

Does prior transurethral resection of prostate have a negative impact on the outcome of holmium laser enucleation of prostate? Results from a prospective comparative study

Usama Khater, Nicholas Anthony Smith, Jonathan E. Katz, Abhishek Bhat, Indraneel Banerjee, Rashmi H. Shah¹, Hemendra N. Shah

Department of Urology, University of Miami, Miller School of Medicine, Miami, Florida, USA, ¹Urolap Superspeciality Clinic and S. L. Raheja (Fortis Associate Hospital), Mumbai, Maharashtra, India

Abstract

Objectives: To prospectively evaluate safety and efficacy of holmium laser enucleation of prostate (HoLEP) for surgical treatment of recurrent symptoms due to prostatomegaly after prior transurethral resection of prostate (TURP).

Materials and Methods: We prospectively evaluated 43 patients with a history of TURP who underwent HoLEP (study group). Patients in chronological order who underwent HoLEP without prior TURP were included in the control group. We hypothesized that prior TURP would increase technical difficulties, thereby leading to a reduction in procedure efficiency by 25%. Patients' demographic, intraoperative, and postoperative data were compared, and statistical analysis was performed.

Results: Demographic data in both groups were comparable. The average interval between past TURP and HoLEP was 4.22 years. There was no difficulty in identifying the dissection plane in the study group and the difference in the procedure efficiency between the study and the control groups were statistically insignificant (0.75 ± 0.31 g/min-study group vs. 0.69 ± 0.36 g/min-control group; $P = 0.665$). The intraoperative parameters and postoperative outcomes were comparable in both groups.

Conclusions: Prior TURP does not negatively impact the outcome of HoLEP in treating symptomatic recurrence for enlarged prostate after initial TURP.

Keywords: Complication, enucleation, hematuria, holmium laser enucleation, prostatectomy, transurethral resection of prostate

Address for correspondence: Dr. Hemendra N. Shah, Department of Urology, University of Miami, Miller School of Medicine, Miami, Florida, USA.

E-mail: drhemendrashah@yahoo.co.in

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INTRODUCTION

Holmium laser enucleation of prostate (HoLEP) is now considered a size-independent treatment option to

treat patients with BPH. HoLEP is effective and less morbid when compared with transurethral resection of prostate (TURP) or open prostatectomy.^[1,2] It is

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also a preferred option in patients who have associated cardiopulmonary comorbidities or on anticoagulants,^[3] and the benefits include maximum volume reduction and increased durability. Although prior TURP is presumed to increase technical difficulties in HoLEP, the outcome benefits are consistent.^[4,5] There is limited information on the outcomes of HoLEP for recurrent symptoms due to enlarged prostate after prior TURP. All four published series that presented outcomes of HoLEP as a secondary or salvage procedure, are retrospective in nature and included patients who failed all prior interventions for BPH, including TURP.^[6-9] Hence, it is difficult to differentiate the impact of prior TURP alone on HoLEP outcomes. The primary outcome of our study was to prospectively evaluate technical difficulties during HoLEP that occur due to prior TURP. We used procedure efficiency as surrogate marker of technical difficulties. The secondary outcome was to evaluate the safety and efficacy of HoLEP in patients with recurrent symptoms secondary to enlarged prostate after prior TURP by looking into the functional outcomes and complications.

MATERIALS AND METHODS

Patients

All patients who underwent HoLEP by a single surgeon (SHN) for recurrent symptoms secondary to enlarged prostate after initial TURP, at R. G. Stone Urological and Laparoscopy Hospital, S. L. Raheja (Fortis Associate) Hospital and Criticare Superspeciality hospital, Mumbai, India, from June 2003 to May 2016 were prospectively enrolled in the study. All patients in the study arm had their prior TURP done at an outside institution. This study was conducted in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The clinical study was exempt from our institutional IRB as HoLEP was accepted as a standard surgical procedure for treating BPH and patients were not randomized. All patients provided informed consent. In 2003, our overall HoLEP procedure efficiency was 0.41 g/min.^[10] It was our hypothesis that prior TURP will increase technical difficulties during surgery, leading to reduction in procedure efficiency by 25%. To show a 25% difference in HoLEP efficiency, a sample size of 45 individuals per treatment arm was required ($\alpha = 0.05$; $\beta = 0.80$). All patients who underwent HoLEP with a past history of TURP were consented for the procedure. These patients were included in the study group. Each patient who underwent HoLEP without prior history of TURP was included individually into the control group, immediately following the treatment patient, in that chronological order. It was our impression

that this would serve as pseudo-randomization and thereby minimize selection bias.

Preoperative evaluation

All patients were evaluated with a detailed history, American Urological Association (AUA) symptom score, physical examination, serum prostate-specific antigen measurement (PSA), pelvic ultrasound, uroflowmetry, and postvoid urine volume estimation. Ascending urethrography and micturating cystourethrography were also performed in all patients with the past history of TURP to rule out urethral stricture or bladder neck stenosis. Patients presenting with recurrent hematuria underwent contrast computerized tomography scan, urine cytology, and diagnostic cystoscopy. After confirmation of the prostatic origin of hematuria, patients who were not on finasteride therapy were started on it. Transrectal ultrasound-guided prostate biopsy was performed in patients with either raised PSA and/or abnormal digital rectal examination findings after shared decision-making. Patients who were diagnosed with urethral stricture, bladder neck stenosis, prostate cancer, or having associated neurogenic bladder were excluded from the study group. Patients with large bladder diverticula were treated with simultaneous laparoscopic diverticulectomy and excluded from this study.

Procedure

All HoLEP's were performed using a 100W holmium laser with a 550 μ end firing laser fiber (Lumenis, Israel). Initially, we employed a two-lobe or three-lobe technique and used laser settings of 2J and 40 Hz as described earlier.^[11] However, from 2014, we performed our HoLEP's at 2J and 25–30 W settings and also gradually transitioned to the En-bloc technique. The technique needed modification based on the morphology of prostate regrowth [Figure 1].

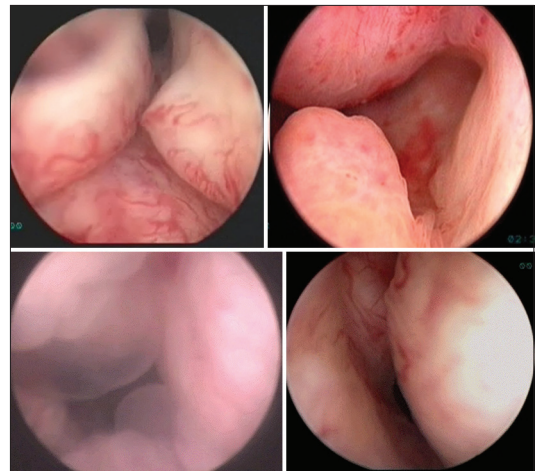


Figure 1: Cystoscopy appearance of post-TURP recurrent or residual prostate after prior TURP. TURP: Transurethral resection of prostate

Patients who had only apical tissue or only one lateral lobe or an anterior lobe, as shown in Figure 1 underwent initial enucleation of that lobe. The rest of the prostatic fossa was then evaluated for any residual adenoma for further removal. Transurethral morcellation of enucleated adenoma was performed using a Versa Cut morcellator™, which was introduced through an offset rigid nephroscope. Two patients in each group with associated calculi were treated synchronously with holmium laser cystolitholapaxy before HoLEP and the time duration of cystolitholapaxy was excluded from the calculation of procedure efficiency. At the end of the procedure, no traction was placed on the Foley catheter; however, all patients received overnight slow continuous bladder irrigation.

Postoperative management and follow-up

The urethral catheter was usually removed on the 1st postoperative day if urine remained clear. Patients were observed for one more night in the hospital and discharged on the 2nd postoperative day. The protocol for management after HoLEP did not change in patients with coagulopathy. Patients were restarted on antiplatelet medications 2–3 days after surgery. Immediate complications, if any, were recorded. Patients were followed up at 1-month, 6 months, and yearly thereafter. Follow-up evaluation included AUA symptoms score (AUA-SS) assessment, uroflowmetry, and sonographic estimation of postvoid residual urine. All patients were asked about any involuntary leakage of urine during each follow-up visit. We did not quantify amount of incontinence.

Statistical analysis

For patients in the study group, the time interval between previous TURP and HoLEP was noted. HoLEP efficiency was considered a surrogate marker for the measure of difficulty during enucleation and morcellation and was calculated by dividing resected prostate weight by the operation time (from the insertion of cystoscope to placement of Foley catheter) in g/min. It was our assumption that morcellation time would be unchanged due to prior TURP, and hence, we did not separately record enucleation and morcellation time. Demographic, perioperative, and postoperative follow-up data were compared among both group and statistical analysis was performed with IBM SPSS Statistics-24 software. Descriptive statistics were reported in number or means (\pm standard deviation) for categorical and continuous variables, respectively. It is well established that two times standard deviation usually provides the range which is the same as 95% of the observation. The outcome between the two groups was compared using independent sample *t*-test (2-tailed) for quantitative variables and Chi-squared

test for qualitative data. $P < 0.05$ was considered statistically significant. We performed the interim analysis in October 2016 and noted that it was futile to continue the study and ended enrollment with 43 patients in each arm. We did not perform multivariate analysis as we wanted to report data in the raw state as performing multivariable analysis could potentially risk performing an under-adjustment.

RESULTS

During the study period, 1292 patients underwent HoLEP, of which 58 patients had a history of TURP. Among those patients with prior TURP, three patients were diagnosed to have prostate cancer before HoLEP and opted for active surveillance. Twelve patients had concurrent sub-meatal stenosis and/or urethral stricture needing internal urethrotomy along with HoLEP for recurrent BPH. After excluding these 15 patients, the data of the remaining 43 patients were included in the study group. The control group consisted of 43 patients who underwent HoLEP without a history of TURP. The average interval between TURP and HoLEP in the study group patients was 4.22 years (range 1 month – 16 years).

The demographic data in both groups were comparable except indication for surgery [Table 1]. The data of post-TURP patients were after initial TURP when they presented for HoLEP. The mean prostate size of 72.34 ± 38.22 cc in the study group was after prior TURP and before they underwent HoLEP. Gross hematuria was seen in 58.13% of patients in the study group as compared with 4.6% in the control group. The primary endpoint of procedure efficiency in the study group was 0.75 ± 0.31 g/min and in the control group was 0.69 ± 0.36 g/min. The difference in the procedure efficiency between the study and control groups was statistically insignificant ($P = 0.665$). The mean weight of the resected prostatic tissue was 48.38 g and 51.73 g in the study and control group, respectively ($P = 0.612$). Capsular perforation occurred in two patients in the study group and in three patients in the control group and the difference was not significant. This did not have any impact on the postoperative management of patients. No cases were aborted or converted to TURP form either group. Incidental prostate cancer was detected in 9.3% of patients in the study group and 13.9% in the control group. Morcellation does not impact the ability of pathologists to detect incidental prostate cancer.^[11] During the follow-up period up to 12 months, there was no difference between the two groups in AUA-SSs, Qmax, and PVR [Table 2]. Postoperative complications, organized by Clavien-Dindo classification, were

Table 1: Patient's demographics and preoperative parameters

Variables	Mean±SD		P
	Group 1 (post-TURP)	Group 2 (no prior history of TURP)	
Number of patients	43	43	
Age (years)	69.6±11.0	67.6±8.2	0.344
Associated medical co-morbidities			0.810
Diabetes mellitus	7	3	
Hypertension	11	12	
Ischemic heart disease	3	2	
Multiple	10	12	
Others	2	3	
Associated anti-platelet medication or anti-coagulant	16	19	0.510
Indication for surgery			
Failure of medical management	7	18	<0.001
Recurrent urinary retention	4	12	
Recurrent hematuria	25	2	
Recurrent infection	2	3	
Bladder diverticulum	1	2	
Obstructive uropathy	2	1	
Associated vesical calculi	2	2	
Refusal of medical management	0	3	
Preoperative weight of prostate (g)	72.34±38.22	76.02±48.31	0.697
PSA (ng/dl)	5.36±5.09	5.88±5.54	0.648
Preoperative AUA symptom score	17.58±4.63	24.19±5.60	<0.001
Preoperative postvoid residual urine (ml)	186.98±303.30	257.28±335.22	0.311
Preoperative maximum uroflow rate (ml/s)	8.09±4.70	5.39±3.86	0.005

SD: Standard deviation, AUA: American Urological Association, TURP: Transurethral resection of prostate, PSA: Prostate-specific antigen

comparable in both groups. Transient incontinence was seen in 9 patients in patients who had prior TURP and in 6 patients in patients who underwent initial HoLEP [Table 2]. All except 1 patient in the study group were continent at 6-month follow-up period. None of the patients had incontinence at 1-year follow-up.

DISCUSSION

HoLEP in patients with symptomatic BPH regardless of the size of the prostate has been confirmed by multiple randomized control trials.^[12-14] However, many of these studies excluded patients with prior prostate surgery, including TURP presumably due to perceived technical difficulties that might arise secondary to earlier surgical intervention.^[15-17] The first randomized trial comparing TURP with HoLEP noted that at 7-year follow-up, none of the patients initially enrolled for HoLEP required surgery for prostate regrowth. On the contrary, 3 patients initially assigned to the TURP arm had prostate regrowth and all were safely treated by HoLEP.^[18]

In our institution, patients with the previous history of TURP were offered benefits of HoLEP. We considered measuring HoLEP procedure efficiency as a marker for technical difficulty during HoLEP. When we started the study in 2003, our HoLEP procedure efficiency was 0.41 g/min.^[10] However, over the study period, our technique was refined and with increasing experience, our efficiency improved.

Our initial hypothesis, that adhesions and fibrosis in the plane of enucleation would make these patients more prone to intraoperative capsular perforation, was not supported by our findings. We did not find any technical difficulty in performing HoLEP in patients with prior history of TURP. There was no difficulty in identifying the enucleation plane and there was no significant difference in the procedure efficiency between the patients who had TURP before HoLEP and the patients who had HoLEP as initial prostate surgery. Due to the lack of significant differences in the primary endpoint, our hypothesis was rejected. Our findings are comparable to other retrospective studies published in the literature [Table 3].^[6-9] Capsular perforation was noted in 5 patients, 2 in the study group and 3 in the control group and the difference was statistically insignificant. We noted that prior TURP did not cause significant adhesions between the residual adenoma and the surgical capsule. While we did note more bladder neck fibrosis, this did not impact outcomes. Similar findings were noted by Jaeger *et al.* while evaluating the outcome of HoLEP in 37 patients with prior prostate surgery, of which 16 patients had previous TURP.^[6] Elshal *et al.* noted that increased need for sharp dissection with laser after prior prostate surgeries, thereby increasing energy utilization in patient undergoing a secondary HoLEP (226.7 vs. 186.3 KJ).^[7] Contradicting our experience and those of others, Oh *et al.* noted that 3/35 patients undergoing salvage HoLEP after prior prostate surgeries that included TURP, photo-selective vaporization of prostate and transurethral needle ablation of prostate had ill-defined

Table 2: Patient's intraoperative parameters and postoperative outcomes

Parameters	Study group (prior TURP)		Control group (no prior TURP)		P
	Mean±SD	Number (n)	Mean±SD	Number (n)	
Duration of surgery (min)	63.35±20.35	43	74.91±31.64	43	0.472
Postoperative catheterization (h)	35.00±5.84	43	36.49±5.58	43	0.231
Hospital stay (h)	39.19±5.48	43	40.30±5.80	43	0.326
Resected prostate weight (g)	48.38±30.42	43	51.73±28.21	43	0.612
HoLEP efficiency (g/min)	0.75±0.31	43	0.69±0.36	43	0.665
Hemoglobin drop (g/dl)	0.76±0.38	43	0.70±0.43	43	0.484
1- month AUA symptom score (AUA-SS)	6.37±2.64	38	6.45±2.86	31	0.901
1-month Qmax (ml/min)	28.80±11.09	29	27.17±11.39	27	0.590
1-month PVR (ml)	32.58±36.81	31	29.09±32.08	29	0.697
3-month AUA-SS	5.0±2.17	26	4.93±2.43	29	0.914
3-month Qmax (ml/min)	24.96±7.63	26	21.41±7.00	25	0.840
3-month PVR (ml)	21.64±26.19	24	20.50±15.44	21	0.832
6-month AUA-SS	4.83±1.92	29	4.53±2.00	28	0.578
6-month Qmax (ml/min)	22.48±7.34	26	22.20±7.10	24	0.889
6-month PVR (ml)	24.89±26.66	28	22.93±26.01	27	0.781
1-year AUA-SS	4.90±1.85	21	4.74±2.08	20	0.769
1-year Qmax (ml/min)	22.34±6.94	19	22.09±6.18	18	0.893
1-year PVR (ml)	21.81±17.48	18	19.58±19.91	18	0.665
Complications#	Number (percentage)		Number (percentage)		P
Intraoperative complications					0.775
Bleeding	1 (2.3)		2 (4.6)		
Capsular perforation	2 (4.6)		3 (6.9)		
Superficial mucosal injury	3 (6.9)		2 (4.6)		
Superficial ureteric orifice injury	0		1 (2.3)		
Intraoperative blood transfusion	0		1 (2.3)		
Postoperative complications					
Clavien-dindo I					
Urine incontinence					
Immediate postoperatively	9 (20.9)		6 (13.9)		0.798
At 6 months	1 (2.3)		0		
At 1 year	0		0		
Clavien-dindo II					
Blood transfusion	1 (2.3)		0		
Urinary tract infection	3 (6.9)		3 (6.9)		
Epididymitis	1 (2.3)		0		
Clavien-dindo IIIa					
Recatheterization	1 (2.3)		0		
Clavien-dindo IIIb					
Meatal/sub-meatal stenosis	0		1 (2.3)		
Bulbar urethral stricture	1 (2.3)		0		
Bladder neck contracture	0		1 (2.3)		
Incidental adenocarcinoma prostate	4 (9.3)		6 (13.9)		0.797

SD: Standard deviation, AUA: American Urological Association, TURP: Transurethral resection of prostate, HoLEP: Holmium laser enucleation of prostate, SS: Symptom score, PVR: Post void residual urine

and nonprominent plane for enucleation.^[8] They did not specify which prostate surgery these patients had before HoLEP as their study group included patients with varieties of previous prostate surgeries, including TURP.

We did not notice any significant difference in the postoperative complications and outcome amongst both groups of patients. These findings were comparable to other published retrospective series in the literature.^[6-8] Contradictory to our results, the largest multi-centric retrospective study from 4 tertiary referral centers in the United States evaluating outcomes of 360 patients who underwent salvage HoLEP after varieties of initial BPH procedures noted that salvage HoLEP was associated with marginal increase in risk of clot retention and urethral

stricture at 6 months follow-up.^[9] Despite these marginal differences, the outcome was favorable and comparable to patients undergoing HoLEP as the primary procedure to treat BPH in this study. In our study, the technique of HoLEP changed over time. Although various surgical techniques result in similar outcomes, their impact on the duration of surgery is controversial. Rucker *et al.* noted that en-bloc and two-lobe enucleation were significantly faster with respect to enucleation time as compared to the three-lobe technique.^[19] However, Enikeev *et al.* noted no such difference in the duration of surgery.^[20]

We also noted gross hematuria to be the most common indication of surgical intervention in study group patients (58.13% in the study group vs. 4.6% in the control

Table 3: Review of studies published on outcome of secondary or salvage holmium laser enucleation of prostate after prior prostate surgery

Author/year of publication	Control group patients	Number of patients undergoing secondary prostatectomy	Patient with past TURP	Time interval between primary and salvage prostatectomy (year), mean (range) or mean±SD	Preoperative prostate size (g)/ method used for size calculation US, CT, MRI, DRE	Comments
Elshal <i>et al.</i> , 2012 ^[7]	978	76	48	5.5 (1.08-10.08)	79.3/TRUS	More sharp dissection with laser needed causing increasing laser energy consumption
Jaeger and Krambeck 2013 ^[6]	74 (2:1 match control)	37	17 ^s	5.4±4.6	93.6±47.1/TRUS	More scar tissue at bladder neck and less efficient morcellation
Oh <i>et al.</i> , 2014 ^[8]	500	35	16	10.3 years for TURP	59.7v21.9/TRUS	Higher laser energy consumption needed.
Marien <i>et al.</i> , 2017 ^[9]	1882	360	183	8.2 years for TURP	98±55/TRUS, CT, MRI	Planes identified easily
Present study 2020	43	43	43	4.22 (0.08-16)	72.34±38.22 Pelvic US	Planes identified easily

TRUS: Ultrasonography, CT: Computerized tomography scan, MRI: Magnetic resonance imaging, DRE: Digital rectal examination, TURP: Transurethral resection of prostate

group). Similar to our findings, Bowden *et al.* analyzed 100 patients with gross hematuria and a history of TURP and noted that 63% of patients had prostatic regrowth responsible for bleeding. Based on their findings, they considered hematuria as a late complication of TURP.^[21] Similarly, Wang *et al.* noted that the primary reason for admission in patients with recurrent BPH (post-TURP) was severe hematuria (44.4%).^[22] On pathologic evaluation, postTURP recurrent prostate tissue was more irregular and friable. The tissue also had a higher microvessel density with thinner blood vessels, making them more likely to bleed. Other authors who evaluated the efficacy of salvage HoLEP did not find a high incidence of recurrent hematuria in their patients.^[7,9] This might be attributable to the inclusion of patients with prostatic intervention other than TURP in their series.

One of the limitations of our study is that it describes a single surgeon's experience with prostate sizes averaging <80 g. Therefore, our results might not be relevant to HoLEP's performed for larger prostate sizes. Another limitation is that the enrollment period for this prospective study was 13 years, since we strictly included only patients with prior TURP, as opposed to other prior BPH interventions. Even so, our study stands out since all four previously published series that presented outcomes of HoLEP as a secondary or salvage procedure are retrospective in nature and included patients who failed not just TURP but a variety of different prior interventions for BPH.^[6-9] This makes it difficult to differentiate the impact of prior TURP on HoLEP outcomes based on those earlier published studies alone. We also believe that early symptoms after TURP can also be attributable to incomplete adenomectomy for larger prostates done at outside institutions. It is possible that our ability to find and maintain the plane of enucleation might

be attributable to nonviolation of the capsule resulting from incomplete resection in some patients. We did not perform subgroup analysis of the impact of time interval from the previous TURP on the duration of surgery. It would be interesting to perform subgroup analysis of the impact of time interval from initial TURP on the difficulty of enucleation and incidence of postoperative transient urine incontinence. Finally, our study lacks long-term data. However, the long-term durability of HoLEP is well established. Despite these limitations, our study is the first and only prospective study confirming safety and efficacy of HoLEP in treating patients with recurrent symptoms due to enlarged prostate after prior TURP.

CONCLUSIONS

Our study reveals that prior TURP does not negatively impact the outcome of HoLEP in treating recurrent symptoms due to enlarged prostate.

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Conflicts of interest

Dr. Hemendra N. Shah served as trainer for HoLEP for LUMENIS and received 1000\$ remuneration in 2018. All other authors have no disclosures or conflicts of interest.

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