0022-5347/04/1725-1926/0
THE JOURNAL OF UROLOGY®

Reprinted from Vol. 172, 1926–1929, November 2004
Printed in U.S.A.
DOI: 10.1097/01.ju.0000140501.68841.a1

HOLMIUM LASER ENUCLEATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE: RESULTS FROM A 2-CENTER, PROSPECTIVE, RANDOMIZED TRIAL IN PATIENTS WITH OBSTRUCTIVE BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Purpose: To our knowledge we report the first multicenter, prospective, randomized study comparing holmium laser enucleation (HoLEP) and transurethral prostate resection (TURP) for obstructive benign prostatic hyperplasia.

Materials and Methods: From January to October 2002, 100 consecutive patients with symptomatic obstructive benign prostatic hyperplasia were randomized at 2 centers to surgical treatment with HoLEP (52 in group 1) or TURP (48 in group 2). Patients in the 2 groups were preoperatively assessed by scoring subjective symptoms questionnaires. Preoperative and perioperative parameters were also evaluated, the latter at 1, 6 and 12 months of followup.

Results: At baseline all patients had obstruction (Schäfer grade greater than 2). At the 1, 6 and 12-month followups no statistically significant differences were observed between the 2 groups in terms of urodynamic findings and subjective symptom scoring. In the HoLEP group mean total time in the operating room ± SD was significantly longer than for TURP (74 ± 19.5 vs 57 ± 15 minutes, $p < 0.05$), while catheterization time (31 ± 13 vs 57.78 ± 17.5 minutes, $p < 0.001$ and hospital stay (59 ± 19.9 vs 85.8 ± 18.9 hours, $p < 0.001$) were significantly shorter in the HoLEP group. Transient stress and urge incontinence were more common in the HoLEP group, although at the 12-month followup results were comparable. The overall complication rate was comparable in the 2 groups. Erectile function was also maintained in the followup period from baseline in each group, as expected.

Conclusions: HoLEP and TURP were equally effective for relieving obstruction and lower urinary tract symptoms. HoLEP was associated with shorter catheterization time and hospital stay. At 1 year of followup complications were similar in the 2 groups.

KEY WORDS: prostate, prostatic hyperplasia, transurethral resection of prostate, laser surgery, prostatectomy

Benign prostatic hyperplasia (BPH) is a prevalent medical condition. It has been calculated that approximately 30% of the male population in Europe and the United States have a chance of undergoing standard transurethral resection of the prostate (TURP) during their lifetimes.[1] TURP has been the gold standard for BPH for the last 30 years. Complications and morbidity related to this procedure, including blood loss, fluid balance disturbances, excessive fluid absorption, incontinence and erectile dysfunction, have been estimated to develop in approximately 15% of the patients[2] and they may sometimes be of clinical relevance.[3] Therefore, high interest has developed in minimally invasive and alternative surgical techniques.

Currently holmium laser prostate enucleation (HoLEP), introduced by Gilling et al,[4] seems to be an attractive alternative to standard TURP. The holmium:YAG laser (Lumenis, Tel Aviv, Israel) is a pulse solid state laser with many characteristics that make it ideal for endourological surgery. It has a wavelength of 2,140 nm that allows it to be strongly absorbed by tissue water, therefore, causing rapid vaporization of exposed tissues at a depth of approximately 0.4 mm and producing tissue coagulation 3 to 4 mm below the vaporization surface tissue. This is useful and allows a precise, bloodless field, preventing systemic fluid absorption. To our knowledge we describe the first multicenter, prospective, randomized trial comparing HoLEP and TURP for urodynamically obstructed BPH.

Accepted for publication June 18, 2004.
Study received ethics committee approval.
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PATIENTS AND METHODS

From January 2002 to October 2002, 100 consecutive patients with BPH and documented obstructed voiding symptoms in whom previous pharmacological therapy had failed were considered candidates for surgical treatment and were included in this study. All patients were evaluated preoperatively by scoring subjective symptoms with the International Prostate Symptom Score (I-PSS), quality of life (QoL) and International Index of Erectile Function (IIEF-15) questionnaires, physical examination with digital rectal examination, laboratory analysis with total serum prostate specific antigen, and kidney-bladder and transrectal prostatic ultrasound. For study purposes all patients were also evaluated with a complete urodynamic study at baseline and 12 months postoperatively. Inclusion criteria were younger than age 75 years, peak urinary flow rate less than 15 ml per second,

post-void residual urine less than 100 cc, medical therapy failure, transrectal ultrasound adenoma volume less than 100 gm and urodynamic obstruction (Schäfer grade greater than 2). Exclusion criteria were neurogenic bladder, a diagnosis of prostate cancer and any previous prostatic, bladder neck or urethral surgery. At baseline no patient had an indwelling catheter. Of these 100 patients 52 were randomized to HoLEP (group 1, including 28 from Milan and 25 from Bergamo) and 48 were randomized to TURP (group 2, including 25 from Milan and 23 from Bergamo). In the HoLEP and TURP groups 12 and 10 men, respectively, had preoperatively donated autologous blood according to the anesthesiologist decision.

The surgical technique used for HoLEP was the one previously described by Gilling et al.[4,5] It included tissue morcellation of the prostatic lobes into fragments that were retrieved from the bladder cavity.[6] All procedures in the 2 groups were performed by urologists on staff at the 2 study institutions. Holmium laser energy was delivered by a 360 μ fiber placed in a 24Fr resectoscope. Enucleation was performed at 2.0 J and 35 Hz, while transurethral resection was performed using a standard tungsten wire loop with a cutting current of 80 W and a coagulating current of 160 W. At the end of the procedures a 22Fr triple lumen catheter was inserted into the bladder and irrigation was started. Recorded intraoperative data included total time in the operating room (ie total time with the resectoscope or laser in place), the quantity of tissue removed in gm and the rate of tissue retrieved per minute. In the HoLEP group only enucleation and morcellation time in minutes was also documented. All retrieved tissue specimen were weighed and sent for histological evaluation. Catheterization time and hospital stay were recorded.

All patients were assessed at the 1, 6 and 12-month followups by interview, subjective symptom scoring, physical examination, uroflowmetry and urinary tract ultrasound. Complete urodynamic testing was performed at baseline and at the 12-month followup date in all patients. Only pressure flow studies are shown in our report. Indeed, free uroflowmetry, cystomanometry with multivariate analysis and urethral pressure profiles were performed in each patient (data not shown) before and after surgery. All data were statistically analyzed using the Student t test for paired and unpaired data. Data are presented as the mean ± SD. For all statistical comparisons significance was defined at $p < 0.05$. The study was approved by our ethics committee and all patients provided informed consent.

RESULTS

Table 1 lists main patient characteristics. Mean preoperative prostatic volume, time in the operating room and total tissue removed were greater in the HoLEP group than in the TURP group. Incidental prostate adenocarcinoma and high grade prostatic intraepithelial neoplasia (HGPIN) were diagnosed similarly in the HoLEP and TURP groups. In the HoLEP group catheterization time and hospital stay were significantly shorter than in the TURP group. We did not find a statistical difference between preoperative and postoperative serum hemoglobin in either group and no difference in blood loss between the 2 groups. Only 1 patient in the TURP group and none in the HoLEP group underwent blood transfusion. Table 2 lists these results.

At the 1, 6 and 12-month followups we did not find any statistical difference between the 2 groups in I-PSS, the QoL question or uroflowmetry. Tables 3 and 4, and the figure show followup data, including urodynamic findings. In each group bladder outlet obstruction had clearly resolved since the 1-month followup visit. As measured with the erectile function domain of the IIEF-15 (questions 1 to 5 and 15), erectile function did not show a decrease during followup from baseline in either groups. As expected, we noted a similar decrease in the ejaculatory domain in the 2 groups (table 5). At the 1-month followup 25 patients (44%) in the HoLEP group reported some degree of urge incontinence (burning in 33 or 58.9% and stress incontinence in 1 or 1.7%), while the same symptoms were recorded in the TURP group in 17 (38.6%) (13 or 29.5% and 1 or 2.2%, respectively). All patients with irritative symptoms received specific medical therapy with a significant progressive improvement within the following months.

TABLE 1. *Patient characteristics*

	HoLEP	TURP
No. pts	52	48
Mean age	65.14	64.5
Mean total serum prostate specific antigen ± SD (ng/ml)	2.3 ± 1.6	2.5 ± 2
Mean TRUS vol ± SD (gm)	70.3 ± 36.7	56.2 ± 19.4*
No. incidental adenoca (%)	6 (11.5)	4 (8.3)
No. prostate HGPIN (%)	3 (5.3)	3 (6.2)

* $p < 0.05$.

TABLE 2. *Perioperative data*

	Mean HoLEP ± SD	Mean TURP ± SD	p Value
Operative time (mins):			
Total	74 ± 19.5	57 ± 15	<0.05
Enucleation	38.57 ± 19.8		
Morcellation	12.09 ± 10		
Resected wt (gm)	36.08 ± 27.03	25.4 ± 13.9	<0.05
Retrieval rate (gm/min)	0.48	0.44	Not significant
Hemoglobin (gm/dl):			
Preop	14.57 ± 1.35	15.1 ± 1.43	Not significant
Postop	13.22 ± 1.45	13.7 ± 1.42	Not significant
Blood loss (gm/dl)	1.32 ± 1.8	1.29 ± 2.1	Not significant
Catheterization time (hrs)	31 ± 13	57.78 ± 17.5	<0.001
Hospital stay (hrs)	59 ± 19.9	85.8 ± 18.9	<0.001

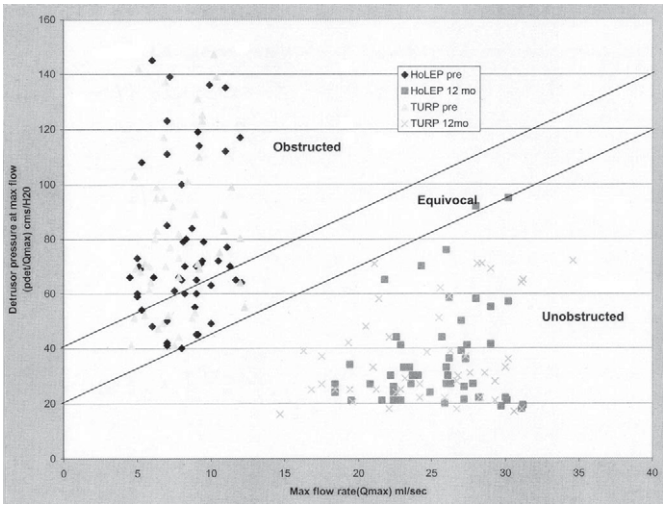
TABLE 3. *Followup data*

	Mean Baseline ± SD	Mean 1 Mo ± SD	Mean 6 Mos ± SD	Mean 12 Mos ± SD
Max flow (ml/sec):				
HoLEP	8.2 ± 3.2	23.36 ± 9.9	23.1 ± 8.6	25.1 ± 7.2
TURP	7.8 ± 3.6	19.1 ± 3.8	26.5 ± 15.5	24.7 ± 10
p Value	0.61	0.07	0.007	0.25
Av flow (ml/sec):				
HoLEP	4.3 ± 2.0	13.3 ± 5.7	13.3 ± 5.9	15.5 ± 4.2
TURP	4.3 ± 2.3	10.1 ± 2.1	9.1 ± 3.6	12.1 ± 3.3
p Value	0.94	0.02	0.01	0.01
I-PSS:				
HoLEP	21.6 ± 6.7	4.9 ± 4.2	3.9 ± 2.9	4.1 ± 2.3
TURP	21.9 ± 7.2	4.7 ± 2.1	2.9 ± 2.6	3.9 ± 3.6
p Value	0.83	0.14	0.72	0.58
QoL question:				
HoLEP	4.6 ± 1.1	1.4 ± 1.4	1 ± 0.8	1.4 ± 0.9
TURP	4.7 ± 1	1.3 ± 0.7	0.6 ± 0.2	0.8 ± 1.28
p Value	0.7	0.66	0.25	0.31

TABLE 4. *Urodynamic findings*

	Mean Baseline (range)	Mean 12 Mos (range)
Detrusor pressure at max flow (cm H_2O):		
HoLEP	77.3 (41–145)	36.2 (18–95)
TURP	81.8 (41–147)	38.5 (16–75)
p Value	0.67	0.85
Schäfer grade:		
HoLEP	3.4 (2–6)	0.9 (1–4)
TURP	3.5 (2–6)	1.2 (0–4)
p Value	0.75	0.55

Baseline to 12 months p <0.001.



Nomogram comparing detrusor pressure at maximum (*max*) flow (*pdet*/*Qmax*) and maximum urinary flow (*Qmax*) at baseline (*pre*) and after 12-month (*mo*) followup in HoLEP and TURP groups.

TABLE 5. *HoLEP vs TURP IIEF-15 scores*

Domains	Mean HoLEP ± SD	Mean TURP ± SD
Preop:		
Erectile function[1–5, 15]	22.3 ± 3.6	21.4 ± 3.1
Orgasmic function[9, 10]	8.5 ± 2.1	8.7 ± 1.9
Sexual desire[11, 12]	6.9 ± 2.3	6.8 ± 1.7
Intercourse satisfaction[6–8]	8.8 ± 1.6	8.1 ± 1.2
Overall satisfaction[13, 14]	7.2 ± 0.9	6.8 ± 1.1
6 Mos:		
Erectile function	23.5 ± 3.6	23.4 ± 3.5
Orgasmic function	6.5 ± 1.2	5.9 ± 1.1
Sexual desire	6.3 ± 2.0	6.1 ± 1.6
Intercourse satisfaction	7.9 ± 1.9	7.8 ± 1.6
Overall satisfaction	6.9 ± 0.7	6.2 ± 0.5
12 Mos:		
Erectile function	23.8 ± 3.9	24.1 ± 3.7
Orgasmic function	6.5 ± 1.3	6.3 ± 1.1
Sexual desire	6.9 ± 2.6	6.7 ± 1.9
Intercourse satisfaction	8.2 ± 1.8	8.4 ± 1.9
Overall satisfaction	7.1 ± 0.9	6.9 ± 0.7

HoLEP vs TURP p not significant.

TABLE 6. *Early and late adverse events*

	No. HoLEP (%)	No. TURP (%)
First followup:		
Bladder mucosal injury*	10 (18.2)	0
Re-intervention for bleeding	1 (1.7)	1 (2.2)
Transurethral resection syndrome	0	1 (2.2)
Early acute urinary retention	3 (5.3)	1 (2.2)
Dysuria (burning)†	33 (58.9)	13 (29.5)
Transitory urge incontinence	25 (44)	17 (38.6)
6 & 12-Mo followups:		
Urethral stricture	1 (1.7)	4 (7.4)
Stress incontinence	1 (1.7)	1 (2.2)

* p = 0.0012.
† p = 0.0002.

Table 6 lists adverse events. In particular, when analyzing complications following HoLEP, the acute urinary retention rate was higher than after TURP and minor bladder lesions that occurred during morcellation were treated with bladder irrigation only. In the HoLEP group 3 episodes (5.3%) of post-catheter removal acute urine retention were noted compared to 1 in the TURP group. These cases were treated with subsequent temporary re-catheterization. In the TURP group 1 case of transurethral resection syndrome was observed. In each group only 1 case of early re-intervention due to bleeding was noted. At the 12-month followup no urethral stricture was observed in the HoLEP group compared to 4 (7.4%) in the TURP group. Treatment consisted of internal urethrotomy in 3 cases and urethral dilation in 1.

DISCUSSION

Holmium laser enucleation of the prostate with morcellation has increasingly been gaining use as a therapeutic option for symptomatic BPH. In our study HoLEP was as effective as TURP in terms of improved subjective symptoms and urodynamic findings at the 12-month followup. At study inclusion all patients in the 2 groups had obstruction due to BPH according to accepted urodynamic criteria and postoperatively most patients were relieved of obstruction. We used validated questionnaires to assess the impact of HoLEP and TURP on subjective symptoms and we were able to note that at the 12-month followup the 2 procedures produced similar positive results. Of note, we observed that erectile function did not deteriorate in either group, while ejaculatory function worsened due to the expected development of retrograde ejaculation, which did not differ within the groups. When our 2 center long-term HoLEP results were compared to those in previously reported studies, no significant differences in terms of urodynamic findings and subjective symptoms were found.[7–9]

The HoLEP technique mimics open prostatectomy, hence, producing a similar wide cavity but allowing a practically bloodless field due to accurate intraoperative hemostasis, thus, requiring shorter catheterization time.[10–12] This was also reflected in decreased bleeding and an easier way to control bleeding volume after HoLEP. Therefore, systematic irrigation was often unnecessary and applied only when macroscopic hematuria occurred. However, the duration was typically only a couple of hours and it was generally self-limiting. Although it did not attain statistical significance in terms of hemoglobin loss, the hemostatic nature of this laser wavelength seems to be the key point for enabling safe early catheter removal.

Catheterization time and hospital stay recorded in patients after HoLEP compared to TURP were significantly shorter, which was much appreciated by patients. According to this finding it has been suggested that HoLEP can be an attractive option as an outpatient procedure in select patients.[13] In our experience operative time is still longer compared to standard TURP, which probably seems to be due to the longer learning curve needed.[14, 15]

The issue of a learning curve is challenging, and extremely difficult to quantify and compare between the 2 techniques. The only 2 groups to study the subject indicated that the HoLEP technique can be learned but it requires longer training than standard transurethral resection, stressing the need for an endourological background with correct mentoring, as with all endourological procedures. We may add that this tutoring is also necessary for TURP but the belief is that it seems easier and more surgeon friendly for new residents to perform accurate HoLEP than TURP. However, currently this remains only a belief and it is difficult to demonstrate. Furthermore, when referring to this study, it is also difficult

to compare learning curves because surgeons performing HoLEP had had previous endoscopic experience with TURP.

When analyzing our data, we note that there is a statistical difference between preoperative prostate volume on ultrasound and between the 2 groups. This can be explained by the ample inclusion criteria (prostates less than 100 gm), which was purposely chosen. However, this difference did not seem to have an impact on other preoperative clinical parameters. A certain degree of subjective burning and urge incontinence was more frequently recorded after HoLEP than after TURP, which was probably due to the high energy applied to the capsule during the procedure. Moreover, this was always short term and self-limiting. Surprisingly when comparing long-term complications in our series with those in the literature, urethral stricture was more frequent in our TURP group[16] and less so in the HoLEP group.[10] We do not have a precise explanation for these findings, although one may speculate that avoiding any use of electrical current may decrease the risk of iatrogenic stricture formation.

Pathological diagnosis was possible in the 2 groups and in particular no difference in terms of cancer and HGPIN detection was noted. This is an important issue due to well-known alterations caused to tissue by all types of lasers.[17] Furthermore, in our experience radical prostatectomy performed in patients with HoLEP diagnosed incidental prostate cancer does not appear to be technically more difficult than procedures performed after TURP. In our study surgeons had been performing TURP for a mean of 12 years, while HoLEP was started only 18 months prior to starting the study. Our study was specifically designed for prostates less than 100 gm because we have not yet completed our learning curve for the enucleation of prostates larger than 100 gm. However, increasing data in the literature[7, 10, 11, 16] seem to confirm our belief that this technique is ideal for large prostates as an attractive alternative to open prostatectomy. Future research will also evaluate this comparison from a cost-effectiveness point of view.

CONCLUSIONS

Holmium laser enucleation of the prostate is a safe and minimally invasive technique that can guarantee results at the 1-year followup that are similar to those of standard transurethral resection in terms of relief of subjective symptoms and urodynamic findings due to bladder outlet obstruction in patients with BPH. Nevertheless, although the HoLEP technique requires more time to perform than standard TURP, it is associated with significantly shorter catheterization time and hospital stay. Complications are similar with the 2 procedures. This first multicenter, randomized study confirms the reproducibility and feasibility of the HoLEP technique and opens the way to extending the indication to larger prostates as an attractive alternative to open surgical prostatectomy.

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