

Holmium Laser Enucleation of the Prostate: Long-Term Durability of Clinical Outcomes and Complication Rates During 10 Years of Followup

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Abbreviations and Acronyms

BPH = benign prostatic hyperplasia

HoLEP = holmium laser enucleation of the prostate

I-PSS = International Prostate Symptom Score

OP = open prostatectomy

PSA = prostate specific antigen

PVR = post-void residual volume

Qmax = maximal flow rate

QOL = quality of life

SUI = stress urinary incontinence

TURP = transurethral resection of the prostate

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Purpose: We assessed the long-term durability of subjective and objective outcomes and complication rates after holmium laser enucleation of the prostate.

Materials and Methods: We conducted a retrospective analysis of 949 evaluable patients treated with holmium laser enucleation of the prostate between March 1998 and September 2010 at a single center. Study variables included International Prostate Symptom Score, quality of life, maximum urinary flow rate, post-void residual urine volume and prostate specific antigen.

Results: Mean followup was 62 months. Mean preoperative post-void residual volume, maximal flow rate, International Prostate Symptom Score and quality of life were 311 ml, 7.9 ml per second, 19 and 3.8, respectively. Postoperatively all variables showed significant improvement starting at month 1 of followup and remained improved for the entire followup period. Patients with acute urinary retention represented 36% (343) of the cohort. Postoperative mean post-void residual volume was 45, 25.7 and 52 ml, mean maximal flow rate was 21.5, 24.3 and 23.4 ml per second, mean International Prostate Symptom Score was 7.3, 4.4 and 3.8, and mean quality of life was 1.7, 1 and 0.7 at 1 month, 1 year and 10 years, respectively. Persistent urge and stress incontinence were found in 1% and 0.5% of patients, respectively. Bladder neck contracture, urethral stricture and reoperation due to residual adenoma developed in 0.8%, 1.6% and 0.7% of patients.

Conclusions: Holmium laser enucleation of the prostate represents an effective treatment modality for men with symptomatic benign prostatic hyperplasia with a low rate of complications during a long followup. Patients who experience improvement from baseline to early followup maintain improvement at later followup.

Key Words: lasers, solid-state; prostatic hyperplasia; transurethral resection of prostate; treatment outcome

FOR many years TURP has been considered the standard surgical therapy for lower urinary tract symptoms secondary to BPH despite perioperative morbidity.¹ This success rate is reflected in substantial improvements in clinical outcomes and a low re-treatment rate on long-term followup.^{2,3}

HoLEP has been used for the treatment of symptomatic BPH since 1996. Many publications have demonstrated the durability of HoLEP for most prostate sizes at long-term followup with low complication rates.⁴⁻⁷ HoLEP has demonstrated good short-term to mid-term clinical improvement up to 5 years.

However, data on long-term durability (greater than 5 years) are still accumulating.

Patients with urinary retention represent a particular challenge to urologists as they often experience inferior functional outcomes and higher complication rates compared to those without urinary retention. HoLEP has been reported to be safe and highly effective in treating urinary retention in men with a large prostate.^{8,9} The most frustrating aspect of minimally invasive techniques is the high rate of recurrence and the need for re-treatment due to the failure of the treatment over time.¹⁰ In this study we document the durability of HoLEP outcomes in a large cohort of patients during a longer followup period.

PATIENTS AND METHODS

We performed a retrospective analysis of patients treated with HoLEP performed by a single surgeon between March 1998 and September 2010 at McGill University Health Centre. Of the 949 patients included in the study 161 and 89 were followed to 9 and 10 years, respectively. Variables studied included I-PSS, QOL, uroflowmetry (Qmax) and PVR. Analysis was done at 1, 3, 6 and 12 months, and then yearly for a maximum of 10 years. In our cohort 343 patients presented preoperatively with acute urinary retention. After they were included in the initial analysis a subset analysis was done for that challenging group of patients.

Postoperative complications including urethral stricture, bladder neck contracture, reoperation due to residual adenoma or regrowth and urinary incontinence were assessed and included in the study. Descriptive analysis was performed, with comparative analysis at each followup period using the paired t test.

RESULTS

Mean patient age was 70 years. Mean preoperative serum PSA was 4.3 ng/ml and mean prostate volume was 81 cc. Mean operative time was 96 minutes, and mean preoperative I-PSS, QOL, Qmax and PVR

were 19, 3.8, 7.9 ml per second and 311 ml, respectively. All studied variables showed a significant improvement starting from the first month of followup and remained significantly improved during the entire followup period.

At 1 month, 1 year and 10 years mean I-PSS was 7, 4.4 and 3.6, mean QOL was 1.6, 1 and 0.7, mean Qmax was 22, 24.6 and 27 ml per second, and mean PVR was 48, 31.7 and 20.7 ml, respectively. Table 1 shows the descriptive analysis of these data during each point of followup while table 2 shows the paired t test at followup. The number of patients included in the PSA analysis was 809 at 3 months, 132 at 9 years and 72 at 10 years. The percent reduction of PSA was 86%, 83% and 84% at 3 months, 9 years and 10 years of followup, respectively.

In our cohort 343 patients (36%) presented with acute urinary retention. Postoperatively mean I-PSS was 7.3, 4.4 and 3.8, mean QOL was 1.7, 1 and 0.7, mean Qmax was 21.5, 24.3 and 23.4 ml per second, and mean PVR was 45, 25.7 and 52 ml at 1 month, 1 year and 10 years, respectively. Table 3 shows the data for this challenging cohort of patients.

Of our patients 4 (0.4%) were on anticoagulant therapy intraoperatively and required intraoperative blood transfusion. In addition, 7 (0.7%) patients had superficial bladder mucosal injury which did not necessitate any further treatment. Compared to the overall durability means, patients who completed 10-year followup had significant improvement of all variables measured in terms of I-PSS (4.5 vs 3.6), QOL (1.1 vs 0.7), PVR (34.2 vs 20.7 ml) and Qmax (18.8 vs 26.9 ml per second) ($p < 0.001$).

Complications were minimal in our cohort of patients. Bladder neck contracture and urethral stricture developed in 0.8% and 1.6% of patients, respectively. The reoperation rate as a result of recurrent obstruction from residual adenoma was 0.7%. Transient SUI was found in 47 men (4.9%)

Table 1. Descriptive analysis of HoLEP outcomes

Followup	No. Pts	I-PSS Mean (range)/Median	QOL Mean (range)/Median	Qmax Mean (range)/Median	PVR Mean (range)/Median
Preop	949	19 (0–35)/19	3.8 (0–6)/4	8 (1.3–20)/8	311 (10–2,500)/192
1 Mo	909	7 (0–32)/6	1.6 (0–6)/1	22 (1.6–67.4)/20	48 (0–500)/32
3 Mos	876	5.2 (0–35)/4	1.2 (0–6)/1	23.2 (2.1–67.4)/21.8	36 (0–999)/22
6 Mos	823	4.7 (0–32)/4	1 (0–6)/1	24.3 (4.8–65.3)/23.2	33 (0–823)/18
1 Yr	771	4.4 (0–27)/3	1 (0–6)/1	24.6 (2.3–70)/23.2	31.7 (0–637)/15
2 Yrs	722	4 (0–30)/3	0.99 (0–6)/1	24.6 (2.4–72.5)/22.6	34 (0–511)/15
3 Yrs	676	4.3 (0–26)/3	0.99 (0–6)/1	24.5 (5.1–72)/22.9	32 (0–575)/14
4 Yrs	623	4.6 (0–27)/3	1 (0–6)/1	23.7 (3.7–67.6)/22.3	36 (0–644)/13
5 Yrs	563	4.6 (0–25)/3	1 (0–5)/1	23.7 (5.1–67.4)/22.8	36 (0–669)/15
6 Yrs	486	4.7 (0–25)/3	1 (0–5)/1	24.7 (0–62.6)/24.1	30 (0–559)/16
7 Yrs	324	4.3 (0–29)/3	1 (0–4)/1	25.6 (1–62.5)/25.1	27 (0–637)/18
8 Yrs	263	4 (0–20)/3	0.8 (0–5)/1	25.8 (4–67.6)/25.8	27.8 (0–528)/15
9 Yrs	161	3.5 (0–16)/2	0.7 (0–3)/1	26.6 (5.8–57.9)/27.1	27.1 (0–456)/15
10 Yrs	89	3.6 (0–12)/3	0.7 (0–3)/1	26.9 (6.6–44.5)/27.8	20.7 (0–654)/12

Table 2. Comparative analysis of HoLEP outcomes

	Mean I-PSS	p Value
Pair 1:		
Preop	18.9	<0.0001
1 Mo	7.2	
Pair 2:		
1 Mo	6.7	<0.0001
1 Yr	4.4	
Pair 3:		
1 Yr	4.2	<0.0001
10 Yrs	3.6	
	Mean QOL	
Pair 4:		
Preop	3.8	<0.0001
1 Mo	1.6	
Pair 5:		
1 Mo	1.5	<0.0001
1 Yr	0.99	
Pair 6:		
1 Yr	0.97	<0.0001
10 Yrs	0.77	
	Mean Qmax	
Pair 7:		
Preop	8	0.002
1 Mo	21.9	
Pair 8:		
1 Mo	21.7	<0.0001
1 Yr	24.9	
Pair 9:		
1 Yr	23.5	<0.0001
10 Yrs	26.8	
	Mean PVR	
Pair 10:		
Preop	311	<0.0001
1 Mo	48	
Pair 11:		
1 Mo	45.7	<0.0001
1 Yr	31.7	
Pair 12:		
1 Yr	35.3	<0.0001
10 Yrs	20.7	

at the first 3-month followup visit and only 5 (0.5%) still had SUI up to the last followup visit. Persistent urge incontinence was found in 1% of our cohort.

The effect of the learning curve on the clinical outcomes was further examined by comparing the results of patients treated in the first 3 years to the results of those treated in the last 3 years. There was a significant improvement of all variables measured in terms of I-PSS (6.2 vs 3.6), QOL (1.2 vs 0.9), PVR (36.7 vs 24.2 ml) and Qmax (14.4 vs 24.6 ml per second), comparing the outcome of treatment in the first 3 years vs the last 3 years, respectively (p <0.001).

DISCUSSION

The technique of HoLEP is currently challenging TURP as a size independent gold standard associ-

ated with at least equal durable outcomes and a lower complication rate. However, the replacement of TURP with HoLEP as a gold standard has not been recommended due to the lack of durability studies on a sufficient number of cases. Krambeck et al recently published results on more than 1,000 cases managed with HoLEP.¹¹ They could draw a strong conclusion with durable long-term results using HoLEP in 83 patients with followup of more than 5 years. At short-term, intermediate term and long-term followup, mean symptom score was 8.7, 5.9 and 5.3, and maximum urinary flow was 17.9, 19.5 and 22.7 cc per second, respectively.

Gilling et al reported on 38 patients with a mean followup of 6 years.⁶ They also demonstrated durable outcomes using HoLEP, with persistent reductions in I-PSS score (8.5 vs 25.7), QOL score (1.8 vs 4.9) and improvement in Qmax (19 vs 8.1 ml per second), as well as a 92% overall patient satisfaction rate.

Kuntz et al reported their 5-year followup results of a randomized clinical trial comparing HoLEP to OP.¹² Interestingly the mean postoperative AUA symptom score was 3.0 in both groups (p = 0.98), mean Qmax was 24.4 ml per second in both groups (p = 0.97), and PVR was 11 ml in the HoLEP and 5 ml in the OP group (p = 0.25). Late complications included urethral stricture and bladder neck contracture, with reoperation rates of 5% in the HoLEP and 6.7% in the OP group (p = 1.0) to correct these complications. No patient had recurrence of benign prostatic hyperplasia. The same group prospectively followed 100 patients treated with HoLEP vs 100 treated with TURP with 3 years of followup,¹³ and again they demonstrated equal efficacy and safe outcomes.

Our study strongly supports previous publications in terms of the durability of outcomes obtained by HoLEP because we obtained followup data for 9 years in 161 patients and for 10 years in 89 patients from a large cohort. To the best of our knowledge this represents the longest followup in the published literature obtained for this number of cases. We were able to provide immediate excellent outcomes following the HoLEP technique as measured by improvement in I-PSS, QOL, Qmax and PVR. That improvement was persistent and even increasing during followup.

Table 3. Descriptive analysis of the acute retention group

	1 Mo Mean (range)/ Median	1 Yr Mean (range)/ Median	10 Yrs Mean (range)/ Median
I-PSS	7.3 (0-26)/6	4.4 (0-25)/3	3.8 (1-8)/3
QOL	1.7 (0-6)/1	1 (0-6)/1	0.7 (0-2)/1
Qmax	21.5 (1.6-67.4)/19	24.4 (5.8-65.5)/22	23.4 (6.6-42.1)/24.7
PVR	45.2 (0-338)/30	25.7 (0-205)/10	52.2 (0-654)/0

In a longitudinal study we evaluated 335 patients treated with HoLEP between 1998 and 2006.⁷ Mean PSA reduction was 75.4%. Postoperative PSA and percent PSA reduction were indicators that HoLEP was an effective technique in nearly complete adenoma removal. Moreover, this percent reduction in PSA remained at lower levels for up to 7 years of followup, suggesting that the glandular size reduction after HoLEP is durable and more complete, possibly explaining the lower reoperation rates previously reported for residual tissue. In addition, we proposed that if the reduction in PSA after HoLEP was 50% or less, these patients should be followed more closely with PSA measurements every 3 to 6 months for the first 2 to 3 years to allow the earlier detection of prostate cancer. In our cohort the percent reduction in PSA was 86% at 3 months postoperatively, and remained durable at 9 (83%) and 10 years (84%) of followup.

In terms of acute urinary retention, the 36% of our cohort who presented preoperatively with retention was reanalyzed separately. On long-term followup we determined that those patients had excellent outcomes similar to those of the overall cohort with no extra morbidity or complications. Peterson et al performed a retrospective study evaluating 164 patients with urinary retention treated with HoLEP.⁹ Their results confirmed the safety and reliability of this procedure for urinary retention in men with a large prostate. Mean duration of urinary retention was 28.9 days (range 2 to 365). All patients were able to void following treatment and remained catheter-free at followup to 1 year. Mean urine flow rate was 26.7 ml per second (range 4.3 to 54.8) and mean PVR was 32.5 ml (range 0 to 150). Anderson et al studied 87 patients treated with HoLEP.¹⁴ They found holmium enucleation to be safe and equally effective for patients with acute retention as for those without retention.¹⁴ We previously published our short-term followup for a cohort of 169 patients with acute urinary retention, and demonstrated the safety and efficacy of HoLEP for this cohort.⁸

Kuo et al studied 108 patients treated with HoLEP for a prostate greater than 75 gm.¹⁵ They reported bladder neck contracture in 0.9% of cases. Krambeck et al reported bladder neck contracture in 1.3% and 6% of patients followed for more than 1 and 5 years, respectively.¹¹ Aho and Gilling reported bladder neck contracture and urethral stricture in 0.35% and 2.1% of their cases after 3 years of followup.¹⁶ Moody and Lingeman reported their initial experience with HoLEP in 2000, with an acceptable rate of complications of 3% and 0% for bladder neck contracture and urethral stricture, respectively.¹⁷ In our cohort bladder neck contracture and urethral

stricture developed in 0.8% and 1.6%, respectively, comparable to previous publications and confirming the safety of the technique.

HoLEP results in SUI at a rate comparable to that of other surgical techniques for the treatment of BPH. In our cohort SUI was found in 47 (4.9%) of 949 men during the first 3-month followup visit. However, after 3 months it was still present in only 13 men (1.3%). In most of the 13 patients SUI resolved within the first year of followup with only 5 (0.5%) still having SUI up to the last followup visit.

Vavassori et al evaluated 330 patients after HoLEP with 3 years of followup.¹⁸ They reported transient SUI in 7.3% of patients (58.3% in prostates less than 50 gm vs 41.6% in prostates greater than 50 gm) without any significant difference regarding prostate size. The rate of persistent stress incontinence up to last followup (36 months) was 0.6%. Krambeck et al found that at short-term, intermediate term, long-term and greater than 5-year followup stress incontinence was noted in 12.5%, 3.4%, 1.8% and 4.8% of patients, respectively.¹¹ At last followup 9 (0.8%) patients had stress incontinence. The persistence of improved outcomes and even more improvement during longer followup are reassuring, and confirm the initial report by Elzayat and Elhilali.¹⁹

However, adoption of holmium laser enucleation of the prostate has been limited by its steep learning curve, a limitation often stated by urologists attempting to perform HoLEP. However, there is an increasing interest in HoLEP as the new gold standard for the surgical management of BPH of any size replacing open prostatectomy and TURP. Baazeem et al recently published new modifications to the HoLEP technique.²⁰ They emphasized the importance of blunt dissection facilitating the early separation of the adenoma near the verumontanum proximal to the external sphincter.

Another modification they propose is that when the adenoma is separated laterally and the anterior aspect of the prostate is reached, the dissection is extended across the midline to facilitate the separation of the 2 lobes in the midline anteriorly when we make the 12 o'clock incision, eliminating any guesswork about the depth needed and avoiding the creation of multiple planes. We believe that it is also important for the learning process to be achieved by performing approximately 20 cases closer to each other during the learning period to avoid restarting to learn every time. One of the limitations of this study is that the mean followup period was 5 years, and 263 (27.7%), 161 (17%) and 89 (9%) patients completed 8, 9 and 10 year followup.

CONCLUSIONS

HoLEP represents a successful, safe and durable treatment for the symptomatic enlarged prostate with a lower recurrence rate on long-term followup.

Subjective and objective measures of patient outcomes remained durable on followup. Thus, HoLEP may be safely considered a new, size independent, gold standard for symptomatic BPH.

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