

Outcomes of transurethral resection and holmium laser enucleation in more than 60 g of prostate: A prospective randomized study

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Abstract

Aim: Transurethral resection of prostate (TURP) is considered a gold standard surgical procedure. The management of benign prostatic hyperplasia (BPH) has undergone tremendous change in recent years and shifted from open to minimal invasive procedure. With the advancement in technology and skills of surgeons, lasers have been used more liberally, particularly holmium laser. Holmium laser enucleation of prostate (HoLEP) is seen as close rival of TURP. The objective of this study is to observe long- and short-term outcomes of transurethral resection and holmium laser enucleation in the prostate of more than 60 g.

Materials and Methods: This prospective randomized study includes 164 patients. Inclusion criteria were age <75 years after failed or poor response to medical therapy, prostatic size >60 g, gross hematuria secondary to BPH, recurrent urinary tract infection, acute urinary retention, postvoid residual >150 ml, and Schafer Grade II or more. BPH associated with neurogenic bladder, stricture urethra, and carcinoma prostate were excluded from the study. Group 1 comprises patients who underwent TURP and Group 2 comprises who underwent HoLEP. Follow-up was done at 1, 3, 6, 12, and 24 months after the surgery.

Results: Data of 144 patients were analyzed. The mean age of patients in TURP and HoLEP group was 66.78 ± 7.81 and 67.70 ± 7.44 years, respectively ($P = 0.47$), mean prostatic volume was 74.5 ± 12.56 and 75.6 ± 12.84 g, respectively ($P = 0.60$), operative time was 73.10 ± 10.49 and 89.56 ± 13.81 min, respectively ($P = 0.0001$). Mean resected tissue was 44.80 ± 9.87 and 48.49 ± 10.87 , respectively ($P = 0.03$). The sexual function did not change significantly in postoperative follow-up.

Conclusion: HoLEP is associated with less blood loss, lower transfusion rates, and a shorter hospital stay. The disadvantage of HoLEP is longer operative time and postoperative dysuria.

Key Words: Holmium laser enucleation of prostate, prostate, transurethral resection of prostate

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Received: 23.05.2016, **Accepted:** 29.06.2016

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.198904

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How to cite this article: Jhanwar A, Sinha RJ, Bansal A, Prakash G, Singh K, Singh V. Outcomes of transurethral resection and holmium laser enucleation in more than 60 g of prostate: A prospective randomized study. Urol Ann 2017;9:45-50.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common urological disease of aging man. Transurethral resection of the prostate (TURP) is now established as a gold standard surgical procedure for BPH.^[1-3] TURP is the reference surgical treatment for small and medium size prostates (80–100 g) refractory to medical therapy and open prostatectomy (OP) is the surgical choice for larger glands.^[4,5] However, complications noted in 15–20% of patients underwent TURP, and 10–15% patients require second intervention within 10 years.^[6,7] The management of BPH has undergone tremendous change in recent years and shifted from open to minimal invasive procedure. With the advancement in technology and skills of surgeons, lasers have been used more liberally, particularly holmium laser. Holmium laser enucleation of prostate (HoLEP) is seen as a close rival of TURP. HoLEP introduced by Gillling *et al.*^[8] and seems to be an attractive alternative to standard TURP, because of its shallow penetration, excellent hemostatic property, and can be applied to prostate irrespective of size.

MATERIALS AND METHODS

This prospective randomized study performed in the Department of Urology, King George's Medical University, India, after obtaining institutional review board approval from August 2012 to July 2015. Informed written consent was taken from all included patients. A total of 164 patients were randomized either into HoLEP or TURP using computer-generated randomization table. Inclusion criteria were age younger than 75 years after failed or poor response to medical therapy, Qmax <15 ml/s, prostatic size of more than 60 g, gross hematuria secondary to BPH, recurrent urinary tract infection (UTI), acute urinary retention, postvoid residual (PVR) more than 150 ml, and Schafer Grade II or more in pressure flow study. Exclusion criteria were patients of BPH with associated neurogenic bladder, stricture urethra, and carcinoma prostate, or previous history of intervention. Group 1 comprises patients who underwent TURP and Group 2 comprises who underwent HoLEP. Data include duration and severity of lower urinary tract symptoms, including the American Urological Association (AUA) symptom score, International Index of Erectile Function 5 (IIEF5) questionnaire, prostate volume, and serum prostate-specific antigen. All men underwent preoperative hematological and biochemical workup. A urine sample was also sent for routine examination and culture sensitivity. Men with UTI were treated with appropriate antibiotics preoperatively. Transrectal ultrasound was performed to assess the size of prostate by a single well-experienced radiologist, and renal ultrasound was done for the evaluation of upper tracts. The urodynamic study was performed in all included patients for the study purpose.

All patients were underwent TURP and HoLEP with the standard technique.^[9-12]

Follow-up was done at 1, 3, 6, 12, and 24 months after the surgery. International Prostate Symptom Score (IPSS), PVR, Qmax (ml/s), were assessed as the primary outcome and sexual function score and complication as a secondary outcome. The urodynamic study was performed at 6 month follow-up.

Surgical procedure

All procedures were performed under spinal/general anesthesia. HoLEP performed by end firing holmium laser fiber (550 μ m, versa power suit) with power setting (2 J at 40–50 Hz, 80–100 W). A 26 F continuous flow resectoscope was used the standard 3 lobe technique (median lobe resected first followed by lateral lobes). Endoscopic morcellation of enucleated lobes was performed with the help of morcellator (VersaCut tissue morcellator, swivel technique). After achieving hemostasis, cystoscopy was done to assess the integrity of bladder. During the procedure, 0.9% normal saline solution was used as irrigant. TURP was performed with a tungsten cutting wire loop with settings, current 160 W, and coagulations at 80 W (Mauermayer technique) with glycine as irrigating fluid. Postoperatively, bladder irrigation was done until hematuria settled sufficiently.

Statistical analysis

Baseline characteristics, pre- and post-operative parameters were compared in two groups. Results were given as mean (standard deviation). Two-sided Mann–Whitney test, Chi-square, and Fisher's exact tests were used. $P < 0.05$ was considered statistically significant.

Sample size

The reported cumulative incidence of perioperative and postoperative complications after endoscopic treatment for BPH is 5%.^[3] Assuming 80% power, 5% significance level ($\alpha = 0.05$, $\beta = 0.20$), the minimum sample size per treatment arm required was 72 as per Dawson and Trapp.^[13]

RESULTS

A total of 164 patients who met the inclusion criteria were included in the study. Eleven patients excluded due to unwillingness, and nine patients were lost to follow-up. Data of 144 patients were analyzed. Baseline characteristics were comparable between the groups [Table I]. The mean age of patients in TURP and HoLEP group was 66.78 ± 7.81 and 67.70 ± 7.44 , respectively ($P = 0.47$), mean prostatic volume TURP and HoLEP were 74.5 ± 12.56 and 75.6 ± 12.84 g, respectively ($P = 0.60$), the total operative time in TURP and HoLEP group was 73.10 ± 10.49 and 89.56 ± 13.81 min, respectively ($P = 0.0001$). Mean resected tissue in TURP

and HoLEP was 44.80 ± 9.87 and 48.49 ± 10.87 , respectively ($P = 0.03$), mean volume of irrigant used in TURP and HoLEP was 33.27 ± 7.77 and 40.08 ± 8.83 L, respectively ($P = 0.0001$). Mean hemoglobin loss (g/dl) in TURP and HoLEP was 0.63 ± 0.6 and 0.47 ± 0.46 g/dl, respectively ($P = 0.08$). None of the patients in both the groups required blood transfusion, and none had complication such as TUR syndrome. The fall of serum sodium level was significantly more in TURP group, but none of the patients developed hyponatremia (2.61 mmol/L in TURP vs. 0.8 mmol/L in HoLEP, $P = 0.0001$).

Postoperative total bladder irrigation time, catheterization time, and total postoperative stay were significantly higher in TURP group in comparison to HoLEP as shown in [Table 2]. Seven patients (9.7%) in TURP and 2 (2.76%) in HoLEP group developed fever due to UTI, which were managed with intravenous antibiotics. Three of the patients in TURP

required blood transfusion because of postoperatively drop in Hb % (<8 g/dl) while none of the patients in HoLEP group required blood transfusion. Two (2.76%) patients in HoLEP group developed stress urinary incontinence transiently, which was managed conservatively with Kegel exercise. Both of these patients become asymptomatic at 3 months of follow-up. None of the patients developed stricture/required any surgical intervention during follow-up. None of the patients among TURP group developed incontinence. [Table 3] compares Qmax, IPSS and PVRU between two group during follow up. The sexual function did not changed significantly in postoperative follow-up and was also not significantly different among both groups [Table 4]. [Figure 1] describes flow of patients during the study period.

DISCUSSION

With the development and refinements of endourological and laser techniques, there has been shifting from more invasive to minimally invasive and less morbid treatment alternatives for the management of BPH to achieve high efficacy (remove a significant amount of prostatic adenoma) with minimal perioperative morbidity. According to the latest AUA guideline, TURP is considered as the gold standard procedure for the management of BPH. In the last two decades, lasers have been included in the urological armamentarium for the management of BPH. HoLEP is now accepted and recommended internationally as a minimally invasive alternative to TURP (level I evidence),^[1] because of its shallow penetration, low morbidity, low blood transfusion rate, short hospital stay, suitable for patients on anticoagulants, and can be applied to wide range of prostate size.^[14] HoLEP has been shown to be as effective as open surgery in generating cavity, since the tip of the fiber mimics that of the surgeon's index finger during OP.

Many studies reported HoLEP better postoperative and perioperative results (Qmax, IPSS, PVR) with lower complication rates.^[15,16] There are some studies reported a significant difference in operating time between HoLEP and TURP, favoring TURP.^[9,14,16-18] In this study, we also observed statistically significant difference in operating time between TURP and HoLEP (73.10 ± 10.49 and 89.56 ± 13.81 min respectively) ($P = 0.0001$). It seems reasonable due to additional time required for morcellation. In a recently conducted meta-analysis, it has been shown that HoLEP required more time than TURP, mean difference was 15.9 min.^[9] However, some studies in English literature reported that with increasing prostate volume tissue ablation by HoLEP become more effective than by TURP leading to shorter operating time for HoLEP and also with the increasing number of HoLEP procedure performed.^[15,19] Similarly,

Table 1: Baseline patients characteristics

Parameters	TURP	HoLEP	P
Number (n)	72	72	1
Age (years), mean (SD)	66.78±7.81	67.70±7.44	0.47
IPSS, mean (SD) (patient without AUR)	25.85±2.22	26.01±2.08	0.65
Qmax (ml/s), mean (SD)	8.7±1.02	8.4±1.48	0.15
PVRU (ml), mean (SD)	187.1±38.5	184.8±32.2	0.69
No AUR patients	40	48	0.47
Prostate size (cm ³), mean (SD)	74.5±12.56	75.6±12.84	0.60
S. PSA (ng/ml), mean (SD)	1.77±1.23	2.01±0.79	0.16
Mean Schafer grade	4.1 (3-6)	3.9 (3-6)	1

IPSS: International Prostate Symptom Score, AUR: Acute urinary retention. PVRU: Postvoid residual urine, S. PSA: Serial prostate-specific antigen, TURP: Transurethral resection of prostate, HoLEP: Holmium laser enucleation of prostate, SD: Standard deviation

Table 2: Perioperative parameters and postoperative complications

	TURP	HoLEP	P
Intraoperative variables			
Total operative time (min), mean (SD)	73±10.49	89±13.81	0.0001
Volume of irrigant (L), mean (SD)	33.27±7.77	40.08±8.83	0.0001
Mean resected tissue (g) (SD)	44.80±9.87	48.49±10.87	0.03
Hemoglobin drop (g/dl) mean (SD)	0.63±0.6	0.47±0.46	0.08
Serum sodium decrease (mmol/L) mean (SD)	2.61±3.51	0.8±1.77	0.0001
Postoperative variables			
Bladder irrigation (h), mean (SD)	12.20±3.38	8.40±2.29	0.0001
Catheter time (h), mean (SD)	48.06±13.36	30.94±5.49	0.0001
Postoperative stay (h), mean (SD)	54.58±12.36	41.81±9.17	0.0001
Postoperative complications (%)			
Fever	7 (9.7)	2 (2.76)	0.16
Blood transfusion	3 (4.14)	0	0.24
Transient dysuria	12 (16.32)	20 (27.6)	0.16
Stricture	2 (2.76)	0	0.49
Transient stress incontinence	0	2 (2.76)	0.49
Clinical hyponatremia	0	0	0.49
Re-catheterization	0	0	

TURP: Transurethral resection of prostate, HoLEP: Holmium laser enucleation of prostate, SD: Standard deviation

significantly more irrigation fluids required for HoLEP as compared to TURP, 33.27 ± 7.77 versus 40.08 ± 8.83 L, respectively, ($P = 0.0001$). This is directly related to the length of operation, wherein longer the operating time more irrigant is used. Gupta *et al.* reported significantly more resection of prostatic tissue in HoLEP procedure as compared to TURP.^[17] In a similar study, Yang *et al.* also observed similar finding. In

this study, we also found more tissue resected in HoLEP group than TURP, which is in accordance with the studies reported earlier. Some trials reported the reduction of hemoglobin level but did not observed statistically significant difference between TURP and HoLEP.^[9,16,20] Rebecca *et al.* observed that rates of perioperative and postoperative blood transfusion were comparatively low in HoLEP as compared to TURP. Similarly, in this study, we also observed more drop of hemoglobin level in TURP group but this observation was statistically insignificant. However, 3 (4.1%) patients in TURP group required blood transfusion in postoperative period due to drop in hemoglobin level below 8 g/dl. None of the patients in HoLEP group required blood transfusion. This might be due to the excellent hemostatic property of holmium laser.

Gilling *et al.* observed longer duration of postoperative irrigation in TURP group as compared to HoLEP.^[21] Das *et al.* another study reported a similar observation.^[22] In the present study, we also observed the same finding (12.20 ± 3.38 h in TURP vs. 8.40 ± 2.29 h in HoLEP, $P = 0.001$).

Gilling *et al.* observed shorter postoperative catheterization duration in HoLEP as compared to TURP.^[21] Tan *et al.* also reported shorter postoperative catheterization duration in HoLEP group.^[23] Similarly, in this study, we also observed shorter duration of catheterization postoperatively in HoLEP group when compared to TURP group (48.06 ± 13.36 h vs. 30.9 ± 5.49 , $P = 0.001$). This might be due to less blood loss in HoLEP group as the duration of catheterization may be a surrogate indicator of blood loss. Kuntz *et al.* did not observed any statistically significant difference in serum sodium level between TURP and HoLEP.^[9] However, this is in contrast to our study; wherein we observed statistically significant difference in reduction of serum sodium level between both groups (2.61 ± 3.51 vs. 0.8 ± 1.77 mmol/L, respectively, $P = 0.001$) but none of the patients developed clinical hyponatremia. None of the patients in our study had any major complication related to procedures such as subtrigonal dissection, capsular perforation, and TUR syndrome. Many trails reported shorter hospital stay in HoLEP group as compared to TURP.^[9,16,20] We also observed statistically significant shorter hospital stay in HoLEP group (54.58 ± 12.36 h vs. 41.81 ± 9.17) $P = 0.0001$. This might be due to better hemostatic property, less postoperative irrigation, and duration of catheterization. Some studies

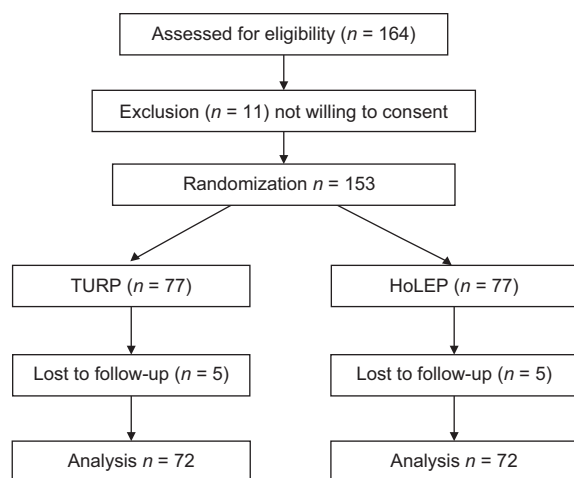


Figure 1: Flow of patients during the study period. TURP: Transurethral resection of prostate, HoLEP: Holmium laser enucleation of prostate

Table 3: Follow-up variables

Parameters	Mean±SD		
	Qmax (ml/s)	IPSS	PVRU (ml)
1 month			
TURP	23.08±2.93	6.94±1.53	21.02 (7.41)
HoLEP	24.03±3.52	6.47±1.52	19.02±8.53
P	0.08	0.06	0.13
3 months			
TURP	24.72±1.81	6.25±0.94	20.02±6.77
HoLEP	25.12±2.01	6.11±1.01	18.10±6.68
P	0.21	0.39	0.08
6 months			
TURP	24.25±3.18	5.03±1.50	18.39±8.26
HoLEP	25.03±2.97	5.28±1.52	16.14±8.88
P	0.13	0.32	0.11
12 months			
TURP	24.98±3.37	5.19±1.31	18.5±8.06
HoLEP	26.61±3.38	5±1.66	17.03±5.55
P	0.004	0.441	0.2
24 months			
TURP	24.9±3.06	5±1.22	19.22±9.09
HoLEP	26.1±3.11	5.01±1.26	17.22±6.63
P	0.02	0.96	0.13

IPSS: International Prostate Symptom Score, HoLEP: Holmium laser enucleation of prostate, TURP: Transurethral resection of prostate, PVRU: Postvoid residual urine, SD: Standard deviation

Table 4: Sexual function score (International Index of Erectile Function 5)

IIEF5 score	Baseline	1 month	3 months	6 months	12 months	24 months
TURP	12.65±2.36	12.79±2.45	13.05±1.96	12.91±2.02	12.68±2.33	12.52±2.12
HoLEP	12.67±1.73	12.90±2.38	13.10±2.40	13.04±1.98	12.79±1.73	12.72±1.82
P	0.95	0.78	0.89	0.69	0.74	0.54

IIEF5: International Index of Erectile Function 5, HoLEP: Holmium laser enucleation of prostate, TURP: Transurethral resection of prostate

reported no significant difference in IPSS score between TURP and HoLEP at 3 and 6 months, but they observed significant decrease in IPSS score at 12 months of follow-up and favoring HoLEP.^[16,20,21] However, in this study, we observed a significant difference in IPSS score in both modalities from baseline but did not observe any statistically significant difference in IPSS score until 24 months of follow-up. Some trials reported results which showed (random effect model) significant difference in Qmax between both the modalities and favoring HoLEP.^[16,20,21] We also observed the difference in Qmax between TURP and HoLEP at all follow-ups and significantly at 12 months afterward. PVR also decreases in both groups significantly from baseline, but our results favor HoLEP although no statistically significant difference was observed. Very few studies reported on postoperative urodynamic parameters. Gilling *et al.* in their study reported postoperative better urodynamic pattern favoring HoLEP (Schafer grade was I grade lower than TURP). Similar results were also reported by Tan *et al.* In this study, we did not observe any significant difference between TURP and HoLEP, which is in contrast to other studies reported earlier. However, urodynamic pattern improved significantly in both modalities from baseline at 6 months follow-up. There are trials which reported stress urinary incontinence and transient dysuria and showed no significant difference between HoLEP and TURP.^[9,17] We also observed stress urinary incontinence and transient dysuria more in HoLEP group, which was managed conservatively and resolved after 6 months of follow-up. This might be due to transient mild thermal injury to external urinary sphincter. Madersbacher and Marberger in a randomized study between TURP and other minimally invasive procedures for BPH reported mean stricture rate of 3.8% in TURP group.^[24] Rassweiler *et al.* also reported 3.1–5.6% stricture rate in TURP.^[3] We also observed 2.7% stricture rate in TURP group and none in HoLEP group. Data on sexual function after HoLEP and TURP are indeed lacking. Very few studies emphasize on sexual function after TURP and HoLEP. Briganti *et al.*^[25] observed a slight postoperative nonsignificant increment in IIEF score and significantly higher retrograde ejaculation rate in each group. In our study, the sexual function score (IIEF5) remains unchanged postoperatively in either group.

CONCLUSION

HoLEP is associated with less blood loss, lower transfusion rates, and a shorter hospital stay in comparison to TURP. The disadvantage of HoLEP is longer operative time and postoperative dysuria. However, the sexual function scores (IIEF5) remain similar in both groups.

Acknowledgment

We acknowledge the cooperation of residents of the Urology Department of King George Medical University who

participated in appointing the patient and following up. We also appreciate the commitment and compliance of the patient who reported the required data and attended for the regular follow.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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