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ORIGINAL RESEARCH Efficacy and safety of prostate artery embolization on lower urinary tract symptoms related to benign prostatic hyperplasia: a systematic review and meta-analysis

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Background: Prostate artery embolization (PAE) is emerging and is a promising minimally invasive therapy that improves lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH). The purpose of this article was to evaluate the efficacy and safety of PAE on LUTS related to BPH.

Materials and methods: A literature review was performed to identify all published articles of PAE for BPH. The sources included MEDLINE, EMBASE and Cochrane Library from 1980 to 2016. A systematic review and meta-analysis was conducted. The outcome measurements were combined by calculating the mean difference with 95% confidence interval. Statistical analysis was carried out using Review Manager 5.3.0.

Results: Twelve studies involving 840 participants were included. Compared with baseline, the International Index of Erectile Function (IIEF-5; International Prostate Symptom Score) scores, the quality of life scores, peak urinary flow rate (Q_{max}) and postvoid residual volume all had significant improvements during the 24-month follow-up (all P < 0.00001). Both prostate volume (PV) and prostate-specific antigen had significant decrease during the 12-month follow-up (P<0.00001 and P=0.005, respectively), except postoperative 24 months (P=0.47 and P=0.32, respectively). The IIEF-5 short form scores had significant increase at postoperative 6 months (P=0.002) and 12 months (P<0.0001), except postoperative 1 month (P=0.23) and 24 months (P=0.21). For large volume ($PV \ge 80 \text{ mL}$) BPH, the results were similar. There were no life-threatening complications.

Conclusion: PAE is an effective, safe and well-tolerable treatment for LUTS related to BPH, including large volume (PV \ge 80 mL) BPH, with a good short-term follow-up. Studies with large number of cases and longer follow-up time are needed to validate our results.

Keywords: lower urinary tract symptoms, benign prostatic hyperplasia, meta-analysis, prostate artery embolization

Introduction

Lower urinary tract symptoms (LUTS) are main complaints resulting from benign prostatic hyperplasia (BPH), which is one of the most common diseases of aging men.¹ LUTS can range in severity and have a significant impact on the quality of life (QoL).

The current treatment options include watchful waiting, medical therapy and surgical intervention. The patients refractory to preliminary treatments can be treated with surgical intervention. Transurethral resection of the prostate (TURP) is the gold standard therapy for LUTS/BPH and, for many years, has been considered the surgical treatment

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of choice and the standard of care when other treatment methods fail.² However, TURP has significant complications, including short-term bleeding, dilutional hyponatremia, sexual dysfunction and incontinence. The complication rate is higher for patients with large volume BPH.³

Recently, prostate artery embolization (PAE) has started emerging and is a promising minimally invasive therapy that improves LUTS related to BPH and is associated with a decrease in prostate volume (PV).⁴ However, it is reported that as many as 25% of patients show no significant improvement in symptoms and peak flow rate. In addition, the average reduction rate in the PV after PAE was only 20%.⁵

The aim of this meta-analysis was to evaluate the efficacy and safety of PAE on LUTS related to BPH, which may help urologists make better choices in the case of elderly patients with large volume BPH.

Materials and methods Search strategy

A comprehensive literature search was carried out by two independent reviewers using MEDLINE (from 1980 to 2016), EMBASE (from 1980 to 2016) and the Cochrane Central Register of Controlled Trials. The reference lists of the retrieved studies were also checked. The following search terms were used: "prostate artery embolization", "lower urinary tract symptoms" and "benign prostatic hyperplasia".

Inclusion criteria

Studies that met the following criteria were included: 1) a study design that included PAE for BPH; 2) a study that provided data on International Prostate Symptom Score (IPSS), QoL, PV, prostate-specific antigen (PSA), peak urine flow rate (Q_{max}), postvoid residual (PVR) volume and International Index of Erectile Function (IIEF-5) short form at different follow-up times, and 3) a study where its full text could be accessed. If these inclusion criteria were not met, then the study was excluded.

Trial selection

When the same study was published in various journals or in different years, the most frequently cited one was used. If the same group of researchers studied a group of subjects with multiple experiments, then each study was included. Together, we discussed each of the studies that were included and excluded.

Quality assessment

The quality of included studies was assessed using the Newcastle–Ottawa scale generating a maximum of nine

stars to each study, including four stars for the selection of participants, two stars for the comparability of participants and three stars for the assessment of outcomes. Quality was assigned according to the scores so that seven to nine stars indicated high quality, four to six stars indicated middle quality and zero to three stars indicated low quality.

Data extraction

Two independent reviewers extracted the data using a predesigned form. The following information was collected from each study: 1) the name of the first author and the publication year; 2) the sample size; 3) the country in which the study was conducted; 4) data on IPSS, QoL, PV, PSA, $Q_{\rm max}$, PVR volume and IIEF-5 at different follow-up times and 5) the number of participants with complications. Any disputes were resolved by group consensus.

Statistical analysis

Statistical analysis was carried out using Review Manager 5.3.0. The changes in seven functional indexes were determined as differences between baseline and study completion. Outcome measurements were combined by calculating the mean difference with 95% confidence interval (CI). To quantify the effect of heterogeneity test result, l^2 heterogeneity test was used. A random-effects model was used if l^2 value was >50%; if not, a fixed-effects model was used. Publication bias was evaluated using the funnel plot.

Results

Characteristic and quality assessment of eligible studies

Figure 1 shows the flow diagram of the study selection process. Finally, there were nine articles involving 12 studies eligible for this meta-analysis.^{6–14} All of the 12 studies reported the baseline IPSSs, QoL scores, PV, PSA levels, $Q_{\rm max}$, PVR volume and IIEF-5 scores. All 12 studies excluded patients with malignancy, advanced atherosclerosis and tortuosity of the iliac arteries and/or prostate arteries, secondary renal insufficiency, large bladder diverticula or stones, neurogenic bladder, detrusor muscle failure, active urinary tract infection and unregulated coagulation parameters. The main characteristic and quality assessment of eligible studies are presented in Table 1.

Changes after PAE IPSSs

Six studies involving 582 participants, five studies involving 451 participants, six studies involving 479 participants and three studies involving 117 participants included

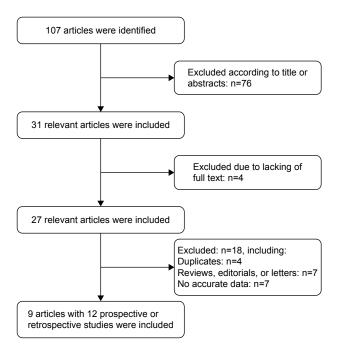


Figure I The flow diagram of the study selection process.

data representing IPSS changes at postoperative 1 month (Figure 2A), 6 months (Figure 2B), 12 months (Figure 2C) and 24 months (Figure 2D), respectively.

Compared with baseline, the IPSSs had significant decreases at postoperative 1 month (weighted mean difference (WMD) -12.74,95% CI -15.10 to -10.39, P < 0.00001), 6 months (WMD -14.13,95% CI -17.73 to -10.54, P < 0.00001), 12 months (WMD -16.07,95% CI -18.16 to -13.98, P < 0.00001) and 24 months (WMD -15.62,95% CI -17.41 to -13.82, P < 0.00001).

QoL scores

Nine studies involving 660 participants, eight studies involving 528 participants, six studies involving 414 participants and three studies involving 117 participants included data representing QoL score changes at postoperative 1 month (Figure 3A), 6 months (Figure 3B), 12 months (Figure 3C) and 24 months (Figure 3D), respectively.

Compared with baseline, the QoL scores had significant decreases at postoperative 1 month (WMD -2.07, 95% CI -2.37 to -1.76, P < 0.00001), 6 months (WMD -2.15, 95% CI -2.44 to -1.86, P < 0.00001), 12 months (WMD -2.81, 95% CI -3.45 to -2.17, P < 0.00001) and 24 months (WMD -2.15, 95% CI -2.60 to -1.69, P < 0.00001).

Prostate volume

Five studies involving 507 participants, five studies involving 386 participants, six studies involving 366 participants and three studies involving 106 participants included data representing PV changes at postoperative 1 month (Figure 4A), 6 months (Figure 4B), 12 months (Figure 4C) and 24 months (Figure 4D), respectively.

Compared with baseline, PV had significant decreases at postoperative 1 month (WMD -17.33, 95% CI -21.19 to -13.47, P < 0.00001), 6 months (WMD -31.62, 95% CI -46.75 to -16.48, P < 0.0001) and 12 months (WMD -30.72, 95% CI -42.91 to -18.53, P < 0.00001). Although PV was also less at postoperative 24 months (WMD -16.89, 95% CI -62.61 to -28.83), the difference was not statistically significant (P=0.47).

Prostate-specific antigen

Five studies involving 520 participants, five studies involving 383 participants, six studies involving 379 participants and three studies involving 104 participants included data representing PSA changes at postoperative 1 month (Figure 5A), 6 months (Figure 5B), 12 months (Figure 5C) and 24 months (Figure 5D), respectively.

Compared with baseline, PSA had significant decreases at postoperative 1 month (WMD -0.80, 95% CI -1.44 to -0.16, P=0.01), 6 months (WMD -1.15, 95% CI -1.69 to -0.60, P<0.0001) and 12 months (WMD -0.97, 95% CI -1.65 to -0.29, P=0.005). Although PSA was also less at postoperative 24 months (WMD -0.80, 95% CI -2.37 to -0.77), the difference was not statistically significant (P=0.32).

Q_{\max}

Six studies involving 502 participants, five studies involving 368 participants, six studies involving 368 participants and three studies involving 104 participants included data representing $Q_{\rm max}$ changes at postoperative 1 month (Figure 6A), 6 months (Figure 6B), 12 months (Figure 6C) and 24 months (Figure 6D), respectively.

Compared with baseline, Q_{max} had significant increases at postoperative 1 month (WMD 4.40, 95% CI 3.00–5.80, P<0.00001), 6 months (WMD 4.71, 95% CI 2.62–6.81, P<0.0001), 12 months (WMD 5.60, 95% CI 4.19–7.02, P<0.00001) and 24 months (WMD 5.89, 95% CI 5.08–6.7, P<0.00001).

PVR volume

Six studies involving 476 participants, five studies involving 348 participants, six studies involving 369 participants and three studies involving 104 participants included data representing PVR volume changes at postoperative 1 month (Figure 7A), 6 months (Figure 7B), 12 months (Figure 7C) and 24 months (Figure 7D), respectively.

Studies	Sample size	Study design	Country	Age (years)	PV (mL)	Other inclusion criteria	Outcome measures	Follow-up (month)	Quality assessment ^a
Gabr et al ⁶	22	Retrospective study	Saudi Arabia	>50	z	BPH patients with LUTS refractory to BPH- related medical therapy or those who had an indwelling urethral catheter due to refractory urine retention	IPSS, QoL, PV, PSA, Q _{mat} , PVR volume, IIEF-5	I, 3, 9	Four stars
Bilhim et al ⁷	186	Retrospective study	Portugal	~ 55	>30	BPH patients, IPSS >18 and QoL scores \ge 3, refractory to medical treatment for at least 6 months; $Q_{max} \le 12$ mL/s or those with acute urinary retention	IPSS, QoL, PV, PSA, Q _{mat} , PVR volume, IIEF-5	I, 6, 12, 18, 24	Seven stars
Wang et al ⁸	47	Prospective study	China	≥ 75	>40	BPH patients, IPSS >18 and QoL scores \ge 3, refractory to medical treatment for at least 6 months, $Q_{max} \le 12$ mL/s or those with acute urinary retention	IPSS, QoL, PV, PSA, Q _{max} , PVR volume, IIEF-5	12	Five stars
Wang et al ⁸	001			<75					Seven stars
lsaacson et al ⁹	12	Prospective study	NSA	√40	80-150	Previous trial of BPH medication, IPSS \ge 18, life expectancy $>$ 1 vear	IPSS, QoL, PV, PSA, 0, PVR volume, IIEF-5	l, 3	Three stars
Bagla et al ¹⁰	16	Prospective study	USA	> 45	<50	BPH patients with moderate- or severe-grade symptoms	QoL, IIEF-5	I, 3, 6	Four stars
Bagla et al ¹⁰ Bagla et al ¹⁰	26 36				50–80 > 80				Four stars Four stars
Li et al''	22	Prospective study	China	>65	> 80	BPH patients, IPSS $>$ 12, Q_{max} $<$ 15 mL/s,	IPSS, QoL, PV, PSA,	1, 3, 6, 12	Four stars
						PSA <4 ng/mL or PSA level between 4 and 10 ng/mL but negative prostate biopsy	Q _{max} , PVR volume, IIEF-5		
Wang et al ¹²	601	Prospective study	China	>50	× 80	BPH patients, IPSS >18 and QoL scores >3, refractory to medical treatment for at least 6 months, Q _{max} <12 mL/s	IPSS, QoL, PV, PSA, Q _{max} , PVR volume, IIEF-5	I, 3, 6, 12, 24	Six stars
Pisco et al ¹³	250	Prospective study	Portugal	√45	√40	BPH patients, IPSS >18, and QoL score ≥ 3 , refractory to medical treatment for at least 6 months; $Q_{max} < 12 \text{ mL/s}$, sexual dysfunction or accepting the risk of developing sexual dysfunction after treatment	IPSS, Qol., PV, PSA, Q _{max} , PVR volume, IIEF-5	I, 3, 6, 12, 18, 24	Eight stars
Pisco et al ¹⁴	<u>+</u>	Prospective study	Portugal	>60	z	BPH patients, IPSS >18 and QoL score \ge 3, refractory to medical treatment for at least 6 months; $Q_{max} < 12$ mL/s or those with acute urinary retention	IPSS, Qol., PV, PSA, Q _{mar} , PVR volume, IIEF-5	v	Three stars

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Total (95% Cl) 451 561 100 -14.13 (-17.73 to -10.54) \bullet Heterogeneity: $r^2=14.88$: $r^2=e2.27$: $dr=4$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=7.71$ ($P=0.00001$); $r^2=95\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=58\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=86\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$); $r^2=88\%$ Test for overall effect: $Z=15.06$ ($P=0.00001$) Test for $P=12.20$ <td< td=""><td>Wang e</td><td></td><td></td><td></td><td>105</td><td>26.1</td><td>5.5</td><td>109</td><td>22.0</td><td>-12.00 (-13.00 to -11.32) -18.50 (-19.79 to -17.21)</td><td>•</td><td></td><td></td></td<>	Wang e				105	26.1	5.5	109	22.0	-12.00 (-13.00 to -11.32) -18.50 (-19.79 to -17.21)	•		
Heterogeneity: $r^2 = 14.88$; $\chi^2 = 22.7$, $df^2 4$ (P-0.00001); $r^2 = 95\%$ Test for overall effect: $Z = 7.71$ (P<0.00001); $r^2 = 95\%$ Fill thim et al. 7.5 4.9 22.4 6.1 186 16.4 -12.20 (-14.22 to -10.18) Li et al. 7.5 4.5 22 27 4.5 22 14.8 -19.50 (-22.16 to -16.84) Pisco et al. 7.5 4.5 22 7. 4.5 22 14.8 -13.00 (-17.81 to -13.98) Mang et al. 8.5 5.5 100 24.5 6.5 100 17.3 -18.00 (-17.67 to -14.33) Wang et al. 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -13.98) Heterogeneity: $r^2 = 5.87$; $\chi^2 = 41.67$, $df = 5$ (P<0.00001); $r^2 = 88\%$ Total (95% CI) 4.79 2.41.67, $df = 5$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 15.06$ (P<0.00001); $r^2 = 88\%$ Test for overall effect: $Z = 17.06$ (P<0.00001) Test for overall effect: $Z = 17.06$ (P<0.0001); $r^2 = 65\%$ 100 15.22 25.4 -15.10 (-17.80 to -12.40) Wang et al. 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.57 to -12.23) Fest for overall effect: $Z = 17.05$ (P<0.0001) Test for $Z = 50\%$ Test for for $Z = 50\%$	Total (9	5% CI)		•	451			581	100	-14.13 (-17.73 to -10.54)	•	•	
Test for overall effect: $Z = f_1 \cdot f_1 \left(P^{-Q_1} \cup 0001 \right)$ Hiltim et al" 10.2 6.5 49 22.4 6.1 186 16.4 -12.20 (-14.22 to -10.18) Li et al" 7.5 4.5 22 14.8 -19.50 (-21.61 to -16.84) Pisco et al" 7.5 4.5 22 14.8 -19.50 (-21.4.39 to -12.41) Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Total (95% CI) 479 7.1 5.6 -17.50 (-19.84 to -13.96) Heterogeneity: r^2 =5.87; r^2 =4.1 6.57 100 -16.07 (-18.16 to -13.96) Heterogeneity: r^2 =5.87; r^2 =4.16.7 4f=5 (P<0.00001); P =88% Test for overall effect: Z=15.06 (P<0.00001); P =88% Test for overall effect: Z=15.06 (P<0.00001) Fiest for overall effect: Z=15.06 (P<0.00001); P =88% Test for overall effect: Z=17.05 (P<0.00001); P =66% Test for overall effect: Z=17.05 (P<0.00001)	Heteroc	eneity: $r^{2_{\pm}}$	=14.88;	$\chi^2 = 82.$	27, df=	=4 (P<0	.00001); /²=9!	2%		•		
Bilhim et al? 10.2 6.5 49 22.4 6.1 186 16.4 -12.20 (-14.22 to -10.18) Li et al" 7.5 4.5 22 27 4.5 186 16.4 -13.50 (-22.16 to -16.84) Pisco et al" 7.5 4.5 22 27 4.5 193 17.9 (-14.99 to -12.41) Wang et al" 8.45 94 26 5.5 109 17.9 (-18.00 (-19.38 to -16.62) Wang et al" 9.5 6.5 4.7 27 5 4.7 15.6 (-19.84 to -15.16) Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Total (35% CI) 479 714 100 -16.07 (-18.16 to -13.98) Heterogeneity: \vec{r}^2 =5.87; \vec{x}^2 =4.1.67, $d\vec{r}$ =5 (P <0.00001); \vec{l}^2 =88% Test for overall effect: Z=15.06 (P <0.00001); \vec{l}^2 =88% Fiblim et al" 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.37 to -12.23) Pisco et al" 9 6.58 25 24.1 6.5 25.4 100 -112.03 Pisco et al" 9 6.58 25 24.1 6.5 25.4 100 -112.03 Pisco et al" 9 6.58 25 24.1 6.5 25.4 100 -112.03 Pisco et al" 9 6.58 25 24.1 6.5 7 100 -112.60 Pisco et al" 9 6.58 25 24.1 6.5 7 100 -112.03 Total (35% CI) 117 542 (-17.41 to -13.82) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Pisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Total (35% CI) 117 543 (-16.00001) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.23) Fisco et al" 9 6.58 25 24.1 6.5 7 109 41.2 -17.00 (-18.57 to -12.40) Fisco et al" 9 6.68 25 6.5 0.00001) Fisco et al" 9 6.68 25 6.5 0.00001) Fisco et al" 9 6.68 25 6.5 0.00001) Fisco et al" 9 6.58 25 24.1 6.5 7 6.5 0.00001) Fisco et al 0.5 7 6-10.0001) Fisco et al 0.5 7 6-10.0001) Fisco et al 0.6 7 2-17.05 (P <0.00001)	lest ror	overall en	ect: Z=)00 [.] 0>	(1.00							
Li et al" 7.5 4.5 22 27 4.5 22 14.8 $-19.50(-22.16 \text{ to} -16.84)$ Pisco et al" 10.4 6.61 167 24.1 6.57 250 18.1 $-13.70(-14.996 \text{ to} -12.41)$ Wang et al" 8 4.5 94 26 5.5 109 17.9 $-18.00(-19.84 \text{ to} -15.16)$ Wang et al" 9.5 6.5 47 27 5 4.7 15.6 $-17.50(-19.84 \text{ to} -15.16)$ Wang et al" 8.5 5.5 100 24.5 6.5 100 17.3 $-16.00(-17.67 \text{ to} -14.33)$ Total (95% CI) 479 714 100 $-16.07(-18.16 \text{ to} -13.38)$ Heterogeneity: r^2 =5.87; χ^2 =4.167, dr =5 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=17.05 (P <0.00001); l^2 =88% Test for overall effect: Z=17.05 (P <0.00001); l^2 =66% Test for overall effect: Z=17.05 (P <0.00001); l^2 =56%					64	22.4	6.1	186	16.4	-12.20 (-14.22 to -10.18)		•	
Pisco et al ¹³ 10.4 6.61 167 24.1 6.57 250 18.1 -13.70 (-14.99 to -12.41) Wang et al ¹⁸ 8.5 6.5 4.7 27 5 4.7 15.6 -17.50 (-19.84 to -16.62) Wang et al ¹⁸ 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) Total (95% CI) 479 714 100 -16.07 (-18.16 to -13.38) Heterogeneity: r^2 =5.87; χ^2 =4.41.67, dr =5 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=4.16.7 dr=5 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =88% Test for overall effect: Z=15.06 (P <0.00001); l^2 =68% Test for overall effect: Z=17.05 (P <0.00001); l^2 =60 -12.23) Test for overall effect: Z=17.05 (P <0.00001); l^2 =56% Test for overall effect: Z=17.05 (P <0.00001); l^2 =56% Test for overall effect: Z=17.05 (P <0.00001); l^2 =56%	Li et al⁺				22	27	4.5	22	14.8	-19.50 (-22.16 to -16.84)	ł		
Wang et ali wang et ali wang et ali s84.594265.510017.9 $-18.00(-19.38 \text{ to} -16.62)$ *Wang et ali wang et ali wang et ali s8.55.510024.56.510017.3 $-16.00(-17.67 \text{ to} -14.33)$ *Wang et ali wang et ali wang et ali s8.55.510024.56.510017.3 $-16.00(-17.67 \text{ to} -14.33)$ *Total (95% CI)479714100 $-16.07(-18.16 \text{ to} -13.98)$ *Heterogeneity: z^2 =5.87; z^2 =41.67, df =5 (P <0.00001); l^2 =88%714100 $-16.07(-18.16 \text{ to} -13.98)$ *Heterogeneity: z^2 =5.87; z^2 =41.67, df =5 (P <0.00001); l^2 =88%714100 $-16.07(-18.16 \text{ to} -12.38)$ *Fistion cali solution to ali wang et ali 96.582525.4 $-17.00(-18.57 \text{ to} -12.23)$ *Fisco et ali wang et ali2 96.582525.4 $-17.00(-18.57 \text{ to} -12.23)$ *Total (95% CI)117545100 $-15.62(-17.41 \text{ to} -13.38)$ *Heterogeneity: z^2 =4.53, df =2 (P =0.10); l^2 =56%-17.05 (P <0.00001)	Pisco e		+		167	24.1	6.57	250	18.1	-13.70 (-14.99 to -12.41)	Ŧ		
Wang et al* by ang et al* by an et al*9.5 6.5 6.5 47 47 27 5 6.5 47 100 27 16.00 5 17.3 479 16.00 714 17.57 100 16.07 -16.07 $(-17.67$ -14.33 17.3 -16.00 $(-17.67$ -14.33 17.3 -16.00 -16.07 -16.33 17.3 -16.00 $(-17.67$ -16.33 17.3 -16.00 $(-17.67$ -16.33 17.3 -16.07 $(-18.16 to -13.38)$ -16.07 (-18.57) -16.07 (-18.57) -16.07 (-18.57) -16.07 (-18.57) -16.07 (-18.57) -16.37 (-18.57) -16.37 (-18.57) -16.37 (-18.57) -16.30 (-18.57) -12.23 (-18.57) -12.23 (-17.00) -12.23 (-18.57) -12.23 (-18.57) -12.23 (-17.00) -12.23 (-18.57) -12.23 (-17.00) -12.23 (-18.57) -12.23 (-17.41) -12	Wang e				2	26	5.5	109	17.9	-18.00 (-19.38 to -16.62)	•		
Wang et al* 8.5 5.5 100 24.5 6.5 100 17.3 -16.00 (-17.67 to -14.33) + Total (95% CI) 479 714 100 -16.07 (-18.16 to -13.98) + + Total (95% CI) 479 714 100 -16.07 (-18.16 to -13.98) + + Heterogeneity: $z^2=5.87$; $z^2=41.67$, $df=5$ ($P<0.00001$); $l^2=88\%$ 714 100 -16.07 (-18.16 to -13.98) + Test for overall effect: $z=1.50.6$ ($P<0.00001$); $l^2=88\%$ 714 100 -16.01 (-18.36 to -12.23) + Billinin et al? 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.37 to -12.23) + Pisco et al?3 9 6.58 22.4 6.1 186 -17.00 (-18.57 to -12.23) + Pisco et al?3 9 6.57 250 25.4 -17.00 (-18.57 to -12.40) + Wang et al?2 9 6.57 250 25.4 -17.00 (-18.57 to -12.43) + Otal (95% CI) 117 545 100 -15.22 (-17.41 to -13.32	Wang e					27		47	15.6	-17.50 (-19.84 to -15.16)	+		
Total (95% CI)479714100 -16.07 (-18.16 to -13.38) \bullet Heterogeneity: $r^2=5.87$; $\chi^2=41.67$, $df=5$ ($P<0.00001$); $l^2=88\%$ Test for overall effect: $Z=15.06$ ($P<0.00001$); $l^2=88\%$ Test for overall effect: $Z=15.06$ ($P<0.00001$);Billhim et all8.1 2.7 8.22.46.1Billhim et all'8.1 2.7 8.22.46.1 132 96.58 25 24.16.57 256 25.4 $-15.10(-17.80 \text{ to } -12.23)$ Ψ and get all'96.58 25 8426 5.5 8426 5.5 8426 5.5 8426 7100 -15.62 (-17.41 to -13.82) \bullet -17.00 (-18.57 to -12.40) \bullet -17.00 (-18.57 to -12.33)Total (95% CI) 117 5.5 84 26 5.5 5.5 84 26 26.4 -15.05 ($P<0.00001$) $Pietorogeneity: r^2=1.40; \chi^2=4.53, df=2 (P=0.10); l^2=56\%Test for overall effect: Z=17.05 (P<0.00001)$	Wang e					24.5		100	17.3	-16.00 (-17.67 to -14.33)	•		
Heterogeneity: r^2 =5.87; χ^2 =4.167, df=5 (P<0.00001); l ² =88% Test for overall effect: Z=15.06 (P<0.00001) Bilhim et al ⁷ 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.37 to -12.23) Pisco et al ¹³ 9 6.58 25 24.1 6.57 250 25.4 -15.10 (-17.80 to -12.40) Wang et al ¹² 9 5.5 84 26 5.5 109 41.2 -17.00 (-18.57 to -15.42) Total (95% CI) 117 545 100 -15.62 (-17.41 to -13.82)	Total (9	5% CI)		•	479			714	100	-16.07 (-18.16 to -13.98)	•		
lest for overall effect: $Z=15.06$ ($P<0.00001$) Bilhim et al? 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.37 to -12.23) Pisco et al ¹³ 9 6.58 25 24.1 6.57 250 25.4 -15.10 (-17.80 to -12.40) Wang et al ¹² 9 5.5 84 26 5.5 109 41.2 -17.00 (-18.57 to -15.43) Total (95% CI) 117 545 100 -15.62 (-17.41 to -13.82) Heterogeneity: $r^2=1.40$; $r^2=4.53$, $dr=2$ ($P=0.10$); $l^2=56\%$ Test for overall effect: $Z=17.05$ ($P<0.00001$) Test for overall effect: $Z=17.05$ ($P<0.00001$)	Heteroc	eneity: r^2	=5.87; 2	2=41.6	7, df={	5 (P<0.(00001);	/ ² =88 ⁹	%				
Biltime tal ⁷ 8.1 2.7 8 22.4 6.1 186 33.4 -14.30 (-16.37 to -12.23) * Pisco et al ¹³ 9 6.58 25 24.1 6.57 250 25.4 -15.10 (-17.80 to -12.40) * Wang et al ¹² 9 5.5 84 26 5.5 109 41.2 -17.00 (-18.57 to -15.43) * Total (95% CI) 117 545 100 -15.62 (-17.41 to -13.82) * Heterogeneity: r^2 =1.40; χ^2 =4.53, df =2 (P =0.10); l^2 =56% Test for overall effect: Z=17.05 (P <0.00001)	lest tor	overall en	ect: Z=) 00.61	10.0>4	(1.000							
Planmaterial 9 6.58 25 24.1 6.57 250 25.4 -15.10 (-17.08 to -12.40)					~	1 00	5	186	73.1	_11 30 /_16 37 to _12 23)		_	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$					52	24.1	0.1 6.57	250 250	25.4	-15.10 (-17.80 to -12.40)			
5 100 -15.62 (-17.41 to -13.82) $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$ -50 -25 0 25	Wang e				2	26	5.5	109	41.2	-17.00 (-18.57 to -15.43)			
-50 -25 0 25	Total (9	5% CI)		•	117			545	100	-15.62 (-17.41 to -13.82)	•		
G7 0 G7- 0G-	Heteroc	eneity: $r^{2=}$	=1.40; <i>ž</i>	2=4.53	, <i>df=</i> 2	(<i>P</i> =0.1(); /2=5	6%				- (- L
	Test for	overall eff	ect: Z=	17.05 (P<0.0(001)					GZ- NG-	0 1	C2

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∢			5	lotal	Mean	ק	lotal	(%)	random, 95% Cl	random, 95% CI	כ
	Bagla et al ¹⁰	2.79	1.31	16	4.6	1.5	16	6.4	-1.81 (-2.79 to -0.83)	ł	
	Bagla et al ¹⁰ Badla et al ¹⁰	3.14 9.02	1.50 1.46	202	א 4 ט		202	9.0 11 F	-1./6 (-2.49 to -1.03) -2 72 (-3 28 to -2 16)	+ +	
	Bilhim et al7	2.5	1.2	185	4.2		186	17.3	-1.70 (-1.90 to -1.50)	•	
-	Gabr et al ⁶	2.8	1.58	22	4.2		22	8.4	-1.40 (-2.18 to -0.62)	ł	
	Isaacson et al ⁹	1.7	1.8	12	4.8	-	12	5.0	-3.10 (-4.27 to -1.93)	ł	
	Li et al ¹¹	2.5	-	22	4.5		22	8.7	-2.00 (-2.75 to -1.25)	ł	
	Pisco et al ¹³	2.48	1.24	236	4.39	0.95	250	17.3	-1.91 (-2.11 to -1.71)	•	
	Wang et al¹²	2.5	-	105	5		109	16.3	-2.50 (-2.77 to -2.23)	•	
	Total (95% CI)			660			679	100	-2.07 (-2.37 to -1.76)	•	
	Heterogeneity: r^2 =0.13; χ^2 =35.30, df=8 (P<0.0001); l ² =77% Test for overall effect: Z=13.28 (P<0.00001)	r²=0.13; effect: Z=	χ²=35.3 =13.28 (30, <i>df</i> =8 (P<0.00	(P<0.0	001); /²:	=77%				
ш	Badla et al ¹⁰	2.7	1.77	16	46	ر ت	16	50	-1 90 (-3 04 to -0 76)	ł	
	Bagla et al ¹⁰	2.08	1.38	26	0.4	; . .	26	10.0	-2.82 (-3.50 to -2.14)	ł	
	Bagla et al ¹⁰	2	1.75	36	2	0.9	36	10.6	-3.00 (-3.64 to -2.36)	ł	
	Bilhim et al7	2.4	1.2	142	4.2	0.7	186	19.9	-1.80 (-2.02 to -1.58)	•	
	Li et al ¹¹	2	-	22	4.5	1.5	22	8.9	-2.50 (-3.25 to -1.75)	ł	
	Pisco et al ¹⁴	2.71	1.38	4	3.86	1.07	14	6.9	-1.15 (-2.06 to -0.24)	ł	
	Pisco et al ¹³	2.27	1.31	167	4.39	0.95	250	19.7	-2.12 (-2.35 to -1.89)	•	
	Wang et al ¹²	с	-	105	£	-	109	18.9	-2.00 (-2.27 to -1.73)	+	
	Total (95% CI) Heterogeneity: r^2 =0.10; χ^2 =23.82, df =7 (P=0.001); l^2 =71% Test for overall effect: Z=14.61 (P<0.00001)	<i>t</i> ²=0.10; effect: <i>Z</i> ⁼	χ²=23.8 =14.61 (528 32, <i>df</i> =7 (P<0.00	(<i>P</i> =0.0	01); /²=	659 71%	100	-2.15 (-2.44 to -1.86)	•	
ပ	Bilhim et al ⁷	2.3	1.1	49	4.2	0.7	186	17.4	-1.90 (-2.22 to -1.58)	•	
	Li et al ¹¹	7	1.5	22	4.5	1.5	22	13.5	-2.50 (-3.39 to -1.61)	ł	
	Pisco et al ¹³	1.96	1.23	102	4.39	0.95	250	17.6	-2.43 (-2.70 to -2.16)	•	
	Wang et al ¹²	2.5	1.5	94	5	-	109	17.2	-2.50 (-2.86 to -2.14)	+	
	Wang et al ⁸	ל ד היה	ч С	47	5.5 7	т т	47	16.9 17.4	-4.00 (-4.40 to -3.60)	+ '	
	Total (95% CI)	2	2	414)	2	714	100	-2.81 (-3.45 to -2.17)		
	Heterogeneity: r^2 =0.59; χ^2 =93.38, df =5 (P<0.00001); l^2 =95% Test for overall effect: Z=8.61 (P<0.00001)	r ² =0.59; effect: Z=	χ²=93.3 =8.61 (F	38, <i>df</i> =5 ><0.000	(P<0.0	0001); /	/2=95%			•	
	Bilhim et al ⁷	2.4	0.7	œ	4.2	0.7	186	29.3	-1.80 (-2.30 to -1.30)	+	
	Pisco et al ¹³ Wang et al ¹²	1.76 3	1.01	25 84	4.39 5	0.95	250 109	32.7 38.0	-2.63 (-2.28 to -1.72) -2.00 (-2.28 to -1.72)	••	
	Total (95% CI)			117			545	100	–2.15 (–2.60 to –1.69)	•	
	Heterogeneity: $r^2=0.12$; $\chi^2=8.14$, $df=2$ ($P=0.02$); $l^2=75\%$	$t^2 = 0.12;$	$\chi^2 = 8.14$	l, <i>df</i> =2 (P=0.02); <i>I</i> ² =75	%		16	c	
	LEST IOL OVERAIL C		1) 77.6=		(1)						2

Figure 3 A forest plot about QoL score changes after PAE at postoperative 1 month (A), 6 months (B), 12 months (C), and 24 months (D). Abbreviations: Cl, confidence interval; IV, intravenous; PAE, prostate artery embolization; SD, standard deviation; QoL, quality of life.

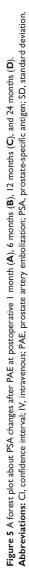
Wang et al

Postoperation Baseline Weight Mean difference (V, mean SD Total Weight Mean difference (V, random, 95% CI 66.6 39.7 175 88.6 51.3 186 61.7 -22.00 (-31.43 to 12.57) 56.8 57.7 22 14.89 22 68.8 51.7 14.80 22.648 56.8 57.72 110 25 58.9 100 -22.92 to -5.48 66.8 30.7 158 31.6 12.67 -22.90 to -10.54 $77.7^{22}289.$ 412.886 51.3 186 51.3 186 51.349 100 $77.7^{22}289.$ $412.479.666.9$ 38.134 88.65 51.349 $20.43.006$ -57.34 66.9 38 13.44 10.93 52.3 -40.006 $-57.716-96.239$ -90.23 66.9 38.134 88.65 51.346 100 -17.33 -21.100 $-57.716-96.239$ -90.23 66.9 38	Mean difference IV, random, 95% Cl	<u>↓</u> ↓ ↓	• + + + +		 ↓ ↓ ↓ ↓ ↓ 	-100 -50 0 50 Favors (postoperation) Favors (baseline)
Postoperation Baseline Total Mean SD	Mean difference IV, random, 95% Cl	-22.00 (-31.43 to 12.57) -20.50 (-29.56 to 11.44) -10.00 (-24.77 to 4.77) -16.70 (-22.90 to -10.50) -14.20 (-22.92 to -5.48)	-17.33 (-21.19 to -13.47) -21.70 (-31.49 to -11.91) -43.00 (-57.77 to -28.23) -48.00 (-52.88 to -4.92) -16.70 (-24.06 to -9.34) -48.00 (-55.17 to -40.83)	-31.62 (-46.75 to -16.48) -17.50 (-33.60 to -1.40) -41.00 (-54.38 to -27.62) -16.60 (-25.85 to -7.35) -49.50 (-66.74 to -42.26) -36.00 (-48.28 to -23.72) -22.50 (-29.25 to -15.75)	-30.72 (-42.91 to -18.53) 1.40 (-58.30 to 61.10) 7.40 (-20.95 to 35.75) -49.00 (-56.62 to -41.38)	-
Study or Postoperation Baseline Stole Total Mean SD Mean <t< td=""><th>-</th><td>16.7 18.1 6.8 38.8 19.6</td><td>100 21.4 19.2 22.3 22.3</td><td>100 =91% 15.7 17.4 18.1 16.2 18.2</td><td>100 =89% 24.1 35.4 40.5</td><td>100 ²=88%</td></t<>	-	16.7 18.1 6.8 38.8 19.6	100 21.4 19.2 22.3 22.3	100 =91% 15.7 17.4 18.1 16.2 18.2	100 =89% 24.1 35.4 40.5	100 ²=88%
Study or subgroup Postoperation Mean SD Baseline Total Baseline Mean SD Stop Fillhim et al ⁷ 66.6 39.7 175 88.6 51.3 Gab et al ⁸ 56.8 15.77 22 77.3 14.8 Li et al ¹¹ 100 25 22 77.3 314.8 Disco et al ¹³ 66.8 28.7 183 35.7 314.8 Wang et al ¹² 103.8 30 474 (Po.00001) 25 Total (95% ct) 507 110 25 31.3 816.5 31.3 36.3 Heterogeneity: χ^2 =2.89, df=4 (Po.50001) 51.3 113 35.3 37 Wang et al ¹² 66.9 38 134 88.6 51.3 Pisco et al ¹³ 66.8 30.92 111 33.5 37 Pisco et al ¹³ 66.8 30.92 114 33.5 37 Pisco et al ¹³ 66.8 30.92 114 33.5 37 Pisco et al ¹³ 66.9	Total			581 3001); <i>I</i> ² : 186 22 250 109 47 47	714 3001); <i>I</i> ² : 186 250 109	545 0003); <i>I</i> ²
Study or subgroup Postoperation Mean SD Base Total Base Mean SD Total Mean Mean SD Total Mean SS Mean SS<	line SD	51.3 14.89 25 37 35	0% 51.3 25 36.3 35	(P<0.00 51.3 37 33 33 33 33 33	(P<0.00 51.3 35 35	2 (P=0.
Study or subgroup Postoperation Mean SD Tota Billhim et al ⁷ Gabr et al ⁸ Li et al ¹¹ S56 39.7 175 22 22 22 22 22 22 20 20 20 20 20 20 20		88.6 77.3 110 83.5 118	58); /²= 00001) 88.6 110 104.5 83.5 118	<i>df=4</i> 0001) 88.6 110 83.5 118 86 71	, <i>df</i> =5 ₁ 00001) 88.6 83.5 118	49, <i>df=</i> : 47)
Study or subgroupPostoperati leal by theanSD subgroupBillhim et al? Gab et al? Li et al? Li et al? Li et al? 10056.8 56.8 56.8 15.77 10056.8 25.73 25 25 25 25 25 25 25 25 25 25 25 25 25 25 25 26 20 20 2097.6 26 26 25 25 25 25 25 25 25 26 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20 20	on Total		507 507 1 (P=0.1) 1 (P<0.1) 1 134 1 134 1 134 1 14 1 111 1 105 1 105	386 =42.12 3 (<i>P</i> <0. 40 22 22 94 94 94 100	366 =45.92 t (<i>P</i> <0. 8 14 84	106 χ ² =16.4 2 (P=0.
Stucky or subgroupPost MearBillhim et al Gabr et al Gabr et al Heterogenetity66.6 66.8 66.9Di et al Heterogenetity70.3.8 66.9Pisco et al Pisco et al Total (95% CI)66.9 66.9Bilhim et al Catal (95% CI)66.9 66.9Pisco et al Et et al Nang et al Pisco et al Bilhim et al Pisco et al 66.966.9 66.9Pisco et al Nang et al Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.968.5 60.9 60.9Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.968.5 90.9 90.9Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.969.5 90.9Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.990.9 90.9Pisco et al Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.990.9 90.9Pisco et al Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 90.990.9 90.9Pisco et al Pisco et al Bilhim et al Pisco et al Bilhim et al Pisco et al 	operati 		.9, df=√ 	3.76; χ^2 Z=4.06 46.2 32.54 15 20 15 15).17; χ^2 Z=4.94 85.5 53.4 18	28.37; , Z=0.72
Study or subgroup Ballhim et al ⁶ Gabr et al ⁶ Li et al ¹¹ Pisco et al ¹² Wang et al ¹² Total (95% Ci Heterogeneity Pisco et al ¹⁴ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Wang et al ¹⁷ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Wang et al ¹⁷ Pisco et al ¹³ Wang et al ¹⁷ Pisco et al ¹³ Wang et al ¹⁷ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Wang et al ¹⁷ Pisco et al ¹³ Pisco et al ¹³ Pisco et al ¹³ Wang et al ¹⁶ Pisco et al ¹³ Pisco et al ¹³ Vang et al ¹⁷ Pisco et al ¹³ Pisco et al ¹³ Pisco et al ¹³ Vang et al ¹⁷ Pisco et al ¹³ Vang et al ¹⁷ Vang et al ¹⁷ Vang et al ¹⁷ Vang et al ¹⁷ Vang et al ¹⁷	Posto Mean	66.6 56.8 100 66.8 103.8) $\chi^{2}=2.8$ 1 effect: 66.9 67 76 66.8 66.8 70) : τ^2 =25(l effect: 71.1 69 66.9 68.5 50 48.5) : τ^2 =20(l effect: 90 90.9 69) : <i>t</i> ² =1,3 l effect:
	Study or subgroup	^a Bilhim et al ⁷ Gabr et al ⁶ Li et al ¹¹ Pisco et al ¹³ Wang et al ¹²	Total (95% CI) Heterogeneity: Test for overall Bilhim et al ⁷ Li et al ¹¹ Pisco et al ¹⁴ Pisco et al ¹² Wang et al ¹²	Total (95% CI) Heterogeneity. Test for overall Bilhim et al″ Li et al″ Pisco et al° Wang et al° Wang et al ⁸ Wang et al ⁸	Total (95% CI) Heterogeneity: Test for overall Bilhim et al ⁷ Pisco et al ¹³ Wang et al ¹²	Total (95% CI Heterogeneity. Test for overall

Figure 4 A forest plot about PV changes after PAE at postoperative 1 month (A), 6 months (B), 12 months (C), and 24 months (D). Note: ^aUsing the fixed-effects model. Abbreviations: CI, confidence interval; IV, intravenous; PAE, prostate artery embolization; PV, prostate volume; SD, standard deviation.

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	Study or subgroup	Postop Mean	Postoperation Mean SD 7	on Total	Baseli Mean	sD	Total	weight (%)	wean difference IV, random, 95% CI		Mean difference IV, random, 95% CI
∢	Bilhim et al ⁷ Gabr et al ⁶ Isaacson et al ⁹ Li et al ¹¹ Pisco et al ¹³ Wang et al ¹²	13.3 14.31 9.8 11.9 11.9	7.3 3.6 3.5 3.5 3.5 3.5	156 22 185 105	10.3 8.06 6.1 9.19 8.5	5.5 5.5 2.95 2.8 2.5 2.5 2.5	186 22 22 250 109	18.5 12.3 14.7 20.4 21.2	3.00 (1.61 to 4.39) 6.25 (3.56 to 8.94) 3.70 (1.12 to 6.28) 6.00 (3.85 to 8.15) 2.71 (1.74 to 3.68) 5.50 (4.73 to 6.27)		₊ + ₊ + ₊ +
	Total (95% CI) 502 601 Heterogeneity: $\tau^2=2.25$; $\chi^2=27.67$, $df=5$ (P<0.0001); $l^2=82\%$ Test for overall effect: $Z=6.17$ (P<0.00001)	<i>t</i> ²=2.25; ∋ffect: Z	;	502 ∵67, <i>d</i> 1= (P<0.00	:5 (P<0.(001)	, (1000	601 /²=82%	100	4.40 (3.00 to 5.80)		•
Ш	Bilhim et al ⁷ Li et al' ¹¹ Pisco et al ¹⁴ Pisco et al ¹³ Wang et al ¹²	13.1 13 10.91 15.5	6.7 3.5 5.34 6.5	122 22 105 105	10.3 6 7.06 9.19 8.5	5.5 2.5 2.63 2.63 2.63 2	186 22 14 109	21.2 20.0 21.8 21.6	2.80 (1.37 to 4.23) 7.00 (5.20 to 8.80) 3.85 (0.73 to 6.97) 2.81 (1.59 to 4.03) 7.00 (5.70 to 8.30)		+ ⁺ ++ ⁺
	Total (95% CI) 368 581 • Heterogeneity: <i>τ</i> ²=4.86; <i>χ</i> ²=34.53, <i>df</i> =4 (P<0.00001); <i>l</i> ²=88% Test for overall effect: Z=4.41 (P<0.0001)	τ²=4.86; ∋ffect: Z	;	368 .53, <i>df</i> = (P<0.00	-4 (<i>P</i> <0.)	00001)	581 ; /²=88%	100 %	4.71 (2.62 to 6.81)		•
с О	Bilhim et al ⁷ Li et al ¹¹ Pisco et al ¹³ Wang et al ¹² Wang et al ⁸	13 12 14 16 16	ຕິດ ບັນ ດິດ ອີດ ບັນ ດີ	36 22 60 47 94	10.3 6 9.19 8.5 8.5 8.5	5.5 2.5 4.47 2.5 1.5	186 22 250 109 47 100	13.6 15.9 16.8 18.3 19.3	2.70 (0.50 to 4.90) 6.00 (4.37 to 7.63) 3.61 (2.21 to 5.01) 6.00 (4.99 to 7.01) 7.00 (5.40 to 8.60) 7.50 (6.83 to 8.17)		++++*
	Total (95% CI) 368 714 Heterogeneity: r^2 =2.58; χ^2 =37.59, df =5 (P<0.00001); l^2 =87% Test for overall effect: Z=7.76 (P<0.00001)	<i>r</i> ²=2.58; ∋ffect: Z	;	368 .59, <i>df</i> = (P<0.00	=5 (<i>P</i> <0.⊢	00001)	714 ; /²=87º	100 %	5.60 (4.19 to 7.02)		٠
Δ	^a Bilhim et al ⁷ Pisco et al ¹³ Wang et al ¹²	13.1 13.9 14.5	8.4 7.2 3.5	8 84 84	10.3 9.19 8.5	5.5 4.47 2	186 250 109	1.9 3.9 94.2	2.80 (-3.07 to 8.67) 4.71 (0.60 to 8.82) 6.00 (5.16 to 6.84)		
	Total (95% Cl) Heterogeneity. <i>≵</i> ² =1.45, <i>df</i> =2 (<i>P</i> =0.49); <i>f</i> ²=0% Test for overall effect: Z=14.20 (<i>P</i> <0.00001)	χ^2 =1.45 effect: Z	, <i>df</i> =2 (=14.20	104 (<i>P</i> =0.49) (<i>P</i> <0.0); /²=0% 0001)		545	100	5.89 (5.08 to 6.70)	-20 -10 C	0 10 Favors (baseline)

Figure 6 A forest plot about Q_{max} changes after PAE at postoperative I month (**A**), 6 months (**B**), 12 months (**C**), and 24 months (**D**). **Note:** ^aUsing the fixed-effects model. **Abbreviations:** CJ, confidence interval; IV, intravenous; PAE, prostate artery embolization; SD, standard deviation; Q_{max}, peak urinary flow rate.

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													- 50 - 50 - 1	iseline)
rence IV, 5% CI									1				- 100	Favors (baseline)
Mean difference IV, random, 95% CI	+	+	•		ŧ.	+ +	++++		† +	+ _	•	+	- 0 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1	Favors (postoperation)
									·	ł	·		-200	
ence IV, % CI	-25.90 (-43.84 to -7.96) -64.12 (-83.32 to -44.92) 60.207 128 70 to 8.30	-00.20 (-120.79 (0.0.39) -70.00 (-85.07 to -54.93) 37.30 (53.00 to -54.54)	-80.00 (-90.14 to -69.86)	-56.23 (-76.02 to -36.43)	-37.50 (-54.51 to -20.49)	-00.00 (-99.04 to -70.96) -79.50 (-99.27 to -59.73)	-40.10 (-56.84 to -23.36) -90.00 (-99.82 to -80.18)	-66.82 (-89.34 to -44.29)	-15.30 (-49.58 to -18.9) -100.00 (-113.21 to -86.7) -51.20 (-69.48 to -32.9)	-54.00 (-64.11 to -43.8) -160.00 (-184.59 to -135.4) -110.00 (-119.80 to -100.2)	-82.69 (-113.64 to -51.74)	-30.90 (-67.42 to -5.62) -11.00 (-79.05 to -57.05) -85.00 (-94.92 to -75.08)	-49.07 (-97.67 to -0.47) -	
Weight Mean difference IV, (%) random, 95% Cl	-25.90 (-43 -64.12 (-83 60.20 (-12	-70.00 (-85. -70.00 (-85. -27.30 (-85.		-56.23 (-76	-37.50 (-54	-79.50 (-99.	40.10 (56 90.00 (99	-66.82 (-89	-15.30 (-49 -100.00 (-1 -51.20 (-69	-54.00 (-64. -160.00 (-11 -110.00 (-11	-82.69 (-11 : 3%	-30.90 (-67. -11.00 (-79. -85.00 (-94.	-49.07 (-97	
	18.2 17.8 6.0	0.0 19.0	20.2	100 ²=87%	19.7	20.4 18.9	19.7 21.3	100 2=91%	14.7 17.3 16.8	17.5 16.1 17.6	100); <i>I</i> ² =96	34.5 23.3 42.2	100 =83%	
Total	7 22 136			601 0001); /		7 4	250 109	581 3001); /		109 47 100	714 0.00001	186 250 109	545 003); <i>I</i> ²	
line SD	91.4 2 38.27 116			(P<0.0(91.4	30.8	88.9 50	(P<0.0(50 40	=5 (P<	91.4 88.9 50	2 (P=0.	
r Baseline Total Mean SD	91.9 111.62	140	125	, <i>df</i> =5 , 00001)	91.9	130.8	102.9 125	348 =46.30, <i>df</i> =4 (P<0.00001)	91.9 140 102.9	94 160 120	.81, <i>df</i> : 00001)	91 102.9 125	37, df=: 05)	
on Total	140 22			476 =38.19 ' (<i>P</i> <0.(108		99 105	348 =46.30 <i>(P<</i> 0.(33 28 23 33	109 47 100	369 χ²=130 . (<i>P</i> <0.(7 3 13 84	104 χ ² =11.8 (<i>P</i> =0.0	
Postoperation Mean SD 7	73.8 25.43	20.2 20 76 37	20.02	7.65; χ²: Z=5.57	57.3 15	21.8	63.95 15).03; $\chi^{2:}$ Z=5_81	92.8 10 56.66	30 20 30 20	94.51;	46 123.53 15	32.88;	
Postopera Mean SD	66 47.5 57 8		45	τ^2 =477 effect:	54.4 55	51.3	62.8 35	τ^2 =596 effect:	76.6 40 51.7	0 0 6	τ^2 =1,3: effect:	61 91.9 40	τ^2 =1,4. effect:	1
Study or subgroup	Bilhim et al ⁷ Gabr et al ⁶ Issaccon et al ⁹	Li et al ¹¹ Disco et al ¹³	Wang et al ¹²	Total (95% CI) 476 601 100 Heterogeneity: x^2 =34.19, df =5 (P<0.00001); l^2 =87% Test for overall effect: Z=5.57 (P=0.00001)	Bilhim et al ⁷	LI et al" Pisco et al ¹⁴	Pisco et al ¹³ Wang et al ¹²	Total (95% CI) 348 581 100 Heterogeneity: r^2 =596.03; χ^2 =46.30, df =4 (P<0.00001); l^2 =91% Test for overall effect: Z=5 81 (P<0.00001)	Bilhim et al ⁷ Li et al ¹¹ Pisco et al ¹³	Wang et al ¹² Wang et al ⁸ Wang et al ⁸	Total (95% CI) 369 714 100 Heterogeneity: r^2 =1,394.51; χ^2 =130.81, df =5 (P <0.00001); β =96% Test for overall effect: Z=5.24 (P <0.00001)	Bilhim et al ⁷ Pisco et al ¹³ Wang et al ¹²	Total (95% Cl) 104 545 100 Heterogeneity: r^2 =1,432.88; χ^2 =11.87, df=2 (P=0.003); l²=83% Test for overall effect: Z=1.98 (P=0.05)	
	⋖				Ш				C)		e c



Compared with baseline, PVR volume had significant decreases at postoperative 1 month (WMD -56.23, 95% CI -76.02 to -36.34, P < 0.00001), 6 months (WMD -66.82, 95% CI -89.34 to -44.29, P < 0.00001), 12 months (WMD -82.69, 95% CI -113.64 to -51.74, P < 0.00001) and 24 months (WMD -49.07, 95% CI -97.67 to -0.47, P=0.05).

IIEF-5 scores

Nine studies involving 609 participants, eight studies involving 463 participants, six studies involving 372 participants and three studies involving 102 participants included data representing IIEF-5 score changes at postoperative 1 month (Figure 8A), 6 months (Figure 8B), 12 months (Figure 8C) and 24 months (Figure 8D), respectively.

Compared with baseline, the IIEF-5 scores were slightly increased at postoperative 1 month (WMD 0.49, 95%

CI -0.30-1.28), but the difference was not statistically significant (*P*=0.23). There were significant increases at postoperative 6 months (WMD 1.29, 95% CI 0.48–2.10, *P*=0.002) and 12 months (WMD 1.36, 95% CI 0.69–2.02, *P*<0.0001). However, a slight decrease turned up at postoperative 24 months (WMD -0.81, 95% CI -2.08-0.46), which was not statistically significant (*P*=0.21).

Changes after PAE on large volume (PV \geq 80 mL) BPH

Four studies, involving 179 participants, included data representing changes in the large volume BPH (PV>80 mL).⁹⁻¹² All the results matched the earlier findings, except that PSA had no obvious decrease during the 3-month follow-up and that the IIEF-5 scores had no significant changes during the 12-month follow-up. The comparison of changes after

	Study or subgroup	Posto Mean		on Total	Baseli Mean		Total		Mean difference IV, random, 95% CI		ean difference IV, xed, 95% Cl	
	Bagla et al ¹⁰	14.75	8	16	15	7.3	16	2.2	-0.25 (-5.56 to 5.06))		
	Bagla et al ¹⁰	14.41	6.64		14.8	6.9	26	4.6	-0.39 (-4.07 to 3.29)			
	Bagla et al ¹⁰	13.15	8.26	36	12.7	5.5	36	6.0	0.45 (-2.79 to 3.69)	/		
	Bilhim et al ⁷	16.8	8	173	16.6	7.8	186	23.4	0.20 (-1.44 to 1.84)			
	Gabr et al ⁶	16.5	6.14	22	15.8	6.79	22	4.3	0.70 (-3.13 to 4.53)			
					13.0	8.3			· · · ·	\ \		
	Isaacson et al ⁹	17	7.2	12			12	1.6	4.00 (-2.22 to 10.22)			
	Li et al ¹¹	18	6	22	20	5.5	22	5.4	-2.00 (-5.40 to 1.40))		
	Pisco et al ¹³	20.6	7.81	197	18.9	8.73	250	26.5	1.70 (0.16 to 3.24)			
	Wang et al ¹²	11	5	105	11	6.5	109	26.0	0.00 (-1.55 to 1.55)		+	
	Total (95% CI)	2-0.40		609	N: 12-00		679	100	0.49 (-0.30 to 1.28)		•	
	Heterogeneity: Test for overall e					D						
	Bagla et al ¹⁰	17.57	6.58	16	15	7.3	16	2.8	2.57 (-2.25 to 7.39)			
	Bagla et al ¹⁰	16.91	6.61	26	14.8	6.9	26	2.0 4.8	2.11 (-1.56 to 5.78)			
	Bagla et al ¹⁰	16.39	8.8	36	14.0	5.5	36	4.0 5.7	3.69 (0.30 to 7.08)			
						5.5 7.8					_	
	Bilhim et al ⁷	18.1	7.9	134	16.6		186	21.4	1.50 (-0.25 to 3.25)			
	Li et al ¹¹	18	5	22	20	5.5	22	6.8	-2.00 (-5.11 to 1.11)			
	Pisco et al ¹⁴	17.9	8.77	14	16.2	9.42	14	1.4	1.70 (-5.04 to 8.44)			
	Pisco et al ¹³	20.5	7.43	110	18.9	8.73	250	21.1	1.60 (-0.16 to 3.36)		-	
,	Wang et al ¹²	12	3	105	11	6.5	109	35.9	1.00 (-0.35 to 2.35)		-	
	Total (95% CI)			463			659	100	1.29 (0.48 to 2.10)		•	
	Heterogeneity: ;			·		D						
	Test for overall e				,							
	Bilhim et al ⁷	18.4	7	44	16.6	7.8	186	8.0	1.80 (-0.55 to 4.15)			
	Li et al ¹¹	17	6	22	20	5.5	22	3.8	-3.00 (-6.40 to 0.40)) -		
	Pisco et al ¹³	20.1	3.67	65	18.9	8.73	250	22.5	1.20 (-0.20 to 2.60)			
1	Wang et al ¹²	13	2	94	11	6.5	109	26.7	2.00 (0.71 to 3.29)			
	Wang et al ⁸	8.5	3.5	47	7.5	3	47	25.4	1.00 (-0.32 to 2.32)			
,	Wang et al ⁸	18	7	100	16	6	100	13.5	2.00 (0.19 to 3.81)			
	Total (95% CI)			372			714	100	1.36 (0.69 to 2.02)		•	
	Heterogeneity: Test for overall e					%						
	Bilhim et al ⁷	18.8	7	6	16.6	7.8	186	5.0	2.20 (-3.51 to 7.91)			
	Pisco et al ¹³	18.7	11.4	12	18.9	8.73	250	3.8	-0.20 (-6.74 to 6.34)) —		
,	Wang et al ¹²	10	2.5	84	11	6.5	109	91.3	-1.00 (-2.33 to 0.33))	-	
	Total (95% CI)			102			545	100	-0.81 (-2.08 to 0.46)	•	
	Heterogeneity:					Ď						10
	Test for overall e	effect: Z	=1.25	(P=0.2 ⁻	1)				-	-20 –10	0	10

Figure 8 A forest plot about IIEF-5 score changes after PAE at postoperative 1 month (A), 6 months (B), 12 months (C), and 24 months (D). Abbreviations: CI, confidence interval; IIEF-5, International Index of Erectile Function; IV, intravenous; PAE, prostate artery embolization; SD, standard deviation.

Variables	I month		3 months		6 months		I2 months	
	MD (95% CI)	P-value	MD (95% CI)	P-value	MD (95% CI)	P-value	MD (95% CI)	P-value
IPSSs	-15.97 (-17.25 to -14.68)	<0.00001	-17.97 (-19.00 to -16.94)	<0.00001	-18.61 (-19.74 to -17.48)	<0.0000	-18.32 (-19.54 to -17.09)	<0.00001
QoL scores	-2.51 (-2.74 to -2.29)	<0.00001	-2.64 (-3.30 to -1.98)	<0.00001	-2.45 (-3.10 to -1.80)	<0.0000	-2.50 (-2.83 to -2.17)	<0.00001
PV	-13.11 (-20.63 to -5.60)	0.0006	-43.39 (-49.92 to -36.85)	<0.00001	-47.05 (-53.50 to -40.60)	<0.0000	-47.58 (-53.94 to -41.21)	<0.00001
PSA	-0.23 (-1.21 to 0.74)	0.64	-0.45 (-1.41 to -0.52)	0.36	-0.74 (-1.15 to -0.33)	0.0004	-0.42 (-0.82 to -0.03)	0.04
Qmax	5.42 (4.73 to 6.12)	<0.00001	6.66 (5.9 to 7.43)	<0.00001	7.00 (5.95 to 8.05)	<0.0000	6.00 (5.14 to 6.86)	<0.00001
PVR volume	-76.64 (-84.98 to -68.29)	<0.00001	-82.73 (-91.10 to -74.36)	<0.00001	-88.35 (-96.39 to -80.31)	<0.0000	-76.80 (-121.87 to -31.72)	0.0008
IIEF-5 scores	-0.04 (-1.31 to 1.22)	0.95	-0.65 (-1.93 to 3.23)	0.62	0.85 (-1.70 to 3.41)	0.51	-0.24 (-5.12 to 4.63)	0.92
Note: Data fror	Note: Data from Isaacson et al, ⁹ Bagla et al, ¹⁰ Li et al, ¹¹ and Wang et al. ¹²	¹ and Wang et al. ¹²						

prostate-specific antigen; PV, prostate volume; PVR, postvoid residual; \mathcal{Q}_{mx} , peak urinary flow rate; QoL, quality of life

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PAE on large volume (PV \geq 80 mL) BPH with baseline is presented in Table 2.

Complications

There were no life-threatening complications. Only one serious adverse event was seen in the study by Pisco et al:14 a case of a small area (1.5 cm²) of bladder wall ischemia in the right side of the base without involvement of the urethra or urethral orifices. The area of ischemia at the bladder base was removed by surgery without further complications.

Burning sensation in urethra (87/840, 10.4%) during the procedure seemed to be the main complication. Hematuria occurred in 57/840 (6.8%) participants, hematospermia in 49/840 (5.8%), a small rectal bleeding in 38/840 (4.5%) and inguinal hematoma in 16/840 (1.9%). All these complications disappeared spontaneously without any treatment. In all, 21/840 (2.9%) participants developed urinary tract infection and all responded to suitable antibiotics. A total of 80/840 (9.5%) participants had acute urinary retention (AUR) at 1-3 days after PAE. For relief, a temporary bladder catheter was placed, and they were able to void spontaneously before discharge. There were no cases of sexual impotence or retrograde ejaculation. Complications reported in the eligible studies are presented in Table 3.

Discussion

PAE was first utilized in the 1970s to treat refractory bleeding following prostatic interventions as well as for intractable hematuria.15 It demonstrated a successful reduction in PV without serious complications in human beings in 2010.² The rationale for PAE is that prostate ischemia leads to PV reduction and hence clinical improvement.¹⁶

In this meta-analysis, compared with baseline, there were significant improvements in the IPSSs (-12.74 points), QoL scores (-2.07 points), PV (-17.33 mL), PSA (-0.80 ng/mL), $Q_{\rm max}$ (+4.4 mL/s) and PVR volume (-56.23 mL) after PAE at postoperative 1 month. It implied that PAE could take effect quickly. Furthermore, the IPSSs (-15.62 points), QoL scores (-2.15 points), $Q_{\rm max}$ (+5.89 mL/s) and PVR volume (-49.07 mL) still had significant improvements during the 24-month follow-up, suggesting that PAE had good control of symptoms within 2 years.

For PV and PSA, significant decreases were found during the 12-month follow-up, but not at postoperative 24 months. We thought that the effect of PAE cannot be maintained in the long-term period. Besides prostate size increasing with

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Studies	Sample	Complicat	ions					
	size	Urethral burning	Urinary tract infection	Hematuria	Hematospermia	Rectal bleeding	AUR	Inguinal hematoma
Gabr et al ⁶	22	15	0	0	0	0	0	0
Bilhim et al ⁷	186	0	I	14	15	10	9	6
Wang et al ⁸	47	10	0	6	4	4	16	3
Wang et al ⁸	100	12	0	8	8	7	9	3
lsaacson et al ⁹	12	0	I	I	I	0	I.	0
Bagla et al ¹⁰	78	0	I	0	0	0	0	I
Li et al''	22	8	0	3	2	3	7	0
Wang et al ¹²	109	19	0	11	9	8	31	3
Pisco et al ¹³	250	23	19	14	10	6	6	0
Pisco et al ¹⁴	14	0	2	0	0	0	I	0
Total	840	87	24	57	49	38	80	16

Table 3	Complications	reported in	the eligible	studies
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Abbreviation: AUR, acute urinary retention.

age, revascularization of the prostatic arteries after PAE may play a role in prostate regrowth. Pisco et al¹³ observed this kind of revascularization in their patients with second PAE. Interestingly, the IPSSs still had a significant decrease despite prostatic enlargement at postoperative 24 months. This may suggest that physical reduction of the obstructing tissue was not the only reason for the improvement in LUTS after PAE.

In terms of the IIEF-5 scores, there was no significant increase until 6 months after PAE. The epidemiological evidence had suggested a clear and clinically meaningful association between LUTS and sexual dysfunction that was independent of age and comorbidity.¹⁷ Along with the continuous improvement in LUTS, the IIEF-5 scores started to increase.

In addition, patients with large volume (PV \geq 80 mL) BPH are often elderly and may have severe comorbidities. They have increased operative risk of undergoing TURP/open surgery or refuse any surgical treatment.¹⁸ In this meta-analysis, for large volume (PV \geq 80 mL) BPH, there were significant improvements in the IPSSs (-18.32 points), QoL scores (-2.50 points), PV (-47.58 mL), Q_{max} (+6.00 mL/s) and PVR volume (-76.80 mL) after PAE during the 12-month follow-up, and there were no lifethreatening complications. PAE does offer the ability to treat BPH in these patients, due to its minimally invasive nature with low morbidity and the possibility to use local anesthetic without sedation.⁸

Subsequent studies have further compared the clinical outcome of PAE versus TURP. Carnevale et al¹⁹ reported that both groups experienced significant improvement in IPSS, QoL, PV, and $Q_{\rm max}$ during the 12-month follow-up. TURP resulted in significantly higher $Q_{\rm max}$ and smaller PV

than PAE but required spinal anesthesia and hospitalization, while IIEF scores were significantly higher in the PAE group. Gao et al²⁰ reported a similar result during the 24-month follow-up, except that the PAE group showed more complications, mostly related to AUR (25.9%), postembolization syndrome (11.1%) and treatment failures (5.3% technical; 9.4% clinical).

Nevertheless, there are some limitations to our analysis. The major limitations include heterogeneity in the participants chosen, different materials and sizes of embolic agents and bilateral or unilateral embolization. The subgroup and sensitivity analysis or a random-effects model might reduce these limitations, but cannot eliminate. Additionally, the sample sizes of some included studies were small, and there was no long-term follow-up study. Data in the studies covered by this meta-analysis are insufficient to determine whether or not PAE is as good as TURP. Stratified trials with high volume and long follow-up time are awaited to strengthen the evidence and to update our findings.

PAE is an effective, safe and well-tolerable treatment for LUTS related to BPH, including large volume (PV \ge 80 mL) BPH, with good short-term follow-up. Studies with large number of cases and longer follow-up time are needed to validate our results.

Disclosure

The authors report no conflicts of interest in this work.

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