; PVR: post void residual; Qmax: maximum flow rate; QoL: quality of life.

Appendix 4. Assessment for risk of bias for NRS using ROBINS-I

Bias domain	Outcome	Author's judgement	Support for judgement
Bias due to confounding	Set 1	Ray 2018: serious risk of bias	Although Ray 2018 used an statistical method to adjust confounding factors, residual or unmeasured confounding can occur.

(Continued)

		Soluyanov 2018: critical risk of bias	Soluyanov 2018 did not perform any such method to adjust for potential confounding.
	Set 2 and 3	Ray 2018: serious risk of bias	Same reason listed above.
Bias in selection of participants into the study	Set 1	Ray 2018: moderate risk of bias Soluyanov 2018: critical risk of bias	As Ray 2018 recruited the participants based on predefined protocol, selection based on participant characteristics appears unlikely to have occurred. In Soluyanov 2018, participants were selected to each intervention based on prostate volume.
	Set 2 and 3	Ray 2018: moderate risk of bias	Same reason listed above.
Bias in classification of interventions	Set 1	Ray 2018, Soluyanov 2018: moderate risk of bias	Both studies used predefined criteria for the intervention (Ray 2018: ongoing authorized registry, Soluyanov 2018: prospective study design).
	Set 2 and 3	Ray 2018: moderate risk of bias	Same reason listed above.
Bias due to deviations from intended interventions	All review outcomes	Ray 2018, Soluyanov 2018: no information	Both studies reported no information on whether there was deviation from the intended intervention.
Bias due to missing data	Set 1	Ray 2018: serious risk of bias Soluyanov 2018: low risk of bias	Ray 2018 showed a large proportion of missing data, while Soluyanov 2018 reported the data of all participants who were assigned to each intervention completed follow-up by the end of the study.
	Set 2	Ray 2018: serious risk of bias	Same reason listed above.
	Set 3	Ray 2018: low risk of bias	All participants were included in the analysis.
Bias in measurement of outcomes	Set 1 (subjective outcome)	Ray 2018, Soluyanov 2018: serious risk of bias	Lack of blinding for participants, personnel, and/or outcome assessors.
	Set 2 and 3 (other subjective outcomes[a])	Ray 2018: serious risk of bias	Same reason listed above.
	Set 2 and 3 (objective outcomes[b])	Ray 2018: serious risk of bias	Although objective outcomes are unlikely influenced by knowledge of the intervention received in outcome assessment, participants and personnel were not blinded.
Bias in selection of the reported result	Set 1	Ray 2018: low risk of bias Soluyanov 2018: no information	Ray 2018 was based on a published protocol, while Soluyanov 2018 did not reported any protocol available.
	Set 2 and 3	Ray 2018: low risk of bias	Same reason listed above.
Overall bias	-	Ray 2018: serious risk of bias	-

(Continued)

	Soluyanov 2018: critical risk of bias

Footnotes

Set 1: urologic symptom scores; Set 2: quality of life, erectile function, ejaculatory disorders, and hospital stay; Set 3: major adverse events, re-treatment, minor adverse events, and acute urinary retention.

[a]Quality of life, major adverse events, erectile function, ejaculatory disorders, and minor adverse events

[b]Re-treatment, acute urinary retention, and hospital stay

NRS: non-randomized study; ROBINS-I: risk of bias tool to assess non-randomized studies of interventions.

HISTORY

Protocol first published: Issue 11, 2017
Review first published: Issue 12, 2020

CONTRIBUTIONS OF AUTHORS

Jae Hung Jung (JHJ): conceived, designed, and wrote the protocol and performed all aspects of data abstraction, analysis, risk of bias assessment, and certainty of evidence ratings.
Balaji Reddy (BR): performed data abstraction and risk of bias assessments.
Karen Ann McCutcheon (KAM): provided clinical and methodological input to the protocol and the review.

Michael Borofsky (MB): provided critical content expertise input to the protocol and review from a urology perspective.
Jafar Golzarian (JG): provided critical content expertise input to the protocol and review from a urology perspective.
Shamar Young (SY): provided critical content expertise input to the protocol and review from an interventional radiology perspective.
Jafar Golzarian (JG): provided critical content expertise input to the protocol and review from an interventional radiology perspective.

Tae Young Shin (TYS): provided clinical and methodological input to the protocol and the review.
Myung Ha Kim (MHK): created search strategies and executed the searches.

Vikram Narayan (VN): provided critical content expertise input to the protocol and the review.
Philipp Dahm (PD): conceived, designed, and wrote the protocol, reviewed critical content, and gave final approval.

DECLARATIONS OF INTEREST

JHJ: none known.

BR: none known.

KAM: none known.

MB: Boston Scientific (consultant for endourology and stone management), Auris Health (consultant for robotic surgery and endourology).

SY: none known.

JG: none known.

TYS: none known.

MHK: none known.

VN: none known.

PD: none known.

SOURCES OF SUPPORT

Internal sources

- Department of Urology, Yonsei University Wonju College of Medicine, Korea, South

  Salary support for Jae Hung Jung
- Minneapolis VA Health Care System, USA

  Salary support for Philipp Dahm
- Department of Urology, University of Minnesota, USA

  Salary support for Philipp Dahm

External sources

- N/A, USA

  No external support was received for this review

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review was based on a published protocol (Jung 2017), and differences are described here.

- Types of studies: we included only NRSs designed as prospective comparative studies, as other studies were very unlikely to provide evidence other than evidence of very low certainty.
- Types of outcome measures: we used an MCID of 0.5 to assess the quality of life outcome based on a newly cited reference (Rees 2015). In addition, we used final values instead of changes from baseline to make the fullest use of the results (half or more studies reported only final values).
- Types of outcome measures: we have changed the outcome of ejaculatory function to ejaculatory disorder due to lack of data based on the questionnaire. Therefore, we used incidence rate of ejaculatory disorders such as postoperative retrograde ejaculation or reduction of ejaculation volume.
- We revised the definition of 'retreatment' to "Participants undergoing the same or other surgical treatment modalities due to insufficient treatment response" for clarity, also omitting the time horizon of up to six months since later retreatments would also be of interest.
- Electronic searches: we additionally searched Google Scholar.
- Assessment of risk of bias in included studies: we listed baseline confounding factors and co-interventions to assess risk of bias in NRSs.
- "Summary of findings" table: we referenced GRADE guidance to rate certainty of evidence in RCTs and NRSs (Schünemann 2018).

NOTES

We based parts of the Methods section of this protocol on a standard template developed by the Cochrane Metabolic and Endocrine Disorders Group, which has been modified and adapted for use by Cochrane Urology.

INDEX TERMS

Medical Subject Headings (MeSH)

Arteries; Ejaculation; Embolization, Therapeutic [adverse effects] [*methods]; Lower Urinary Tract Symptoms [*therapy]; Penile Erection; Postoperative Complications [etiology]; Prostate [*blood supply]; Prostatic Hyperplasia [*complications]; Quality of Life; Randomized Controlled Trials as Topic; Retreatment [statistics & numerical data]; Sexual Dysfunction, Physiological [etiology]; *Transurethral Resection of Prostate [adverse effects]; Treatment Outcome

MeSH check words

Aged; Humans; Male