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INVITED REVIEW

Transurethral enucleation of the prostate versus transvesical open prostatectomy for large benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials

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Abstract
Purpose To evaluate the efficacy and safety of transurethral enucleation of the prostate (TUEP) versus transvesical open prostatectomy (OP) for the management of large benign prostatic hyperplasia (BPH).
Methods Randomized controlled trials (RCTs) comparing TUEP and OP were identified from PubMed, Embase and Web of Science up to February 28, 2015. A meta-analysis was conducted with the STATA 12.0 software.
Results Nine RCTs including 758 patients were enrolled in our meta-analysis. There were no significant differences between the two groups in the maximum urinary flow rate at 1, 3, 6 months, 1 and 2 years: postvoiding residual urinary volume, prostate-specific antigen, international prostate symptom score and quality of life score at 1, 3, 6 months and 1 year; or international index of erectile function at 3, 6 months and 1 year. Perioperative outcomes including hemoglobin level drop, catheter period, irrigation length and hospital stay favored TUEP, while operative time and resected prostate weight favored OP. There was significantly less blood transfusion with TUEP, but no significant differences were found in other complications such as recatheterization, urinary tract infection, reintervention for clots and bleeding control, incidence of pneumonia and infarction, transient incontinence, bladder neck contracture, urethral stricture and recurrent adenoma.
Conclusions TUEP can be performed effectively and safely with functional outcomes and complications similar to OP for large BPH, whereas it has the advantages of a shorter catheter period, shorter hospital stays and less blood transfusion. These findings seem to support TUEP as the next-generation "gold standard" of surgery for large BPH.

Keywords Transurethral enucleation · Open prostatectomy · Large benign prostatic hyperplasia · Meta-analysis · Bipolar enucleation · PKEP · International Consultation in Bipolar Enucleation of the Prostate · ICBEP

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Introduction

Transurethral resection of the prostate (TURP) has been generally considered the gold standard surgical treatment for benign prostatic hyperplasia (BPH) [1–3]. TURP for large BPH has been associated with major problems including blood loss, transurethral resection syndrome in monopolar resection and a high reoperation rate [4–7]. The European Urological Association guidelines recommended open prostatectomy (OP) as the first-line alternative for prostates >80–100 ml in volume [8]. Though OP is an effective and durable procedure for the treatment of large prostates [9], it is an invasive procedure and is associated with substantial perioperative morbidity as well as longer hospital stay and prolonged recovery [10]. Therefore, newer minimally invasive procedures have focused on achieving improvements in the endoscopic management of large BPH [11–16].

Transurethral enucleation of the prostate (TUEP) has been available as a monopolar current-based enucleation–resection since it was first described by Hiraoka in 1983 [17]. Although it was the blueprint for all other transurethral enucleations to come, it remained a local phenomenon in Japan [18]. Only when enucleation was teamed up with laser technology and the mechanical tissue morcellator, did it come into focus after publication of a paper on holmium laser enucleation of the prostate (HoLEP) in 1998 by Fraundorfer and Gilling [19]. HoLEP is regarded as a standard approach for the treatment of large prostate glands, and the great evidence base is mentioned in support of that. However, only in 2006 there was the first randomized controlled trial on HoLEP versus bipolar enucleation (plasmakinetic enucleation of the prostate, PKEP) published by the same group [20]. The only differences that could be demonstrated at that time were operative time (43.6 vs. 60.5 min), recovery room time (47.1 vs. 65.6 min) and bladder irrigation requirement (5 vs. 35 %), all in favor of HoLEP. Given the fact that HoLEP had been in use for 6 years at the beginning of the study, these differences may have resulted from the learning curve for PKEP.

Since 2006 more than 15 randomized controlled trials have been published comparing bipolar enucleation with a standard treatment arm (OP or TURP). Despite that, bipolar enucleation has not been regarded to be as valuable with regard to the evidence base as HoLEP and has consequently been neglected in the current EAU guidelines and systematic reviews [1].

Numerous studies have demonstrated that bipolar TUEP (i.e., PKEP) is an attractive minimally invasive alternative to OP for large BPH, with comparable functional results and significantly lower perioperative morbidity [11, 21–24]. However, there is a lack of data synthesis through meta-analysis to provide evidence with regard to this issue. To overcome this scientific reception bias, the International Consultation in Bipolar Enucleation of the Prostate (ICBEP) was founded by dedicated surgeons in the field of transurethral and functional urology in 2014. In this study, we aim to provide stronger scientific evidence by performing a systematic review and meta-analysis to compare the efficacy and safety of TUEP (including PKEP and HoLEP) and OP, thus providing current evidence for this treatment option in large benign prostatic enlargement (BPE).

Methods

Literature search strategy

We conducted a systematic review of the literature to identify articles published up to February 28, 2015, on the management of large BPH. We performed a systematic search of the electronic databases, including PubMed, Embase and Web of Science, using the terms "enucleation," "open" and "prostate." Additionally, a full manual search of the references of identified articles was conducted. Searches were restricted to randomized controlled and English language publications.

Inclusion and exclusion criteria

All RCTs comparing the efficacy and safety of TUEP with those of OP in large BPH and having at least one of the quantitative outcomes to be described were included in the analysis. Non-randomized controlled studies were excluded from this study.

Quality assessment

We scored the methodological quality of RCTs with the Jadad composite scale, which ranges from 0 to 5 points. According to this scale, a score ≤ 2 indicates low quality, while a score ≥ 3 indicates high quality [25]. Two independent reviewers independently allocated quality scores to the identified studies. Disagreements were resolved by consensus.

Data extraction and outcome measures

The baseline and outcome data were extracted from each eligible study by two authors independently. Patients' baseline characteristics are presented in Table 1. Outcome data were extracted as follows: maximum flow rate (Qmax), postvoid residual (PVR), international prostate symptom score (IPSS), quality of life (QoL), prostate-specific antigen (PSA), international index of erectile function (IIEF), operative time, resected prostate weight, hemoglobin level drop, irrigation length, catheterization time, hospital stay and various complications. Complications were classified using the modified Clavien–Dindo system [26].

Table 1 Characteristics of the included randomized controlled trials (RCTs)

Studies	Publication (year)	Treatments	TUEP device	No. of patients	Definition of "large prostate"	Age (years)	Qmax (mL/s)	PVR (mL)	QoL	IPSS	Prostate size	Follow-up (mo)	Jadad score
Chen et al. [10]	2014	PKEP	Gyrus generator	80	>100 g	64.7 ± 3.7	4 (3–6)	240 (160–390)	4 (4–5)	25.6 ± 3.3	110 (102–130) g	72	3
		OP		80		63.7 ± 4.5	4 (2.25–5)	249 (180–400)	5 (4–6)	25.7 ± 3.3	114.5 (104–128) g		
Geavlete et al. [16]	2015	PKEP	SurgMaster UES-40 generator	80	>80 mL	68.5 ± 8.5	6.6 ± 1.6	134.1 ± 86.8	4.1 ± 1.1	24.7 ± 3.3	122.6–30.7 mL	12	2
		OP		80		68.7 ± 8.6	6.5 ± 1.7	142.1 ± 93.1	4.0 ± 1.2	24.9 ± 3.0	128.7 ± 32.7 mL		
Kuntz et al. [14]	2008	HoLEP	VersaPulse PowerSuite	60	>100 mL	69.2 ± 8.4	3.8 ± 3.6	280 ± 273	NA	NA	114.6 ± 21.6 mL	60	3
		OP		60		71.2 ± 8.3	3.6 ± 3.8	292 ± 191	NA	NA	113.0 ± 19.2 mL		
Kuntz et al. [18]	2004	HoLEP	VersaPulse PowerSuite	60	>100 g	69.2 ± 8.4	3.8 ± 3.6	280 ± 273	NA	NA	114.6 ± 21.6 mL	18	3
		OP		60		71.2 ± 8.3	3.6 ± 3.8	292 ± 191	NA	NA	113.0 ± 19.2 mL		
Kuntz et al. [17]	2002	HoLEP	VersaPulse PowerSuite	60	>100 g	69.2 ± 8.4	3.8 ± 3.6	280 ± 273	NA	NA	114.6 ± 21.6 mL	6	3
		OP		60		71.2 ± 8.3	3.6 ± 3.8	292 ± 191	NA	NA	113.0 ± 19.2 mL		
Naspro et al. [19]	2006	HoLEP	VersaPulse PowerSuite	41	>70 g	66.26 ± 6.55	7.83 ± 3.42	NA	4.07 ± 0.93	20.11 ± 5.84	113.27 ± 35.33 g	24	2
		OP		39		67.27 ± 6.72	8.32 ± 2.37	NA	4.44 ± 0.96	21.60 ± 3.24	124.21 ± 38.52 g		
Ou et al. [20]	2013	PKEP	Gyrus generator	47	>80 mL	69.8 ± 10.2	5.9 ± 2.1	89.6 ± 52.7	4.1 ± 0.4	23.2 ± 5.7	132.2 ± 36.9 mL	12	2
		OP		45		71.5 ± 9.5	5.1 ± 2.3	81.3 ± 48.6	4.3 ± 0.5	25.1 ± 5.4	139.5 ± 36.2 mL		
Rao et al. [21]	2013	PKEP	Gyrus generator	43	>80 mL	NA	5.8 ± 2.0	83.4 ± 11.8	5.2 ± 0.7	24.8 ± 3.1	116.2 ± 32.4 mL	12	2
		OP		40		NA	5.9 ± 2.3	81.4 ± 15.7	5.1 ± 0.9	24.5 ± 3.6	110.2 ± 32.1 mL		
Salonia et al. [22]	2006	HoLEP	VersaPulse PowerSuite	34	70–220 g	67.4 ± 6.7	8.9 ± 4.2	87.4 ± 83.5	4.6 ± 1.0	19.6 ± 7.0	113.8 ± 37.0 mL	NA	2
		OP		29		68.0 ± 6.4	8.4 ± 2.4	106.3 ± 71.8	4.4 ± 1.0	21.6 ± 3.5	121.0 ± 34.9 mL		

PKEP plasmakinetic enucleation of the prostate, *OP* open prostatectomy, *HoLEP* holmium laser enucleation of the prostate, *TUEP* transurethral enucleation of the prostate, *Qmax* maximum flow rate, *PVR* postvoid residual, *QoL* quality of life, *IPSS* international prostate symptom score, *NA* not available

Statistical analysis

A meta-analysis was performed to generate summary statistics when two or more RCTs adequate for pooling were available for any outcome including perioperative data, efficacy and complications. We also conducted subgroup meta-analyses on the type of enucleation technology: PKEP and HoLEP. Continuous data were expressed as weighted mean difference (WMD) with a 95 % confidence interval (CI) and dichotomous data as an odds ratio (OR) with a 95 % CI. The Chi-square test was used to test statistical heterogeneity. In the case of statistically significant heterogeneity ($p < 0.10$), the random effects model was used for the meta-analyses. Otherwise, the fixed effects model was used. Forest plots and funnel plots were produced to reflect the pooled indicators and publication bias. Statistical tests were performed using STATA version 12.0 (StataCorp, College Station, TX, USA).

Results

Characteristics of eligible studies

The initial database search yielded 504 records. After the removal of duplicates, 293 articles were considered. Editorials or comments ($n = 19$), reviews ($n = 78$) and irrelevant topics ($n = 178$) were also excluded based on the title and abstract. Two articles [27, 28] were eliminated because they were not RCTs. After the review of the full text, one of the eligible studies [24] was excluded because it provided data from an overlapping population. Additionally, six other articles were excluded: These studies were published as abstracts, and outcomes of interest were not available. At the end of the process, nine studies [11, 15, 21–23, 29–32] including 758 patients were enrolled in our meta-analysis. Figure 1 shows the flow diagram. All included studies were RCTs and were published in English. Among enrolled studies, four [11, 21–23] compared PKEP with OP for large BPH, and the remaining five [15, 29–32] compared HoLEP with OP for the disease. Three studies [15, 29, 30] enrolled the same cohort of patients, but reported outcomes of interest at different follow-up times. Multi-lobes enucleation method was used in all these TUEPs. The baseline characteristics of included studies are described in Table 1.

Outcomes of efficacy variables including Qmax, PVR, IPSS, QoL, PSA and IIEF

Qmax

The Qmax data were acquired from seven trials [11, 15, 21–23, 30, 31]. Five studies reported Qmax at 1 postoperative month [11, 21, 23, 30, 31], five at 3 months [21–23, 30, 31], four at 6 months [11, 21, 23, 30], six at 1 year [11, 15, 21–23, 31] and three at 2 years [11, 15, 31]. There were no significant differences in Qmax between TUEP and OP during the postoperative 1, 3, 6, 12 months and 2 years, and no significant differences were observed in subgroup analysis (all $p > 0.05$, Table 2).

PVR

The PVR data were obtained from four trials [21–23, 30]. Three trials reported PVR at 1 and 6 months [21, 23, 30], and four trials reported PVR at 3 months and 1 year [21–23, 30]. TUEP and OP showed no significant differences in PVR during the postoperative 1, 3, 6 months and 1 year (all $p > 0.05$, Table 2).

IPSS

The IPSS data were obtained from four trials [21–23, 31]. Three trials reported IPSS at 1 month [21, 23, 31]. Four trials reported IPSS at 3 months and 1 year [21–23, 31]. Two trials reported IPSS at 6 months [21, 23]. TUEP and OP showed no significant differences in IPSS during the postoperative 1, 3, 6 months and 1 year (all $p > 0.05$, Table 2).

QoL

The QoL data were obtained from four trials [21–23, 31]. Three trials reported QoL at 1 month [21, 23, 31], four at 3 months and 1 year [21–23, 31] and two at 6 months [21, 23]. Pooled analysis showed no significant differences in QoL between TUEP and OP at each follow-up time point (all $p > 0.05$, Table 2). There were no significant differences in subgroup analysis (PKEP vs. OP; HoLEP vs. OP) of QoL at any follow-up time point, except for PKEP versus OP at 3 months ($p = 0.020$, Table 2).

PSA

Three trials of PKEP versus OP evaluated the postoperative PSA levels [11, 21, 23]. No significant differences were observed between TUEP and OP at any follow-up time point (all $p > 0.05$, Table 2).

IIEF

The IIEF scores were also obtained from a PKEP versus OP [23] and a HoLEP versus OP trial [31], representatively. Pooled analysis of IIEF scores at postoperative 3, 6 months and 1 year showed no significant differences (all $p > 0.05$, Table 2).

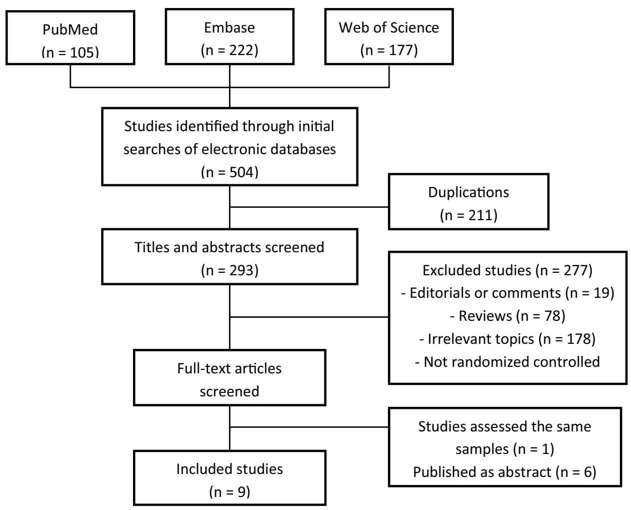


Fig. 1 Flow diagram of studies identified, included and excluded from analysis

Outcomes of perioperative variables

Operative time

TUEP was observed to be associated with longer operative time (WMD 14.163 min; 95 % CI 3.225–25.100; $p = 0.011$; Fig. 2a) in pooled data from the seven studies [11, 21–23, 30–32]. Three studies (HoLEP vs. OP) also supported OP ($p = 0.011$) [30–32], while there was no significant difference in four PKEP versus OP RCTs ($p = 0.364$) [11, 21–23].

Resected prostate weight

Seven trials reported resected prostate weight concerning 758 patients. The pooled results of analysis showed a statistically significant difference between TUEP and OP (WMD −8.713 g; 95 % CI −12.667 to −4.758; $p < 0.001$; Fig. 2b) [11, 21–23, 30–32]. In subgroup analysis, similar results were obtained for both PKEP versus OP ($p < 0.001$) [11, 21–23] and HoLEP versus OP ($p = 0.015$) [30–32].

Hemoglobin level drop

We extracted data on drop of serum hemoglobin level from five studies [21–23, 30, 31]. TUEP generated a smaller drop in serum hemoglobin level compared with OP (WMD: −0.937 g/dL; 95 % CI −1.392 to −0.482; $p < 0.001$; Fig. 2c). In the subgroup analysis, three studies [21–23] (PKEP vs. OP) and two studies [30, 31] (HoLEP vs. OP) also supported PKEP ($p = 0.007$) and HoLEP ($p < 0.001$), respectively.

Irrigation length, catheterization time and hospital stay

Three RCTs compared irrigation length between TUEP and OP. There was a shorter irrigation length in TUEP than in OP (WMD: −2.143 days; 95 % CI −2.629 to −1.657; $p = 0.004$; Fig. 2d). Six RCTs involving 598 patients reported on catheterization duration time and hospital stay [21–23, 30–32]. The pooled data showed a significant difference favoring TUEP with shorter catheterization time (WMD: −3.734 days; 95 % CI −5.391 to −2.076; $p < 0.001$; Fig. 2e) and shorter hospital stay (WMD: −4.113 days; 95 % CI −5.455 to −2.770; $p < 0.001$; Fig. 2f). Significant differences also existed in subgroup analysis of HoLEP versus OP, whereas significant differences were not found between PKEP and OP (Fig. 2e, f).

Outcomes of complications

Perioperative complications

A significant difference favoring TUEP was found with regard to incidence of blood transfusion (Clavien 2; OR 0.251; 95 % CI 0.132–0.477; $p < 0.001$; Fig. 3a) [11, 21–23, 29, 31, 32]. There was no significant difference in recatheterization (Clavien 1; OR 1.150; 95 % CI 0.486–2.722; $p = 0.750$; Fig. 3b) [11, 21–23, 29], urinary tract infection (UTI) (Clavien 2; OR 0.570; 95 % CI 0.288–1.130; $p = 0.107$; Fig. 3c) [11, 21–23], reintervention for clots and bleeding control (Clavien 3; OR 0.7370; 95 % CI 0.251–2.166; $p = 0.579$; Fig. 3d) [21, 22, 29, 31] or incidence of pneumonia and infarction (Clavien 2/4a; OR 0.333; 95 % CI 0.034–3.244; $p = 0.344$; Fig. 3e) [11, 29] between the two groups.

Postoperative complications

There were no statistical differences between TUEP and OP with respect to transient incontinence (Clavien 1; OR 0.673; 95 % CI 0.379–1.195; $p = 0.176$; Fig. 3f) [11, 21–23, 31], bladder neck contracture (Clavien 3b; OR 0.436; 95 % CI 0.170–1.116; $p = 0.084$; Fig. 3g) [11, 21–23, 29, 31] or urethral stricture (Clavien 3a; OR 1.475; 95 % CI 0.518–4.194; $p = 0.466$; Fig. 3h) [11, 21–23, 29]. Also, two studies did not find any recurrent adenoma case in PKEP/HoLEP or OP during 5- and 6-year follow-up, respectively [11, 15].

Bias analyses

We used funnel plots to assess publication bias. The funnel plot for resected prostate weight showed no obvious asymmetry (Fig. 4).

Table 2 Overall analysis of postoperative efficacy parameters comparing TUEP and OP

Outcome of interest	No. of studies	No. of patients, TUEP/OP	WMD (95 % CI)	*p* value	Favors	Heterogeneity *p* value
Qmax (mL/s)						
1 month						
TUEP	5	304/302	−0.05 [−0.710, 0.611]	0.883	None	0.662
PKEP	3	203/203	−0.175 [−0.873, 0.523]	0.624	None	0.823
HoLEP	2	101/99	1.008 [−1.022, 3.038]	0.331	None	0.356
3 months						
TUEP	5	271/264	−0.815 [−2.410, 0.779]	0.316	None	0.002
PKEP	3	170/165	−0.735 [−2.768, 1.298]	0.479	None	0.001
HoLEP	2	101/99	−1.059 [−4.480, 2.361]	0.544	None	0.145
6 months						
TUEP	4	263/160	0.705 [−0.124, 1.534]	0.095	None	0.211
PKEP	3	203/200	0.353 [−0.540, 1.246]	0.438	None	0.904
1 year						
TUEP	6	351/344	−0.228 [−0.975, 0.518]	0.549	None	0.330
PKEP	4	250/245	0.018 [−0.796, 0.832]	0.965	None	0.347
HoLEP	2	101/99	−1.53 [−3.401, 0.341]	0.109	None	0.618
2 years						
TUEP	3	181/179	−0.344 [−1.839, 1.152]	0.652	None	0.840
HoLEP	2	101/99	−0.787 [−2.900, 1.327]	0.466	None	0.921
PVR (mL)						
1 month						
TUEP	3	183/180	−2.946 [−9.753, 3.860]	0.396	None	0.001
PKEP	2	123/120	−5.688 [−16.255, 4.878]	0.291	None	0.001
3 months						
TUEP	4	230/225	−1.72 [−6.472, 3.033]	0.478	None	0.001
PKEP	3	170/165	−3.533 [−9.105, 2.038]	0.214	None	0.003
6 months						
TUEP	3	183/180	−2.373 [−8.140, 3.394]	0.420	None	0.000
PKEP	2	123/120	−4.681 [−13.498, 4.136]	0.298	None	0.000
1 year						
TUEP	4	230/225	−0.748 [−1.824, 0.328]	0.173	None	0.037
PKEP	3	170/165	−0.754 [−1.854, 0.345]	0.179	None	0.014
IPSS						
1 month						
TUEP	3	164/159	0.528 [−0.023, 1.078]	0.060	None	0.049
PKEP	2	123/120	0.243 [−0.353, 0.839]	0.424	None	0.871
3 months						
TUEP	4	211/204	0.323 [−0.112, 0.758]	0.146	None	0.607
PKEP	3	170/165	0.222 [−0.245, 0.688]	0.352	None	0.801
6 months						
TUEP	2	164/159	0.2 [−0.267, 0.667]	0.401	None	1.000
PKEP	2	164/159	0.2 [−0.267, 0.667]	0.401	None	1.000
1 year						
TUEP	4	211/204	0.006 [−0.310, 0.322]	0.970	None	0.549
PKEP	3	170/165	0.005 [−0.313, 0.324]	0.973	None	0.347
QoL						
1 month						
TUEP	3	164/159	−0.08 [−0.268, 0.109]	0.407	None	0.694
PKEP	2	123/120	−0.112 [−0.317, 0.093]	0.283	None	0.753

Table 2 continued

Outcome of interest	No. of studies	No. of patients, TUEP/OP	WMD (95 % CI)	*p* value	Favors	Heterogeneity *p* value
3 months						
TUEP	4	211/204	0.005 [−0.304, 0.314]	0.976	None	0.002
PKEP	3	170/165	−0.168 [− 0.309, −0.027]	0.020	OP	0.811
6 months						
TUEP	2	164/159	−0.054 [−0.177, 0.069]	0.392	None	0.835
PKEP	2	164/159	−0.054 [−0.177, 0.069]	0.392	None	0.835
1 year						
TUEP	4	211/204	−0.748 [−1.824, 0.328]	0.173	None	0.037
PKEP	3	170/165	−0.754 [−1.854, 0.345]	0.179	None	0.014
PSA (ng/dl)						
1 month						
TUEP	3	203/200	0.156 [−0.050, 0.361]	0.138	None	0.497
PKEP	3	203/200	0.156 [−0.050, 0.361]	0.138	None	0.497
3 months						
TUEP	2	123/120	−0.06 [− 0.232, 0.112]	0.494	None	1.000
PKEP	2	123/120	−0.06 [−0.232, 0.112]	0.494	None	1.000
6 months						
TUEP	3	203/200	−0.011 [−0.079, 0.057]	0.749	None	0.270
PKEP	3	203/200	−0.011 [−0.079, 0.057]	0.749	None	0.270
1 year						
TUEP	3	203/200	0.007 [−0.060, 0.073]	0.845	None	0.561
PKEP	3	203/200	0.007 [−0.060, 0.073]	0.845	None	0.561
IIEF						
3 months						
TUEP	2	84/79	0.473 [−0.644, 1.589]	0.407	None	0.677
6 months						
TUEP	2	84/79	−0.954 [−1.981, 0.073]	0.069	None	0.086
1 year						
TUEP	2	84/79	0.97 [−0.066, 2.005]	0.066	None	0.031

TUEP transurethral enucleation of the prostate, *WMD* weighted mean difference; other abbreviations as in Table 1

Discussion

The search for the optimal surgical management for large BPH causing benign prostatic obstruction (BPO)/bladder outlet obstruction (BOO) presents a challenge. OP was the first and is still considered to be the standard treatment for the surgical treatment for BPH, with a definite therapeutic effect [33]. However, it is an invasive procedure and is associated with increased morbidity [34]. In recent years, TUEP, in which the prostate is transurethrally and anatomically enucleated, has been approved as an effective and safe option to treat large BPH [35]. Some RCTs have compared efficacy and safety of TUEP and OP for the treatment of large BPH. In this study, we enrolled nine RCTs involving 758 patients and meta-analyzed the overall efficacy and safety between TUEP and OP. We found that TUEP obtains a similar treatment effect and has a more desirable perioperative profile, compared with OP.

The present meta-analysis showed that TUEP had functional results comparable with those of OP for both the subjective (IPSS, QoL, IIEF) and objective (Qmax, PVR) variables. Our study showed that TUEP was equivalent to OP in improving subjective symptoms and urodynamic measurements in the early follow-up. Unfortunately, due to the lack of data, we failed to evaluate the long-term efficacy. However, two papers reported similar long-term efficacy outcomes between the two groups analyzed in our study [11, 15].

Pooled analysis of operative time revealed that TUEP was associated with longer operative time compared with OP. In subgroup analyses, the operation time was similar between PKEP and OP in the four pooled studies. However, the three pooled HoLEP versus OP studies demonstrated that operative time was significantly longer for HoLEP. Difficulties in the HoLEP operation and an unskilled surgeon might have influenced the results. Moreover, the

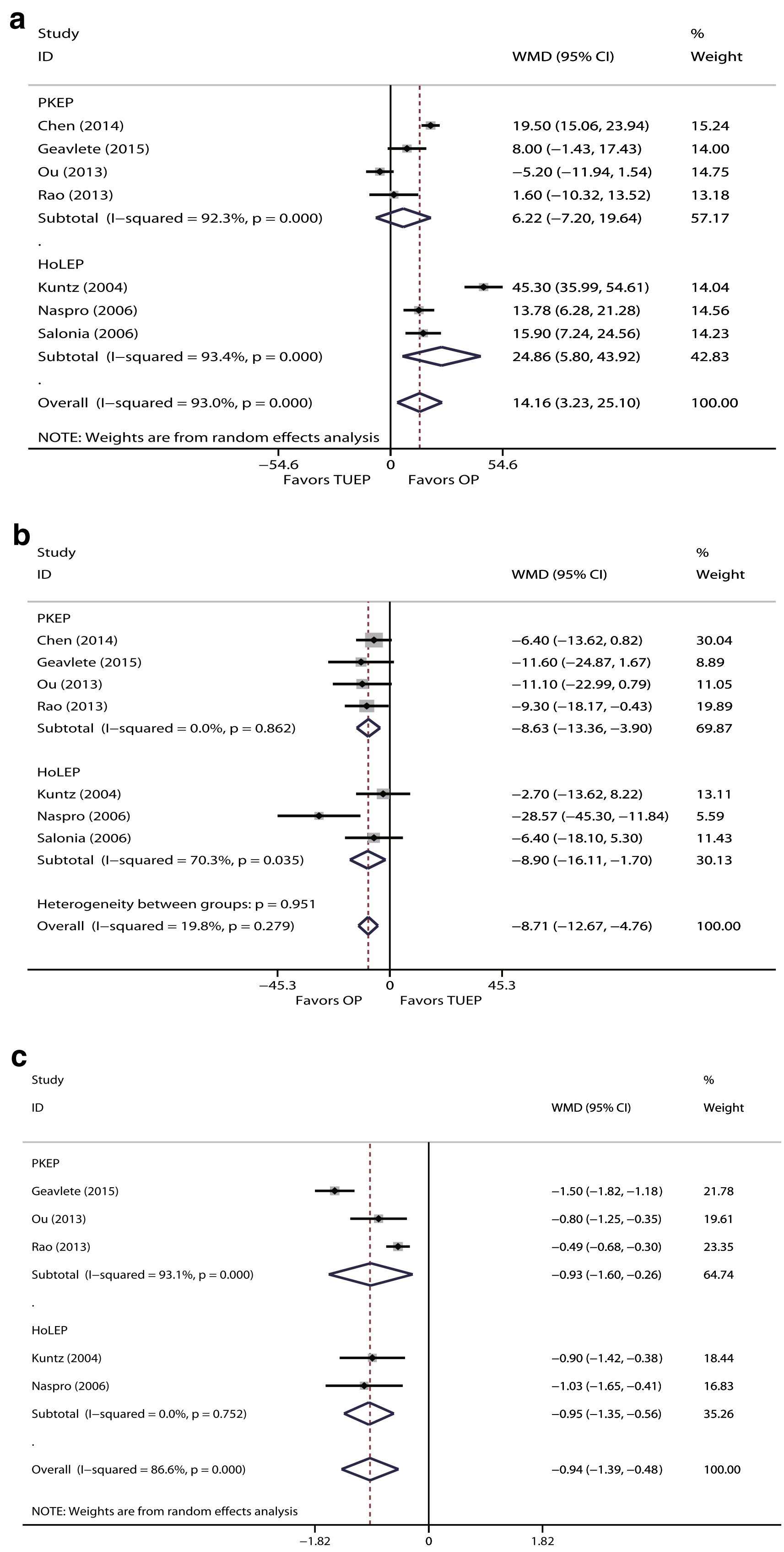
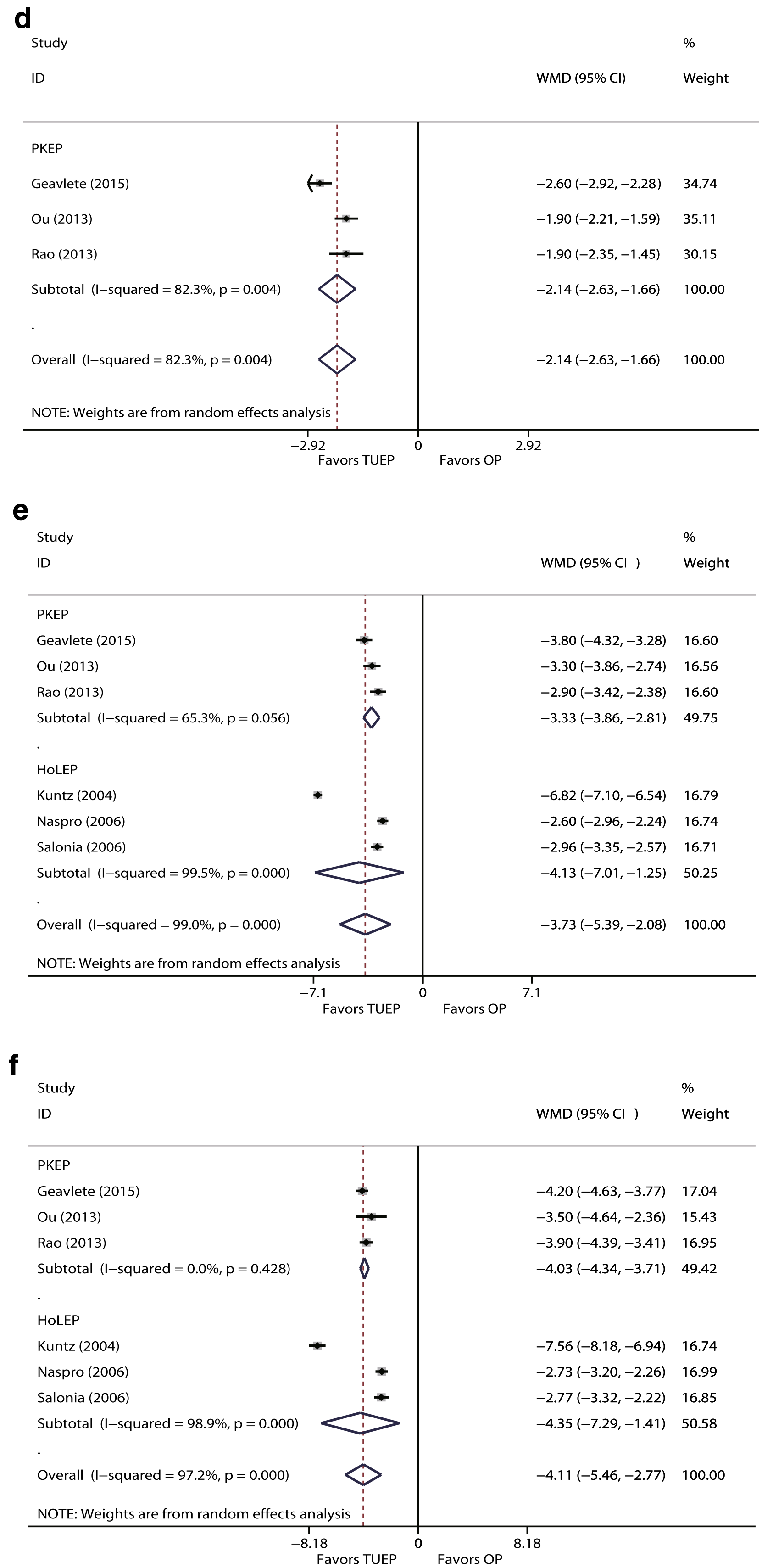


Fig. 2 Forest plot and meta-analysis of perioperative variables between TUEP and OP. **a** Operative time. **b** Resected prostate weight. **c** Hemoglobin level drop. **d** Irrigation length. **e** Catheterization time. **f** Hospital stay

Fig. 2 continued



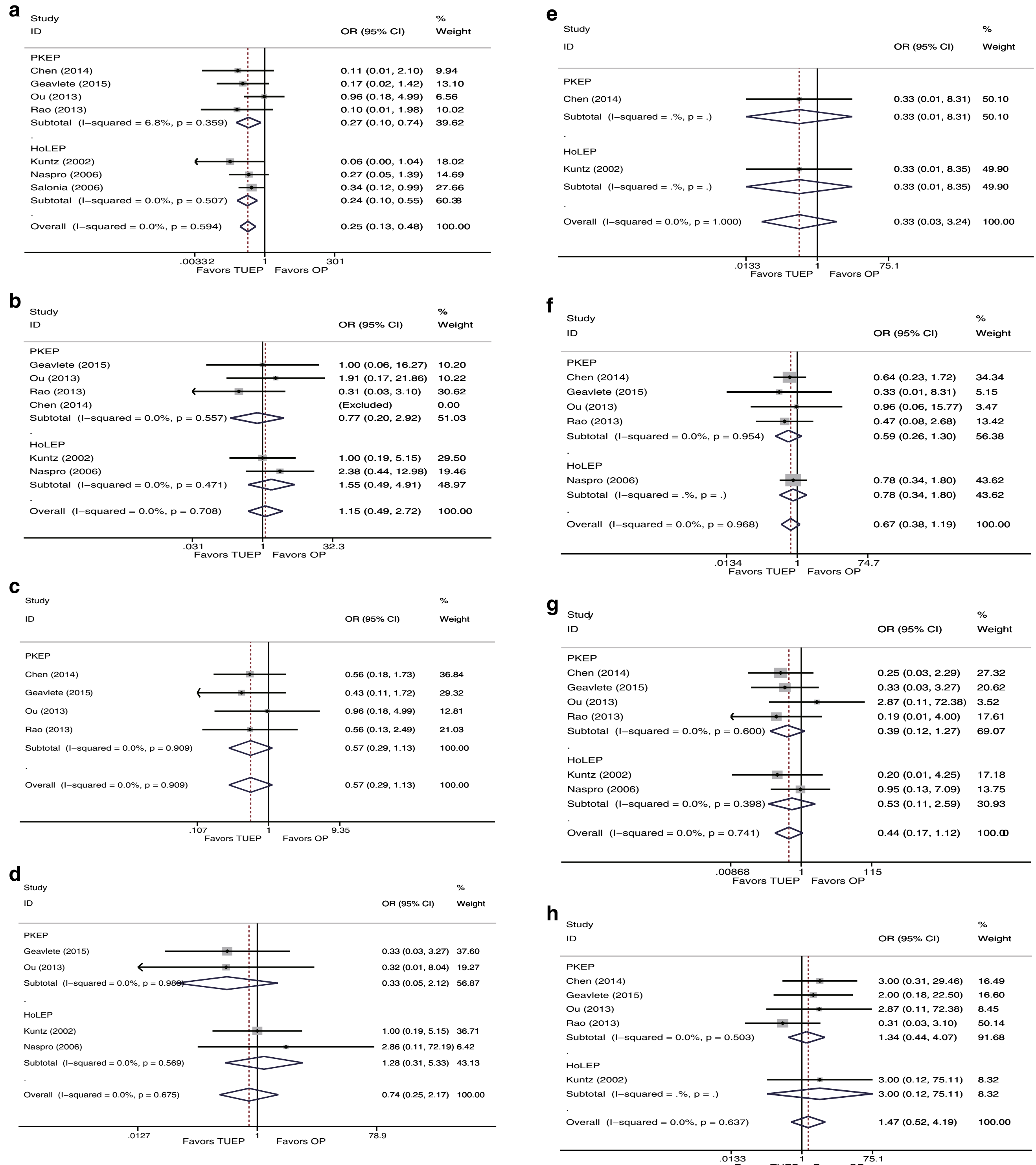


Fig. 3 Forest plot and meta-analysis of complications between TUEP and OP. **a** Blood transfusion. **b** Recatheterization. **c** Urinary tract infection (UTI). **d** Reintervention for clots and bleeding control. **e** Incidence of pneumonia and infarction. **f** Transient incontinence. **g** Bladder neck contracture. **h** Urethral stricture

resected prostate weight in TUEP was less than that in OP. This result might be explained by the fact that some of the tissue retrieved by TUEP is vaporized in the enucleation procedure [36].

Length of catheterization, irrigation and hospital stay was markedly shorter in the TUEP group. Reduced length of catheterization, irrigation and hospital stay may reduce the costs of postoperative care. However, the economic

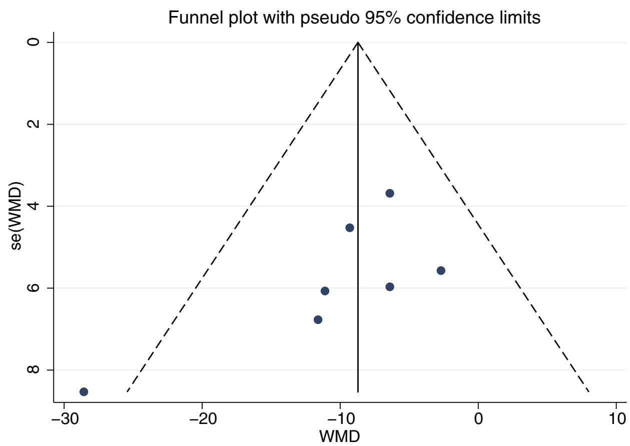


Fig. 4 Funnel plot for resected prostate weight

advantages of a shorter hospital stay and lower transfusion rate should be evaluated in conjunction with overall costs of the laser and plasmakinetic equipment. We could not pool the cost data in our meta-analysis, because only one RCT performed a cost analysis between TUEP and OP. Salonia's data demonstrated that HoLEP was associated with a significant hospital net cost saving compared with OP [32]. Further well-designed studies are needed to provide a more comprehensive economic evaluation between TUEP and OP.

No differences were observed between groups for postoperative complications including UTI, transient incontinence, bladder neck contracture, urethral stricture, recatheterization, or pneumonia and infarction. Hemorrhage requiring blood transfusion was a common complication in both TUEP and OP groups. Our analysis showed that TUEP reduced the risk of blood transfusion. This result might be associated with better laser and plasmakinetic coagulation technology. However, clinical criteria on the ideal moment to start the transfusion therapy are not always clear, and therefore, different practices between hospitals may bias our results. In addition, though no significant difference was observed between TUEP and OP in pneumonia and infarction complications, the two patients developing such complications in our study were both from the OP group.

We cannot integrate the reoperation data because of multifarious definitions and follow-up times in these RCTs. While four studies reported reoperation in the short and medium term, none of these studies revealed a significant difference in reoperation rate between TUEP and OP [22, 23, 29, 30]. The other two studies discussed reoperation in the long term (5 and 6 years), and no significant differences were observed between the two groups [11, 15]. It is remarkable that no patients developed recurrence reobstruction in these two studies.

We should admit that there are certain intrinsic limitations that cannot be ignored when analyzing our data. Though we regarded TUEP as a modality of ablation of prostatic tissue and innovatively included both PKEP and HoLEP in our study, there are some differences between bipolar and laser devices. Furthermore, in our included articles we lacked other techniques of TUEP, such as thulium laser and diode laser. Moreover, there are various definitions of "large BPH" in the eligible studies. Additionally, the statistical power of some outcomes was limited due to the relatively small sample size of the indicators. Despite these limitations, this study is the first systematic review that includes a considerably large patient group and detailed follow-up comparison to evaluate the efficacy and safety between TUEP and OP in treatment of large prostates. In future, we will also systematically evaluate the clinical efficacy and safety of TUEP compared with TURP for BPH patients.

Conclusions

We identified nine randomized trials that compared TUEP with OP in the management of large prostates. No differences between TUEP and OP were observed in the short- and intermediate-term functional outcomes. Perioperative outcomes of irrigation time, catheterization time and length of hospital stay were shorter with TUEP. Postoperative complications of blood transfusion were significantly fewer with TUEP, whereas no difference was noted in the complications of recatheterization, UTI, reintervention for clots and bleeding control, incidence of pneumonia and infarction, transient incontinence, bladder neck contracture, urethral stricture or recurrent adenoma. We consider that TUEP as a current-based technique could evolve as the next-generation gold standard of transurethral surgery for large BPE.

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Author contribution Youcheng Lin, Xun Wu, Chunxiao Liu, Zexuan Su and Thomas RW Herrmann involved in protocol/project development; Youcheng Lin, Xun Wu, Abai Xu, Rui Ren and Mancheng Gong involved in data collection or management; Youcheng Lin, Xun Wu, Xueqiong Zhou, Yong Wen and Yong Zou involved in data analysis; and Youcheng Lin, Thomas RW Herrmann and Xun Wu involved in manuscript writing/editing.

Compliance with ethical standards

Conflict of interest Thomas R. W. Herrmann declares Karl Storz GmbH, Honoraria, Financial Support for attending Symposia, financial support for educational programs, Consultancy, Advisory, Royalties; Boston Scientific AG Honoraria, Financial support for attending Symposia, financial support for educational programs, Consultancy, Advisory Board; LISA Laser OHG AG Honoraria, Financial support for attending Symposia, financial support for educational programs; Ipsen Pharma Honoraria, Financial support for attending Symposia, Advisory Board. All other authors declare that they have no conflict of interest.

Ethical standard As the present study is a meta-analysis and structured review, this manuscript is in line with the Declaration of Helsinki.

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