REVIEW ARTICLE

Enucleation of the prostate for benign prostatic hyperplasia thulium laser versus holmium laser: a systematic review and meta-analysis

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Abstract

To evaluate the clinical efficacy and safety of thulium laser vapoenucleation/enucleation of the prostate (ThuEP) versus holmium laser enucleation of the prostate (HoLEP) in the management of benign prostatic hyperplasia (BPH). A systematic literature search was performed using PubMed, Embase, and Web of Science to identify eligible studies published before July 2018. Meta-analysis of extracted data was performed with RevMan version 5.3. We chose the fixed- or random-effect model to fit the pooled heterogeneity. Five eligible studies including two randomized controlled trials (RCTs) and three non-RCTs involving 1010 patients were enrolled in our meta-analysis. ThuEP provided less enucleation time when compared with HoLEP (WMD = − 7.73, 95% CI − 14.39–1.07, $P = 0.02$). During the 1st, 6th, and 12th months of postoperative follow-ups, statistically significant differences were found in Qmax (WMD = 2.05, 95% CI 0.52~3.58) and PVR (WMD = − 6.50, 95% CI − 7.35~− 5.66, $P < 0.001$) in the 1st month after the operation, also in IPSS (IPSS: WMD = − 1.29, 95% CI − 2.39~− 0.19, $P = 0.02$) in the 12th month after the operation. As regards other perioperative, postoperative parameters, and complication rates, we found no significant difference. Both ThuEP and HoLEP provided satisfactory micturition improvement with low morbidity after the 1st and 6th months of the operation. However, ThuEP showed higher enucleation efficacy and less intraoperative blood loss and may get a better outcome as compared to the HoLEP group in the early postoperative period with regard to Qmax/PVR and IPSS after the 1st and 12th months of the operation respectively.

Keywords Thulium laser · Holmium laser · Enucleation · Safety · Efficacy · Meta-analysis

Introduction

Benign prostatic hyperplasia (BPH) is a common pathologic condition which is mightily connected with increasing age [1]. BPH can eventually result in benign prostatic obstruction (BPO), which is a crucial cause of lower urinary tract symptoms (LUTS). LUTS is known as one of the most common and unpleasant nonmalignant conditions impairing the quality of life in aging men with significant social-economic importance to public health systems worldwide [2]. The efficacy of drugs, such as 5-alpha reductase inhibitors and alpha-blockers, is limited to severe symptoms. Therefore, as the disease progresses, more invasive treatment options have to be taken into consideration [3].

Transurethral resection of the prostate (TURP) has stood the test of time and is properly considered the surgical reference method that provides enduring clinical improvement in patients with symptomatic BPH and a prostate volume ranges from 30 to 80 ml that are refractory or cannot tolerate medical therapy [4]. However, TURP is also associated with considerably increasing intraoperative or postoperative complication rates with age and prostate volume, such as unsatisfactory hemostatic effect, genitourinary infections, transurethral resection syndrome (TURS), fluid volume absorption, prolonged recovery, and postoperative erectile dysfunction [5, 6].

To overcome these known pitfalls, many minimally invasive procedures have come into view. Prostate artery

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embolization (PAE) has recently been proposed as a new minimally invasive alternative treatment for standard surgical procedures in patients with LUTS caused by BPO [7]. This endovascular approach consists in a selective embolization of the prostatic arteries to induce a reduction of prostate size and thus a subsequent decrease in LUTS. Following the first randomized clinical trial comparing the efficacy and safety of PAE with TURP, there have been several subsequent studies from around the world (including two non-inferiority, randomized trials); nevertheless, the results were highly contradictory. On the basis of above trials, a recently published meta-analysis with 708 patients presenting that compared with classical surgical procedures, PAE treatment for BPH is associated with significant advantages of safety and sexual function but with clear disadvantages of other functional outcomes [8]. However, current studies are sparse; hence, the evidence are not sufficient enough to conclude on the ideal indication, feasibility, mid-term and long-term efficacy, and safety of PAE. Greenlight photoselective vaporization of the prostate (PVP) is another substitute surgical option for conventional TURP in the management of LUTS from BPH [9]. Due to the optical characteristics of green light laser, it provides efficient vaporization of prostate tissue and excellent perioperative hemostasis with a clear surgical view. One major disadvantage of PVP is the limitation of resectable volume, especially for large glands. Another main disadvantage of PVP is that no tissue specimen could be reserved for pathologic examination, which carries the risk of missing an opportunity for prostate cancer diagnosis [10].

Endoscopic enucleation of the prostate (EEP) has been developed and recognized as a viable treatment option [3]. EEP can be performed through several sources of energy, the most well recognized of which is holmium laser enucleation of the prostate (HoLEP). This surgical procedure has been proven to be a minimally invasive, size-independent method with a comparable surgical outcome as conventional TURP in several meta-analyses based on numerous randomized controlled trials (RCTs) [11–14]. Development of novel technologies resulted in the emergence of additional laser energy sources. Thulium laser is a burgeoning surgical laser followed by the development of holmium laser prostatectomy. Due to its 2-μm wavelength which is close to the 1.92-μm water absorption peak and the continuous wave mode, thulium laser is reported to be superior to the other lasers in some aspects such as minimal blood loss, high ablation rate with minimal thermal injury, and precise incision [15]. In 2008, it was first introduced as a viable resection method in a comparison with TURP for the treatment of BPH [16]. Subsequently, the thulium laser was gradually applied to endoscopic enucleation surgeries, resulting in the procedures known as thulium vapoenucleation of the prostate (ThuVEP) and thulium laser enucleation of the prostate (ThuLEP) [17, 18].

Both thulium and holmium laser enucleation have been shown to be size-independent methods for the operative treatment of BPH with low perioperative and postoperative morbidity and good long-term outcomes [19, 20]. Though several comparative studies of the two enucleation modifications have been published recently, no systematic assessment was performed. The aim of this meta-analysis is to compare the clinical efficacy and safety of ThuVEP/ThuLEP with those of HoLEP for the treatment of patients with LUTS related to BPH.

Materials and methods

Search strategy

A systematic literature search using the Pubmed, Embase, and Web of Science databases of controlled trials was conducted. Before the literature search, the inclusion and exclusion criteria were defined. Studies meeting the following criteria were included: (1) compared ThuVEP/ThuLEP with standard HoLEP; (2) patients with benign prostatic obstruction who suffered from LUTS; (3) full papers reporting on at least one of the two primary outcomes of efficacy and safety; (4) publications dated from January 1, 2000, to July 30, 2018; (5) no language restriction was used in the searches. On the contrast, studies meeting the following criteria were excluded: (1) not met the inclusion criteria; (2) contained patients with suspicion of prostate cancer or neurogenic bladder; (3) review articles, non-comparative studies, case reports, letters, and editorial commentaries. The search terms were used as follows: ("holmium" or "thulium") AND ("benign prostatic hyperplasia" or "BPH"). This systematic review was performed basing on the Preferred Reporting Items for Systematic Reviews and Meta-analyses protocols (PRISMA-P) 2015 guidelines [21].

Study selection

Two independent researchers(K.-W.X and L.Z.) performed the first screening of titles and abstracts of all the studies that were identified by the retrieval strategy for the identification of eligible studies. A full-text review was required if sufficient information could not be obtained based on the title and the abstract alone. All the studies that appeared to fit the inclusion criteria were independently screened for full review, and the records were extracted and evaluated. The reference lists of retrieved studies were further screened for additional eligible publications. We also tried to contact the corresponding author of studies which data was unclear or incomplete to confirm data extraction. Any disagreement between the reviewers was discussed and resolved by consensus, and the third reviewer (K.-J.W.) was involved in the judgment if an agreement could not be reached.

The level of evidence (LE) of every included study was graded based on the EAU guidelines. Risk of bias (RoB) assessment was undertaken using the recommended tool in the Cochrane Handbook 5.1 for Systematic Reviews of Interventions for RCTs [22]. For non-randomized controlled studies, study quality was assessed by the Newcastle-Ottawa Scale (NOS) [23]. The scale ranges from 0 to 9 scores, and only studies with a score > 7 were considered qualified enough to be included in our analysis.

Data extraction and analysis

Five standardized forms were applied to extract data of the basic characteristics of patients, physical parameters of laser devices, perioperative outcome parameters, postoperative outcome parameters, and complication index. The following information of the included studies was extracted independently by two authors (K.-W.X and L.Z.): baseline characteristics of patients involving author's name, date of publication, study design, number of patients, age of patients; perioperative and postoperative parameters comprising PSA level, prostate volume, postvoid residual (PVR), maximum flow rate (Qmax), international prostate symptom score (IPSS), quality of life (QoL), operative time, postoperative sodium and hemoglobin decrease, catheter time, and hospital stay; physical parameters of laser devices including laser type, wave mode, output power, and fiber diameter; complications including blood transfusion, incomplete enucleation, recatheterization, urinary incontinence, urinary tract infections, and prolonged drainage.

This meta-analysis was performed with the RevMan analytical software package (RevMan version .5.3, Cochrane Collaboration, Oxford, UK). Continuous variables were presented as the mean ± standard deviation. If the included studies presented medium (IQR) instead of mean ± standard deviation, sample sizes were large ($n > 25$) and the outcome

distribution was similar to the normal distribution, then the following formula was applied: mean = medium, IQR = 1.35SD [22]. If standard deviations were not reported and could not be calculated from available data, we asked authors to supply the data. The odds ratio (OR) and 95% confidence interval (CI) were used for the dichotomous variables. If the event rates were 0, a half-integer continuity correction was applied to all four cells [22].

The pooled effects were determined by the Z-test, and $P < 0.05$ was considered statistically significant. Chi-squared test and the I^2 statistic were used to examine the heterogeneity among the studies. If $P > 0.1$ or $I^2 < 50\%$, the fixed-effected model was used, which showed that the eligible included studies are homogeneous. If not, the random-effected model was performed to estimate the relative risk (risk ratios) with 95% CI, because the high heterogeneity was across the studies.
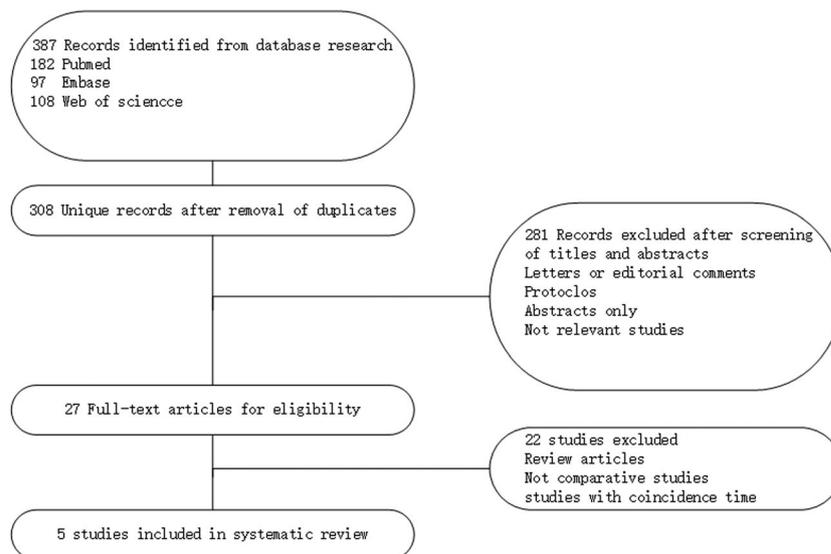
Results

The characteristics of patients included in different studies are summarized in Table 1 [24–28]. A total of 1010 patients from five independent studies were included in our present review and a total of 483 patients were treated with thulium laser while the rest were treated with holmium laser. The physical parameters of different laser devices are shown in Supplementary Table 1. The literature selection process is illustrated in Fig. 1. All five studies were involved in our meta-analysis, including two RCTs and three non-RCTs. The results of quality estimates of RCTs and non-RCTs are shown in Tables 2 and 3, respectively. For RCTs, blinding of the surgeons was impossible as regards the nature of clinical intervention; hence, if the blinding of the patients and the outcome estimators were described in the methodology part, the study

Table 1 Baseline characteristic of included studies

Studies	Treatments	No. of patients	Age (years)	IPSS baseline	Qmax baseline (ml/s)	PSA (ng/ml)	PVR (ml)	Prostate volume (ml)	QoL data	LE	Study design
Enikeev (2018)	ThuEP	202	67.1 ± 7.2	21.8 ± 1.6	7.6 ± 1.9	4.5 ± 3.1	70.1 ± 28.7	91.0 ± 32.1	4.0 ± 0.8	3b	CCT
	HoLEP	254	66.5 ± 7.7	21.9 ± 1.1	7.5 ± 1.7	4.5 ± 2.6	72.4 ± 28.6	89.7 ± 43.3	4.1 ± 0.8		
B. Becker (2018)	ThuEP	48	74 ± 6.5	20 ± 6.6	9.6 ± 4.6	4.14 ± 3.19	100 ± 156.1	82.5 ± 38.7	4.0 ± 0.7	2b	RCT
	HoLEP	46	71.5 ± 5.9	22 ± 8.1	12.1 ± 5.8	4.14 ± 4.59	105 ± 112.4	77.5 ± 47.7	4.0 ± 0.7		
Pirloa (2018)	ThuEP	117	70 ± 7.4	20 ± 4.3	7.0 ± 2.22	3.8 ± 1.91	90 ± 59.3	75 ± 25.9	5.0 ± 0.7	3b	CCT
	HoLEP	117	71 ± 6.6	21 ± 5.9	7.0 ± 3.26	5.48 ± 3.9	103.5 ± 104.8	75 ± 29.6	5.0 ± 0.7		
Zhang (2012)	TmLEP	71	74.2 ± 9.8	24.6 ± 3.2	6.8 ± 3.9	2.56 ± 2.19	64.6 ± 32.5	46.6 ± 25.2	NR	2b	RCT
	HoLEP	62	76.2 ± 9.7	22.8 ± 2.6	7.3 ± 3.7	2.07 ± 2.22	64.6 ± 33.4	43.5 ± 23.0	NR		
Hong (2015)	TmLEP	45	72.1 ± 4.0	26.4 ± 6.0	6.44 ± 2.42	2.75 ± 1.36	115.7 ± 98.2	59.7 ± 10.7	5.06 ± 0.91	3b	CCT
	HoLEP	48	70.3 ± 5.2	27.3 ± 5.3	5.87 ± 2.67	3.08 ± 1.97	138.6 ± 91.5	56.2 ± 13.4	4.77 ± 1.09		

ThuEP thulium laser enucleation of the prostate (ThuLEP)/thulium vapoenucleation of the prostate (ThuVEP); *HoLEP* holmium laser enucleation of the prostate; *IPSS* international prostate symptom score; *Qmax* maximum flow rate; *PSA* serum prostate-specific antigen; *PVR* post-void residual urine; *QoL* quality of life; *LE* level of evidence; *RCT* randomized controlled trial; *CCT* case control trials, *NR* not recorded

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│ 387 Records identified from database research │
│ 182 Pubmed                                │
│ 97  Embase                                │
│ 108 Web of sciencce                       │
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│ 308 Unique records after removal of duplicates │
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                    │                    │ 281 Records excluded after screening │
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                    │                    │ Letters or editorial comments    │
                    │                    │ Protoclos                        │
                    │                    │ Abstracts only                   │
                    │                    │ Not relevant studies             │
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│ 27 Full-text articles for eligibility    │
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                    │                    │ 22 studies excluded              │
                    │                    │ Review articles                  │
                    │                    │ Not comparative studies          │
                    │                    │ studies with coincidence time    │
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│ 5 studies included in systematic review  │
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was deemed as blinded. For non-RCTs, all the included studies showed high quality.

The efficacy and safety of ThuVEP and ThuLEP were mainly determined by the optical features of thulium laser. Due to the smooth transition from each technique, it was difficult to define a clear differentiation of the ThuLEP technique from the ThuVEP technique [29]. In our study, thulium vaporization was used in all the included studies in various degrees; therefore, we inclined to determine this procedure as thulium enucleation of the prostate (ThuEP) rather than ThuLEP or ThuVEP.

Management of enucleated prostatic lobes was different among studies. Tissue morcellation was performed either conventionally via a mechanical tissue morcellator or with a mushroom technique. As the morcellator was not available at the beginning of Zhang's study, so the "mushroom technique" was applied. The enucleated lobes were fragmented with the use of the electrocautery loop. As reported by Zhang et al., the mean time of mushroom fragmenting by electro-resection and evacuation was approximately 17 min, which was comparable to mechanical tissue morcellation [20, 30]. Hence, the data were also included. On the whole, no major effects were observed on the meta-analysis of baseline parameters.

Significant differences were observed in enucleation time between groups (enucleation time: WMD = − 7.73, 95% CI −

14.39~1.07, $P = 0.02$). Two studies reported significant differences in enucleation efficiency (g/min) between ThuVEP and HoLEP, which was in accordance with the result of meta-analysis, suggesting the advantages of ThuEP over HoLEP. All the included studies recorded less hemoglobin decrease in ThuEP when compared with HoLEP; however, the difference was not statistically significant. Only one study reported intraoperative blood loss, and the data showed less intraoperative blood loss in the ThuEP group when compared with the HoLEP group. With regard to operation time, catheterization time, hospital stay, and the decrease of sodium, no statistical difference was obtained between the groups. However, great heterogeneity was found among the studies (Fig. 2).

Functional measures including symptom scores (IPSS, QoL) and voiding parameters (Qmax, PVR) were used for preoperative and postoperative assessments. All the included studies reported statistically significant improvement after surgery. Meta-analysis of follow-up data between groups showed significant difference in Qmax (WMD = 2.05, 95% CI 0.52~3.58, $P < 0.001$) and PVR (WMD = − 6.50, 95% CI − 7.35 ~ − 5.66, $P < 0.001$) in the 1st month after the operation, while no significant difference was shown in other variables. During the 6th month and the 12th month of postoperative follow-ups, no statistically significant difference was observed in QoL, Qmax, and PVR between the groups. Interestingly, a significant difference was observed in IPSS (WMD = − 1.29,

Table 2 Risk of bias for RCTs

Author, year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Other bias
B. Becker 2018	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk
Zhang 2012	Low risk	Low risk	Unclear	Low risk	High risk	Unclear

Table 3 Newcastle-Ottawa Scale for quality assessment of CCTs

Author, year	Selection				Comparability	Outcome			Total score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Based on the design or analysis	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Enikeev 2018	1	1	1	1	2	1	1	1	9
Pirloa	1	1	1	1	2	1	1	1	9
Ma 2015	1	1	1	1	2	1	1	1	9

95% CI $-2.39 \sim -0.19$, $P = 0.02$) during the 12th month of postoperative follow-up (Figs. 3, 4, and 5). Two studies recorded these functional and voiding parameters in the 3rd month and the 18th month after surgery; however, the data was not enough to be included in the meta-analysis.

Meta-analysis on major reported complications showed no differences between ThuEP and HoLEP, including blood transfusion, recatheterization, prolonged drainage, urinary tract infections, incomplete enucleation due to perforation of the surgical capsule of the prostate, urinary incontinence (the first month), and urinary incontinence (the sixth month) (Table 4). Other minor complications, e.g., retrograde ejaculation, urethral stricture, bladder contracture, and ureteral orifice injury, were also reported in the included studies, but, however, the data were not enough to be used in our meta-analysis. The modified Clavien classification system was used to classify the medical and surgical complications in three studies. However, the meta-analysis could not be performed because of the difference among classification definition of complications.

Discussions

TURP is properly considered as the surgical reference method that provides an enduring clinical improvement of BPO. Despite the modification of the technique that promoted the security of TURP, the considerable morbidity, long-term complications including ejaculatory dysfunction, erectile dysfunction, urethral strictures, bladder neck contractures, urinary incontinence, urinary tract infection, and blood transfusion, and a relatively high retreatment rate still existed [31].

Laser enucleation of the prostate has developed as an efficient and more minimally invasive method which may provide similar outcomes compared with TURP and OP (open prostatectomy). In 1995, the first clinical report on holmium laser treatment of BPH was reported by Gilling et al. [32]. A number of urologists claimed that HoLEP has no size limitations, and it enables complete gland removal with minimal bleeding, which is associated with decreased morbidity [19, 20, 33]. Superior long-term endurability has also been reported. However, HoLEP is considered a difficult surgical procedure, and the shallow learning curve has limited its application in clinical urologic practice worldwide. It has been reported that HoLEP has a learning curve of at least 20–30 cases and even approximately 50 cases are thought to be sufficient enough for performing this technique without difficulty [34–36]. The minimally invasive laser techniques are developing with an incredible rate in modern urology. In 2008, the thulium laser was first introduced as a feasible resection procedure for the treatment of BPH in a comparison with TURP [16]. The technology was further modified by Bach and colleagues in 2009 using the thulium:YAG laser for

Fig. 2 Forest plot of perioperative outcomes between ThuEP and HoLEP. (A) Operation time. (B) Enucleation time. (C) Morcellation time. (D) Catherization time. (E) Hospital stay. (F) Hemoglobin decrease. (G) Sodium decrease
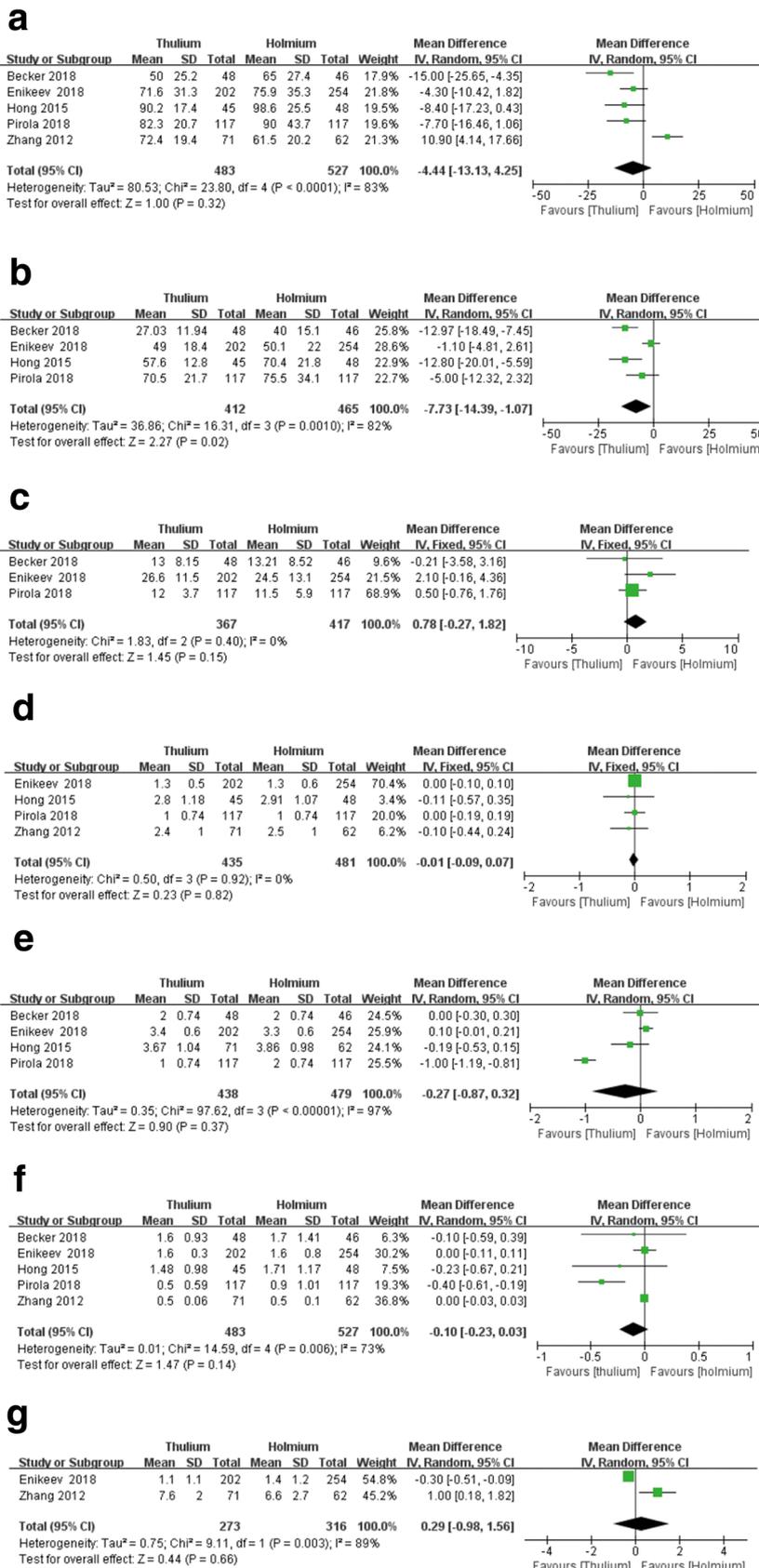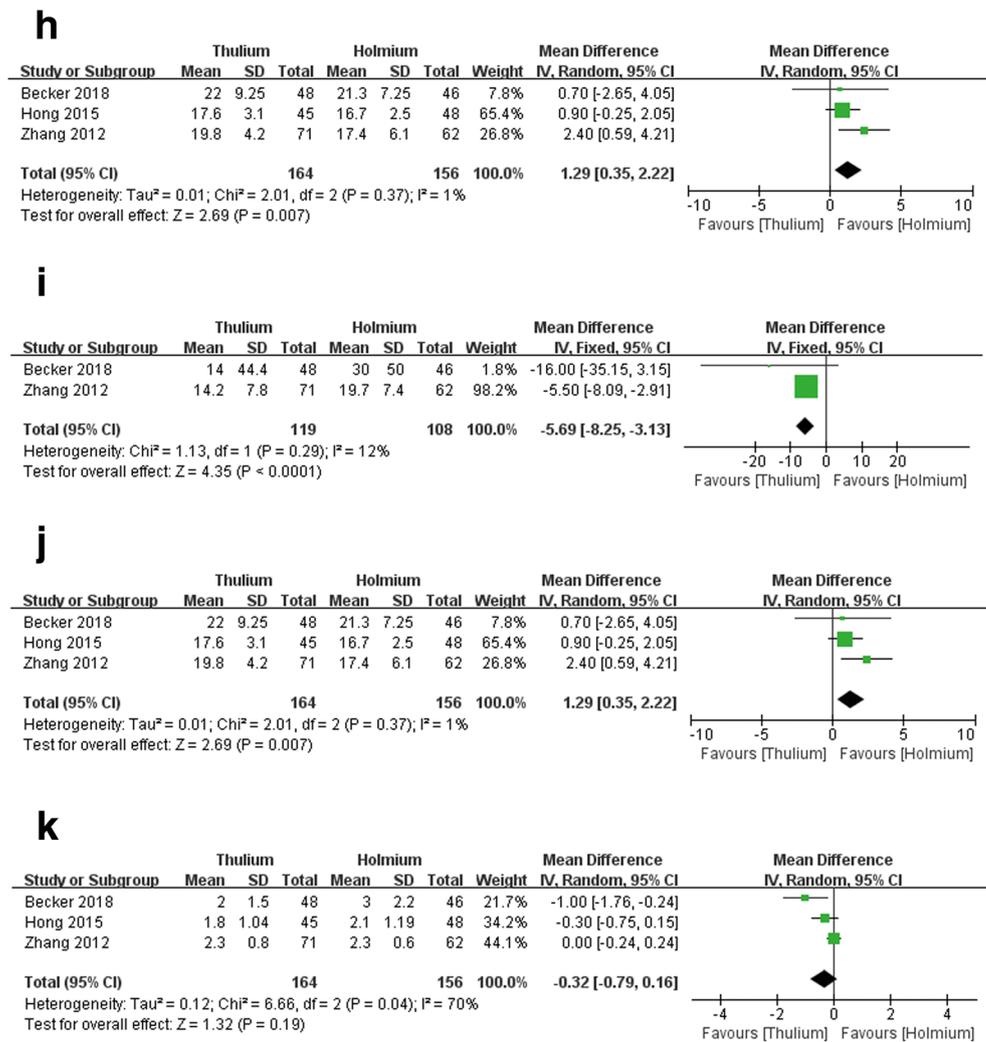
Fig. 3 Forest plot of postoperative outcomes (1-month) between ThuEP and HoLEP. (H) Qmax. (I) PVR. (J) IPSS. (K) QoL
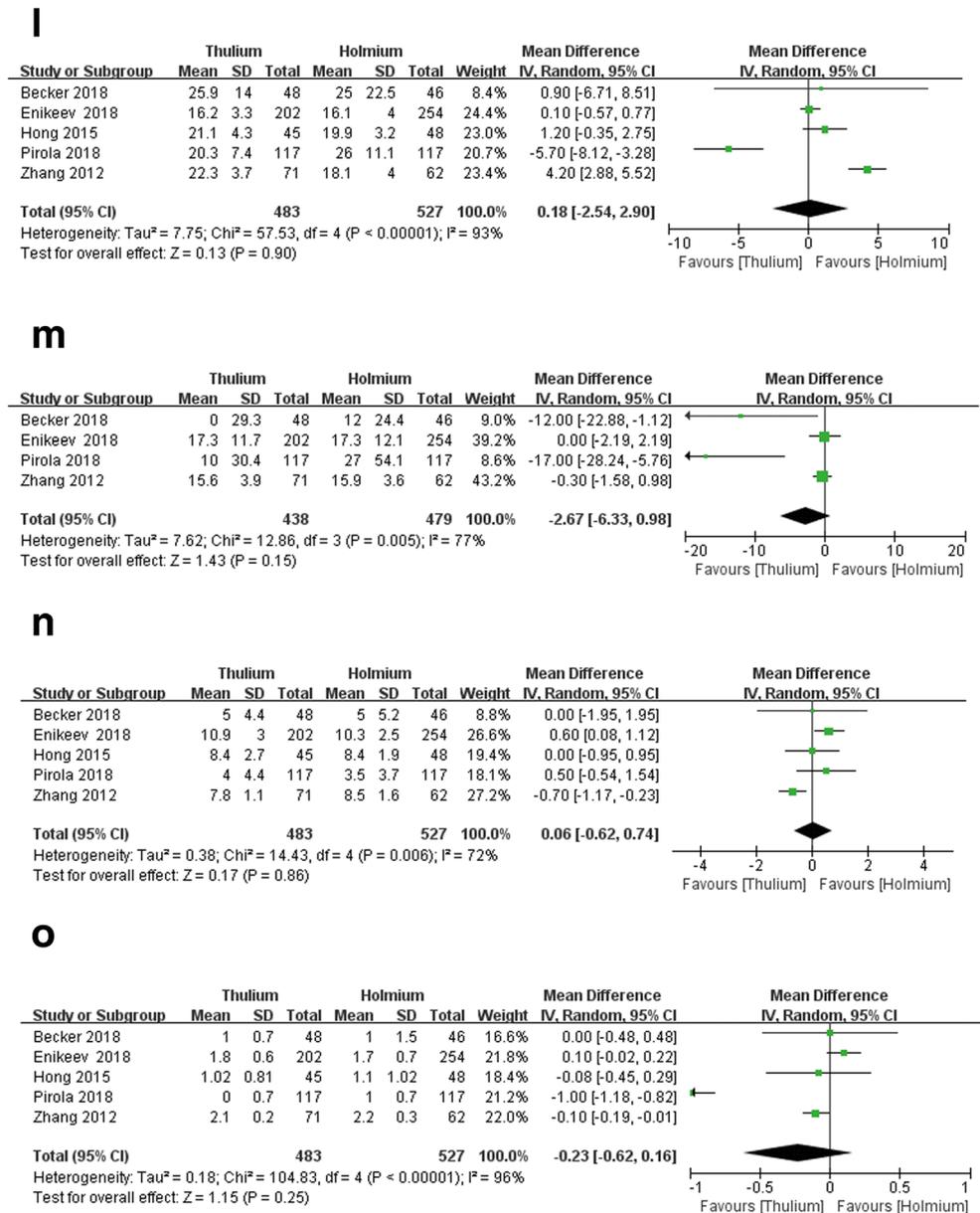

In our analysis, we could notice a significant difference in enucleation time which favors the ThuEP technique. High enucleation efficacy of the ThuEP technique was also reported in three included studies. This can be explained by two features of the thulium laser [15]: (1) the wavelength of thulium laser is close to the water absorption peak, and water is the main absorbing substance which comprises about two-thirds of the prostate, thus results in a high energy absorption rate and instantaneous tissue vaporization; (2) compared with the pulsed mode of the holmium:YAG laser, the continuous wave mode of the thulium:YAG laser might provide a faster enucleation.

Interestingly, no statistical difference was observed between the total operation time of the procedures, and the analysis of morcellation time also showed no significant difference. The difference in coagulation depth between thulium:YAG laser (2 mm) and holmium:YAG laser (4 mm) may be an explanation; for the final coagulation, more time may be required after ThuEP compared with HoLEP [18, 38].

vapoenucleation of the prostate (ThuVEP). ThuVEP is an energy-based transurethral enucleating procedure; the wave of thulium:YAG laser was continuously applied to the enucleation plane for separating the prostate from the surgical capsule [17]. Subsequently, the thulium laser was fully enrolled into endoscopic enucleation of the prostate surgeries, generating the procedure known as thulium laser enucleation of the prostate (ThuLEP). In contrast to the rest of energy-based transurethral enucleating techniques, ThuLEP is characterized by the blunt enucleation of the enlarged gland without using energy, and thulium laser retrogradely separates the gland over its surgical capsule with the tip of laser fiber [18]. Gross et al. evaluated postoperative outcomes and complications of ThuVEP in regard to prostate size [37]. No difference was observed in transfusion rates or other complications. The findings indicated that the enucleation efficacy (g/min) was improved with enhanced prostate size, further proofing that thulium laser endoscopic enucleation is also a size-independent procedure as HoLEP.

There is also another explanation; different studies may record the operation time in different criteria, and none of the included studies has a clear definition of this parameter. Also, the proficiency of the surgeons may influence the results. In general, all the possible explanations may be responsible for the high heterogeneity. In addition, the diversity in the energy settings among the studies may be a potential factor for the difference in the enucleation rate next to the mode of laser piled. Netsch and colleagues compared the efficacy of 70-w with 120-w ThuVEP in patients with enlarged prostates. Results showed that compared with the 70-w Tm:YAG device, the 120-w Tm:YAG device enhanced the effectiveness of ThuVEP in regard to enucleation as well as overall

operation efficiency, and no statistical difference was found in the incidence of complications among patients treated with the different laser devices [39]. No RCT which compares high-powered HoLEP with low-powered HoLEP has been published. However, a recently published report suggested that low-power HoLEP could be performed safely and without any technical problems. When compared with the data of high-power HoLEP reported in the literature, it could also provide a comparable functional outcome [40]. Enikeev et al. reported that the enucleation energy was set at 70 W for holmium laser and 60 W for the thulium laser, no difference was observed among the baseline characteristics of patients between the groups, while the enucleation time in

Fig. 5 Forest plot of postoperative outcomes (12-month) between ThuEP and HoLEP. (P) Qmax. (Q) PVR. (R) IPSS. (S) QoL
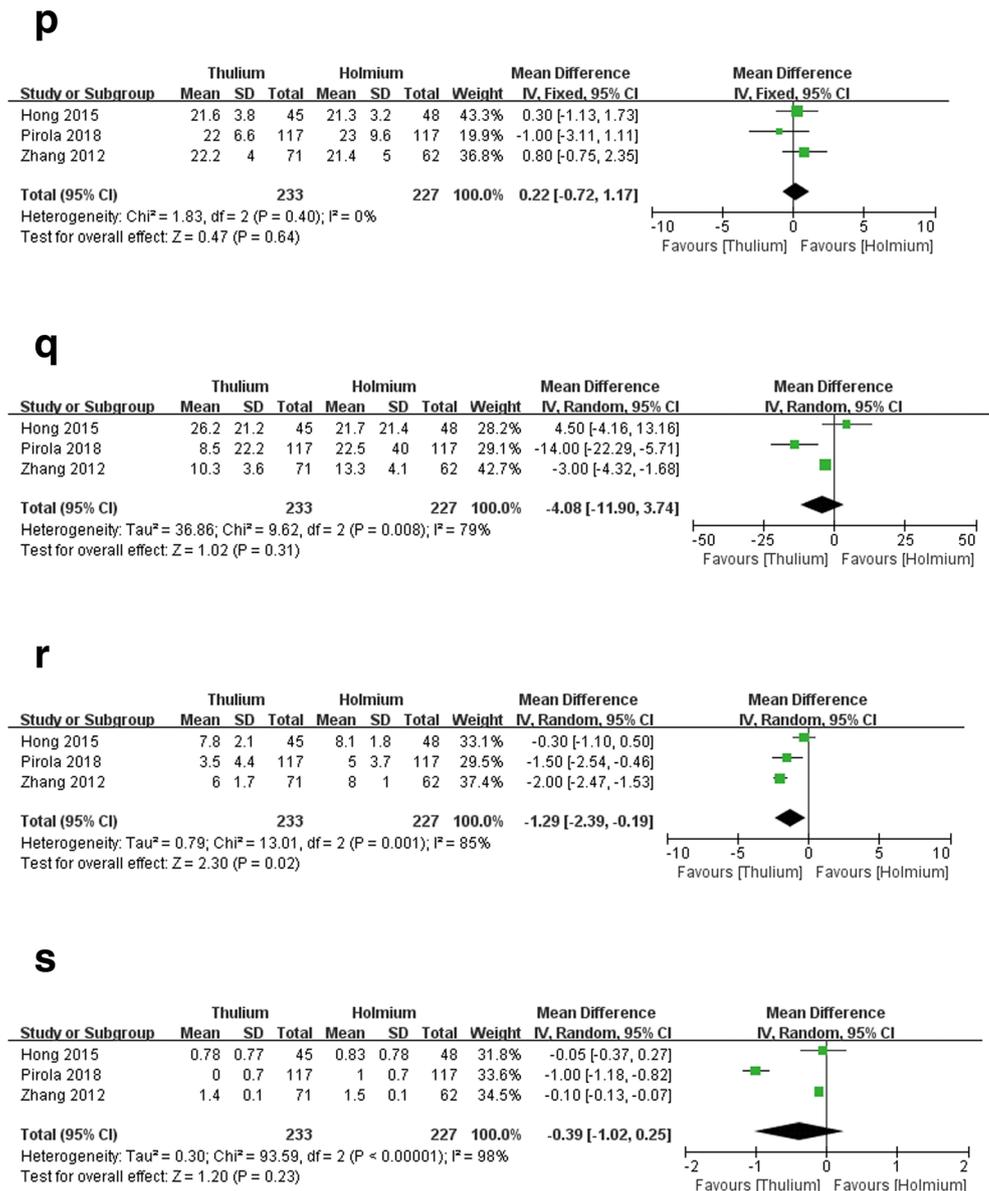
thulium group still slightly less than the holmium group [25]. This might support the features of thulium laser as we mentioned previously.

In our review, all the included studies recorded less perioperative blood loss (decrease of hemoglobin); however, in terms of the results of our meta-analysis, the difference was not significant. This point was supported by the analysis of postoperative blood transfusion rate which also showed no statistical difference. Based on the above results, we assume that the wavelength of thulium laser may offer superior coagulation and intraoperative blood loss control compared with the holmium laser [41]. In terms of other perioperative parameters, for example, sodium decrease, catheterization time, and hospital stay, the pooled analysis showed no significant difference. However, some perioperative parameters, like catheterization time and hospital stay, are most likely triggered by differences in reimbursement in the different national health systems and should be taken into account when comparing these parameters from different series [37].

The meta-analysis of postoperative parameters suggested that ThuEP exhibited an evidently higher Qmax when compared with HoLEP in the 1st month of postoperative follow-up; however, the difference was not statistically significant in the 6th month and the 12th month of follow-ups. The pooled analysis of postoperative data has also shown a lower PVR in ThuEP group compared with HoLEP group in the 1st month of follow-up. In the 6th month and the 12th month of follow-ups, this difference was no longer significant. With regard to

Table 4 Meta-analysis of major postoperative complications

Complications	No. of studies	No. of patients ThuEP/HoLEP	OR (95% CI)	P value	Chi^2	df	I^2 (%)	P value	Favors
					Study heterogeneity				
Blood transfusion	20–24	483/527	0.46 (0.10, 2.06)	0.31	0.42	2	0	0.81	None
Infection	20–24	483/527	1.17 (0.56, 2.43)	0.67	0.63	3	0	0.89	None
Recatheterization	20, 21, 23	321/362	0.62 (0.29, 1.31)	0.21	3.21	2	38	0.2	None
In complete enucleation	21–24	438/479	1.05 (0.46, 2.41)	0.91	2.33	3	0	0.51	None
Prolonged drainage	20, 21, 24	367/417	0.77 (0.24, 2.46)	0.66	0.18	2	0	0.91	None
Urinary incontinence (1 months)	20–23	366/410	0.61 (0.33, 1.13)	0.12	0.41	3	0	0.94	None
Urinary incontinence (6 months)	20–23	366/410	0.52 (1.10, 2.86)	0.45	0.6	1	0	0.45	None

OR odds ratios, *CI* confidence interval

subjective variables, ThuEP and HoLEP demonstrated equivalent micturition improvement in IPSS and QoL in the 1st and 6th month of follow-up. In the 12th month of follow-up, statistically higher IPSS was recorded in HoLEP group, and slightly higher QoL was also recorded in HoLEP group; however, the difference was not significant. Unfortunately, we could not compare the long-term curative effect 1 year later between the two procedures because of the lack of data. In conclusion, our analysis indicated that ThuEP might get a more satisfying effect as compared with the HoLEP group in the early postoperative period. But the difference among functional parameters became insignificant during the later follow-up, which suggested comparable mid-term outcomes between the groups. It is also worth noticing that ThuEP may apply better symptom resolution on IPSS and QoL in late follow-up.

Besides transfusion, the meta-analysis of other major postoperative complications was also performed between the two groups, including recatheterization, urinary tract infections, incomplete enucleation (prostate capsule damage associated with considerable bleeding from the venous sinus), prolonged drainage, and urinary incontinence in the 1st month and the 6th month postoperatively. The result showed that no significant difference was found between the two groups. However, we noticed that all the studies which recorded postoperative urinary incontinence data reported a lower urinary incontinence rate in the 1st month after the operation. This also supported the opinion that ThuEP may obtain a more satisfying effect in the early postoperative period when compared to HoLEP.

As no study includes in a direct comparison of cost-effectiveness between HoLEP and ThuEP, the cost-effectiveness of these two fiber optic delivery systems was discussed as per the following parts: the equipment costs, the operative costs, and the hospital stay as well as complications [42]. Both HoLEP and ThuEP utilize almost the same equipment as many other urological procedures; hence, direct costs that can attributable to the procedure are minimal. Except for enucleation of the prostate, holmium laser can be

used for many other purposes, for instance, lithotripsy and urethrotomy, thus dispersing the cost. Recent studies demonstrated that thulium laser is a novel alternative for lithotripsy owing to its use of a more suitable wavelength, smaller fibers, and potential for using a smaller, less expensive laser system; thus, the thulium technique still remains cost competitive [43]. Both holmium and thulium laser fibers are reusable, with respect to the hospital stay and major complications, and we found no significant difference in the pooled analysis of these parameters. As regards servicing or upkeeping difference between the two laser types, no relevant study was found. Moreover, in consideration of the difference among regional or national health systems, a prudent systematic assessment is needed.

Our meta-analysis has several limitations, which should be taken into consideration when interpreting the results. First, three studies were retrospective studies and the results should be interpreted with caution, giving the potential for selection and treatment bias due to the inherent limitations of the retrospective study. Second, the follow-up was not long enough. Zhang et al. recorded both functional and voiding parameters of the two laser types in the 18th month postoperative follow-up. As far as we know, among the published studies on ThuEP, this is the study with the longest follow-up. Though it is difficult to keep in contact with the patients after a more or less successful operation, long-term data are very helpful for us to further evaluate the two laser devices. Third, a prospective analysis of learning curves of ThuVEP procedure demonstrated that even surgeon with initial learning experience can make reasonable efficiency when closely mentored, which might lead to a significantly gentle learning curve [44]. However, no study included in a comparison of the learning curve between thulium and holmium. Fourth, for some parameters, such as perioperative sodium decrease, one study dominated the result, for it providing 456 patients out of the whole 589 patients, which might influence the credibility of the result. Fifth, high heterogeneity was observed in several outcomes among studies, including operation time, enucleation

time, sodium decrease, and all the postoperative functional parameters. The high heterogeneity might be explained by the difference in surgical techniques (ThuVEP and ThuLEP), energy settings, surgical experience, and outcome definitions. Though the random-effect model was applied in these items, there might be some influences on the efficiency of our meta-analysis. Nevertheless, we could not perform the sensitivity analysis by removing the single study to test those potential deficiencies, because only five studies could be included in the final analysis. And such a small number of studies were unable to make a strong conclusion. Thus, well-designed and high-quality multicenter long-term RCTs with large sample size are required to validate our findings.

Conclusions

Both ThuEP and HoLEP are effective and safe procedures for the treatment of symptomatic BPH. Both procedures provide satisfactory micturition improvement with low morbidity in the 1st month, 6th month, and 12th month of follow-up. However, ThuEP may contain several advantages over HoLEP with regard to enucleation time and efficacy, perioperative blood loss, Qmax, and PVR in the 1st month and IPSS in the 12th month postoperatively. Due to the existing limitations of the included studies, more scientifically designed, prospective comparative studies with large sample size, multicenter and long-term follow-up should be undertaken to confirm the effectiveness and safety of these two procedures.

Compliance with ethical standards

Ethical approval Meta-analysis does not require ethical review.

Informed consent Meta-analysis does not require informed consent.

Conflict of interest The authors declare that they have no conflict of interest.

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