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Holmium Laser Enucleation of the Prostate for Benign Prostatic Hyperplasia: Effectiveness, Safety, and Overcoming of the Learning Curve

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Purpose: To examine the efficacy and safety of holmium laser enucleation of the prostate (HoLEP) for the surgical treatment of benign prostatic hyperplasia and to estimate the time to overcome the learning curve.

Materials and Methods: From May 2008 to October 2009, 164 consecutive patients treated with HoLEP were enrolled in this study. International Prostate Symptom Score (IPSS), peak urinary flow rate (Qmax), and postvoid residual urine (PVR) were documented preoperatively and at 6 weeks and 3, 6, 12, and 18 months postoperatively. The 164 study subjects were divided into 3 groups (group 1 the first 50 patients treated, group 2 the second 50, and group 3 the third 64), and perioperative data and complications were analyzed in these groups to determine the learning curve. In addition, the inverse and upward techniques were compared in terms of the effects and the stability of morcellation.

Results: The mean patient age was 69 years, and the average operation time was 62 minutes (range, 20-208 minutes). Mean prostate volume was 54.2 ml and mean resected tissue weight was 18.6 g. Postoperatively, IPSS and PVR decreased and Qmax increased significantly. Postoperative complications were transient incontinence (8.5%), urinary retention (4.3%), hematuria (3.0%), urinary tract infection (1.2%), and urethral stricture (0.6%), and intraoperative complications were minor capsular perforation (4%) and bladder injury (8%).

Conclusions: HoLEP was found to be effective and safe regardless of prostate size. We recommend that a systematic educational program be established to reduce the learning curve.

Key Words: *Holmium; Lasers; Prostate; Prostatic hyperplasia*

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INTRODUCTION

Transurethral resection of the prostate (TURP) has been considered as the standard for the surgical treatment for bladder outlet obstruction induced by benign prostatic hyperplasia (BPH). However, ever since Gilling and Fraundorfer reported the concept of holmium laser enucleation of the prostate (HoLEP) in 1998 [1], HoLEP has been increasingly used. HoLEP is considered to be at least equivalent to or better than TURP, has been reported to have the same long-term record as open prostatectomy, and also has been suggested as an endourological surgery that could replace open prostatectomy [2,3]. Recently, HoLEP has been adopted by several hospitals in South Korea. However, no domestic study has been conducted on HoLEP as yet. Thus, we decided to describe our early experiences regarding the effectiveness and safety of HoLEP and to estimate the learning curve, which has been reported to be the largest disadvantage of HoLEP [4-6].

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MATERIALS AND METHODS

1. Subjects

From May 2008 through October 2009, 164 consecutive patients who underwent HoLEP for BPH were included in this study. Patients were included when their International Prostate Symptom Score (IPSS) was 8 or higher, their peak urinary flow rate (Qmax) was 15 ml/s or less, or their postvoid residual urine (PVR) was significant. Patients were excluded if they had prostate cancer, had neurogenic bladder, or had undergone urethral surgery. Prostate biopsies were performed to exclude prostate cancer when clinically necessary. All procedures were performed by a single surgeon (JBL). Before HoLEP, all patients underwent a digital rectal examination, serum prostate-specific antigen (PSA), transrectal ultrasonography, uroflowmetry, and residual urine measurement, and IPSS and quality of life (QoL) scores were determined.

2. Surgical skills

The HoLEP procedure is composed of two parts: enucleation for prostate adenoma and morcellation of the removed tissues within the bladder [3,7]. Briefly, the median and the lateral prostate lobes were dissected off the surgical capsule of the prostate in a retrograde direction from the apex and released into the bladder [1,4]. With the capsule plane secured, the capsule is peeled off continuously from its top and bottom sides in a nine o'clock (right side) and three o'clock (left side) direction by using the "push and cut" technique. In this manner, all lateral lobes are removed; remaining tissues are then trimmed and hemostasis applied [4,7]. Morcellation is then performed within the bladder. After the bladder is sufficiently filled, the removed tissues are grasped with the morcellator by suction [4,7]. The tissues are then ground into small pieces by using forward and backward movements of the blades before being totally evacuated.

After HoLEP, a 3-way 22 Fr urethral catheter was inserted and continuous irrigation was carried out. Bladder filling during HoLEP may cause temporary postoperative hypotonicity [8]; thus, the urethral catheter was generally removed 1 to 2 days later. All retrieved tissues were examined histologically.

3. Instruments

The VersaPulse PowerSuite™ (Lumenis, Israel) Holmium Laser was used for the enucleation of prostatic adenoma at a laser power of 80-100 W. Morcellation was conducted by using a percutaneous nephrolithotomy (PNL) nephroscope and a VersaCut® Morcellator (Lumenis, Israel).

4. Outcomes

IPSS and QoL scores and uroflowmetry and residual urine were determined at 6 weeks and 3, 6, 12, and 18 months after HoLEP and were compared with data obtained preoperatively. A questionnaire on complications was also administered at the same time. Serum PSA was assessed at 6 months and 1 year postoperatively.

5. Learning curve

With respect to the learning curve, the 164 consecutive patients were divided into three groups, that is, the first 50 patients, the second 50 patients, and the third 64 patients treated, and perioperative data and complications were compared between the groups.

6. Morcellation technique

Morcellation using an inverse (downward) technique was used to improve the safety of the morcellation procedure from the 85th patient. Morcellation effectiveness and safety of the inverse and upward techniques were compared. During inverse morcellation, the blade is hung upside down such that it is directed toward the base of the bladder. By positioning a morcellator on top of prostatic tissues, the tissues can be held and evacuated from above by suction.

7. Statistical analysis

The mean values of continuous variables were used in the analysis. Ranges are shown in parentheses. The unpaired Student's t-test was used to analyze differences between group mean values, and the Mann-Whitney U test was used to analyze non-normally distributed continuous variables. p-values of less than 0.05 were considered significant.

RESULTS

1. Baseline characteristics

Baseline characteristics are listed in Table 1. Forty-three patients (26%) had a prostate volume of <40 ml, 82 (50%) a prostrate volume of 41-59 ml, and 39 (24%) had a volume of >60 ml as shown in Table 2.

TABLE 1. Baseline characteristics of the 164 patients who underwent HoLEP

	Mean (range)
Age (years)	69 (54-92)
Prostate volume (ml)	54.2 (28-170)
PSA (ng/ml)	5.1 (0.16-36.32)
AUR (No.)	25
Urologic medical Hx. (No.)	
α-blocker	56
5ARI	4
Combined	25
Urologic surgical Hx. (No.)	
TURP	8
PVP	2

Data are presented as means, with ranges in parentheses, with minimum to maximum in parentheses, or numbers. HoLEP: holmium laser enucleation of the prostate, PSA: prostate-specific antigen, AUR: acute urinary retention, Hx.: history, 5ARI: 5α reductase inhibitor, Combined means that α-blocker and 5ARI were co-administered, TUPR: transurethral resection of the prostate, PVP: photoselective vaporization of the prostate

2. Outcomes

The mean operative time was 62 minutes (range, 20-208 minutes) and the mean amount of retrieved prostate tissue was 18.6 g (range, 2-144 g), which represented 34.3% of the total volume of the prostates. The larger the volume of the prostatic gland, the greater the amount of tissue resected, as shown in Table 2.

Changes in clinical parameters after HoLEP are listed in Table 3. At 6 months postoperatively, median PVR had declined by 87.5%, whereas the mean Qmax rate had increased by 94%, and mean IPSS and median QoL scores had decreased by 63.2%, and 56.6%, respectively. In addition, mean serum PSA was 1.5 (range, 0.1-11.8), a decrease of 70.6%.

Hemoglobin and electrolytes decreased postoperatively but not significantly, and there was no case of blood transfusion. The mean catheterization time was 2.5 days (range, 1-7 days).

During HoLEP, visual internal urethrotomy was performed in 2 cases for mild urethral stricture, and lithotripsy was performed in 5 cases for accompanying bladder stones.

3. Learning curve

About 50 cases showed a large change in the learning curve. Later, a stable learning curve could be maintained. Table 4 and 5 detail the operative data and the complications encountered.

4. Complications

Postoperative complications included transient incontinence (8.5%), urinary retention (4.3%), urinary tract infection (1.2%), and urethral stricture (0.6%). After discharge, 3% of patients required readmission due to hematuria, which was resolved conservatively by an indwelling urethral catheter for 2 to 3 days. Furthermore, a distinctive decrease in transient incontinence was shown in 50 cases as seen in Table 5.

5. Morcellation technique

As seen in Table 6, bladder injury was effectively overcome by securing stable visual sites during morcellation by the

TABLE 2. Classification of resected weight proportion according to prostate volume

	Prostate volume (ml)			Total
	≤40	41-59	≥60	
No. of patients (%)	43 (26)	82 (50)	39 (24)	164 (100)
Ratio of the resected weight (%)	22.6	30.5	48.1	34.3

Statistical significance was accepted for p-values of <0.05

TABLE 3. Changes in clinical parameters after HoLEP

	Preoperative (n=164)	Postoperative		
		3 months (n=160)	6 months (n=152)	12 months (n=38)
IPSS	25.0 (7-35)	11.4 (5-19)	9.2 (2-16)	7.1 (1-13)
QoL	5.3 (4-6)	3.4 (1-5)	2.3 (0-4)	2.1 (0-4)
Qmax (ml/s)	11.4 (1.1-17.5)	25.2 (14.4-38.0)	22.1 (10.9-33.8)	23.8 (11.8-40.6)
PVR (ml)	88 (22-260)	39 (0-80)	11 (0-40)	10 (0-37)

Data are presented as means, with ranges in parentheses, with minimum to maximum in parentheses. Statistical significance was accepted for p-values of <0.05. HoLEP: holmium laser enucleation of the prostate, IPSS: International Prostate Symptom Score, QoL: quality of life, Qmax: peak urinary flow rate, PVR: postvoid residual urine

TABLE 4. Evolution of operative data during the learning curve

	Patients No.		
	1-50	51-100	101-164
Age (years)	68.9 (57-83)	69.3 (54-92)	68.3 (55-87)
Used laser energy (kJ)[a]	142.0 (38.4-330.0)	82.1 (18.5-264.3)	80.1 (20.9-222.3)
Operation time (min)[a]	74.2 (40-208)	58.3 (20-133)	56.9 (20-126)
Operation efficiency (g/min)[a]	0.25 (0.07-0.49)	0.34 (0.11-0.81)	0.35 (0.09-0.79)
Prostate volume (ml)	53.8 (28-104)	55.0 (33-170)	54.0 (34-159)
Resected weight (g)	17.9 (2-51)	19.2 (4-144)	18.8 (3-126)
Hb loss	0.69	0.71	0.44
Na decrease	0.88	0.09	0.61
Catheterization time (days)[a]	2.7 (2-7)	2.3 (1-6)	2.0 (1-4)

Data are presented as means, with ranges in parentheses, with minimum to maximum in parentheses. Hb: hemoglobin, Na: serum sodium, [a]: statistically significant at the $p<0.05$ level

TABLE 5. Intraoperative and postoperative complications during the learning curve

	Patients No.			Total
	1-50	51-100	101-164	
Change to TURP during HoLEP[a]	6[c]	0	0	6
Minor capsular perforation[a]	4	1	1	6
Bladder injury[b]	9	3	1	13
Transfusion	0	0	0	0
Recatheterization due to retention[b]	4	2	1	7
Re-admission due to hematuria	2	2	1	5
Transient incontinence[b,d]	7	4	3	14
Urinary tract infection	1	1	0	2
Urethral sticture[a]	1	0	0	1
Bladder neck contracture	0	0	0	0
Re-operation due to remnant adenoma	0	0	0	0

TURP: transurethral resection of the prostate, HoLEP: holmium laser enucleation of the prostate, [a]: statistically significant differences between patients 1-50 and 51-100 ($p<0.05$), [b]: statistically significant differences between patients 1-50, 51-100, and 101-164 ($p<0.05$), [c]: all were within 20 consecutive cases, [d]: usually resolved <3 months after HoLEP

TABLE 6. Comparison of operative data regarding morcellation for the upward and inverse (downward) techniques

	Upward technique	Inverse (downward) technique
Patients No.	1-84	85-164
Mean morcellation time (min)	14.3±8.6	6.1±7.4
Morcellation efficiency (g/min)	1.93±1.14	4.06±0.95
Bladder injury	11	2
Superficial	6	2
Deep[a]	5	0
Catheter time (days)	2.6±1.7	2.0±1.2

Data presented are Means±SD or numbers. Statistical significance was accepted for p values of <0.05. [a]: injury involved the muscular layer and required an indwelling urethral catheter for more than 3 days postoperatively

inverse (downward) technique.

6. Pathology

Prostate cancer was detected histologically in 3 (2%) patients postoperatively.

DISCUSSION

Recently, HoLEP has emerged as an attractive surgical alternative to the treatment of bladder outlet obstruction due to BPH [9]. The HoLEP technique is a method of removing all prostatic adenoma endourologically and might be as effective as open prostatectomy and theoretically reduce complications [3,10,11]. Kuntz et al reported in a study involving 120 patients with a 5-year follow-up study that HoLEP and open prostatectomy showed the same level of clinical improvement and that BPH did not recur; thus, it was concluded that HoLEP is an endourological alternative for open prostatectomy [3]. In addition, other studies reported that open prostatectomy was better in the indices of operation time and removed tissue weight, but that HoLEP was better in the indices of catheterization time, hospital stay, and bleeding or transfusion. The reason for HoLEP having less removed weight was thought to be due to tissue evaporation by laser during HoLEP [3,6,9,12].

Previous studies have compared HoLEP and TURP and found that TURP was better in terms of operation time, whereas HoLEP was better in terms of resected tissue weight, catheterization time, hospital stay, and bleeding or transfusion [6,13-15]. Furthermore, there was no difference in the uroflowmetry or change of symptom scores between both groups after 2 years of follow-up observations [14,15]. Kuntz et al reported in a randomized study of 200 patients with a 1-year follow-up that HoLEP was better than TURP in terms of hospital stays, hemoglobin decrease, clinical improvement, and residual urine [2]. Furthermore, HoLEP was shown to be effective and safe for treating concurrent BPH in patients administered anticoagulants, in patients with a hemorrhagic disorder, and in patients with stones in the upper urinary tract or bladder [16-20].

However, the major disadvantage of HoLEP concerns overcoming the learning curve, which requires experience and time. Many surgeons have mentioned that although the HoLEP method was more difficult than TURP, one could overcome the difficulty with self-learning [5,21-23]. Seki et al reported an enucleation efficiency study involving 70 patients who underwent HoLEP and were divided into 7 groups of 10 patients each. In the first group, enucleation efficiency was 0.3 g/min but in the last group it had increased to 0.75 g/min, showing that the accumulation of experience improved the learning curve [24]. Placer et al studied the learning curve of HoLEP in 125 patients who were divided into 5 groups in time-sequence order; they compared the first and last groups [4]. Enucleation efficiency was found to markedly increase from 0.3 g/min to 1 g/min, and mean operation times and the amount of energy used showed decreases of 47% and 45%, respectively, between these groups. Furthermore, regarding transient incontinence, which is representative of the complications of HoLEP, the prevalence in the first group of 50 patients was 28%, but that in the last group of 50 patients was markedly reduced by 6%. Thus, they mentioned that improvement of the learning curve had a direct effect of decreasing complications [4].

Recently, Shah et al reported the results of a study involving 162 patients who were divided into 3 groups by sequence of HoLEP (first group: 1-50, second group: 51-100, and third group: 101-162). Eight patients (5%) out of 162 showed a failure of lateral lobe enucleation, and thereby were switched to TURP. All 8 were among the first 25 treated, and enucleation efficiency was improved approaching a high point plateau after 50 cases. Experience with about 50 cases would be necessary to reach the expert level in this

surgical technique, HoLEP. Also, instruction by more experienced urologists would bring about better results and shorten the learning curve [21]. In our study, HoLEP learning was self-taught and accomplished alone after attending as an observer and watching the self-learning video, because the opportunity to be supervised by an experienced urologist was not available in Korea. In the case of our study, enucleation failure for the first 20 cases led to switching to TURP in 6 patients (4%). This asserts the necessity of a systemized mentoring program.

The most significant complication that can develop in HoLEP is bladder injury during morcellation. Generally, its frequency is less than 10%, and most degrees of the injury are not severe [22]. However, introduction of morcellation by the inverse (downward) technique was effective at reducing bladder injury. The inverse (downward) technique could prevent blocking of the view of the posterior wall of the bladder by the tissues during morcellation and helped to maintain a sufficient distance of the morcellator from the bladder wall. A bladder wall injury by the blade during HoLEP would grasp the bladder trigon area, which is relatively safer, thus preventing the worst scenario or sequelae. In the case of our study, the morcellation time was significantly reduced and bladder injury and urethral catheterization time were also distinctively reduced (Table 6).

The frequency of urethral stricture and bladder neck contracture by HoLEP was also within the 5% range, which was similar to that of TURP [2,25]. In our study, the short follow-up observation period did not allow assessment of this issue.

Transient incontinence is a postoperative complication of HoLEP that distresses many surgeons. The surgical features of total prostatic adenoma removal by HoLEP tend to induce higher frequencies of incontinence than does TURP and the condition lasts longer [26,27]. The incontinence frequency was reported to be 1% through 44%. However, 3-10% is most common [4,5,22,28,29]. Higher incontinence frequency is reported during the initial try with less experience and is thought to be associated with the learning curve [4,5]. The duration of postoperative incontinence is usually 3 to 6 months. Some surgeons reported permanent incontinence. However, incontinence is mostly a transient occurrence [4,22,28,29]. An antiinflammatory or anticholinergic drug could be used to regulate incontinence [22,28]. We also realized that the frequency of transient incontinence was markedly reduced as the number of cases increased. The reasons for such a decrease in the frequency of incontinence were considered to be improvement of the learning curve, efforts to reduce thermal injuries on the apex level by a laser, and the process of saving some amount of anterior fibromuscular stroma tissues [13,28,30].

CONCLUSIONS

HoLEP has fewer complication and is effective. It is a method that may completely remove prostatic adenoma tissues. In particular, its clinical effectiveness is excellent regardless of prostate size, and it is effective even in cases with a prostate volume of 100 ml or more. However, for self- taught surgeons, about 50 cases are needed to reach the experienced level; thus, we suggest the establishment of a systematic educational program to shorten the learning period.

Conflicts of Interest

The authors have nothing to disclose.

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