

The Efficacy and Safety of HoLEP for Benign Prostatic Hyperplasia With Large Volume: A Systematic Review and Meta-Analysis

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Abstract

This meta-analysis was to evaluate the efficacy and safety of holmium laser enucleation of prostate (HoLEP) in the treatment of benign prostatic hyperplasia (BPH) with large volume. PubMed, Embase, and Cochrane Library databases (until March 2022) were used to search related randomized controlled trials. A total of 11 studies including 1,258 patients were involved. HoLEP could significantly decrease the length of hospital stay and accelerate recovery. In subanalysis, HoLEP had better perioperative outcomes than bipolar transurethral resection of the prostate (B-TURP) and bipolar transurethral enucleation of the prostate (BPEP). The improvement in operative time and enucleation time was better in thulium laser enucleation of the prostate (ThuLEP) than HoLEP. In the follow-up period, the HoLEP decreased post-void residual urine (PVR) in short-term intervals and improved patients' maximum flow rate (Q_{max}) and prostate-specific antigen (PSA) in mid- and long-term intervals. In subanalysis, HoLEP presented significant improvements in Q_{max}, PSA, and quality of life (QoL) than B-TURP, and HoLEP could also improve Q_{max} than ThuLEP after 6 months of surgery. The HoLEP reduced the risk of postoperative bleeding compared with other surgeries in safety. In our study, we confirmed the advantages of HoLEP in treating BPH when the prostate size was larger than 80 mL, which indicated that HoLEP could be the best choice for treatment of large volume of prostate.

Keywords

HoLEP, BPH, B-TURP, BPEP, ThuLEP, randomized controlled trials, meta-analysis

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Introduction

The incidence rate of benign prostatic hyperplasia (BPH) is higher in middle-aged and elderly men. Its lower urinary tract symptoms (LUTS) seriously affect the quality of life in patients, especially for those with a prostate volume larger than 80 mL (M. W. Zhang et al., 2017). The LUTS is also strongly associated with sexual function (Rosen et al., 2003). For patients with BPH, medical treatment may be the first-line treatment, such as tamsulosin and finasteride; when medical treatment is ineffective or the LUTS are not relieved, surgical treatment may be the preferred method (Gratzke et al., 2015).

Transurethral resection of the prostate (TURP) used to be the standard treatment for benign prostatic hyperplasia. The effects of this technique are limited by the volume of prostate (Oelke et al., 2012; Rieken & Bachmann, 2014). Various methods were later developed to manage large volumes of the prostate with better outcomes (Office, 2021). The bipolar transurethral resection of the prostate (B-TURP) and bipolar transurethral enucleation of the prostate (BPEP) showed lower perioperative morbidity and favorable mid- to long-term efficacy (Office, 2021). With the development of the laser technique, the holmium laser technique was used to treat patients with BPH without limitation of prostate size and



also presented better security and relatively fewer complications than TURP (Naspro et al., 2017; Sun et al., 2018; Zhong et al., 2019). The thulium laser enucleation of the prostate (ThuLEP) and greenlight laser photoselective vapo-enucleation of the prostate (GLPVEP) also played important roles in the treatment of BPH (Office, 2021). These techniques were also widely used with less bleeding and better excision when the prostate volume is greater than 80 mL. The guideline pointed out the therapeutic role of holmium laser enucleation of the prostate (HoLEP) in large prostate (Office, 2021), there was still a lack of strong evidence on the advantages of HoLEP in treating a large volume of prostate.

In this systematic review and meta-analysis, we assessed the efficacy and safety of HoLEP in treating a large volume of prostate from all published randomized controlled trials (RCTs).

Method

Search Strategy

The PRISMA guideline was applied to our study (Page et al., 2021), and we searched PubMed (until March 2022), Embase (until to March 2022), and Cochrane Library databases (until March 2022) to evaluate the efficacy and safety of HoLEP in treating patients with LUTS when the volume of the prostate was more than 80 mL, using related search terms including holmium laser, prostatectomy, enucleation, BPH, LUTS, and RCTs. This study only included published articles and had no restrictions on the language of the articles. All included studies were reviewed by different authors to confirm the availability and identify additional relevant articles.

Inclusion Criteria

The included criterion was as follows: (1) Patient: The volume of the prostate was more than 80 mL, 80cc; (2) intervention: The patients in the trial group were treated with HoLEP; (3) comparator: The patients in the control

group were treated with B-TURP, bipolar transurethral resection of the prostate (BPRP), ThuLEP, and GLPVEP; (4) outcome: The study provided accurate data, including perioperative data (operative time, enucleation time et al.), postoperative data (international prostate symptom score [IPSS], maximum flow rate [Qmax], etc.), and complication (bladder injury, bladder neck contracture et al.); and (5) study: All studies were RCTs. The related detail of inclusion criteria was summarized in Table 1. Compared with retrospective studies, the RCTs had stricter inclusion and exclusion criteria. If the same group of participants was studied by one group of researchers in different years, all studies were included.

Quality Assessment

Cochrane collaborations revised risk-of-bias tool for randomized trials (RoB 2) was used to evaluate the quality of all included RCTs (Sterne et al., 2019). Domains recorded included randomization process, deviations from the intended outcomes, missing outcome data, measurement of the outcome, and selection of the reported result. The accompanying manual provided by Cochrane provided guidance for determining the risk of bias in each domain. Included papers were rated "high risk," "low risk," or "some concerns" across five domains. The different opinions of classification were solved by discussion among all authors. The included studies were evaluated by two independent authors, and after verification, the risk of bias was finally determined.

Data Extraction

A series of valuable information was collected from all included studies: (1) study type and country; (2) the name of the first author; (3) publication time; (4) sample size; (5) eligibility criteria, and excluded criteria, interventions, postoperative follow-up period, date of study; and (6) perioperative data including operation time, enucleation time, morcellation time, hemoglobin decrease, catheterization time and length of hospital stay. The

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Table 1. Search Strategy According to Populations, Interventions, Comparators, Outcomes, and Study Designs (PICOS).

Items	Population	Intervention	Comparator	Outcomes	Study design
Inclusion criteria	The size of prostate was more than 80 mL, 80cc; International prostate symptom score (IPSS) > 1; Quality of life (QOL) score ≥ 3; Peak flow rate (Qmax) < 15 mL/sec; Patients with acute urine retention secondary to BPH who failed trial of voiding.	HoLEP	B-TURP BPEP GLPVEP ThuLEP	Perioperative data (operative time, enucleation time, morcellation time, hemoglobin decrease, catheterization time and length of hospital stay), postoperative data (Qmax, IPSS, PVR, PSA, QoL and IIEF-5) and complication (bladder injury, bladder neck contracture, postoperative bleeding, orchitis, retention, stress urinary incontinence, urethral stricture, urinary tract infection and urge urinary incontinence)	Randomized Controlled Trials
Exclusion criteria	The average size of prostate was less than 80 mL, 80 cc; International prostate symptom score (IPSS) < 1; Quality of life (QOL) score < 3; Peak flow rate (Qmax) > 15 mL/s;	Not performed	Not performed	Qualitative outcomes such as patient feelings; inadequate indicators;	Letters, comments, reviews, qualitative studies

Note. BPH = benign prostatic hyperplasia; HoLEP = holmium laser enucleation of prostate; B-TURP = bipolar transurethral resection of prostate; BPEP = bipolar transurethral enucleation of the prostate; GLPVEP = greenlight laser photoselective vapo-enucleation of the prostate; ThuLEP = thulium laser enucleation of the prostate; PVR = post-void residual urine; PSA = prostate-specific antigen; IIEF-5 = international index of erectile function-5.

postoperative indexes were also evaluated, including IPSS, Qmax, post-void residual urine (PVR), quality of life (QoL) score, prostate-specific antigen (PSA) at 1-, 3-, 12-, 24-, and 36-month intervals; and the postoperative complication was also collected. This study does not need ethical approval because it is a retrospective analysis of existing studies.

Statistical and Meta-Analysis

We analyzed the data of this data by Review Manager software (RevMan, version 5.4.0, Cochrane Collaboration; Cumpston et al., 2019). The continuous data were analyzed by mean difference (MD), and the dichotomous data were evaluated by odds ratio (OR) with 95% confidence interval (95% CI; DerSimonian & Laird, 2015). If the p value for the I^2 statistic was higher than .05, the study was deemed to be homogeneous as a fixed-effects model was applied; by contraries, the random-effects model was used. If p value was less than .05, the results were considered to indicate statistical significance.

Result

Selection and Characteristics of Included Studies

A total of 449 articles were searched in the database, and there were only 57 articles left after reading the title and abstract. By reviewing the full-text articles and qualitative synthesis, 11 studies were finally included in our

meta-analysis (Elshal et al., 2020; Fuschi et al., 2021; Ghobrial et al., 2021; Guo, 2020; Habib et al., 2020, 2022; Higazy et al., 2021; Kuntz et al., 2004, 2008; Kuntz & Lehrich, 2002; J. Zhang et al., 2020). The details of included studies were presented in Figure 1, and the characteristics and baseline are summarized in Table 2.

The Quality of Eligible Studies

The included studies were all RCTs. One study offered less useful data, so the quality of the study was “high risk.” The detail was presented in Figure 2. Three articles that were three different follow-up times of one RCT were all included. If two intervention groups were set in article, we regarded the article as two individual RCTs. The detail was summarized in the Table 2.

Intraoperative and Perioperative Outcomes

Operative Time, Enucleation Time, and Morcellation Time. Operative time: the forest plots identified a mean difference (MD) of -2.83 and 95% confidence interval (CI) of -13.28 to 7.63 ($p = .60$; Figure 3A). Enucleation time: the forest plots identified a MD of 0.92 and 95% CI of -4.67 to 6.51 ($p = .75$; Figure 3B). Morcellation time: the forest plots identified a MD of 0.26 and 95% CI of -1.30 to 1.83 ($p = .74$; Figure 3C). The results suggested that that the HoLEP was not inferior in operative time, enucleation time and morcellation time than other surgeries.

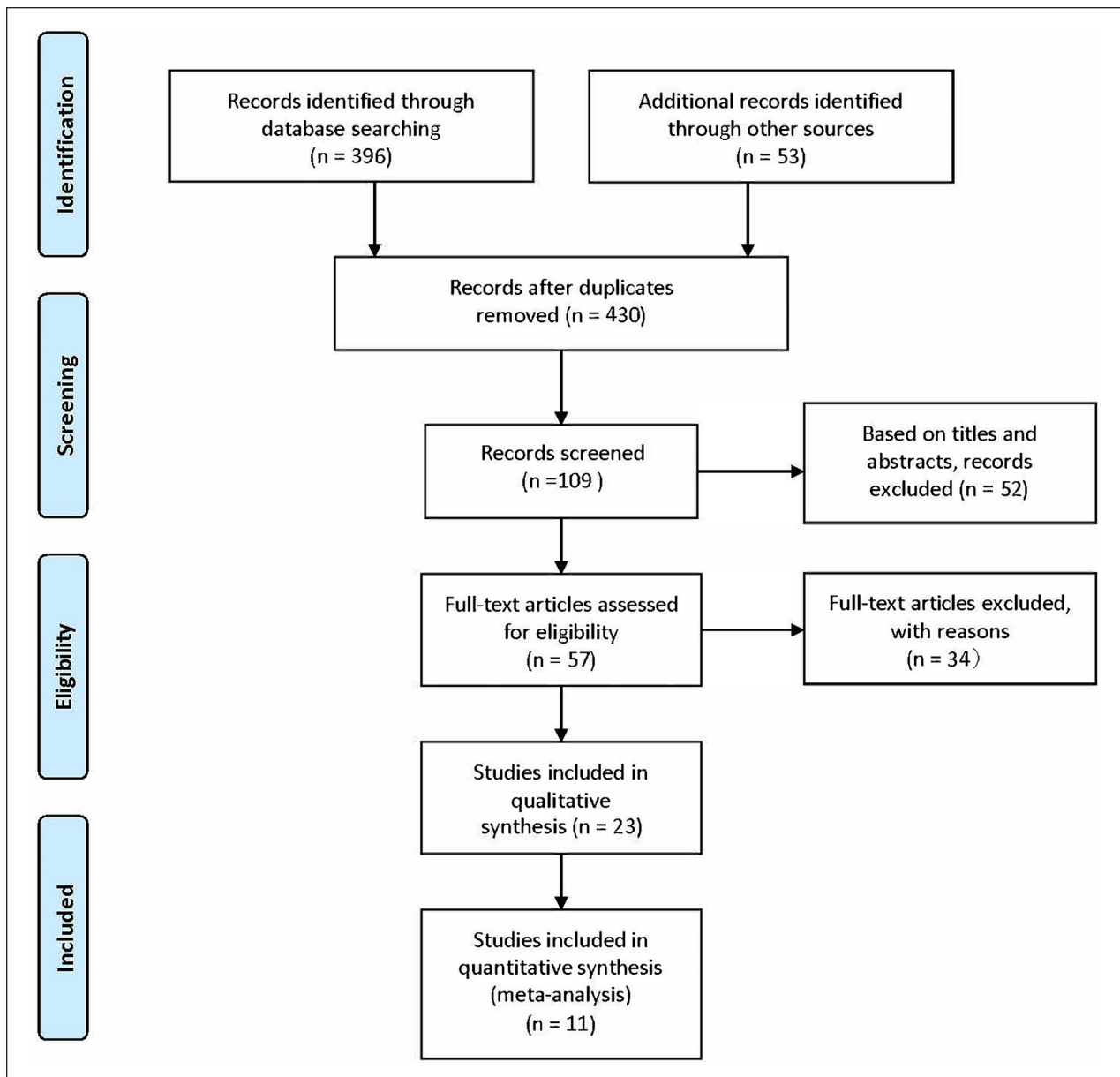


Figure 1. Flowchart of the Study Selection Process.

Hemoglobin Decrease. The HoLEP presented less perioperative hemoglobin decrease compared with other surgeries. (MD, -0.34 ; 95%CI, $[-0.58, -0.10]$; $p = .006$; Figure 3D).

Catheterization Time. Catheterization time between HoLEP and other surgeries was not statistically significant (MD, -1.28 ; 95%CI, $[-2.93, 0.37]$; $p = .13$; Figure 3E).

Length of Hospital Stay. Thirteen articles with 1,258 patients were absorbed in this group. The random-effects

model was applied for analysis because the trials were not homogeneous. The results presented that there was a significant difference in hospitalization time between the HoLEP and other surgical methods (MD, -1.16 ; 95% CI, -1.89 to -0.43 ; $p = .002$), indicating that the HoLEP could significantly accelerate the recovery.

Sub-Analysis of Intraoperative and Perioperative Outcomes

HoLEP and B-TURP. The HoLEP presented better outcomes in operative time (MD, -10.67 ; 95%CI, $[-17.53,$

Table 2. Study and Patient Characteristics.

Study (years)	Treatment	Age (year)	Patients	Qmax baseline	IPSS baseline	PVR (mL)	QoL data	PSA baseline	Prostate volume	Laser power	Postoperative follow-up period
Fuschi et al. (2021)	HoLEP MISP	68.21 ± 6.09 66.41 ± 7.49	42 68	7.05 ± 1.88 7.19 ± 1.28	24.15 ± 3 23.9 ± 1.85	130.13 ± 33.53 128.64 ± 26.49	3.89 ± 0.83 3.84 ± 0.91	5.64 ± 3.27 5.47 ± 2.97	142.21 ± 30.14 146.94 ± 30.67	100W NA	3, 6, 12, and 24 months
J. Zhang et al. (2020)	HoLEP ThuLEP	71.8 ± 3.9 72.7 ± 3.1	54 53	7.1 ± 2.8 6.6 ± 2.3	23.9 ± 3.9 22.8 ± 3.7	172.7 ± 39.4 165.5 ± 46.2	5 ± 0.74 5 ± 0.74	5.09 ± 1.49 4.96 ± 1.40	93.0 ± 7.2 91.8 ± 6.9	90W 120W	1, 3, 6, 12, and 18 months
Kuntz et al. (2004, 2008), Kuntz & Lehnrich, (2002)	HoLEP OP	69.2 ± 8.4 71.2 ± 8.3	60 60	3.8 ± 3.6 3.6 ± 3.8	NA NA	280 ± 273 292 ± 191	NA NA	NA NA	114.6 ± 21.6 113.0 ± 19.2	80W NA	1, 3, 6, 12, 18, and 24 months
Habib et al. (2020)	HoLEP BPPEP	66.81 ± 7.77 67.48 ± 6.46	33 31	0 (0–13.9) 2.5(0–10)	25.24 ± 4.87 25.35 ± 4.17	135.37 ± 46.83 159.41 ± 63.16	5 (3–6) 5 (4–6)	6.5 (0.71–33) 6.2 (18.75)	125 (80–270) 102 (80–243)	100W NA	12 months
Higazy et al. (2021)	HoLEP BPPEP	66.17 ± 7.22 67.72 ± 6.48	54 53	3.3 ± 3.4 3.9 ± 3.3	28.8 ± 2.1 28.9 ± 2.1	160 ± 52.8 168.5 ± 55.8	4.37 ± 0.49 4.43 ± 0.5	7.6 ± 2.5 6.2 ± 3.2	135.19 ± 34.84 125.0 ± 26.93	100W NA	1, 3, and 12 months
Habib et al. (2022)	HoLEP B-TURP	66.77 ± 6.78 65.47 ± 7.98	57 55	7.42 ± 3.14 6.88 ± 2.19	27.01 ± 4.98 28.32 ± 3.78	161.15 ± 119.9 130.46 ± 70.83	5 (1.48) 5 (1.48)	8.51 ± 6.25 6.7 ± 4.82	128.66 ± 47.61 119.12 ± 32.66	NA NA	36 months
Elsal et al. (2020) ^a	HoLEP GLPVEP	66.2 ± 7 64.5 ± 6	60 60	7 ± 1 9 ± 1	25.8 ± 1.2 27 ± 1	44 ± 12 44 ± 9	4.8 ± 0.3 5 ± 0.2	8.2 ± 4.1 8.3 ± 3.6	103 ± 25 107 ± 21	100W 180W	1, 4, 12, 24, and 36 months
Elsal et al. (2020) ^b	HoLEP B-TURP	66.2 ± 7 66.1 ± 7	60 62	7 ± 1 8.8 ± 0.5	25.8 ± 1.2 24.9 ± 1.1	44 ± 12 71 ± 14	4.8 ± 0.3 4.6 ± 0.4	8.2 ± 4.1 8.7 ± 13.8	103 ± 25 106 ± 23	100W NA	1, 4, 12, 24, and 36 months
Guo (2020)	HoLEP BPPEP	74.2 ± 6.8 75.5 ± 6.6	84 96	6.1 ± 2.1 5.6 ± 1.8	28.2 ± 1.7 28.4 ± 1.6	NA NA	5.21 ± 0.68 5.20 ± 0.66	NA NA	95.2 ± 13.7 94.8 ± 13.3	NA NA	12 months
Ghobrial et al. (2021) ^a	HoLEP ThuLEP	67.7 ± 6.9 67.5 ± 6.1	52 52	NA NA	NA NA	NA NA	NA NA	NA NA	>80 >80	NA NA	6 months
Ghobrial et al. (2021) ^b	HoLEP BPPEP	67.7 ± 6.9 67.5 ± 6.7	52 51	NA NA	NA NA	NA NA	NA NA	NA NA	>80 >80	NA NA	6 months

Note. Data are presented as median (range) or mean SD ± (range) as appropriate. Qmax = maximum urinary flow rate; IPSS = International Prostate Symptom Score; PVR = post-void residual urine volume; PSA = prostate-specific antigen; HoLEP = Holmium laser enucleation of prostate; MISP = minimally invasive simple prostatectomy; ThuLEP = Thulium laser enucleation of prostate; OP = open prostatectomy; BPPEP = bipolar plasmakinetic enucleation of prostate; B-TURP = bipolar transurethral resection of prostate; GLPVEP = greenlight laser photoselective vapo-enucleation of the prostate; QoL = Quality of life; RCT = Randomized controlled trial; NA = not available.

^{a, b} Referred to two different RCTs divided from one study with triple interventions.

	D1	D2	D3	D4	D5	Overall
Elshal 2020 a	+	+	+	+	+	+
Elshal 2020 b	+	+	+	+	+	+
Fuschi 2020	+	+	+	+	+	+
Ghobrial 2021 a	+	+	+	?	?	?
Ghobrial 2021 b	+	+	+	?	?	?
Guo 2020	+	+	+	?	+	?
Habib 2020	+	+	+	+	+	+
Habib 2022	+	+	+	+	+	+
Higazy 2021	+	+	+	+	+	+
Kuntz 2002	+	+	+	+	+	+
Kuntz 2004	+	+	+	+	+	+
Kuntz 2008	+	+	+	+	+	+
Zhang 2020	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process
D2: Bias due to deviations from intended intervention
D3: Bias due to missing outcomes data
D4: Bias in measurement of the outcome
D5: Bias of selection of the reported result




Judgement:
 Low
 Some concerns
 High

Figure 2. The Summary of Risk of Bias.

-3.82]; $p = .002$), perioperative hemoglobin decrease (MD, -1.03; 95%CI, [-1.24, -0.83]; $p < .0001$), catheterization time (MD, -1.06; 95%CI, [-1.30, -0.81]; $p < .00001$) and hospitalization time (MD, -0.84; 95%CI, [-1.03, -0.65]; $p < .00001$) (Supplemental Figure 1). These results meant the HoLEP was better choice than B-TURP in resection of large prostate.

HoLEP and BPEP. In these two groups, significant differences were observed in operative time (MD, -14.41; 95%CI, [-24.23, -4.60]; $p = .004$), enucleation time (MD, -3.65; 95%CI, [-7.05, -0.25]; $p = .04$), perioperative hemoglobin decrease (MD, -0.20; 95%CI, [-0.24, -0.16]; $p < .00001$), catheterization time (MD, -0.52; 95%CI, [-0.77, -0.27]; $p < .0001$) and hospitalization time (MD, -0.30; 95%CI, [-0.57, -0.03]; $p = .03$), suggesting that the HoLEP had better outcomes than BEPE (Figure 4).

HoLEP and ThuLEP. The ThuLEP had less operative time (MD 7.19; 95%CI, [4.61, 9.77], $p < .00001$) and less enucleation time (MD, 5.13; 95%CI, [2.63, 7.62]; $p < .0001$) than HoLEP (Figure 5A and B), which was not differences

in perioperative hemoglobin decrease, catheterization time and hospitalization time (Figure 5C–E). These results meant the ThuLEP saved intraoperation time with similar perioperative outcomes.

Postoperative Outcomes

Short-Term Follow-Up. The follow-up after 1 month of surgery identified the HoLEP had improvement in PVR (MD, -7.81; 95%CI, [-12.43, -3.20]; $p = .0009$; Figure 6C). And the outcomes were not different in Qmax, IPSS, PVR, PSA, QoL, and IIEF-5 after 3 to 4 months and 6 months follow-up between the two groups (Supplemental Figures 2 and 3).

Mid-Term Follow-Up. After 12 months follow-up, the patients treated with HoLEP had better Qmax (MD, 2.14; 95%CI, [0.33, 3.94]; $p = .02$; Figure 7). The patients treated with HoLEP were more satisfied to their postoperative life (12 month: MD, -0.10; 95%CI, [-0.18, -0.01]; $p = .04$; 12-24 months: MD, -0.32; 95%CI, [-0.58, -0.05]; $p = .02$; Figure 7 and Supplemental Figure 4).

Long-Term Follow-Up. After 36 months follow-up, the patients treated with HoLEP had significantly better Qmax (MD, 5.11; 95%CI, [3.22, 7.01]; $p < .00001$) and PSA (MD, -2.11; 95%CI, [-3.07, -1.15]; $p < .0001$; Figure 8A, D).

Subanalysis of Postoperative Outcomes

HoLEP and B-TURP. Compared with B-TURP, patients treated with HoLEP had better prognosis in Qmax (MD, 7.18; 95%CI, [6.34, 8.01]; $p < .00001$), PSA (MD, -1.65; 95%CI, [-2.76, 0.55]; $p = .003$), and QoL (MD, -0.13; 95%CI, [-0.25, -0.01]; $p = .04$) after the 36th month of surgery (Supplemental Figure 5). The HoLEP treatment identified better prognosis in long-term follow-up than B-TURP.

HoLEP and BPEP. The outcomes were not different in 12th-month follow-up between HoLEP and BPEP (Supplemental Figure 6). The advantage of HoLEP should be confirmed in short- and long-term follow-up by more large-volume studies in the future.

HoLEP and ThuLEP. The HoLEP could improve Qmax after 6 months follow-up (MD, 2.73; 95%CI, [1.06, 4.40]; $p = .001$) (Supplemental Figure 7). Two groups were not compared in mid-term and long-term follow-up, which should be analyzed in the future.

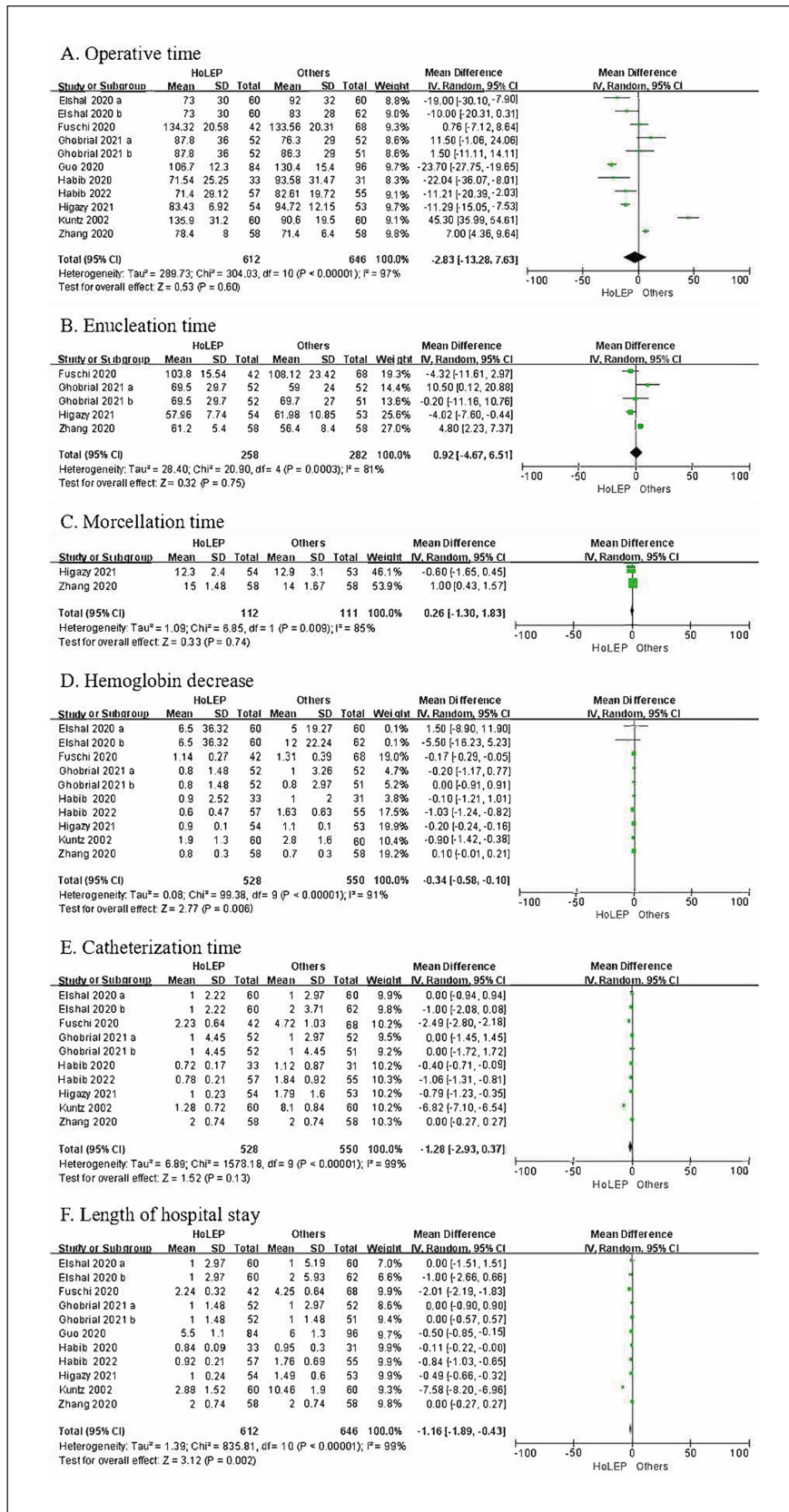
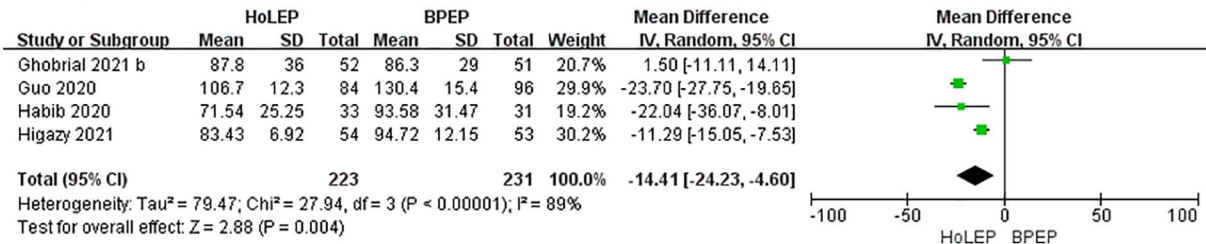
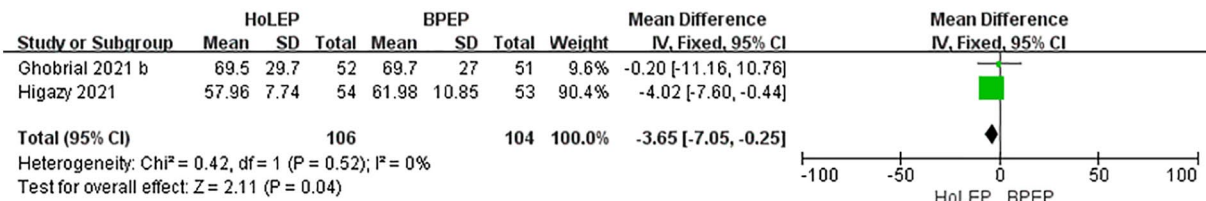


Figure 3. Forest Plots Showing the Result of (A) Operation Time, (B) Enucleation Time, (C) Morcellation Time, (D) Hemoglobin Decrease, (E) Catheterization Time, and (F) Length of Hospital Stay.
Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom.

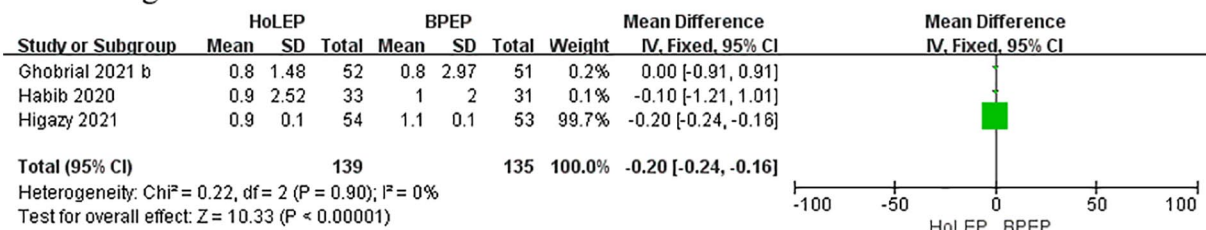
A. Operative time



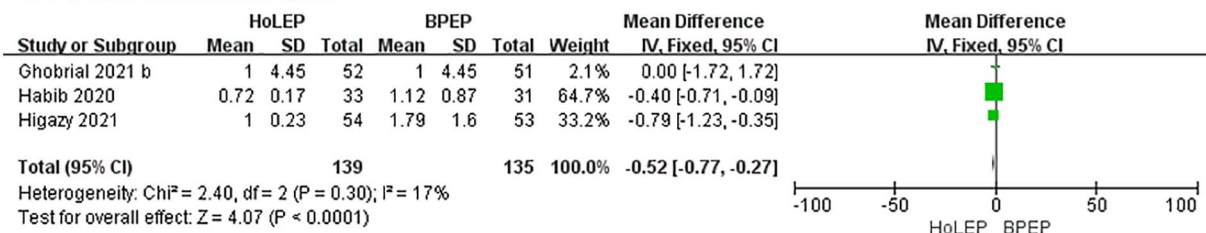
B. Enucleation time



C. Hemoglobin decrease



D. Catheterization time



E. Length of hospital stay

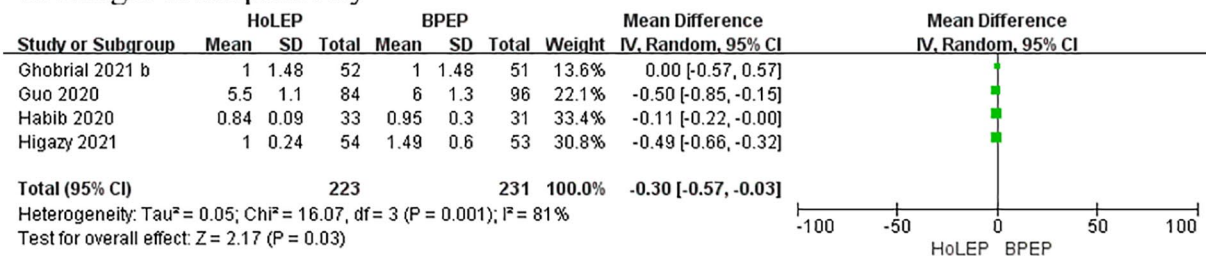


Figure 4. Forest Plot and Meta-Analysis of Perioperative Outcomes Between HoLEP and BPEP: (A) Operation Time, (B) Enucleation Time, (C) Hemoglobin Decrease, (D) Catheterization Time, and (E) Length of Hospital Stay.

Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; HoLEP = holmium laser enucleation of prostate; BPEP = bipolar transurethral enucleation of the prostate.

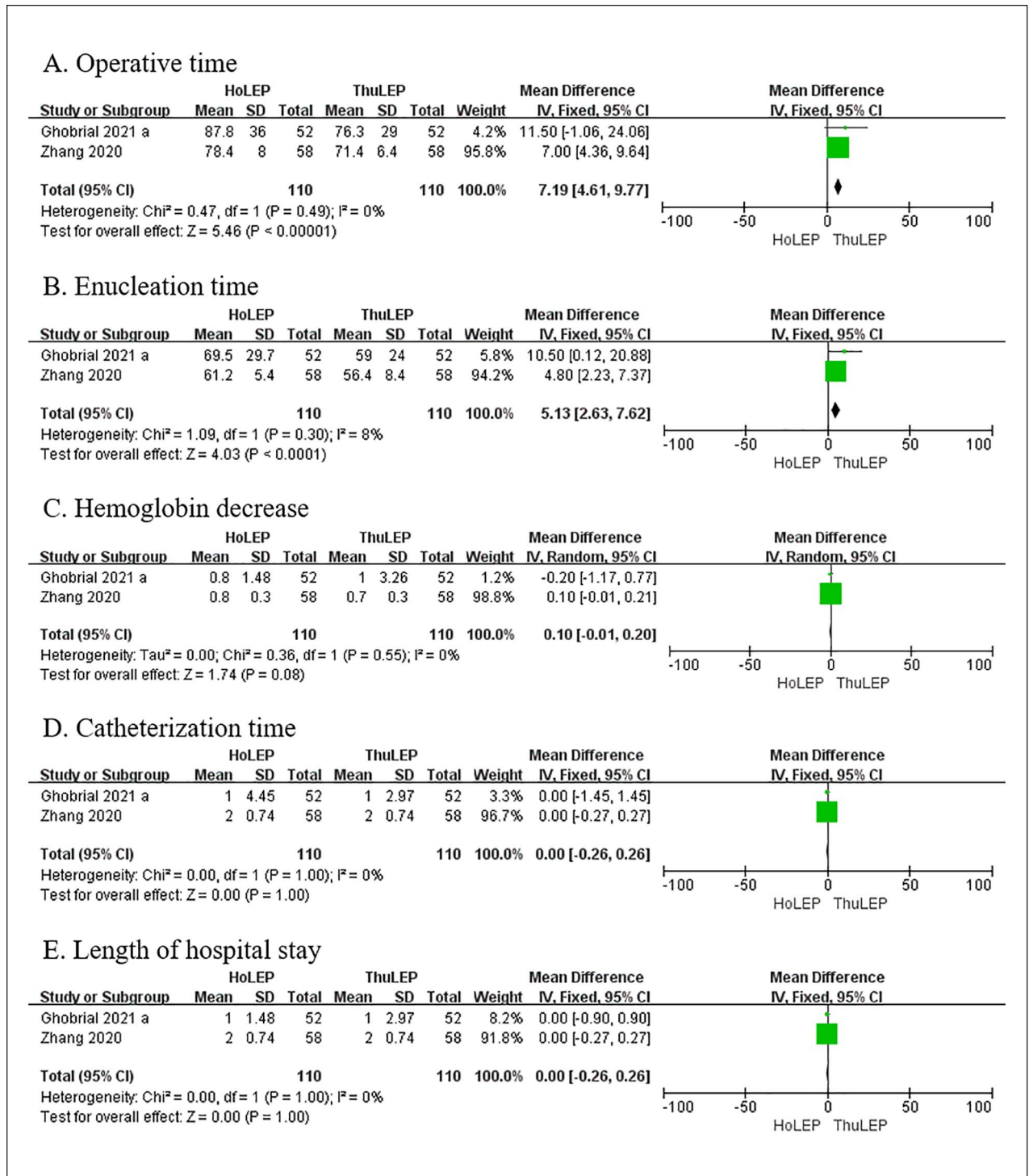


Figure 5. Forest Plot and Meta-Analysis of Perioperative Outcomes Between HoLEP and ThuLEP: (A) Operation Time, (B) Enucleation Time, (C) Hemoglobin Decrease, (D) Catheterization Time, and (E) Length of Hospital Stay.
 Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; HoLEP = holmium laser enucleation of prostate; ThuLEP = thulium laser enucleation of the prostate.

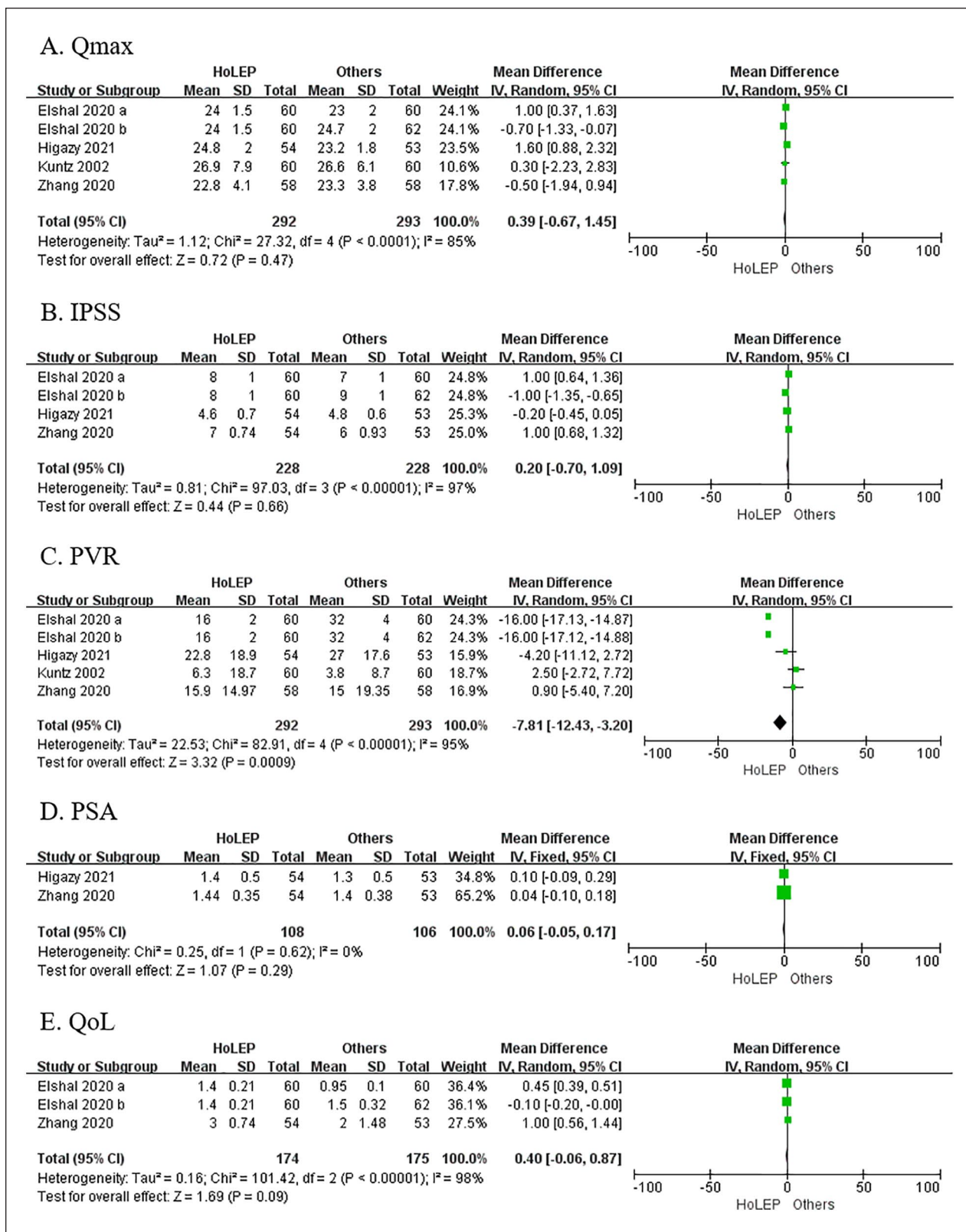


Figure 6. Forest Plots and Meta-Analysis of Postoperative Outcomes After 1 Month of Surgery: (A) Qmax, (B) IPSS, (C) PVR, (D) PSA, and (E) QoL.

Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; Qmax = maximum urinary flow rate; IPSS = International Prostate Symptom Score; PVR = post-void residual urine volume; PSA = prostate-specific antigen; QoL = quality of life.

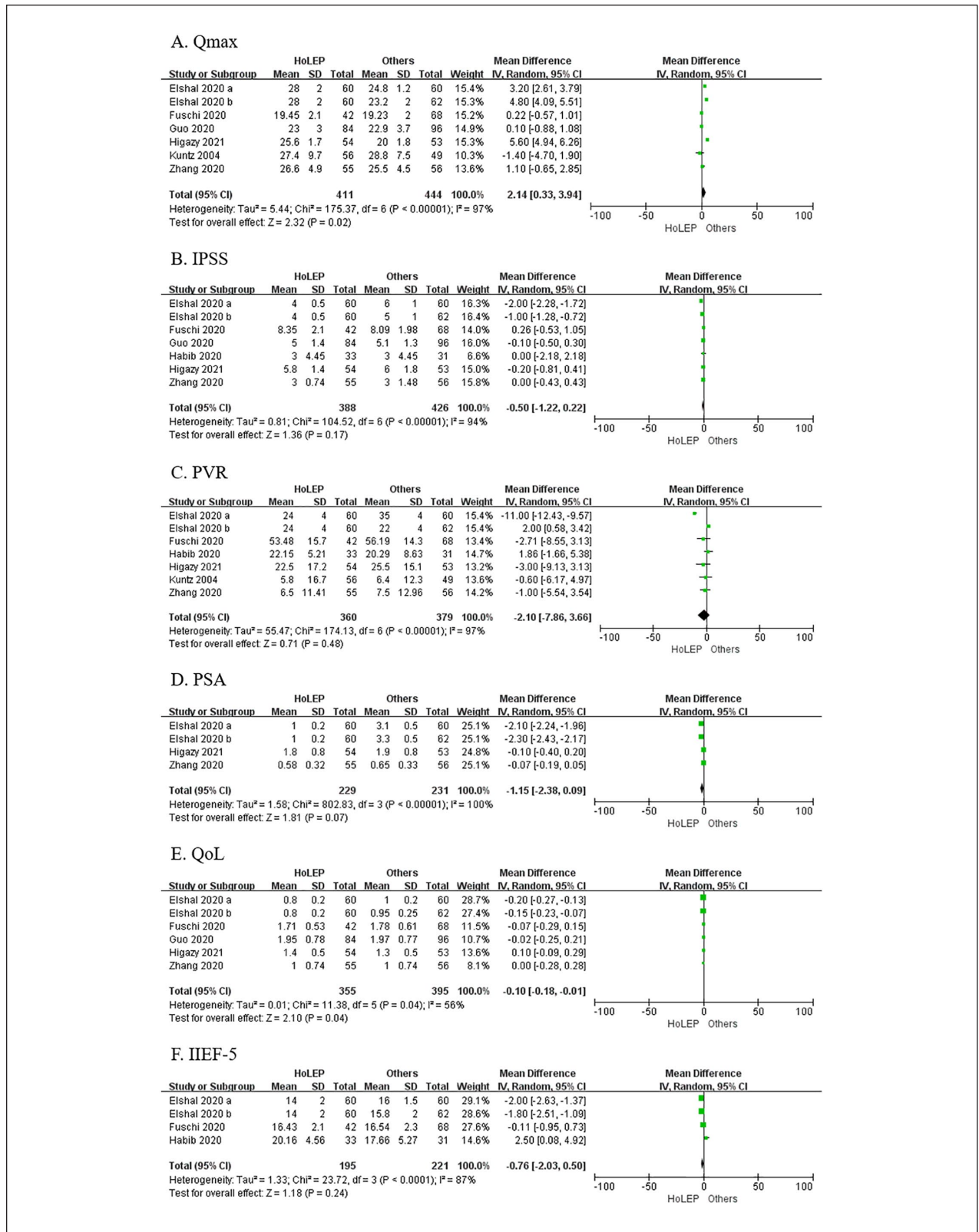
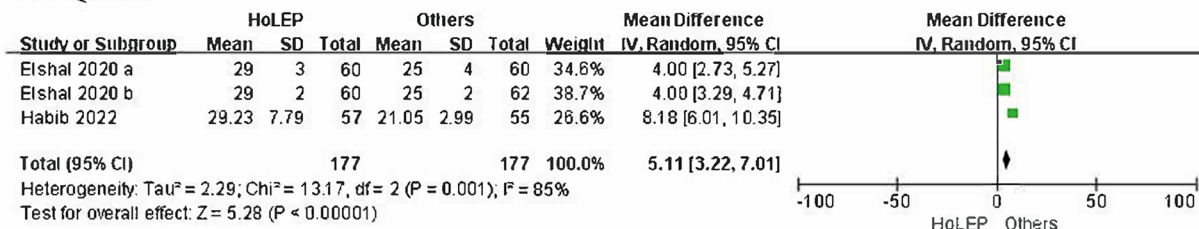
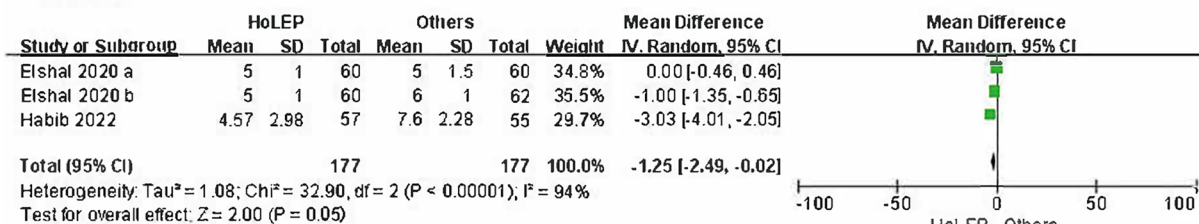


Figure 7. Forest Plots and Meta-Analysis of Postoperative Outcomes After 12 Months of Surgery (A) Qmax, (B) IPSS, (C) PVR, (D) PSA (E) QoL and (F) IIEF-5.
Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; Qmax = maximum urinary flow rate; IPSS = International Prostate Symptom Score; PVR = post-void residual urine volume; PSA = prostate-specific antigen; QoL = quality of life; IIEF-5 = international index of erectile function-5.

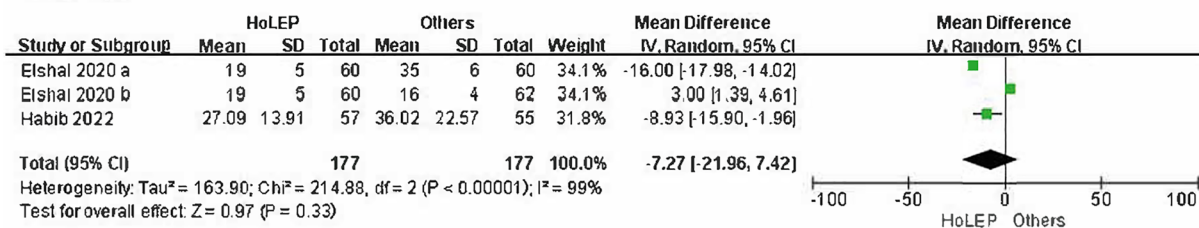
A. Qmax



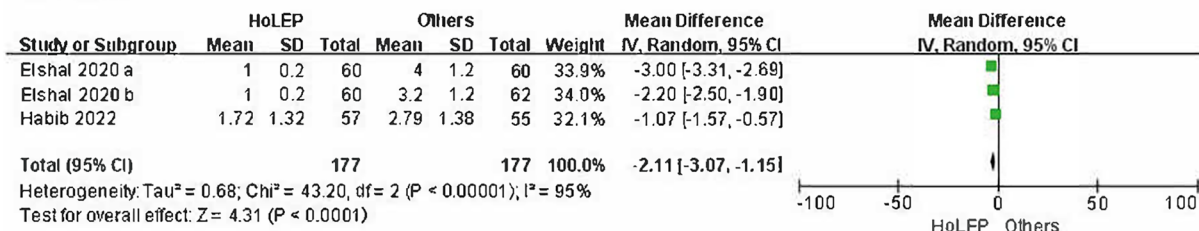
B. IPSS



C. PVR



D. PSA



E. QoL

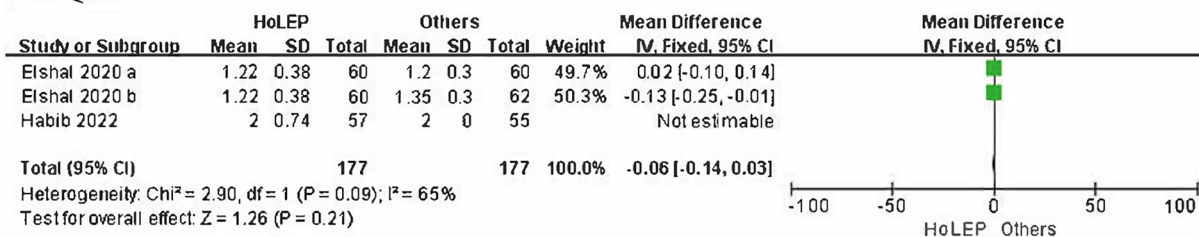


Figure 8. Forest Plots and Meta-Analysis of Postoperative Outcomes After 36 Months of Surgery: (A) Qmax, (B) IPSS, (C) PVR, (D) PSA, and (E) QoL.

Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; Qmax = maximum urinary flow rate; IPSS = International Prostate Symptom Score; PVR = post-void residual urine volume; PSA = prostate-specific antigen; QoL = quality of life.

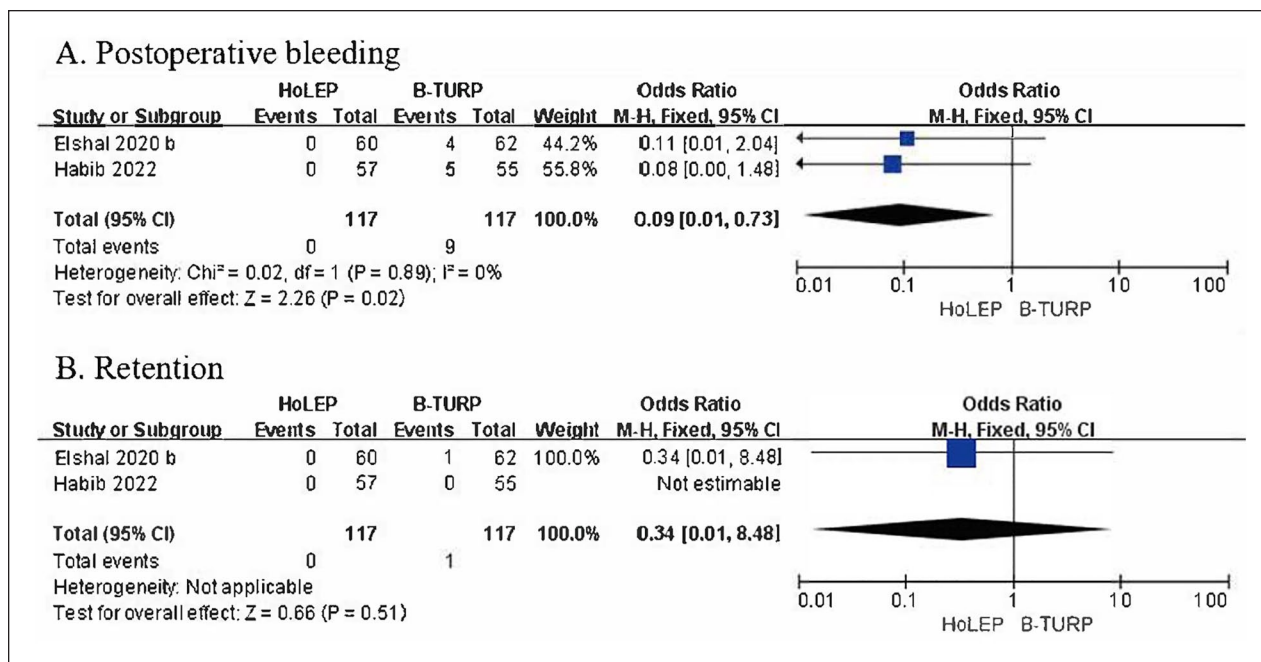


Figure 9. Forest Plots and Meta-Analysis of Postoperative Complication Between HoLEP and B-TURP: (A) Postoperative Bleeding and (B) Retention.

Note. M-H = Mantel-Haenszel; CI = confidence interval; df = degrees of freedom; HoLEP = holmium laser enucleation of prostate; B-TURP = bipolar transurethral resection of prostate.

Postoperative Complication

We analyzed the postoperative complications in bladder injury, bladder neck contracture, bleeding, orchitis, retention, stress urinary incontinence (SUI), urethral stricture, urinary tract infection (UTI), and urge urinary incontinence (UUI), and the HoLEP had less risk of postoperative bleeding (MD, 0.29; 95%CI, [0.12, 0.73]; $p = .008$; Supplemental Figure 8C).

HoLEP and B-TURP. The HoLEP had an advantage in hemostasis with the laser technique (OR, 0.09; 95%CI, [0.01, 0.73]; $p = .02$), and had similar outcomes in retention, which was presented in Figure 9.

HoLEP and BPEP. There were no significant differences between the two groups in postoperative complications (Supplemental Figure 9).

HoLEP and ThuLEP. The HoLEP has not observed less adverse events compared with ThuLEP in postoperative complications (Supplemental Figure 10).

Discussion

BPH is one of the most common diseases affecting the quality of life, especially in mid-aged and elderly men

(Chughtai et al., 2016). LUTS is closely related to aging, in which moderate and severe LUTS have an increased risk of major adverse cardiac events (Kupelian et al., 2006; Martin et al., 2011). The management of LUTS may have an important impact on future changes in population structure, especially in aging countries.

To be specific, the main treatments for LUTS are conservative methods such as observation and medical treatment, and surgical treatment is still treatment for patients with ineffective conservative treatment or aggravating symptoms in which TURP was regarded as the standard treatment for patients (Feng et al., 2016). The latest guideline for BPH pointed out that the upper limitation for TURP was suggested as 80 mL and the incidence of complications increased significantly with the increase in surgical duration (Office, 2021; Riedinger et al., 2019). But the surgical method of a large volume of prostate (>80 mL) was not clear based on limited RCTs.

With the development of the laser technique, the holmium laser with a wave length of 2,140 nm could increase the ability of adequate hemostasia with limited tissue coagulation and necrosis (Gilling et al., 1995). HoLEP has been approved for BPH patients with moderate to severe LUTS as an alternative to TURP (Kuebker & Miller, 2017; Nair et al., 2016; Office, 2021). Many studies have proved that HoLEP was favorable short-term efficacy in Qmax and IPSS, and long-term efficacy was

also significantly better compared with TURP (Cornu et al., 2015; Gilling et al., 2012; Yin et al., 2013; X. Zhang et al., 2016; Y. Zhang et al., 2019). For prostate less than 80 mL, the efficacy of IPSS and Qmax was similar between HoLEP with B-TURP, but HoLEP identified less catheterization time, hospital stay, and lower risk of bleeding (Chen et al., 2013). In our analysis, compared with B-TURP, HoLEP also presented better outcomes in catheterization time, hospital stay, and risk of bleeding, and the HoLEP could significantly improve Qmax, PSA, and QoL during long-term follow-up in a large volume of prostate. These results indicated that the patients who accepted HoLEP had a better prognosis in long term, compared with B-TURP. A novel form of enucleation of the prostate named as BPEP was described based on B-TURP, which appeared to better catheterization time, hospital stay, and lower risk of bleeding (Samir et al., 2019). A previous study demonstrated that HoLEP had a shorter operative time than plasmakinetic enucleation (Neill et al., 2006). The latest study reported different results that the HoLEP had longer operative time and hospital stay than the plasmakinetic enucleation for prostate more than 60 mL (Patard et al., 2021). In our result, the HoLEP appeared better perioperative efficacy in less operative time, catheterization time, and faster recovery in patients with a volume of prostate more than 80 mL. For the medium-time follow-up, the HoLEP did not appear different than BPEP. For less experienced surgeons, the HoLEP had a longer learning curve and procedures, which could cause differential results (Elshal et al., 2017).

ThuLEP also had good tissue gasification and hemostasis by using 2013 mm wavelength. Compared with HoLEP, the ThuLEP could shorten hospital stays and reduce bleeding loss, which also appeared to better outcomes in the early postoperative period with regard to IPSS after the third month of the operation without selection of prostate size (Meng et al., 2022). For a large volume of prostate, ThuLEP shortens operative time and enucleation time. With the extension of follow-up time, Qmax increased significantly in HoLEP group patients during 6 months follow-up. The results concluded that HoLEP had better follow-up outcomes, and the other advantages of HoLEP should be confirmed in short- and long-term follow-up by more studies in the future.

In the treatment of BPH with prostate more than 80 mL, the HoLEP reduced blood loss and shortened the length of hospital stay compared with other surgical procedures in the perioperative period. The different postoperative function of the prostate was not observed during 6 months follow-up. HoLEP significantly improved Qmax and QoL in the medium postoperative period. We reported patients were all satisfied with postoperative

life regardless of different methods. After a 3-year follow-up, the HoLEP presented better Qmax and PSA than other surgical methods, which indicated that the HoLEP could be the best choice for treatment of a large volume of prostate.

The major complications were also performed including bladder injury, bladder neck contracture, postoperative bleeding, retention, urethral stricture, and others. The HoLEP presented less risk of postoperative bleeding. In the sub-analysis, the HoLEP appeared reliably safe compared with BPEP and ThuLEP, and the HoLEP reported better safety in hemostasis than B-TURP. The explanation was that holmium laser reduced the damage to surrounding tissues and vessels with more limited scope of the laser.

Some limitations need to be considered in our study. First, significant heterogeneity existed in some evaluation indexes, so we accepted the fix- and random-effects model in different analysis. Second, the difference between some surgical methods and HoLEP could not be analyzed accurately due to fewer included studies, and long-term follow-up was scarce. We would focus on the future publication in different surgical procedure to complete our conclusion. Finally, the result should be verified by further studies.

Conclusion

In our study, we confirmed the advantages of HoLEP in treating BPH in which the prostate size was larger than 80 mL. And in the subanalysis, the HoLEP also presented better efficacy and safety than BPEP, B-TURP, and ThuLEP, which indicated the HoLEP could be the best choice in the treatment of a large volume of prostate. This result remained to be evaluated by further long-term follow-up and high-quality studies.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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