Review Article
Meta-analysis of the efficacy of prostate artery embolization in prostatic hyperplasia

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Abstract: Objective: The purpose of this article was to assess the efficacy of PAE in the treatment of LUTS related to BPH. Methods: Databases including PubMed, MEDLINE, EMBASE, the Cochrane Library, and other related sources were searched, with the results limited to items published between Jan. 1st, 2000 and Jun. 30th, 2017, for randomized controlled studies concerning PAE/BPH/LUTS and with no language restriction. Eligible randomized controlled trials (RCTs) were selected by independent paired researchers according to the inclusion and exclusion criteria. The overall quality of each of the included RCTs was assessed using the Cochrane risk of bias tool. The main outcome measures included the quality of life score (QoL), prostate volume (PV), the international prostate symptom score (IPSS), the maximum urinary flow rate (Qmax), postvoid residual urine volume (PVR volume), prostate-specific antigen (PSA), and the international index of erectile function (IIEF-5). The fixed effect model or random effect model was selected for the meta-analysis using RevMan 5.2 software. Results: Nine RCTs containing 508 patients were included. Compared with the baseline, the meta-analysis for this study showed that the QoL scores were significantly lowered after PAE at postoperative 1, 3, and 12 months (all P<0.001). The PV showed no significant change after PAE at postoperative 1 and 3 months (P=0.39, P=0.49), but it decreased significantly at postoperative 12 months (P<0.00001). Significant improvements were shown in IPSS (all P<0.00001) and Qmax (all P<0.0001) after PAE at postoperative 1, 3, and 12 months. The PVR volume was significantly improved after PAE at postoperative 1, 3, and 12 months (P=0.009, P=0.010, P=0.004). The PSA presented no improvement after PAE at postoperative 1 and 12 months (P=0.73, P=0.37), but it presented significant improvement after 3 months (P<0.0001). IIEF-5 showed no improvement after PAE at postoperative 1, 3, and 12 months (P=0.46, P=1.00, P=0.67). Conclusion: PAE is an effective treatment for BPH-induced LUTS.

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

Introduction

Lower urinary tract symptoms (LUTS) are the major complications resulting from benign prostatic hyperplasia (BPH), which is one of the most common diseases in elderly men [1]. LUTS ranges in severity and have a relatively significant impact on the quality of life (QoL) of the patients [2-4]. Options like expectant treatment, medical therapy, and surgical intervention are currently put into use for BPH-induced LUTS. Surgical intervention can be initially adopted to treat patients with refractory LUTS. Transurethral resection of the prostate (TURP) has been the gold standard therapy for the treatment of LUTS/BPH for many years and has

been considered the first choice and standard of care for surgery when other treatments have failed [5]. However, significant complications, including short-term bleeding, dilutional hyponatremia, sexual dysfunction, and urinary incontinence often occur after TURP, and the complication rate in larger BPH is relatively higher [6].

Recently, prostate artery embolization (PAE) has gradually been emerging as a minimally invasive therapy, which can improve the BPH-induced LUTS and significantly reduce the prostate volume (PV) [7, 8]. However, it is reported in the literature that there is no significant improvement in the symptoms or in the maxi-

mum urinary flow rate (Qmax) in 25% of patients. In addition, the mean rate of prostate volume reduction after PAE is only 20% [9].

The purpose of this meta-analysis was to assess the effectiveness of PAE for BPH-induced LUTS, hoping to provide a reliable basis for the treatment in urological surgery.

Materials and methods

This meta-analysis followed the preferred reporting items for systematic reviews (PRISM) [10].

Database and keywords for search

Various databases, including PubMed, MEDLINE, EMBASE, and the Cochrane Library, were searched for this meta-analysis. The keywords searched in this study were "prostate artery embolization", "lower urinary tract symptoms", and "benign prostatic hyperplasia". The results were limited to items published between Jan. 1st, 2000 and Jun. 30th, 2017.

Literature screening

The studies were screened according to the inclusion and exclusion criteria following keyword searches.

Inclusion criteria

Study design: Randomized controlled trials (RCTs) on PAE for the treatment of male LUTS/ BPH patients were selected, and there was no restriction in the RCTs on blinding method, the follow-up time, or the language.

Diagnostic criteria: Patients with symptoms such as frequent and urgent urination, nocturia, and urge incontinence and/or with urethral obstruction due to benign prostatic hyperplasia who were diagnosed with LUTS/BPH [11].

Treatment method: Patients with LUTS/BPH in the RCTs were treated with transurethral resection of the prostate (TURP) or PAE.

Baseline standard: The international prostate symptom scores (IPSSs) were categorized as either mild (0-7), moderate (8-19), or severe (20-35). Regarding the IIEF-5 classification, a score of ≥22 points was considered normal erectile function, while ED was classified as mild (12-21 points), moderate (8-11 points), or severe (5-7 points). QoL was assigned a score

of 0-6, which graded the patients' subjective feelings about their current LUTS. The higher the score, the worse the quality. Normal Qmax in males should be greater than 15 mL/sec. Under normal conditions, the postvoid residual urine volume (PVR volume) should be less than 5 mL. PV<25 mL was considered normal in the patients. Total prostate specific antigen (tPSA) <4.0 μg/mL was considered normal. Outcome measures containing IPSS, IIEF-5, QoL, Qmax, PVR volume, PV, or PSA were included in the RCTs. The full texts of the RCTs could be accessed. If the above inclusion criteria were not met, the RCT was excluded.

Literature screening: One researcher read the titles of all the studies and removed the duplicates. The other two researchers independently read the titles and abstracts of all the articles screened out by the former researcher and screened them according to the inclusion and exclusion criteria. Then the two carefully read the full texts of the articles and independently extracted the clinical indicators and data and made forms. Any disputes were resolved by group consensus.

Quality assessment

The Cochrane risk of bias tool was used to score the included studies for quality assessment. The Cochrane risk of bias tool includes 7 evidence-based domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. These 7 domains aimed to assess the risk of bias of the sources. Each domain could be judged as "low risk of bias", "high risk of bias", or "unclear risk of bias" according to the criteria for judging the risk of bias. The included studies whose outcome measures were all clearly stated were judged as having a low risk of bias. If an included study clearly stated that the trial was not implemented according to the above 7 domains, it would be judged as having a high risk of bias. If an included study showed no related risk of bias, it would be judged as having an unclear risk of bias.

Data extraction

The extracted data included date of publication, sample size, randomizing method, blinding, age, IPSS, IIEF-5, QoL, Qmax, PVR volume,
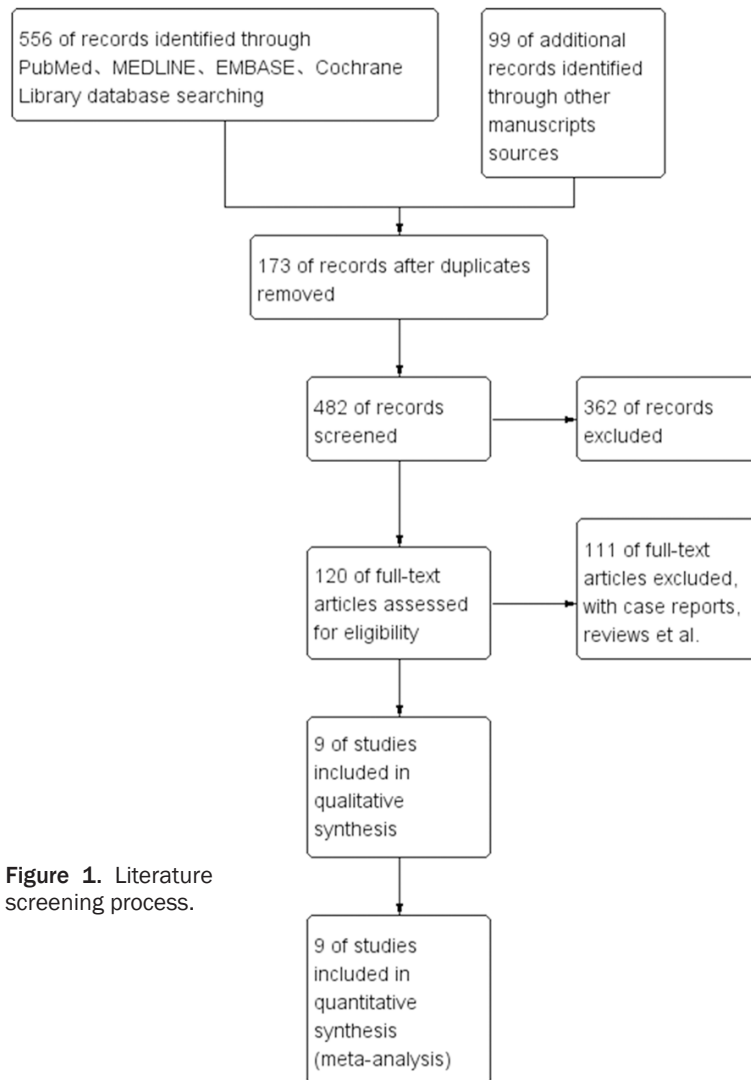
Figure 1. Literature screening process.

the data. Each effect size was expressed by a 95% confidence interval (CI).

The I^2 statistics were used to assess heterogeneity. $0\% < I^2 < 25\%$ indicated no heterogeneity, $25\% < I^2 < 50\%$ indicated mild heterogeneity, $50\% < I^2 < 75\%$ indicated moderate heterogeneity, and $75\% < I^2 < 100\%$ indicated strong heterogeneity. The fixed effects model was used for the analysis when no significant heterogeneity ($P \geq 0.1$, $I^2 < 50\%$) was observed among the studies. The random effects model was used when significant heterogeneity ($P < 0.1$, $I^2 > 50\%$) was observed among the studies, and a sensitivity analysis was also used to explore the possible sources of the heterogeneity. The possible sources of heterogeneity were research year, multi-center or single-center study, author, or small sample size. The significance level of $\alpha = 0.05$ was adopted for testing.

Results

Characteristic of eligible studies

PV, and PSA. In order to ensure the high credibility of the literature collection process, the indicators included in the articles were screened by two major independent researchers in a double-blind manner, and inconsistencies were resolved by group consensus. The literature screening process is shown in **Figure 1**.

Statistical analysis

The statistical analysis was performed using RevMan 5.2 software provided by the Cochrane Collaboration for the effect of pooled values. The measurement data were expressed by the Standard Mean Difference (SMD) and 95% confidence intervals (CIs). The SMD was adopted due to different measurement tools for recording data and different measurement units for

A total of 9 eligible RTCs involving 508 patients who underwent PAE were eventually included in this analysis according to the inclusion and exclusion criteria after careful searching and screening [2, 4, 12-18]. The data included IPSS, IIEF-5, QoL, Qmax, PVR volume, PV, and PSA. The literature screening process and its results are shown in **Table 1** and **Figure 1**.

Risk assessment

The overall bias of the included studies was assessed according to the risk of bias table recommended by the Cochrane Collaboration. Each study showed more than one bias, and the biases were mainly reflected in allocation concealment, selective reporting, and incomplete outcome data (**Figures 2**, **3**).

Table 1. Characteristic of eligible literatures

Randomized controlled trials (RCTs)	RCT design	Sample size	Country	Age (years)	Outcome measures
Ari J. Isaacson 2015 [12]	Retrospective study	12	USA	59.5±2.1	IPSSs, QoL, PV, Qmax, PVR volume, IIEF-5, PSA
Charles R. Tapping 2017 [13]	Retrospective study	8	UK	64.4±1.2	IPSSs, QoL, PV
Francisco Cesar Carnevale 2017 [14]	Retrospective study	59	Brazil	62.7±7.2	IPSSs, QoL, PV, Qmax,
Jin Ho Hwang 2017 [15]	Retrospective study	9	South Korea	78.1±12.3	IPSSs, QoL, PV, Qmax
Joao Martins Pisco 2013 [16]	Retrospective study	250	Portugal	65.5±7.4	IPSSs, QoL, PV, Qmax, PVR volume, IIEF-5, PSA
Mao Qiang Wang 2015 [2]	Retrospective study	117	China	71.5±13.5	IPSSs, QoL, PV, Qmax, PVR volume, IIEF-5, PSA
M. W. Little 2017 [17]	Retrospective study	12	UK	69.6±3.7	IPSSs, QoL, PV
Qiang Li 2015 [4]	Retrospective study	24	China	74.5±7.5	IPSSs, QoL, PV, Qmax, PVR volume, IIEF-5, PSA
Zhilei Qiu 2017 [18]	Retrospective study	17	China	75.53±4.74	IPSSs, QoL, PV, Qmax,

Figure 2. The risk of bias table of the included literatures.

Changes in measurements after PAE

Quality of life score (QoL score): Nine studies involving 491 participants included data represent-ing QoL scores after PAE in LUTS/BPH patients [2, 4, 12-18]. Compared with the baseline, the QoL scores had significant decreases after PAE at postoperative 1 month (SMD -1.87, 95% CI -2.87 to -0.88, P=0.0002), 3 months (SMD -1.73, 95% CI -2.48 to -0.99, P<0.00001), and 12 months (SMD -1.89, 95% CI -2.43 to -1.36, P<0.00001) (**Figure 4**).

Prostate volume (PV): Nine studies involving 508 participants included data representing PV after PAE in LUTS/BPH patients [2, 4, 12-18]. Compared with the baseline, the PV showed no significant change after PAE at postoperative 1 month (SMD -0.3, 95% CI -0.98 to 0.39, P=0.39) and 3 months (SMD -0.85, 95% CI -3.27 to 1.57, P=0.49), while it decreased significantly at postoperative 12 months (SMD -1.74, 95% CI -2.49 to -0.99, P<0.00001) (**Figure 5**).

International prostate symptom score (IPSS): Eight studies involving 408 participants included data representing IPSS after PAE in LUTS/BPH patients [2, 4, 12-14, 16-18]. Compared with the baseline, significant improvement was shown in IPSS after PAE at postoperative 1 month (SMD -2.32, 95% CI -3.27 to -1.37, P<0.00001), 3 months (SMD -3.81, 95% CI -5.01 to -2.6, P<0.00001),
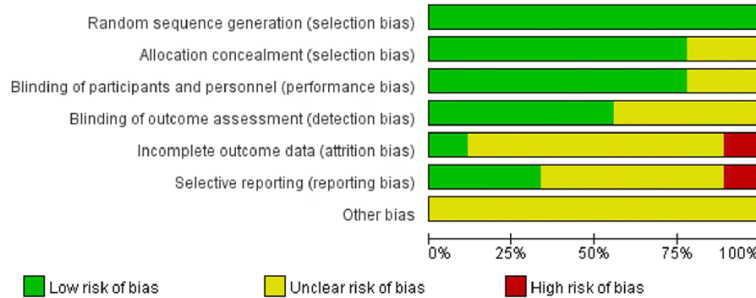
Figure 3. The overall bias of the included studies.

and 12 months (SMD -2.57, 95% CI -3.47 to -1.67, P<0.00001) (**Figure 6**).

Maximum urinary flow rate (Qmax): Six studies involving 479 participants included data representing Qmax after PAE in LUTS/BPH patients [2, 4, 12, 14, 16, 18]. Compared with the baseline, significant improvement was shown in Qmax after PAE at postoperative 1 month (SMD 1.31, 95% CI 0.68 to 1.94, P<0.0001), 3 months (SMD 1.65, 95% CI 0.83 to 2.48, P<0.0001) and 12 months (SMD 1.34, 95% CI 0.9 to 1.79, P<0.00001) (**Figure 7**).

Postvoid residual urine volume (PVR volume): Five studies involving 403 participants included data representing PVR volume after PAE in LUTS/BPH patients [2, 4, 12, 16, 18]. Compared with the baseline, the PVR volume was significantly improved after PAE at postoperative 1 month (SMD -1.59, 95% CI -2.78 to -0.39, P=0.009), 3 months (SMD -1.00, 95% CI -1.76 to -0.24, P=0.010) and 12 months (SMD -2.32, 95% CI -3.88 to -0.76, P=0.004) (**Figure 8**).

Prostate specific antigen (PSA): Five studies involving 462 participants included data representing PSA after PAE in the LUTS/BPH patients [2, 4, 12, 14, 16]. Compared with the baseline, the PSA was not improved after PAE at postoperative 1 month (SMD 0.02, 95% CI -0.11 to 0.16, P=0.73) and 12 months (SMD -0.07, 95% CI -0.23 to 0.09, P=0.37), but it was significantly improved at postoperative 3 months (SMD -0.29, 95% CI -0.44 to -0.15, P<0.0001) (**Figure 9**).

International index of erectile function score (IIEF-5 score): Seven studies involving 423 participants included data representing the IIEF-5 score after PAE in LUTS/BPH patients [2, 4, 12, 13, 16-18]. Compared with the baseline, the IIEF-5 score showed no improvement after PAE

at postoperative 1 month (SMD 0.08, 95% CI -0.14 to 0.31, P=0.46), 3 months (SMD -0.00, 95% CI -0.25 to 0.25, P=1.00), and 12 months (SMD -0.13, 95% CI -0.74 to 0.48, P=0.67) (**Figure 10**).

Discussion

BPH commonly occurs in elderly men, and glandular hyperplasia can cause obstructions within the lower urinary tract when the gland reaches a certain size. With the widespread use of PAE in clinical surgery, treatment for BPH has achieved a good therapeutic effect. However, postoperative complications of PAE are increasingly common, which is still raising concern about PAE applied to the treatment of LUTS/BPH [19]. PAE was first used in the 1970s as a remedy for refractory bleeding following prostatic interventions [20]. It was demonstrated in 2010 that PAE could successfully reduce PV in LUTS/BPH patients without serious complications [21].

BPH is a hormone-dependent disease. Currently, drugs such as α1-receptor antagonist, 5α-reductase inhibitor, M-receptor antagonist, and TURP are the main choices for the treatment of BPH. However, the long-term administration of these drugs can lead to adverse reactions like breast tenderness and enlargement, ejaculation disorders and sexual dysfunction. It was reported that 19 cases (14 males and 5 females) who were administrated finasteride for the treatment of hair loss had moderate or severe depression [22]. PAE will mechanically embolize the prostate capillary bed and the major arteries, which can reduce the blood supply and further cause ischemic necrosis, leaving fewer or no adverse effects on the whole body. The QoL scores in this study also showed significant improvements after PAE at postoperative 1, 3 and 12 months.

Regarding the changes on PV after PAE, the reduction rate of PV after PAE is about 15% to 40%, which is far lower than the reduction rate (50%-60%) of the entire uterus after PAE for uterine fibroids. The reason for this difference is not clear, and further exploration is needed. In addition, previous studies have reported that the improvement in the clinical symptoms and

Study or Subgroup	PAE Mean	SD	Total	baseline Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
A								
Ari J. Isaacson 2015	1.7	1.8	12	4.8	1	12	4.4%	-2.06 [-3.08, -1.03]
Francisco Cesar Carnevale 2017	1.5	0.9	59	4.9	0.6	59	5.3%	-4.42 [-5.09, -3.74]
Joao Martins Pisco 2013	2.71	1.38	236	4.39	0.95	250	6.2%	-1.42 [-1.62, -1.22]
Mao Qiang Wang 2015	2.5	1	117	5	1	117	6.0%	-2.49 [-2.83, -2.15]
Qiang Li 2015	2.5	1	24	4.5	1.5	24	5.4%	-1.54 [-2.19, -0.89]
Zhilei Qiu 2017	2.8	1.1	17	2.1	0.9	17	5.3%	0.68 [-0.01, 1.37]
Subtotal (95% CI)			465			479	32.5%	-1.87 [-2.87, -0.88]
Heterogeneity: Tau² = 1.43; Chi² = 135.54, df = 5 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 3.70 (P = 0.0002)								
B								
Ari J. Isaacson 2015	1.3	1.4	12	4.8	1	12	4.1%	-2.78 [-3.95, -1.60]
Joao Martins Pisco 2013	1.96	1.23	167	4.39	0.95	250	6.1%	-2.27 [-2.51, -2.02]
M. W. Little 2017	1	0.2	12	0.85	0.1	12	4.9%	0.92 [0.07, 1.76]
Mao Qiang Wang 2015	3	0.5	117	5	1	117	6.0%	-2.52 [-2.87, -2.18]
Qiang Li 2015	2	1	24	4.5	1.5	24	5.3%	-1.93 [-2.62, -1.23]
Zhilei Qiu 2017	2.5	1.1	17	4.1	0.7	17	5.0%	-1.69 [-2.49, -0.90]
Subtotal (95% CI)			349			432	31.3%	-1.73 [-2.48, -0.99]
Heterogeneity: Tau² = 0.73; Chi² = 58.14, df = 5 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 4.58 (P < 0.00001)								
C								
Charles R. Tapping 2017	0.9	0.1	8	0.75	0.2	8	4.4%	0.90 [-0.15, 1.94]
Francisco Cesar Carnevale 2017	3	0.8	59	4.9	0.6	59	5.7%	-2.67 [-3.17, -2.17]
Jin Ho Hwang 2017	2.6	1.3	9	4.9	1.1	9	4.1%	-1.82 [-2.96, -0.68]
Joao Martins Pisco 2013	1.96	1.23	167	4.39	0.95	250	6.1%	-2.27 [-2.51, -2.02]
Mao Qiang Wang 2015	2.5	1.5	117	5	1	117	6.0%	-1.95 [-2.27, -1.64]
Qiang Li 2015	2	1	24	4.5	1.5	24	5.3%	-1.93 [-2.62, -1.23]
Zhilei Qiu 2017	2.1	0.7	17	4.1	0.7	17	4.6%	-2.79 [-3.76, -1.82]
Subtotal (95% CI)			401			484	36.2%	-1.89 [-2.43, -1.36]
Heterogeneity: Tau² = 0.38; Chi² = 41.50, df = 6 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 6.99 (P < 0.00001)								
Total (95% CI)			1215			1395	100.0%	-1.83 [-2.22, -1.43]
Heterogeneity: Tau² = 0.66; Chi² = 252.27, df = 18 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 9.01 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.12. df = 2 (P = 0.94). I² = 0%								

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Figure 4. A forest plot of QoL score changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

the changes in patients' urinary flow dynamics after PAE are not completely consistent with the degree of PV reduction: the PV was clearly reduced after PAE, but the symptoms were not improved; or no change was seen in the PV after PAE, but the symptoms were significantly improved [23].

At the same time, Carnelvale et al. found that the PV decreased by 27.8% after unilateral PAE at postoperative 6 months, and the PV decreased by 47.8% after bilateral PAE at postoperative 6 months, indicating that PAE could significantly reduce PV [24]. In this meta-analysis, no significant changes in the PV after PAE at postoperative 1 and 3 months were seen, but the PV decreased significantly after PAE at postoperative 12 months, indicating that the reduction of PV after PAE was not the only factor to alleviate the symptoms. Also, histological changes in the prostate and changes in tension caused by the decrease in blood flow (decrease in hormone level) of the prostate after embolization may affect bladder emptying, which could also alleviate the symptoms.

PAE is the embolization of a small prostate artery, which eventually causes ischemia and atrophy in the enlarged prostate tissue and further reduces the symptoms of urinary tract obstruction without harm to penile erection [25]. A significant improvement was seen in Qmax after PAE at postoperative 1, 3, and 12 months in this study. But the IIEF-5 score showed no significant improvement after PAE at postoperative 1, 3, and 12 months. Epidemiological studies have shown a clear correlation between clinical sexual dysfunction and LUTS, regardless of age or disease [26].

The measurement of the PVR volume is also one of the main diagnostic approaches for BPH. As the obstruction in urinary tract worsens, the urine in the bladder cannot be completely emptied due to difficulty in urinating caused by prostatic hyperplasia. The volume of the remaining urine in the bladder is called the PVR volume [27]. Urodynamic examination is extremely important in the diagnosis of benign prostatic hyperplasia and is an indispensable instrument for the examination of lower urinary tract syndrome. After arterial embolization, the

Study or Subgroup	PAE Mean	SD	Total	baseline Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
A									
Ari J. Isaacson 2015	0	0	0	0	0	0		Not estimable	
Charles R. Tapping 2017	0	0	0	0	0	0		Not estimable	
Francisco Cesar Carnevale 2017	51.3	23.6	59	61.1	24.7	59	6.1%	-0.40 [-0.77, -0.04]	
Jin Ho Hwang 2017	0	0	0	0	0	0		Not estimable	
Joao Martins Pisco 2013	66.8	28.75	183	83.5	37	250	6.1%	-0.49 [-0.69, -0.30]	
M. W. Little 2017	0	0	0	0	0	0		Not estimable	
Mao Qiang Wang 2015	103.8	30	117	118	35	117	6.1%	-0.43 [-0.69, -0.17]	
Qiang Li 2015	100	25	24	110	25	24	6.0%	-0.39 [-0.97, 0.18]	
Zhilei Qiu 2017	523	5.9	17	64.6	10.2	17	0.3%	53.72 [40.12, 67.31]	
Subtotal (95% CI)			400			467	24.7%	-0.30 [-0.98, 0.39]	
Heterogeneity: Tau² = 0.45; Chi² = 61.29, df = 4 (P < 0.00001); I² = 93%									
Test for overall effect: Z = 0.85 (P = 0.39)									
B									
Ari J. Isaacson 2015	76.7	19.6	12	111.1	27.8	12	5.7%	-1.38 [-2.29, -0.47]	
Joao Martins Pisco 2013	66.8	28.75	183	1.96	1.23	250	6.1%	3.46 [3.16, 3.76]	
M. W. Little 2017	70	24	12	110	23	12	5.7%	-1.64 [-2.59, -0.70]	
Mao Qiang Wang 2015	72.5	25	117	118	35	117	6.1%	-1.49 [-1.78, -1.20]	
Qiang Li 2015	68	20	24	110	25	24	5.9%	-1.82 [-2.51, -1.14]	
Zhilei Qiu 2017	45.2	5.9	17	64.6	10.2	17	5.7%	-2.27 [-3.16, -1.39]	
Subtotal (95% CI)			365			432	35.3%	-0.85 [-3.27, 1.57]	
Heterogeneity: Tau² = 9.02; Chi² = 671.50, df = 5 (P < 0.00001); I² = 99%									
Test for overall effect: Z = 0.69 (P = 0.49)									
C									
Charles R. Tapping 2017	65.4	23	8	125	24	8	5.2%	-2.40 [-3.77, -1.03]	
Francisco Cesar Carnevale 2017	57	26.8	59	62.7	7.2	59	6.1%	-0.29 [-0.65, 0.07]	
Jin Ho Hwang 2017	61.3	31.2	9	89.4	12.3	9	5.6%	-1.13 [-2.14, -0.11]	
M. W. Little 2017	60	12	12	130	32	12	5.4%	-2.80 [-3.98, -1.62]	
Mao Qiang Wang 2015	68.5	15	117	118	35	117	6.1%	-1.83 [-2.14, -1.53]	
Qiang Li 2015	69	20	24	110	25	24	5.9%	-1.78 [-2.46, -1.10]	
Zhilei Qiu 2017	42	7.5	17	64.6	10.2	17	5.7%	-2.46 [-3.38, -1.55]	
Subtotal (95% CI)			246			246	40.1%	-1.74 [-2.49, -0.99]	
Heterogeneity: Tau² = 0.82; Chi² = 57.79, df = 6 (P < 0.00001); I² = 90%									
Test for overall effect: Z = 4.56 (P < 0.00001)									
Total (95% CI)			1011			1145	100.0%	-0.94 [-1.73, -0.14]	
Heterogeneity: Tau² = 2.65; Chi² = 942.94, df = 17 (P < 0.00001); I² = 98%									
Test for overall effect: Z = 2.32 (P = 0.02)									
Test for subgroup differences: Chi² = 7.79, df = 2 (P = 0.02), I² = 74.3%									

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Figure 5. A forest plot of PV changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

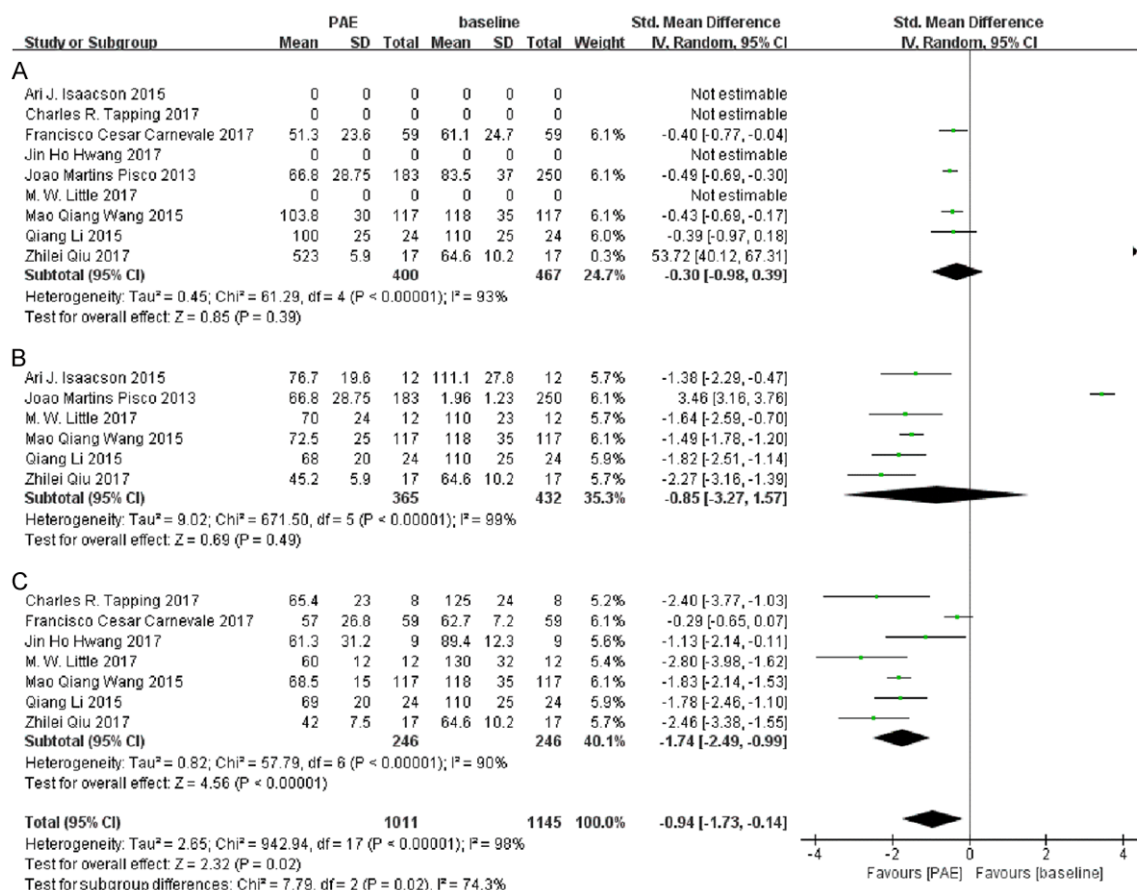size of the prostate is reduced, and the urine remaining in the bladder is easier to discharge. It was also found in this study that PVR volume was significantly improved after PAE at postoperative 1, 3, and 12 months, indicating that PAE could significantly relieve the residual urine volume in the bladder.

PSA is a member of the chymotrypsin-like serine protease family and can be produced and secreted by the epithelial cells of the normal prostate gland or the prostate gland with pathological and non-pathological changes. It is a single-chain polypeptide with the ability to decompose the main gelatinous protein in semen and therefore has the effect of diluting semen. PSA is tissue-specific. It exists only in the cytoplasm of human prostatic acinar and ductal epithelial cells and is not expressed in other cells. However, it has no tumor-specificity. The total PSA levels (free PSA plus complexed PSA) could be elevated duo to prostatitis, benign prostatic hyperplasia, or prostate can-

cer [28]. After the above causes were relieved, the concentrations of PSA in the serum could be measurably decreased and the volume of prostatic hyperplasia after PAE reduced.

In conclusion, PAE is effective in the treatment of male BPH, and more eligible cases with longer follow-up times are needed to be included in later studies to confirm the findings.

Disclosure of conflict of interest

None.

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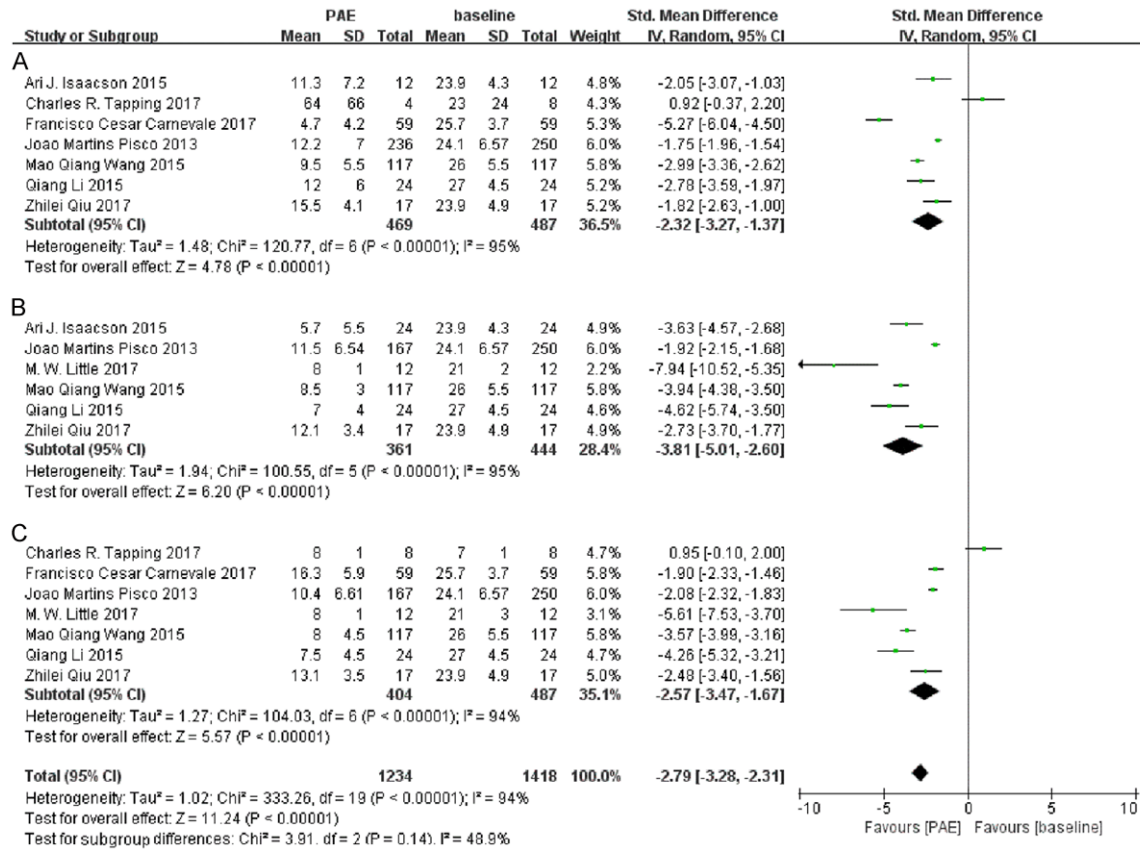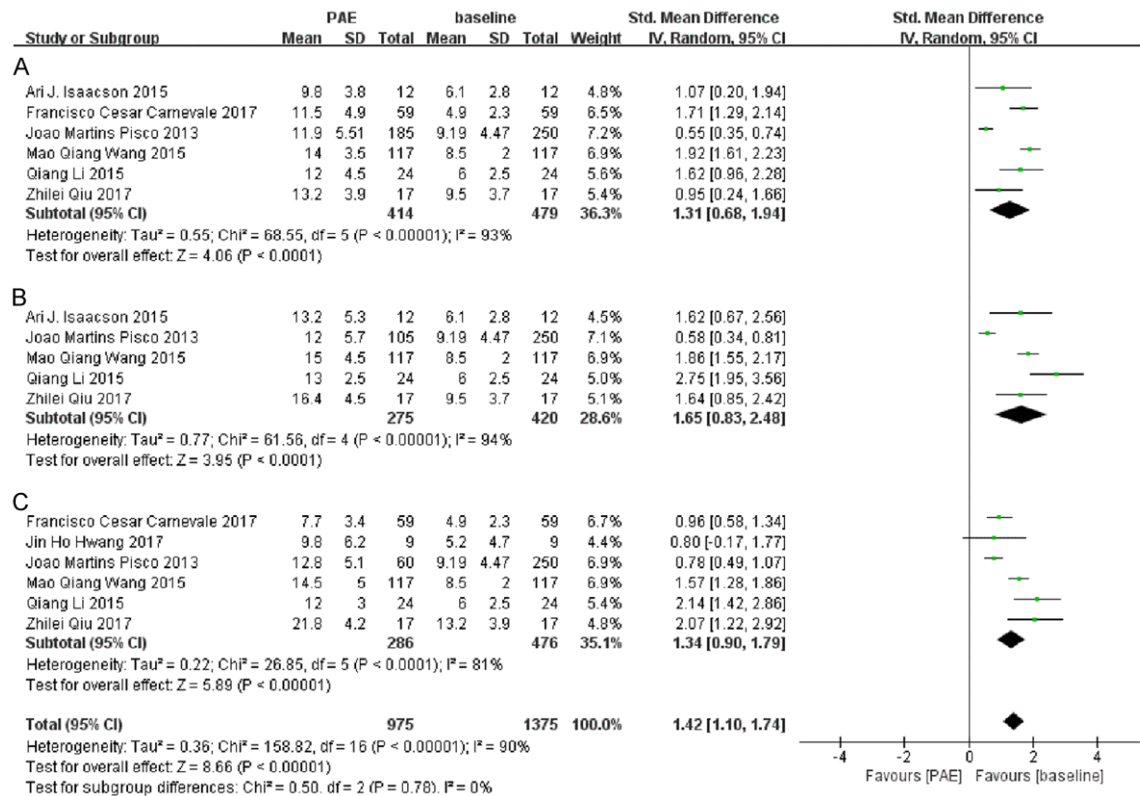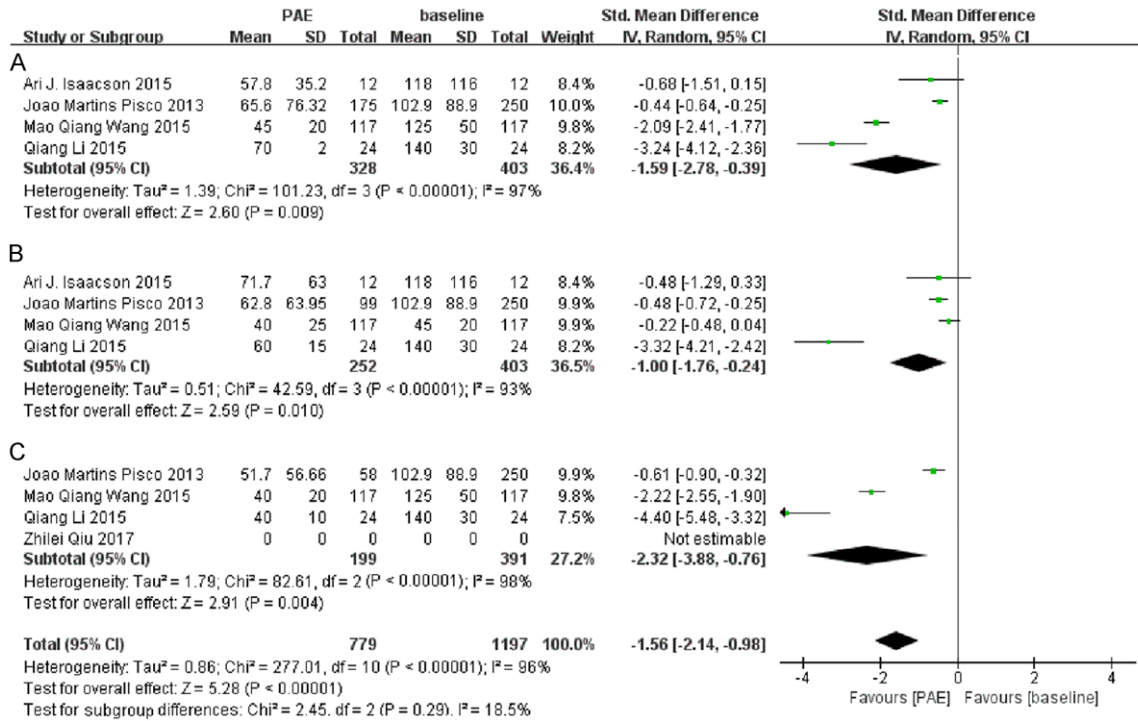| Study or Subgroup	PAE Mean	SD	Total	baseline Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
A								
Ari J. Isaacson 2015	11.3	7.2	12	23.9	4.3	12	4.8%	-2.05 [-3.07, -1.03]
Charles R. Tapping 2017	64	66	4	23	24	8	4.3%	0.92 [-0.37, 2.20]
Francisco Cesar Carnevale 2017	4.7	4.2	59	25.7	3.7	59	5.3%	-5.27 [-6.04, -4.50]
Joao Martins Pisco 2013	12.2	7	236	24.1	6.57	250	6.0%	-1.75 [-1.96, -1.54]
Mao Qiang Wang 2015	9.5	5.5	117	26	5.5	117	5.8%	-2.99 [-3.36, -2.62]
Qiang Li 2015	12	6	24	27	4.5	24	5.2%	-2.78 [-3.59, -1.97]
Zhilei Qiu 2017	15.5	4.1	17	23.9	4.9	17	5.2%	-1.82 [-2.63, -1.00]
Subtotal (95% CI)			469			487	36.5%	-2.32 [-3.27, -1.37]
Heterogeneity: Tau² = 1.48; Chi² = 120.77, df = 6 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 4.78 (P < 0.00001)								
B								
Ari J. Isaacson 2015	5.7	5.5	24	23.9	4.3	24	4.9%	-3.63 [-4.57, -2.68]
Joao Martins Pisco 2013	11.5	6.54	167	24.1	6.57	250	6.0%	-1.92 [-2.15, -1.68]
M. W. Little 2017	8	1	12	21	2	12	2.2%	-7.94 [-10.52, -5.35]
Mao Qiang Wang 2015	8.5	3	117	26	5.5	117	5.8%	-3.94 [-4.38, -3.50]
Qiang Li 2015	7	4	24	27	4.5	24	4.6%	-4.62 [-5.74, -3.50]
Zhilei Qiu 2017	12.1	3.4	17	23.9	4.9	17	4.9%	-2.73 [-3.70, -1.77]
Subtotal (95% CI)			361			444	28.4%	-3.81 [-5.01, -2.60]
Heterogeneity: Tau² = 1.94; Chi² = 100.55, df = 5 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 6.20 (P < 0.00001)								
C								
Charles R. Tapping 2017	8	1	8	7	1	8	4.7%	0.95 [-0.10, 2.00]
Francisco Cesar Carnevale 2017	16.3	5.9	59	25.7	3.7	59	5.8%	-1.90 [-2.33, -1.46]
Joao Martins Pisco 2013	10.4	6.61	167	24.1	6.57	250	6.0%	-2.08 [-2.32, -1.83]
M. W. Little 2017	8	1	12	21	3	12	3.1%	-5.61 [-7.53, -3.70]
Mao Qiang Wang 2015	8	4.5	117	26	5.5	117	5.8%	-3.57 [-3.99, -3.16]
Qiang Li 2015	7.5	4.5	24	27	4.5	24	4.7%	-4.26 [-5.32, -3.21]
Zhilei Qiu 2017	13.1	3.5	17	23.9	4.9	17	5.0%	-2.48 [-3.40, -1.56]
Subtotal (95% CI)			404			487	35.1%	-2.57 [-3.47, -1.67]
Heterogeneity: Tau² = 1.27; Chi² = 104.03, df = 6 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 5.57 (P < 0.00001)								
Total (95% CI)			1234			1418	100.0%	-2.79 [-3.28, -2.31]
Heterogeneity: Tau² = 1.02; Chi² = 333.26, df = 19 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 11.24 (P < 0.00001)								
Test for subgroup differences: Chi² = 3.91, df = 2 (P = 0.14), I² = 48.9%								

Favours [PAE] Favours [baseline]

Figure 6. A forest plot about IPSS changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

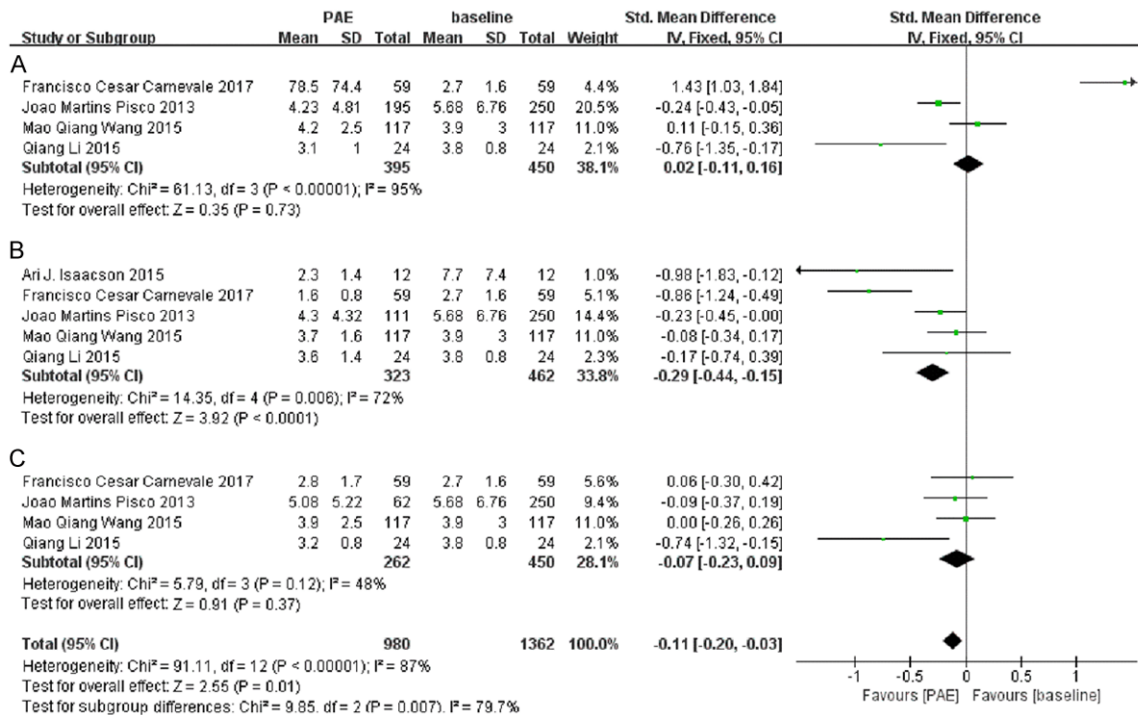| Study or Subgroup	PAE Mean	SD	Total	baseline Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
A								
Ari J. Isaacson 2015	9.8	3.8	12	6.1	2.8	12	4.8%	1.07 [0.20, 1.94]
Francisco Cesar Carnevale 2017	11.5	4.9	59	4.9	2.3	59	6.5%	1.71 [1.29, 2.14]
Joao Martins Pisco 2013	11.9	5.51	185	9.19	4.47	250	7.2%	0.55 [0.35, 0.74]
Mao Qiang Wang 2015	14	3.5	117	8.5	2	117	6.9%	1.92 [1.61, 2.23]
Qiang Li 2015	12	4.5	24	6	2.5	24	5.6%	1.62 [0.96, 2.28]
Zhilei Qiu 2017	13.2	3.9	17	9.5	3.7	17	5.4%	0.95 [0.24, 1.66]
Subtotal (95% CI)			414			479	36.3%	1.31 [0.68, 1.94]
Heterogeneity: Tau² = 0.55; Chi² = 68.55, df = 5 (P < 0.0001); I² = 93%								
Test for overall effect: Z = 4.06 (P < 0.0001)								
B								
Ari J. Isaacson 2015	13.2	5.3	12	6.1	2.8	12	4.5%	1.62 [0.67, 2.56]
Joao Martins Pisco 2013	12	5.7	105	9.19	4.47	250	7.1%	0.58 [0.34, 0.81]
Mao Qiang Wang 2015	15	4.5	117	8.5	2	117	6.9%	1.86 [1.55, 2.17]
Qiang Li 2015	13	2.5	24	6	2.5	24	5.0%	2.75 [1.95, 3.56]
Zhilei Qiu 2017	16.4	4.5	17	9.5	3.7	17	5.1%	1.64 [0.85, 2.42]
Subtotal (95% CI)			275			420	28.6%	1.65 [0.83, 2.48]
Heterogeneity: Tau² = 0.77; Chi² = 61.56, df = 4 (P < 0.0001); I² = 94%								
Test for overall effect: Z = 3.95 (P < 0.0001)								
C								
Francisco Cesar Carnevale 2017	7.7	3.4	59	4.9	2.3	59	6.7%	0.96 [0.58, 1.34]
Jin Ho Hwang 2017	9.8	6.2	9	5.2	4.7	9	4.4%	0.80 [-0.17, 1.77]
Joao Martins Pisco 2013	12.8	5.1	60	9.19	4.47	250	6.9%	0.78 [0.49, 1.07]
Mao Qiang Wang 2015	14.5	5	117	8.5	2	117	6.9%	1.57 [1.28, 1.86]
Qiang Li 2015	12	3	24	6	2.5	24	5.4%	2.14 [1.42, 2.86]
Zhilei Qiu 2017	21.8	4.2	17	13.2	3.9	17	4.8%	2.07 [1.22, 2.92]
Subtotal (95% CI)			286			476	35.1%	1.34 [0.90, 1.79]
Heterogeneity: Tau² = 0.22; Chi² = 26.85, df = 5 (P < 0.0001); I² = 81%								
Test for overall effect: Z = 5.89 (P < 0.00001)								
Total (95% CI)			975			1375	100.0%	1.42 [1.10, 1.74]
Heterogeneity: Tau² = 0.36; Chi² = 158.82, df = 16 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 8.66 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.50, df = 2 (P = 0.78), I² = 0%								

Favours [PAE] Favours [baseline]

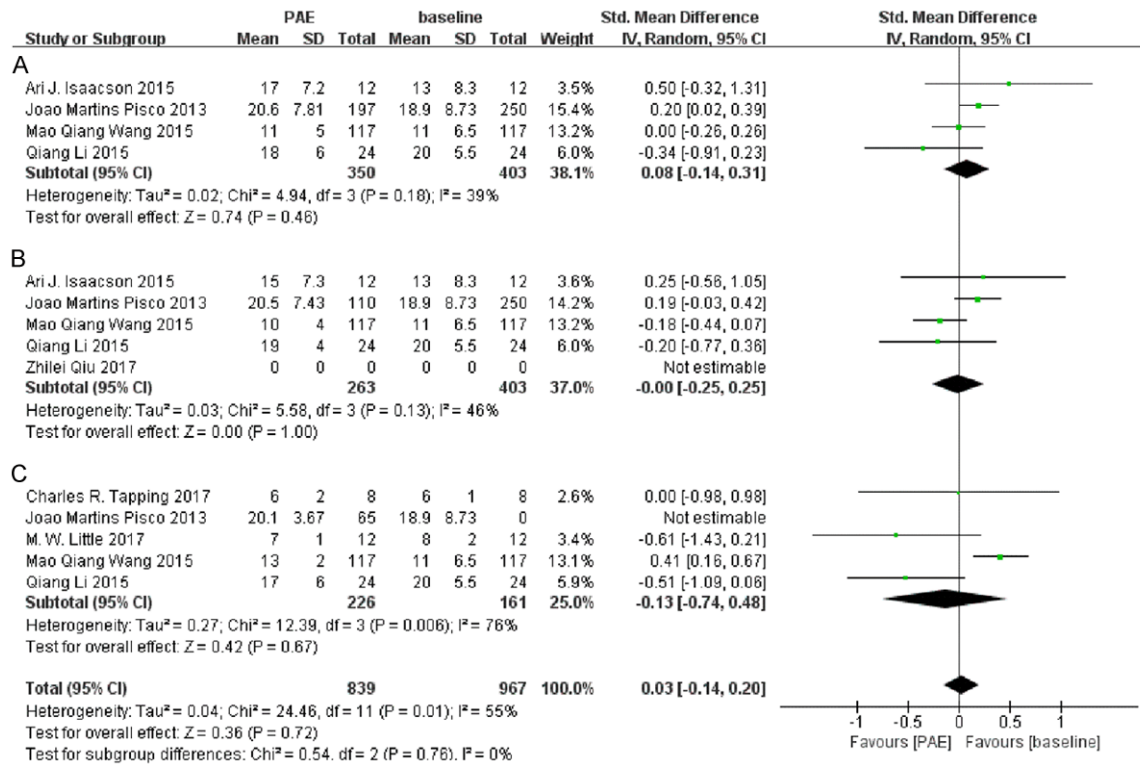Figure 7. A forest plot of Qmax changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

Figure 8. A forest plot of PVR volume changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

Figure 9. A forest plot of PSA changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

Figure 10. A forest plot of IIEF-5 score changes after PAE at postoperative 1 month (A), 3 months (B), and 12 months (C).

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