Holmium laser enucleation versus transurethral resection of the prostate

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Introduction: *This was a prospective, randomized clinical trial to compare the safety, efficacy, and medium-term durability of holmium laser enucleation of the prostate (HoLEP) combined with mechanical morcellation versus standard transurethral resection of the prostate (TURP) for the surgical treatment of patients with bladder outlet obstruction due to benign prostatic hyperplasia (BPH). The patients had prostates that were greater than 30 g and less than 100 g and were followed for 1 year.*

Patients and methods: *From April 2008 to December 2009, 80 consecutive patients with lower urinary tract obstruction (LUTS) due to BPH were randomized to either surgical treatment with HoLEP (group 1, n = 40) or standard TURP (group 2, n = 40). Preoperative assessments included American Urological Association (AUA) symptom score, serum prostate-specific antigen (PSA), post-voiding residual (PVR) urine volume, transrectal ultrasound (TRUS), and urodynamic studies. Perioperative parameters included total operating time, resected tissue weight, hemoglobin loss, presence or absence of blood transfusion, time of catheter removal, and duration of hospital stay. Postoperative evaluations were conducted at 1, 6, and 12 months.*

Results: *Patients in the HoLEP group had shorter catheterization times and hospital stays than patients in the TURP group. There was no significant difference in operating times between the two groups. Mean hemoglobin loss was lower in the HoLEP group (1.8 ± 1.3 g/dL versus 2.9 ± 1.5 g/dL). There was a significantly greater improvement from baseline AUA symptom scores and PVR urine volumes in the HoLEP group versus the TURP group, at all postoperative assessments. Postoperatively, 25% of patients in group 1 (HoLEP) and 20% of patients in group 2 (TURP) had irritative voiding symptoms. Urethral stricture occurred in three cases (one case in the HoLEP group and two cases in the TURP group).*

Conclusion: *HoLEP proved to be a safe and highly effective technique for surgical treatment of bladder outlet obstruction due to BPH.*

Key Words: benign prostatic hyperplasia, HoLEP, LUTS, TURP

Introduction

Transurethral resection of the prostate (TURP) is considered to be the gold standard for surgical treatment of bladder outlet obstruction due to benign prostatic hyperplasia (BPH). However, TURP is associated with relatively high morbidity,[1] partly due to high blood loss (a blood transfusion rate between 5% and 11%)[2] and partly due to TUR syndrome when treating larger prostates.[3] Holmium laser enucleation of the prostate (HoLEP), was first described in 1996 by Peter Gilling and colleagues[4] as an alternate technique for enucleation of the prostate that minimizes blood loss, since it involves the use of a laser and mechanical soft tissue morcellation, and which offers good hemostatic qualities and effective removal of obstructions.[5] Other studies have also demonstrated that compared to TURP, HoLEP is associated with a significant reduction in blood loss and other perioperative morbidities, as well as reductions in urethral catheterization time and hospital stay, and it provides comparable short term urinary function results.[6,7] Since many authors advocate the use of HoLEP as a potential new gold standard

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for the treatment of bladder outlet obstruction,[8,9] and to investigate the durability of results following HoLEP, we conducted a randomized clinical trial in 80 patients with bladder outlet obstruction due to BPH and prostates that were less than 100 g, to compare perioperative and 1 year (medium term) postoperative outcomes in patients who underwent surgical treatment with HoLEP versus TURP.

Patients and methods

From April 2008 to December 2009, 80 consecutive patients who presented to the Urology Department at King Fahd Specialist Hospital in Al Qassin, Saudi Arabia, with bladder outlet obstruction caused by BPH, with related voiding symptoms, and prostate volume greater than 30 g but less than 100 g (as determined by TRUS), who had not responded to pharmacologic therapy, and who were eligible for surgical treatment were enrolled in this randomized, prospective study. Other inclusion criteria were an AUA symptom score of 12 or higher and a peak urinary flow rate of 15 mL/sec or lower. Exclusion criteria were neurogenic bladder; previous urethral, bladder neck, or prostate surgery; suspected prostatic cancer by abnormal digital rectal examination (DRE), total serum PSA > 4 ng/mL or abnormal TRUS; and TRUS-guided prostate biopsy. Patient evaluation included a complete medical history and physical examination, DRE, urinalysis and culture, urinary tract ultrasound (including measurement of PVR volume), TRUS of the prostate and seminal vesicles (including measurement of prostatic volume), urodynamic pressure flow studies (including measurement of the peak urinary flow rate [Qmax]), and AUA symptom score.[2]

Surgical techniques

All patients provided written informed consent, and within 1 month of randomization they were operated under general or epidural anesthesia. TURP was carried out by two urologists (MAE and HS) and HoLEP was performed by two urologists (MAE and AAH). HoLEP was performed as previously described by Gilling et al.[4] The technique included enucleation of the prostatic lobes with a maximum average power of 100w (2.0 j at 50 Hz) followed by tissue morcellation into fragments by a mechanical tissue morcellator (Lumenis, Palo Alto, CA, USA) and subsequent retrieval of fragments from the bladder cavity. Standard TURP technique was performed with a tungsten wire loop at 160 w cutting and 80 w coagulating current. For TURP, 1.5% glycine was used for irrigation during the procedure, and normal saline was used for postoperative irrigation. For HoLEP, normal saline was used during the procedure and postoperatively. At the end of each operation, for all patients, a 20 Fr double-lumen urethral catheter was inserted, and the bladder was continuously irrigated depending on the amount of bleeding.

Outcome measurements

The study was designed as a prospective, randomized clinical trial with a 1 year follow up to determine medium term results. AUA symptom scores, peak urinary flow rates, and PVR urine volume were chosen as primary treatment-related postoperative outcomes. Perioperative outcomes included total operative time, resected tissue weight, hemoglobin loss, blood transfusion, catheterization time, and duration of hospital stay. Postoperative evaluation at 1, 6, and 12 months included AUA symptom scores, peak urinary flow rates, PVR urine volume, and the presence of any complications (including urgency, frequency, hematuria, and incontinence [especially persistent stress incontinence]).

Statistical methods

Data were presented as mean ± standard deviation (SD). Perioperative data also included range. The comparison of outcomes between the both groups was carried out by the paired Student t test, and significance was defined as a p value < 0.05.

Results

Eighty patients participated in the study and were followed for 12 months. At baseline, no patients had an indwelling urethral catheter. The patients were randomized, using a computer-generated table, to either receive HoLEP (group 1, n = 40) or TURP (group 2, n = 40) surgical treatment. Table 1 lists baseline preoperative patient characteristics. There were no statistically significant differences in baseline characteristics between the two groups.

Table 2 lists the perioperative data. Catheterization times and hospital stays were significantly shorter for patients in the HoLEP group. Although the operating times were almost identical in the two groups, more tissue was removed during HoLEP than during TURP (0.6 g/min versus 0.5 g/ min). In addition, blood loss was smaller for patients in the HoLEP group, and none of the patients in this group required a blood transfusion.

Table 3 lists the postoperative follow up findings for the two groups at 1, 6, and 12 months. At each assessment time, both surgical modalities resulted in

TABLE 1. **Preoperative patient characteristics**

Variable	HoLEP (mean ± SD)	TURP (mean ± SD)	p value
No. of cases	40	40	
Age, years	67.5 ± 8.1 (56-82)	68.3 ± 9.2 (53-84)	0.48
Prostate volume*, g	62.4 ± 24.1 (32-87)	58.5 ± 31.6 (30-92)	0.23
Qmax, mL/sec	8.4 ± 2.3 (3-15)	8.1 ± 2.7 (2-14)	0.09
PVR urine volume, mL	130 ± 96.5 (50-650)	105 ± 89.7 (50-550)	0.57
PSA, ng/mL	2.9 ± 0.5 (0.2-4)	3.1 ± 0.71 (0.2-4)	0.07
AUA symptom score	23 ± 3.6 (13-33)	25 ± 5.1 (14-32)	0.52

AUA = American Urological Association; HoLEP = holmium laser enucleation of the prostate; PSA = prostate-specific antigen; PVR = post-voiding residual; Qmax = peak urinary flow rate; TURP = transurethral resection of the prostate
*determined by transrectal ultrasound (TRUS)

TABLE 2. **Perioperative data**

Variable	HoLEP (mean ± SD)	TURP (mean ± SD)	p value
Total operating time, min	72.8 ± 21.7	73.6 ± 22.3	0.15
Specimen weight, g	44.2 ± 16.5	37.4 ± 19.2	0.08
Hemoglobin loss, g/dL	1.8 ± 1.3	2.9 ± 1.5	< 0.05*
Blood transfusion, number (%)	0	3 (7.5%)	< 0.007*
Catheterization time, days	1.5 ± 1.4	2.1 ± 1.1	< 0.0001*
Hospital stay, days	2.6 ± 1.2	3.8 ± 1.6	< 0.0001*

HoLEP = holmium laser enucleation of the prostate; TURP = transurethral resection of the prostate
*significant difference

TABLE 3. **Postoperative follow up**

Parameter	HoLEP (mean ± SD)	TURP (mean ± SD)	p value
1 month			
AUA score	4.1 ± 2.7	5.3 ± 3.4	0.05*
Qmax, mL/sec	22.3 ± 12.2	23.1 ± 10.6	0.64
PVR, mL	9.6 ± 20.1	15.3 ± 22.4	0.005*
6 months			
AUA score	2.6 ± 1.3	3.8 ± 3.1	0.005*
Qmax, mL/sec	23.5 ± 9.2	24.3 ± 6.8	0.72
PVR, mL	5.7 ± 12.6	17.6 ± 18.3	< 0.0001*
12 months			
AUA score	2.2 ± 1.4	3.7 ± 1.6	< 0.0001*
Qmax, mL/sec	24.9 ± 11.7	25.5 ± 7.4	0.78
PVR, mL	5.3 ± 15.2	24.1 ± 16.8	< 0.0001*

AUA = American Urological Association; HoLEP = holmium laser enucleation of the prostate; PSA = prostate-specific antigen; PVR = post-voiding residual (urine volume); Qmax = peak urinary flow rate; TURP = transurethral resection of the prostate.
*significant difference

TABLE 4 **Postoperative complications**

Variable	HoLEP (number [%])	TURP (number [%])	p value
Irritative voiding symptoms (at 1 month)	10 (25%)	8 (20%)	0.61
Urinary incontinence (at 6 months)	8 (20%)	12 (30%)	0.08
Urge	3 (7.5%)	5 (12.5%)	
Stress	2 (5%)	3 (7.5%)	
Mixed	3 (7.5%)	4 (10%)	
Urethral stricture (at 12 months)	1 (2.5%)	2 (5%)	0.72

HoLEP = holmium laser enucleation of the prostate; TURP = transurethral resection of the prostate

statistically significant improvements from baseline in AUA symptom score, Qmax, and PVR urine volume. The AUA symptom scores and PVR urine volumes were significantly better in the HoLEP group than in the TURP group at all postoperative assessments. In contrast, Qmax did not differ significantly between the two groups at any time. Compared to baseline, at 1 year after surgery, AUA symptom scores improved 10-fold in the HoLEP group and 7-fold in the TURP group, while mean Qmax increased 3-fold in both groups, and mean PVR urine volume decreased by 96% in the HoLEP group and by 76% in the TURP group.

There was no statistically significant difference between the two groups in postoperative complications, as shown in Table 4. Irritative voiding symptoms that occurred at 1 month of follow up were self limited and treated by nonsteroidal anti-inflammatory drugs. While urge, stress or mixed urinary incontinence occurred at 6 months of follow up, these were temporary. Three urethral strictures occurred at 1 year follow up (one in HoLEP group and two in TURP group), but these were all short and treated by visual internal urethrotomy.

Discussion

Although many treatments for bladder outlet obstruction due to BPH have been suggested as alternatives to TURP, most of these other treatments have not proven to be as effective or as durable as TURP, although morbidity was often improved. The holmium laser wave length makes it a versatile tool that can provide an endoscopic alternative to TURP when used for enucleation of the prostate.[10]

In this study, HoLEP was superior to TURP in terms of perioperative morbidity. There was significantly less blood loss ($p < 0.05$) with HoLEP, and none of the patients who underwent HoLEP required blood transfusions, whereas two patients in the TURP group required transfusions. The excellent hemostatic characteristics of the holmium procedure result in a significantly less bladder irrigation, with shorter catheterization time (1.5 versus 2.1 days; $p < 0.0001$) and shorter hospital stay (2.6 versus 3.8 days; $p < 0.0001$). These findings agree with those of Ahyai et al[11] who reported significantly lower intraoperative and early postoperative complication rates in HoLEP patients than in TURP patients (9.5% versus 13.3%; $p = 0.08$). Similarly, Wilson et al[12] reported improved perioperative morbidity for HoLEP patients (shorter catheterization time and reduced hospital stay), even though more prostate tissue was retrieved.

The overall operating time for patients who underwent HoLEP in our series is similar to that reported for TURP.[11,13] This result is likely due to use of the mechanical morcellator with new morcellator blades to fragment the enucleated prostatic lobes within the bladder, which reduces the overall operating time so that it is comparable to that for TURP. In contrast, Kuntz and colleagues reported a 25% increase in operating time when using electroresection to fragment prostatic lobes into pieces small enough to be evacuated through the resectoscope sheath.[14] There are number of important factors that might influence the efficiency of morcellation, such as low performance of the blades and potential tissue resistance due to the presence of small fibrotic spheres against the morcellator sheath (called the "crazy ball effect"). Therefore, it is mandatory to keep at least two spare, new, sharp blades available during the operation and to keep the optimum morcellation rate between 5 and10 g/min.[15]

HoLEP, like TURP, results in an open prostatic cavity. This may explain why, in this study, the improvement in micturition was immediate, and the mean AUA symptom scores, peak urinary flow rates, and PVR urine volumes had returned to normal within the postoperative first month in each group. However, AUA symptom scores and PVR urine volumes were significantly better in the HoLEP group at all postoperative follow up examinations up to 12 months. Our postoperative results were in accordance with studies by Tan et al,[16] Kuntz et al,[14] and Ahyai et al,[11] who demonstrated significantly better AUA symptom scores and PVR volumes with HoLEP compared to TURP.

Our randomized clinical trial clarified the safety and efficacy of HoLEP for the removal of obstructing prostatic tissue. It demonstrated the advantages of this minimally invasive procedure, which included reduced blood loss, short catheterization time and short hospital stay. In addition, HoLEP resulted in greater postoperative improvement than TURP, which was generally evident immediately at the first month and was consistent up to 12 months, without any significant worsening in study endpoints or clinical outcomes. The superiority of results with HoLEP may be related to the efficacious enucleation provided, especially at the apex of the prostate.

Our study lacked long term follow up to determine the durability of HoLEP, unlike the study by Kuntz and colleagues (with 5 years of follow up)[17] or the study by Gilling and colleagues (with 6 years of follow up),[18] which both concluded that HoLEP produces durable results that are comparable to results after TURP. In addition, the study by Ahyai et al (with 3 years of follow up)[11] reported that the re-operation rate (7.2 % versus 6.7 %; p = 1) as well as urethral strictures (4.1 versus 3.3; p = 1) were not significantly different in HoLEP and TURP groups. Follow up (l year) also demonstrated no significant difference in urethral stricture between the two groups (2.5 % versus 5 %; p = 0.7).

In our opinion, the two most debated drawbacks of HoLEP that may have limited its spread in the urologist community namely, the long learning curve and high cost are not entirely justified. The learning curve can be minimized with proper case selection and a short period of structured supervision. In general, after performing transurethral surgery on about 20 to 30 patients, a urologist will likely be able to perform HoLEP on prostates between 30 and 100 grams, especially since the anatomical nature of enucleation makes it inherently easier to master HoLEP than TURP.[19]

The present study did not address cost. Nevertheless, the high initial and maintenance cost of laser therapy may be partially compensated by the shorter hospital stay and the more rapid return to work. A previous study demonstrated that HoLEP is more cost effective than TURP, since it may spare the costs of higher early morbidity with TURP.[20] Also, the multi-use nature of the holmium laser, which can also be used to treat stones, further improves its cost effectiveness; it has a 93% success rate for treatment of ureteric stones.[21]

Conclusion

HoLEP proved to be a safe and highly effective technique for the surgical treatment of bladder outlet obstruction due to BPH. Results after HoLEP compared favorably with results after TURP. Blood loss, catheterization time, and hospital stay were significantly decreased with HoLEP. Postoperative improvement in symptoms and micturition parameters were significantly better with HoLEP than with TURP; these occurred within the first month and lasted up to 12 months of follow up. □

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