Comparison of holmium laser enucleation prostatectomy and open transvesical prostatectomy in large prostate more than 80 g in Egyptian men: a randomized controlled trial

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Objective
The aim was to assess the safety and efficacy of holmium laser enucleation prostatectomy (HoLEP) vs open prostatectomy (OP) for prostate of more than 80 g owing to benign prostatic hyperplasia in Egyptian men regarding micturition parameters and complications.
Patients and methods
A total of 110 patients were randomly divided into HoLEP (55 patients) and OP (55 patients). The inclusion criteria were American Urological Association-Symptom Score (AUA-SS) of eight or higher, maximum urinary flow rate (Qmax) of 10 ml/s or less, postvoiding residual urine (PVUR) of 50 ml or more, and a total prostate volume of 80 ml or more in transrectal ultrasound. The exclusion criteria included previous prostate or urethral surgery and non-benign prostatic hyperplasia related voiding disorders. Follow-up was done at first week, second week, first month, third month, sixth month, and 12th month postoperatively. Perioperative parameters were operative time, enucleation specimen weight, postoperative hemoglobin, length of hospital stay, and the duration of indwelling catheter. The assessment was done in the form of AUA-SS, Qmax, PVUR, and reported complications.
Results
Operative time was statistically significantly shorter in HoLEP compared with OP (102.45 vs 170.45 min, respectively). Drop-in hemoglobin concentration was statistically significantly higher in OP compared with HoLEP. Moreover, the duration of catheterization and hospital stay were statistically significantly shorter in HoLEP compared with OP. On the contrary, AUA-SS, PVUR, and Qmax did not reveal statistically significant differences between the two groups.
Conclusion
Both modalities have similar efficacy; however, HoLEP was superior to OP regarding hospital stay, the duration of catheterization, and the rate of hemoglobin concentration drop.

Keywords:
benign prostatic hyperplasia, holmium laser enucleation prostatectomy, open prostatectomy

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Introduction

Benign prostatic hyperplasia (BPH) is considered one of the most common medical conditions in elderly men, affecting their quality of life. BPH is also responsible for a high magnitude of lower urinary tract symptoms of those men. The prevalence of BPH increases from the age of 40 years to the age of 90 years, at which the prevalence becomes 100% [1].

After the failure of medical options for those men or developing complications of bladder outlet obstruction owing to BPH, the surgical options arise such as transurethral resection of the prostate (TURP) in small gland and open prostatectomy (OP) in the large gland [2]. TURP is a very good and effective option, but many complications may occur, such as TURP syndrome and the need for a blood transfusion [3].

New laser techniques, which were developed along the past years, have provided many advantages compared with open or endoscopic modalities. These advantages are better control of bleeding, shorter hospital stay, and minimum duration of both catheterization and postoperative irrigation [3]. Because of these positive points, there was a trend toward the implementation and development of laser techniques along the past years [4].

For the prostate larger than 75 g, OP is the preferred technique in areas with restricted access to modern

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technology [5], but unfortunately OP has more risks such as the need for a blood transfusion and postoperative hemorrhage [6]. Many laser enucleation techniques were studied, and holmium laser enucleation prostatectomy (HoLEP) proved its safety and efficacy in large prostate. However, it was found that the literature did not provide sufficient effective randomized controlled trials comparing HoLEP with OP [7,8].

Consequently, our goal was to compare and evaluate the safety and efficacy of HoLEP and OP in large prostate volume more than 80 g owing to BPH in Egyptian men.

Patients and methods

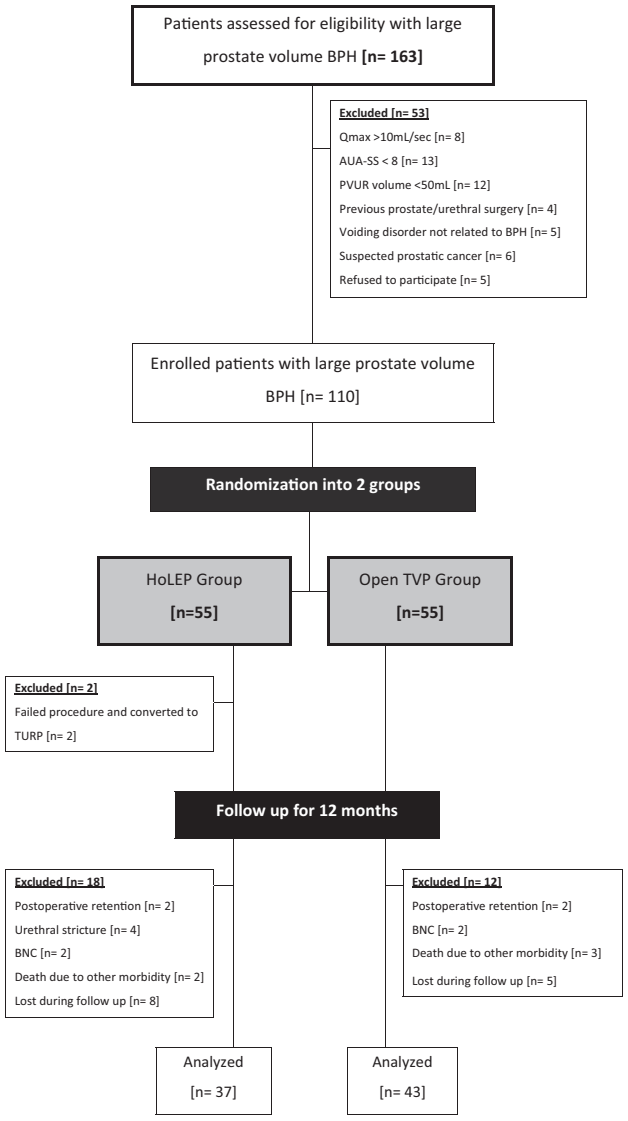
From April 2018 to April 2020, 110 male patients were assigned and randomly divided by a closed envelope method to HoLEP (55 patients) and OP (55 patients) after the approval of the Ethical Committee, and written consents of the patients had been obtained.

The inclusion criteria were American Urological Association-Symptom Score (AUA-SS) of eight or higher, maximum urinary flow rate (Qmax) of 10 ml/s or less, post-void residual urine (PVUR) volume of 50 ml or more, and a total prostate volume of 80 ml or more in transrectal ultrasound. The exclusion criteria included a previous prostate or urethral surgery and non-BPH-related voiding disorders. Preoperatively, the patients were screened for prostate cancer by prostate specific antigen (PSA) and excluded by prostate biopsy if indicated.

Follow-up for each group was assessed in first week, second week, first month, third month, sixth month, and 12th months postoperatively by AUA-SS, Qmax, and estimation of PVUR. Perioperative parameters for each group included operative time, enucleation specimen weight, serum hemoglobin concentration on day 1 postoperatively, need for a blood transfusion, length of hospital stay, and the duration of catheterization. Reporting on complications intraoperatively and postoperatively as the rate of hemoglobin concentration drop and presence of voiding or storage symptoms in both groups was done.

The process of recruitment and handling the study population during the study is shown in the flow diagram according to the CONSORT (CONsoildated Standards of Reporting Trials), 2010 guidelines (Fig. 1).

Figure 1



CONSORT 2010 flow diagram showing the recruitment and handling of the study population during the course of the study.

Surgical procedures

Holmium laser enucleation of the prostate

A Cyber HO 100 is a holmium laser device producing energy up to 105 W. manufactured by Quanta (Milan, Italy). The laser fibers used were end firing and 550 mm in diameter. These laser fibers were sterilized many times, and they were used in 5 up to 20 operations for each fiber. A continuous flow resectoscope (Karl Storz, Tuttlingen, Germany) was used with a laser bridge for good visualization and stabilization of the laser fiber.

During the operation, the median and the lateral prostatic lobes were dissected off the surgical capsule in a retrograde fashion from the apex toward the bladder. The laser fiber was enucleating the adenoma exactly like the surgeon's index finger while doing OP. Then, removal of the lobes was

done by the morcellator device (Richard Wolf Inc., Knittlingen, Germany) with reusable blades.

Overall, 0.9% of saline solution was used as irrigation fluid in HoLEP. All removed tissues were examined histologically. Postoperative bladder irrigation was done for one day till urine became clear and then the catheter was removed and the patient was discharged on the second day postoperatively.

Open prostatectomy

OP was performed by a suprapubic transvesical approach via a midline incision, as described by Hryntschack and published in 1951 [9]. The patients were discharged on the fifth day postoperatively, and the bladder catheter was removed on the tenth day postoperatively.

Statistical methods

Data were analyzed using SPSS version 24.0 (SPSS Inc., Chicago, Illinois, USA). Data were analyzed on an intention-to-treat basis. Parametric numerical data were presented as mean±SD, whereas nonparametric numerical data were presented as median with interquartile range. Categorical data were presented as numbers and percentages. A two-group comparison for numerical data was done using the Student *t*-test for parametric data and using the Mann–Whitney test for nonparametric data. Categorical data were compared using χ^2 test or Fisher exact test. Repeated measure data were analyzed using repeated measure two-way analysis of variance. The significance level was set at P less than or equal to 0.05.

The sample size was calculated using G*Power version 3.1.9.2, (Heinrich-Heine-Universitat, Dusseldorf, Germany), setting the power (β) at 0.02 and the significance level (α) at 0.05. Data from previous reports [10] indicated that the mean hemoglobin loss (g/dl) after HoLEP and OP was 1.9±1.3 and 2.8±1.6, respectively.

Calculations according to these values produced a minimal sample size of 85 patients to be randomized equally to both groups. Assuming a drop-out rate of 20%, a minimum drop-out inflated enrollment sample size of ~110 patients will be needed.

Table 1 Comparison between study groups regarding basic demographic and clinical characteristics

	HoLEP group	Open TVP group	*P*
Age (years)			
Range	55.0–76.0	55.0–83.0	0.63
Mean±SD	68.07±5.58	67.49±6.91	
Prostate specific antigen			
Total PSA (ng/ml)	5.42±1.42	5.76±1.18	0.17
Free PSA (mg/ml)	2.24±0.62	2.22±0.60	0.84
Ratio	0.42±0.08	0.39±0.09	0.06
Prostate volume (g)			
Range	82.0–158.0	82.0–166.0	0.32
Mean±SD	116.09±21.03	119.89±19.02	
Preoperative AUA-SS			
Range	15.0–26.0	17.0–30.0	0.07
Mean±SD	20.64±3.11	21.75±3.16	
Preoperative PVUR (ml)			
Range	150.0–977.0	120.0–998.0	0.85
Mean±SD	447.98±176.11	441.12±224.20	
Preoperative Qmax (ml/s)			
Range	0.0–9.0	0.0–10.0	0.67
Mean±SD	4.20±2.78	4.0±2.23	

AUA-SS, American Urological Association-Symptom Score; HoLEP, holmium laser enucleation prostatectomy; PSA, prostate specific antigen; PVUR, postvoiding residual urine; TVP, transvesical prostatectomy.

Results

No statistically significant differences were found between the two groups regarding the basal demographic and clinical characteristics including age, PSA levels, prostate volume by transrectal ultrasound, and preoperative AUA-SS, PVUR, and Qmax (Table 1).

Operative time was statistically significantly shorter in the HoLEP group compared with the OP group (102.45 vs 170.45 min, respectively). However, the weight of the resected specimen did not differ significantly between the two groups (Table 2).

Duration of catheterization and hospital stay were statistically significantly shorter in the HoLEP group compared with the OP group (Table 3).

Regarding the efficacy, repeated measure analysis of preoperative and follow-up data of AUA-SS, PVUR volume, and Qmax did not reveal statistically significant differences between the two groups. Moreover, despite the statistically significant improvement in AUA-SS, PVUR, and Qmax over time (owing to the marked improvement when comparing the preoperative values

Table 2 Comparison between study groups regarding operative time and weight of resected specimen

	HoLEP group	Open TVP group	*P*
Operative time (min)			
Mean±SD	102.45±14.27	170.45±11.41	<**0.001**
95%CI	98.52–106.39	167.37–173.54	
Resected specimen weight (g)			
Mean±SD	87.15±16.25	92.38±17.18	0.10
95%CI	82.67–91.63	87.74–97.03	

CI, confidence interval; HoLEP, holmium laser enucleation prostatectomy; TVP, transvesical prostatectomy.

Table 3 Comparison between study groups regarding catheterization duration and hospital stay

	HoLEP Group	Open TVP Group	*P*
Catheterization duration (days)			
Median (IQR)	1 (1–1)	10 (10–10)	<0.001
95%CI	1–1	10–10	
Hospital stay (days)			
Median (IQR)	2 (2–2)	6 (6–7)	<0.001
95%CI	2–2	6–7	

CI, confidence interval; HoLEP, holmium laser enucleation prostatectomy; IQR, interquartile range; TVP, transvesical prostatectomy.

Table 4 Comparison between the two groups regarding AUA-SS, PVUR, and Qmax preoperatively and during follow-up

Time	AUA-SS		PVUR (ml)		Qmax (ml/s)	
	HoLEP group (*n*=37)	Open TVP group (*n*=43)	HoLEP group (*n*=37)	Open TVP group (*n*=43)	HoLEP group (*n*=37)	Open TVP group (*n*=43)
Preoperative	20.68±3.09	22.50±3.61	453.94±186.17	462.91±210.63	3.84±2.89	3.79±2.22
Postoperative	3.10±1.62	3.08±1.81	26.78±6.41	25.25±6.60	29.21±7.84	26.91±8.96
2 weeks	2.94±1.84	2.54±1.47	26.57±6.39	25.58±8.74	26.47±4.04	26.37±6.49
1 month	2.78±1.71	2.37±1.24	27.15±7.58	28.66±6.37	29.42±9.54	24.50±7.41
3 months	3.57±2.31	3.04±1.45	23.0±4.87	24.50±5.34	22.26±8.85	25.04±6.72
6 months	2.78±1.96	2.41±1.01	28.78±6.91	27.70±8.30	26.78±6.49	27.95±7.56
12 months	3.47±1.98	2.79±1.21	19.52±8.09	21.29±7.83	27.94±7.05	29.91±6.03
P	Group effect: 0.71		Group effect: 0.87		Group effect: 0.84	
	Time effect: <0.001		Time effect: <0.001		Time effect: <0.001	
	Group×time interaction: 0.09		Group×time interaction: 0.88		Group×time interaction: 0.12	

AUA-SS, American Urological Association-Symptom Score; HoLEP, holmium laser enucleation prostatectomy; PVUR, postvoiding residual urine; TVP, transvesical prostatectomy.

with the postoperative ones), the magnitude and rate of this improvement were not statistically significantly influenced by the usage of either of surgical modalities (Table 4 and Fig. 2).

Regarding perioperative complications, drop-in hemoglobin concentration was statistically significantly higher in the OP group compared with the HoLEP group. However, it should be noted that this difference might lack clinical significance. Only two patients required blood transfusion in the HoLEP group, whereas five patients in the OP group required blood transfusion. However, this difference failed to reach statistical significance (Fig. 3).

Perforation of the prostatic capsule occurred in two cases in the HoLEP group with no statistically significant difference compared with the OP group. Urinary tract infection (UTI) was more frequent in the OP group compared with the HoLEP group. However, this difference failed to reach statistical significance.

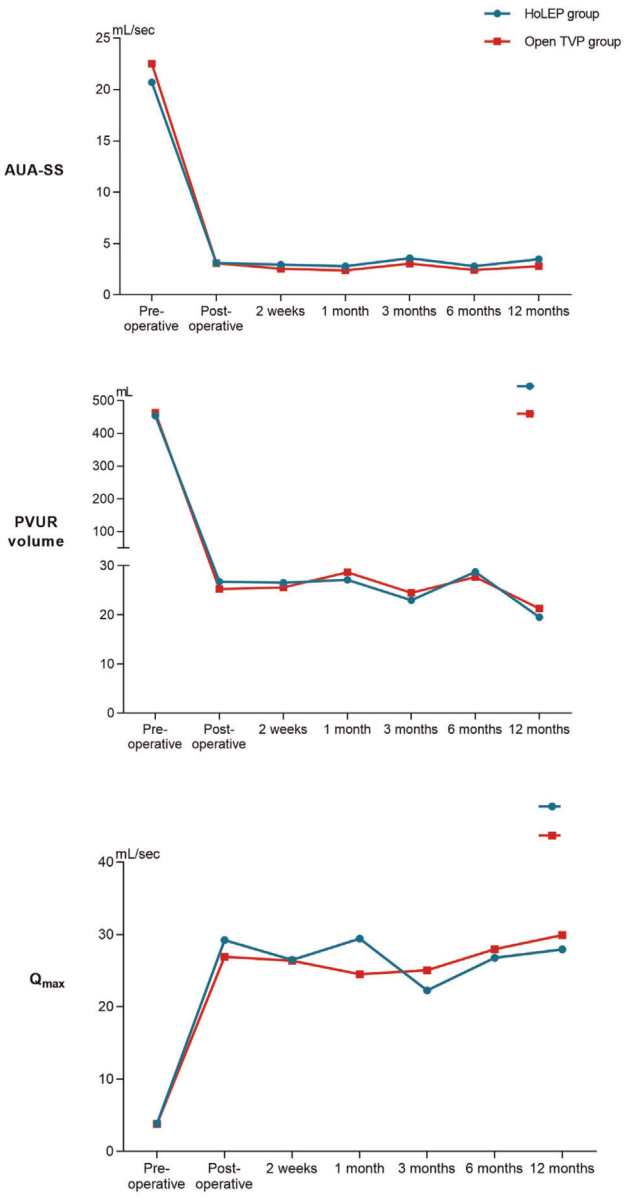
Regarding long-term complications, urethral stricture was more frequent in the HoLEP group compared with the OP group (4 in HoLEP group vs 0 in the OP group), yet with no statistically significant difference. The incidences of postoperative urinary retention, stress urinary incontinence (SUI), and bladder neck contracture (BNC) were comparable in the two groups (Table 5).

Discussion

In our study, the preoperative parameters in the compared groups such as patient's age, PSA, prostate volume, AUA-SS, PVUR, and Qmax did not show statistically significant difference and so did not have any confounding effect on the results in the two techniques.

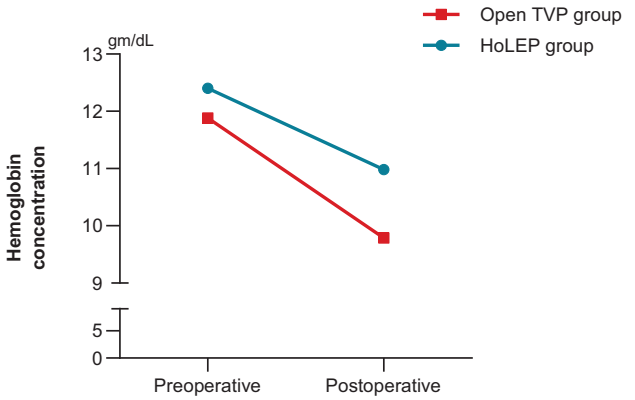
Comparing the hemoglobin drop in our study, we have found a statistically significant higher drop in hemoglobin concentration in the OP group compared with the HoLEP group. Moreover, the need for a blood transfusion in the OP group was 9.1% and only 3.8% in HOLEP group. These data were similar to multiple studies in which they reported that the rate of hemoglobin drop was statistically significantly higher in the OP group [10–13]; moreover, the need for a blood transfusion was statistically significantly higher in the OP group than in the HoLEP group [10–12]. Only two patients who needed blood transfusion in HoLEP arm underwent the operation with low hemoglobin concentration and so they needed blood

Figure 2



Line graph showing the AUA-SS (top), PVUR volume (middle), and Qmax (bottom) in the two groups along the different preoperative and postoperative time points.

Figure 3



Bar graph for change in perioperative hemoglobin concentration in the two groups.

transfusion postoperatively owing to the low amount of allowable blood loss.

Regarding operative time, Naspro *et al.* [11] revealed that the operative time in minutes in the OP group (58.31±11.95) was statistically significantly shorter compared with HoLEP group (72.09±21.22), and similar results were obtained from other researches [10,13]. These data were different from our results, and it might be owing to long morcellation time that took about a third of the total operative time [13]. However, in our study, all HoLEP cases were performed by a single expert senior staff who was well trained on laser techniques and we used a modern morcellator device with excellent performance.

Elshal *et al.* [12] revealed that the total operative time in HoLEP ranged from 50 to 185 min, and in OP, it was not mentioned, and these data were similar to our data. Moreover, the operative time in our study was significantly shorter in HoLEP than OP, and this may be owing to the more advanced morcellator device and more proper training on HoLEP than at the beginning of using this technique.

Hospital stay and catheter duration were statistically significantly shorter in HoLEP [10–13]. This was in agreement with our results.

Regarding the weight of the resected specimens in this study, it was statistically insignificant between the studied groups, and these data were in agreement with Kuntz *et al.* [10], where they reported that the resected weight in HoLEP and OP was 83.9±21.9 and 96.4±36.4 g, and it was also statistically insignificant. Moreover, Elshal *et al.* [12] reported that the mean resected prostate weight in HoLEP and OP was 99.2±34 and 103.7±25 g, respectively, and it was also statistically insignificant. On the contrary, Moody and Lingeman [13] revealed that the resected weight was statistically significantly higher in the open group. This might be owing to limited sample size, as they compared only among 10 patients in the two groups.

Regarding the safety, we have reported that the capsular perforation was 3.8% in HoLEP group and required longer catheterization time and passed almost unnoticed. This was in agreement with a similar study that revealed a rate of perforation of 2.1% in both groups, and it was statistically insignificant [12].

Regarding UTI, it was more frequent in OP than HoLEP, and these data were statistically

Table 5 Comparison between study groups regarding incidence of intraoperative and postoperative surgical complications

	HoLEP group [*n* (%)]	Open TVP group [*n* (%)]	*P*
Failed procedure and conversion to the other modality	2 (3.6)	0	0.49
Hemorrhage requiring blood transfusion	2 (3.8)	5 (9.1)	0.43
Perforation	2 (3.8)	0	0.24
Urinary retention	2 (3.6)	2 (3.6)	0.99
Urinary tract infection	2 (3.6)	6 (10.9)	0.27
Stress urinary incontinence			
Transient SUI	2 (3.6)	4 (7.3)	0.70
Persistent SUI	2 (3.6)	2 (3.6)	
Bladder neck contracture	2 (3.6)	2 (3.6)	0.99
Urethral stricture	4 (7.3)	0	0.12

HoLEP, holmium laser enucleation prostatectomy; SUI, stress urinary incontinence; TVP, transvesical prostatectomy.

insignificant and resolved with adequate medical treatment. This was different from what was reported by Naspro *et al.* [11], where dysuria was more frequent in HoLEP group (10.8%) than OP (8.5%); however, these results were statistically insignificant. Longer catheterization time in OP than HoLEP may be the reason, and also Naspro *et al.* [11] reported that patients were complaining of dysuria only not UTI, as we have reported in our study and was proved by urine analysis.

We reported that transient SUI was 7.3% in OP and 3.6% in HoLEP, and these data were statistically insignificant between the two groups. Similar results were obtained from Naspro *et al.* [11], where transient SUI was 2.4% in HoLEP and 2.5% in OP, and also from Moody and Lingeman, where they reported 4 cases of transient SUI in HoLEP and 1 permanent SUI in OP [13]. We think that this rate of SUI was mainly owing to continuous traction on the mucosal strip over the sphincter and late separation of it during the procedure, and this was the cause of this transient SUI in HoLEP patients, and now after early separation of the mucosal strip, our patients did not complain of SUI.

Kuntz and Lehrich and also Naspro and colleagues reported that the rate of urinary retention postoperatively that required catheterization was 12.1 and 5%, respectively, in HoLEP vs 5.1 and 5% in OP; this was similar to our study results [10,11].

Naspro *et al.* [11] reported that the rate of BNC/urethral stricture was 5.4% in HoLEP group and 5.7% in OP group after 1 year of follow-up, and this was statistically insignificant. Similar results were reported by Moody and Lingeman where they reported only two cases of BNC in OP group, and again, these results were statistically insignificant [13]. Moreover, Kuntz and Lehrich [10] reported that BNC/urethral stricture was 6.7% in OP group and 5% in HoLEP, and it was statistically insignificant. All these data were similar to our results.

Regarding the efficacy, we have found dramatic significant improvement postoperatively of the AUA-SS in both groups. These results were similar to Naspro and colleagues, Kuntz and Lehrich, and Kuntz and colleagues who all reported similar changes in this score along the first year postoperatively, and these results were insignificant on comparison between the two modalities [10,11,14].

Regarding Qmax preoperatively and postoperatively, the literature showed significant improvement in the postoperative values in both modalities, and the serial follow-up of Qmax after that did not show any significant change from the immediate postoperative results in both modalities or even in each modality over time, and this was in agreement with our study results [10,11,14].

In our study, one of the main postoperative functional outcomes is the estimation of PVUR, which did not reveal any statistically significant differences between the two groups. Moreover, despite the statistically significant improvement in PVUR (owing to the marked improvement when comparing the preoperative values with the postoperative ones), the magnitude and rate of this improvement were not statistically influenced by usage of either surgical modality. These results were similar to Naspro and colleagues and Kuntz and colleagues [10,14].

The limitations of this study were the limited sample size and the short time of the follow-up. Consequently, the absence of a statistically significant difference between the two groups regarding the complication rate does not imply the absence of difference in the incidence of

complications of one surgical modality compared with the other. This is attributed to the limited sample size, which was consequently underpowered to detect the difference in such relatively rare complications. In other words, the limited sample size confers a high probability of type II statistical error.

This study was the first in our institution and all surgeries whether OP or HoLEP were done by only two persons equally performing the two techniques to avoid surgeons bias and it revealed the ability to replace our gold standard OP with the newer technique (HoLEP) as long as it is effective as proved by our results in comparison with OP. These points are considered our points of strength.

Conclusion

Both modalities have similar efficacy with some more advantages in HoLEP than OP in hospital stay, duration of catheter, and bleeding control. Consequently, we could say that HoLEP is safer than OP. In the end, we have found the technique that can replace OP in Egypt because HoLEP proved its efficacy and safety compared with the common modality (OP).

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Conflicts of interest

There are no conflicts of interest.

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