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Laser enucleation for prostates larger than 100 mL: Comparison of HoLEP and ThuLEP

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Summary

Recently, with the advancements in laser technology, Holmium laser enucleation of the prostate (HoLEP) and Thulium laser enucleation of the prostate (ThuLEP) have come to the fore in the surgical treatment of benign prostatic hyperplasia (BPH). We aimed to evaluate and compare the outcomes of HoLEP and ThuLEP in patients with >100 ml prostate volume. Patients who underwent HoLEP and ThuLEP between July 2017 and March 2020 were reviewed retrospectively. The patients were divided into two groups as HoLEP (Group 1, $n = 121$) and ThuLEP (Group 2, $n = 104$). Perioperative parameters, functional outcomes, continence status, intra and post-operative complications were compared between groups in the post-operative 1st and 6th month. No significant difference was found in terms of total laser energy (TLE), morcellation efficiency (ME), enucleated tissue weight (ETW), complication rates (CR) and continence status of patients between both groups ($p > .05$). In favour of ThuLEP group, there were statistically significant differences regarding total operation time (TOT), laser efficiency (LE), enucleation time (ET) and enucleation efficiency (EE) between groups ($p \leq .05$). HoLEP and ThuLEP can be used safely and effectively in prostates larger than 100 ml.

KEYWORDS

BPH, endoscopic enucleation of the prostate, HoLEP, Large prostate, ThuLEP

1 | INTRODUCTION

Benign prostatic hyperplasia (BPH) is a significant health condition worldwide that affects up to 50% of men over 60 years and is clinically characterised by lower urinary tract symptoms (LUTS) (Vartak & Raghuvanshi, 2019). Until recently, transurethral resection of the prostate (TUR-P) was the first-line treatment for prostates under 80 ml, while open prostatectomy (OP) was recommended for prostate with volumes above 80 ml (Becker et al., 2018; Castellani et al., 2019). In recent years, in parallel to the advancements in laser technology, Holmium laser enucleation of the prostate (HoLEP) and Thulium laser enucleation of the prostate (ThuLEP) have come to the fore in the surgical treatment of BPH.

HoLEP was introduced by Gilling in 1998 and began to be applied especially in high prostate volumes (Gilling et al., 2000; Zell et al., 2020). Compared to OP, similar post-operative results were obtained with lower complication rates (Elshal et al., 2016; Kuntz et al., 2008). In 2010, Herrmann et al. reported the results of BPH surgery with a different laser technology named ThuLEP (Herrmann et al., 2010). Its safety and efficacy for prostates <80 ml (Pirola

et al., 2018) and >80 ml (Chang et al., 2019) has been reported in several studies. The number of studies comparing functional outcomes and complication rates between these two different laser types are limited in large prostates. Therefore, we aimed to compare peri- and post-operative outcomes between HoLEP and ThuLEP in prostates larger than 100 ml.

2 | MATERIALS AND METHODS

2.1 | Study design and enrolment

We obtained ethical approval from the Local Ethics Committee (Nr: 2020-06/2). Data from 444 patients that underwent HoLEP and ThuLEP between July 2017 and March 2020 were reviewed retrospectively. All men received alpha-blocker medication with or without 5-alpha reductase inhibitor. Among patients that used 5-alpha reductase inhibitor, only those who did not use it for the last 6 months were included. Inclusion criteria were Qmax ≤15 ml/s, IPSS-T ≥ 8 and PVR ≥50 ml. Since we aimed to evaluate our previously described HoLEP technique, the first 200 enucleation cases performed with standard technique excluded. Nineteen patients were excluded from the study: previous BPH surgery (4), prostate or bladder cancer (5), patients with a history of neurogenic bladder or urethral strictures (10). Ultimately, data from 225 patients were included for analysis. Patients were divided as HoLEP (Group 1) and ThuLEP (Group 2).

2.2 | Data collection

Patient baseline characteristics such as age, prostate-specific antigen (PSA) and prostate size were recorded. Abdominal ultrasonography (US) was performed to measure prostate volume preoperatively. Functional outcomes such as the International prostate symptom score (IPSS), maximum flow rate (Q_{max}), average urinary flow rate (Q_{ave}) and post-voiding residual volume (PVR) were recorded pre- and post-operatively at months 1 and 6 respectively. Perioperative parameters such as enucleation time (ET—min), morcellation time (MT— min), total operation time (TOT—min), total laser energy (TLE—joule), laser efficiency (LE—joule/g), enucleation efficiency (EE—g/min), morcellation efficiency (ME—g/min), enucleated tissue weight (ETW—g), complication rate (CR) according to Clavien-Dindo, hospitalisation time (HT), catheterisation removal time (CRT) were also recorded. Continence was evaluated according to the International Continence Society (ICS) recommendations(Abrams et al., 2002). All patients were inquired about urinary leaks due to exertion, effort, sneezing or coughing. Any urine leak was considered positive for SUI. No SUI was evaluated by defining complete urinary control. Urge urinary incontinence (UUI) was defined as involuntarily leakage immediately preceded by urgency. Complete dryness was rated as continence.

2.3 | Interventions

All procedures were performed by a single surgeon (LT) using the previously described 'Omega Sign' technique, under regional or general anaesthesia (Tunc et al., 2020). A 26-Fr continuous flow resectoscope was used in both groups. A laser-fibre stabilising bridge, a 120 W holmium laser (VersaPulse; Lumenis Ltd.,) with a 550 μm fibre (SlimLine; Lumenis Ltd.) was used for group 1. Power settings were 100 W for cutting, 60 W for coagulation. In group 2, a Thulium:YAG laser (Cyber TM 200W; Quanta System) with a 550 μm fibre was utilised. Power settings were 60 W for left and 40 W for right pedal. A 26-Fr nephroscope and a Hawk Jaws tissue morcellator (Hawk, Minitech Co.) were used to remove enucleated tissue in both groups.

2.4 | Statistical analysis

The Statistical Package for Social Sciences 23.0 software was employed. The Kolmogorov–Smirnov, Kurtosis and Skewness Tests were used to assess the normality of data. Descriptive statistics of scale samples were expressed as mean ± standard deviation or median [inter-quartile range]. If the defined group had normal distribution, it was expressed as mean ± standard deviation; otherwise expressed as median [inter-quartile range]. The clinical characteristics of two groups were compared with Mann–Whitney U or Student *t*-test for continuous variables. Pearson Chi-Square test or Fisher's Exact test were used to assess categorical variables. All statistical tests were two-sided and $p \leq .05$ was considered as statistically significant.

3 | RESULTS

In Group 1 and 2, there were 121 and 104 patients respectively. Patients' characteristics and pre-operative data are shown in Table 1. There were no significant differences between groups regarding baseline characteristics (Table 1). Perioperative data of both groups are shown in Table 2. Total operation time (TOT), enucleation efficiency (EE), enucleation time (ET), laser efficiency (LE) were significantly different between groups ($p = .009$, $p = .001$, $p = .004$, $p = .001$ respectively). TOT, LE, ET were significantly lower and EE was higher in group 2 [85.5 ± 20.47 (min) versus. 89 ± 23.47 (min), $p = .009$; 0.73 ± 0.09 (j/g) versus. 0.8 ± 0.06 (j/g), $p = .001$; 79.5 ± 18.09 (min) versus. 83 ± 21.2 (min), $p = .004$ and 1.76 ± 0.17 (g/min) versus. 1.5 ± 0.09 (g/min), $p = .001$ respectively]. There we no significant differences in terms of hospitalisation time and catheterisation removal time (Table 2). Baseline and follow-up data are shown in Table 3. When pre-operative and post-operative functional outcomes are compared, a statistically significant improvement was observed in both groups from baseline to last follow-up ($p \leq .001$). There was no difference in terms of functional parameters such as IPSS Total, Qmax, Qave and QoL at post-operative months 1 and 6 between both groups. Stress urinary incontinence was found

TABLE 1 Patients' baseline characteristics and pre-operative data

	Group 1 (*N*: 121)	Group 2 (*N*: 104)	*p*-value
Median age (y) [IQR]	65 [7.47]	68.5 [7.92]	.077
Median PSA (ng/ml) [IQR]	4.35 [4.21]	4.28 [5.82]	.498
Median Hb (ng/ml) [IQR]	14.86 [0.6]	15.4 [1.33]	.067
Mean Post-op Hb (g/dl)*	14.65 ± 0.65	15.1 ± 1.36	.484
Median prostate volume on TAUS (ml) [IQR]	125 [33.83]	135 [29.67]	.058
IPSS Total	28 ± 3.94	29 ± 4.99	.17
Mean quality of life	5 ± 0.65	5 ± 0.47	.057
Mean maximal urinary flow rate (ml/s)	8.8 ± 2.38	9 ± 3.96	.94
Mean average urinary flow rate (ml/s)	3.6 ± 1.06	3.8 ± 1.63	.052
Post-voiding residual urine volume (ml)	147.5 ± 66.52	125 ± 88.14	.055

Note: Abbreviations: Hb, haemoglobin; IPSS, International Prostate Symptom Score; IQR, inter-quartile range; PSA, prostate-specific antigen; TAUS, transabdominal ultrasonography.

*Statistically analysed with Student *t*-test; others analysed with Mann–Whitney U test.

TABLE 2 Perioperative data

	Group 1 (*N*: 121)	Group 2 (*N*: 104)	*p*-value
Enucleation Time (min)	83 ± 21.2	79.5 ± 18.09	**.004**
Enucleation Efficiency (g/min)	1.5 ± 0.09	1.76 ± 0.17	**.001**
Morcellation Time (min)	6 ± 2.38	6 ± 2.41	.789
Morcellation Efficiency (g/min)	21.67 ± 3.19	21.87 ± 4.05	.056
Total Laser Energy (j)	101.5 ± 27.86	104 ± 22.24	0.899
Laser Efficiency (j/g)	0.8 ± 0.06	0.73 ± 0.09	**.001**
Total Operation Time (min)	89 ± 23.47	85.5 ± 20.47	**.009**
Enucleated Tissue Weight (g)	103 ± 31.52	112 ± 27.85	.085
Hospital Time (h)	28 ± 6	30 ± 5.15	.071
Catheterisation removal time (h)	25 ± 5.87	28 ± 5.73	.1

Note: Statistically analysed with Mann–Whitney U test. Values in bold statistically significantly different.

under 2% of cases at post-operative month 1 and was similar in both groups (Table 3). Pre- and post-operative complications are shown in Table 4. There were no significant differences between groups regarding intra and post-operative complications. Post-operative haematuria was observed in three patients in group 1 and in one patient in group 2. For these patients, prolonged bladder irrigation was undertaken. After catheter removal, only one patient in group 1 was recatheterised due to clot retention. Superficial bladder injury was observed in only one patient. Urinary tract infection was seen in two patients in Group 1 and three patient in Group 2. All were treated with broad-spectrum parenteral antibiotics.

4 | DISCUSSION

Large prostates have always been a challenge for urologists regarding benign prostate surgery. In the present study, we compared the efficiency and safety of HoLEP and ThuLEP in prostates larger than 100 ml. We demonstrated that functional outcomes of HoLEP and ThuLEP were similar, and both techniques have low complications rates in prostates larger than 100 ml.

Laser endoscopic enucleation (LEP) has gained momentum in recent years by mimicking OP in a minimally invasive approach. HoLEP has made continuous progress since its first description, and the European Association of Urology (EAU) and American Urological Association (AUA) guidelines currently recommend it as one of the primary options in BPH surgery independent of prostate size (Gravas et al., 2020; Parsons et al., 2020). Recently, with the increasing use of laser, different laser types have been utilised in BPH surgery. Among these, Thulium laser and Holmium laser came into prominence and became one of the first-line surgical options in large prostates especially when using enucleation techniques (Gilling et al., 2000; Gravas et al., 2020). There are several studies comparing HoLEP to OP, and HoLEP has shown lower complication rates, less catheterisation time and a shorter length of hospital stay (Herrmann et al., 2010; Pirola et al., 2018). While OP has shown advantages in terms of TOT, no statistically significant differences were reported when compared to HoLEP group regarding post-operative Qmax, Qave, QoL and PVR (Jones et al., 2016). On the other hand, an alternative method recommended for large prostates is bipolar prostate enucleation, which also includes the principle of enucleation. In a study comparing HoLEP and bipolar enucleation, HoLEP had shorter TOT and CRT, however, there was no difference in post-operative functional results. In addition, studies for bipolar enucleation of prostate above 200 grams are very limited(Habib et al., 2020).

In parallel with the developments in Thulium laser technology, several ThuLEP methods have been described. With effective functional post-operative results and low complication rates, it is reported that ThuLEP is a suitable alternative treatment to HoLEP and OP for large prostates (Chang et al., 2019). There are limited number of studies comparing HoLEP and ThuLEP surgery. Despite both procedures being technically different, the surgical principle is

TABLE 3 Patients' baseline and follow-up data

Parameters	IPSS Total	QoL	Qmax (ml/s)	Qave (ml/s)	PVR	SUI (*n* %)*	UUI (*n* %)*	PMS (*n* %)*
Preoperative								
Group 1	28 ± 3.94	5 ± 0.65	8.8 ± 2.38	3.6 ± 1.06	147.5 ± 66.52			
Group 2	29 ± 4.99	5 ± 0.47	9 ± 3.96	3.8 ± 1.63	125 ± 88.14			
p-value	.17	.057	.94	.052	.055			
1th month								
Group 1	1 ± 1.28+	1 ± 0.69+	26.5 ± 4.26+	13.5 ± 2.25+	0 ± 16.06+	2(1.7%)	2(1.7%)	9(7.4%)
Group 2	2 ± 1.37+	0 ± 1+	27.3 ± 9.57+	13.6 ± 5.62+	0 ± 14.37+	2(1.9%)	1(1%)	7(6.7%)
p-value	.29	.086	.61	.7	.27	1	1	1
6th month								
Group 1	0 ± 0.89+	0 ± 0.5+	29.1 ± 4.6+	14.08 ± 2.53+	0 ± 12.37+	0%	0 (0%)	1(1.7%)
Group 2	1 ± 0.83+	0 ± 0.56+	31 ± 8.01+	14.5 ± 3.53+	0 ± 12.13+	0 (0%)	0 (0%)	0(0%)
p-value	.11	.152	.68	.15	.74	NA	NA	1

Note: Statistically analysed with Wilcoxon and Mann–Whitney U test.

Abbreviations: IPSS, International Prostate Symptom Score; *N*, number of patients; PVR, Post-voiding Residual Volume; Qmax, Maximum flow rate; QoL, Quality of Life; SUI, Stress Urinary Incontinence; UUI, Urge Urinary Incontinence.

*Others analysed with Fisher's Exact test.

+p <.001 compared to baseline.

TABLE 4 Intraoperative and post-operative complications

	Group 1	Group 2	*p*	Evaluation
Intraoperative complications				
Superficial bladder mucosal injury	1	0	1	3 days of catheterisation (G1)
Capsular perforation	1	1	1	3 days of catheterisation (G1)
Haematuria requiring prolonged irrigation	3	1	.62	Irrigation (G3a)
Post-operative complications				
UTI	2	3	.66	Intravenous antibiotic applications (G2)
Clot evacuation using urethral catheter	1	1	1	Bladder irrigation (G3a)
Clot evacuation with cystoscopy	0	0	NA	Cystoscopy (G3b)
Re-catheterisation	1	0	1	Anti-inflammatory drug application for 3 days (G3a)
Bladder neck contracture	1	1	1	Laser incision of the bladder neck (G3b)
Urethral stricture	1	1	1	Internal urethrotomy (G3b)
Meatal stenosis	1	0	1	Meatoplasty (G3b)

Note: Statistically analysed with Pearson Chi-Square test.

Abbreviation: UTI, Urinary tract infection.

similar (Becker et al., 2018). Zhang et al. reported that TOT and ET were lower in ThuLEP group compared with HoLEP group (Zhang et al., 2020). In another study, no difference was detected in perioperative data except for ET and TOT in ThuLEP and HoLEP groups (p <.001) (Chang et al., 2019). In terms of CRT and HT, there was no difference in two studies (Habib et al., 2020; Pirola et al., 2018). In our study, lower ET, TOT, LE were found in ThuLEP groups. As expected, EE was better in group 2 thanks to an improved coagulation in Thulium:YAG laser surgery which can be performed in a shorter time with less laser use. The shorter duration of ThuLEP surgery may be due to different energy setups or pulse modes. Despite the difference in perioperative data, CRT, HT and ETW were similar in groups.

In 2020, Bozzini et al. conducted a multicentre, prospective and randomised matched-pair analysis comparing HoLEP and ThuLEP. In terms of Qmax, PVR, IPSS and QoL score, the procedures did not show any differences at 3 and 12 months of follow-up(Bozzini et al., 2020). Similarly, in our study, no difference was found between groups in terms of post-operative functional results. When compared to baseline functional data, there was a significant improvement in post-operative Qmax, PVR, IPSS and QoL score in both groups.

Urinary incontinence after HoLEP has been a source of concern for urologists. In HoLEP surgery, several factors that affect stress urinary incontinence have been identified such as the technique used, the duration of surgery, diabetes mellitus and the surgeon´s experience (Elmansy et al., 2011) Although different techniques have been studied with HoLEP surgery, the Omega sign technique, which minimises the stress urinary incontinence rates according to the principles defined by Gilling, is a potential candidate to be the standard technique because it defines the enucleation steps well and defines the proper protection of the external sphincter (Gilling, 2020; Tunc et al., 2020). Houssin et al. reported significantly higher post-operative SUI rates at month 3 of 14.5% and 4.2% at month 6 (Houssin et al., 2020). In other study, the post-operative SUI rate was 5.8, 1.5 and 0.7% at 1, 3 and 6 months respectively(Saitta et al., 2019). With the Omega sign technique, SUI rates were reported at 1% during the first month, 0% at months 3 and 6 (Tunc et al., 2020). It was emphasised that the mucosal flap formed between 2 and 10 o'clock region protects the external sphincter. In the ThuLEP procedure, early and late post-operative SUI rates were reported as 13.2% and 0.5% respectively(Yuan et al., 2019). In the present study, we compared HoLEP and ThuLEP results using the Omega sign technique. No difference was found between groups in terms of SUI rates ($p = 1$). We show that low SUI rates can be achieved regardless of the laser type used with the Omega sign technique.

It has been reported that both HoLEP and ThuLEP are safe procedures, but acute urinary retention (AUR), blood transfusion rates and SUI rates were significantly higher in the HoLEP group (Bozzini et al., 2020). For AUR and SUI rate, Holmium laser tears the adenoma and capsule tissue with its pulse output feature and causes the mechanical effect of the resectescope´s tip to be used more. Alternatively, Thulium laser has a better coagulation effect. In Thulium laser, the mechanical effect is observed less frequently due to tissue being cut in a clean line with the effect of a continuous wave (Gilling, 2020). In another study, intraoperative, perioperative and late post-operative complications were similar in HoLEP and ThuLEP groups. Clavien grade II complications were most commonly seen, mainly transient haematuria which was managed with prolonged bladder catheterisation. Two were Clavien grade IIIb, requiring a re-intervention (one in the HoLEP group because of incomplete morcellation and one in ThuLEP group for bipolar haemostatic coagulation) (Chang et al., 2019). In our study, there were no statistically significant differences regarding complications. Although transient haematuria was reported in the HoLEP group, no difference was observed. These patients were treated with prolonged catheterisation and irrigation.

Our study has certain limitations that must be acknowledged. Firstly, our study was retrospective in nature. Secondly, we did not evaluate erectile, ejaculatory and sexual function between groups. TRUS was not used to measure prostate volume and can thus lead to deviations in measurements. In addition, the follow-up duration was short. The evaluation of erectile function and ejaculation level would also contribute to our study.

5 | CONCLUSIONS

HoLEP and ThuLEP can be used safely and effectively in prostates ≥100 ml. If a standardised technique is used with both laser types, a low rate of SUI results can be expected. Multicentric and prospective randomised controlled trials with longer follow-up and larger number of patients are required to confirm our findings.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

EK involved in project development and manuscript writing. SYil involved in data collection and manuscript writing. OA involved in data collection. HCA involved in data analysis. MY involved in data collection. EG involved in data analysis and manuscript writing. SY involved in data collection. RSI involved in review. LT involved in supervision and project development. All authors read and approved the final manuscript.

ETHICS APPROVAL

Approval was obtained from Local Ethical Committee (2020-06/2).

CONSENT TO PARTICIPATE

Informed consent was obtained from all men included in the study.

STATEMENT OF HUMAN RIGHTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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