


Comparison of outcomes of Holmium enucleation of the prostate for small- and moderate-sized prostates

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Abstract

There is an ongoing discussion in the literature on the surgical treatment option for small prostate size benign prostate hyperplasia (BPH) patients. This study aimed to evaluate the efficacy of Holmium laser enucleation of the prostate (HoLEP) surgery in small (<30 ml) and moderate (30–80 ml) prostate size as accepted in European Association of Urology guideline. We retrospectively analysed our database between May 2016 and May 2019 and patients who underwent HoLEP surgery. Patients who have prostate size <80 ml were included the study. These patients were divided into two group: group 1 with prostate size <30 ml ($n = 64$) and group 2 with prostate size 30–80 ml ($n = 101$). Enucleation time (ET), morcellation time (MT), total operation time (OT), enucleation efficiency (EE), morcellation efficiency (ME), intra- and post-operative complications were analysed. While EE and Hb drop were better in favour of group 2; PSA drop, ET, MT, OT and ME were superior in favour of group 1. In group 1, intra-operative complications were higher (6 vs. 2; $p < .05$) and post-operative complications did not differ statistically between groups ($p = .14$). No statistically significant finding was found between groups regarding incontinence. In conclusion, HoLEP is a reliable method in terms of its results in patients with small prostates.

KEYWORDS

HoLEP, holmium, moderate, prostate, small

1 | INTRODUCTION

There is an ongoing discussion in the literature on the surgical treatment option for small prostate size benign prostate hyperplasia (BPH) patients. A small prostate is defined as <30 ml in the guidelines, and the surgical algorithms are designed based on this value (Foster et al., 2018; Gratzke et al., 2015). However, limited number of papers in the literature have evaluated and compared surgical efficacy with a small prostate definition of ≤ 40 ml (Elshal et al., 2014; Gupta et al., 2006; Haraguchi et al., 2009; Kim et al., 2016, 2019; Kuntz et al., 2004; Lee et al., 2014; Tan et al., 2003; Wilson et al., 2006). The size of the prostate is one of the most important determinants of the surgical technique to be selected. Both European Urology

Association (EAU) and American Urology Association (AUA) guidelines on lower urinary tract symptoms (LUTS) attributed to BPH classify surgical treatment options into three main categories according to size of prostate: small (<30 ml), moderate (30–80 ml) and large (>80 ml) and offer several minimal invasive surgical treatment options for small prostates (Foster et al., 2018; Gratzke et al., 2015).

The holmium laser enucleation of the prostate (HoLEP) treatment has come a long way since its introduction and has taken its place in prostate surgical treatment as the 'size-independent' procedure in AUA guideline (Das et al., 2019). Although HoLEP is addressed as a surgical treatment option of small prostate flow chart in AUA guidelines, it is still stayed behind transurethral incision of the prostate and transurethral resection of the prostate (TURP) for small

prostate treatment options in EAU guidelines (Foster et al., 2018; Gratzke et al., 2015). The effect of prostate size on the outcome of HoLEP surgery has been studied in the literature; most of the published papers compared the large prostates above 80 or 100 ml (Gazel et al., 2019; Glybochko et al., 2017; Hettiarachchi et al., 2002; Jones et al., 2016; Kuntz et al., 2008; Zhang et al., 2020) and some compared small prostates below 40 or 30 ml (Kim et al., 2016, 2019; Park et al., 2017).

There are a number of studies that compare the efficacy of HoLEP in small- and moderate-size prostates, however, all defined the threshold as 40 ml (Kuntz et al., 2004; Lee et al., 2014). This study aimed to evaluate the efficacy of HoLEP surgery in small (<30 ml) and moderate (30–80 ml) prostate size as accepted in EAU guideline.

2 | MATERIALS AND METHODS

2.1 | Patient selection

After institutional ethical committee approval (ID: 2020-149), we retrospectively analysed our database between May 2016 and May 2019 and patients who underwent HoLEP surgery were determined. Patients who have prostate size <80 ml were included the study. All patients were performed by a single surgeon (LT) who has his own technique and experience of more than 1,000 cases. These patients were divided into two groups: group 1 with prostate size <30 ml (n: 64) and group 2 with prostate size 30–80 ml (n: 101). The study included patients who met inclusion criteria as follows: prostate size <80 ml, a maximum urinary flow rate (Q_{\max}) ≤ 15 ml/s, International Prostate Symptom Score (IPSS) ≥ 12 , post-voiding residue (PVR) >100 ml, patients with no benefit of medical therapy (alpha-blocker and/or 5-alpha reductase inhibitor), recurrent or refractory urinary retention, and bladder stones. Exclusion criteria were included as previous urethral/prostate surgery, urethral stricture, prostate cancer, neurogenic bladder and patients whose prostate size determined with transrectal ultrasonography.

2.2 | Demographic data

Demographic data including age, body mass index, prostate-specific antigen (PSA) level, haemoglobin (Hb) level, prostate volume (PV), IPSS, quality of life (QoL) score, Q_{\max} and PVR were included the study database. The preop IPSS score with indwelling catheters were excluded.

2.3 | Surgical procedure and equipment

Under regional or general anaesthesia, Omega Sign HoLEP technique that previously described by our team was performed in all procedures (Tunc et al., 2020). Two-pedal 120 W Holmium: YAG Laser (VersaPulse; Lumenis Ltd.) with 550- μ m end-firing fibre (SlimLine

TM 550, Lumenis Inc.) was used as energy source. 26-F continuous-flow resectoscope with a laser bridge (Karl Storz Endoscopy) was used. Enucleated prostate tissues were removed by a morcellator (VersaCut, Lumenis) introduced through a nephroscope (Karl Storz Endoscopy). At the end of the procedure, a three-way 22-F urethral catheter was placed.

2.4 | Peri-operative and post-operative data

All data routinely included the patient database by our team were checked, and enucleation time (ET), morcellation time (MT), total operation time (TOT), enucleation efficiency (amount of enucleated tissue per minute) (EE), morcellation efficiency (amount of morcellated tissue per minute; ME) and percentage of enucleated weight (percentage of enucleated tissue volume to total PV; PEW) parameters and intra-operative complications of all patients were included the study database.

The urethral catheter was removed once the urine is clear, and the catheter time (CT) and hospitalisation time (HT) were recorded. Patients were asked for follow-up at the first, third and sixth post-operative months, and uroflowmetry, PVR and IPSS forms were collected. Continence status were noted according to recommendations by the International Continence Society (ICS) (Abrams et al., 2002). Incontinence status was evaluated on the basis of medical interview with the patients. All patients were asked about any leak because of exertion, effort, sneezing or coughing. Any urine leak was considered positive for stress urinary incontinence (SUI). The condition of no SUI was evaluated by defining complete urinary control. UUI was defined as involuntary leakage accompanied by or immediately preceded by urgency. Continence was defined as complete dryness.

2.5 | Statistical analysis

The Statistical Package for Social Sciences 23.0 software (SPSS 23.0) was used. The Kolmogorov–Smirnov, Kurtosis and Skewness tests were used to assess the normality of the data. Descriptive statistics of scale samples were expressed as mean \pm standard deviation. The clinical characteristics of the two groups were compared with the Mann–Whitney *U* or Student's *t* test for continuous variables. The Wilcoxon or paired *t* test was used to assess the changes in continuous measures between before and after surgery. Haemoglobin, the IPSS, QoL, Q_{\max} and PVR were compared pre- and post-operatively in each patient group. All statistical tests were two-sided, with $p < .05$ considered as statistically significant.

3 | RESULTS

Patients' characteristics and preoperative data are given in Table 1. In group 1 and group 2, the mean age was 61.5 ± 4.8 years,

TABLE 1 Patients' characteristics and preoperative data

Parameters	Group 1 (N: 64)	Group 2 (N: 101)	p-value ^a
Median age (year)	61.5 ± 4.8	62 ± 4.94	.13
BMI (kg/m ²)	24.6 ± 3.15	24.5 ± 2.61	.75
Median PSA (ng/ml)	2.9 ± 2.33	2.6 ± 2.28	.08
Median Hb (ng/ml)	14.7 ± 1.07	14.57 ± 1.12	.26
Median prostate volume (ml)	26 ± 1.81	61 ± 10.88	.001
IPSS-S preop	10 ± 1.58	7 ± 1.09	.36
IPSS-V preop	13 ± 3.35	14 ± 3.56	.19
IPSS total	24 ± 3.95	25 ± 3.89	.64
Mean IPSS quality of life	5 ± 1.01	5 ± 1.02	.4
Mean Q _{max} (ml/s)	7.7 ± 2.13	8 ± 2.32	.04
PVR (ml)	145 ± 71.74	126 ± 65.92	.09

Abbreviations: BMI, Median body mass index; Hb, haemoglobin; IPSS, International Prostate Symptom Score; IPSS-S, International Prostate Symptom Score-Storage; IPSS-V, International Prostate Symptom Score-Voiding; PSA, prostate-specific antigen; PVR, Post-void residual urine volume; Q_{max}, maximal urinary flow rate; TRUS, transrectal ultrasonography.

^aStatistically analysed with Mann-Whitney *U* test.

TABLE 2 Peri-operative data

	Group 1 (N: 64)	Group 2 (N: 101)	p-value ^b
EE (g/min)	1.1 ± 0.21	1.3 ± 0.26	.001
Mean Postop Hb (g/dL)	14.17 ± 1.09	14.1 ± 1.15	.55
Hb drop (g/dl)	0.5 ± 0.25	0.45 ± 0.3	.01
ET (min)	20 ± 2.34	40.95 ± 8.79	.001
MT (min)	5 ± 0.91	9 ± 4.11	.001
OT (min)	24 ± 2.79	52 ± 9.76	.001
ME (g/min)	7 ± 3.15	4 ± 0.81	.001
RW (g)	19 ± 2.31	40 ± 13.37	.001
PEW (%)	70.5 ± 7.08	69.7 ± 21.18	.08
CT (hr)	18 ± 3.51	21 ± 4.2	.001
HT (hr)	22 ± 3.43	23 ± 3.63	.001

Abbreviations: CT, catheterisation time; EE, enucleation efficiency; ET, enucleation time; Hb, haemoglobin; HT, hospitalisation time; ME, morcellation efficiency; MT, morcellation time; OT, operation time; PRW, percentage of enucleated weight; RW, resected weight.

^bStatistically analysed with Mann-Whitney *U* test.

Values in bold statistically significantly different

62 ± 4.94 years respectively. Both groups showed no statistical difference in patients' characteristics and preoperative data except median PV and mean Q_{max}. However, median PV for the groups were 26 ± 1.81 ml and 61 ± 10.88 ml (*p* = .001) respectively. Table 2 shows peri-operative data of the study. While EE and Hb drop was in favour of group 2; PSA drop, ET, MT, OT and ME were in favour

of group 1. PEW did not show statistically significant difference between groups (70.5 ± 7.08 vs. 69.7 ± 21.18; *p* = .08). CT and HT were shorter in group 1 (*p* = .001). Table 3 shows the first, third and sixth months' functional results comparison in groups. First and third month results comparison showed statistically significant difference in QoL values (*p* = .02 and *p* = .01 respectively). In other parameters, no statistically significant difference was detected between groups. Intra-operative and post-operative complications are listed in Table 4. While total number of intra-operative complications of group 1 showed more complication rate (6 vs. 2; *p* < .05), post-operative complications did not differ statistically between groups (13 vs. 12; *p* = .14). Re-catheterisation rate was higher in group 1 (6 vs. 2; *p* < .05) while all other complication parameters both intra-operative and post-operative in the Table 4 showed no statistically significant difference between groups. No bladder neck contracture or urethral stricture was detected in the study groups. No Clavien grade 4 complication was recorded. No patient needed conversion to open or other endoscopic surgery. No patient needed reoperation because of bladder outlet obstruction, but only one of the patients in group 2 needed meatotomy under regional anaesthesia. Continence status of the patients according to ICS including UUI, SUI and PMS are given in Table 5. No statistically significant finding was found between the groups.

4 | DISCUSSION

Holmium laser enucleation of the prostate surgery, which is accepted as feasible and safe 'size-independent' surgical treatment of BPH in both AUA and EAU guidelines, has gained the popularity it deserves, and publications on this subject are rapidly increasing (Das et al., 2019; Foster et al., 2018; Gratzke et al., 2015). There are several studies in the literature, assessing the efficacy of BPH and holmium laser treatment surgeries according to prostate size; however, these studies compare large prostates to small- and medium-sized prostates together, or small prostates to medium and large prostates together, or small and moderate prostates together to large prostates (Gazel et al., 2019; Glybochko et al., 2017; Park et al., 2017).

Studies comparing small prostates specifically with medium-sized prostates are rare in the literature (Kuntz et al., 2004; Lee et al., 2014; Park et al., 2017). In the study by Park et al. comparing the results of patients who underwent HoLEP with prostate sizes of ≤30 ml and >30 ml, it is reported that there were no significant differences between the groups in the levels of haemoglobin, IPSS, QoL, Q_{max} and PVR between before surgery and 3 months after surgery. Considering functional outcomes, it is shown that the improvement in IPSS voiding subscore after HoLEP was significant, but storage subscore was not (Park et al., 2017). In our study, although there was no significant difference in haemoglobin levels between groups, haemoglobin drop was significantly higher in the group with ≤30 ml size of prostate. Our results showed that there was statistically significant difference in QoL values between

TABLE 3 Functional results comparison of groups in 1st, 3rd and 6th months

	IPSS-S	IPSS-V	IPSS Total	QoL	Q _{max} (ml/s)	PVR
Preoperative						
Group 1	11 ± 1.69	14 ± 3.66	26 ± 3.65	5 ± 1.01	7.7 ± 2.13	145 ± 71.74
Group 2	7 ± 2.05	16 ± 3.25	27 ± 3.77	5 ± 1.02	8 ± 2.32	126 ± 65.92
<i>p</i> -value	.23	.08	.24	.4	.04	.09
1st month						
Group 1	6 ± 1.69 ⁺	4 ± 1.43 ⁺	10 ± 2.44 ⁺	3 ± 1.29 ⁺	25.4 ± 4.87 ⁺	25 ± 15.89 ⁺
Group 2	6 ± 1.64 ⁺	4 ± 1.24 ⁺	10 ± 2.37 ⁺	3 ± 1.31 ⁺	24.6 ± 5.75 ⁺	25 ± 15.06 ⁺
<i>p</i> -value	.23	.054	.06	.02	.8	.77
3rd month						
Group 1	6 ± 1.85 ⁺	3 ± 0.85 ⁺	9 ± 2.17 ⁺	3 ± 1.2 ⁺	26.1 ± 4.73 ⁺	24 ± 15.88 ⁺
Group 2	6 ± 1.91 ⁺	3 ± 0.82 ⁺	9 ± 2.33 ⁺	3 ± 1.16 ⁺	25.5 ± 5.52 ⁺	24 ± 14.74 ⁺
<i>p</i> -value	.22	.3	.17	.01	.76	.73
6th month						
Group 1	4 ± 1.69 ⁺	2 ± 0.55 ⁺	6 ± 1.77 ⁺	2 ± 1.03 ⁺	26.7 ± 4.91 ⁺	21.5 ± 16.2 ⁺
Group 2	4 ± 1.59 ⁺	2 ± 0.63 ⁺	6 ± 1.73 ⁺	2 ± 1.15 ⁺	26.8 ± 5.58 ⁺	21 ± 14.6 ⁺
<i>p</i> -value	.99	.13	.63	.31	.35	.61

Abbreviations: IPSS, International Prostate Symptom Score; IPSS-S, International Prostate Symptom Score-Storage; IPSS-V, International Prostate Symptom Score-Voiding; PVR, Post-void residual urine volume; Q_{max}, maximal urinary flow rate; QoL, Quality of Life

Values in bold statistically significantly different, + *p* < 0.001 compared to baseline.

groups in the first and third month post-operatively, and no statistically significant difference was detected between groups with respect to the other parameters in the first and third month post-operatively. In contrast to the study Park et al, in our study, in patients with prostate size ≤30 ml, IPSS voiding subscore significantly decreased (14 ± 3.66 vs. 2 ± 0.55, *p* < .05) and also the IPSS storage subscore was significantly improved (11 ± 1.69 vs. 4 ± 1.69, *p* < .05) in the sixth month post-operatively. Additionally, there was no significant difference between the two groups in terms of IPSS-S, IPSS-V, IPSS-T, Q_{max} and PVR at the post-operative first, third and sixth months.

Kuntz et al. (2004) compared peri-operative outcomes of small (<40 ml), moderate (40–79 ml) and large (>80 ml) prostate groups underwent HoLEP. The authors emphasised that the improvement in voiding parameters of all sizes of prostate groups was similar, and there were no statistically significant differences. Furthermore, CT and HT did not differ and depend on prostate size between small and moderate prostates (Kuntz et al., 2004). However, in our study, CT and HT were shorter in smaller prostate group. In a study by Lee et al, HoLEP results was compared with TURP in small (<40 ml), moderate (40–79 ml) and large (>80 ml) prostate groups but did not provide the comparative results of HoLEP between groups. In this study, it is reported that there was no significant difference between TURP and HoLEP groups in terms of IPSS improvement in all prostate sizes. It is also observed that OT affected by prostate size in HoLEP group (Lee et al., 2014). In another study, ET was significantly shorter in small prostate groups (≤30 ml) (Park et al., 2017). In accordance with the literature, our results showed shorter ET and OT in small prostate groups.

Enucleation efficiency ranges between 0.34 and 1.48 g/min for different size of PV (Becker et al., 2018). EE can be found to be lower in small prostates. This may be due to the fact that the surgical capsule is distinct, and the planes between the adenoma and the capsule are more difficult to identify in small prostates during enucleation (Rapisarda et al., 2019). In our study, EE for moderate prostate patients was significantly higher (1.1 ± 0.21 vs. 1.3 ± 0.26, *p* < .05). Contrary to the study, which reported that the enucleation efficiency did not change in patients with HoLEP and prostate size of ≤80 ml (Gazel et al., 2019), our study demonstrated that the increase in size increased EE comparing the small and moderate PVs to support the study by Ibrahim et al. (Ibrahim et al., 2019).

Despite the advantages of HoLEP, post-operative SUI continues to be a major problem both for surgeons as an annoying complication and for patients by affecting the QoL (Cho et al., 2011; Oh, 2019). The results of the studies on this subject are controversial in the literature. Cho et al concluded that patients with transition zone volume <30 ml may complain from persistent SUI following HoLEP. The authors interpreted that a surgical option other than HoLEP may be better in patients with prostate <30 ml (Cho et al., 2018). Elmansy et al reported that patients whose PV was >81 g was significantly associated with post-operative SUI development after HoLEP (Elmansy et al., 2011). Our study showed post-operative lower incontinence rates, and incontinence rates were not different in moderate and small prostates even in first post-operative month (%3.1 vs. %2; *p* = .64). No SUI and also UUI were recorded in the post-operative third and sixth months.

Complication rates were found to be higher in patients with small prostate (<30 ml) on treating them with HoLEP surgery, which was

TABLE 4 Intra-operative and post-operative complications

	Group 1 n (%)	Group 2 n (%)	p	Evaluation
Intra-operative complications				
Haematuria	1 (1.6)	0 (0)	.38	Transfusion (G2)
Capsular perforation	2 (3.1)	1 (1)	.56	Longer catheterisation, 3 days (G1)
Superficial bladder mucosal injury	3 (4.7)	1 (1)	.3	Longer catheterisation, 3 days (G1)
Device malfunction	0 (0)	0 (0)	NA	—
Total	6 (9)	2 (2)	.03	
Post-operative complications				
Deviations from the normal post-operative course (post-operative emesis, electrolyte imbalance, pain ect...)ª	3 (4.7)	4 (4)	.82	Treated with antiemetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy (G1)
UTI	2 (3.1)	3 (3)	1	Intravenous antibiotic (G2)
Clot evacuation using urethral catheter	0 (0)	1 (1)	1	Irrigation (G3a)
Clot evacuation with cystoscopy	0 (0)	0 (0)	NA	—
Re-catheterisation	6 (9)	2 (2)	.03	3 days with anti-inflammatory drug (G3a)
Bladder neck contracture	0 (0)	0 (0)	NA	—
Urethral stricture	0 (0)	0 (0)	NA	—
Meatal stenosis	0 (0)	1 (1)	1	Meatoplasty (G3b)
Transient haematuria	2 (3.1)	1 (1)	.56	Transfusion (G2)
Totalª	13 (20)	12 (12)	.14	

ªStatistically analysed with Pearson chi-square test; others analysed with Fisher's Exact test. (bold numbers are $p < .05$ value that considered statistically significant).

attributed to poorly capsule development in small glands (Ibrahim et al., 2019). In the comparison study for sizes below 30 ml and above, although the complication rate was not significantly different between the groups, the patients in small prostate group were more likely to have higher-grade complications requiring further procedures (\geq grade 3) (Park et al., 2017). In another study, no significant difference was observed relating to complications between groups of all prostate sizes (Kuntz et al., 2004). We observed more intra-operative complications in prostates with a volume of <30 ml. However, in accordance with the literature, in terms of intra-operative and post-operative complications, there was no statistically significant difference between groups in the present study.

Bladder neck contracture (BNC) is emerging as one of the most common complications leading to retreatment after surgical management of benign prostatic obstruction (BPO) due to BPH, especially in patients with smaller prostates (Reich et al., 2008). A positive correlation was shown between prostate size and post-operative BNC and routine bladder neck incision in patients with prostate size <40 ml (Krambeck et al., 2010). In a study that compared the resection and enucleation of small (<30 ml) prostate

TABLE 5 Post-operative continence status of the patients

	Group 1 (<30) n = 64 (%)	Group 2 (30–80) n = 101 (%)	p-value
UUI 1. month	2 (3.1)	3 (3)	1
UUI 3. month	0	0	NA
UUI 6. month	0	0	NA
SUI 1. month	2 (3.1)	2 (2)	.64
SUI 3. month	0	0	NA
SUI 6. month	0	0	NA
PMS 1. monthª	4 (6.3)	5 (5)	.72
PMS 3. month	1 (1.6)	1 (1)	1
PMS 6. month	0	0	NA

Abbreviation: UUI, Urge Urinary Incontinence; SUI, Stress Urinary Incontinence; PMS, Post-micturition symptoms.

ªAnalysed with Pearson chi-square test; others analysed with Fisher's exact test.

with thulium energy system, it was concluded that both of the methods were safe and efficient procedures for small prostates, and also thulium laser enucleation of the prostate (ThuLEP) could

significantly reduce the BNC risk (Sun et al., 2019). BNC was detected in 10% of patients with a prostate size of 30 ml who underwent HoLEP, whereas BNC was not developed in any patient with a prostate size >30 ml (Park et al., 2017). On the other hand, another study showed no BNC at 1-month follow-up. In our study, no BNC was observed during 6 months of follow-up. The low complication rate in our study can be explained by the HoLEP experience of a single surgeon (LT) in >700 cases and the surgical technique performed (Yalçın et al., 2020).

One of the most important limitations of HoLEP surgery is that the learning curve is upright, and it should also be kept in mind that the procedure requires skill, and the risk of capsule perforation is more frequent especially in patients with small prostates (Kim et al., 2015; Nam et al., 2015). The most important reason for this may be that it is difficult to determine the apical plane for enucleation in small prostates (Haraguchi et al., 2009). Adequate HoLEP experience is necessary to decrease the complication rates especially in patients with smaller prostate. All operations in our study were performed after the surgeon had completed the learning curve.

4.1 | Study limitations

This study has several limitations. First, number of patients is small, follow-up period is relatively short, and the study is retrospective nature. This study included patients with only ≤80-ml PVs. The strength of our study is that we could prove the safety and efficacy of the HoLEP surgery for treating patients with small and moderate PVs, although the guideline of European Association of Urology about this surgery procedure recommend only for patients with >30-ml PVs in the flowcharts. Finally, in our study for the purpose of evaluate the efficacy and safety of enucleation we did not try to determine the sexual complications and it may be a limitation of this study.

5 | CONCLUSION

It is clear that HoLEP is a safe and effective method for patients with LUTS because of BPO. HoLEP is a reliable method in terms of its results in patients with small prostates as well as in large prostates.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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