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Efficacy of holmium laser enucleation in patients with a small (less than 30 mL) prostate volume

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Purpose: To evaluate the efficacy of holmium laser enucleation of the prostate (HoLEP) in patients with a small prostate volume (≤30 mL).

Materials and Methods: We retrospectively evaluated 1,135 patients who underwent HoLEP at two institutions between July 2007 and March 2020. Patients who were not evaluated for the International Prostate Symptom Score (IPSS) before or after HoLEP were excluded. We divided patients into two groups according to estimated prostate volume (ePV): ≤30 (n=198) and >30 mL (n=539). The patient characteristics, IPSS, peak urinary flow rate (Qmax), postvoid residual urine volume (PVR), and other data were compared before and after surgery in each group and between the two groups. Multivariate analysis was performed to identify the factors associated with the efficacy of HoLEP in the group with ePV ≤30 mL.

Results: A total of 737 patients were included in this retrospective study. ePV (23.4 mL vs. 50 mL; p<0.001) and PVR differed significantly between the two groups. The IPSS, IPSS-quality of life, PVR, and Qmax significantly improved after HoLEP in both groups. Improvements in the IPSS, IPSS-quality of life, Qmax, and PVR were greater in the >30 mL group (p<0.001), whereas operation time and morcellation time were significantly shorter in the ≤30 mL group. In the multivariate analysis, age <70 years was independently associated with improvement by HoLEP.

Conclusions: HoLEP is an effective treatment for patients with a small prostate, even though the extent of improvement after HoLEP was greater in those with a larger prostate.

Keywords: Enucleation; Holmium; Laser therapy; Prostatic hyperplasia; Transurethral resection of prostate

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common cause of lower urinary tract symptoms (LUTS) in older men [1-3]. Surgical treatment is recommended for patients with urinary retention, bladder diverticulum, no satisfactory response to medical therapy, or any other complication related to BPH [4,5]. Holmium laser enucleation of the prostate (Ho-

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LEP) is the gold standard surgical treatment for patients with symptomatic BPH [3]. Especially, HoLEP for large BPH is an effective, minimally invasive treatment with no size limitation that allows complete enucleation of the transitional zone [6].

However, the efficacy of HoLEP for symptomatic small BPH is not well known. Because the evidence regarding HoLEP for small prostate volumes is insufficient, clinicians may be hesitant to perform surgical treatment, preferring to continue medical treatment despite the indications for HoLEP. A few recent studies, albeit small retrospective studies, have reported that HoLEP is safe and effective for small as well as larger prostates [7,8]. However, the success rate of the entire treatment may be reduced in patients with bladder decompensation due to delayed surgery. Thus, further accumulation of evidence on the efficacy of HoLEP for small-sized BPH is required.

In the current study, to determine the efficacy of HoLEP for small-sized BPH, we compared the efficacy of HoLEP between patient groups with smaller (≤30 mL) and larger (>30 mL) prostate volumes.

MATERIALS AND METHODS

1. Patients

In this retrospective study, 1,135 patients who underwent HoLEP at Kochi Health Sciences Center and Tottori Municipal Hospital from July 2007 to March 2020 were recruited. The application of HoLEP was decided by each clinician according to the patient's symptoms, including being refractory to medication, having a high International Prostate Symptom Score (IPSS), and having urinary retention, and patient preference with full informed consent. Patients were excluded from the study if they had been previously diagnosed with prostate cancer of if they had no IPSS data either before or after surgery. In 398 patients, the IPSS was missing either before or after HoLEP. The remaining 737 patients, with a mean age of 72 years (range, 49–93 years), were included in this study. The following patient characteristics were collected: age, hypertension, diabetes mellitus, preoperative medical therapy (α-blocker, phosphodiesterase type 5 inhibitor, and 5α-reductase inhibitors), urinary retention, hemoglobin (Hb) level, prostate-specific antigen level, estimated prostate volume (ePV) measured by transabdominal ultrasonography or magnetic resonance imaging, operation time, morcellation time, enucleation tissue weight, enucleation tissue ratio, admission duration, and catheterization duration. IPSS, IPSS-quality of life (QoL), peak urinary flow rate (Qmax), and postvoid residual urine volume (PVR) were evaluated before and within 1 year after surgery. The seven IPSS questions address either voiding or storage symptoms, and thus voiding and storage subscores were calculated separately. The patients were divided into two groups according to their ePV: ≤30 mL (n=198) and >30 mL (n=539).

2. Surgical procedure

We used an 80–120-W holmium laser (VersaPulse Select, Lumenis Pulse 120H with Moses; Lumenis Ltd., Yokneam, Israel), 550-μm end-firing laser fibers (SlimLine; Lumenis Ltd.), and a 26-Fr continuous flow laser resectoscope for enucleation. A 26-Fr nephroscope and a tissue morcellator (Versacut; Lumenis Ltd.) were used for morcellation. We used transurethral resection in saline for coagulation. All BPH cases were enucleated by using the two- or three-lobe technique. A three-way 22-Fr Foley catheter was inserted with continuous bladder irrigation and removed 2 to 3 days after surgery unless there were no complications such as urethral injury or urinary tract infection.

Evaluation after HoLEP was conducted during follow-up visits at 1, 3, 6, and 12 months in almost all patients. At each visit, we performed IPSS and IPSS-QoL evaluations, uroflowmetry, and transabdominal ultrasonography to determine the PVR. If the patient did not visit our institution at the scheduled follow-ups, we used the latest data obtained within 1 year after surgery.

3. Statistical analysis

All statistical analyses were performed by using EZR version 1.36 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [9]. Patient characteristics were compared between the two groups by using Fisher's exact test and the Mann–Whitney U-test, and the difference in each variable from before to after surgery was compared by using the Mann–Whitney U-test. To identify factors associated with the efficacy of HoLEP in the ≤30 mL group (small prostate group), we defined improvement after HoLEP as total IPSS score ≤7 according to the Japanese clinical guideline for male LUTS [10]. Factors associated with the efficacy of HoLEP were analyzed by using logistic repression analysis, including age <70 years, history of hypertension and diabetes mellitus, pre-medical therapy, urinary retention, ePV ≥22 mL, Qmax ≥10 mL/s, total IPSS score >20, and IPSS-QoL score >3. The cutoff values of age and ePV were determined by a receiver operating characteristic analysis, and other factors were determined on the basis of severity grading from the guidelines [10]. Variables considered to be significant in the univariate analysis were entered in the multivariate analysis. A p-value <0.05 was considered significant.

Quantitative data are expressed as means with standard deviations.

4. Ethics statement

This study complied with the standards of the Declaration of Helsinki and with current ethical guidelines and was approved by the Institutional Review Board of Kochi Health Sciences Center and Tottori Municipal Hospital (registration number: 201018). Written informed consent was obtained from all participants.

RESULTS

The mean ePV of the 737 patients included in this study was 48.3 mL (range, 11–239 mL). Of the 737 patients, 146 (19.8%) presented with urinary retention, and 158 (21.4%) received anticoagulation therapy.

The preoperative characteristics of the patients in each group are described in Table 1. Compared with the patients in the >30 mL group, the patients in the ≤30 mL group had a lower prostate-specific antigen level (2.4 ng/mL vs. 4.6 ng/mL; p<0.001), a smaller ePV (23.4 mL vs. 50 mL; p<0.001), and a lower PVR (48.6 mL vs. 65.5 mL; p=0.009). There were no significant differences between the two groups in terms of the other variables evaluated, including age, hypertension, diabetes mellitus, preoperative medical therapy (α-blocker, phosphodiesterase type 5 inhibitor, and 5α-reductase inhibitors), urinary retention, Hb level, IPSS-total, voiding subscore, storage subscore, IPSS-QoL, and Qmax.

Table 2 shows the preoperative and postoperative data of

Table 1. Characteristics of patients and preoperative data

Variable	Group 1 (≤30 mL) (n=198)	Group 2 (>30 mL) (n=539)	p-value
Age (y)	72 (66–78)	72 (67–79)	0.601
Hypertension	97 (49.0)	239 (44.3)	0.279
Diabetes mellitus	31 (15.7)	77 (14.3)	0.640
PSA (ng/mL)	2.4 (1.1–4.7)	4.6 (2.7–8.1)	<0.001
Urinary retention	37 (18.7)	109 (20.2)	0.678
Hb (mg/mL)	14.2 (13.2–14.9)	14.2 (13.2–15.0)	0.858
Estimated prostate volume (mL)	23.4 (20–28)	50 (38–69)	<0.001
Preoperative medical therapy for BPH	113 (57.1)	296 (54.9)	0.617
α-Blocker	112 (56.6)	292 (54.2)	0.616
Phosphodiesterase-type 5 inhibitor	3 (1.5)	16 (3.0)	0.431
5α-reductase inhibitors	5 (2.5)	11 (2.0)	0.776
Combination therapy	8 (4.0)	22 (4.1)	>0.999
IPSS-total	19 (14–25)	18 (13–24)	0.267
Voiding subscore	11 (7–15)	10 (6–14)	0.087
Storage subscore	8 (5–10)	8 (6–10)	0.556
IPSS-quality of life	5 (4–6)	5 (3–6)	0.169
Maximal urinary flow rate (mL/s)	11.2 (8.1–15.5)	10.9 (7.8–14.5)	0.467
Postvoid residual urine volume (mL)	48.6 (15–130)	65.5 (28–150)	0.009

Values are presented as median (interquartile range) or number (%).
PSA, prostate-specific antigen; Hb, hemoglobin; BPH, benign prostatic hyperplasia; IPSS, International Prostate Symptom Score.

Table 2. Preoperative data and postoperative outcomes of the group with prostate volume ≤30 mL (n=198)

Variable	Before	After	p-value
Hb (mg/mL)	14.2 (13.2–14.9)	12.9 (11.8–13.7)	<0.001
IPSS total	19 (14–25)	11 (6.3–14.8)	<0.001
Voiding subscore	11 (7–15)	5 (3–8)	<0.001
Storage subscore	8 (5–10)	5 (4–7)	<0.001
IPSS-quality of life	5 (4–6)	2 (1–4)	<0.001
Maximal urinary flow rate (mL/s)	11.2 (8.1–15.5)	15.4 (10.3–21.9)	<0.001
Postvoid residual urine volume (mL)	48.6 (15.0–130.0)	13.6 (3.1–38.8)	<0.001

Values are presented as median (interquartile range).
Hb, hemoglobin; IPSS, International Prostate Symptom Score.

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Table 3. Preoperative data and postoperative outcomes of the group with prostate volume >30 mL (n=539)

Variable	Before	After	p-value
Hb (mg/mL)	14.2 (13.2–15.0)	12.9 (11.7–13.7)	<0.001
IPSS total	18 (13–24)	8 (4–11)	<0.001
Voiding subscore	10 (6–14)	3 (1–6)	<0.001
Storage subscore	8 (6–10)	4 (3–6)	<0.001
IPSS-quality of life	5 (3–6)	2 (1–3)	<0.001
Maximal urinary flow rate (mL/s)	10.9 (7.8–14.5)	19.7 (12.5–27.2)	<0.001
Postvoid residual urine volume (mL)	65.5 (27.8–150)	14 (4.1–33)	<0.001

Values are presented as median (interquartile range).
Hb, hemoglobin; IPSS, International Prostate Symptom Score.

Table 4. Comparison of preoperative data and postoperative outcomes between the two groups

Variable	Group 1 (≤30 mL) (n=198)	Group 2 (>30 mL) (n=539)	p-value
Hb decrease (mg/mL)	1.2 (0.8–1.6)	1.2 (0.7–1.8)	0.397
Operation time (min)	49 (39–60)	78 (59–104)	<0.001
Morcellation time (min)	3 (1.5–4.8)	8.3 (5.0–15.0)	<0.001
Enucleated tissue weight (g)	5 (3–9)	23 (13–38)	<0.001
Enucleated tissue ratio	22.8 (15.0–35.2)	46.1 (29.2–62.9)	<0.001
Admission duration (d)	6 (6–7)	6 (6–7)	0.292
Urine catheterization duration (d)	2 (2–3)	3 (2–3)	0.021
IPSS total improvement	8 (3–13)	9 (4–16)	0.012
Voiding subscore improvement	5.5 (2–9)	6 (2–11)	0.041
Storage subscore improvement	2 (0–5)	4 (1–6)	<0.001
IPSS-quality of life improvement	2 (1–3)	3 (1–4)	0.023
Maximal urinary flow rate improvement (mL/s)	4.2 (0–11)	7.7 (0–17)	<0.001
PVR urine volume decrease (mL)	9.9 (-9 to 67)	23 (-5 to 99)	0.048

Values are presented as median (interquartile range).
Hb, hemoglobin; IPSS, International Prostate Symptom Score; PVR, postvoid residual urine volume.

the ≤30 mL group. There were significant decreases in the Hb level, IPSS-total, voiding subscore, storage subscore, IPSS-QoL, and PVR (p<0.001) from before to after HoLEP. The Qmax was significantly increased after HoLEP (p<0.001).

Table 3 shows the preoperative and postoperative data of the >30 mL group. In this group, as in the ≤30 mL group, each factor evaluated showed a significant change after HoLEP, including the Hb level, IPSS-total, voiding subscore, storage subscore, IPSS-QoL, and PVR (p<0.001). The Qmax also increased significantly (p<0.001).

There were no significant differences between the two groups in terms of the change in the Hb level or admission duration after HoLEP. The patients in the ≤30 mL group had a shorter operation time (49 min vs. 78 min; p<0.001) and morcellation time (3 min vs. 8.3 min; p<0.001) and a lower enucleated tissue weight (5 g vs. 23 g; p<0.001) and enucleated tissue ratio (22.8% vs. 46.1%; p<0.001) compared with the >30 mL group. Furthermore, the >30 mL group showed greater improvements in the IPSS-total (p=0.012), voiding subscore (p=0.041), storage subscore (p<0.001), IPSS-QoL (p=0.023), Qmax (p<0.001), and PVR (p=0.048), compared with the ≤30 mL group (Table 4).

In the small prostate group, univariate and multivariate analysis were performed to identify which cases were more suitable for HoLEP (Table 5). In the univariate analysis, age <70 years (p<0.001), ePV ≥22 mL (p=0.037), and total IPSS score >20 (p=0.012) were significantly associated with the efficacy of HoLEP. In the multivariate analysis including all the factors with p<0.05 in the univariate analysis, only age <70 years remained as an independent factor for which HoLEP was more effective.

DISCUSSION

We detected significant improvements both in patients with an ePV ≤30 mL and in those with an ePV >30 mL. The IPSS, IPSS-QoL, Qmax, and PVR were improved after HoLEP in the patients with an ePV ≤30 mL. Furthermore, the storage and voiding subscores and Qmax were significantly improved in the ≤30 mL group. Our results reveal the ef-

Table 5. Univariate and multivariate analysis of factors associated with the efficacy of HoLEP

Risk factor	Univariate			Multivariate		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Age <70 years	3.57	1.89–6.73	<0.001	3.70	1.93–7.09	<0.001
Hypertension	1.17	0.64–2.14	0.619			
Diabetes mellitus	0.93	0.40–2.16	0.867			
Pre-medical therapy	0.66	0.36–1.22	0.186			
Urinary retention	0.69	0.31–1.58	0.382			
Estimated prostate volume ≥22 mL	2.12	1.05–4.29	0.037	2.05	0.98–4.29	0.058
Maximal urinary flow rate ≥10 mL/s	1.28	0.61–2.69	0.517			
Total IPSS score >20	0.43	0.22–0.83	0.012	0.60	0.31–1.15	0.126
IPSS-QoL score >3	0.69	0.33–1.45	0.331			

HoLEP, holmium laser enucleation of the prostate; CI, confidence interval; IPSS, International Prostate Symptom Score; QoL, quality of life.

ficacy of HoLEP for small-sized BPH with LUTS, especially for younger patients.

BPH is characterized by LUTS caused by benign hyperplasia of the prostate, which is associated with enlargement of the prostate and LUTS suggestive of bladder outlet obstruction [10]. Previous studies showed that the volume of the prostate increases 2.6% per year, and that the IPSS and IPSS-QoL decrease [11,12]. Consequently, BPH should be treated with the appropriate medical therapy or surgery. Most urologists prescribe alpha-adrenergic receptor antagonists or 5α-reductase inhibitors as the initial treatment for BPH [13], especially for smaller prostates regardless of whether the LUTS are severe. When the first-line internal medical therapy for BPH fails, we consider surgery or a different internal therapy. However, a previous study indicated that clinicians are hesitant to perform surgery in patients with a small prostate and instead continue the internal medicine treatment [7]. In this study, age <70 years was independently associated with the efficacy of HoLEP in the group with small prostates. This result is consistent with previous reports that detrusor underactivity will progress and result in detrusor acontractility if a patient cannot undergo surgery within an appropriate length of time [14]. Therefore, the success rate of surgery may increase by performing surgery for patients with severe symptoms, even in those with small prostate glands [15,16].

In our patients with an ePV ≤30 mL, the IPSS-total, voiding subscore, storage subscore, and IPSS-QoL decreased significantly after HoLEP. In previous studies, the voiding subscore and IPSS-QoL improved significantly after HoLEP and after transurethral resection of the prostate in patients with a prostate volume >30 mL, although the IPSS storage subscore did not change significantly after either procedure [7,17]. We speculate that the discrepancy in the IPSS voiding subscore between our study and those previous studies is that we evaluated a larger number of patients, and skill with the HoLEP technique depends on the number of operations performed [18].

In addition, Park et al. [7] reported no significant differences in the change in the IPSS-total, voiding subscore, storage subscore, IPSS-QoL, Qmax, or PVR after HoLEP according to prostate volume (≤30 mL vs. >30 mL). In contrast, our study indicated significant differences between the two groups (ePV ≤30 mL vs. >30 mL) (Table 4). The reason for this difference is not clear, but we suspect that patients with smaller prostates (ePV ≤30 mL) with LUTS have more pathophysiologies, including neurogenic bladder, chronic heart failure, sleep apnea syndrome, and chronic kidney disease, than do patients with larger prostates. However, patients in the ≤30 mL group showed significant decreases in all scores. Similar to a previous report, we recommend surgery for BPH with a small prostate [7].

Unfortunately, both groups included patients whose LUTS did not improve after HoLEP. We successfully performed HoLEP in patients with suspected detrusor underactivity or acontractility to remove a urinary catheter. As we did not perform a pressure-flow urodynamic study, the number of such patients included in this study is not known. However, we think it is appropriate to perform HoLEP in catheter-free patients. Lomas and Krambeck [15] reported that nine patients with detrusor underactivity and eight patients with acontractile bladders and urinary retention underwent HoLEP, of whom seven (77.8%) and five (62.5%) were catheter-free, respectively. Another study reported that HoLEP was effective for catheter-dependent patients with acontractile bladders to remove urinary catheters (18 of 19 patients [94.7%]) [16]. However, the success rate was not as good for patients without a catheter. Future studies evalu-

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ating how we select the appropriate patients for HoLEP, to avoid unnecessary surgery, are needed.

This study had several limitations. First, the data were collected retrospectively, thus potentially introducing selection bias. However, the preoperative data were similar between the two groups, and thus we believe our results are meaningful. Second, the follow-up period was relatively short, and we used follow-up data performed at different time points (3 months, 6 months, or 1 year after surgery). Previous reports revealed that the IPSS, IPSS-QoL, and Qmax at 1 year after HoLEP are similar to those at 3 months [19]. Although data collection at the same time points among patients is preferred, we do not believe this affected our results based on those reports. Third, several characteristics for more accurate discrimination were not available in this study, including pressure-flow urodynamic studies and grade of trabeculation by cystoscopy. Although we lacked accurate data from urodynamic studies, we can predict which patients have detrusor underactivity or bladder outlet obstruction or detrusor underactivity and bladder outlet obstruction by using uroflowmetry parameters, the IPSS, and the intravesical prostatic protrusion ratio. Thus, patients can avoid the discomfort and potential complications of catheterization [20,21]. Finally, surgery was performed by multiple surgeons.

CONCLUSIONS

The results of our current study showed that HoLEP was an effective therapy in patients with larger (≤30 mL) and smaller (>30 mL) prostate volumes. Regardless of prostate size, there were significant improvements after HoLEP in our patients, but the extent of improvement was greater in patients with the larger prostate volume (>30 mL). HoLEP might be a good treatment option for small-sized prostates.

CONFLICTS OF INTEREST

The author has nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Ichiro Tsuboi and Yuki Maruyama. Data acquisition: Ichiro Tsuboi and Takuya Sadahira. Statistical analysis: Ichiro Tsuboi, Noriaki Ono, Toyohiko Watanabe, and Syunji Hayata. Data analysis and interpretation: Nobuyoshi Ando, Yasuhiro Nishiyama, and Motoo Araki. Drafting of the manuscript: Ichiro Tsuboi, Yuki Maruyama, and Takuya Sadahira. Critical revision of the manuscript: Takushi Kurashige, Takaharu Ichikawa, and Ryoji Arata. Supervision: Hiroaki Shiina and Yasutomo Nasu.

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