



Predictors of urgency improvement after Holmium laser enucleation of the prostate in men with benign prostatic hyperplasia

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Purpose: To investigate the change in urinary urgency and predictors of urgency improvement after holmium laser enucleation of the prostate (HoLEP) in men with benign prostatic hyperplasia (BPH).

Materials and Methods: We retrospectively analyzed the medical records of patients who were treated with HoLEP for BPH and had preoperative urgency measuring ≥ 3 on a 5-point urinary sensation scale. Those with prostate cancer diagnosed prior to or after HoLEP, a history of other prostatic and/or urethral surgery, moderate to severe postoperative complications, and neurogenic causes were excluded. Patients who had improved urgency with antimuscarinic medication after HoLEP were excluded. We divided the patients into 2 groups based on urgency symptoms 3 months after HoLEP: improved and unimproved urgency. Improved urgency was defined as a reduction of 2 or more points on the 5-point urinary sensation scale. Preoperative clinical and urodynamic factors as well as perioperative factors were compared between groups.

Results: In total, 139 patients were included in this study. Voiding parameters in all patients improved significantly after HoLEP. Seventy-one patients (51.1%) had improved urgency, while 68 (48.9%) did not show any improvement. A history of acute urinary retention (AUR) and postvoid residual were associated with postoperative urgency improvement in univariate analysis. In multivariate analysis, a history of AUR was an independent factor affecting urgency improvement.

Conclusions: A preoperative history of AUR could influence the change in urgency after HoLEP surgery in patients with BPH.

Keywords: Holmium; Laser therapy; Overactive urinary bladder; Prostatic hyperplasia

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INTRODUCTION

A considerable number of patients with benign prostatic hyperplasia (BPH) have overactive bladder (OAB) symptoms such as urgency, frequency, nocturia, and urgency incontinence [1]. These symptoms have a greater impact on the quality of life (QoL) than voiding symptoms in men

with BPH [2]. The pathophysiology of OAB remains unclear, but it is presumed that the secondary functional and structural changes in the bladder caused by BPH-induced bladder outlet obstruction (BOO) lead to OAB symptoms. BOO is known to cause hypertrophy of the detrusor muscle, alter several neurotransmitters and neuroreceptors in the urothelium and detrusor muscle, and bladder ischemia.

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These alterations consequently lead to a change in the sensory and motor neurons, which has been suggested to be the pathophysiological mechanism of OAB [3,4]. Therefore, if a patient with BPH receives appropriate treatment for BOO, his OAB symptoms are expected to improve. Prior studies reported that medical treatment, such as with an alpha-blocker or 5-alpha-reductase inhibitor, and surgical treatment via transurethral resection of prostate (TURP) both significantly improve voiding symptoms as well as BPH-induced OAB symptoms [5-7].

Holmium laser enucleation of the prostate (HoLEP) treats BPH effectively and safely, irrespective of prostate volume [8]; therefore, it has recently been widely used in place of the TURP procedure as a surgical intervention for BPH. It has also been reported that OAB symptoms and urodynamic parameters improved after the HoLEP surgery [9]. However, OAB symptoms can still remain in some patients even after appropriate surgical treatment and one study showed that urge incontinence lasted longer after the HoLEP than the TURP procedure [10]. Therefore, more studies are required to investigate the relationship between HoLEP and OAB symptoms. Research is especially lacking on a key of OAB symptom, urinary urgency, which has significant negative effects on health-related QoL. In this study, we investigated the change in urgency and predictors of urgency improvement after HoLEP in men with BPH to evaluate the efficacy of HoLEP in urgency and to help decide when treating urgency after HoLEP.

MATERIALS AND METHODS

The present study retrospectively analyzed the medical records of patients who presented with complaints of urgency ≥ 3 on a 5-point urinary sensation scale [11] and who underwent HoLEP from December 2011 to May 2015. Five-point urinary sensation scale was administered by investigator after the patient interview. The patients needed at least 3 months of postoperative follow-up data, and the following cases were excluded: those with prostate cancer diagnosed before or after the HoLEP based on a prostate biopsy; a history of prior prostatic and/or urethral surgery; complications impacting voiding symptoms after a HoLEP such as a urethral stricture; suspected neurogenic causes for urgency; and use of anticholinergics prescribed as treatment for urgency within the 3 months after surgery. The surgery was performed at two centers by 2 surgeons (JCK, HWK) experienced in the HoLEP procedure. Transrectal needle biopsies of the prostate were performed to exclude a prostatic cancer when clinically indicated. Improvement

in urgency was defined as a reduction of 2 or more points on the 5-point urinary sensation scale 3 months after surgery. Patients were divided into 2 groups: improved and unimproved urgency. Preoperative clinical factors and perioperative results were compared between these groups. The preoperative clinical factors investigated were age, total prostate volume, transition zone volume, serum prostate-specific antigen levels, history of acute urinary retention (AUR), urgency incontinence, and the International Prostate Symptom Score (IPSS). Prostate volumes were measured via transrectal ultrasonography. We also compared urodynamic parameters between the 2 groups, which included the maximum flow rate (Qmax), postvoid residual urine volume (PVR), maximum bladder capacity, detrusor pressure at the maximum flow rate (PdetQmax), BOO grade, BOO index, bladder contractility index (BCI), detrusor overactivity (DO), and detrusor underactivity (DUA). BOO grade was measured by using the Schafer obstruction grade. The presence of DO was defined as either spontaneous or provoked involuntary detrusor contractions of ≥ 5 cmH₂O with urgency during filling cystometry. DUA was defined as a BCI less than 100 on the urodynamic study (UDS). The perioperative results considered included enucleation time, morcellation time, laser energy used, enucleation weight, enucleation efficiency, morcellation efficiency, and the enucleation ratio (enucleation weight/transition zone volume).

Continuous variables were reported as means and standard deviations, and categorical variables were expressed as frequencies and percentages. The clinical and urodynamic characteristics in the improved and nonimproved urgency groups were evaluated for statistically significant differences using the Student t-test for continuous variables and the chi-square and Fisher exact tests for categorical variables. We compared the preoperative voiding parameters to postoperative voiding parameters with paired t-test. We used logistic regression analysis to identify factors influencing postoperative urgency. To construct a multivariate model, logistic regression was performed. A 5% level of significance was used for all statistical testing. All statistical analyses were performed using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA). This study was approved by the local ethics committee (Catholic Medical Center, Clinical Research Coordination Center, approval number: HIRB-00200_2-002).

RESULTS

Of 648 patients who underwent HoLEP, 139 patients were included and analyzed; 51.1% (n=71) showed an

improvement in urgency, while 48.9% (n=68) did not show any improvement. The preoperative clinical characteristics and urodynamic parameters are shown in Table 1. A preoperative history of AUR was more frequently observed in the group with improved urgency. Preoperative PVR in unimproved urgency group was larger than that in improved urgency group. The perioperative results are

demonstrated in Table 2, and there was no significant difference between the 2 groups significantly. In follow-up voiding parameters, they were significantly improved 3 months after the surgery [Qmax (p<0.001), PVR (p<0.001), IPSS total score (p<0.001), IPSS storage subscore (p=0.001), IPSS voiding subscore (p<0.001), IPSS QoL score (p<0.001)].

Univariate analysis data showed that the preoperative

Table 1. Baseline characteristics of enrolled patients

Variable	Total (n=139)	Improved urgency group (n=71)	Unimproved urgency group (n=68)	p-value
Age (yr)	68.7±7.5	68.0±7.7	69.4±7.4	0.290
History of AUR	24 (17.3)	18 (25.4)	6 (8.8)	0.010*
Urgency incontinence	34 (24.5)	20 (28.2)	14 (20.6)	0.299
PSA (µg/mL)	5.41±9.9	7.1±3.4	3.7±3.6	0.051
Total prostate volume (mL)	56.3±32.8	58.3±38.5	54.3±25.7	0.472
Transitional zone volume (mL)	29.8±22.7	31.5±25.1	28.2±20.0	0.415
IPSS Total	22.2±7.2	21.9±7.4	22.3±6.9	0.775
IPSS storage subscore	9.0±3.5	8.8±3.7	9.3±3.3	0.439
IPSS voiding subscore	13.1±4.7	13.2±4.8	13.1±4.6	0.891
IPSS QoL score	4.3±0.9	4.3±1.0	4.2±0.9	0.759
Urodynamic parameters				
Qmax (mL/s)	8.1±4.1	7.9±4.1	8.4±4.2	0.436
PVR (mL)	90.0±113.1	110.6±129.9	69.4±91.5	0.035*
Maximum bladder capacity (mL)	356.4±133.1	364.1±144.0	348.3±121.2	0.511
MUCP (cmH ₂ O)	86.7±34.3	88.1±35.6	85.3±33.3	0.713
PdetQmax (cmH ₂ O)	61.4±31.1	65.9±33.4	56.7±27.9	0.104
BOOI	49.1±32.2	54.6±36.5	43.1±25.9	0.051
BOO grade				0.712
3–6	88 (63.3)	46 (64.8)	42 (61.8)	
0–2	51 (36.7)	25 (35.2)	26 (38.2)	
BCI	98.3±36.7	102.6±37.1	93.6±36.0	0.179
DO	19 (13.7)	7 (9.8)	12 (17.6)	0.149
DUA	63 (45.3)	29 (40.8)	34 (50.0)	0.190

Values are presented as mean±standard deviation or number (%).

AUR, acuter urinary retention; PSA, prostate specific antigen; IPSS, international prostate symptom score; QoL, quality of life; Qmax, maximal flow rate; PVR, postvoid residual; MUCP, maximal urethral closure pressure; PdetQmax, detrusor pressure on maximal flow; BOO, bladder outlet obstruction; BOOI, bladder obstruction index; BCI, bladder contractility index; DO, detrusor overactivity; DUA, detrusor underactivity.

*p<0.05, statistically significant.

Table 2. Comparison of perioperative results between urgency improvement and nonimprovement groups

Variable	Total (n=139)	Improved urgency group (n=71)	Unimproved urgency group (n=68)	p-value
Enucleation time (min)	55.4±31.1	59.1±37.2	51.6±22.9	0.159
Morcellation time (min)	9.7±7.6	10.9±9.1	8.5±5.5	0.069
Laser energy used (KJ)	125.1±61.4	126.2±62.3	123.8±61.0	0.819
Enucleation weight (g)	28.5±29.6	31.1±35.2	25.9±22.6	0.307
Enucleation efficiency (g/min)	0.82±3.84	1.1±5.3	0.5±0.5	0.382
Morcellation efficiency (g/min)	3.0±2.2	2.7±1.5	3.3±2.8	0.113
Enucleation ratio	0.94±0.79	0.92±0.66	0.98±0.91	0.638

Values are presented as mean±standard deviation.

Table 3. Multivariate analyses of preoperative factors affecting urgency after Holmium laser enucleation of the prostate

Variable	Odds ratio (95% CI)	p-value
History of AUR	3.107 (1.105–9.510)	0.047
PVR	1.002 (0.999–1.006)	0.225

CI, confidence interval; AUR, acute urinary retention; PVR, postvoid residual.

factors predicting an improvement in perioperative urinary urgency were a history of AUR and the PVR (Table 1). Multivariate analyses revealed that a preoperative history of AUR signified an improvement in perioperative urinary urgency (Table 3).

DISCUSSION

In this study, 51% of the BPH patients with OAB symptoms showed significant improvement in urgency 3 months after surgery, and a history of AUR appeared to be a relevant predictor of this change. Verhamme et al. [12] conducted a study with Dutch general practitioners to investigate the incidence rate of AUR and reported that 2.2 of every 1,000 men suffered from this condition. In addition, AUR was the first of the lower urinary tract symptoms (LUTS)/BPH in 50% of patients with AUR. AUR is correlated with LUTS severity in that the incidence rate of AUR rises with an increase in the American Urologic Association Symptom Index (AUA-SI) [13]. HoLEP relieves LUTS in patients with preoperative symptomatic AUR, which in turn can result in significant IPSS and QoL improvement [14,15]. When comparing patients who underwent HoLEP with and without a history of AUR, patients with preoperative AUR showed greater improvement in the AUA-SI and QoL scores and a lower PVR [16]. Patients with elevated PVRs had higher incidence rates of urinary frequency and nocturia as well as urgency incontinence [17]. Therefore, improvement in the accompanying urgency can also be expected in patients with a history of AUR who show a postoperative PVR reduction and significant improvement in voiding symptoms. The univariate analysis in the present study showed a relationship between higher PVR and improved urgency; although, this was not true on multivariate analysis.

Why storage symptoms are not resolved despite appropriate BOO treatment remains unclear. One potential explanation for this is that BOO causes irreversible changes in the bladder, the storage symptoms can last even after receiving an appropriate treatment for BOO [18]. Also, once an irreversible change is made, it is likely that voiding symptoms are not going to be resolved. In addition, long-term

BOO decreases blood flow in the detrusor muscle, which then depresses a contractile function of the bladder [19]. However, in the present study, voiding parameters improved significantly by 3 months post-HoLEP. Thus, there were presumably few, if any, cases of irreversible bladder changes included in our study.

Although OAB symptoms can be caused by BOO-induced secondary changes, they may also occur in the absence of BOO. If OAB symptoms improve after HoLEP in patients with BOO, it may be assumed that their symptoms were the result of BOO. Therefore, a history of AUR highlights the importance of BOO in the pathophysiology of the bladder.

The pathophysiology of OAB is not perfectly understood, but bladder ischemia is considered to be a key factor. As intravesical pressure increases, bladder blood flow decreases, resulting in a progressive partial denervation of the detrusor muscle. In a study by Wada et al. [20], urgency improvement after TURP was dependent on an improvement in bladder vascular resistance. It is assumed that urgency persists after surgical treatment for BPH due to unresolved bladder ischemia. Bladder vascular resistance increases when the PVR is high or the obstruction is severe. A modest improvement in the postoperative PVR could signify ongoing bladder ischemia and, consequently, continued urgency.

AUR accounts for approximately 30% of the indications for BPH surgery [13]. In 50% of these cases, AUR was the presenting sign of LUTS/BPH and surgical intervention quickly follows the onset of symptoms. Although the exact treatment of AUR has not been established, surgical treatment seems to be the end point of this disease. According to multiple cross-sectional studies worldwide, the immediate treatment of AUR is the urethral catheterization followed by a trial without catheter (TWOC) [21]. But there are studies that TWOC is not enough for successful treatment of AUR. Only 55% of patients were able to void spontaneously after TWOC [22]. Also 67% of patients who experienced AUR eventually underwent BPH related surgery [23]. AUR had an impact on patients' health-related QoL with high pain scores and economic burden reported [24]. Thus, patients with AUR tend to get early surgical treatment for their voiding problems. Early

surgical treatment results in rapid symptom resolution, before the changes in the bladder caused by BOO become severe. Moreover, as HoLEP effectively removes the whole adenoma regardless of the prostate size, a complete release of BOO is possible. This could be another explanation for the relationship between a history of AUR and urgency improvement after HoLEP. Anderson et al. [16] reported that BPH patients without AUR had persistent storage symptoms that were responsive to anticholinergics after HoLEP.

In this study, perioperative urgency improvement was measured on a 5-point urinary sensation scale. This is one of the limitations of our study, as this is a subjective assessment without supporting objective data such as postoperative UDS, voiding diary and OAB symptom score. However, because a UDS is an invasive test with low compliance in perioperative patients, there were no suitable alternatives to a subjective indicator in this study. Also, this study retrospectively analyzed a small group of patients, and thus the statistical power was limited accordingly. Performed retrospectively, this study might have been affected by selection bias.

CONCLUSIONS

A preoperative history of AUR could influence the degree of urinary urgency improvement after a HoLEP, a procedure that is effective for BOO symptom control, particularly when performed early. In other words, a HoLEP can resolve early urgency symptoms for at least 3 months without adjunctive drug treatment in patients with preoperative AUR. However, in patients expected to have persistent urinary urgency, an active treatment, such as early administration of antimuscarinic agents, is necessary.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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