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Original Article

Holmium laser enucleation of the prostate for the treatment of size-independent BPH: A single-center experience of 600 cases

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ABSTRACT

Objective: Holmium laser enucleation of the prostate (HoLEP) is an endourologic minimal invasive intervention of benign prostate hyperplasia (BPH). The interest on HoLEP is increasing in the literature. The aim of the present study was to evaluate the learning curve and our preliminary results.

Material and methods: A retrospective analysis on 600 patients with BPH who underwent HoLEP between July 2015 and April 2019 was performed. Perioperative measures including enucleation efficiency (EE), morcellation efficiency (ME), and percentage of resected tissue weight (PRW) were recorded. Hospitalization time (HT) and catheterization time (CT) were measured. Functional outcomes, Clavien–Dindo classification complications, and continence status were assessed at 1-, 3-, and 6-month follow-up.

Results: The mean age, prostate size, and prostate-specific antigen levels of the patients were 64.54 years, 91 g, and 4.54 ng/mL, respectively. There were 38.3% of patients with ≥100 g prostate size. The measured EE, ME, and PRW were 1.12 g/min, 4 g/min, and 72%, respectively. The mean HT and CT were 24.53 h and 21.50 h, respectively. Functional outcomes showed significant improvement at 1-, 3-, and 6-month follow-up. Intraoperative and postoperative complications were comparable with the literature. The most common perioperative complication was superficial bladder mucosal injury (n=8, 1.33%). Only one patient had persistent stress urinary incontinence at 6-month follow-up.

Conclusion: As mentioned in the literature, HoLEP indications are independent from prostate size. Our results showed similarity with the literature on functional outcomes, complication rates, and continence status. With its superior results, our HoLEP series from Turkey supports that HoLEP will replace transurethral resection of the prostate as the known current gold standard.

Keywords: Benign prostatic hyperplasia; BPH; HoLEP; holmium laser; laser enucleation.

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Introduction

Holmium laser resection of the prostate was first described by Gilling et al. in 1995. After a few years, this technique evolved to holmium laser enucleation of the prostate (HoLEP).[1] HoLEP procedure has the advantage of the complete enucleation of the entire transitional zone from the prostate capsule as the endoscopic equivalent of an open prostatectomy (OP).[2-4] The classical well-known gold standards for the surgical treatment of benign prostate hyperplasia (BPH) have been OP and transurethral resection of the prostate (TURP) depending on prostate sizes.[5] Surgical outcomes, such as urinary parameter improvements, postoperative complications, and durability, based on re-operation rates are equal or better than TURP with HoLEP.[6] The number of studies and meta-analyses concluding better voiding parameters, lower morbidity, and shorter hospitalization for HoLEP rather than for TURP has been gradually increasing.[2,6-9] In addition, HoLEP has less catheterization time (CT) and hospitalization time (HT) than TURP.[3,4] HoLEP is one of the most commonly used endoscopic enucleation of prostate (EEP) intervention that is recommended by the European Association of Urology (EAU) and American Urological Association (AUA) as a minimal invasive treatment method regarding patients with BPH independent from prostate sizes.[10-12]

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In Turkey, the interest of EEP has recently begun to rise. The aim of the present study was to evaluate the size-independent HoLEP results in our first 600 patients and to compare these results with the literature.

Material and methods

Patient selection

The study was approved by the ethics committee of the institutional review board (protocol no. 77082166-302.08.01). Patients who underwent the HoLEP procedure between July 2015 and April 2019 were reviewed retrospectively. Informed consent was obtained from all participants. Diagnosis of obstruction was confirmed by obstructed urinary flow rate, post-void residual urine (PVR), and preoperative International Prostate Symptom Score (IPSS). All patients received an alpha-blocker medication, with or without 5-alpha reductase inhibitor, for at least 6 months prior to surgery. All patients consulted to the anesthesia department, and the patients with comorbidities were recorded. Antiplatelet therapy was terminated 5–7 days before surgery in individuals taking these drugs. Urethrocystoscopy was performed for all the cases exactly before the HoLEP procedure to examine obstruction, bladder trabeculation, and urethral and bladder pathologies and to exclude bladder tumor. Inclusion criteria were IPSS of ≥8, maximum urinary flow rate (Qmax) of ≤15 mL/s, and PVR of ≥50 mL. A total number of 17 patients were excluded from the study. These were 6 patients with prostate cancer, 4 patients with bladder cancer, 2 patients with neurogenic bladder, and 5 patients with urethral stricture. Before the surgery, all patients signed an informed consent form.

Demographic data

Demographic data were collected by our patient medical information database. The patients were evaluated by IPSS, total prostate-specific antigen (PSA), hemoglobin (Hb) digital rectal examination, suprapubic ultrasonography, Qmax, and PVR preoperatively. Age, comorbidities, and preoperative biopsy results were noted.

Surgical procedure and technique

Under regional or general anesthesia, the patients were placed in the lithotomy position. All procedures were performed by a single surgeon (LT). A two-pedal 120 W Holmium:YAG Laser (VersaPulse; Lumenis Ltd., Yokneam, Israel) was used as the energy source. A 550-μm end-firing laser fiber (SlimLine TM 550, Lumenis Inc.) was used. A 26 F continuous flow resectoscope with a laser bridge (Karl Storz Endoscopy, CA, USA) was also used. The three-lobe technique was used in all procedures. Median lobe and both lateral lobes were enucleated retrogradely off the surgical capsule exposing the correct plane and released at the level of the bladder neck. Enucleated floating prostate tissues were removed by a morcellator (VersaCut, Lumenis, Santa Clara, CA, USA) introduced through a nephroscope (Karl Storz Endoscopy). During morcellation, the bladder was kept distended with continuous irrigation of both inflow channels of resectoscope and nephroscope. Enucleation time (ET), morcellation time (MT), overall operation time (OT), enucleation efficiency (EE), and morcellation efficiency (ME) were recorded separately. At the end of the procedure, a three-way 22 F urethral catheter was placed. Intraoperative complications were noted.

Main Points:

- HoLEP surgery provides size-independent high enucleation efficiency, comparable functional outcomes, and low complication and incontinence rates in the surgical treatment of BPO.
- Although HoLEP is a safe surgery, it has some kind of intraoperative complications due to procedure or device failure. Surgeons planning to perform this surgery should know the types of the complications and how to manage.
- This surgery offers superior continence results both early and late time period, if performed in a manner that respects tissue and external urethral sphincter and using correct anatomical plans.

Postoperative follow-up and data

The urethral catheter was removed once the urine is clear, and the CT and HT were recorded. All patients were planned for follow-up at 1, 3, and 6 months postoperatively. The uroflowmetry variables including PVR, IPSS, and quality of life (QoL) were re-assessed, and the continence status was noted. Postoperative complications were noted and graded using the Clavien–Dindo classification.[13] Storage and voiding lower urinary tract symptoms (LUTS) were assessed using questions from the validated IPSS that consists of seven questions that are used to assess voiding symptoms (IPSS-V) (incomplete emptying, intermittency, weak stream, and straining to void using questions 1, 3, 5, and 6, respectively) and storage symptoms (IPSS-S) (frequency, urgency, and nocturia using questions 2, 4, and 7, respectively). Continence status and post-micturition symptoms (PMS) were evaluated according to the standards recommended by the International Continence Society (ICS).[14] According to the ICS–PMS scoring system, 1–4 scores of patients were accepted as the presence of PMS.

Statistical analysis

The Statistical Package for Social Sciences 23.0 software (IBM SPSS Corp.; Armonk, NY, USA) was utilized for statistical analysis. The Kolmogorov–Smirnov, kurtosis, and skewness tests were used to assess the normality of the data. Descriptive statistics of scale samples were expressed as mean±standard deviation. The clinical characteristics of the two groups were compared using the Mann–Whitney U test or Student's t-test for continuous variables. The Wilcoxon or paired t-test was used to assess the changes in continuous measures between before and after surgery. All statistical tests were two-sided. A p value <0.05 was considered as statistically significant.

Results

A total of 600 patients who underwent the HoLEP procedure between July 2015 and April 2019 were enrolled in the study.

Preoperative data and patient's characteristics

The mean age of the patients was 64.54 (47–87) years. The largest prostate size detected in operated patients was 430 g, whereas the smallest prostate was 21 g. The most common comorbidities among the patients were diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease, and hyperlipidemia. Some of the patients were diagnosed with metabolic syndrome. Comorbidities were observed in 385 (64.16%) patients, and all of them were consulted to the related clinics and anesthesia department before the operation. The preoperative patient demographics, peri- and postoperative PSA, and Hb levels of the patients are shown in Table 1.

Table 1. Preoperative demographic measures, Hb, and PSA level changes

Value	Mean	Minimum	Maximum	p
Age (years)	64.54	47	87	
BMI (kg/m^2)	24.63	17.10	33.20	
Prostate size (g)	91	21	430	
PSA-pre* (ng/mL)	4.54	0.33	20.00	<0.001*
PSA-post* (ng/mL)	0.92	0.20	2.20	
Hb-pre** (g/dL)	14.29	10.20	17.60	>0.05**
Hb-post** (g/dL)	13.90	9.60	17.34	
Hb-drop (g/dL)	0.51	0.25	1.20	

*Statistically analyzed by Mann–Whitney U test. **Statistically analyzed by Wilcoxon test. BMI: body mass index; Hb: hemoglobin; PSA: prostate-specific antigen; PSA-pre: preoperative PSA value; PSA-post: postoperative PSA value; Hb-pre: preoperative hemoglobin level; Hb-post: postoperative hemoglobin level; Hb-drop: hemoglobin change

Table 2. Perioperative measures

Value	Mean	Minimum	Maximum
ET (min)	61	12	301
EE (g/min)	1.12	0.65	1.60
MT (min)	17	2	88
ME (g/min)	4	2	10
OT-total (min)	78	16	341
RW (g)	66	14	289
PRW (%)	72	41	88
HT (h)	24.53	14	54
CT (h)	21.50	10	50

ET: enucleation time; EE: enucleation efficiency; MT: morcellation time; ME: morcellation efficiency; OT-total: total operation time; RW: resected weight; PRW: percentage of resected tissue weight; HT: hospitalization time (length of stay); CT: catheterization time

Perioperative data

Perioperative measures are given in Table 2. The mean ET, EE, MT, ME, OT, resected tissue weight, and percentage of resected tissue weight were 61 min, 1.12 g/min, 17 min, 4 g/min, 78 min, 66 g, and 72%, respectively.

Postoperative data

The preoperative and postoperative 1-, 3-, and 6-month Qmax, PVR, IPSS-V, IPSS-S, and QoL measures are shown in Table 3. A statistically significant improvement was observed in all postoperative parameters compared with preoperative values. HT and CT are also given in Table 2. The mean HT and CT were measured as 24.53 h and 21.50 h, respectively.

The intraoperative and postoperative complications, management for complications, and Clavien–Dindo classification are

Table 3. Postoperative measures

Value	Mean	Minimum	Maximum	p
Qmax-pre (mL/s)	7.46	2.00	16.80	<0.001
Qmax-post 1 mo (mL/s)	25.86	15.00	53.00	
Qmax-post 3 mo (mL/s)	26.35	16.50	53.50	
Qmax-post 6 mo (mL/s)	27.54	17.00	55.50	
PVR-pre (mL)	148.70	20	365	<0.001
PVR-post 1 mo (mL)	29.70	0	85.00	
PVR-post 3 mo (mL)	28.33	0	84.00	
PVR-post 6 mo (mL)	26.24	0	84.00	
IPSS-V-pre	14.52	6	19	<0.001
IPSS-V-post 1 mo	3.94	1	8	
IPSS-V-post 3 mo	2.82	1	6	
IPSS-V-post 6 mo	2.01	1	4	
IPSS-S-pre	11.28	6	15	<0.001
IPSS-S-post 1 mo	6.28	1	10	
IPSS-S-post 3 mo	5.89	1	10	
IPSS-S-post 6 mo	4.63	1	10	
QoL pre	5	3	6	<0.001
QoL-post 1 mo	3.28	0	5	
QoL-post 3 mo	3.15	0	5	
QoL-post 6 mo	2.17	0	4	

Statistically analyzed by Wilcoxon test. Qmax: maximum urinary flow rate; PVR: post-void residual urine; IPSS-V: International Prostate Symptom Score, Voiding Subscore; IPSS-S: International Prostate Symptom Score, Storage Subscore; QoL: quality of life

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Table 4. Intra- and postoperative complications-related managements

Intraoperative complications	**n (%)**	**Management (Clavien–Dindo classification)**
Bleeding (required transfusion)	3 (0.5)	Transfusion (G2)
Bleeding (required transfusion)	1 (0.17)	Conversion to open surgery, under general anesthesia (G3b)
Capsular perforation	6 (1)	Longer catheterization, 3 days (G1)
Superficial bladder mucosal injury	8 (1.33)	Longer catheterization, 3 days (G1)
Device malfunction	4 (0.67)	
-Laser system malfunction	3 (0.5)	Conversion to TURP, under regional anesthesia (G3a)
Cooling system failure	- 1	
Laser scope detachment	- 2	
-Morcellator malfunction	1 (0.17)	Cystotomy to collect the free floating prostate tissue, under general anesthesia (G3b)
Blade failure	- 1	
Postoperative complications	**n (%)**	**Management (Clavien–Dindo classification)**
UTI	7 (1.17)	Intravenous antibiotic (G2)
Clot retention	4 (0.67)	Clot evacuation using urethral catheter, irrigation (G3a)
Clot retention	2 (0.33)	Clot evacuation with cystoscopy, cystoscopic intervention under general anesthesia (G3b)
Re-catheterization	9 (1.5)	3 days with anti-inflammatory drug (G3a)
Bladder neck contracture	5 (0.83)	Bladder neck laser incision (G3b)
Urethral stricture	5 (0.83)	Internal urethrotomy (G3b)
Meatal stenosis	4 (0.67)	Meatoplasty (G3b)
Deviations from the normal postoperative course (e.g., postoperative emesis, electrolyte imbalance, and pain)	21 (3.5)	Treated with antiemetics, antipyretics, analgesics, diuretics, and electrolytes and physiotherapy (G1)

UTI: urinary tract infection

Table 5. The continence status of patients during the follow-up period

Continence status	**SUI**	**UUI**	**PMS**
1 month after HoLEP, n (%)	14 (2.33%)	17 (2.83%)	43 (7.17%)
3 months after HoLEP, n (%)	1 (0.17%)	0	11 (1.83%)
6 months after HoLEP, n (%)	1 (0.17%)	0	0

SUI: stress urinary incontinence; UUI: urge urinary incontinence; PMS: post-micturition symptoms

given in Table 4. The most common perioperative complication was superficial bladder mucosal injury (n=8, 1.33%), which is classified as Clavien–Dindo Grade 1 complication. Four device malfunction complications were reported. Three of them were laser system malfunction, including one cooling system failure and two laser scope detachment with one of them with morcellator blade malfunction (Table 4).

The continence status of the patients at 1, 3, and 6 months is given in Table 5. On postoperative month 1, stress urinary incontinence (SUI), urge urinary incontinence (UUI), and PMS were observed in 14 (2.33%), 17 (2.83%), and 43 (7.17%) patients, respectively. SUI was observed in only one patient at 3 and 6 months, whereas UUI was not observed in any patient at 3 and 6 months. PMS was also evaluated with scoring. Forty-three (7.17%) patients had a complaint about PMS at 1 month after the surgery. It decreased over time and was not seen at 6-month follow-up as shown in Table 5.

Pathologic examinations were reported as benign prostatic hyperplasia in all patients except for 2 (0.33%) patients. The pathologic examination was reported as prostate cancer for these patients, and further treatment was planned.

Discussion

Our HoLEP outcomes showed significant improvement regarding LUTS during 6 months of the postoperative follow-up period. Intraoperative and postoperative complications appeared to be comparable with the literature.

HoLEP surgery is stated in both EAU and AUA guidelines as a minimal invasive treatment method for size-independent BPH.

[10,11] In a recent meta-analysis, Zhong et al.[15] reviewed 11 studies with a prostate size <100 g and compared HoLEP with TURP. Their study concluded that even in small- to mid-sized prostates, HoLEP offers less blood loss, less blood transfusion rates, shorter HT, shorter CT, and potentially better long-term results in Qmax, PVR, and IPSS. In another study consisting of 57 patients with prostates >175 g, HoLEP outcomes were satisfactory, safer, and better than OP.[16] Gazel et al.[17] compared prostates below and over 80 g treated with HoLEP and found no significant difference in IPSS, QoL score, Qmax, Q average, voiding time, PVR, and Hb levels between the two groups. In addition, no significant difference was observed in postoperative complications between the groups, and they concluded that HoLEP is an effective procedure for treating both small and large prostates. In our study, we have presented our size-independent experience of HoLEP in the treatment of BPH ranging from 21 to 430 g. In the current study, 600 patients benefited from HoLEP surgery with high EE, excellent functional outcomes, and low complication and incontinence rates even in huge prostates.

Preoperative and postoperative PSA and Hb levels have been screened in HoLEP surgeries. In our study, we found that the mean postoperative PSA and Hb levels decreased to 0.92 (0.20–2.20) ng/mL and 0.51 g/dL (0.25–1.20) g/dL, respectively, which is comparable with the literature.[18-21]

In HoLEP surgery, EE and ME are the parameters used to evaluate the effectiveness of enucleation and morcellation. EE and ME show the information of the amount of prostate removed in 1 min in grams during enucleation and morcellation. Most of the studies about HoLEP surgery give EE results to show their work as considerable and make the comparison using EE.[22] In the current study, EE was found to be 1.12 (0.65–1.60) g/min, which is comparable with the literature. In the literature, to our knowledge, EE ranges between 0.34 and 1.48 g/min.[23] Morcellation is the last part of the HoLEP surgery, and the effectiveness of this step is evaluated using ME. In the present study, the mean ME was 4 (2–10) g/min, which is comparable with the literature. ME shows the efficacy of the morcellator device, but there are some variables affecting ME, such as tissue density[22] and brand of the morcellator.[24]

Most of the current studies in the literature define TURP as the historical gold standard of BPH surgical treatment methods. When compared with newer methods, TURP is most commonly used for small prostates and shows poor hemostasis and increased morbidity. These well-known morbidities are transurethral resection syndrome, which can cause severe electrolyte imbalance, prolonged CT, higher retreatment rates, and prolonged HT.[3] These limitations of TURP led to the development of new techniques. A recent review article compared new modalities on the surgical treatment of BPH. Monopolar TURP, bipolar TURP, OP, HoLEP, and photoselective vaporization of the prostate (PVP) were compared in a meta-analysis with 2245 patients. HoLEP showed significant improvement over TURP in IPSS and Qmax. In the same review, regarding durability, HoLEP was the only procedure that did not require re-operation within 5 years.[7] According to another review, HoLEP was found to be superior than TURP, OP, PVP, plasmakinetic resection of the prostate, and thulium laser transurethral enucleation of the prostate separately.[3] Yin et al.[8] published a meta-analysis comparing HoLEP versus TURP in six randomized controlled trials. HoLEP patients showed superiority over TURP in both Qmax and IPSS scores at 1 year. Less intraoperative blood loss, shorter CT, shorter HT, and lower transfusion rates were also reported. Kuntz et al.[25] compared the HoLEP and OP results of patients with prostate volumes >100 g in a 5-year follow-up. The results supported HoLEP as a strong endourological alternative to OP. Zhang et al.[20] compared HoLEP with robotic simple prostatectomy (RSP) and found HoLEP to be superior than RSP, with lower OT, decreased postoperative Hb and transfusion rates, and shorter HT and CT. In our study, the mean prostate volume was 91 (21–430) g. Two hundred thirty (38.3%) patients had a prostate volume >100 g. HT was 24.53 (14–54) h, and CT was 21.50 (10–50) h, which are comparable with the published literature.

Capsular perforation and superficial bladder mucosal injury were shown to be the most common complications in the intraoperative period.[26] As regarding complications of our HoLEP experience, intraoperative and postoperative complications and Clavien–Dindo classification are summarized in Table 4. The most common complications that were also found in our study were superficial bladder injury in 8 (1.33%) patients and capsular perforation in 6 (1%) patients. As mentioned in a recent review[27], the leading device malfunction related to HoLEP is morcellator malfunction, usually with higher-grade complications, such as conversion to open surgery, hemorrhage, or need of intensive care unit. In our 600 cases of experience, we converted to TURP in 3 (0.5%) cases, and for 1 (0.17%) case, open approach was performed to remove the free floating prostate tissue out of the bladder due to various device malfunction as shown in Table 4.

SUI and UUI are the annoying problems following HoLEP surgery that patients struggle. In addition, PMS is another challenging problem following transurethral prostate surgeries. The SUI rate reaches up to 42.7% in the early postoperative period. It is shown that SUI rates decrease to almost none in the 6-month period.[27] A French study gave 86.1% of post-HoLEP patients with pure SUI at 1 month of surgery, and 32.7% of the whole patients were still having incontinence at 6 months after surgery.[28] A very recent study from Russia compared en-bloc technique with two-lobe technique and gave their SUI rates at 3 and 6 months, 2.96% versus 4.23% and 1.47% versus 1.69%, respectively.[29]

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In our study, we evaluated continence status with SUI, UUI, and PMS according to the ICS.[15] During postoperative month 1, only 2.33% of the patients complained about SUI and 2.83% about UUI, whereas 7.17% complained about PMS. We noticed 1 patient with persistent SUI and 11 patients with PMS during month 3. At month 6 control, we noticed only 1 patient with SUI, whereas we observed no UUI or PMS in other patients. The mean early postoperative transient incontinence after HoLEP was 10.7%.[26] Therefore, our continence results were comparable and even appeared to be better than the above results belonging to the literature.

In the present study, we evaluated our initial results of HoLEP in our first 600 cases. Despite the widespread utilization of this technique in developed countries, HoLEP is an uncommon procedure in our country. As limitations of the present study, sexual functional questioning and retrograde ejaculation were evaluated. The limitation of this technique may be the length of the procedure, the steep learning curve, and the high actual prices of the holmium laser device and the other equipment, such as morcellator and laser fibers. Lack of experience may be the other cause of hesitation from this technique.

In conclusion, to the best of our knowledge, this is the first study presenting the results of the HoLEP procedure from Turkey with high volume cases. The present study aims to pay attention to size-independent high EE, comparable functional outcomes, and low complication and incontinence rates of HoLEP surgery. Our initial results showed similarity with the literature in functional outcomes, complication rates, and continence status. We believe that, with its superior results as in the literature, this first HoLEP series from Turkey supports that whenever it becomes easy to reach the equipment for surgeons and patients, HoLEP will replace the current gold standard TURP.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gazi University School of Medicine (protocol number 77082166-302.08.01).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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