REVIEW PAPER

FUNCTIONAL UROLOGY

Complications and functional outcomes of endoscopic enucleation of the prostate: a systematic review and meta-analysis of randomised-controlled studies

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Introduction There are several endoscopic enucleation procedures (EEP) using different energy sources: holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation of the prostate (ThuLEP), Greenlight® (GreenVEP) and diode (DiLEP) lasers, and plasma kinetic enucleation of the prostate (PKEP). The comparative outcomes among these EEPs are unclear. We aimed to compare the peri-operative and post-operative outcomes, complications and functional outcomes among different EEPs.
Material and methods A systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist. Only randomised-controlled trials (RCT) comparing EEPs were included. The risk of bias was assessed using the Cochrane tool for RCTs.
Results The search identified 1153 articles and 12 RCTs were included. The number of RCTs for each comparison was, HoLEP vs ThuLEP; n = 3, HoLEP vs PKEP; n = 3, PKEP vs DiLEP; n = 3, HoLEP vs GreenVEP; n = 1, HoLEP vs DiLEP; n = 1, ThuLEP vs PKEP; n = 1. Operative time was shorter and blood loss was lower with ThuLEP compared with HoLEP, whereas operative time was shorter for HoLEP compared with PKEP. Blood loss was lower with HoLEP and DiLEP compared with PKEP. There were no Clavien-Dindo IV–V complications, and the incidence of Clavien-Dindo I complications was lower with ThuLEP compared with HoLEP. No significant differences were detected among EEPs regarding urinary retention, stress urinary incontinence, bladder neck contracture or urethral stricture. Lower International Prostate Symptom Score (IPSS) and higher quality of life (QoL) scores were in favour of ThuLEP compared with HoLEP at 1 month.
Conclusions EEP improves symptoms and uroflowmetry parameters with a low incidence of high-grade complications. ThuLEP was associated with shorter operative time, lower blood loss, and lower incidence of low-grade complications compared with HoLEP.

Key Words: benign prostate enlargement ‹› enucleation ‹› laser ‹› holmium ‹› thulium

INTRODUCTION

Benign prostate hyperplasia (BPH) may induce lower urinary tract symptoms (LUTS) and complications, such as urinary retention and renal failure. Many options are available to manage BPH, including medical drug and surgical treatment, and radiological embolization [1]. Refinements in technology

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and technique aim to improve efficacy and functional outcomes and reduce peri- and post-operative complications. Historically, transurethral resection of the prostate (TURP) has been the gold standard for prostate sizes ≤80 cc, and open prostatectomy for larger prostates. Endoscopic enucleation of the prostate (EEP) has been used to overcome size limitations, and to avoid the morbidity associated with open surgery. Available laser options to perform EEP include: holmium laser enucleation of the prostate (HoLEP), thulium (ThuLEP/ThuVEP/ThuVAP), greenlight (GreenVEP/GreenLEP) and diode (DiLEP). Plasma kinetic enucleation of the prostate (PKEP), or bipolar enucleation (BipoLEP) represent important alternatives when lasers are not available for clinical use [1–3]. Researchers have compared all energy sources with TURP in randomized-controlled trials (RCTs) and meta-analyses [4–7], however, the European Association of Urology (EAU) guidelines concluded that EEP with holmium, thulium and diode demonstrate similar efficacy and safety profile compared with TURP [1].

There are not many RCTs comparing different enucleation techniques, therefore, the optimum approach is yet to be defined. Surgical RCTs are uncommon because they are difficult to conduct, especially the randomisation step. The most studied technique is HoLEP versus ThuLEP, and a recent meta-analysis concluded that both procedures offer comparable improvement in symptoms, but ThuLEP is associated with less blood loss and incidence of transient urinary incontinence [8].

With the lack of evidence in comparing individual enucleation techniques, the aim of our systematic review is to evaluate the efficacy, incidence of complications and functional outcomes among various enucleation methods.

Evidence acquisition

Search strategy

The systematic review was registered on the PROSPERO database (CRD42022306747) and performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA, Appendix 1) checklist [9]. We searched the Medline, Cochrane and Embase databases on 07-Feb-2022 (Appendix 4), and filtered for English articles, humans, and randomised studies, with no date restrictions.

Study eligibility

A population (P), intervention (I), comparator (C), outcome (O), and study design (S) (PICOS) framework defined the study eligibility. We included studies if they fulfilled, (P): men undergoing EEP for BPH; (I): any enucleation method, e.g. using holmium, thulium, greenlight or diode laser, or plasma kinetic; (C) any of the 'intervention' methods listed above; (O) peri- and post-operative outcomes and complications functional outcomes [maximum flow rate (Qmax)], post-void residual (PVR), the International Prostate Symptom Score (IPSS), quality of life (QoL) and International Index of Erectile Function (IIEF) questionnaires; (S) RCTs only. We excluded case reports, conference abstracts, reviews, letters, commentaries, and editorials.

Two reviewers (KHP and GO) screened articles, and reference lists of included manuscripts for eligibility. Disagreement during study inclusion was resolved by a judgement of one of the senior authors (CSB, TT).

Risk of bias assessment

The risk of bias (RoB) assessment of included studies was performed (KHP and GO) using the Cochrane RoB tool for RCTs [10].

Data extraction and analysis

Data extracted (GO and KHP) included, the number of patients, EEP technique, baseline characteristics [age, prostate size, prostate-specific antigen (PSA) level, IPSS, Qmax and PVR, and IIEF], operative time, length of stay, catheter duration, blood loss, post-operative complications (urinary retention/incontinence, urethral stricture, retrograde ejaculation), Clavien-Dindo (CD) grade [11], post-operative Qmax and PVR, IPSS and IIEF scores, and follow-up duration.

We performed a qualitative synthesis and meta-analyses using Review Manager 5.4.1 (The Cochrane Collaboration, Oxford, UK). We used the inverse variance weighted mean difference (WMD) with 95% confidence intervals (95% CI) as a summary measure for continuous variables. If studies reported the median and interquartile ranges (IQR), we estimated the mean and standard deviation (SD) based on formulas by Hozo et al. [12]. For dichotomous outcomes, we calculated odds ratio (OR) according to Mantel-Haenszel (MH) test, as an effect measure with 95% CI. We considered a p-value <0.05 as statistically significant. Pooled estimates were calculated using the random-effect model for all outcome variables. We quantified study heterogeneity with the Chi-squared and I^2 statistics.

Table 1. *Baseline patient characteristics*

Author	Year	Intervention arm		No. patients analysed, n (%)			Age, years (mean/SD)			Prostate size, mL/cc (mean/SD, median/IQR)			PSA (ng/ml)			IPSS (mean/SD)			QoL (mean/SD, median/IQR)			Qmax, mL/s (mean/SD, median/IQR)			PVR, mL (mean/SD)			IIEF (mean/SD, median/IQR)		
		EEP1	EEP2	Overall	EEP1	EEP2	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value
Becker et al. [13]	2018	HoLEP	ThuLEP	94	46	48	71.5 ±2	74 ±1.9	0.207	77.5 ±16.13	82.5 ±6.31	0.826	4.14 ±1.55	4.14 ±1.08	0.698	22 ±2.75	20 ±2.25	0.809	4 ±0.25	4 ±0.25	0.889	12.1 ±1.95	9.6 ±1.55	0.181	105 ±37.94	100 ±52.69	0.962	20 ±4.56	16.5 ±4.63	0.642
Bozzini et al. [14]	2021	HoLEP	ThuLEP	236	121	115	69.5 ±15.54	67.1 ±17.83	0.12	86.3 ±46.7	90.2 ±42.7	0.17	2.9 ±5.25	3.2 ±4.14	0.31	17.9 ±6.95	18.2 ±7.31	0.16	NR	NR	NR	8.2 ±6.71	7.9 ±8.05	0.15	90.4 ± 120.44	115.5 ± 130.54	0.24	NR	NR	NR
Zhang et al. [17]	2020	HoLEP	ThuLEP	116, 107 (18 m)	58, 54 (18 m)	58, 53 (18 m)	71.8 ±3.9	72.7 ±3.1	0.17	93.0 ±7.2	91.8 ±6.9	0.37	5.09 ±1.49	4.96 ±1.40	0.63	23.9 ±3.9	22.8 ±3.7	0.13	5 (4–6)	5 (4–6)	0.65	7.1 ±2.8	6.6 ±2.3	0.37	172.7 ±39.4	165.5 ±46.2	0.37	NR	NR	NR
Habib et al. [18]	2020	HoLEP	PKEP	64	33	31	66.81 ±7.77	67. 48 ±6.46	0.71	125 (80–270)	102 (80–243)	0.073	6.5 (0.71–33)	6.2 (1–18.75)	0.379	25.24 ±4.87	25.35 ±4.17	0.92	5 (3–6)	5 (4–6)	0.387	0 (0–13.9)	2.5 (0–10)	0.88	135.37 ±46.83	159.41 ±63.16	0.23	19.84 ±4.82	17.48 ±5.34	0.1
Higazy et al. [19]	2021	HoLEP	PKEP	107	54	53	66.17 ±7.22	67.72 ±6.48	0.09	135.19 ±34.84	125.00 ±26.93	0.09	7.6 ±2.5	6.2 ±3.2	**0.007**	28.8 ±2.1	28.9 ±2.1	0.85	4.37 ±0.49	4.43 ±0.5	0.65	3.3 ±3.4	3.9 ±3.3	0.45	160 ±52.8	168.5 ±55.8	0.64	NR	NR	NR
Wei et al. [20]	2021	HoLEP	PKEP	160, 159 (12 m), 141 (24 m), 126 (36 m)	80, 80 (12 m), 69 (24 m), 62 (36 m)	80,79 (12 m), 72 (24 m), 64 (36 m)	70.95 ±7.50	70.28 ±8.16	0.67	63.71 ±21.63	61.23 ±20.99	0.46	3.74 ±2.17	3.63 ±1.92	0.74	22.63 ±3.15	22.20 ±3.60	0.43	4.69 ±0.84	4.66 ±0.80	0.85	7.28 ±2.37	7.10 ±2.46	0.65	132.44 ±71.01	121.35 66.13	0.31	17.46 ±1.70	17.59 ±1.70	0.64
Elshal et al. [24]	2015	HoLEP	GreenVEP	103	50	53	71 ±9.3	74.1 ±.8	0.09	87.1 ±28.1	83.3 ±27.8	0.49	5.6 ±4.4	5.3 ±12.6	0.88	22.4 ±5.6	23 ±4.8	0.6	3.8 ±1.2	4 ±1.1	0.4	7.5 ±1.3	8 ±3	0.5	146 ±105	172 ±137	0.4	55.6 ±15.4 (IIEF-15)	45.8 ±17 (IIEF-15)	0.27
He et al. [15]	2019	HoLEP	DiLEP	126	63	63	71.6 ±9.8	71.7 ±8.7	0.95	75.6 ±28.9	83.0 ±34.8	0.193	2.2 ±1.8	2.7 ±1.2	0.1	24.2 ±4.0	23.4 ±5.5	0.32	3.9 ±0.7	3.7 ±0.8	0.073	6.7 ±3.9	6.7 ±3.7	0.981	85. ±98.2	92.1 ±127.5	0.76	NR	NR	NR
Feng et al. [16]	2016	ThuLEP	PKEP	127	61	66	67.66 ±8.99	70.03 ±7.84	0.11	69.02 ±22.29	67.05 ±16.28	0.57	2.70 ±1.03	2.49 ±1.18	0.29	23.82 ±4.65	24.13 ±4.08	0.69	4.35 ±0.62	4.43 ±0.61	0.48	7.48 ±3.66	7.14 ±3.13	0.62	88.87 ±44.83	95.19 ±49.03	0.53	NR	NR	NR
Wu et al. [21]	2016	PKEP	DiLEP	80	40	40	73.6 ±6.2	75.4 ±8.4	0.28	93.3 ±18.5	98.6 ±21.6	0.24	6.2 ±3.8	5.6 ±3.2	0.45	21.8 ±4.5	22.4 ±5.3	0.59	4.9 ±1.1	4.8 ±0.9	0.66	7.6 ±3.1	6.8 ±2.8	0.23	147.5 ±47.2	162.8 ±41.7	0.13	17.5 ±2.6	17.1 ±2.7	0.5
Xu et al. [22]	2013	PKEP	DiLEP	80	40	40	NR	NR	NR	65.79 ±24.63	68.72 ±22.28	0.58	2.67 ±1.17	2.79 ±1.25	0.64	23.73 ±4.60	23.50 ±4.89	0.83	4.58 ±0.81	4.40 ±0.84	0.35	7.77 ±2.10	7.91 ±2.22	0.78	66.57 ±64.64	52.60 ±49.47	0.28	NR	NR	NR
Zou et al. [23]	2018	PKEP	DiLEP	114	57	57	69.4 ±7.5	67.3 ±7.7	0.14	63.4 ±36.4	59.5 ±28.8	0.98	5.2 (2.0–11.2)	4.4 (2.3–8.2	0.7	22.8 ±7.0	23.1 ±6.1	0.9	5 (5–6)	5 (4–6)	0.2	5.4 ±5.1	6.9 ±5.0	0.11	63.4 ±36.4	59.5 ±28.8	0.98	8 (5–19)	9 (6–18)	0.35

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-analyses; EEP – endoscopic enucleation of the prostate; HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium EP; PKEP – plasma kinetic EP; GreenVEP – greenlight vaporisation EP; DiLEP – diode EP; SD – standard deviation; PSA – prostate-specific antigen; IPSS – International Prostate Symptom Score; QoL – quality of life; Qmax – maximum flow rate; PVR – post-void residual; IIEF – International Index of Erectile Function

Evidence synthesis

The initial search identified 1153 articles, overall, 12 RCTs [13–24] were included for analysis (PRISMA diagram, Figure 1). In total, 1,406 patients were included: HoLEP, n = 505; PKEK, n = 366; ThuLEP, n = 284 (vaporisation n = 48); DiLEP, n = 200; GreenVEP, n = 53. Baseline characteristics of the patients, including age, prostate size, PSA level, IPSS scores, Qmax and PVR, and IIEF scores, are presented in Table 1. The prostate size was comparable and are detailed in Table 1. Appendix 2 summarises the study inclusion and exclusion criteria, and EEP characteristics. We performed meta-analyses when more than one RCT compared the same outcome: 1) HoLEP with ThuLEP [13, 14, 17]; 2) HoLEP with PKEP [18, 19, 20], and; 3) PKEP with DiLEP [21, 22] (Figure 2). Only one RCT compared HoLEP with GreenVEP [24], HoLEP with DiLEP [15] or, ThuLEP with PKEP [16], therefore, meta-analyses comparing these techniques were impossible, and we performed a descriptive analysis.

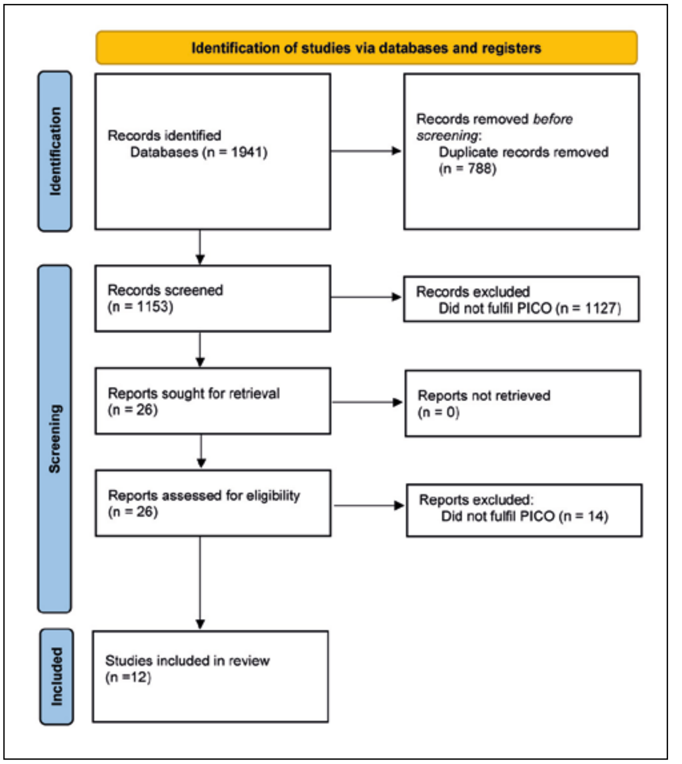


Figure 1. *PRISMA 2020 flow chart for the current systematic review.*

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-analyses; n – number of patients

Peri- and post-operative parameters

Operative time

The mean operative time (mins) was HoLEP, 65–114; PKEP, 38.8–98.7; ThuLEP, 63.7–71.4; DiLEP, 33.7–113.5, and; GreenVEP, 103 (Table 2).

The operative time (Figure 2a) was significantly shorter in the ThuLEP group compared to HoLEP (WMD, 10.3; 95% CI, 3.95–16.3; p = 0.001), and longer in the PKEP group compared to HoLEP §(WMD, -12.1; 95% CI, -15.7– -8.44; p <0.001).

There were no significant differences in operative time in the single RCTs that compared HoLEP with GreenVEP, HoLEP with DiLEP or, ThuLEP with PKEP (Table 2).

Enucleation weight

The mean enucleation weight (grams) across all studies was HoLEP, 48–105; PKEP, 37.2–99.9; ThuLEP, 41.3–66.5; DiLEP, 33.7–65.8 and; GreenVEP, 11.6 (Table 2). However, when comparing HoLEP versus ThuLEP, the enucleation weight was 48–65 grams and 48.8–66.5 grams respectively (Table 2).

In meta-analyses, there were no significant differences about the weight of tissue removed between techniques (Figure 2b).

Haemoglobin decrease

The decrease in haemoglobin (g/dL) was with HoLEP, 0.5–2.8; PKEP, 0.36–1.6; ThuLEP, 0.5–2.6; DiLEP, 0.3–0.9 and; GreenVEP, 0.7. Other peri- and post-operative parameters are detailed in Table 1.

In meta-analyses, haemoglobin decrease was lower with ThuLEP compared with HoLEP (WMD, 0.8; 95% CI, 0.08–1.5; p = 0.03); higher with HoLEP compared with PKEP (WMD, -0.2; 95% CI, -0.23– -0.1; p <0.001) and; lower with DiLEP compared with PKEP (WMD, 0.32; 95% CI, 0.06–0.59; p = 0.02) (Figure 2c).

There was no significance between comparable EEPs about the transfusion rate (Figure 1).

Catheter duration and length of stay

The urinary catheter time was between 1–3 days for all enucleation methods (Table 2). Catheter duration was significantly shorter in with HoLEP compared with PKEP (WMD, -0.43; 95% CI, -0.79– -0.07; p = 0.02) (Figure 2e).

Data from the single RCTs showed that ThuLEP was associated with shorter catheter duration (mean, 1.85 days) when compared with PKEP (mean, 2.3 days; p = 0.04) (Table 2).

The mean LOS (days) was HoLEP, 2–5.8; PKEP, 0.95–5.3; ThuLEP, 2–2.6; DiLEP, 3.6-6.2 and; GreenVEP, 1.5 (Table 2). HoLEP was associated with

Table 2. *Peri- and post-operative outcomes*

Author	Year	Intervention arm		Operation time, mins (mean/SD)			Enucleation time, mins (mean/SD)			Enucleated tissue weight, grams (mean/SD)			Hb decrease, g/dl (mean/SD)			Catheter duration, days (mean/SD)			LOS, days (mean/SD)		
		EEP1	EEP2	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value
Becker et al. [13]	2018	HoLEP	ThuLEP	65 ±9.25	50 ±8.5	0.275	40 ±5.09	27.03 ±4,02	**≤0.004**	48 ±13.75	58 ±13.44	0.421	1.7 ±0.475	1.6 ±0.31	0.97	2 ±0.25	2 ±0.25	0.966	2 ±0.25	2 ±0.25	0.809
Bozzini et al. [14]	2021	HoLEP	ThuLEP	71.66 ±38.70	63.69 ±41.44	0.245	NR	NR	NR	51.13 ±23.14	48.84 ±18.23	0.321	2.77 ±1.23	0.45 ±1.78	**0.005**	2.0 ±3.55	1.9 ±2.81	0.45	2.8 ±3.89	2.2 ±4.05	0.316
Zhang et al. [17]	2020	HoLEP	ThuLEP	78.4 ±8.0	71.4 ±6.4	**<0.001**	61.2 ±5.4	56.4 ±8.4	**<0.001**	65.0 ±7.6	66.5 ±5.8	0.23	0.8 ±0.1	0.7 ±0.1	**0.15**	2 ±0.25	2 ±0.25	0.694	2 ±0.25	2 ±0.25	0.5
Habib et al. [18]	2020	HoLEP	PKEP	71.54 ±25.25	93.58 ±31.47	**0.003**	NR	NR	NR	79 ±44	78 ±37	0.88	0.9 ±0.85	1 ±0.7	1	0.72 ±0.17	1.17 ±0.87	**0.019**	0.84 ±0.09	0.95 ±0.3	0.066
Higazy et al. [19]	2021	HoLEP	PKEP	83.43 ±6.92	94.72 ±12.15	**<0.001**	57.96 ±7.74	61.98 ±10.85	**0.029**	105 ±34.20	99.91 ±21.69	0.36	0.9 ±0.1	1.1 ±0.1	0.96	1 ±0.23	1.79 ±1.6	**0.02**	1 ±0.24	1.49 ±0.6	**0.01**
Wei et al. [20]	2021	HoLEP	PKEP	66.56 ±22.59	78.21 ±27.78	**<0.01**	53.68 ±19.33	49.71 ±18.32	0.19	53.93 ±19.29	51.61 ±18.62	0.44	0.96 ±0.52	1.13 ±0.51	**0.03**	3.27 ±0.62	3.54 ±0.69	**0.01**	3.59 ±0.58	3.94 ±0.68	**<0.001**
Elshal et al. [24]	2015	HoLEP	Gre-enVEP	114 ±35	103 ±35	0.1	NR	NR	NR	48 ±22	11.6 ±20	**0.00**	0.74 ±0.82	0.74 ±1.1	0.9	1.2 ±1	2.3 ±3.8	0.055	1.1 ±0.7	1.5 ±1.3	0.055
He et al. [15]	2019	HoLEP	DiLEP	68.7 ±19.7	62.9 ±18.2	0.091	44.7 ±12.2	40.7 ±10.9	0.054	55.2 ±27.3	60.4 ±34.2	0.34	0.51 ±0.22	0.4. ±0.23	**0.007**	2.3 ±0.39	2.23 ±0.44	0.33	5.8±2.3	6.2±2.7	0.418
Feng et al. [16]	2016	ThuLEP	PKEP	67.90 ±20.88	69.21 ±19.80	0.72	NR	NR	NR	41.29 ±14.33	39.47 ±11.66	0.43	0.80 ±0.49	0.99 ±0.52	**0.037**	1.85 ±0.94	2.28 ±1.34	**0.042**	2.64 ±1.08	3.02 ±1.45	0.1
Wu et al. [21]	2016	PKEP	DiLEP	98.7 ±31.5	113.5 ±25.4	**0.02**	NR	NR	NR	62.3 ±20.2	65.8 ±15.6	0.39	1.1 ±0.5	0.8 ±0.3	**<0.01**	1.6 ±0.7	1.2 ±0.4	**<0.01**	4.8 ±1.8	3.6 ±1.5	**<0.01**
Xu et al. [22]	2013	PKEP	DiLEP	50.28 ±6.24	33.73 ±6.96	**0.00**	17.18 ±4.08	18.55 ±3.68	0.12	47.93 ±22.69	51.30 ±21.09	0.49	1.61 ±0.85	0.93 ±1.02	**0.002**	1.94 ±0.36	1.15 ±0.33	**0.00**	5.30 ±0.93	4.95 ±0.95	0.103
Zou et al. [23]	2018	PKEP	DiLEP	38.8 ±16.9	41.4 ±18.1	0.43	35.1 ±15.6	37.8 ±16.9	0.38	37.2 ±10.9	33.7 ±8.5	0.84	0.36 ±0.75	0.33 ±0.66	0.82	1.97 ±0.2	1.86 ±0.2	0.77	4 ±0.25	4 ±0.5	0.06

Hb – haemoglobin; LOS – length of stay

Table 3. *Post-operative complications*

Author	Year	Intervention arm		Clavien-Dindo I, n (%)			Urinary retention, n (%)			Clavien-Dindo II, n (%)			Clavien-Dindo IIIa, n (%)			Clavien-Dindo IIIb, n (%)			Urge incontinence overall			Stress incontinence overall		
		EEP1	EEP2	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value
Becker et al. [13]	2018	HoLEP	ThuLEP	9 (19,6)	4 (8,3)	NR	3 (6.5)	1 (2.1)	0.254	2 (4.3)	1 (2.1)	NR	2 (4.3)	0 (0)	NR	3 (6.5)	1 (2.1)	NR	4 (8.7)	1 (2.1)	0.149	8 (17.4)	9 (18.8)	0.491
Bozzini et al. [14]	2021	HoLEP	ThuLEP	14 (11.6)	7 (6.08)	NR	13 (10.7)	7 (6.1)	**0.04**	8 (6.6)	2 (1.7)	NR	NR	NR	NR	1 (0.08)	1 (0.08)	0.4	10 (8.2)	8 (6.9)	0.2	9 (7.4)	2 (1.7)	**0.03**
Zhang et al. [17]	2020	HoLEP	ThuLEP	8 (13.8)	2 (3.4)	NR	1 (1.7)	0 (0)	NR	1 (1.7)	3 (5.2)	0.62	0 (0)	0 (0)	–	2 (3.4)	2 (3.4)	1	NR	NR	NR	5 (8.6)	2 (3.4)	0.44
Habib et al. [18]	2020	HoLEP	PKEP	0 (0)	1 (3.2)	NR	0 (0)	0 (0)	–	1 (3)	3 (9.7)	NR	NR	NR	NR	1 (3)	0 (0)		NR	NR	NR	3 (9.1)	5 (16.1)	0.47
Higazy et al. [19]	2021	HoLEP	PKEP	1 (1.9)	2 (3.7)	NR	0 (0)	0 (0)	–	3 (5.6)	5 (9.4)	NR	0 (0)	0 (0)	-	1 (1.9)	1 (1.9)	1	NR	NR	NR	5 (9.3)	5 (9.4)	0.74
Wei et al. [20]	2021	HoLEP	PKEP	0 (0)	4 (5)	NR	4 (2.5)	0 (0)	**0.04**	NR	NR	NR	NR	NR	NR	2 (3.2)	4 (6.3)	NR	6 (7.5)	7 (8.8)	0.77	3 (3.8)	2 (2.5)	NR
Elshal et al. [24]	2015	HoLEP	Gre-enVEP	7 (14)	10 (18.9)	NR	1 (2)	3 (5.7)	0.6	0 (0)	5 (9.4)	NR	NR	NR	NR	3 (6)	4 (7.5)	NR	5 (10)	6 (9.4)	0.22	7 (14)	3 (5.7)	NR
He et al. [15]	2019	HoLEP	DiLEP	1 (1.6)	1 (1.6)	NR	1 (1.6)	1 (1.6)	1	4 (6.3)	3 (4.8)	NR	0 (0)	0 (0)	–	1 (1.6)	3 (4.8)	NR	NR	NR	NR	5 (7.9)	4(6.3)	0.729
Feng et al. [16]	2016	ThuLEP	PKEP	1 (1.6)	2 (3)	NR	1 (1.6)	1 (1.5)	0.96	1 (1.6)	3 (4.5)	NR	NR	NR	NR	1 (1.6)	2 (3)	NR	NR	NR	NR	3 (4.9)	3 (4.5)	0.921
Wu et al. [21]	2016	PKEP	DiLEP	4 (10)	2 (5)	NR	3 (7.5)	2 (5)	0.64	1 (2.5)	0 (0)	NR	NR	NR	NR	3 (7.5)	1 (2.5)	NR	15 (37.5)	7 (17.5)	**0.05**	5 (12.5)	4 (10)	0.72
Xu et al. [22]	2013	PKEP	DiLEP	1 (2.5)	2 (5)	NR	0 (0)	0 (0)	–	0 (0)	0 (0)	-	NR	NR	NR	0 (0)	0 (0)	–	14 (35)	5 (12.5)	**0.02**	4 (10)	3 (7.5)	0.692
Zou et al. [23]	2018	PKEP	DiLEP	1 (1.8)	2 (3.0)	NR	1 (1.8)	2 (3.0)	1	5 (8.8)	3 (5.3)	NR	NR	NR	NR	1 (1.8)	3 (5.3)	NR	NR	NR	NR	5 (8.8)	5 (8.8)	1

EEP – endoscopic enucleation procedures; HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; PKEP – plasma kinetic enucleation of the prostate; GreenVEP – greenlight vaporisation EP; DiLEP – diode EP a shorter LOS when compared with PKEP (WMD – 0.31; 95% CI, -0.53– -0.09; p = 0.006) (Figure 2f).

Complications according to Clavien-Dindo

Complications following different forms of EEP are shown in Table 3. The incidence of CD-I, CD-II, CD-IIIb was HoLEP, n = 140 (27.7%), n = 19 (4.5%), n = 14 (2.8%); PKEP, n = 18 (4.9%), n = 17 (5.9%), n = 11 (3%); ThuLEP, n = 4 (4.9%), n = 7 (2.5%), n = 5 (1.8%); DiLEP, n = 7 (3.5%), n = 9 (4.5%), n = 7 (3.5%); GreenVEP, n = 10 (18.9%), n = 5 (9.4%), n = 4 (7.5%) respectively. CD-IIIa occurred in two (0.9%) of HoLEP patients, CD-IIIa did not occur in the other EEP groups. There were no encountered CD-IV-V complications.

There were lower cases of CD-I with ThuLEP compared with HoLEP (OR, 2.45; 95% CI, 1.28-5.03;

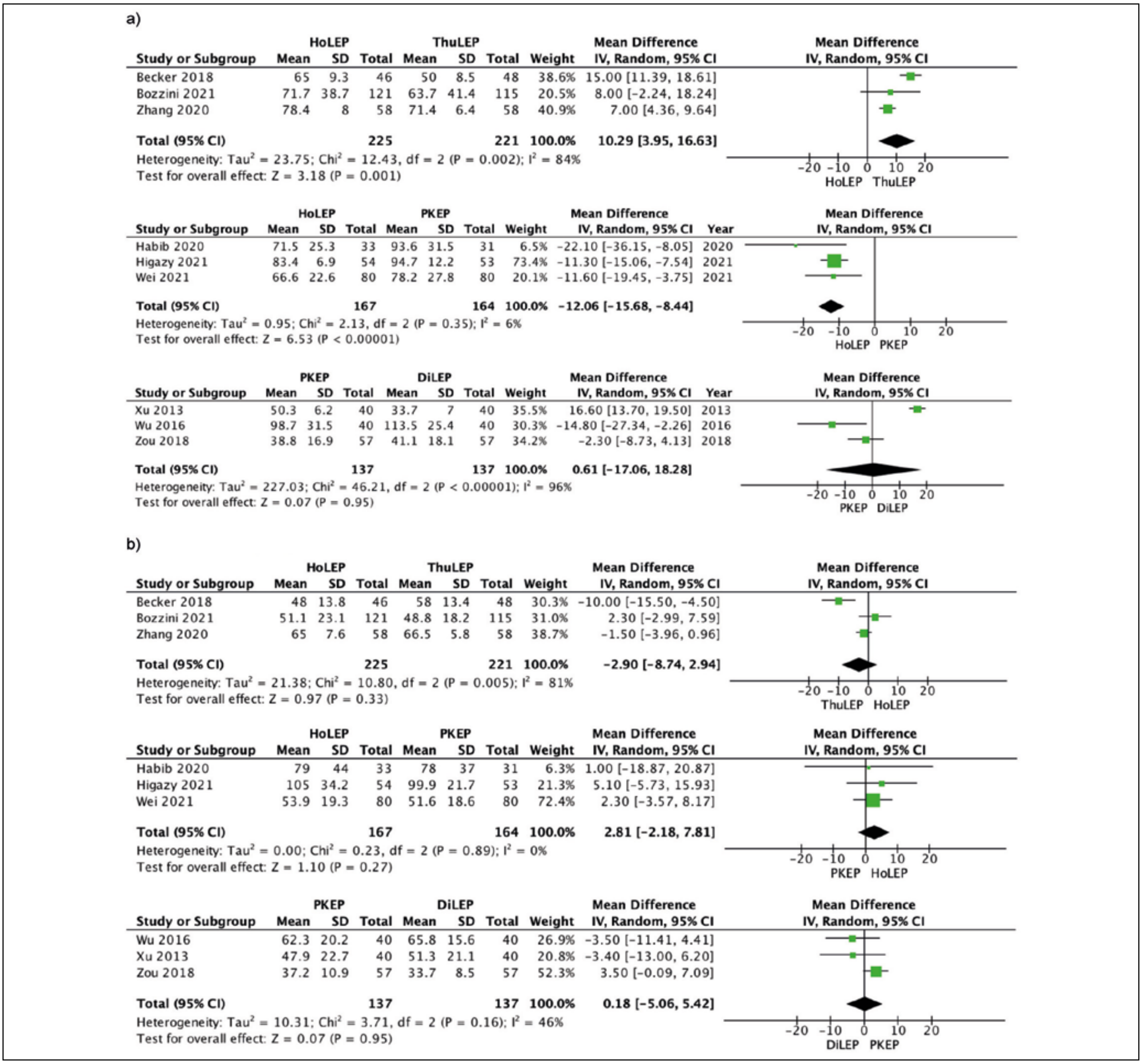


Figure 2. *Meta-analysis of outcomes. Peri-operative and post-operative outcomes:* **a)** *operation time (mins),* **b)** *enucleated weight (grams).*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

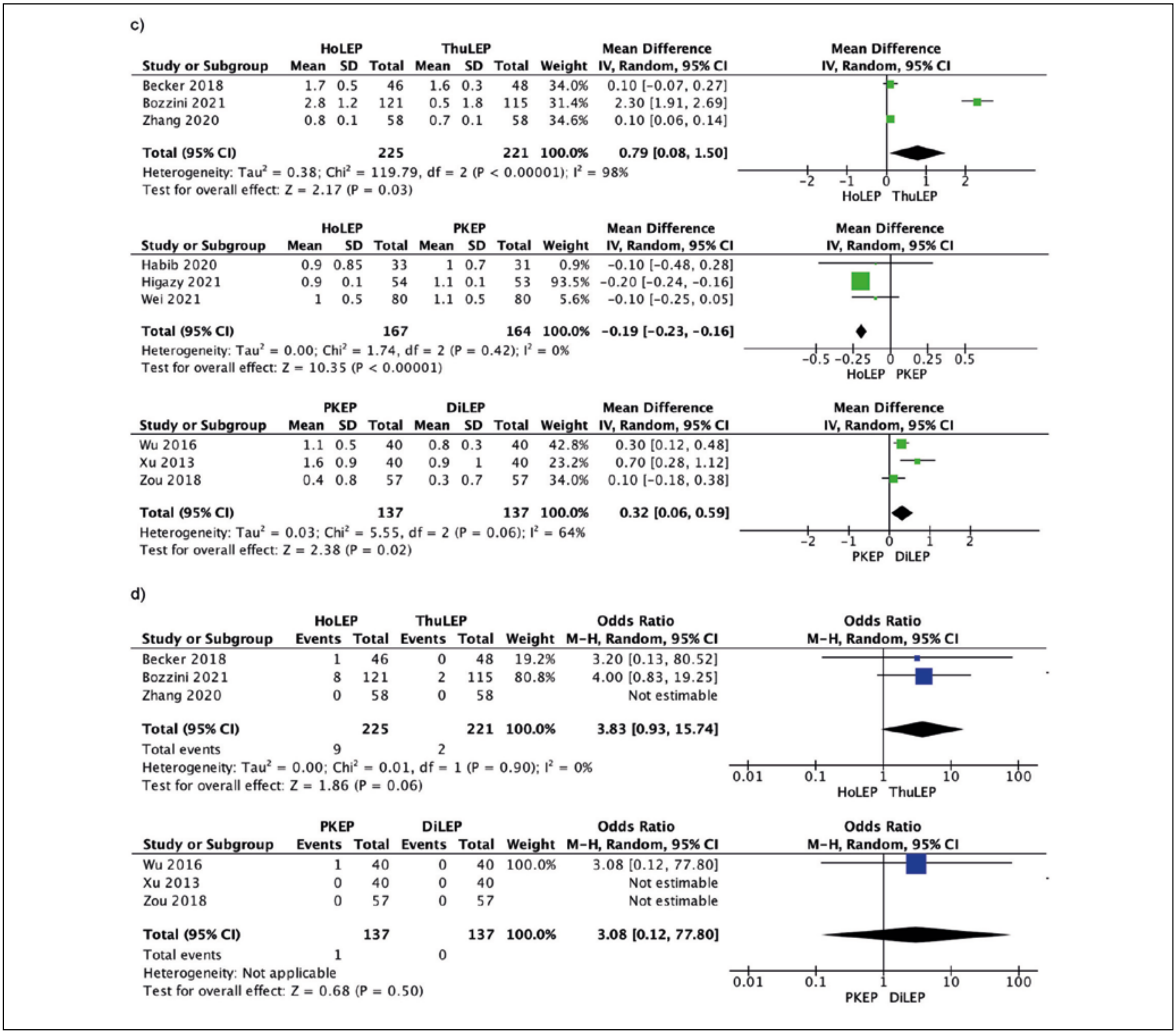


Figure 2. *Meta-analysis of outcomes. Peri-operative and post-operative outcomes:* **c)** *haemoglobin decrease (g/dL),* **d)** *transfusion.*
HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

p = 0.007) (Figure 3a). No other statistical significance was found in meta-analyses with regards to CD-I, CD-II and CD-IIIb when comparing other techniques (Figure 3a–c).

Specific complications

Specific complications, including urinary retention, urinary incontinence, bladder neck contracture, and urethral stricture, are summarised in Table 3 and Appendix 3. Figure 4a-e illustrates meta-analyses, and the only significance identified was the higher incidence of urge urinary incontinence (UUI) with PKEP than DiLEP (OR, 3.22; 95% CI, 1.50–6.94; p = 0.003 (Figure 4c).

Functional outcomes

International Prostate Symptom Score and quality of life

Table 4 summarises IPSS scores at 1, 3, 6 and 12 months. Men who underwent ThuLEP had a lower IPSS score compared to HoLEP at 1 month (WMD,

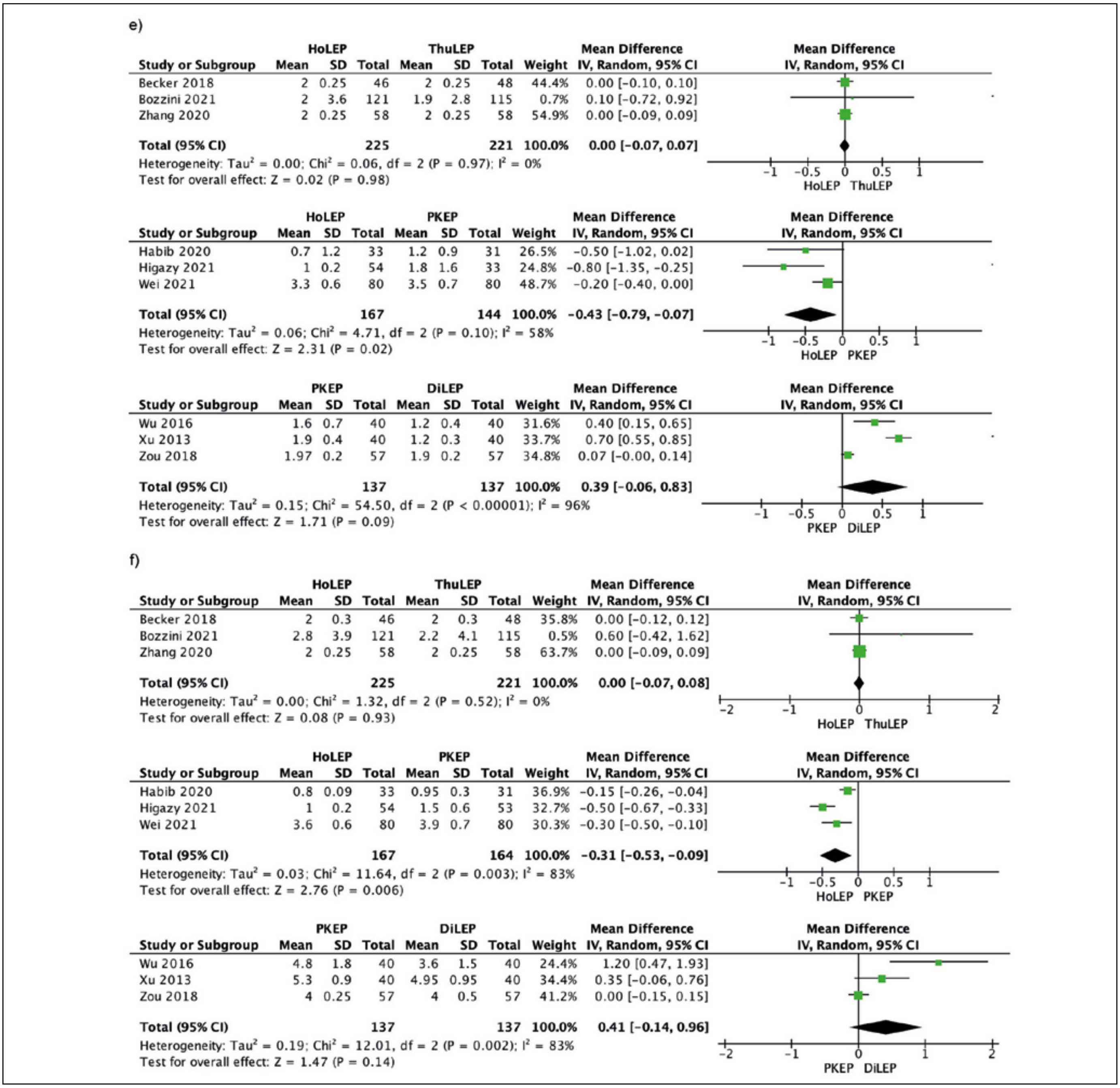


Figure 2. *Meta-analysis of outcomes. Peri-operative and post-operative outcomes:* **e)** *catheter duration (days),* **f)** *length of hospital stay (days)*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

1.4; 95% CI, 0.44–2.37; p = 0.004) and 3 months (WMD, 1.0; 95% CI, 0.85–1.15; p <0.001), however, IPSS scores were similar at 6 and 12 months post-operatively. No other significant differences were identified (Figure 5a).

QoL score was lower in the ThuLEP group compared with HoLEP at 1 months (WMD, 1.0; 95% CI, 0.87–1.13; p <0.001), but this was not significant at 6 or 12 months (Figure 5b).

Maximum flow rate and peri- and post-operative

Qmax and PVR, among different techniques, are shown in Table 4. There were no significant differences

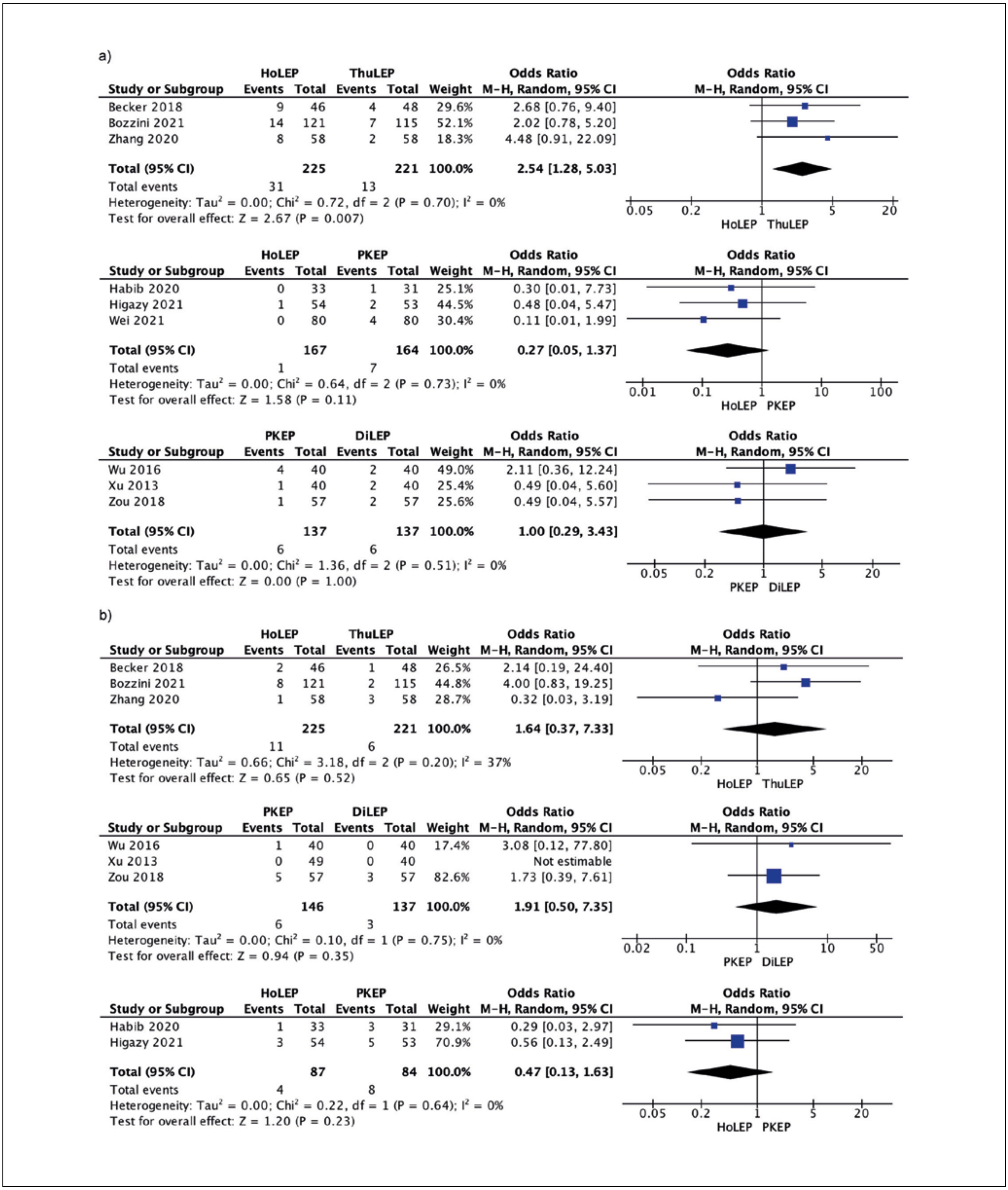


Figure 3. *Meta-analysis of outcomes. Complications according to the Clavien-Dindo classification:* **a)** *Clavien-Dindo I,* **b)** *Clavien-Dindo II.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

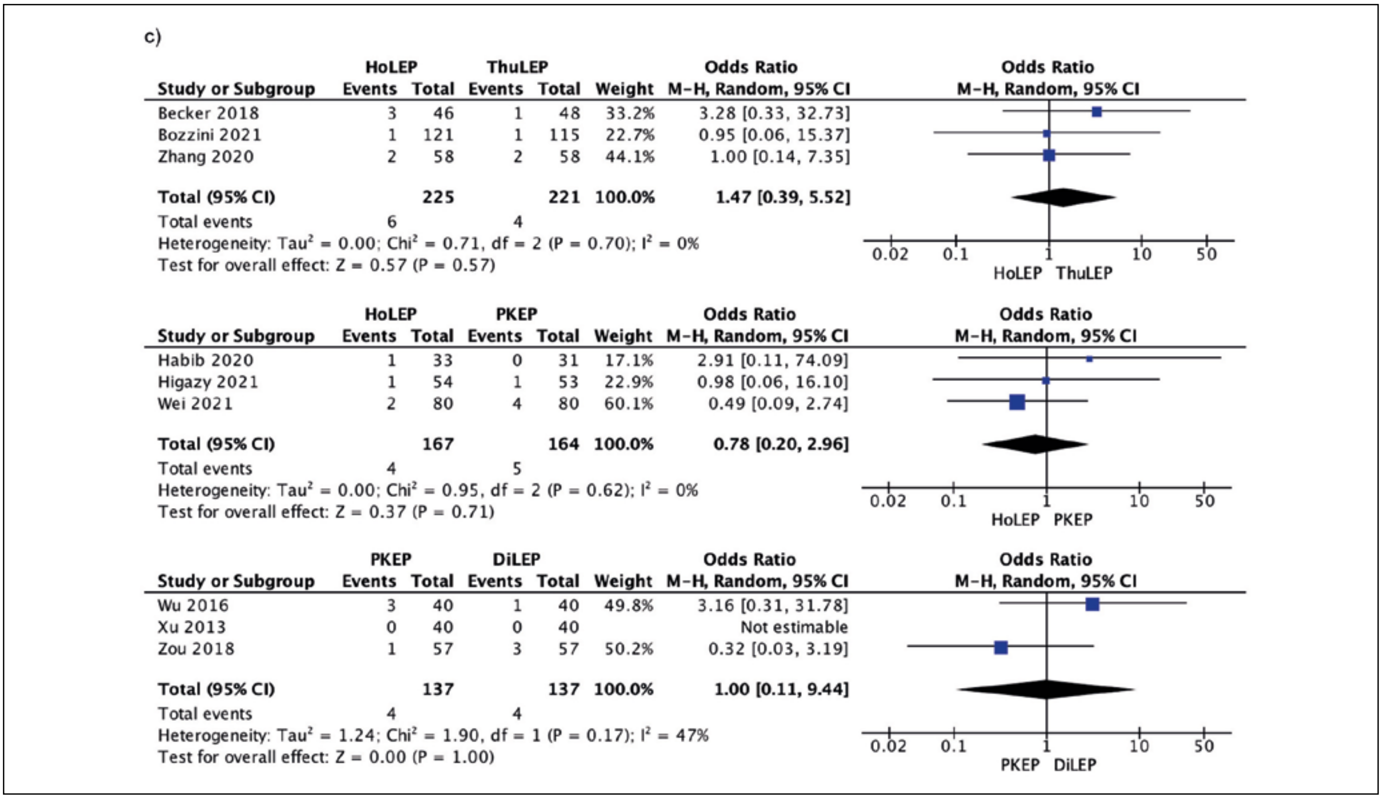


Figure 3. *Meta-analysis of outcomes. Complications according to the Clavien-Dindo classification:* **c)** *Clavien-Dindo IIIb.*
HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

when comparing HoLEP with ThuLEP, or PKEP with DiLEP. However, at 1 month, patients who had HoLEP had a higher Qmax than those who had PKEP (WMD, 1.17; 95% CI, 0.28–2.05; p = 0.01), but this was not significant at 12 months post-operatively (Figure 5c). Qmax was significantly lower with GreenVEP when compared with HoLEP at 3 and 6 months (Table 4).
PVR was lower in the HoLEP group versus ThuLEP at 3 months (WMD, -2,85; 95% CI, -4.90– -0.79; p = 0.007), but this was not significant at 6 or 12 months (Figure 5d).

Index of Erectile Function

Meta-analyses were only possible to compare PKEP with DiLEP, and HoLEP with PKEP, and there was no statistical significance regarding post-operative IIEF scores (Table 4 and Figure 5e).

Risk of bias assessment

We performed the RoB assessment of the included studies using the Cochrane RoB tool. Figure 6 demonstrates the results, and the domain with the highest RoB was blinding of participants and personnel. We decided to judge all studies in which the authors performed only patient blinding as non-blinded studies. The allocation concealment domain had an 'unclear' RoB in 75% of the studies. The randomisation domain had a low RoB in 92% of the studies.

DISCUSSION

Herein, to our knowledge, we report the first systematic review and meta-analysis of published RCTs comparing various EEP techniques to treat symptomatic benign prostate enlargement. Overall, study heterogeneity was high, which is a commonly observed issue in prior publications of studies on EEPs [5, 6]. EEPs appear to offer similar efficacy and safety to TURP, but overcome the limitations over larger prostates and provide an alternative to the more invasive open prostatectomy [1, 25, 26].
In contrary to the meta-analysis comparing ThuLEP and HoLEP by Hartung et al. [8], we excluded one RCT (Zhang et al., [27]) in our analyses due to the high study heterogeneity and bias. Our results seem more homogenous when compared to the functional results of the mentioned study.

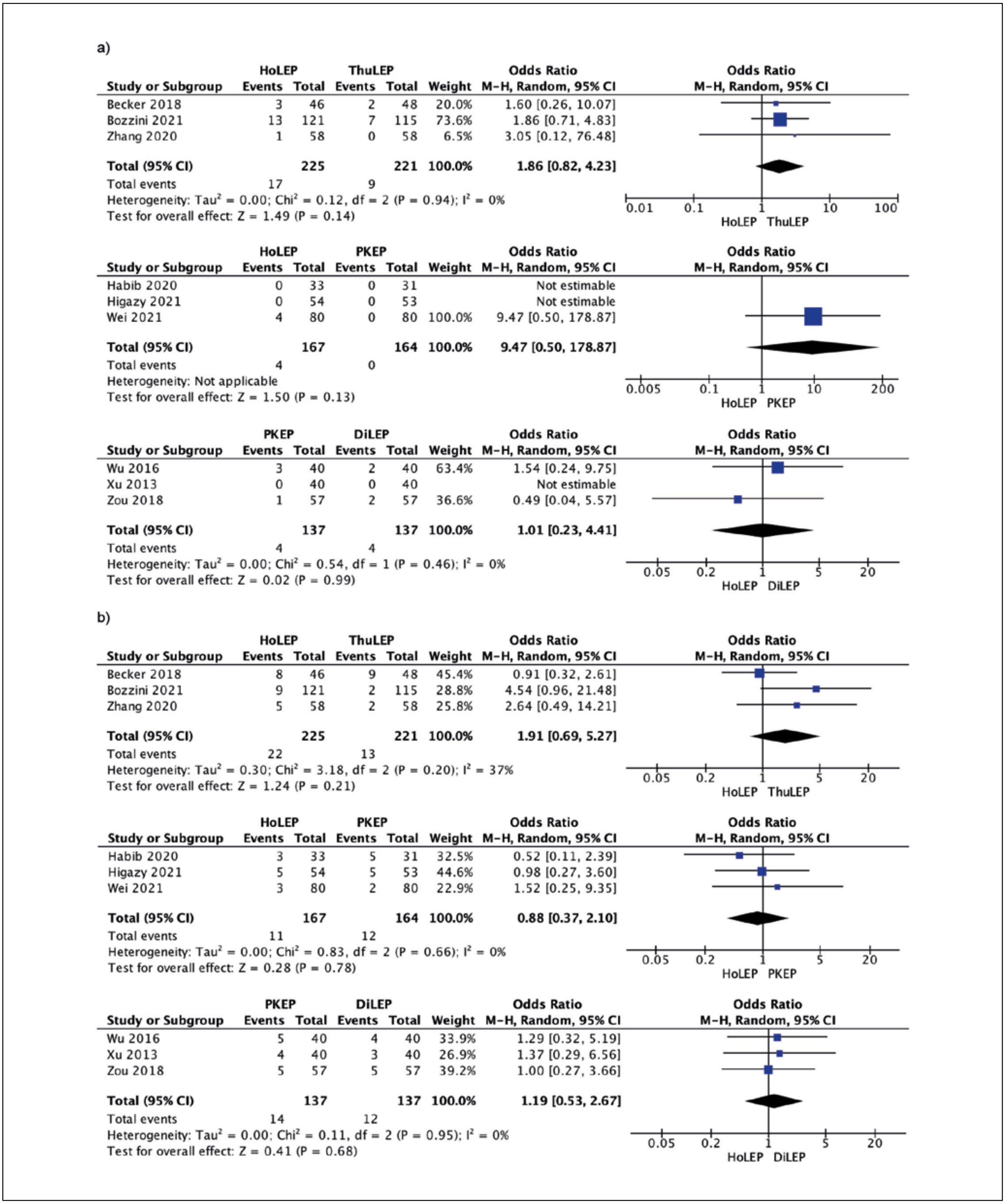


Figure 4. *Meta-analysis of outcomes. Specific complications: **a)** urinary retention, **b)** stress urinary incontinence.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

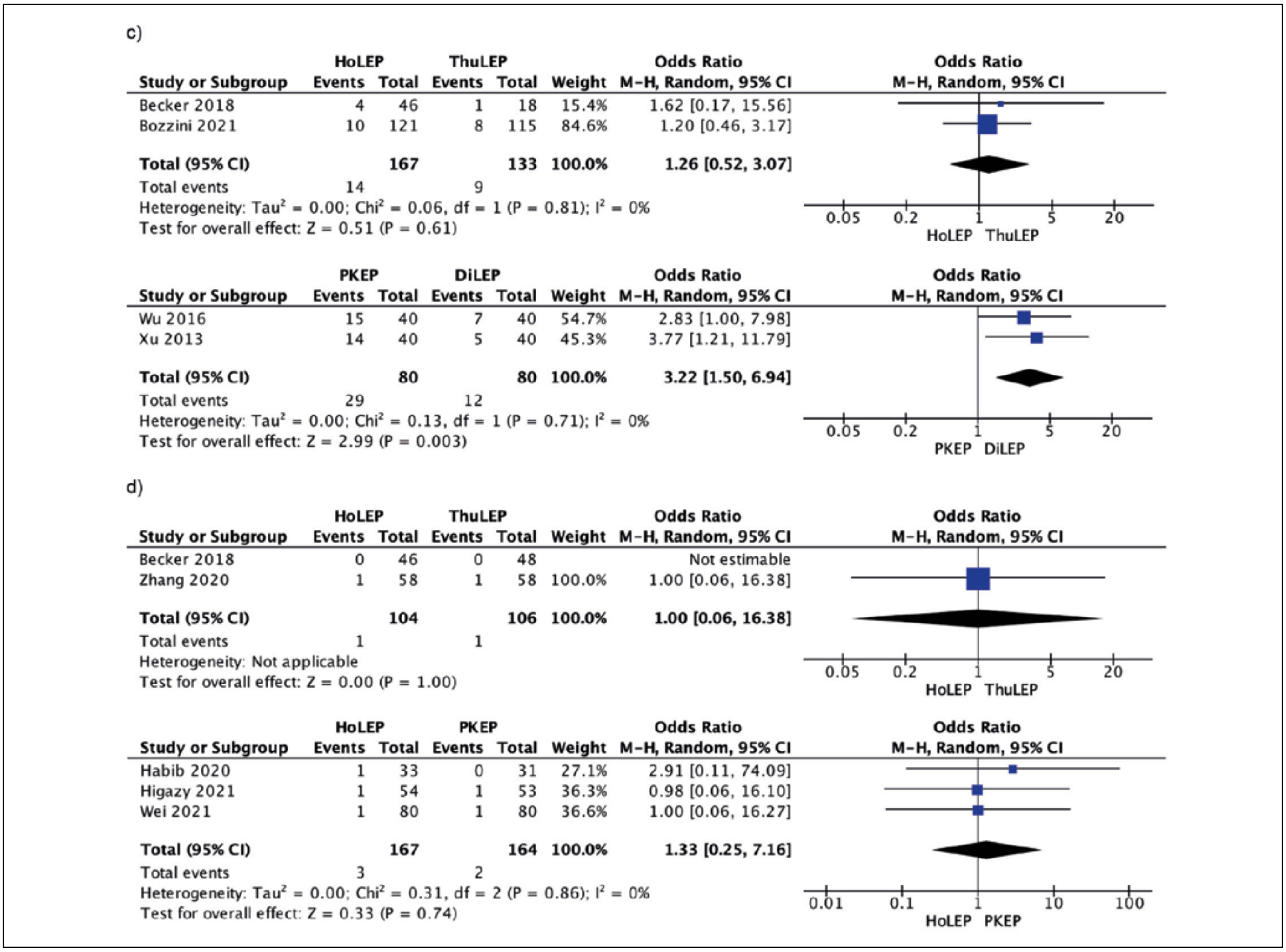


Figure 4. *Meta-analysis of outcomes. Specific complications:* **c)** *urge urinary incontinence,* **d)** *bladder neck contracture.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

Principle findings

The most studied EEP was HoLEP. There were at least one RCT comparing HoLEP with ThuLEP (n = 3), PKEP (n = 3), GreenVEP (n = 1) or DilEP (n = 1). The least studied was GreenVEP; our search did not identify any RCTs on GreenVEP compared with ThuLEP, PKEP, or DiLEP. Without 2-arm RCTs comparing all possible EEP combinations, or RCTs comparing all EEPs, it is impossible to draw conclusions on which EEP is superior.

Our analyses showed that ThuLEP was associated with the shortest operative time compared with HoLEP. Enucleated tissue weight was similar in most comparisons, except that one RCT showed that the enucleation weight was lower with GreenVEP compared with HoLEP [24]. Regarding haemoglobin drop, all methods were associated with less blood loss than PKEP, and ThuLEP and DiLEP were associated with less blood loss than HoLEP. Catheter duration and LOS were longest with PKEP.

There were significant variations in reporting of complications among studies, and some did not use the CD classification. However, EEP is generally a safe procedure, there were no CD IV-V complications, and CD-IIIb occurred in up to 7.5% of cases. Regarding specific complications, meta-analyses did not identify any significant differences with regards to the incidence of urinary retention, urinary incontinence, bladder neck contracture, and urethral stricture among the EEPs studied, except that DiLEP was associated with less UUI compared with PKEP.

Although not statistically significant, the incidence of transfusion, urinary retention, urge and SUI were lower with ThuLEP compared with HoLEP. This observation may be associated with the deeper penetration

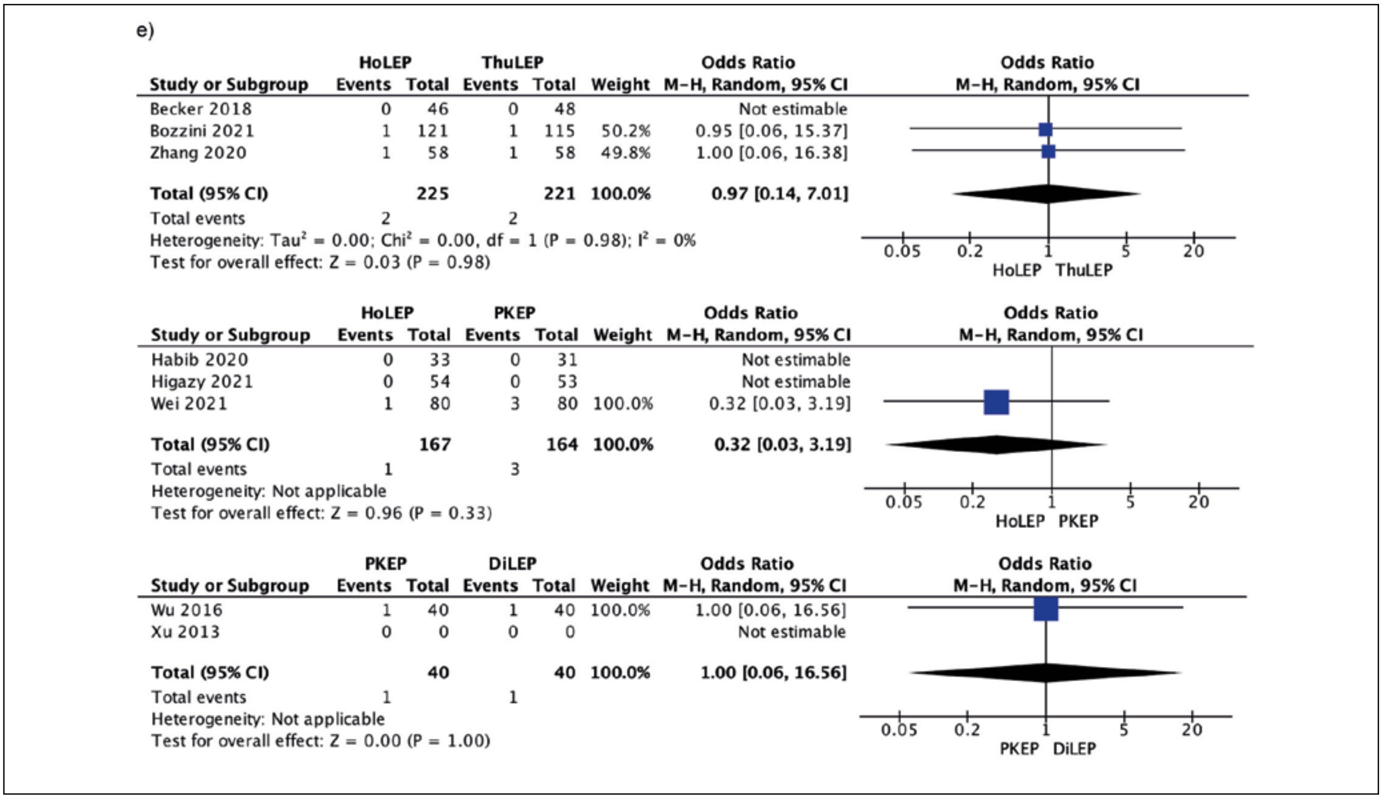


Figure 4. *Meta-analysis of outcomes. Specific complications:* **e)** *urethral stricture.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

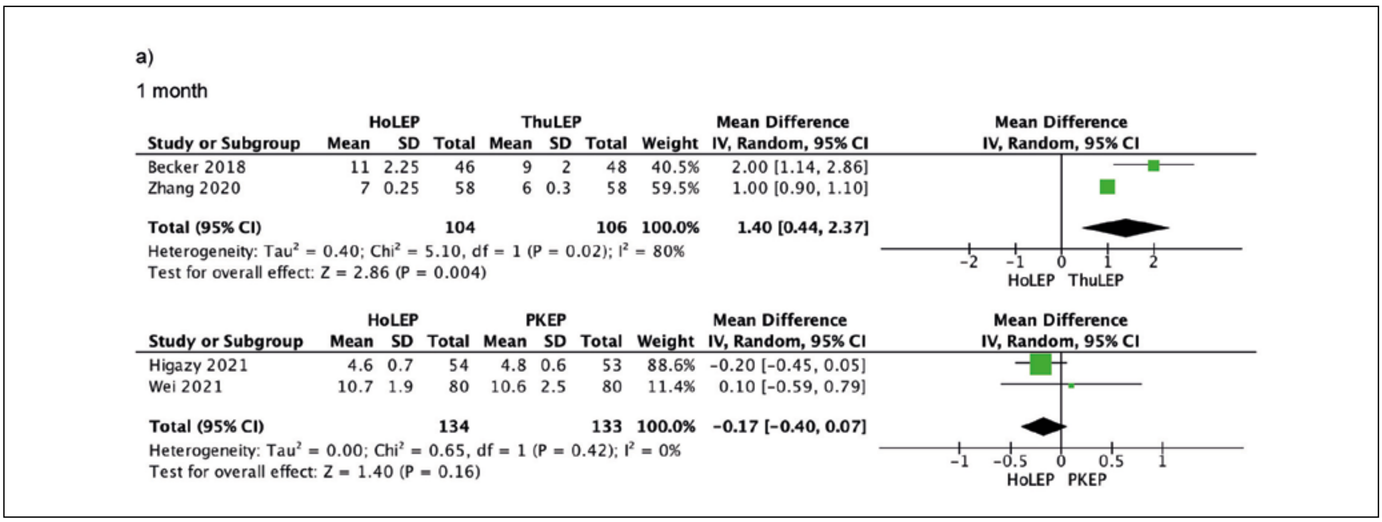
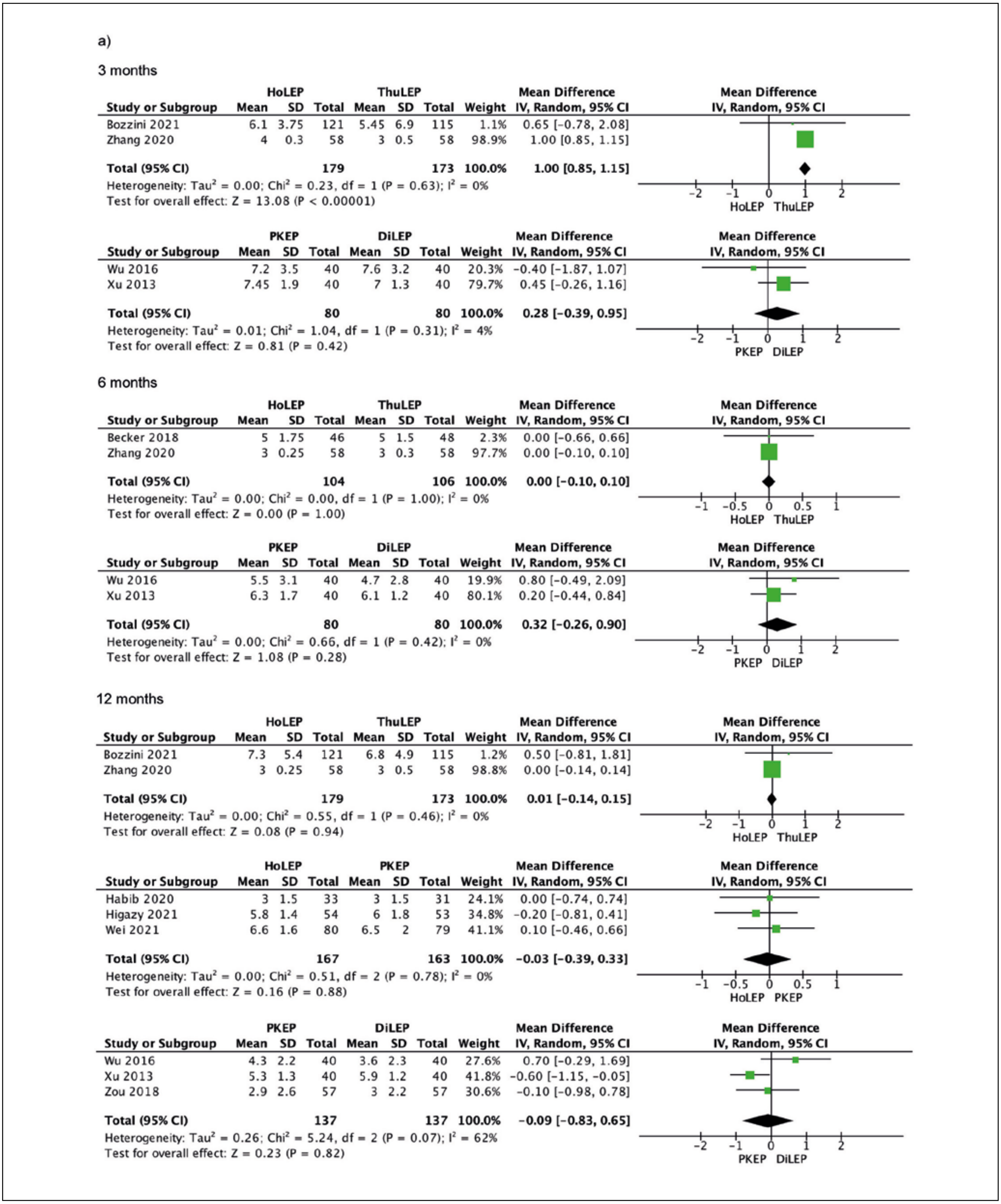


Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **a)** *IPSS.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate



a)

3 months

Study or Subgroup	HoLEP Mean	HoLEP SD	HoLEP Total	ThuLEP Mean	ThuLEP SD	ThuLEP Total	Weight	Mean Difference IV, Random, 95% CI
Bozzini 2021	6.1	3.75	121	5.45	6.9	115	1.1%	0.65 [-0.78, 2.08]
Zhang 2020	4	0.3	58	3	0.5	58	98.9%	1.00 [0.85, 1.15]
Total (95% CI)			**179**			**173**	**100.0%**	**1.00 [0.85, 1.15]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.23$, df = 1 (P = 0.63); $I^2 = 0\%$
Test for overall effect: Z = 13.08 (P < 0.00001)

Study or Subgroup	PKEP Mean	PKEP SD	PKEP Total	DiLEP Mean	DiLEP SD	DiLEP Total	Weight	Mean Difference IV, Random, 95% CI
Wu 2016	7.2	3.5	40	7.6	3.2	40	20.3%	-0.40 [-1.87, 1.07]
Xu 2013	7.45	1.9	40	7	1.3	40	79.7%	0.45 [-0.26, 1.16]
Total (95% CI)			**80**			**80**	**100.0%**	**0.28 [-0.39, 0.95]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 1.04$, df = 1 (P = 0.31); $I^2 = 4\%$
Test for overall effect: Z = 0.81 (P = 0.42)

6 months

Study or Subgroup	HoLEP Mean	HoLEP SD	HoLEP Total	ThuLEP Mean	ThuLEP SD	ThuLEP Total	Weight	Mean Difference IV, Random, 95% CI
Becker 2018	5	1.75	46	5	1.5	48	2.3%	0.00 [-0.66, 0.66]
Zhang 2020	3	0.25	58	3	0.3	58	97.7%	0.00 [-0.10, 0.10]
Total (95% CI)			**104**			**106**	**100.0%**	**0.00 [-0.10, 0.10]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 (P = 1.00); $I^2 = 0\%$
Test for overall effect: Z = 0.00 (P = 1.00)

Study or Subgroup	PKEP Mean	PKEP SD	PKEP Total	DiLEP Mean	DiLEP SD	DiLEP Total	Weight	Mean Difference IV, Random, 95% CI
Wu 2016	5.5	3.1	40	4.7	2.8	40	19.9%	0.80 [-0.49, 2.09]
Xu 2013	6.3	1.7	40	6.1	1.2	40	80.1%	0.20 [-0.44, 0.84]
Total (95% CI)			**80**			**80**	**100.0%**	**0.32 [-0.26, 0.90]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.66$, df = 1 (P = 0.42); $I^2 = 0\%$
Test for overall effect: Z = 1.08 (P = 0.28)

12 months

Study or Subgroup	HoLEP Mean	HoLEP SD	HoLEP Total	ThuLEP Mean	ThuLEP SD	ThuLEP Total	Weight	Mean Difference IV, Random, 95% CI
Bozzini 2021	7.3	5.4	121	6.8	4.9	115	1.2%	0.50 [-0.81, 1.81]
Zhang 2020	3	0.25	58	3	0.5	58	98.8%	0.00 [-0.14, 0.14]
Total (95% CI)			**179**			**173**	**100.0%**	**0.01 [-0.14, 0.15]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.55$, df = 1 (P = 0.46); $I^2 = 0\%$
Test for overall effect: Z = 0.08 (P = 0.94)

Study or Subgroup	HoLEP Mean	HoLEP SD	HoLEP Total	PKEP Mean	PKEP SD	PKEP Total	Weight	Mean Difference IV, Random, 95% CI
Habib 2020	3	1.5	33	3	1.5	31	24.1%	0.00 [-0.74, 0.74]
Higazy 2021	5.8	1.4	54	6	1.8	53	34.8%	-0.20 [-0.81, 0.41]
Wei 2021	6.6	1.6	80	6.5	2	79	41.1%	0.10 [-0.46, 0.66]
Total (95% CI)			**167**			**163**	**100.0%**	**-0.03 [-0.39, 0.33]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.51$, df = 2 (P = 0.78); $I^2 = 0\%$
Test for overall effect: Z = 0.16 (P = 0.88)

Study or Subgroup	PKEP Mean	PKEP SD	PKEP Total	DiLEP Mean	DiLEP SD	DiLEP Total	Weight	Mean Difference IV, Random, 95% CI
Wu 2016	4.3	2.2	40	3.6	2.3	40	27.6%	0.70 [-0.29, 1.69]
Xu 2013	5.3	1.3	40	5.9	1.2	40	41.8%	-0.60 [-1.15, -0.05]
Zou 2018	2.9	2.6	57	3	2.2	57	30.6%	-0.10 [-0.98, 0.78]
Total (95% CI)			**137**			**137**	**100.0%**	**-0.09 [-0.83, 0.65]**

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 5.24$, df = 2 (P = 0.07); $I^2 = 62\%$
Test for overall effect: Z = 0.23 (P = 0.82)

Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **a)** *IPSS.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

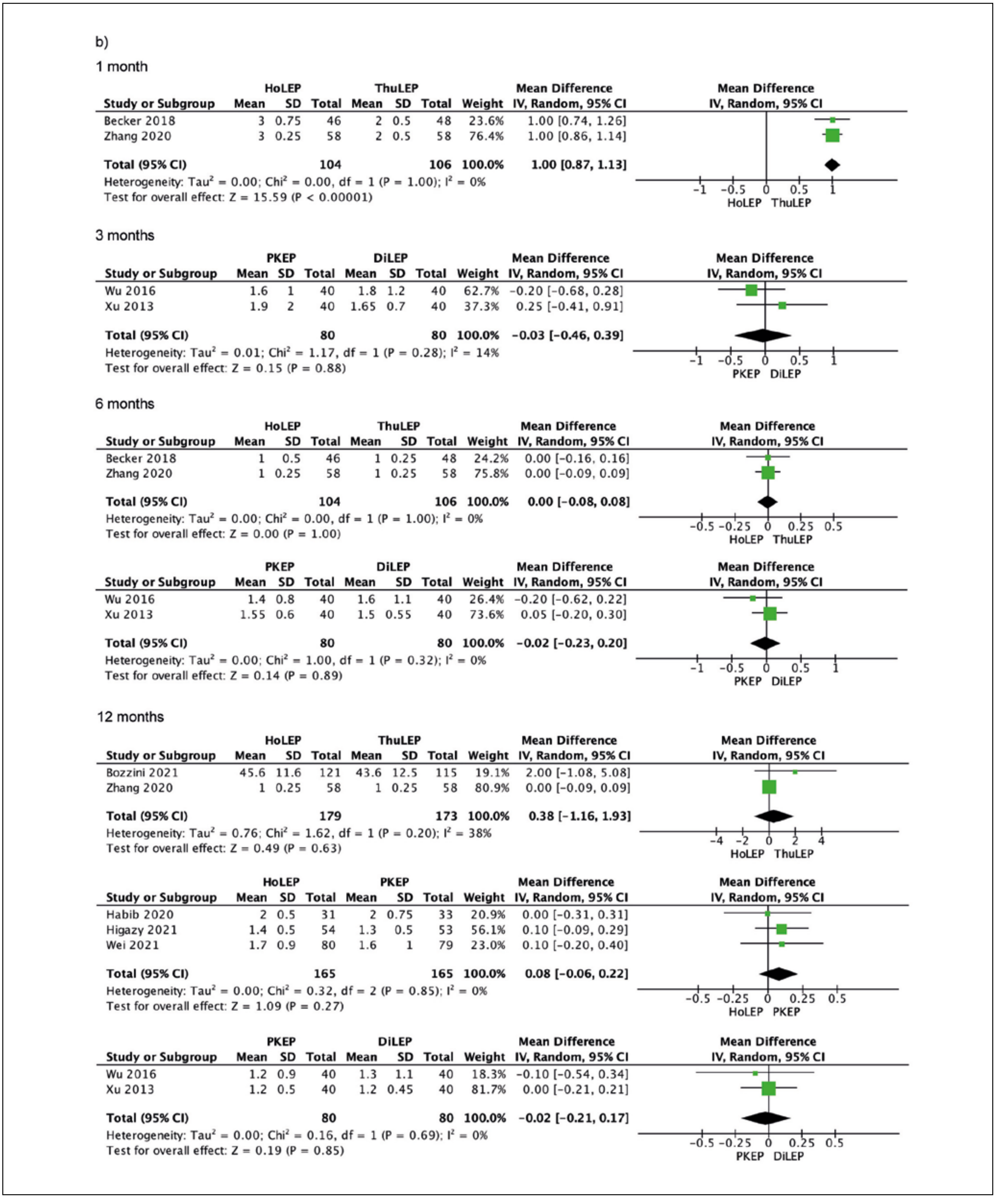


Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **b)** *QoL.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

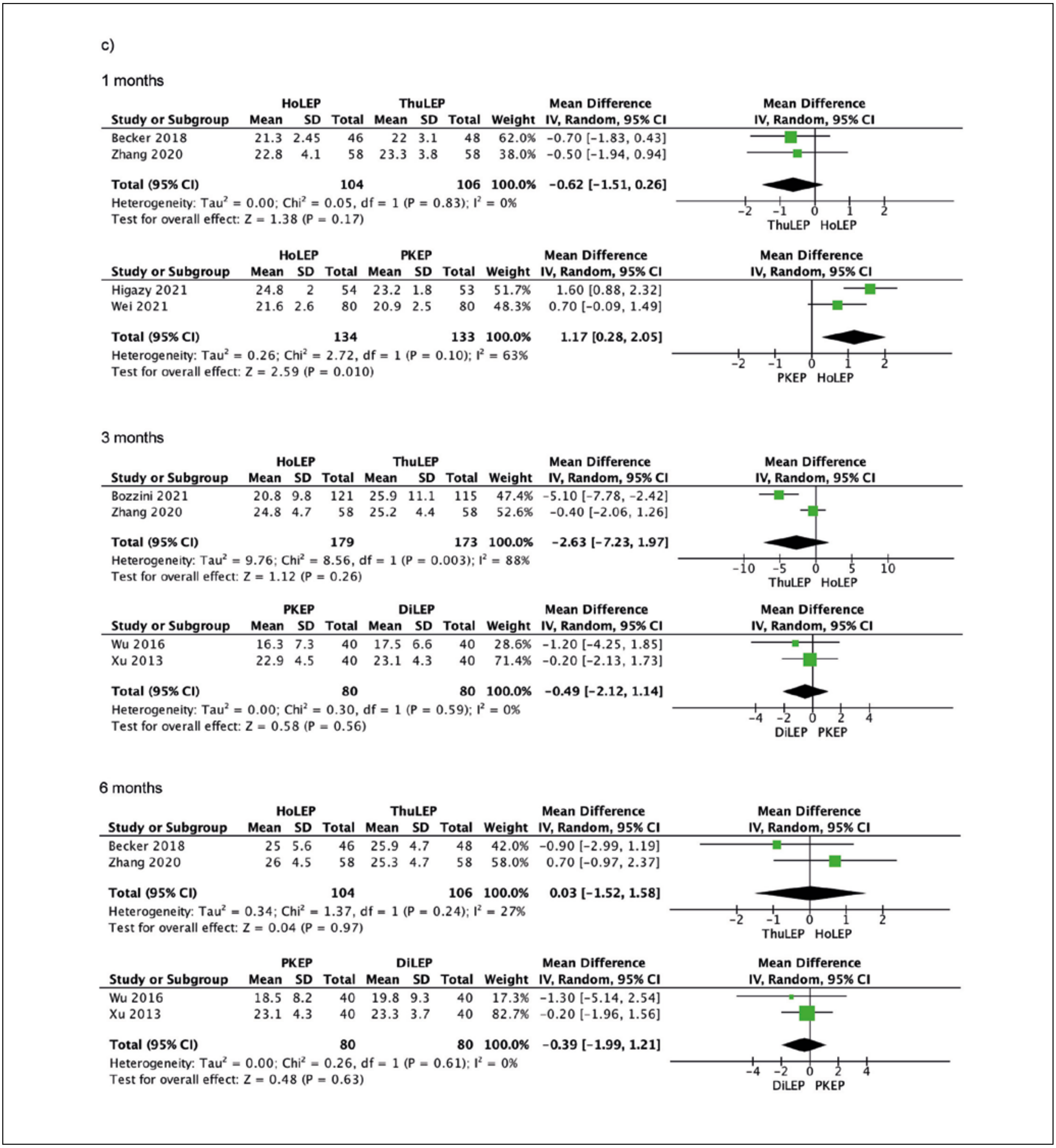


Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **c)** *QoL.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

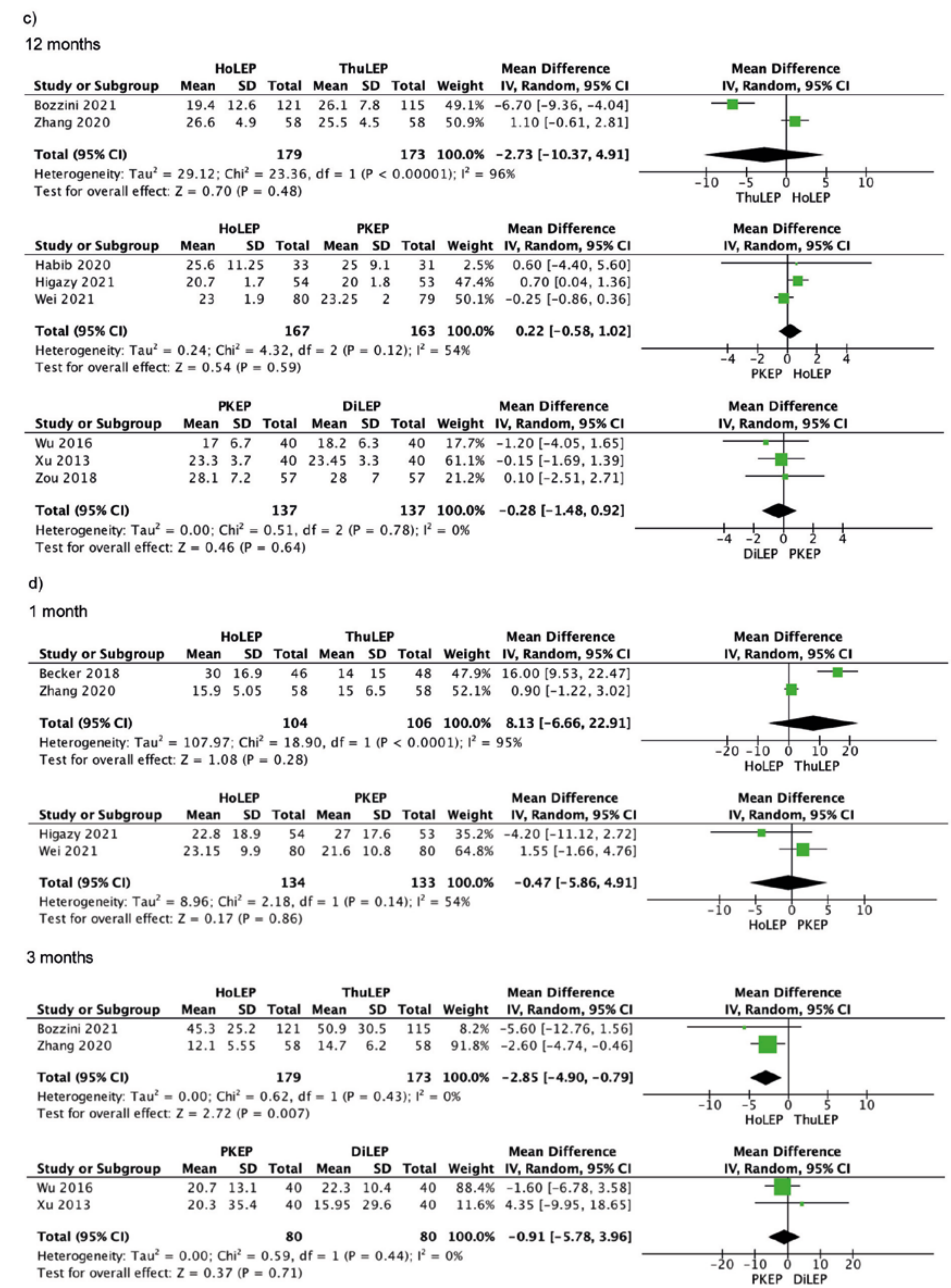


Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **c)** *QoL,* **d)** *PVR.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

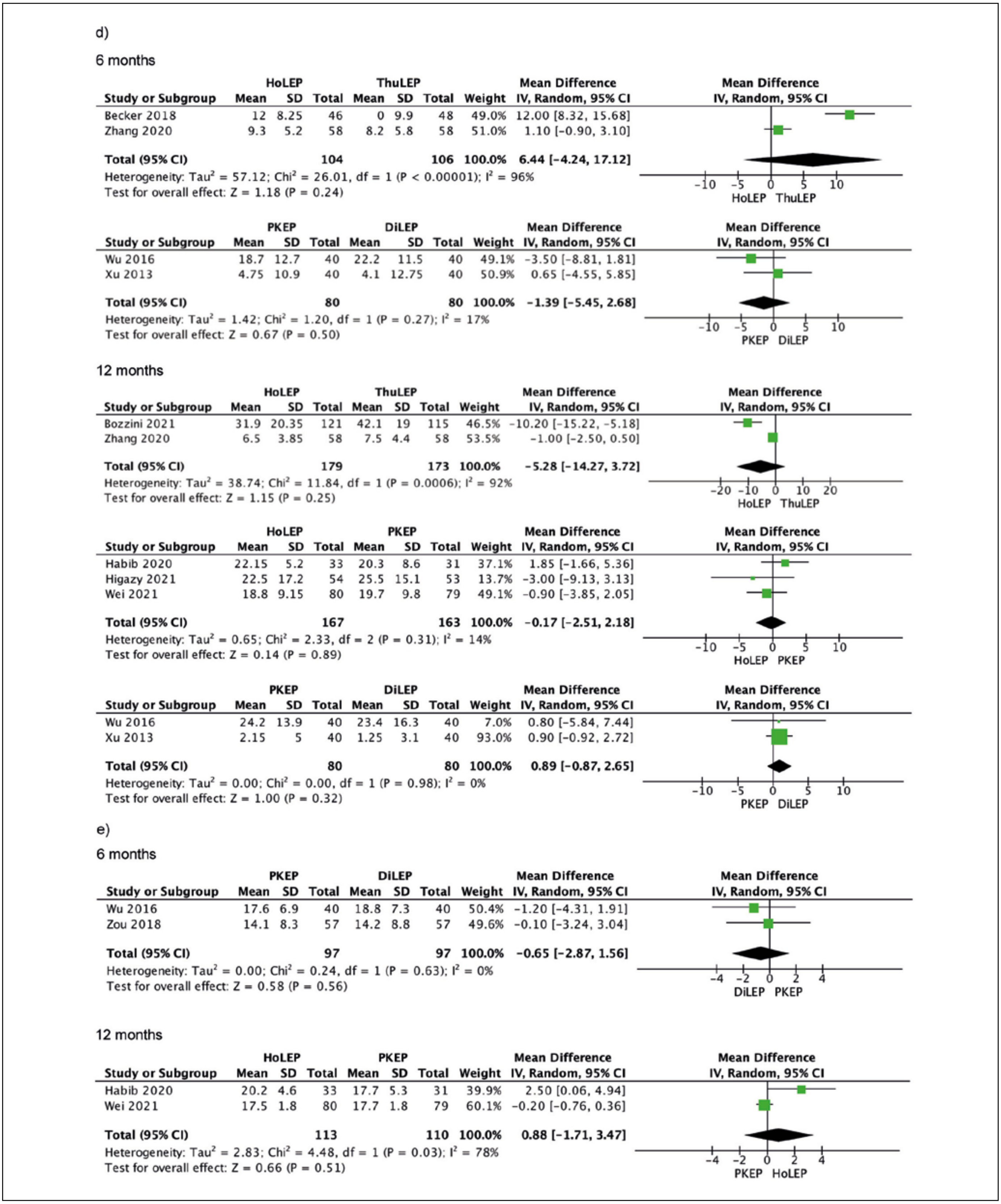


Figure 5. *Meta-analysis of outcomes. Functional outcomes:* **d)** *PVR,* **e)** *IIEF.*

HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; SD – standard deviation; CI – confidence interval; PKEP – plasma kinetic enucleation of the prostate; DiLEP – diode laser enucleation of the prostate

Table 4. *Post-operative functional outcomes*

Author	Year	Intervention arm			IPSS (mean/SD)			QoL (mean/SD)			Qmax, mL/s (mean/SD)			PVR, mL (mean/SD)			IIEF (mean/SD)		
		EEP1	EEP2	Follow-up	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value
Becker et al. [13]	2018	HoLEP	ThuLEP	1 m	11 ±2.25	9 ±2	0.429	3 ±0.75	2 ±0.5	≤0.040	21.3 ±2.45	22 ±3.13	0.8	30 ±16.88	14 ±15	0.351	NR	NR	NR
				3 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				6 m	5 ±1.75	5 ±1.5	0.73	1 ±0.5	1 ±0.25	0.824	25 ±5.62	25.9 ±4.73	0.616	12 ±8.25	0 ±9.88	0.527	NR	NR	NR
				12 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bozzini et al. [14]	2021	HoLEP	ThuLEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	6.12 ±3.75	5.45 ±6.88	0.16	44.2 ±13.22	40.9 ±15.22	0.13	20.76 ±9.78	25.87 ±11.09	0.12	45.3 ±25.16	50.9 ±30.46	0.07	NR	NR	NR
				6 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				12 m	7.34 ±5.43	6.81 ±4.92	0.21	45.6 ±11.59	43.6 ±12.49	0.17	19.43 ±12.56	26.12 ±7.76	0.08	31.9 ±20.35	42.1 ±18.99	0.11	NR	NR	NR
Zhang et al. [17]	2020	HoLEP	ThuLEP	1 m	7 ±0.25	6 ±0.3	0.63	3 ±0.25	2 ±0.5	0.077	22.8 ±4.1	23.3 ±3.8	0.51	15.9 ±5.05	15.0 ±6.5	0.72	NR	NR	NR
				3 m	4 ±0.3	3 ±0.5	0.18	2 (1–2.25)	2 (1–2)	0.22	24.8 ±4.7	25.2 ±4.4	0.68	12.1 ±5.55	14.7 ±6.2	0.19	NR	NR	NR
				6 m	3 ±0.25	3 ±0.3	0.99	1 ±0.25	1 ±0.25	0.48	26.0 ±4.5	25.3 ±4.7	0.45	9.3 ±5.2	8.2 ±5.8	0.76	NR	NR	NR
				12 m	3 ±0.25	3 ±0.5	0.4	1 ±0.25	1 ±0.25	0.48	26.6 ±4.9	25.5 ±4.5	0.2	6.5 ±3.85	7.5 ±4.4	0.34	NR	NR	NR
Habib et al. [18]	2020	HoLEP	PKEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				6 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				12 m	3 ±1.5	3 ±1.5	0.48	2 ±0.5	2 ±0.75	0.22	25.6 ±11.25	25 ±9.1	0.78	22.15 ±5.21	20.29 ±8.63	0.3	20.16 ±4.56	17.68 ±5.27	0.074
Higazy et al. [19]	2021	HoLEP	PKEP	1 m	4.6 ±0.7	4.8 ±0.6	0.2	NR	NR	NR	24.8 ±2	23.2 ±1.8	0.65	22.8 ±18.9	27 ±17.6	0.31	NR	NR	NR
				3 m	5.1 ±1	5.23 ±0.97	0.56	NR	NR	NR	22.22 ±1.85	21.94 ±1.79	0.43	24.8 ±18.9	28 ±17.6	0.23	NR	NR	NR
				6 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				12 m	5.8 ±1.4	6 ±1.8	0.11	1.4 ±0.5	1.3 ±0.5	0.9	20.74 ±1.7	20 ±1.8	0.523	22.5 ±17.2	25.5 ±15.1	0.41	NR	NR	NR
Wei et al. [20]	2021	HoLEP	PKEP	1 m	10.71 ±1.93	10.63 ±2.52	0.81	2.55 ±0.63	2.61 ±0.61	0.53	21.60 ±2.59	20.94 ±2.49	0.1	23.15 ±9.94	21.56 ±10.77	0.33	NR	NR	NR
				3 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				6 m	7.63 ±1.95	7.94 ±2.13	0.33	2.18 ±0.81	2.21 ±0.84	0.77	22.36 ±1.96	22.31 ±1.75	0.87	21.30 ±9.77	21.11 ±9.18	0.9	NR	NR	NR
				12 m	6.58 ±1.64	6.52 ±2.04	0.85	1.69 ±0.89	1.56 ±1.04	0.4	23.00 ±1.91	23.25 ±2.02	0.42	18.83 ±9.15	19.72 ±9.82	0.55	17.46 ±1.77	17.71 ±1.77	0.38
Elshal et al. [24]	2015	HoLEP	Gre-enVEP	1 m	NR	NR	NR	NR	NR	NR	24.7 ±12.5	20.4 ±9.4	0.06	NR	NR	NR	NR	NR	NR
				3 m	NR	NR	NR	NR	NR	NR	26.4 ±13.2	19.9 ±10.8	**0.02**	NR	NR	NR	NR	NR	NR
				6 m	NR	NR	NR	NR	NR	NR	31.1 ±14	18.5 ±7	**0.01**	NR	NR	NR	NR	NR	NR
				12 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
He et al. [15]	2019	HoLEP	DiLEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	9.8 ±3.7	9.9 ±3.3	0.92	1.4 ±0.9	1.5 ±0.9	0.566	22.8 ±2.7	22.5 ±2.5	0.589	20.7 ±16.1	20.3 ±13.5	0.881	NR	NR	NR
				6 m	6.5 ±3.4	7.5 ±3.9	0.137	1.3 ±0.7	1.3 ±0.8	0.816	24.2 ±3.6	23.9 ±2.8	0.598	10.2 ±8.7	12.3 ±9.1	0.178	NR	NR	NR
				12 m	5.9 ±2.6	6.2 ±2.7	0.55	0.8 ±0.1	0.7 ±0.1	0.281	24.3 ±3.3	24.6 ±3.1	0.655	8.3 ±8.2	10.2 ±6.6	0.152	NR	NR	NR
Feng et al. [16]	2016	ThuLEP	PKEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	8.07 ±2.57	8.85 ±2.94	0.11	1.64 ±0.59	1.74 ±0.71	0.2	20.13 ±4.33	19.14 ±5.34	0.25	21.05 ±12.49	22.62 ±13.04	0.49	NR	NR	NR
				6 m	7.69 ±2.29	8.15 ±2.22	0.25	1.54 ±0.53	1.64 ±0.58	0.43	21.07 ±3.85	20.62 ±3.47	0.31	18.41 ±12.44	19.27 ±11.19	0.68	NR	NR	NR
				12 m	6.87 ±2.54	7.03 ±2.38	0.71	1.32 ±0.47	1.38 ±0.49	0.49	21.46 ±4.05	21.09 ±3.29	0.57	17.56 ±11.75	18.33 ±10.47	0.7	NR	NR	NR
Wu et al. [21]	2016	PKEP	DiLEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	7.2 ±3.5	7.6 ±3.2	0.6	1.6 ±1.0	1.8 ±1.2	0.42	16.3 ±7.3	17.5 ±6.6	0.44	20.7 ±13.1	22.3 ±10.4	0.55	16.3 ±5.8	15.5 ±6.2	0.55
				6 m	5.5 ±3.1	4.7 ±2.8	0.23	1.4 ±0.8	1.6 ±1.1	0.36	18.5 ±8.2	19.8 ±9.3	0.51	18.7 ±12.7	20.2 ±11.5	0.58	17.6 ±6.9	18.8 ±7.3	0.45
				12 m	4.3 ±2.2	3.6 ±2.3	0.16	1.2 ±0.9	1.3 ±1.1	0.65	17.0 ±6.7	18.2 ±6.3	0.41	24.2 ±13.9	23.4 ±16.3	0.81	17.2 ±7.4	16.8 ±8.3	0.82

Table 4. *Continued*

Author	Year	Intervention arm		Follow-up	IPSS (mean/SD)			QoL (mean/SD)			Qmax, mL/s (mean/SD)			PVR, mL (mean/SD)			IIEF (mean/SD)		
		EEP1	EEP2		EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value	EEP1	EEP2	p-value
Xu et al. [22]	2013	PKEP	DiLEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	7.45 ±1.89	7.03 ±1.29	0.24	1.88 ±0.97	1.65 ±0.74	0.25	22.86 ±4.51	23.09 ±4.29	0.82	20.30 ±35.43	15.95 ±29.58	0.55	NR	NR	NR
				6 m	6.30 ±1.74	6.08 ±1.23	0.51	1.55 ±0.60	1.48 ±0.55	0.56	23.11 ±4.29	23.33 ±3.73	0.812	4.75 ±10.89	4.07 ±12.75	0.8	NR	NR	NR
				12 m	5.28 ±1.32	4.88 ±1.24	0.17	1.23 ±0.48	1.18 ±0.45	0.63	23.32 ±3.67	23.45 ±3.33	0.87	2.15 ±5.02	1.25 ±3.10	0.34	NR	NR	NR
Zou et al. [23]	2018	PKEP	DiLEP	1 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				3 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
				6 m	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	14.1 ±8.3	14.2 ±8.8	NR
				12 m	2.9 ±2.6	3.0 ±2.2	NR	NR	NR	NR	28.1 ±7.2	28.0 ±7.0	NR	NR	NR	NR	NR	NR	NR

IPSS – International Prostate Symptom Score; SD – standard deviation; QoL – quality of life; PVR – post-void residual; IIEF – International Index of Erectile Function; EEP – endoscopic enucleation procedures; HoLEP – holmium laser enucleation of the prostate; ThuLEP – thulium laser enucleation of the prostate; PKEP – plasma kinetic enucleation of the prostate; VEP; DiLEP – diode EP

of the holmium laser (~0.4 mm) compared with thulium (~0.25 mm), and the tissue tearing caused by Ho:YAG's pulsed emission [28].

EEP improves IPSS, QoL, Qmax, and PVR regarding efficacy. On comparing different EEP, ThuLEP significantly improves IPSS and QoL scores more than HoLEP in the short term (1 month), but not in the longer-term (12 months). We identified no other functional outcome differences in meta-analyses.

Although the efficacy and safety among different EEPs are similar, it has been shown that the length of learning may differ. The learning curve is steep, with a plateau of around 30–40 cases for HoLEP [29]. Therefore, the complications and functional outcomes reported in the current study may be skewed by surgeons who were still mastering the procedure. In addition, outcomes may well be affected by the differences in power settings [30], variations in the technique, such as the number of lobes enucleated [31], and the type of morcellators [32] used.

Enucleation using plasma kinetic energy is an alternative option where laser facilities are not readily available. Most of the outcomes following PKEP are similar to enucleation using lasers, but may be superior due to lower cost and hospital expenses [20]. In addition, it achieves less blood loss and improved IPSS, QoL, and Qmax compared with TURP [33].

Implication for clinical practice and future research

All enucleation methods appeared to improve short-term IPSS with a low incidence of severe complications. However, there are not enough RCTs with consistent reporting to conclude on which enucleation method is more superior. More RCTs are needed to compare different EEPs, and future research should focus on 'standardised' reporting, i.e., reporting pre- and post-operative IPSS/IIEF and uroflowmetry parameters and, using the Clavien-Dindo system for complications.

Strengths and limitations

Strengths of this review include the systematic approach, adherence to the PRISMA checklist, and RoB assessment of individual studies. A limitation was the heterogeneity among studies regarding their primary endpoints, follow-up duration, and reporting of IPSS/IIEF at different time points. Due to the small number of studies included in the meta-analysis for each outcome, we did not perform a subgroup analysis (sensitivity analysis).

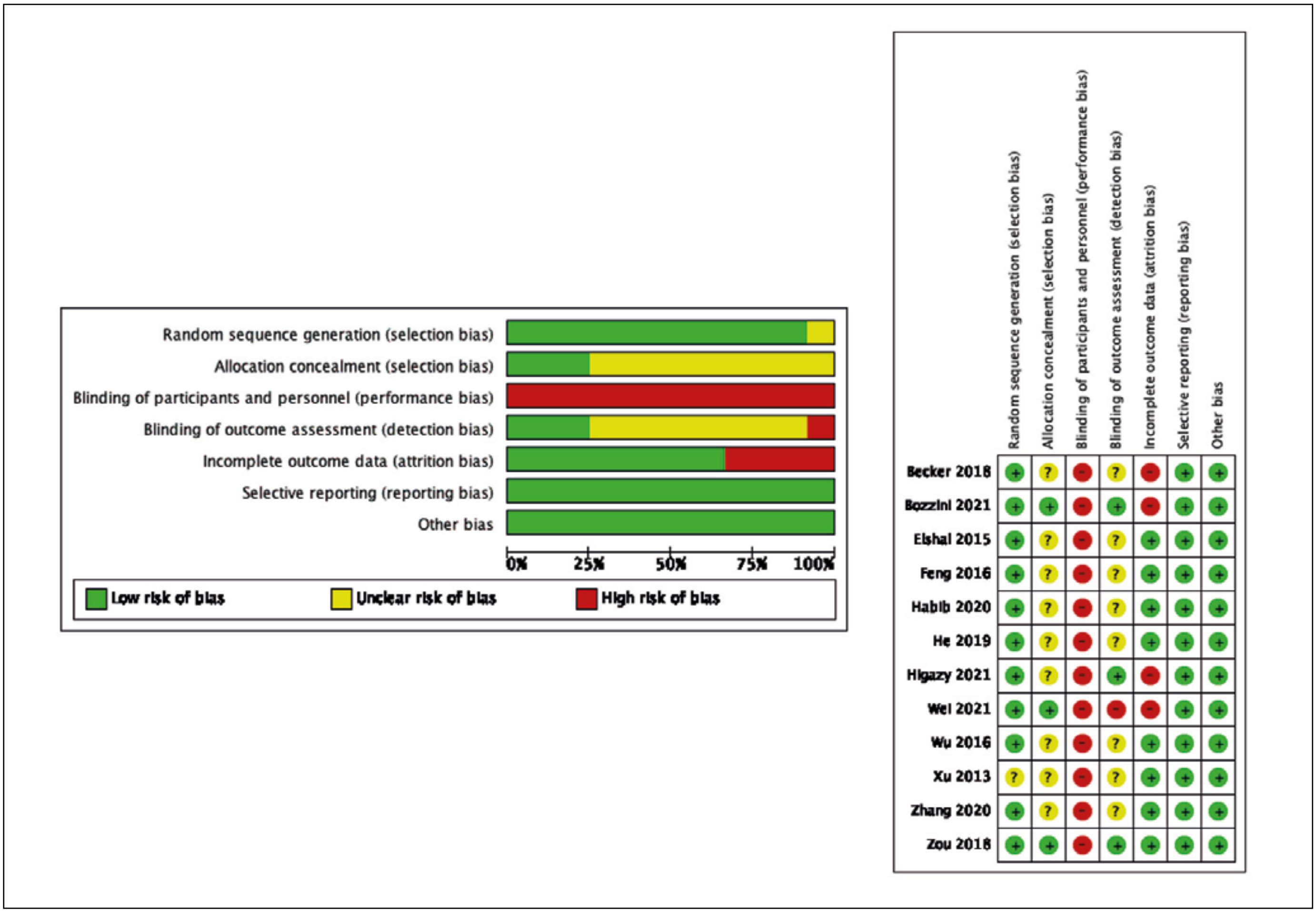


Figure 6. *Risk of bias assessment of included studies using the Cochrane RoB for RCTs tools.*
RoB – risk of bias; RCTs – randomised-controlled trials

Although most studies did report patient blinding during hospitalization, performance bias was judged high in all of the included studies. In addition, we did not stratify the enucleation details further, such as the energy level used and the number of lobes enucleated.

CONCLUSIONS

EEPs improve symptom and QoL scores and Qmax. Procedures are safe with a low incidence of Clavien-Dindo I–III complications. However, ThuLEP was associated with shorter operative time, lower haemoglobin decrease, and lower incidence of low-grade complications compared with HoLEP. Thorough meta-analyses were not possible due to the lack of RCTs for some EEP comparisons. RCTs comparing various EEPs are highly needed to gather further information about the possible advantages of different energy sources and enucleation techniques. Reporting of complications should be done uniformly to avoid a high inter-study bias for essential safety outcomes.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

KHP and GO had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: CSB, TT
Acquisition of data: KHP, GO, YY
Analysis and interpretation: KHP, GO
Drafting of the manuscript: KHP, GO
Critical revision of the manuscript: KHP, GO, CYY, CSB, TT
Statistical analysis: KHP, GO
Obtaining funding: None
Administrative, technical or material support: KHP, GO, CYY, CSB, TT
Supervision: CSB, TT

APPENDIX

Appendix 1. *PRISMA 2020 Checklist*

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-analyses

Section and Topic	Item #	Checklist item	Location where item is reported (page)
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract page
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	1
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	2
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	2
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	2
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	2
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	2, 3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	2
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	2, 3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	2, 3
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NR
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NR
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	2
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	2, 3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6, suppl figure 2
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	3

Appendix 1. *Continued*

Section and Topic	Item #	Checklist item	Location where item is reported (page)
Study characteristics	17	Cite each included study and present its characteristics.	3-6, tables 1-3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	6, suppl figure 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	3-6, figure 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	6, suppl figure 3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	3-6, figure 1
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	3-6, figure 1, tables 1-3
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NR
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	6, suppl figure 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	figure 1
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	6-9
	23b	Discuss any limitations of the evidence included in the review.	9
	23c	Discuss any limitations of the review processes used.	9
	23d	Discuss implications of the results for practice, policy, and future research.	9
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NR
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NR
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NR

From: Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

Appendix 2. *Inclusion and exclusion of included studies*

Author	Year	Inclusion criteria	Exclusion criteria
Becker et al. [13]	2018	Qmax ≤15 ml/s, IPSS ≥12, age ≥18, failed medical therapy for BPO, recurrent UTI, acute or recurrent episodes of urinary retention or postrenal acute kidney injury	Previous urethral/prostatic surgery, active prostate cancer (PCa), urethral strictures, urodynamically diagnosed neurogenic bladder
Bozzini et al. [14]	2021a	IPSS ≥8, weak or no response to previous medical treatments, Qmax <15 ml/sec, acute urinary retention	History of prostatic surgery, prostate or bladder cancer suspicion/history, documented/suspected neurogenic bladder, urethral stricture, anticoagulant/antiaggregant therapy, concurrent bladder stones, patients unfit for surgery, failure to sign informed consent
Zhang et al. [17]	2019	Prostate size (TRUS) ≥80 ml, Qmax ≤15 ml/sec, IPSS ≥12, urodynamic obstruction without detrusor dysfunction and no response to pharmacologic therapy	Neurogenic bladder, suspicion for prostate cancer, urethral strictures, poor tolerance for surgery
Habib et al. [18]	2020	IPSS ≥13, Qmax <15 ml/sec, prostate size ≥80 g	Urethral stricture, neurological disorder affecting bladder function, bladder or prostate cancer, previous history of TURP or bladder neck surgery
Higazy et al. [19]	2021	LUTS secondary to BPH, prostate volume ≥ 80ml, failed medical treatment, refractory haematuria, recurrent attacks of urine retention, upper urinary tract affected or high IPSS ≥20 that affects Qo 3, IPSS ≥8	Anticoagulant or antiplatelet medication, neurogenic bladder, urethral stricture, bladder stones, prostate cancer, previous prostate urethral surgery
Wei et al. [20]	2021	Patients with LUTS and obstruction due to BPH who had indication for surgical treatment and failed on conservative medical therapy with alpha blockers and 5-alpha reductase inhibitors	Severe pulmonary disease or heart disease, bladder calculus, neurogenic bladder dysfunction, bladder cancer, previous prostate surgery, prostate cancer, urethral stricture or coagulopathy
Elshal et al. [24]	2015	Age >50, refractory LUTS secondary to BPH, I-PSS >15, QoL-score ≥3, Qmax <15 ml/sec, acute urinary retention secondary to BPH in whom trial of voiding failed, prostate volume on TRUS 40–150 ml	Neurological disorder, active UTI, bladder/prostate cancer
He et al. [15]	2019	Qmax ≤15 ml/s, QoL ≥3, IPSS ≥8	Prostate cancer, prior prostate surgery, acute prostatitis or urethritis, neurogenic bladder and urethral injury
Feng et al. [16]	2016	Age ≥50 and ≤85, IPSS ≥7, Qmax < 15 ml/sec, medical therapy failure	Neurogenic bladder, documented or suspected prostate cancer, prior prostatic or urethral surgery, poor tolerance for surgery
Wu et al. [21]	2016	Indication for surgical treatment of BPH	Severe pulmonary or heart disease, bladder calculus, neurogenic bladder dysfunction, bladder or prostate cancer, urethral stricture or coagulopathy
Xu et al. [22]	2013	Age ≥50, IPSS ≥7, Qmax < 1 ml/sec	Neurogenic bladder, history of prostatic or urethral surgery, prostate cancer
Zou et al. [23]	2018	IPSS ≥12, QoL ≥4, Qmax <15 ml/sec and/or Schafer grade ≥2 and/or failed medical therapy for BPO and/or recurrent urinary retention	Previous urethral/prostatic surgery, prostate cancer, urethral stricture, neurogenic bladder, neurologic disorder affecting micturition

IPSS – international prostate symptom score; BPO – benign prostatic obstruction; Pca – prostate cancer; UTI – urinary tract infections; TRUS – transrectal ultrasound; BPH – benign prostatic hyperplasia; LUTS – lower urinary tract symptoms; TURP – transurethral resection of the prostate

Appendix 3. *Post-operative complications*

Author	Year	Intervention arm		Clot retention/prolonged haematuria, n (%)					Superficial bladder injury due to morcellation, n (%)					Capsule violation/perforation intra-operative, n (%)					Haematuria, n (%)				
		EEP1	EEP2	Overall	EEP1	EEP2	Treatment	p-value	Overall	EEP1	EEP2	Treatment	p-value	Overall	EEP1	EEP2	Treatment	p-value	Overall	EEP1	EEP2	Treatment	p-value
Becker et al. [13]	2018	HoLEP	ThuVEP	4 (4.3)	2 (4.3)	2 (4.2)	Bladder irrigation	0.499	1 (1.1)	0 (0)	1 (2.1)	No special therapy	0.281	NR	NR	NR	NR	NR	1 (1.1)	1 (2.2)	0 (0)	Transfusion	0.267
Bozzini et al. [14]	2021	HoLEP	ThuLEP	NR	NR	NR	NR	NR	1 (0.4)	1 (0.8)	0 (0)	NR	0.8	NR	NR	NR	NR	NR	10 (4.2)	8 (6.6)	2 (1.7)	Transfusion	0.03
Zhang et al. [17]	2020	HoLEP	ThuLEP	4 (3.4)	3 (5.2)	1 (1.7)	Bladder irrigation	0.62	5 (4.3)	4 (6.9)	1 (1.7)	no treatment	0.36	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–
Habib et al. [18]	2020	HoLEP	PKEP	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–	1 (1.6)	0 (0)	1 (3.2)	Catheter drainage	0.48	0 (0)	0 (0)	0 (0)	NR	–
Higazy et al. [19]	2021	HoLEP	PKEP	1 (0.9)	1 (1.9)	0 (0)	NR	0.32	1 (0.9)	0 (0)	1 (1.9)	Prolonged catheter duration	0.31	1 (0.9)	0 (0)	1 (1.9)	Prolonged catheter	0.31	NR	NR	NR	NR	NR
Wei et al. [20]	2021	HoLEP	PKEP	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–	NR	NR	NR	NR	NR
Elshal et al. [24]	2015	HoLEP	GreenVEP	3 (2.9)	1 (2)	2 (3.7)	Catheterization	1	5 (4.9)	4 (8)	1 (1.8)	Catheter drainage of bladder	0.19	4 (3.9)	1 (2)	3 (5.6)	Catheter drainage of bladder	0.61	1 (1)	0 (0)	1 (1.8)	Transfusion	1
He et al. [15]	2019	HoLEP	DiLEP	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–
Feng et al. [16]	2016	ThuLEP	PKEP	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–	1 (0.8)	0 (0)	1 (1.5)	NR	0.33	1 (0.8)	0 (0)	1 (1.5)	Transfusion	0.33
Wu et al. [21]	2016	PKEP	DiLEP	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1 (1.3)	1 (2.5)	0 (0)	NR	0.31	1 (1.3)	1 (2.5)	0 (0)	Transfusion	0.31
Xu et al. [22]	2013	PKEP	DiLEP	NR	NR	NR	0	NR	0 (0)	0 (0)	0 (0)	NR	–	3 (3.8)	1 (2.5)	2 (5)	NR	0.56	0 (0)	0 (0)	0 (0)	NR	–
Zou et al. [23]	2018	PKEP	DiLEP	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–

EEP – endoscopic enucleation of the prostate; HoLEP – holmium laser enucleation of the prostate; ThuVEP – thulium laser vapoenucleation prostate; PKEP – plasma kinetic enucleation of the prostate; NR – not reported; DiLEP – diode laser enucleation of the prostate

Appendix 3. *Continued*

Author	Year	Intervention arm		UTI, n (%)					Incomplete morcellation, n (%)					Hydronephrosis due to ureteric orifice injury, n (%)				
		EEP1	EEP2	Overall	EEP1	EEP2	Treat-ment	p-value	Overall	EEP1	EEP2	Treat-ment	p-value	Overall	EEP1	EEP2	Treat-ment	p-value
Becker et al. [13]	2018	HoLEP	ThuVEP	2 (2.1)	1 (2.1)	1 (2.1)	Antibio-tics	0.499 – 4 weeks follow up, 0.31 – be-tween 1–6 months follow up	1 (1.1)	1 (2.2)	0 (0)	Remo-val of enuc-leated tissue in local ana-esthesia	0.267	1 (1.1)	1 (2.2)	0 (0)	Ureteral stent inser-tion	0.267
Bozzini et al. [14]	2021	HoLEP	ThuLEP	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Zhang et al. [17]	2020	HoLEP	ThuLEP	4 (3.5)	1 (1.7)	3 (5.2)	Antibio-tics	0.62	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–
Habib et al. [18]	2020	HoLEP	PKEP	4 (6.3)	1 (3)	3 (9.7)	Antibio-tics	0.347	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Higazy et al. [19]	2021	HoLEP	PKEP	8 (7.5)	3 (5.6)	5 (9.4)	Antibio-tics	0.67	0 (0)	0 (0)	0 (0)	NR	–	0 (0)	0 (0)	0 (0)	NR	–
Wei et al. [20]	2021	HoLEP	PKEP	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Elshal et al. [24]	2015	HoLEP	Gre-enVEP	4 (3.9)	overall: 0 (0)	overall: 4 (7.6); early: 3 (5.7); late: 1 (1.8)	Antibio-tics	1.0 (early); 0.41 (late)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
He et al. [15]	2019	HoLEP	DiLEP	7 (5.6)	4 (6.3)	3 (4.8)	Antibio-tics	0.697	NR	NR	NR	NR	NR	0 (0)	0 (0)	0 (0)	NR	–
Feng et al. [16]	2016	ThuLEP	PKEP	3 (2.4)	1 (1.6)	2 (3)	Antibio-tics	0.61	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Wu et al. [21]	2016	PKEP	DiLEP	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Xu et al. [22]	2013	PKEP	DiLEP	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Zou et al. [23]	2018	PKEP	DiLEP	8 (7)	5 (8.8)	3 (5.3)	Antibio-tics	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

EEP – endoscopic enucleation of the prostate; HoLEP – holmium laser enucleation of the prostate; ThuVEP – thulium laser vapoenucleation prostate; PKEP – plasma kinetic enucleation of the prostate; NR – not reported; DiLEP – diode laser enucleation of the prostate

Database: Embase <1974 to 2022 February 04>, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, EBM Reviews – Cochrane Central Register of Controlled Trials <November 2021>

Search Strategy:

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1 exp prostate hypertrophy/ or exp Prostatic Hyperplasia/ (63820)

2 prostate adenoma/ (1171)

3 (benign adj3 (prostate or prostatic) adj3 (obstruction* or enlargement*)).kw,tw. (4677)

4 ((prostate or prostatic) adj2 (hyperplasia or hypertroph* or adenoma*)).tw,kw. (53611)

5 Prostatism.tw,kw. (1357)

6 or/1-5 (79386)

7 exp lower urinary tract symptoms/ or exp lower urinary tract symptom/ (64188)

8 ((lower urinary or bladder or urethra* or urination or urinating or LUT) adj3 (symptom* or complain*)).tw,kw. (39956)

9 "LUTS".tw. (15818)

10 (Bladder outlet obstruction or BPH or BPO or BPE or BOO or OAB).tw,kw. (59421)

11 bladder obstruction/ (4199)

12 bladder neck stenosis/ or Urinary Bladder Neck Obstruction/ (12275)

13 ((benign or neck) adj3 bladder adj3 (sclerosis or obstruction* or obstructed voiding or neck strangulation or stenosis or stenoses or scleroses or contracture or stricture* or narrow* or fistula*)).tw,kw. (3450)

14 dysuria.tw,kw. (14013)

15 (Sensation adj3 incomplete adj3 emptying).tw,kw. (224)

16 (Chronic adj3 (urine or urinary) adj3 retention).tw,kw. (971)

17 (Incomplete voiding or obstructing voiding).tw,kw. (268)

18 (bladder emptying adj2 (dysfunction* or incomplete or incompetent)).tw. (867)

19 overactive bladder/ (24014)

20 ((Overactive or overactivity or over activit*) adj (bladder or detrusor)).kw,tw. (22604)

21 ((detrusor or bladder) adj (underactivit* or failure or acontractile or hypocontract*)).tw. (1705)

22 or/7-21 (158864)

23 male/ or (men or man or male*).tw,af. (21267456)

24 22 and 23 (86615)

25 6 or 24 (131426)

26 exp Laser Therapy/ (95026)

27 exp holmium laser/ (13150)

28 laser/ (130458)

29 (laser and prostat*).tw,kw. (11250)

30 (holmium or "HoLEP" or thulium or "ThuLEP" or BipolEP or diode or DiLEP or greenlep or MoLEP or EEP or greenlight or greenlep).tw,kw. (67792)

31 ((prostate or laser or bipola or endoscopic) adj5 enucleation).tw,kw. (4328)

32 or/26-31 (286279)

33 25 and 32 (8462)

34 randomized controlled trial.pt. or randomized controlled trial.mp. (2509637)

35 clinical trial.pt. (814043)

36 random*.mp. (4774348)

37 clinical trial:.mp. (3491403)

38 (blind* or double-blind* or placebo*).mp. (1911776)

39 (systematic review or meta-analysis).pt. or (systematic review or meta-analysis).ti. (618248)

40 or/34-39 (7634123)

41 33 and 40 (2554)

42 case report/ or case reports/ or case report.ti. (5016554)

43 41 not 42 (2537)

44 conference abstract.pt. (4326957)

45 43 not 44 (2221)

46 limit 45 to english language (1941)

47 remove duplicates from 46 (1153)

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Appendix 4. *Search strategy and results.*

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