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Review Article

Role of Thulium Laser and Holmium Laser in the Surgical Treatment of Benign Prostatic Hyperplasia: A Systemic Review and Meta-Analysis

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Abstract

Background: Patients with benign prostatic hyperplasia are generally treated holmium laser enucleation of the prostate (HoLEP) and thulium laser enucleation of the prostate (ThuLEP). Therefore, it is important to analyze the several surgical procedures used for benign prostatic hyperplasia in terms of their role, effectiveness and safety.

Methods: We conducted a meta-analysis by searching databases of PubMed, Google Scholar, and Web of Science. Finally, we selected 10 papers including 2,456 patients treated with of thulium laser and holmium laser in the surgical treatment of benign prostatic hyperplasia. We did the analysis using RevMan 5.0 with the selected studies until 26 October 2023.

Results: ThuLEP resulted in a smaller reduction in haemoglobin (MD: -0.22, 95%CI -0.32 to -0.13, P<0.001) and a shorter hospital stay (MD: -0.29, 95%CI -0.38 to -0.20, P <0.001). During the postoperative follow-ups, only the IPSS (MD: -0.03; 95%CI -0.11 to -0.06; P 0.58) at the six-month showed statistically significant differences.

Conclusion: ThuLEP has greater security and faster growth than HoLEP.

Keywords: Benign prostatic hyperplasia; Holmium laser; Thulium laser; Treatment

Introduction

One of the most serious conditions affecting up to 50% of middle-aged and older men (intimately linked to ageing) is benign prostatic hyperplasia (BPH). Everywhere in the world, men over 50 years have varying degrees of BPH (1, 2). This is medically referred to as Lower urinary tract symptom (LUTS) associated with BPH, which can significantly reduce an aged patient's quality of life (1, 3). There are two main categories of current BPH treatment options: medication therapy and surgical intervention. When patients report with unsuccessful conservative treatment or poor remission of lower urinary tract symptoms (LUTS) after medication treatment, surgical surgery is essential (3). Therefore, standard treatment for the condition is still transurethral resection of the prostate (TURP) (1, 4). Until recently, open prostatectomy (OP) was recommended for prostates with volumes greater than 80 mL, whereas transurethral resection of the prostate

(TUR-P) was the preferred treatment for prostates with volumes less than 80 mL (5, 6). As laser technology has advanced quickly in recent years, particularly in enucleation, it has become a persistent threat to the "gold" standard of BPH surgical treatment.
Additionally, the earliest type of prostate enucleation, holmium laser enucleation of the prostate (HoLEP), was a minimally invasive, size-independent procedure. Compared to TURP, this has superior security and comparatively less difficulties. Gilling first presented the HoLEP in 1998, and it quickly gained popularity, especially in cases of high prostate volumes (7-9). The Holmium laser emits pulses of radiation with a wavelength of 2123 nm. Water readily absorbs it because of its wavelength, which is near to the tissue water absorption peak. Additionally, it might produce a steam bubble at the laser fiber's tip that facilitates mechanical dissection. A continuous wave of energy is transmitted by thulium lasers. Its wavelength, which is 2013 nm, is very near the water absorption peak. Both tissue gasification and hemostasis are positively impacted. Thulium laser enucleation of the prostate (ThuLEP) was first proposed in 2008 and has only recently gained some traction in the management of BPH (10–13). It has additional advantages, especially in terms of learning curve (14). Although the clinical effects of ThuLEP and HoLEP in the treatment of BPH have been mentioned in a number of clinical trials, no thorough analysis was done.
In order to assess these two enucleation techniques' efficacy and safety as well as to give more substantial evidence for clinical use, we did a meta-analysis of the available data.

Methods

Search strategy

Databases including PubMed, Google Scholar, and Web of Science have been utilized to locate relevant research that used the correct MeSH terminology up until October 26, 2023. "Benign prostatic hyperplasia" or "benign prostatic enlargement" or "BPH") AND ("holmium" or "thulium" or "HoLEP" or "ThuLEP" or "enucleation") were utilised as MeSH phrases or keywords with Boolean operators. According to PRISMA (15) and STROBE (16) criteria, this study was conducted.

Eligibility Criteria

Inclusion criteria

The PICOS concept (participants, intervention, control, outcome, and study type) was used to determine the inclusion criteria:
Type of Study: All randomized controlled trials (RCTs), Prospective, Retrospective observational are the most common study types. The studies' publishing dates have not been restricted.
Types of participants: people who have been diagnosed with BPH and do not have LUTS or any other systemic chronic or metabolic diseases. The BPH diagnosis criteria were based on the published guidelines of the urological society. No matter the age, gender, or nationality.
Original data, genotypic frequency information for both case and control samples, and odds ratios (ORs) with 95% confidence interval (CI) values were included in the research.

Exclusion criteria

Studies that did not meet the following requirements were not included in the meta-analysis such as a. Review articles, in vitro or animal study, case reports, conference abstracts were not included. b. Newcastle–Ottawa scale (NOS) score was less than 7. c. Jadad scale score was less than 3. d. Studies that did not provide allele frequencies or genotypic for samples, overlapping or duplicate studies. e. Studies published in other language than English.

Screening

Two authors (JW and SW) independently reviewed pertinent studies using the inclusion and exclusion criteria. The PRISMA guidelines were followed, and the PRISMA flow chart was used to display a selection of research based on their titles, abstracts, and full texts. Following communication with a third author (MW), the disagreement among the authors was resolved.

Quality assessment

In prospective and retrospective observational studies, the Newcastle-Ottawa (Questionnaire) Scale (NOS) was employed to assess study quality and quantify the likelihood of bias (17, 18). Quality assessments of the included studies were carried out by two reviewers (JW and SW), and any discrepancies were settled by discussion with the third author (MW). A score of > 7 stars on the quality rating system, which ranges from 0 to 10, indicates high-quality content. Jadad scale was utilised in Randomised Control Trials (RCT). The third (MW) author helped to settle differences after reviewers (JW and SW) conducted quality ratings of the listed studies. Randomization, blinding, withdrawals, and dropouts are the four main elements that make up the quality evaluation. A score of at least three stars (out of a possible five) on the quality rating system denotes high quality.

Data extraction

Each articles were carefully reviewed, and data was separately extracted by two researchers. The following outcome parameters were included: the length of hospital stay (LOS), haemoglobin decrease (HD), the International Prostate Symptom Score (IPSS), the maximum urine flow rate (Qmax), the post-void residual urine volume (PVR), and the quality of life (QoL). We computed the mean and standard deviation for continuous variables that were presented in the major literature as median and range. Any disputes over the extraction procedure were settled through group discussions. We made an effort to get in touch with the author through email if a paper's data is insufficient or unconvincing.

Statistical analysis

The dichotomous and continuous data were evaluated using the ORs and their related 95% CIs, and a 95% confidence interval (CI) and *P*-value were generated. Statistics were considered significant with *P* values under 0.05. Due to differences among the included studies, the random-effect model was chosen over the fixed-effect model. Heterogeneity was assessed using the I^2 z test and the Chi-square statistic. To ascertain whether there was any publishing bias, the funnel plot was used. All the analysis were done using RevMan 5.4 software.

Results

Search results and study characteristics

There were 630 studies found in the initial search. Based on the titles, 95 studies were further reviewed. Additionally, 38 studies that were deemed pertinent and further evaluated based on abstracts. Thirty-two papers' whole texts were also obtained, and 10 of them were considered significant for quantitative analysis in line with the current study's goals. According to the PRISMA flow chart, the step-by-step screening and selection of research is shown in Fig. 1. Out of the 10 studies (5, 19–27) chosen, five were prospective (5, 19-22), four were randomized controlled trials (RCT) (23-26), and the remaining one was a retrospective observational study (27). There were 2,456 patients in total selected studies (Table 1).

Table 1: Characteristics of the studies

Ref. No.	*Place*	*Treatment Type*	*IPSS*	*QMAX*	*PVR*	*Prostate volume*	*QoL*	*Laser power*	*Hospital stay duration*	*Eneuclation Time*	*Catheration Time*	*Score*
(5)	Germany	ThuLEP	22.9±1.8	7.4±2.7	90.3±4.56	92.1±38.3	3.8 ± 0.7	60	3.5±0.8	47.8±21.4	1.3±0.8	8
(25)	Italy	ThuLEP	18.2±7.3	7.9±8.05	115.5±130.5	90.2±42.7	NA	120	2.2±4.05	NA	1.9±2.6	5
(19)	Russia	ThuLEP	21.8±1.6	7.6±1.9	70.1±28.7	91.0±32.1	4.0 ± 0.8	60	3.0±0.6	49.0±18.4	1.3±0.5	7
(20)	Italy	ThuLEP	20.0±4.2	7.0±2.2	90±59.0	75.9±29.6	5 ± 0.74	110	1.0±0.74	70.5±21.7	1.0±0.74	8
(21)	Russia	ThuLEP	NA	NA	NA	NA	NA	60	6.9±0.8	NA	2.15±0.38	7
(24)	China	ThuLEP	24.3±2.1	19.6±2.3	64.6±4.1	40.3±2.4	NA	70	NA	NA	NA	4
(22)	China	ThuLEP	24.6±3.2	6.8±3.9	64.6±32.4	46.6±25.3	NA	70	NA	NA	2.4±1.0	8
(23)	China	ThuLEP	22.8±3.7	6.6±2.3	165.5±46.2	91.8±6.9	5 ± 1.48	120	2.0±0.74	56.4±8.4	2±0.74	5
(27)		ThuLEP	NA	NA	NA	>80	NA	NA	1±2.97	59.0±24	1±2.97	4
(26)	Turkey	ThuLEP	29 ± 4.99	9 ± 3.96	125 ± 88.14	135 ±29.67	5 ± 0.47	104	30 ± 5.15	79.5 ± 18.09	28 ± 5.73	8
(5)	Germany	HoLEP	22.9±1.6	6.8±1.6	88.3±42.5	91.4±32.1	4.1 ± 1.3	70	3.6±0.5	47.8±21.4	1.8±0.9	8
(25)	Italy	HoLEP	17.9±7.1	8.2±6.7	90.4±120.4	86.3±47.0	NA	NA	2.8±3.8	NA	2.0±3.5	5
(19)	Russia	HoLEP	21.9±1.1	7.5±1.5	72.4±28.6	89.7±43.3	4.1 ± 0.8	70	3.3±0.6	50.1±22.0	1.3±0.6	7
(27)		HoLEP	19.9±5.5	8.2±4.2	162.0±128.0	132±34	2.8±1.5	NA	1±4.45	69.5±29.7	1±4.45	4
(26)	Turkey	HoLEP	28 ± 3.94	8.8 ± 2.38	147.5 ± 66.52	125 ±33.83	5 ± 0.65	101	28 ± 6	83 ± 21.2	25 ± 5.87	8
(20)	Italy	HoLEP	21.0±6.1	7.0±3.3	103.5±104.8	75.9±29.6	5 ± 0.74	60	2.0±0.74	75.5±34.07	1.0±0.74	8
(21)	Russia	HoLEP	NA	NA	NA	NA	NA	90	7.5±1.3	NA	2.2±0.39	7
(24)	China	HoLEP	22.4±2.0	16.2±2.0	64.6±5.0	44.7±2.2	NA	90	NA	NA	NA	4
(22)	China	HoLEP	22.8±2.6	7.3±3.7	64.6±33.4	43.5±23.2	NA	90	NA	NA	2.5±1.0	8

Quality evaluation

The Newcastle-Ottawa Scale and the Jadad scale were used to rate the studies' quality. On a scale of 0 to 10, the prospective and retrospective observational studies in the study were evaluated, and all six were found to be of outstanding quality. As shown in table 1, all four RCT studies, which were rated on a scale of 0 to 5, were of excellent quality.

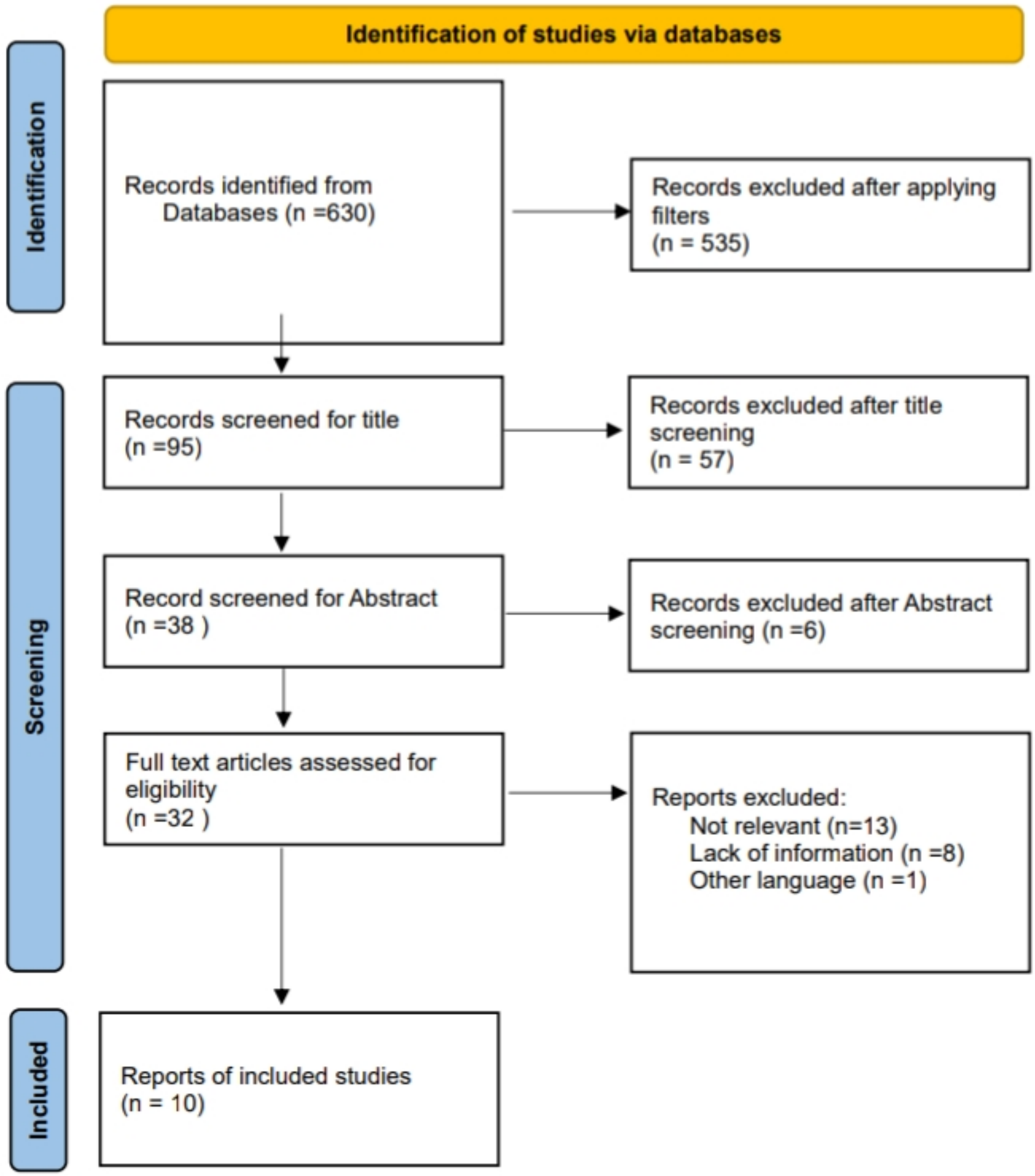

Fig. 1: PRISMA flow chart

Preoperative outcome in surgical treatment of benign prostatic hyperplasia before using thulium laser and holmium laser

Ten studies were included, with 2,456 patients. A total of 1,084 ThoLEP and 1,372 HoLEP were included to study the effect surgical treatment of benign prostatic hyperplasia. The Forest plot and meta-analysis of perioperative outcomes between ThuLEP and HoLEP for Operation time, Enucleation time, Catherization time, hospital stay, and Hemoglobin decrease were analysed. The pooled odds ratio was -0.14 (-0.23, -0.04), -0.12 (-

0.21, -0.03), -0.13 (-0.21, -0.05), -0.29 (-0.38, -0.20), -0.22 (-0.32, -0.13), for Operation time, Enucleation time, Catherization time, hospital stay, Hemoglobin decreases respectively, which indicates signification association (Fig. 2-6). However, the heterogeneity among studies was found to be 93%, 63%, 86%, 92%, 93% for Operation time, Enucleation time, Catherization time, hospital stay, Hemoglobin decreases respectively which is quite high as indicated by I^2 statistics and the Chi-square test (P<0.001). The placement of the diamond to the left of the vertical line suggested that ThuLE resulted in less of a fall in haemoglobin and a shorter amount of time spent in the hospital.

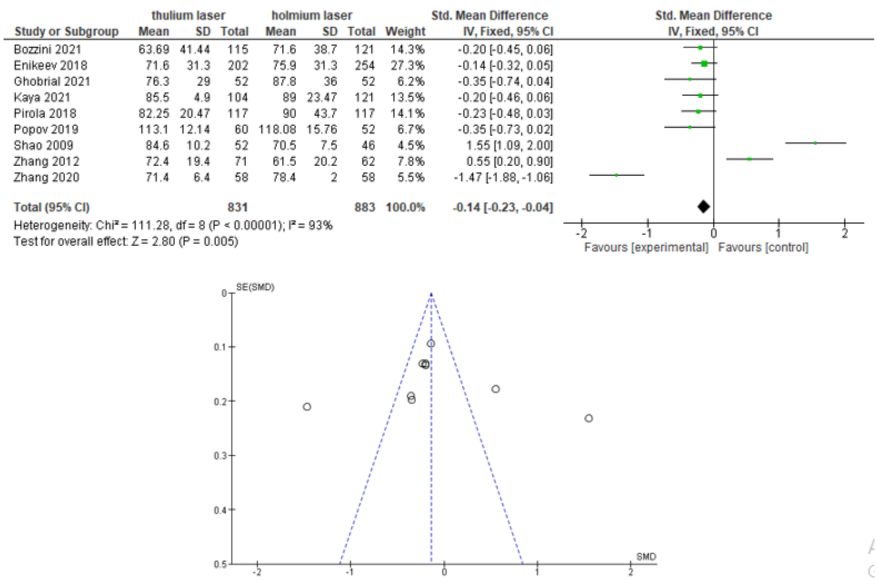

Fig. 2: Preoperative outcomes of ThuLEP and HoLEP for operation time were compared using a forest plot and a meta-analysis

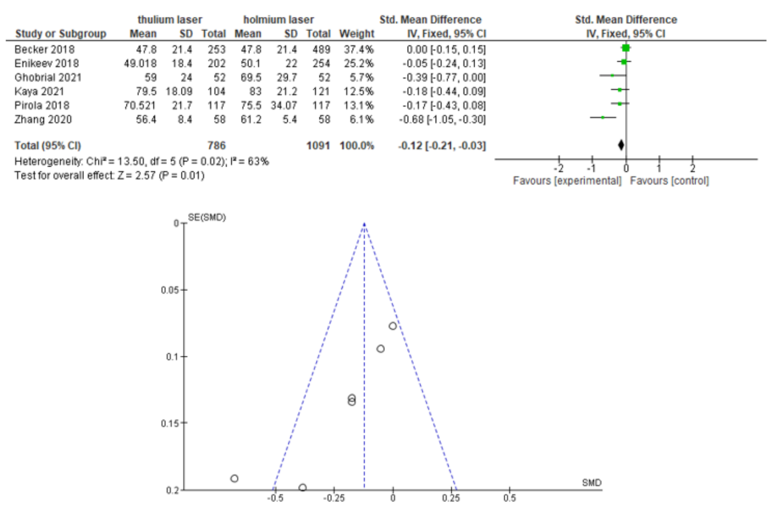

Fig. 3: Preoperative outcomes of ThuLEP and HoLEP for enucleation time were compared using a forest plot and a meta-analysis

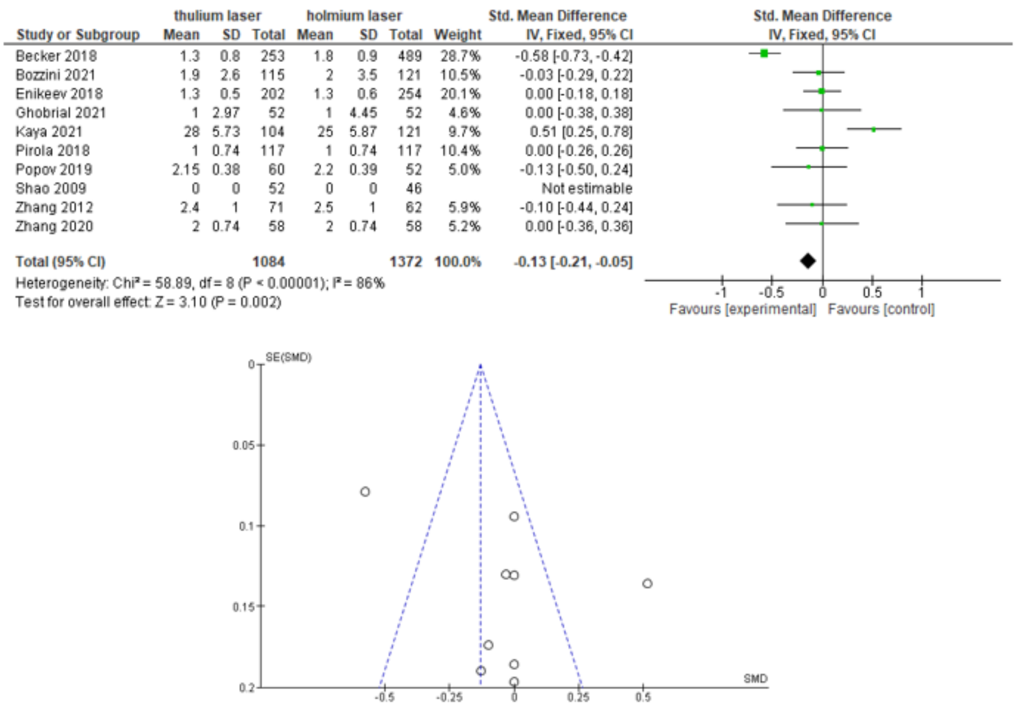

Fig. 4: Preoperative outcomes of ThuLEP and HoLEP for catherization time were compared using a forest plot and a meta-analysis

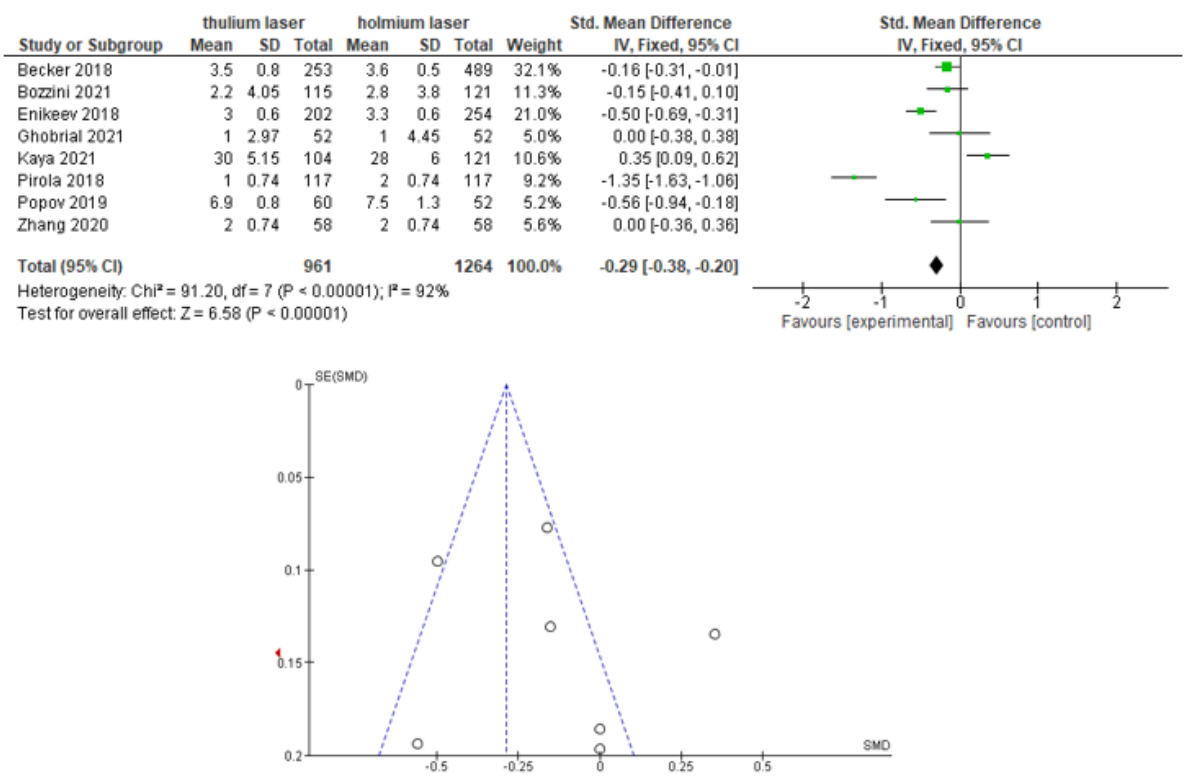

Fig. 5: Preoperative outcomes of ThuLEP and HoLEP for length of hospital stay were compared using a forest plot and a meta-analysis

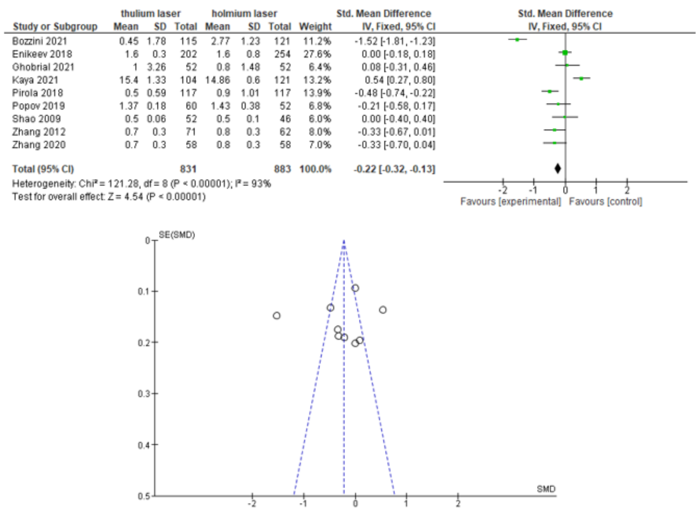

Fig. 6: Preoperative outcomes of ThuLEP and HoLEP for haemoglobin reduction were compared using a forest plot and a meta-analysis

Publication bias

The funnel plot was used for the qualitative assessment of publication bias. The shape of the plot revealed some degree of asymmetry (Fig. 2-6) which indicates publication bias.

Postoperative outcomes at sixth, months

Sixth-month surgical follow-ups revealed statistically significant variations in IPSS (MD: -0.03; 95%CI -0.11 to 0.06; *P* =0.58), QoL (MD: -0.65; 95%CI -0.75 to 0.55; *P* <0.001), PVR (MD: -0.17; 95%CI -0.26 to 0.08; *P* =0.0003) and QMAX (MD: -0.11; 95%CI -0.20 to 0.01; *P* =0.02) at the 6th month. No significant statistical differences were found in other postoperative parameters (Fig. 7-10). However, the heterogeneity among studies was found to be 70%, 97%, 56%, and 92%, for IPSS, Qol, PVR and QMAX, respectively.

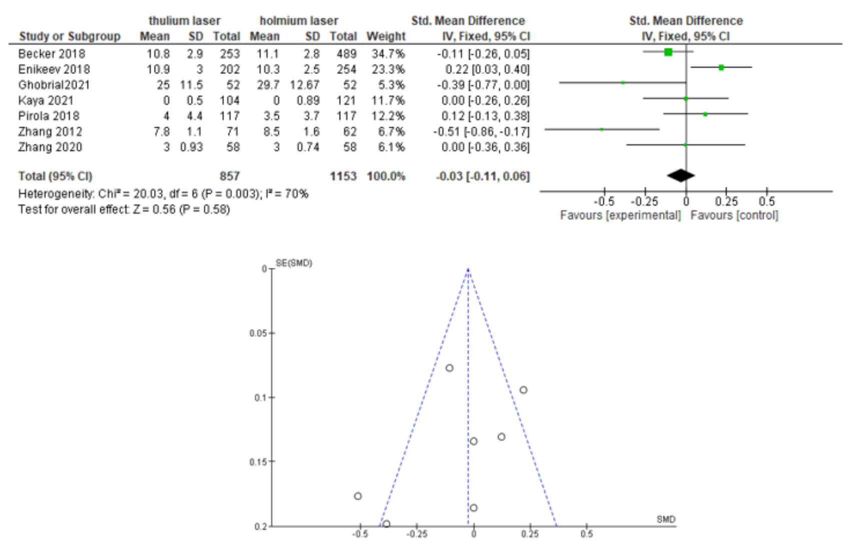

Fig. 7: Postoperative outcomes of ThuLEP and HoLEP for IPSS were compared using a forest plot and a meta-analysis

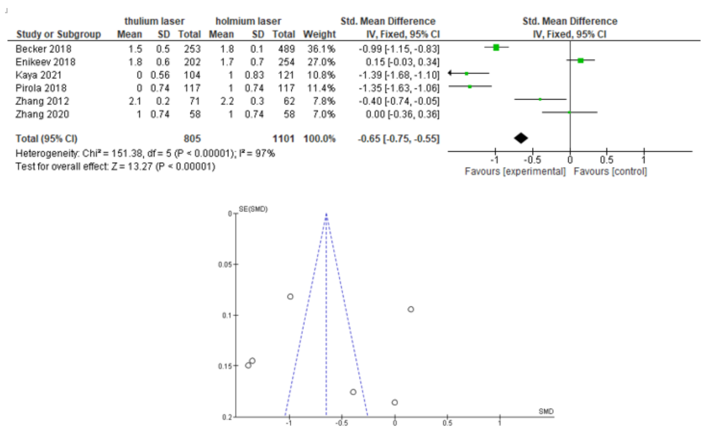

Fig. 8: Postoperative outcomes of ThuLEP and HoLEP for QoL were compared using a forest plot and a meta-analysis

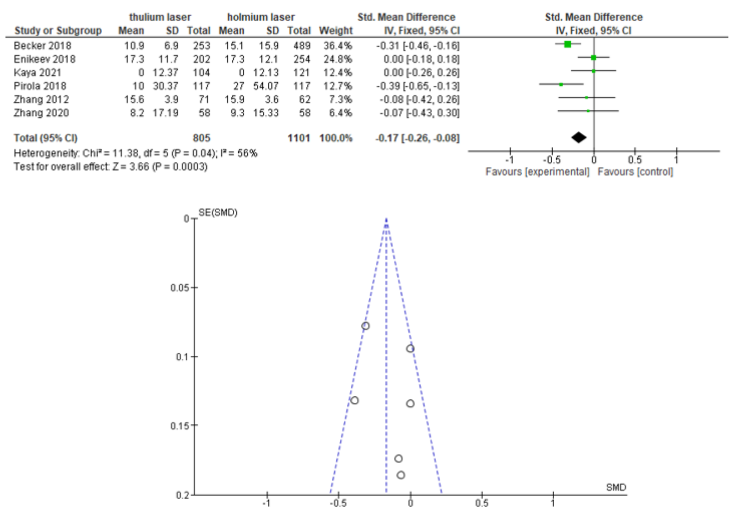

Fig. 9: Postoperative outcomes of ThuLEP and HoLEP for PVR were compared using a forest plot and a meta-analysis

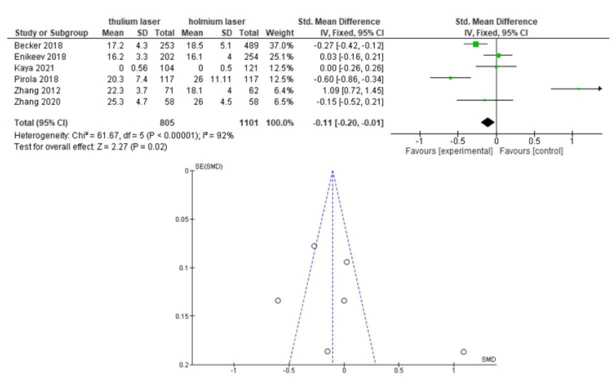

Fig. 10: Postoperative outcomes of ThuLEP and HoLEP for Qmax were compared using a forest plot and a meta-analysis

Publication bias

The funnel plot was used for the qualitative assessment of publication bias. The shape of the plot revealed some degree of asymmetry (Fig. 7-10) which indicates publication bias.

Postoperative complications

No significant differences between ThuLEP and HoLEP were found in a meta-analysis of the primary documented complications (Table 2). Only three of the examined studies classified the surgical complications using the Clavien-Dindo classification system, either modified or unmodified. However, due to the disparities in classification definitions, we were unable to do a meta-analysis.

Table 2: Meta-analysis of major postoperative complications

Complications Type	*No of Studies*	*No of Patients ThoLEP*	*No. Patients HoLEP*	*OR (95% CI)*
Postoperative Bleeding	4	630	918	0.69 (0.58, 0.81)
Clot Retention	3	572	860	0.67 (0.57, 0.78)
Infection	4	617	905	0.68 (0.58, 0.80)
Bladder Tamponade	2	455	743	0.61 (0.52, 0.72)
Bladder Injury	2	173	179	1.27 (1.01, 1.59)
Incomplete Morcellation	2	455	743	0.61 (0.52, 0.72)
Urethral Stricture	4	290	296	1.33 (1.10, 1.60)
Coronary Retention	2	279	296	1.26 (1.04, 1.52)
Bladder-Neck Contracture	3	279	296	1.26 (1.04, 1.52)

Discussion

For decades, transurethral resection of the prostate (TURP) has been the surgical therapy of choice for benign prostatic hyperplasia (BPH). The substantial body of research (10, 28–29) supports its undeniable efficacy in considerably reducing symptoms, particularly in urine flow rate and LUTS. However, 15% to 20% of patients will experience major side effects include transurethral resection syndrome, lower urinary tract infection, postoperative bleeding, and subsequent surgeries. The integration of endoscopy and laser technologies has helped to alter prostate surgery in the current period as science and technology have advanced continuously (29). The prostate laser enucleation is a minimally invasive surgery that has been shown to result in less trauma, improved security, and an improved prognosis (28,30). HoLEP has been demonstrated to be a highly effective and independent surgical technique, particularly for BPH patients with moderate to severe LUTS (30, 31). Additionally, HoLEP had a better postoperative prognosis than TURP. With its benefits of a lower risk of bleeding and a better prognosis, ThuLEP has high safety (32). ThuLEP has become more and more well-liked in recent years as a BPH treatment. Although TURP-related needless issues might be avoided with ThuLEP and HoLEP, there was debate over the two surgical techniques' safety and efficacy (32).

Our meta-analysis was designed to present the most recent data for clinical practise based on this circumstance. There was no discernible change in terms of ET, as could be shown. This outcome was very in line with other findings (5, 19). The ET, however, was shorter in the ThuLEP group, which may be related to device power (22). Both studies (5, 19) reported the same laser power, which was 70 W for a holmium laser and 60 W for a thulium laser, respectively. On the other hand, Zhang et al. utilized a 90 W holmium laser and a 120 W thulium laser (23). According to reports, both low-power and high-power holmium lasers are equally effective for HoLEP surgical procedures (30).

Gloomily, there was no research on ThuLEP's different thulium laser powers. It is interesting to note that professor's study, this would suggest that the enucleation process is affected by the power of the thulium laser. ThuLEP, as is well known, is quite similar to ThuVEP with the exception that the adenoma is removed mechanically rather than energetically. It is difficult to be rigid about not utilising energy, and we hypothesise that the variation in thulium laser power may have the most influence on how ThuLEP proceeds. In addition to the aforementioned aspect, the time of enucleation was significantly influenced by various definitions of time, various pieces of equipment, and the surgeon's technical proficiency. The results of the meta-analysis on the MT did not reveal any appreciable differences between the two groups and were quite consistent with Becker et al. (5). The MT was shorter in the ThuLEP group (22). Therefore, it was clear that different equipment, such as the mechanical tissue morcellator (Piranha TM, Germany) utilized by Zhang et al. (23) and the VersaCut morcellator (Lumenis, Israel) by Becker et al, was a significant interfering element (5).

According to a prospective investigation, the VersaCut and Piranha morcellators both had an effective morcellation rate for HoLEP. In addition, the Piranha morcellator outperformed VersaCut (31). Rather than significant device variations, the discrepancies between the two trials' findings might be attributable to the researchers' improved understanding of Piranha equipment and equipment troubleshooting skills (31). The laser difference ceased to be significant in the morcellation stage, and this finding applied to the ThuLEP stage at that time. Zhang et al.'s findings (23) might have improved their comprehension of and capacity to troubleshoot the equipment as a result.

Heterogeneity among studies are one of important parameter to assess the results of meta-nalysis (32-35). The results of current meta-analysis has demonstrated the heterogeneity among studies. Publication bias is another important parameter, which need to assess by the researchers in the meta-analysis (36-39). The results of current meta-analysis in most of parameters have indicated less involvement of publication bias.

Conclusion

ThuLEP has greater security and quicker symptom alleviation than HoLEP. However, it will take some time for it to establish fully its advantages in the field of benign prostatic hyperplasia in the near future due to limitations on the capacity of various medical institutions, laser power, and surgeon skill. To corroborate our findings, additional randomized controlled studies with a larger sample size, more centres, and longer follow-up periods are still required.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

The authors declare that there is no conflict of interests.

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