OUTCOMES OF HoLEP IN THE RETREATMENT SETTING

Tracy Marien¹ MD, Mustafa Kadihasanoglu¹ MD, Teerayut Tangpaitoon¹ MD, Nadya York² MD, Andrew T. Blackburne³ MD, Haidar Abdul-Muhsin⁴ MD, Michael S. Borofsky² MD, Amy E. Krambeck³ MD, Mitchell R. Humphreys⁴ MD, James E. Lingeman² MD, and Nicole L. Miller¹ MD

¹Vanderbilt University Medical Center, Nashville, TN; ²Indiana University School of Medicine, Indianapolis, IN; ³Mayo Clinic, Rochester, MN; ⁴Mayo Clinic, Scottsdale, AZ

Corresponding Author:

Nicole L. Miller, MD

A1302 Medical Center North

Nashville, TN 37232

Telephone: 615-322-3807

Fax: 615-322-8990

Email: nicole.miller@vanderbilt.edu

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INTRODUCTION: Holmium laser enucleation of the prostate (HoLEP) can also be applied in the retreatment setting when other BPH therapies fail. We sought to compare outcomes of men undergoing HoLEP in the primary versus retreatment setting (pHoLEP versus rHoLEP).

MATERIALS AND METHODS: A retrospective review of 2,242 patients undergoing HoLEP at four academic hospitals between 2003 and 2015 was performed. Patient demographic, operative and perioperative outcomes between rHoLEP and pHoLEP were compared.

RESULTS: The majority of the 360 (16%) men undergoing rHoLEP did so for residual urinary symptoms (71%). The most commonly primary procedure was transurethral resection of the prostate (42%). Mean time between prior BPH surgery and rHoLEP was 68 months (1-444 months). There were no significant differences in age, prostate size, AUA symptom score (AUASS), or average flow rate between cohorts. Perioperatively, rHoLEP was associated with significantly shorter operative times, reduced blood loss, lower specimen weight, and shorter length of stay. AUASS improved in both groups, though remained higher for men undergoing rHoLEP (6.5 versus 5.0, $P < 0.001$). Likelihood of clot retention (4.7% versus 1.8%, $P = 0.01$) and urethral stricture (3.3% versus 1.5%, $P = 0.043$) were slightly higher in the rHoLEP group.

CONCLUSIONS: Immediate perioperative outcomes for HoLEP performed in the retreatment setting are no different from those in the primary setting. While rHoLEP was associated with increases in likelihood of clot retention, urethral stricture, and AUA

symptom score, these minimal differences must be considered against the overall favorable symptom improvement across both cohorts.

INTRODUCTION

While minimally invasive treatments for benign prostatic hyperplasia (BPH) can be effective in the appropriately selected patient, none are absolutely durable, and as life expectancy increases, the need for reoperation for BPH increases. Transurethral resection of the prostate (TURP) has been considered the gold standard endoscopic procedure to treat BPH. Mostly based on anecdotal experience, patients are generally counseled that they may experience prostatic regrowth and need additional treatment in 8-10 years following TURP. Retreatment for BPH occurs in 1-32% of men following various minimally invasive therapies.¹⁻⁵

Holmium laser enucleation of the prostate (HoLEP) is used for the primary treatment of BPH and is known to have a very low retreatment rate (around 1-3%). However, it is a potentially preferable surgical approach to the management of prostatic regrowth given its ability to remove more tissue than other endoscopic approaches⁶ and its ability to dissect along the true anatomic planes of BPH, similar to simple prostatectomy. Some may assume that HoLEP in the retreatment (rHoLEP) setting would be associated with more adverse outcomes and be more technically difficult compared to primary (pHoLEP), though minimal evidence exists to support this.^{7,8} The aim of this series is to compare outcomes of men undergoing HoLEP in the primary versus the retreatment setting.

MATERIALS AND METHODS

After institutional review board approval was obtained, a retrospective chart review was performed on 2,242 men who underwent HoLEP between 2003 and 2015 at four academic institutions: Vanderbilt University Medical Center (Nashville, TN), Indiana University School of Medicine (Indianapolis, IN), Mayo Clinic Minnesota (Rochester, MN), and Mayo Clinic Arizona (Scottsdale, AZ). Men who had undergone prior BPH procedures, regardless of type, were placed in the rHoLEP cohort while those who had not were placed in the pHoLEP cohort. For men undergoing rHoLEP, indication for retreatment, date and type of prior BPH procedure were captured.

For all patients, demographic information including patient age, body mass index (BMI), and ASA score were recorded. Men's voiding habits were characterized prior to surgery by whether or not they were in urinary retention, AUA symptom scores (AUASS), maximum urinary flow rate (Q_m), average urinary flow rate (Q_a), and postvoid residual (PVR). Urinary flow rates were only included in the analysis if the voided volumes were 150 mL or greater. Prostate size was typically estimated on preoperative transrectal ultrasound, cross sectional imaging with Computerized Tomography or Magnetic Resonance Imaging. The ellipsoid volume formula ($\text{volume} = \text{length} \times \text{width} \times \text{height} \times \pi/6$) was used to calculate prostate volume. Urodynamics prior to HoLEP were performed at the discretion of the treating urologist.

A standardized HoLEP was performed using the previously described technique by one urologist at each treating facility: Vanderbilt (NLM), Indiana Health University (JEL), Mayo Clinic Rochester (AEK), and Mayo Clinic Scottsdale (MRH).⁹ Operative time, estimated blood loss (EBL), need for blood transfusions, resected tissue weight, pathologic findings, intraoperative complications, and length of stay (LOS) data were captured in the database. Postoperative outcomes were assessed at the last available follow-up in the 3-12 month postoperative period. Outcomes reviewed included AUASS, Qm, Qa, PVR, and postoperative complications. Urethral stricture, BNC, and new urinary incontinence were only assessed in men with at least 6 months follow-up as not to falsely decrease the rate of these complications with men who have shorter follow-up and perhaps have not had enough time to develop these complications. Similarly, as it sometimes takes several weeks or months for transient urinary incontinence to resolve, only men with 6 months or more follow-up were considered. Statistical analysis to compare patients undergoing rHoLEP to pHoLEP was performed using the STATA statistical package version 11 (StataCorp LP, College Station, TX).

RESULTS

A total of 2,242 patients were included in the series; 320 from Vanderbilt, 1803 from Indiana, 78 from Mayo Rochester, and 41 from Mayo Arizona. Three hundred and sixty

(16%) of these patients had undergone prior BPH surgery. Mean time between prior treatment and rHoLEP was 68 months (range 1 to 444 months). When taking into account men who only underwent a single procedure prior to retreatment, the average time to rHoLEP following: TURP was 98.4 months, laser surgery was 49.4 months, transurethral microwave therapy (TUMT) was 49.6 months, and transurethral needle ablation (TUNA) was 82.2 months. Four men had undergone four prior BPH procedures, six had undergone three, 51 had undergone two, and 299 underwent one. The most common prior BPH surgery was TURP (183, 42%), followed by laser treatment (123, 28%), and then TUMT (97, 22%) (Figure 1). Indication for rHoLEP was known for 253 (70%) patients (Figure 2). The most common reason for retreatment was persistent lower urinary tract symptoms (LUTS) in 179 (71%), followed by urinary retention in 63 (25%), and then gross hematuria in 22 (9%).

Men undergoing rHoLEP and pHoLEP were similar in regards to age, BMI, and ASA scores (Table 1). The preoperative AUASS were similar between both cohorts, 20.4 versus 20.5, $P = 0.82$. The estimated prostate size of those undergoing rHoLEP and pHoLEP was also similar, at 98 cc and 102 cc ($P = 0.17$), respectively. Men undergoing retreatment had significant higher baseline maximum urinary flows (10.3 versus 9.0 mL/sec, $P = 0.017$) and lower PVRs (204 mL versus 281 mL, $P = 0.035$) prior to HoLEP. Urodynamics were performed more often in men undergoing rHoLEP (17% versus 6%, $P = 0.0001$).

The perioperative and postoperative outcomes are presented in Table 2. Men undergoing rHoLEP had shorter operative times (86 versus 97 minutes, $P = 0.003$), lower EBL (36 versus 80 mL), less tissue enucleated (69 versus 76 grams, $P = 0.023$), and a shorter LOS (1.1 versus 1.3 days, $P = 0.010$). There was no difference between the two groups in regards to blood transfusions, finding of cancer on final pathology, or intraoperative complications. Postoperatively, there was significant improvement in AUASS for both groups, though more so for men undergoing pHoLEP (5.0 versus 6.5, $P < 0.0001$). Postoperative urinary flow rates and PVRs were similar between the two groups. Men undergoing rHoLEP had a higher risk of clot retention (4.7% versus 1.8%, $P = 0.01$) and urethral stricture (3.3% versus 1.5%, $P = 0.043$). There was no difference in the incidence of postoperative infection, bladder neck contracture, or new incontinence between the two groups.

DISCUSSION

This is the largest series comparing men undergoing surgical retreatment for BPH with HoLEP to men undergoing primary treatment. As life expectancy increases, not only will more men live long enough to develop symptomatic BPH, but also some who undergo surgical intervention will require retreatment. The retreatment rate for BPH has been reported as 1-32% for various minimally invasive interventions.¹⁻⁴ In the current series,

the average time from prior BPH treatment to retreatment was 5.7 years. TURP was durable for approximately eight years versus laser and TUMT, which lasted for approximately four years for those requiring retreatment.

For men undergoing pHoLEP versus rHoLEP, there was no difference in preoperative prostate volume (102 versus 98 cc, $P = 0.17$). Unfortunately, prostate volume prior to initial BPH treatment was not available for review. Interestingly, when looking at men who had undergone one prior BPH procedure and comparing preoperative prostate volume, there was no difference between men who had undergone TURP, laser treatment, TUMT, or TUNA ($P = 0.46$). The type of prior laser procedure performed as primary treatment was not known for all patients in the rHoLEP group. While, perhaps the patients who had undergone previous TURP had significant prostatic regrowth eight years later, the nearly 100 cc average preoperative prostate volume four years following laser vaporization and TUMT suggests that these men were likely initially under treated. Patient selection may have led to a greater risk of failure and need for secondary therapy, or these men may have multi-nodular BPH with accelerated de-novo growth of BPH tissue necessitating retreatment.

Complaints of bothersome LUTS following prior BPH surgery requires the urologist to distinguish between symptoms related to overactive bladder versus symptoms of

incomplete emptying from an underactive bladder or outlet obstruction to facilitate appropriate treatment. In many cases, men with low urinary flow rates, elevated PVRs, and evidence of obstructive prostatic tissue on cystoscopy will benefit from treatment of BPH and no further testing is required. However, prior to HoLEP in the current series, men who required retreatment had significantly higher average maximum urinary flow rates (10.3 versus 9.0 mL/s, $P = 0.017$) and lower PVRs (204 versus 281 mL, $P = 0.0035$) compared to those men who were undergoing primary BPH treatment. Current guidelines recommend that prior to surgical intervention for BPH, men with maximum urinary flow rates greater than 10 mL/s undergo pressure flow studies to confirm outlet obstruction.^{10,11} Correspondingly, men undergoing rHoLEP were more likely to have urodynamics preoperatively (17% versus 6%, $P = 0.0001$) to determine whether LUTS were secondary to obstruction and to ensure that men in urinary retention had adequate detrusor function.

In the reoperative setting, there is always concern that the initial procedure disrupted the natural tissue planes and may make subsequent surgical intervention more challenging. However, the current series and prior studies have failed to show this to be true in the case of HoLEP. Elshal et al and Jaeger et al both commented that the plane of enucleation was identified without any extra difficulty in their series of men undergoing rHoLEP.^{7,8} In Elshal et al's series, enucleation time was actually significantly shorter for men undergoing retreatment compared to those undergoing pHoLEP (76.0

versus 91.8 minutes, $P = 0.029$), though preoperative prostate size was significantly smaller for the rHoLEP group (79.3 versus 94.3 cc, $P = 0.04$), and significantly less tissue was removed (52.6 versus 64.5 cc, $P = 0.03$), though enucleation rates appear to be similar (1.50 g/m versus 1.46 g/m). In our experience most prior treatments tend to focus on the bladder neck and floor of the prostate, leaving the apical tissue almost untouched. This often facilitates correct identification of the plane between the peripheral and transition zones of the prostate to simplify the retreatment HoLEP. Other series have reported similar operative times, including Krambeck et al who noted similar enucleation times and rates in their series of 37 men undergoing retreatment compared to 74 men undergoing pHoLEP matched based on prostate size.^{7,12} In the current series, men undergoing retreatment had overall shorter operative times (86 versus 97 minutes, $P = 0.003$), in the setting of similar preoperative prostate volumes, though an average of 7 g less tissue was resected for those undergoing rHoLEP ($P = 0.023$). The lower EBL noted in the rHoLEP arm (36 versus 80 cc, $P = 0.0001$), is likely related to the shorter operative time and less tissue resected. While the shorter operative time clearly demonstrates that rHoLEP is technically feasible, the faster time may also reflect more attending participation at these teaching institutions due to the possibility that HoLEP in a reoperative field would be more challenging for a trainee secondary to the altered prostate morphology and anatomy.

Men in the current series undergoing rHoLEP had excellent functional outcomes, similar

to those compared to the pHoLEP arm and other large series.¹³⁻¹⁵ In terms of voiding parameters, PVR improved in both groups by at least 150 mL and Qm by over 14 mL/s. Other large series of 230 to 1000 men undergoing HoLEP have reported similar improvement in maximum urinary flow and PVR.^{13,15} All other series studying rHoLEP also found significantly improved and similar urinary flow rates and PVRs compared to men undergoing primary surgery.^{7,8,12}

In the current series, AUASS improved significantly for both groups, 6.5 from 20.4 (68% improvement) and 5.0 from 20.4 (75% improvement) for the rHoLEP and pHoLEP arms, respectively. However, the postoperative AUASS was slightly higher ($P < 0.0001$) for men undergoing rHoLEP. Men undergoing rHoLEP and pHoLEP in two prior series had similar AUASS postoperatively unlike the current series.^{8,12} However, Jaeger et al noted a slightly higher AUASS (7.52 versus 5.21, $P = 0.0060$) in those men who had undergone retreatment.⁷ The exact reason for this higher AUASS in the men undergoing rHoLEP in this series is unknown. However, one explanation may be that men who had undergone prior BPH surgery are more likely to have co-existing bladder dysfunction, and though the obstruction was relieved by HoLEP as noted by the significant and similar improvement in peak urinary flow rates and PVRs, there may be baseline bladder dysfunction leading to more irritative voiding symptoms. Regardless, men undergoing retreatment had significant improvement in symptomatology, which should be considered when counseling patients on rHoLEP despite the slightly higher overall score.

Retreatment may be more prevalent with other minimally invasive treatment approaches compared to HoLEP because less BPH tissue is removed, especially as prostate size increases. With the increase in patient longevity and the advent of effective medical therapies delaying surgical intervention, prostates are now larger at the time of surgery.¹⁶ HoLEP has previously been shown to have similar durable outcomes for larger glands, compared to simple prostatectomy, without a recurrence of BPH requiring retreatment.¹⁷⁻¹⁸

Men undergoing rHoLEP did experience higher rates of postoperative clot retention (4.7% versus 1.8%, $P = 0.01$) and urethral stricture (3.3% versus 1.5%, $P = 0.043$), though these rates are still quite low and align with outcomes reported in other high volume HoLEP series.¹⁹⁻²¹ The higher urethral stricture rate may be secondary to repeated instrumentation and potential for scarring in the bulbar and penile urethra. There was no difference between rHoLEP and pHoLEP in terms of urinary tract infections, bladder neck contracture, and new urinary incontinence postoperatively. Jaeger and Elshal also found similar low rates of complications without any difference compared to men undergoing primary treatment.^{7,8} A statistical difference between the rates of postoperative clot retention and urethral stricture was likely detected in this series given the much larger number of patients.

The strengths of this study include its large size and its inclusion of multiple centers making it more generalizable. While this study focuses on HoLEP, each institution offers a variety of surgical BPH solutions including monopolar and bipolar TURP, photovaporization of the prostate, transurethral incision of the prostate, button vaporization of the prostate, urolift, and simple prostatectomy. This study is limited by its retrospective nature as well as by the tertiary referral pattern of the included institutions. As many patients will return to their local urologists, this can limit follow-up and attainment of prior records (such as prostate volumes before initial BPH surgery). Additionally, all four centers did not use the same validated questionnaires to assess urinary incontinence, limiting the assessment of this postoperative condition.

CONCLUSIONS

The need for surgical retreatment of BPH secondary to inadequate removal of tissue and prostatic regrowth will only increase as life expectancy increases. HoLEP following prior BPH procedures is not only technically feasible, but safe and effective as demonstrated in this large multicenter series. Though there was a higher rate of postoperative clot retention and urethral stricture, the rate of these complications was still low and on par with other reported series of HoLEP.

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Table 1: Preoperative Characteristics

	pHoLEP N = 1,882	rHoLEP N = 360	P value
Age, years old, mean (range) (n = 2,242)	70 (34-95)	71 (42-93)	0.10*
BMI, kg/m ² , mean (range) (n = 437)	28 (20-48)	28 (19-45)	0.82*
ASA, no. (%) (n = 1,782)			
1	61 (4%)	12 (3.5%)	0.74 [±]
2	662 (46%)	161 (47%)	
3	649 (45%)	161 (46%)	
4	65 (5%)	11 (3.5%)	
Urinary retention, no. (%) (n = 2,234)	685 (36%)	111 (31%)	0.061 [±]
AUASS (mean ± STD) (n = 1,593)	20.4 ± 7.4	20.5 ± 7.5	0.82*
Qm, mL/sec, (mean ± STD) (n = 651)	9.0 ± 7.2	10.3 ± 7.6	0.017*
Qa, mL/sec, (mean ± STD) (n = 444)	5.1 ± 3.9	4.6 ± 2.5	0.28*
PVR, mL, (mean ± STD) (n = 1,360)	281 ± 417	204 ± 202	0.0035*
Prostate size, cc, (mean ± STD) (n = 1,780)	102 ± 56	98 ± 55	0.17*
UDS performed, no. (%) (n = 2,239)	110 (6%)	61 (17%)	0.0001[±]

Abbreviations: BMI, body mass index; kg, kilogram; m, meter; AUASS, AUA symptom score; STD, standard deviation; Qm, peak urinary flow rate; mL, milliliter; sec, second; Qa, average urinary flow rate; PVR, postvoid residual; cc, cubic centimeters; UDS, urodynamic study; no. number

Table 2: Outcomes

	pHoLEP N = 1,882	rHoLEP N = 360	P value
PERIOPERATIVE			
Operative time, min, (mean ± STD) (n = 2,015)	97 ± 54	86 ± 49	0.003[*]
EBL, mL, (mean ± STD) (n = 437)	80 ± 128	36 ± 50	0.0001[*]
Blood transfusions, no. (%) (n = 2,238)	37 (2%)	4 (1%)	0.28 [‡]
Tissue weight, g, (mean ± STD) (n = 2,199)	76 ± 55	69 ± 58	0.023[*]
Cancer on pathology, no. (%) (n = 2,242)	164 (9%)	38 (11%)	0.27 [‡]
Intraop urologic complication, no. (%) (n = 2,242)	22 (1%)	3 (1%)	0.58 [‡]
Urethral false passage	7 (0.4%)	0 (0%)	0.25 [‡]
Minor bladder morcellator injury	11 (0.6%)	2 (0.1%)	0.59 [‡]
Major bladder morcellator injury	3 (0.2%)	1 (<0.1%)	0.38 [‡]
Ureteral orifice injury requiring stent	1 (<0.1%)	0 (0%)	0.71 [‡]
LOS, days, (mean ± STD) (n = 2,171)	1.3 ± 1.5	1.1 ± 0.72	0.01[*]
POSTOPERATIVE			
AUASS (mean ± STD) (n = 1,280)	5.0 ± 4.6	6.5 ± 5.8	<0.0001[*]
Qm, mL/sec, (mean ± STD) (n = 322)	26.7 ± 12.7	24.4 ± 13	0.12 [*]
Qa, mL/sec, (mean ± STD) (n = 316)	14.7 ± 6.6	13.2 ± 7.5	0.081 [*]
PVR, mL, (mean ± STD) (n = 540)	50 ± 6.3	58 ± 6.9	0.44 [*]
Postop urologic complication, no. (%)			
Infection (n = 2,198)	73 (3.9%)	18 (5.3%)	0.23 [‡]
Clot retention (n = 2,197)	34 (1.8%)	16 (4.7%)	0.01[‡]
Urethral stricture (n = 1,770)	23 (1.5%)	8 (3.3%)	0.043[‡]
Bladder neck contracture (n = 1,765)	13 (0.8%)	4 (1.7%)	0.28 [‡]
New incontinence (n = 1,082)	33 (3.7%)	4 (2.1%)	0.26 [‡]

Abbreviations: min, minutes; STD, standard deviation; EBL, estimated blood loss; mL, milliliter; no., number; g, grams; intraop, intraoperative; LOS, length of stay; AUASS, AUA symptom score; Qm, peak urinary flow rate; sec, second; Qa, average urinary flow rate; PVR postvoid residual; postop, postoperative

Figure 1: Prior BPH Therapy*

Abbreviations

- AUASS, American Urological Association symptom score
- BPH, benign prostatic hyperplasia
- EBL, estimated blood loss
- HoLEP, holmium laser enucleation of the prostate
- LOS, length of stay
- LUTS, lower urinary tract symptoms
- pHoLEP, primary holmium laser enucleation of the prostate
- PVR, postvoid residual
- Qa, average urinary flow rate
- Qm, maximum urinary flow rate
- rHoLEP, retreatment holmium laser enucleation of the prostate
- TUMT, transurethral microwave therapy
- TUNA, transurethral needle ablation of the prostate
- TURP, transurethral resection of the prostate