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ORIGINAL PAPER

Is Holmium Laser Enucleation of Prostate equally effective in management of benign prostatic hyperplasia patients with either voiding or storage lower urinary tract symptoms? A comparative study

Mostafa M. Mostafa [1, 2], Nilesh Patil [1], Mahmoud Khalil [2], Mohammed A. Elgammal [2], Ayman Mahdy [1]

[1] Division of Urology, Department of Surgery, University of Cincinnati College of Medicine, Cincinnati (US);
[2] Asiut University Hospitals, Asiut, Egypt.

Summary ***Objective: To evaluate and compare the effectiveness and safety of holmium laser enucleation of prostate (HoLEP) in relieving either voiding or storage lower urinary tract symptoms (LUTS) in benign prostatic hyperplasia (BPH) patients.***
Materials and methods: The charts of patients with BPH who underwent HoLEP for either predominant voiding or predominant storage LUTS at University of Cincinnati hospitals in the period between February 2015 and December 2020 were retrospectively reviewed and analyzed for changes in voiding symptomatology, storage symptomatology, hematuria, International Prostate Symptom Score (IPSS), peak flow rates (Q_{max}), presence of detrusor overactivity (DO), and post-voiding residual urine (PVR) from baseline to up to 6 months postoperatively.
Results: A total of 132 patients were included in the analysis. Patients were divided into two groups: Group 1 included BPH patients with predominant voiding LUTS (68 Patients) while group 2 involved those with predominant storage LUTS (64 Patients). HoLEP was equally effective in management of both groups with significant improvement in urodynamics study (UDS) parameters, patient voiding and storage symptomatology, and IPSS from preoperatively to up to 6 months postoperatively with relatively low procedure complication rate and postoperative need for medication or procedure.
Conclusions: HoLEP is a safe, effective, and reliable minimally invasive surgical modality that can be relied on for BPH patients with either predominant voiding or predominant storage symptoms with relatively low procedure complication rate and postoperative need for medication or procedure.

KEY WORDS: *Holmium Laser Enucleation of Prostate (HoLEP); Benign Prostatic Hyperplasia (BPH); Lower Urinary Tract Symptoms (LUTS).*

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition affecting a large number of men over the age of 50 years and is the major cause of the highly prevalent *lower urinary tract symptoms* (LUTS) in men of this age group that often necessitate surgical intervention (1, 2). The LUTS associated with BPH are generally divided into voiding symptoms (slow stream, splitting or spraying, intermittency, hesitancy, straining, terminal dribbling) and storage symptoms (day-time urinary frequency, nocturia, urgency, urinary incontinence) (3).
These LUTS are among the most common clinical complaints in adult men with reported increasing prevalence with aging (4). The storage LUTS may also be termed *overactive bladder* (OAB) symptoms and are largely encompassed by the term *overactive bladder syndrome* (OABS) (5). While the voiding symptoms are usually more prevalent, the storage symptoms are almost always more bothersome (6). Associated with a significant burden on both patients and society, these LUTS also have a major impact on patients' *quality of life* (QoL) (7). As such, the *American Urological Association* (AUA) has developed the *International Prostate Symptom Score* (IPSS) as one of the most reliable tools to evaluate the severity of LUTS associated with BPH which, in turn, plays a major role in determining the most appropriate treatment option for BPH (8-10).
After being the preferred surgical treatment for BPH patients for more than 30 years, *transurethral resection of prostate* (TURP) has been replaced by *holmium laser enucleation of prostate* (HoLEP) as the gold standard surgical treatment for BPH (5, 11, 12).
Introduced in 1995, HoLEP is a minimally invasive surgical procedure that has become the first line treatment of BPH as it provides both effective and safe surgical treatment option for BPH without any size limitation, although at the expense of occasional complications (11, 13, 14). HoLEP has the advantage of enucleating the enlarging BPH adenoma without destroying the bladder neck thus relieving *bladder outflow obstruction* (BOO) immediately, safely, and effectively (5).
Although improvement in both storage and voiding LUTS has been demonstrated after either medical treatment with an alpha-blocker or a 5-alpha-reductase inhibitor or surgical treatment with TURP for BPH patients, few studies have been made to measure the outcomes of HoLEP in BPH-related voiding and/or storage LUTS (11).
We performed our study with the aim to evaluate and compare the effectiveness and safety of HoLEP in relieving either voiding or storage LUTS in BPH patients.

No conflict of interest declared.

Materials and methods

After our study protocol approval by *University of Cincinnati Institutional Review Board* (IRB ID:2021-0666), we started reviewing the charts of all patients who underwent HoLEP at *University of Cincinnati* hospitals in the period between February 2015 and December 2020. All patients had routine initial evaluation with complete medical history, *digital rectal examination* (DRE), IPSS questionnaire, urinalysis, serum creatinine level, determination of serum *prostate-specific antigen* (PSA) when needed, *transrectal ultrasonography* (TRUS), peak flow rate (Q_{max}), *post-voiding residual urine* (PVR), and *urodynamic study* (UDS) before proceeding to any surgical intervention.

Our inclusion criteria included patients with BPH who underwent HoLEP for either predominant voiding or predominant storage LUTS.

We excluded patients who underwent the procedure for BPH with concomitant bladder stones and/or neurogenic bladder. We also excluded patients with predominant storage LUTS along with PVR of 150 ml or more, patients taking medications that may mimic or aggravate the LUTS such as antidepressants, diuretics, bronchodilators, anticholinergics, sympathomimetics, and antihistamines (15), and those having uncontrolled *diabetes mellitus* (DM) or recurrent *urinary tract infections* (UTIs).

For proper allocation of patients to either of our two comparative groups (BPH patients with predominant voiding symptoms versus those with predominant storage symptoms), we used the principal indication for surgical intervention as determined by both subjective and objective parameters as the main allotment tool. Regarding the subjective parameters, we analyzed nine symptoms in all patients and categorized them into two main categories in order to determine the type of patient predominant symptomatology: storage symptoms (frequency, urgency, nocturia, and urinary incontinence) and voiding symptoms (hesitancy, intermittency, terminal dribbling, straining, and urinary retention) (3). We also analyzed hematuria, a relevant symptom that is not specific for either group. Analysis of symptoms was performed by the attending physician at the patient's first presentation via asking the patient an open-ended question about the patient's main complaint that urged him to seek medical care followed by closed-ended or binary questions to confirm the absence of the other relevant symptoms. Additionally, to both confirm the proper allocation of each patient to the pertinent group and avoid reporting bias, we used UDS as an objective parameter. As such, we identified patients with predominant voiding symptoms as those who reported their voiding symptoms as the more bothersome, whose voiding symptoms were the main drive for intervention, and whose UDS showed a predominant obstructive pattern with urodynamic evidence of BOO (BOO index > 40 using ICS nomogram (16). On the other hand, patients with predominant storage symptoms were defined as those who identified their storage symptoms as the more bothersome, who had no history of urinary retention, whose storage symptoms were the only indication for intervention, and whose UDS showed a predominant OAB pattern with volume to first contraction less than 350 mL and DO (involuntary detrusor contraction ≥ 10 cm H_2O) (17).

All the cases included were performed by one highly skilled surgeon in the procedure (AM) to avoid the interference of below optimum surgical skills or learning curve complications in our results.

Treatment efficacy, which was the primary outcome, was evaluated by comparing the preoperative UDS parameters, patient symptomatology, and IPSS with their postoperative counterparts. UDS parameters (Q_{max}, PVR, and demonstration of DO) were reported twice: at baseline and at the 6-month follow-up visit. We collected and compared them between the two groups. Patient voiding symptomatology, storage symptomatology, hematuria, and IPSS were reported at baseline, 3-month, and 6-month postoperatively.

We also collected, analyzed, and compared them between the two groups. For the secondary outcome (treatment safety), any reported complication within the first 6 postoperative months was collected and analyzed. We also collected, analyzed, and compared the postoperative need for medication (antimuscarinic alone or antimuscarinic+ beta-3 agonist) or procedure (Botox injection, urethral dilatation, or open prostatectomy) within the first 6 postoperative months between the two groups.

Figure 1.
Flowchart on inclusion and exclusion steps.

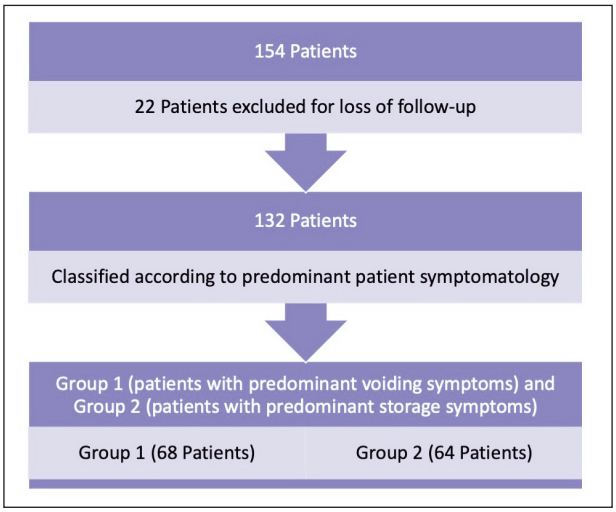

Table 1.
Demographic and baseline characteristics of the studied groups.

Variables	Group 1 (n = 68)	Group 2 (n = 64)	P-value
Age (years)			
Mean ± SD	75.2 ± 6.1	74.9 ± 5.5	0.767
BMI (kg/m^2)			
Mean ± SD	25.6 ± 2.68	25.6 ± 1.2	0.916
Ethnicity			
White	26 (38.2%)	26 (40.0%)	0.214
Black/African American	30 (44.1%)	20 (31.3%)	
Hispanic	12 (17.6%)	18 (28.1%)	
Smoking	32 (47.1%)	30 (46.9%)	0.983
Diabetes mellitus	26 (38.2%)	30 (46.9%)	0.315
Heart failure	25 (36.8%)	21 (32.8%)	0.634
Hypertension	37 (54.4%)	33 (51.6%)	0.743

SD: Standard deviation.

Statistical analysis

All statistical analyses were conducted using the IBM SPSS software package version 20.0 (*Armonk, NY: IBM Corp*). Quantitative variables are presented as means ± standard deviation, and qualitative variables are expressed as frequencies with percentages. Results were compared between two groups using Student's t-test and Mann-Whitney U test for quantitative variables and chi-square test and McNemar's test for qualitative variables.
A P-value of < 0.05 was considered significant.

Results

In total, 132 patients met the inclusion criteria, had complete follow-up data in their charts with preoperative and postoperative documentation of various voiding and storage symptomatology, IPSS, and UDS parameters and were included in our study. We allocated these patients into two groups: Group 1 (68 patients) included those with predominant voiding symptoms while group 2 (64 patients) involved those with predominant storage symptoms (Figure 1).

Demographic and baseline characteristics of the studied groups

The median age was 75.2 ± 6.1 and 74.9 ± 5.5 years for groups 1 and 2, respectively with no significant differences in demographic and baseline characteristics between the two groups (Table 1).

UDS parameters of the studied groups

The mean preoperative peak flow rates (Q_{max}) were 8.6 ± 2 and 12.5 ± 1.9 for groups 1 and 2, respectively with a significant increase in Q_{max} postoperatively with p-value of increase of < 0.001 for both groups.
With reference to DO, there was a remarkable decrease in the presence of DO after the procedure in both groups (4 out of 16 patients and 12 out of 64 patients with preoperative DO for groups 1 and 2, respectively) with significantly higher decrease in DO after the procedure in group 2 (p-value = < 0.001) than in group 1 (p-value = 0.008). As to post-voiding residual urine (PVR), there was a significant decrease in PVR after HoLEP in both groups with p-value of improvement of < 0.001 for both groups (Table 2).

Patient symptomatology of the studied groups

There was a significant decrease in the frequency of the 4 studied storage symptoms and the 5 studied voiding symptoms in both groups from preoperatively to both 3- and 6- month postoperatively.
Eleven (16.2%) and Seven (10.9%) patients from groups 1 and 2, respectively had preoperative hematuria that was completely alleviated after HoLEP (Table 3).

IPSS of the studied groups

The mean preoperative IPSS was 28.4 ± 3.4 and 26.9 ± 3 for groups 1 and 2, respectively, and there was significant decrease in IPSS from preoperatively to both 3- and 6-month postoperatively in both studied groups with p-value of decrease of < 0.001. Interestingly, even though the preoperative IPSS was significantly higher in group 1 than in group 2 (p-value = 0.010), there was non-significant difference in the decrease in IPSS between both groups at both 3-month follow-up (p-value = 0.842) and 6-month follow-up (p-value = 0.483) (Table 4).

Procedure complication rate and postoperative need for medication or procedure in the studied groups

There was no significant difference between the studied groups as regarding procedure complication rate and postoperative need for medication or procedure.
The most encountered complication was urinary tract infection occurring in 22 (32.4%) and 14 (21.9%) group 1 and 2 patients, respectively followed by urinary incontinence, bleeding, urethral stricture, and finally residual prostatic tissue. Most patients didn't require postoperative medication or procedure with only 10.3% and 4.4% of group 1 patients and 23.4% and 4.7% group 2 patients requiring postoperative medication and procedure, respectively (Table 5).

Table 2.
Changes in urodynamic study (UDS) parameters at 6-month postoperatively and comparison with preoperatively.

	Variables	Group 1 (n = 68)	Group 2 (n = 64)	P-value
Peak flow rate (Q_{max}) (ml/s)	Preoperatively (Mean ± SD)	8.6 ± 2	12.5 ± 1.9	< 0.001
	6-month Postoperatively (Mean ± SD)	14.2 ± 2.4	15.6 ± 1.7	< 0.001
	P-value from preoperatively to 6-month postoperatively	< 0.001	< 0.001	
	Increase (Mean ± SD)	5.6 ± 2.2	3.1 ± 1.9	< 0.001
Detrusor over activity (DO)	Preoperatively			
	No	52 (76.5%)	0 (0%)	< 0.001
	Yes	16 (23.5%)	64 (100%)	
	6-month postoperatively			
	No	64 (94.1%)	52 (81.3%)	0.024
	Yes	4 (5.9%)	12 (18.8%)	
	P-value from preoperatively to 6-month postoperatively	0.008	< 0.001	
Post-voiding residual urine (PVR) (ml)	Preoperatively (Mean ± SD)	239.4 ± 69.7	104.7 ± 22.6	< 0.001
	6-month Postoperatively (Mean ± SD)	53.7 ± 26.9	48.3 ± 15.3	0.156
	P-value from preoperatively to 6-month postoperatively	< 0.001	< 0.001	
	Decrease (Mean ± SD)	185.7 ± 72.1	56.4 ± 24.86	< 0.001

SD: Standard deviation.

Discussion

To the best of our knowledge, we performed the first large study comparing the outcomes of HoLEP in BPH patients with predominant voiding symptoms and those with predominant storage symptoms in subjective outcomes (patient symptomatology and IPSS), objective outcomes (UDS parameters), procedure complication rate and postoperative need for medication or procedure. Our study confirms that HoLEP is associated with significant improvement in UDS

Table 3.
Changes in patient symptomatology at 3- and 6-month postoperatively and comparison with preoperatively

	Variables	Group 1 (n = 68)	Group 2 (n = 64)	P-value
Storage symptoms	**Frequency**			
	Preoperatively	24 (35.3%)	54 (84.4%)	< 0.001
	3-month postoperatively	9 (13.2%)	24 (37.5%)	0.001
	6-month postoperatively	6 (8.8%)	16 (25%)	0.013
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	<0.001	
	Urgency			
	Preoperatively	19 (27.9%)	53 (82.8%)	< 0.001
	3-month postoperatively	9 (13.2%)	19 (29.7%)	0.021
	6-month postoperatively	3 (4.4%)	8 (12.5%)	0.093
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	< 0.001	
	Nocturia			
	Preoperatively	30 (44.1%)	52 (81.3%)	< 0.001
	3-month postoperatively	12 (17.6%)	26 (40.6%)	0.004
	6-month postoperatively	6 (8.8%)	6 (9.4%)	0.912
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	< 0.001	
	Urinary incontinence			
	Preoperatively	8 (11.8%)	38 (59.4%)	< 0.001
	3-month postoperatively	2 (2.9%)	9 (14.1%)	0.021
	6-month postoperatively	0 (0%)	3 (4.7%)	0.111
	P-value from preoperatively to 3-and 6-month postoperatively	0.006	< 0.001	
Voiding symptoms	**Hesitancy**			
	Preoperatively	54 (79.4%)	10 (15.6%)	< 0.001
	3-month postoperatively	16 (23.5%)	5 (7.8%)	0.014
	6-month postoperatively	8 (11.8%)	2 (3.1%)	0.098
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	0.047	
	Intermittency			
	Preoperatively	52 (76.5%)	8 (12.5%)	< 0.001
	3-month postoperatively	16 (23.5%)	4 (6.3%)	0.006
	6-month postoperatively	5 (7.4%)	0 (0%)	0.058
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	0.018	
	Terminal dribbling			
	Preoperatively	56 (82.4%)	10 (15.6%)	< 0.001
	3-month postoperatively	22 (32.4%)	4 (6.3%)	< 0.001
	6-month postoperatively	5 (7.4%)	1 (1.6%)	0.209
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	0.011	
	Straining			
	Preoperatively	50 (73.5%)	24 (37.5%)	< 0.001
	3-month postoperatively	34 (50%)	15 (23.4%)	0.002
	6-month postoperatively	9 (13.2%)	6 (9.4%)	0.485
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	< 0.001	
	Urinary retention			
	Preoperatively	68 (100%)	0 (0%)	< 0.001
	3-month postoperatively	1 (1.5%)	0 (0%)	1.000
	6-month postoperatively	0 (0%)	0 (0%)	-
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	-	
	Hematuria			
	Preoperatively	11 (16.2%)	7 (10.9%)	0.381
	3-month postoperatively	2 (2.9%)	1 (1.6%)	1.000
	6-month postoperatively	0 (0%)	0 (0%)	-
	P-value from preoperatively to 3-and 6-month postoperatively	< 0.001	0.005	

parameters, patient storage and voiding symptomatology, and IPSS from preoperatively to both 3- and 6- month postoperatively with remarkably low procedure complication rate and postoperative need for either medication or procedure and with similar efficacy in BPH patients with either predominant voiding or predominant storage symptoms.

Vavassori et al. performed a study evaluating outcomes of HoLEP in 330 consecutive patients and reported significant improvement in Q_{max}, IPSS, and QoL after 3-year follow-up with 8.5% of their patients having postoperative transient irritative symptoms, 7.3% having transient postoperative urinary incontinence, and 2.7% having persistent BOO requiring reoperation (18). Our results confirm the reported improvement in Q_{max} and IPSS and the possibility of transient postoperative irritative symptoms or urinary incontinence after HoLEP. However, we also noted significant improvement in both PVR and DO and comparable efficacy in management of both voiding and storage LUTS after HoLEP.

Pyun et al performed a study to compare the outcomes of HoLEP between 3 groups: BOO-only, BOO with *detrusor underactivity* (DU), and BOO with DO and concluded that the improvement in the IPSS and Q_{max} was higher in the BOO-only group than in the BOO with DO and BOO with DU groups (19).

In contrast to their results, our results confirm that HoLEP has a comparable efficacy in management of BPH patients with either predominant voiding or predominant storage symptoms with significant improvement in UDS parameters, patient symptomatology, and IPSS in both groups of patients, and we can assume that the difference between our results can be attributed to the fact that they had significantly higher number of patients in the BOO-only group (138 patients) compared to BOO with DO group (56 patients) and BOO with DU group (33 patients) and that they included a group having DU in the comparison denoting including patients with late stage bladder dysfunction in their study. Besides, we would like to point that it is better to compare the preoperative with the postoperative Q_{max} for each of the studied groups rather than the degree of increase in Q_{max} between the studied groups because the lower the Q_{max}, the higher the room for increase. For example, in our study, the Q_{max} was preoperatively significantly lower in group 1 having recurrent attacks of urinary retention, and so, although there was a higher increase in Q_{max} after HoLEP in group 1, the postoperative Q_{max} was still higher in group 2.

Jeong et al. conducted a study to evaluate the effect of the presence of preoperative detrusor overactivity on the functional outcomes of HoLEP and concluded that although the storage symptoms improved in patients who had preoperative DO and those who did not, a significant

Table 4.
Changes in International Prostate Symptom Score (IPSS) at 3- and 6- month postoperatively and comparison with preoperatively.

	Group 1 (n = 68)	Group 2 (n = 64)	P-value
IPSS			
Preoperatively (Mean ± SD)	28.4 ± 3.4	26.9 ± 3	0.010
3-month postoperatively (Mean ± SD)	19.9 ± 5.2	18.3 ± 4.3	0.061
6-month postoperatively (Mean ± SD)	12.3 ± 5.7	10.3 ± 5.1	0.036
P-value from preoperatively to 3- and 6-month postoperatively	< 0.001	< 0.001	
Decrease in IPSS			
From preoperatively to 3-month postoperatively (Mean ± SD)	8.5 ± 3.8	8.6 ± 3.4	0.842
From preoperatively to 6-month postoperatively (Mean ± SD)	16 ± 4.6	16.6 ± 4.7	0.483

SD: Standard deviation.

Table 5.
Comparison of procedure complication rate and postoperative need for medication or procedure within the first 6 postoperative months between the two groups.

Variables	Group 1 (n = 68)	Group 2 (n = 64)	P-value
Residual prostatic tissue	1 (1.5%)	0 (0%)	1.000
Bleeding	7 (10.3%)	4 (6.3%)	0.401
Urinary Tract Infection	22 (32.4%)	14 (21.9%)	0.177
Urinary incontinence	5 (7.4%)	7 (10.9%)	0.474
Urethral stricture	2 (2.9%)	1 (1.6%)	1.000
Postoperative need for medication			0.128
No	61 (89.7%)	49 (76.6%)	
Antimuscarinic alone	5 (7.4%)	11 (17.2%)	
Antimuscarinic + Beta-3 Agonist	2 (2.9%)	4 (6.2%)	
Postoperative need for procedure			0.466
No	65 (95.6%)	61 (95.3%)	
Botox	0 (0%)	2 (3.1%)	
Urethral dilatation	2 (2.9%)	1 (1.6%)	
Open prostatectomy	1 (1.5%)	0 (0%)	

number of those who had preoperative DO required postoperative anticholinergics (11). We agree with their results that patients with preoperative DO on UDS would require transient postoperative anticholinergic therapy and can add that there is significant improvement in both voiding and storage symptoms after HoLEP in patients with and without preoperative DO on UDS.

Study limitations

The retrospective nature of the study and the absence of comparative groups including patients who underwent other BPH procedures to compare the effectiveness and complication rate of HoLEP with those of other BPH procedures can affect the generalizability of our results.
Although we would have preferred to use the IPSS voiding subscore (IPSS-V) and the IPSS storage subscore (IPSS-S) rather than the total IPSS (IPSS-T) to facilitate assignment of the patients to either of the two groups, we could not do so as we retrospectively reviewed the charts of patients after the IPSS-T rather than the IPSS-V and IPSS-S had already been calculated at the time of the patients' visits. However, we used both subjective and objective parameters to compensate for the lack of data regarding the IPSS subscores and to ensure the proper allocation of patients to the relevant study groups.

Conclusions

HoLEP is a safe and reliable minimally invasive surgical modality with reported significant improvement in both subjective (measured by patients' symptomatology and IPSS) and objective (measured by UDS parameters) aspects associated with BPH. It is highly efficient in alleviating both voiding and storage symptoms and can be resorted to whether the patient is suffering from predominant voiding or predominant storage symptoms.
Moreover, the procedure complication rate and postoperative need for medication or procedure are relatively low.

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Correspondence

Mostafa M. Mostafa, MD (Corresponding Author)
mostafmm@ucmail.uc.edu
Research Fellow of Urology, Division of Urology, Department of Surgery,
University of Cincinnati College of Medicine,
231 Albert Sabin Way, Cincinnati, OH 45267
Assistant Lecturer of Urology, Asiut University Hospitals, Asiut, Egypt

Nilesh Patil, MD
patilnh@ucmail.uc.edu
Associate Professor of Urology, Department of Surgery,
University of Cincinnati College of Medicine,
231 Albert Sabin Way, Cincinnati, OH 45267

Mahmoud Khalil, MD
mahmoud.magdy51@gmail.com
Lecturer of Urology, Asiut University Hospitals, Asiut, Egypt

Mohammed A. Elgammal, MD
mohammedelgammal@aun.edu.eg
Professor of Urology, Asiut University Hospitals, Asiut, Egypt

Ayman Mahdy, MD, PhD, MBA
mahdyan@uc.edu
Chief of Urology, Professor of Urology,
R. Bruce and Barbara Bracken Endowed Chair in Surgical Urology,
Director of Voiding Dysfunction and Female Urology,
Medical Director of Urology, the West Chester Hospital,
Department of Surgery, University of Cincinnati College of Medicine,
231 Albert Sabin Way, ML 0589, Cincinnati, OH 45267