

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus



Benign Prostatic Hyperplasia

Comparison Between Thulium Fiber Laser and High-power Holmium Laser for Anatomic Endoscopic Enucleation of the Prostate: A Propensity Score–matched Analysis from the REAP Registry

Vineet Gauhar^a, Carlotta Nedbal^{b,c,*}, Daniele Castellani^b, Khi Yung Fong^d, Mario Sofer^e, Moisés Rodríguez Socarrás^f, Azimdjón N. Tursunkulov^g, Lie Kwok Ying^a, Dean Elterman^h, Abhay Mahajanⁱ, Vladislav Petov^j, Sorokin Nikolai Ivanovich^k, Tanuj Paul Bhatia^l, Dmitry Enikeev^{j,m,n}, Nariman Gadzhiev^o, Mallikarjuna Chiruvella^p, Jeremy Yuen-Chun Teoh^q, Andrea Benedetto Galosi^b, Fernando Gómez Sancha^f, Bhaskar Kumar Somani^c, Thomas R.W. Herrmann^r

^a Department of Urology, Ng Teng Fong General Hospital, National University Health System, Singapore; ^b Urology Unit, Azienda Ospedaliero-Universitaria delle Marche, Università Politecnica delle Marche, Ancona, Italy; ^c Department of Urology, University Hospital Southampton NHS Trust, Southampton, UK; ^d Yong Loo Lin School of Medicine, National University of Singapore, Singapore; ^e Department of Urology, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel; ^f Department of Urology and Robotic Surgery, ICUA-Clínica CEMTRO, Madrid, Spain; ^g Urology Division, AkfaMedline Hospital, Tashkent, Uzbekistan; ^h Division of Urology, Department of Surgery, University Health Network, University of Toronto, Toronto, Canada; ⁱ Department of Urology, Sai Urology Hospital and MGM Medical College, Aurangabad, India; ^j Department of Urology, Institute for Urology and Reproductive Health, Sechenov University, Moscow, Russia; ^k Urology Division, Lomonosov Moscow State University, Moscow, Russia; ^l Department of Urology, Sarvodaya Hospital and Research Centre, Faridabad, India; ^m Vienna Medical University, Vienna, Austria; ⁿ Karl Landsteiner Institute of Urology and Andrology, Vienna, Austria; ^o Department of Urology, Saint Petersburg State University Hospital, Saint Petersburg, Russia; ^p Department of Urology, Asian Institute of Nephrology and Urology, Hyderabad, India; ^q S.H. Ho Urology Centre, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China; ^r Department of Urology, Kantonspital Frauenfeld, Spital Thurgau AG, Frauenfeld, Switzerland

Article info

Article history:

Accepted June 22, 2023

Associate Editor: Christian Gratzke

Keywords:

Benign prostatic hyperplasia
Laser therapy
Endoscopic enucleation of the prostate
Holmium laser
Thulium fiber laser

Abstract

Background: Different lasers have been developed for treatment of benign prostatic hyperplasia, with no definitively superior technique identified to date.

Objective: To compare surgical and functional enucleation outcomes in real-world multicentre practice using high-power holmium laser (HP-HoLEP) and thulium fiber laser enucleation of the prostate (ThuFLEP) for different prostate sizes.

Design, setting, and participants: The study included 4216 patients who underwent HP-HoLEP or ThuFLEP at eight centers in seven countries between 2020 and 2022. Exclusion criteria were previous urethral or prostatic surgery, radiotherapy, or concomitant surgery.

Outcome measurements and statistical analysis: To adjust for the bias arising from different characteristics at baseline, propensity score matching (PSM) was used to identify 563 matched patients in each cohort. Outcomes included the incidence of postoperative

* Corresponding author. Urology Unit, Azienda Ospedaliero-Universitaria delle Marche, Università Politecnica delle Marche, Via Conca 71, 60127 Ancona, Italy. Tel. +39 334 3997886.
E-mail address: carlottednedbal@gmail.com (C. Nedbal).

<https://doi.org/10.1016/j.euf.2023.06.009>

2405-4569/© 2023 European Association of Urology. Published by Elsevier B.V. All rights reserved.

Please cite this article as: V. Gauhar, C. Nedbal, D. Castellani et al., Comparison Between Thulium Fiber Laser and High-power Holmium Laser for Anatomic Endoscopic Enucleation of the Prostate: A Propensity Score–matched Analysis from the REAP Registry, Eur Urol Focus (2023), <https://doi.org/10.1016/j.euf.2023.06.009>

incontinence, early complications (30-d), and delayed complications, and results for the International Prostate Symptom Score (IPSS), quality of life (QoL), maximum flow rate (Qmax), and postvoid residual volume (PVR).

Results and limitations: After PSM, 563 patients in each arm were included. Total operative time was similar between the arms, but enucleation and morcellation times were significantly longer for ThuFLEP. The rate of postoperative acute urinary retention was higher in the ThuFLEP arm (3.6% vs 0.9%; $p = 0.005$), but the 30-d readmission rate was higher in the HP-HoLEP arm (22% vs 8%; $p = 0.016$). There was no difference in postoperative incontinence rates (HP-HoLEP:19.7%, ThuFLEP:16.0%; $p = 0.120$). Rates of other early and delayed complications were low and comparable between the arms. The ThuFLEP group had higher Qmax ($p < 0.001$) and lower PVR ($p < 0.001$) than the HP-HoLEP group at 1-yr follow-up. The study is limited by its retrospective nature.

Conclusions: This real-world study shows that early and delayed outcomes of enucleation with ThuFLEP are comparable to those with HP-HoLEP, with similar improvements in micturition parameters and IPSS.

Patient summary: As lasers become readily available for the treatment of enlarged prostates causing urinary bother, urologists should focus on performing good anatomic removal of prostate tissue, with the choice of laser not as important for good outcomes. Patients should be counseled about long-term complications, even when the procedure is being performed by an experienced surgeon.

© 2023 European Association of Urology. Published by Elsevier B.V. All rights reserved.

1. Introduction

Lower urinary tract symptoms (LUTS) associated with benign prostatic enlargement/obstruction have a significant impact on the quality of life (QoL) of men [1]. Transurethral resection of the prostate (TURP) has been established as the treatment of choice for small and medium-sized prostates [2]. Anatomic endoscopic enucleation of the prostate (AEEP), first described by Hirahoka in 1983 [3], was included in the European Association of Urology (EAU) guidelines for benign prostatic hyperplasia (BPH) treatment in 2016 [4]. AEEP is as effective as open prostatectomy with less morbidity for prostates >80 ml, and is superior to “standard” TURP in terms of lower blood loss and shorter catheterization time [5].

After Fraundorfer and Gilling [6] successfully introduced holmium laser enucleation of the prostate (HoLEP) in 1998, different laser energy sources have been developed, the most notable being thulium:YAG laser, introduced in 2010 by Herrman and colleagues [7].

HoLEP is performed at both high-power (HP; 50–100 W) and low-power (LP; 20–50 W) settings. A recent meta-analysis by Pirola and colleagues [8] revealed that HP-HoLEP and LP-HoLEP have comparable surgical times and safety profiles, with similar operative and functional outcomes. Thulium fiber laser (TFL), a woven silica fiber doped with thulium ions, has a shorter wavelength and higher water absorption coefficient in comparison to holmium laser [9], leading to higher energy density at the tip, which translates into deeper ablation and coagulation abilities [10]. TFL enucleation of the prostate (ThuFLEP) achieved similar efficacy and efficiency to HoLEP in both a single-center registry [11] and a single-center randomized controlled trial [12], and both are considered efficient energy sources for AEEP.

However, there are limited real-world studies comparing HP-HoLEP and ThuFLEP. Hence, our aim was to compare HP-HoLEP and ThuFLEP using data from a real-world registry,

with the incidence of postoperative urinary incontinence as a primary outcome, and early and delayed complications as secondary outcomes.

2. Patients and methods

2.1. Registry design and enrolment protocol

The Refinement in Endoscopic Anatomical Enucleation of Prostate (REAP) registry is a retrospective multicenter anonymized database aimed at understanding how enucleation is performed in different parts of the world. It is hoped that data from this registry will strengthen results in the literature, reveal unknown issues, and ultimately help in improving real-world practice of AEEP. Institutional review board approval was obtained by the leading center (AINU 11/2022) and the remaining centers received approval from their respective institutional boards.

2.2. Study population

Data were obtained for 6193 patients treated by 12 surgeons in eight centers with at least 200 cases of enucleation experience. ThuFLEP was performed in three centers and HP-HoLEP in four centers, while one center performed both HP-HoLEP and ThuFLEP. For this study, men who underwent surgery for clinical BPH between January 2020 and January 2022, with specification for either HP-HoLEP or ThuFLEP as the energy choice, irrespective of the brand of device used, were included for analysis.

Patients with LUTS who had no response or worsening symptoms after medical therapy, acute urinary retention (AUR), or any other absolute indication for surgery (recurrent urinary tract infection, bilateral hydronephrosis with renal impairment, recurrent hematuria due to BPH) were eligible for inclusion. Patients with previous prostate/urethral surgery, prostate cancer, or pelvic radiotherapy were excluded. Patients who underwent concomitant lower urinary tract surgery (internal urethrotomy, lithotripsy, or transurethral resection of bladder tumor) were also excluded. Any suspicion of prostate cancer was ruled out via prostate biopsy before enucleation. Oral anticoagulant agents were switched to low-molecular-weight heparin in preparation for surgery and resumed at the discretion of each center. Antibiotic prophylaxis

was administered to all patients according to local protocols. Prostate enucleation was performed using a 26 Ch resectoscope (Karl Storz, Tuttlingen, Germany) with a separate operative channel for the fiber. Enucleation was performed using either TFL (TFL U3, IRE-Polus, Fryazino, Russia, or 60 W super pulse TFL IPG photonics, Oxford, MA, USA) or HP-Ho laser (100 W; Cyber Ho, Quanta System, Varese, Italy, or Lumenis Pulse, Lumenis, Yokneam, Israel) with a 550- μ m fiber in all cases. Morcellation was performed after enucleation in all cases, using different morcellators as available.

2.3. Patient follow-up and secondary treatment

Patients were assessed after surgery according to the local standard of care. Follow-up time intervals were either 3, 6, 12, or 24 mo, or a combination of these. At follow-up, relevant scores and micturition parameters were evaluated. Enucleation time was calculated from the start of enucleation to the start of morcellation. Surgical time was considered from cystoscopy to catheter placement. Incontinence was defined as any urine leakage reported by the patient.

2.4. Statistical analysis

All statistical analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria) with $p < 0.05$ indicating statistical significance. Continuous variables are reported using the median and interquartile range (IQR), while categorical variables are reported as the absolute frequency and percentage. The Shapiro-Wilk test was used to assess for normality. Patient demographics, perioperative parameters, and outcome results were compared between the HP-HoLEP and ThuFLEP groups using a χ^2 test or Fisher's exact test for categorical variables, and the Mann-Whitney U test for continuous variables.

Propensity score matching (PSM) was used to reduce confounding in the statistical comparisons and was calculated using a logistic regression model with one-to-one matching for the following variables: age, prostate volume, diabetes mellitus, hypertension, preoperative indwelling catheter (IDC), preoperative IPSS, preoperative Qmax, preoperative PVR, and enucleation type. An absolute standardized mean difference

(ASMD) threshold of <0.1 was used as the threshold for favorable matching [13]. All variables reported for the overall cohort are also reported for the PSM cohort.

Outcomes were assessed using the PSM cohort only. The primary outcome was the incidence of postoperative urinary incontinence. Secondary outcomes included early complications (up to 30 d after surgery) and delayed complications (within 1 yr).

Univariable logistic regression analysis (UVA) was performed in the PSM population to evaluate factors associated with postoperative urinary incontinence at 12 mo. Relevant potentially prognostic variables on UVA were entered into a multivariable regression analysis model (MVA) to assess their significance as independent predictors. Predictors are reported using an odds ratio (OR), 95% confidence interval (CI), and p value, with $p < 0.05$ indicating statistical significance.

3. Results

Of 6193 men who underwent AEEP in the REAP registry, 4216 met the inclusion criteria and were included in the analysis. Of these, 1954 patients underwent HP-HoLEP and 2262 underwent ThuFLEP. In the unmatched cohort, baseline characteristics were markedly different between the treatment arms (Table 1). PSM yielded 563 patients in each group who were well-matched for the study variables.

In the PSM cohort, median operative time was similar in the two groups (65 min, IQR 50–82 for HP-HoLEP vs 60 min, IQR 40–84 for ThuFLEP; $p = 0.063$), but the HP-HoLEP group had a shorter median enucleation time (45 min, IQR 30–72 min vs 77 min, IQR 45–100; $p < 0.001$) and morcellation time (15 min, IQR 11–25 vs 20 min, IQR 12–75; $p < 0.001$; Table 2). A greater proportion of patients in the ThuFLEP group did not undergo early apical release (46.9% vs 84.7%; $p < 0.001$). The ThuFLEP group had a higher rate of postoperative acute urinary retention (3.6% vs 0.9%; $p = 0.005$), shorter median postoperative catheterization time that reached statistical significance (2.0 d, IQR

Table 1 – Baseline preoperative characteristics.

	Unmatched cohort			PSM cohort ^a		
	HP-HoLEP (n = 1954)	ThuFLEP (n = 2262)	ASMD	HP-HoLEP (n = 563)	ThuFLEP (n = 563)	ASMD
Median age, yr (IQR)	68 (63–74)	67 (61–72)	0.209	67 (62–73)	67 (61.5–72)	0.004
Median prostate volume, cm ³ (IQR)	74 (53–95)	72 (60–90)	0.009	76 (56–95)	80 (60–90)	0.045
Preoperative IDC, n (%)	721 (36.9)	206 (9.1)	0.700	46 (8.2)	41 (7.3)	0.033
Diabetes mellitus, n (%)	339 (32.9)	262 (11.6)	0.530	105 (18.7)	106 (18.8)	0.005
Hypertension, n (%)	552 (53.5)	1308 (57.9)	0.087	303 (53.8)	296 (52.6)	0.025
Ischemic heart disease, n (%)	217 (26.5)	192 (20.6)	0.140	87 (23.9)	53 (37.9)	0.306
Cerebrovascular disease, n (%)	90 (11.0)	125 (13.3)	0.072	33 (9.1)	29 (20.4)	0.325
Median IPSS (IQR)	23 (21–26)	23 (21–26)	0.200	22 (21–24)	22 (21–24)	0.029
Median QoL (IQR)	5.0 (5.0–6.0)	5.0 (4.0–5.0)	0.368	5.0 (4.0–5.0)	4.0 (3.0–5.0)	0.090
Median Qmax, ml/s (IQR)	7.0 (5.0–9.1)	8.6 (7.0–10.9)	0.493	7.0 (5.0–8.8)	7.3 (5.8–8.8)	0.094
Median PVR, ml (IQR)	80 (54–169)	70 (60–90)	0.554	70 (50–100)	70 (50–90)	0.052
Median PSA, ng/ml (IQR)	4.6 (2.8–7.7)	4.0 (2.3–6.3)	0.103	4.5 (3.0–6.7)	4.8 (2.8–7.6)	0.146
Enucleation type, n (%)			1.032			0.004
3 lobes	353 (18.1)	69 (3.1)		62 (11.0)	62 (11.0)	
2 lobes	627 (32.1)	1743 (77.1)		321 (57.0)	322 (57.2)	
En bloc	974 (49.8)	450 (19.9)		180 (32.0)	179 (31.8)	

ASMD = absolute standardized mean difference; HP-HoLEP = high-power holmium laser enucleation of the prostate; IDC = indwelling catheter; IPSS = International Prostate Symptom Score; IQR = interquartile range; PSA = prostate-specific antigen; PSM = propensity score-matched; Qmax = maximum flow rate; QoL = Quality of Life score; PVR = postvoid residual volume; ThuFLEP = thulium:YAG fiber laser enucleation of the prostate.

^a The PSM cohort was matched for age, prostate volume, DM, HTN, preoperative IDC, preoperative IPSS, preoperative Qmax, preoperative PVR, and enucleation type. ASMD <0.1 indicates good matching between the cohorts. Variables for which ASMD >0.1 are highlighted in bold.

Table 2 – Intraoperative and postoperative outcomes

	Unmatched cohort ^a			PSM cohort ^a		
	HP-HoLEP (n = 1954)	ThuFLEP (n = 2262)	p value	HP-HoLEP (n = 563)	ThuFLEP (n = 563)	p value
No early apical release, n (%)	1229 (62.9)	762 (33.7)	<0.001	264 (46.9)	477 (84.7)	<0.001
Spinal anesthesia, n (%)	1417 (72.5)	2074 (91.7)	<0.001	546 (97.0)	561 (99.6)	0.001
Median operation time, min (IQR)	70 (55–100)	70 (55–99)	0.733	65 (50–82)	60 (40–84)	0.063
Median enucleation time, min (IQR)	40 (30–60)	60 (40–80)	<0.001	45 (30–72)	77 (45–100)	<0.001
Median morcellation time, min (IQR)	15 (10–21)	23 (15–35)	<0.001	15 (11–25)	20 (12–75)	<0.001
30-d complications, n (%)						
Acute urinary retention, n (%)	63 (3.2)	71 (3.1)	0.945	5 (0.9)	20 (3.6)	0.005
POB, n (%)	15 (0.8)	24 (1.1)	0.406	5 (0.9)	12 (2.1)	0.143
Urinary tract infection	67 (3.4)	81 (3.6)	0.854	16 (2.8)	10 (1.8)	0.321
Sepsis	5 (0.3)	0	0.050	0	0	-
Median postoperative catheter time, d (IQR)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.652	2.0 (1.0–5.0)	2.0 (1.0–2.0)	<0.001
Postoperative incontinence, n (%)	403 (20.6)	960 (42.4)	<0.001	111 (19.7)	90 (16.0)	0.120
Urge incontinence	106 (26.4)	66 (8.0)		40 (23.8)	16 (16.5)	
Stress incontinence	237 (59.0)	720 (87.0)		97 (57.7)	70 (72.2)	
Mixed incontinence	59 (14.7)	42 (5.1)		31 (18.5)	11 (11.3)	
30-d readmission, n (%)	74 (6.6)	38 (1.9)	<0.001	22 (3.9)	8 (1.4)	0.016
Delayed complications (>30 d), n (%)						
US requiring dilation, n (%)	14 (0.7)	33 (1.5)	0.032	7 (1.2)	4 (0.7)	0.545
US requiring urethrotomy, n (%)	11 (0.6)	4 (0.2)	0.066	3 (0.5)	1 (0.2)	0.616
BNS requiring transurethral incision, n (%)	7 (0.4)	20 (0.9)	0.052	3 (0.5)	6 (1.1)	0.503
Repeat BPH surgery, n (%)	1 (0.1)	1 (0.0)	>0.99	0	0	-

BNS = bladder neck sclerosis; BPH = benign prostatic hyperplasia; HP-HoLEP = high-power holmium laser enucleation of the prostate; IQR = interquartile range; POB = postoperative bleeding needing surgical control or additional hemostasis; PSM = propensity score-matched; ThuFLEP = thulium:YAG fiber laser enucleation of the prostate; US = urethral stricture.

^a p values <0.05 are highlighted in bold.

Table 3 – Postoperative urinary symptoms and micturition parameters at 3 mo and 12 mo in the propensity score-matched cohort

	HP-HoLEP	ThuFLEP	p value ^a
3 mo			
Median IPSS (IQR)	7.0 (5.0–8.0)	6.0 (4.0–8.0)	0.101
Mean IPSS (SD)	9.3 (9.6)	8.3 (10.6)	
Median QoL (IQR)	1.0 (1.0–2.0)	2.0 (1.0–2.0)	0.298
Mean QoL (SD)	2.5 (3.0)	2.7 (3.3)	
Median Qmax, ml/s (IQR)	21.0 (17.5–24.0)	20.0 (17.0–22.4)	0.004
Mean Qmax, ml/s (SD)	19.7 (8.5)	18.3 (7.1)	
Median PVR, ml (IQR)	20 (10–30)	15 (5.0–20)	<0.001
Mean PVR, ml (SD)	22 (16)	14 (11)	
12 mo			
Median IPSS (IQR)	5.0 (3.5–7.0)	4.0 (2.0–7.0)	0.561
Mean IPSS (SD)	4.9 (3.1)	4.7 (5.0)	
Median QoL (IQR)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.016
Mean QoL (SD)	2.6 (2.9)	2.1 (2.7)	
Median Qmax, ml/s (IQR)	21.0 (16.0–24.0)	24.0 (20.0–30.0)	<0.001
Mean Qmax, ml/s (SD)	18.0 (9.9)	22.1 (10.6)	
Median PVR, ml (IQR)	30 (17–44)	0 (0–31)	<0.001
Mean PVR, ml (SD)	32 (18)	15 (7.7)	

HP-HoLEP = high-power holmium laser enucleation of the prostate; IPSS = International Prostate Symptom Score; IQR = interquartile range; Qmax = maximum flow rate; QoL = Quality of Life score; PVR = postvoid residual volume; SD = standard deviation; ThuFLEP = Thulium:YAG fiber laser enucleation of the prostate.

^a p values <0.05 are highlighted in bold.

1.0–2.0 vs 2.0 d, IQR 1.0–5.0; $p < 0.001$), and lower rate of 30-d readmission (1.5% vs 3.9%; $p = 0.016$). Delayed complication rates did not differ significantly between the treatment groups.

The incidence of postoperative incontinence did not differ between the HP-HoLEP and ThuFLEP arms (19.7% vs 16.0%; $p = 0.120$). Stress incontinence was the most common type in both arms (57.7% in HP-HoLEP vs 72.2% in ThuFLEP), followed by urge incontinence (23.8% vs 16.5%) and mixed incontinence (18.5 vs 11.3%).

Follow-up results for IPSS, QoL, Qmax, and PVR are shown in Table 3. There were no significant differences in

IPSS between the groups at 3 and 12 mo. The QoL score did not differ significantly at 3 mo, but was lower in the ThuFLEP group at 12 mo, indicating better QoL (2.1 ± 2.7 vs 2.6 ± 2.9 ; $p = 0.016$). Median Qmax was higher for the HP-HoLEP group at 3 mo (21.0 ml/s, IQR 17.5–24.0 vs 20.0 ml/s, IQR 17.0–22.4; $p = 0.004$), but this trend reversed at 12 mo (21.0 ml/s, IQR 16.0–24.0 vs 24.0 ml/s, IQR 20.0–30.0; $p < 0.001$). The ThuFLEP group had lower median PVR at both 3 mo (15 ml, IQR 5.0–20 vs 20 ml, IQR 10–30; $p < 0.001$) and 12 mo (0 ml, IQR 0–31 vs 30 ml, IQR 17–44; $p < 0.001$), but the differences were not clinically meaningful.

Table 4 – Univariable and multivariable analysis of 12-mo incontinence in the propensity score–matched cohort

Predictor	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
ThuFLEP (vs HP-HoLEP)	0.775 (0.569–1.052)	0.103	–	–
Preoperative IDC	4.641 (2.939–7.305)	<0.001	2.04 (1.16–3.59)	0.013
Diabetes mellitus	0.974 (0.65–1.429)	0.894	–	–
Hypertension	0.647 (0.475–0.878)	0.005	0.48 (0.31–0.75)	0.001
Ischemic heart disease	0.648 (0.406–1.014)	0.063	–	–
Cerebrovascular disease	1.243 (0.69–2.176)	0.456	–	–
Enucleation type (vs 3-lobe)				
2-lobe	1.038 (0.608–1.866)	0.897	–	–
En bloc	2.201 (1.281–3.979)	0.006	2.61 (1.31–5.50)	0.008
No early apical release	0.916 (0.668–1.265)	0.591	–	–
Spinal anesthesia	0.463 (0.181–1.332)	0.124	–	–
Age	0.998 (0.978–1.018)	0.853	–	–
Prostate volume	1.002 (0.997–1.006)	0.393	–	–
Preoperative IPSS	1.039 (1.014–1.068)	0.004	1.08 (1.04–1.12)	<0.001
Preoperative QoL	0.986 (0.957–1.013)	0.336	–	–
Preoperative Qmax	1.041 (0.98–1.105)	0.192	–	–
Preoperative PVR	1.003 (1.001–1.005)	0.003	1.00 (1.00–1.00)	0.244
Preoperative PSA	0.999 (0.994–1.004)	0.836	–	–
Operation time	1.003 (0.999–1.007)	0.120	–	–
Enucleation time	0.996 (0.99–1.002)	0.218	–	–
Morcellation time	0.988 (0.979–0.995)	0.003	1.02 (1.00–1.03)	0.018

CI = confidence interval; HP-HoLEP = high-power holmium laser enucleation of the prostate; IDC = indwelling catheter; IPSS = International Prostate Symptom Score; OR = odds ratio; PSA = prostate-specific antigen; PVR = postvoid residual volume; Qmax = maximum flow rate; QoL = Quality of Life score.

^ap values <0.05 are highlighted in bold.

Table 4 shows UVA and MVA results for postoperative incontinence at 12 mo after surgery. On MVA, patients with a preoperative IDC, two-lobe or en-bloc enucleation, higher preoperative IPSS, and a longer morcellation time had significantly higher odds of being incontinent. Hypertension was associated with lower odds of postoperative incontinence.

4. Discussion

In vitro studies have shown how different lasers interact with prostatic tissue. Cecchetti and colleagues [14] clarified that different holmium laser settings generate different temperatures and shockwaves in soft tissue, with good tissue ablation achieved using LP settings and no additional benefits at HP settings. LP-HoLEP has been proposed as a valid alternative to HP-HoLEP in facilities that do not have access to HP devices [8], with comparable outcomes albeit involving a slightly longer surgical time, especially for larger prostates. HP settings could translate into better hemostatic surgery but at the cost of frequent postoperative irritative symptoms such as dysuria, urgency, and frequency [15]. MOSES technology, whereby an amplified holmium pulse wave can travel for longer and deliver more hemostatic laser-tissue interaction without higher tissue damage [16], has great potential for both lithotripsy and application to soft tissues, and has recently been applied to AEEP (MoLEP). One systematic review comparing MoLEP and HoLEP suggested that MOSES technology could result in shorter enucleation and morcellation times, with great hemostatic ability and a shorter learning curve [17]. The authors concluded that MoLEP may be a game changer for day-surgery AEEP, but this needs confirmation in further studies with long-term outcomes. Petov and colleagues [18] claimed that in the hands of experienced surgeons, 3-yr

outcomes are effective and durable for ThuFLEP and the incidence of complications is low. In a study including 163 men who underwent either ThuFLEP or HoLEP, Enikeev and colleagues [12] found that both techniques had comparable functional results in terms of IPSS and Qmax, with similar irritative symptoms.

For patients with a preoperative IDC in our study, we did not collect data on whether this was a long-term IDC or whether it was inserted because of recurrent or precipitated AUR. Considering the lower incidence of postoperative AUR in the HP-HoLEP arm, this technique may be a good choice to offer to patients with a preoperative IDC. However, urologists should counsel patients with a history of preoperative AUR that they are at higher risk of immediate recatheterization, a longer time to a trial without catheter, a longer hospital stay, and postoperative urinary tract infection and sepsis, as suggested by Law and colleagues [19]. Nonetheless, in our study there were no cases of sepsis after PSM matching, precluding further analysis of this outcome.

Total operative time was not affected by the choice of laser for AEEP in our study. Our data revealed shorter enucleation and morcellation times for the HP-HoLEP procedures, possibly because of variability in surgeon experience. Unfortunately, the retrospective nature of our study does not allow clarification of the reason for this difference, which could be influenced by intraoperative events such as instrument malfunction, pre-enucleation urethral dilatation, or other possible reasons for prolonged surgery.

Taking together the 1-yr follow-up data, functional outcomes that reflect the efficacy of enucleation, such as IPSS and QoL, are excellent and similar for both procedures. This indicates that the promise of TFL as a new, more efficient alternative to HP-holmium laser is a realistic possibility for prostate enucleation [20]. In a recent study of 1003 patients undergoing ThuLEP [21], MVA revealed that

shorter surgical time (OR 0.973, 95% CI 0.957–0.994; $p = 0.002$) and a need for recatheterization (OR 3.956, 95% CI 1.867–8.382; $p < 0.001$) were associated with bladder neck stenosis, while larger prostate volume was significantly associated with lower incidence of urethral stricture (OR 0.984, 95% CI 0.972–0.998; $p = 0.03$). However, there was no difference in the incidence of bladder neck stenosis between our two treatment arms both before and after PSM, demonstrating that holmium laser and TFL do not differ in terms of thermal injury at the bladder neck level.

A comparison of TURP and HoLEP revealed that a longer operative time and a larger prostate volume were risk factors for urethral stricture and bladder neck stenosis with TURP, and that HP-HoLEP was a better alternative [22]. A meta-analysis [23] revealed that the pooled incidence of bladder neck stenosis was 1.3% after TURP and 0.66% after enucleation. These findings are echoed in our study; thus, while it may be premature to say that TFL is the next-best laser energy, the evidence suggests that TFL is safe and effective and in no way inferior to HoLEP. Usability and serviceability are its biggest advantages, and are likely to make TFL more popular [24].

Current evidence on AEEP outcomes with TFL or HP-holmium laser is from ex vivo studies [25,26], single-center studies [12,25], or data extrapolated from systematic reviews and meta-analysis [27]. To the best of our knowledge, our high-volume study is the first to attempt to demonstrate the feasibility and efficacy of both techniques for all prostate sizes and for patients of any age, with potentially no limitation on their application for BPH via any surgical technique.

Limitations of our study include its retrospective nature and some possible biases due to omission of variables and sample reduction for PSM analysis, which may possibly account for MVA identification of the en bloc technique as a risk factor for incontinence; however, this finding requires further evaluation. A drawback of PSM is its assumption that the matched variables are the sole determinants of treatment assignment, whereas in real-world clinical practice the choice of laser is mainly determined by institutional availability and surgeon preference. Nevertheless, recommendations regarding the application of PSM in urology were strictly followed to obtain valid measures with scientific reproducibility. Without PSM, the high variability for IPSS, preoperative IDC use, prostate size, and age at surgery could be considered limitations, but we believe them to be a reflection of real-world populations, demonstrating the wide feasibility of both techniques. Moreover, even though postoperative management was not completely standardized and some minor complications may have been missed, this high-volume study is likely to be a true mirror of daily clinical practice. Another limitation is the lack of a pad test and dedicated questionnaires that might better quantify the amount of leakage and bother. Finally, we acknowledge that having multiple operators in several centers with their own protocols could increase the variability of the intraoperative results, but as all the surgeons were highly experienced in AEEP and followed standardized enucleation techniques, this is paradoxically the exact reason for conducting a real-world outcomes study.

5. Conclusions

This is the first large-volume, real-world study reporting outcomes for patients followed for up to 12 mo after Thu-FLEP or HP-HoLEP. We found that both procedures were safe and effective for AEEP using any surgical approach, with improvements in urinary symptoms and micturition parameters, an acceptable rate of urinary incontinence, and low incidence of early and delayed complications. At 1 yr, all patients had a remarkable reduction in IPPS and increase in Qmax values, with a slightly more promising trend for the latter with TFL devices.

Author contributions: Carlotta Nedbal 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: Gauhar, Castellani, Teoh.

Acquisition of data: Sofer, Rodríguez Socarrás, Tursunkulov, Ying, Elterman, Mahajan, Petov, Ivanovich, Bhatia, Enikeev, Gadzhiev, Chiruvella, Teoh.

Analysis and interpretation of data: Gauhar, Nedbal, Castellani.

Drafting of the manuscript: Gauhar, Nedbal, Castellani.

Critical revision of the manuscript for important intellectual content: Gómez-Sancha, Somani, Herrmann.

Statistical analysis: Castellani, Fong.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: Gómez-Sancha, Galosi, Somani, Herrmann.

Other: None.

Financial disclosures: Carlotta Nedbal certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Fernando Gómez-Sancha is a consultant for Quanta System and Lumenis. Thomas R.W. Herrmann is a consultant for, has received honoraria from, and is involved in research collaboration with Karl Storz. Dean Elterman is an investigator and a consultant for Astellas, Boston Scientific, Teleflex, Prodeon, ProVerum, Procept Biorobotics, Olympus, Urotronic, and Zenflow. The remaining authors have nothing to disclose.

Funding/Support and role of the sponsor: None.

References

- [1] Taub DA, Wei JT. The economics of benign prostatic hyperplasia and lower urinary tract symptoms in the United States. *Curr Urol Rep* 2006;7:272–81. <https://doi.org/10.1007/s11934-996-0006-0>.
- [2] Cornu JN, Ahyai S, Bachmann A, et al. A systematic review and meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic obstruction: an update. *Eur Urol* 2015;67:1066–96. <https://doi.org/10.1016/j.eururo.2014.06.017>.
- [3] Hiraoka Y. A new method of prostatectomy, transurethral detachment and resection of benign prostatic hyperplasia. *Nihon Ika Daigaku Zasshi* 1983;50:896–8. <https://doi.org/10.1272/jnms1923.50.896>.
- [4] Gravas S, Cornu J, Gacci M, et al. EAU guidelines on management of non-neurogenic male lower urinary tract symptoms (LUTS), incl. benign prostatic obstruction (BPO). Arnhem, The Netherlands: European Association of Urology; 2022.

- [5] Reddy SK, Utley V, Gilling PJ. The evolution of endoscopic prostate enucleation: a historical perspective. *Andrologia* 2020;52:e13673.
- [6] Fraundorfer MR, Gilling PJ. Holmium:YAG laser enucleation of the prostate combined with mechanical morcellation: preliminary results. *Eur Urol* 1998;33:69–72. <https://doi.org/10.1159/000019535>.
- [7] Herrmann TR, Bach T, Imkamp F, et al. Thulium laser enucleation of the prostate (ThuLEP): transurethral anatomical prostatectomy with laser support. Introduction of a novel technique for the treatment of benign prostatic obstruction. *World J Urol* 2010;28:45–51. <https://doi.org/10.1007/s00345-009-0503-0>.
- [8] Pirola GM, Castellani D, Maggi M, et al. Does power setting impact surgical outcomes of holmium laser enucleation of the prostate? A systematic review and meta-analysis. *Cent Eur J Urol* 2022;75:153–61. <https://doi.org/10.5173/cej.2022.0104>.
- [9] Teichmann HO, Herrmann TR, Bach T. Technical aspects of lasers in urology. *World J Urol* 2007;25:221–5. <https://doi.org/10.1007/s00345-007-0184-5>.
- [10] Fried NM, Murray KE. High-power thulium fiber laser ablation of urinary tissues at 1.94 μm . *J Endourol* 2005;19:25–31. <https://doi.org/10.1089/end.2005.19.25>.
- [11] Zhang F, Shao Q, Herrmann TR, et al. Thulium laser versus holmium laser transurethral enucleation of the prostate: 18-month follow-up data of a single center. *Urology* 2012;79:869–74. <https://doi.org/10.1016/j.urology.2011.12.018>.
- [12] Enikeev D, Taratkin M, Babaevskaya D, et al. Randomized prospective trial of the severity of irritative symptoms after HoLEP vs ThuFLEP. *World J Urol* 2022;40:2047–53. <https://doi.org/10.1007/s00345-022-04046-8>.
- [13] Lunt M. Selecting an appropriate caliper can be essential for achieving good balance with propensity score matching. *Am J Epidemiol* 2014;179:226–35. <https://doi.org/10.1093/aje/kwt212>.
- [14] Cecchetti W, Zattoni F, Nigro F, Tasca A. Plasma bubble formation induced by holmium laser: an in vitro study. *Urology* 2004;63:586–90. <https://doi.org/10.1016/j.urology.2003.09.010>.
- [15] Scoffone CM, Cracco CM. High-power HoLEP: no thanks! *World J Urol* 2018;36:837–8. <https://doi.org/10.1007/s00345-018-2186-x>.
- [16] Ventimiglia E, Traxer O. What is Moses effect: a historical perspective. *J Endourol* 2019;2019(33):353–7. <https://doi.org/10.1089/end.2019.0012>.
- [17] Gauhar V, Gilling P, Pirola GM, et al. Does MOSES technology enhance the efficiency and outcomes of standard holmium laser enucleation of the prostate? Results of a systematic review and meta-analysis of comparative studies. *Eur Urol Focus* 2022;8:1362–9. <https://doi.org/10.1016/j.euf.2022.01.013>.
- [18] Petov V, Babaevskaya D, Taratkin M, et al. Thulium fiber laser enucleation of the prostate: prospective study of mid- and long-term outcomes in 1328 patients. *J Endourol* 2022;36:1231–6. <https://doi.org/10.1089/end.2022.0029>.
- [19] Law YXT, Castellani D, Dell'atti L, et al. Differences in surgical and functional outcomes in benign prostate hyperplasia patients with only lower urinary tract symptoms versus those in retention: a systematic review and meta-analysis. *Neurourol Urodyn* 2021;40:1389–401. <https://doi.org/10.1002/nau.24708>.
- [20] Enikeev D, Taratkin M. Thulium fiber laser: bringing lasers to a whole new level. *Eur Urol Open Sci* 2022;48:31–3. <https://doi.org/10.1016/j.euro.2022.07.007>.
- [21] Castellani D, Antonucci M, Signoretti M, et al. Urethral and bladder neck stenosis after thulium laser enucleation of the prostate: analysis of risk factors in a series of 1003 patients. *Andrologia* 2022;54:e14523.
- [22] Elsaqa M, Serag M, Leenlani N, et al. The incidence of urethral stricture and bladder neck contracture with transurethral resection vs. holmium laser enucleation of prostate: A matched, dual-center study. *Can Urol Assoc J* 2023;17:E35–8. <https://doi.org/10.5489/cuaj.7967>.
- [23] Castellani D, Wroclawski ML, Pirola GM, et al. Bladder neck stenosis after transurethral prostate surgery: a systematic review and meta-analysis. *World J Urol* 2021;39:4073–83. <https://doi.org/10.1007/s00345-021-03718-1>.
- [24] Taratkin M, Checucci E, Androsov A, et al. Thulium fiber laser in BPH surgery: bench to bedside—a systematic review on behalf of YAU Urotechnology Working Group. *Front Urol* 2022;2:1017069. <https://doi.org/10.3389/fruro.2022.1017069>.
- [25] Taratkin M, Azilgareeva C, Cacciamani GE, Enikeev D. Thulium fiber laser in urology: physics made simple. *Curr Opin Urol* 2022;32:166–72. <https://doi.org/10.1097/MOU.0000000000000967>.
- [26] Taratkin M, Kovalenko A, Laukhtina E, et al. Ex vivo study of Ho:YAG and thulium fiber lasers for soft tissue surgery: which laser for which case? *Lasers Med Sci* 2022;37:149–54. <https://doi.org/10.1007/s10103-020-03189-7>.
- [27] Pallauf M, Kunit T, Ramesmayer C, et al. Endoscopic enucleation of the prostate (EEP). The same but different—a systematic review. *World J Urol* 2021;39:2383–96. <https://doi.org/10.1007/s00345-021-03705-66>.