Holmium laser enucleation of prostate (HoLEP) in nonagenarians and octogenarians: Impact of age and frailty on surgical outcomes

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ABSTRACT

Introduction: Holmium laser enucleation of the prostate (HoLEP) is a well-established technique for management of benign prostatic hyperplasia (BPH). With the growing aging population, a considerable percentage of octogenarians (80–90 years old) and nonagenarians (>90 years old) require surgical management for BPH. We aimed to assess the outcomes of HoLEP in those age groups.
Methods: We reviewed a maintained database for HoLEP patients in a tertiary center. Patients were assigned to two groups: above (group A) and below (group B) 80 years old. Perioperative outcome and postoperative followup data were compared between both groups.
Results: The study included 1090 patients, 201 and 889 in groups A and B, respectively. Median age was 83 and 70 years in groups A and B, respectively. Group A showed longer operative time, longer catheterization time, and higher 30-day emergency room visits and readmission rates. Hemoglobin drop was comparable, although associated with higher rate of blood

KEY MESSAGES

- We report perioperative and postoperative outcomes of HoLEP in octogenarian and nonagenarian patients.
- Our results showed that octogenarian and nonagenarian had longer operation time, higher need for blood transfusion, longer postoperative catheterization time, and higher readmission rates.
- Complications within 30 days of the surgery were higher in octogenarians and nonagenarians, although most complications were mild.
- Followup functional outcome data and long-term complication rates were comparable to younger patients.

transfusion in group A. Overall, 30-day postoperative complications were higher in group A (20.8% vs, 9.3%, p= 0.008), although the majority of complications in both groups were grade I and II. The rate of complications over Clavien-Dindo grade II were statistically comparable (3.4% vs. 1.79%, p= 0.133). Followup at six weeks, three months, and one year showed comparable functional outcomes in both groups.
Conclusions: HoLEP is a safe and effective option in the geriatric population of octogenarians and even nonagenarians. HoLEP is associated with higher overall complication rate in older age groups; however, most complications were minor.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a prevalent condition in aging men and represents a substantial disease burden. The prevalence of BPH proportionately increases with more progressive aging in general population with negative impact on quality of life through the lower urinary tract symptoms (LUTS). Approximately 80% of men over 70 years of age experiences LUTS. The prevalence of LUTS rises to as high as 88% to 90% by 81 years of age. Urinary symptoms of urgency, nocturia, weak stream, intermittency, and incomplete emptying strongly correlates with age. (1-3)

Transurethral resection of the prostate (TURP) using the electrocautery loop has been used as the traditional the gold standard procedure for endoscopic management of BPH. Unfortunately, TURP is associated with significant risk of blood loss and dilutional hyponatremia, especially with prolonged resection using monopolar current. (4,5)

Holmium laser enucleation of the prostate (HoLEP) has become increasingly popular as a surgical alternative for management of BPH of different sizes. HoLEP rivals the success of the traditional TURP due to minimal blood loss, minimal post-operative complications, short lengths of stay, and low reoperation rate. (6,7) HoLEP has been associated with marked improvement in patient's quality of life and high postoperative patient satisfaction rates. (8)

Geriatric patients, mainly nonagenarians (age 90-99) and octogenarian (age 80-89), are often overlooked as surgical candidates for minimally invasive prostate surgery, and few studies have evaluated the outcomes of HoLEP in this population with variable results. (9,10) In the current study, we aimed to evaluate the practicality and morbidity of HoLEP in octogenarian and nonagenarian patients through reporting the perioperative and postoperative outcomes of HoLEP in this age group and compare their outcomes to younger cohorts.

METHODS

This is a retrospective study reviewing data for patients who underwent HoLEP between May 2015 and December 2020 at a single teaching institution. The surgeries were performed by a single surgeon (MET) with 9-year experience with HoLEP. Patients were assigned into two

groups according to their age, above or below 80 years of age. Patients with incomplete follow-up data up to 1 year were excluded.

The data regarding patients' demographics, baseline preoperative characteristics, operative details, perioperative complications, postoperative outcomes at 6 weeks, 3 months, and 1 year follow up, and the long-term follow up complication were collected and compared between both groups (above and below 80 years old).

Frailty evaluation was performed preoperatively through the Modified Hopkins frailty score adopted at our institution. (11,12) The score is calculated based on handgrip strength, assessment of unanticipated weight loss of 10 pounds or greater within the last year (shrinking), hemoglobin in last 30 days and American Society of Anesthesiologists (ASA) physical status classification, A score of 0 is considered low risk/non-frail, 1-2 is considered intermediate risk, and 3-5 is considered high risk/frail. Baseline and follow-up assessment of LUTS and bothersome scores was performed using the International Prostate Symptoms Score (IPSS) and quality of life (QoL) questionnaires. Urine incontinence was assessed using International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF). These parameters were assessed at different follow-up visits at 6 weeks, 3 months, and 12 months.

HoLEP protocol

Prostate volume was estimated in most of the patients before surgery through transabdominal or transrectal ultrasound or multiparametric MRI for elevated PSA. Whenever possible, anticoagulants and antiplatelets, other than aspirin, are held 3-7 days before HoLEP. HoLEP was performed with holmium laser power setting of 2J and frequency of 40 or 20 Hz. Lumenis MOSES^{TM} technology was adopted since January 2019. Throughout the study period, a voiding trial was usually performed on postoperative day 1. Patients who failed the voiding trial were discharged with an indwelling catheter and had a repeat voiding trial after 3 days in the outpatient clinic. Earlier, patients were mostly discharged on a postoperative day 1 while in the last 2 years of the study period, same-day discharge was embraced in suitable patients especially after the adoption of MOSES^{TM} technology.

Statistical analysis

Data was analyzed using the commercially available SAS (Statistical Analysis Software) Version 9.4 (SAS Institute Inc., Cary, NC, USA). Sample characteristics are described using descriptive statistics. Frequencies and percentages are used to describe categorical variables. Means and standard deviations (or medians and interquartile ranges where appropriate) are used to describe continuous variables. A chi-square test (or Fisher's exact test when low cell counts are present) is used to test for associations in bivariate comparisons. A two-sample t-test (or Wilcoxon rank-sum test when appropriate) is used to test for differences in continuous variables between 2 groups. Statistical significance is set at 0.05.

RESULTS

Among 1202 underwent HoLEP during the study period, 112 patients (25 and 87 patients > and < 80 years respectively) were excluded for incomplete follow up data. The study included 1090 patients. There were 201 patients above 80 years old (Group A) with median age of 83 years; 10 and 191 nonagenarians and octogenarians respectively. While (Group B) included 889 patients below 80 years old with median age of 70 years.

The patients in Group A had significantly higher frailty score, higher American Society of Anesthesiology (ASA) score, lower grip strength, lower body mass index (BMI), lower baseline hemoglobin level, higher incidence of cardiovascular disease (CVD) and chronic anticoagulant use. [Table 1] Sixteen (7.9%) and twenty-eight (3.15%) patients in group A and B respectively continued antiplatelets/anticoagulants during HoLEP (P=0.0017).

Regarding the perioperative outcome, Group A was associated with longer operative time, longer catheterization time, higher rates of failed hospital voiding trial, 30-days emergency room (ER) visits. The mean hospital stay in both group A and group B were less than 1.5 days with statistically longer hospital stay in group A. Hemoglobin (Hb) drop [preoperative Hb - lowest Hb in 30 postoperative days] was comparable in both groups although the need for blood transfusion was higher at group A (6.9% vs 1.2%) which may be related to lower preoperative hemoglobin in group A since absolute decrease in hemoglobin was similar. Readmission rate was 11.4% vs 3.1% in group A and B respectively (p<0.001). [Table 2]

The Clavien-Dindo score for complications within the 30 days showed overall higher rate of complications encountered in Group A (20.8% vs 9.3%, p= 0.008) although the majority of the complications in both groups were grade I and II. The complication rate over Clavien-Dindo grade II were statistically comparable in both groups (3.4% vs 1.79%, p= 0.133). [Table 3] Clavien-Dindo class I included mainly postoperative irritative symptoms, hematuria or urine retention requiring reinserting urethral catheter. Class II complications were mainly urinary tract infection or blood transfusion while Class III included patients who required endoscopic intervention under spinal (III a) or general (III b) anesthesia mainly for growth hematuria. Class IV complications were seen in total 5 patients with single or multi-organ failure due to sepsis. To eliminate the effect of variation of antiplatelets/anticoagulants utilization rate during HoLEP, specific analysis of postoperative complications has been performed after excluding the patients who utilized antiplatelets/anticoagulants at the time of HoLEP. The complication rate [32 (15.9%) vs 68 (7.6%), p=0.001] and readmission rate [17 (8.45%) vs 18 (2.02%), p= 0.001] were still significantly higher in group A than group B respectively.

The postoperative outcome data at the 3 appointed follow up periods (6-week, 3-month, and 1-year) were statistically comparable in both groups regarding IPSS (p=0.37, 0.69, 0.13) QOL (0.47, 0.46, 0.12) PVR, incontinence (stress and/or urge) rates (p= 0.65, 0.77, 0.69), serum PSA (0.07, 0.22, 0.47). Only median PVR was statistically higher in group A at 6-week follow up (P= 0.016) while it was comparable at 3-month and 1-year encounters (p= 0.68, 0.28 respectively). [Figure 1] With median follow up of 19 and 17 months in group A and B

respectively, the long-term follow up (beyond 1-year) data showed comparable rates of urethral stricture, bladder neck contracture complications, and long-term incontinence. [Table 3] Within the nonagenarian patients, six patients had HoLEP with anticoagulation or antiplatelets. Only one patient had grade I Clavien-Dindo complications in the form of hematuria. Seven patients had successful voiding trial at POD-1. On follow up, median IPSS was 7 (4-11), 8 (6-16) and 6 (2-11) while urine incontinence was seen in 7, 4 and 2 patients at 6-week, 3-month and 1-year follow up occasions respectively.

DISCUSSION

BPH is one of the most common diseases plaguing the aging male population, and the increasing average life expectancy and aging population is projected to continuously increase the burden in the coming years. (13) This prevalent disease impacts quality of life, particularly in elderly patients who are more susceptible to falls and infection. (14,15)

Mmeje et al have first reported HoLEP results in 45 patients older than 80 years old showing overall morbidity of 22.1% and 4.4% Clavien-Dindo over grade II complications. Hemoglobin drop and length of hospital stay were comparable to younger age groups but showed a longer catheterization time. (10)

Piao et al, in age stratified study, have reported HoLEP results with 38 octogenarian patients showing comparable overall morbidity and 6-month functional outcomes in patients aged ≥80 years compared to the younger age groups. They have reported prolonged operative time, higher enucleation weigh, prolonged hospital-stay in older age group however incidence of perioperative complication with Clavien-Dindo grade was 13.2%. At early follow up, older age group showed lower Qmax but similar QOL and PVR. (9)

Tamalunas et al have also reported their perioperative HoLEP results in 115 octogenarian patients showed overall perioperative Clavien-Dindo over II complications rate of 4.3% with no significant difference regarding perioperative outcomes compared to younger age groups. (16) Heiman et al have recently compared the perioperative and early postoperative outcomes of HoLEP in 74 octogenarian patients to the outcomes of patients of younger age. They reported 10.8% complications rate and 5.7 % readmission rate in octogenarian patients with no significant difference to outcome in younger patients. (17)

The current study is the largest report for HoLEP in the octogenarian patients with complete follow up data up to one year with the first report of HoLEP in nonagenarian patients. The overall complication rate in octogenarian and Nonagenarian patients was 20.9% whereas complications over-grade II Clavien-Dindo were 3.4%, almost close to the rates reported by Mmeje et al and Tamalunas et al while it is higher than the complication rate reported by Piao et al and Heiman et al and as 13.2% and 10.8% respectively. (10, 16) Although the overall complication rate was higher in older group, over-grade II Clavien-Dindo complication rate was comparable to younger group in the current study (3.4 vs 1.79%, p= 0.13). The higher rate of complications may be attributed to higher frailty and comorbidities, lower performance status

and more use of anticoagulants and antiplatelets in octogenarians and nonagenarians. Pio et al have also reported higher overall complication rates in octogenarians (9) whereas Heiman et al reported comparable overall complication rate in octogenarians and younger age group. (17) We suggest that this discrepancy in results is caused by variability and lack of consensus for the definition of grade I and II complications in different studies. Also, this may be attributed to lower number of patients in other studies.

The frailty score has recently emerged as an important comprehensive preoperative evaluation tool to assess the performance status and surgical risk in elderly patients. The frailty score involves multiple factors to evaluate surgical risk rather simple consideration of age or comorbidities. (18, 19) In the current study, the frailty score was significantly higher in the octogenarian and nonagenarian patients however 83% of this group had frailty score of 0 or 1. This emphasizes that the proper preoperative screening and assessment of the patients' general condition and performance status is paramount and is better than simple consideration of age. HoLEP has proven safety with the use of the continuous or intermittent use of anticoagulants or antiplatelets in multiple studies. This is of great value specifically in geriatric age group with high rates of cardiovascular disease and anticoagulants use. (20) Although the older age group had higher rates of anticoagulant use in our study, the hemoglobin drop post-HoLEP was comparable to the younger age group. The transfusion rate of the total cohort was 2.29%; within the range of transfusion for HoLEP in literature (0.8-5%). (21, 22) The transfusion rate in the group A was high (6.96%) however Mmeje et al reported higher transfusion of 11% in octogenarians. (10)

The follow up data showed the great efficacy of HoLEP in older age group with comparable functional outcomes through the IPSS, QOL, and PVR. The incontinence rates in older age group were 40.9%, 14.4%, and 4.9% at 6-week, 3-month and 1-year follow up respectively. Interestingly, incontinence rates in older group were comparable to those of the younger group at the 3 follow up points. This may reflect the less reflection of age and frailty on the incidence of incontinence compared to other factors that may be linked to incontinence as prostate volume, BMI, DM, and surgeon experience. (23)

Limitations of the study include retrospective nature, its origin from a single tertiary care center with all surgeries were performed by a single experienced surgeon, and small number of nonagenarian patients. Despite these limitations, the present study has some strength points as the largest report of HoLEP in octogenarian patients, complete follow up of at least one year, inclusion of multiple variables, and frailty scores assessment as index of general status beside age.

CONCLUSIONS

HoLEP is a safe and very effective minimally invasive technique for management of enlarged prostate in the highly screened geriatric population of octogenarians and even nonagenarians. Although HoLEP is associated with higher early complication rate in octogenarians and

nonagenarians compared to the younger age group, the majority of complications are minor. Postoperative functional outcomes are comparable to younger age group.

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FIGURES AND TABLES

Figure 1. Comparison of IPSS, PSA, incontinence rate, and PVR in both groups at three followup occasions: 6 weeks, 3 months, 1 year.

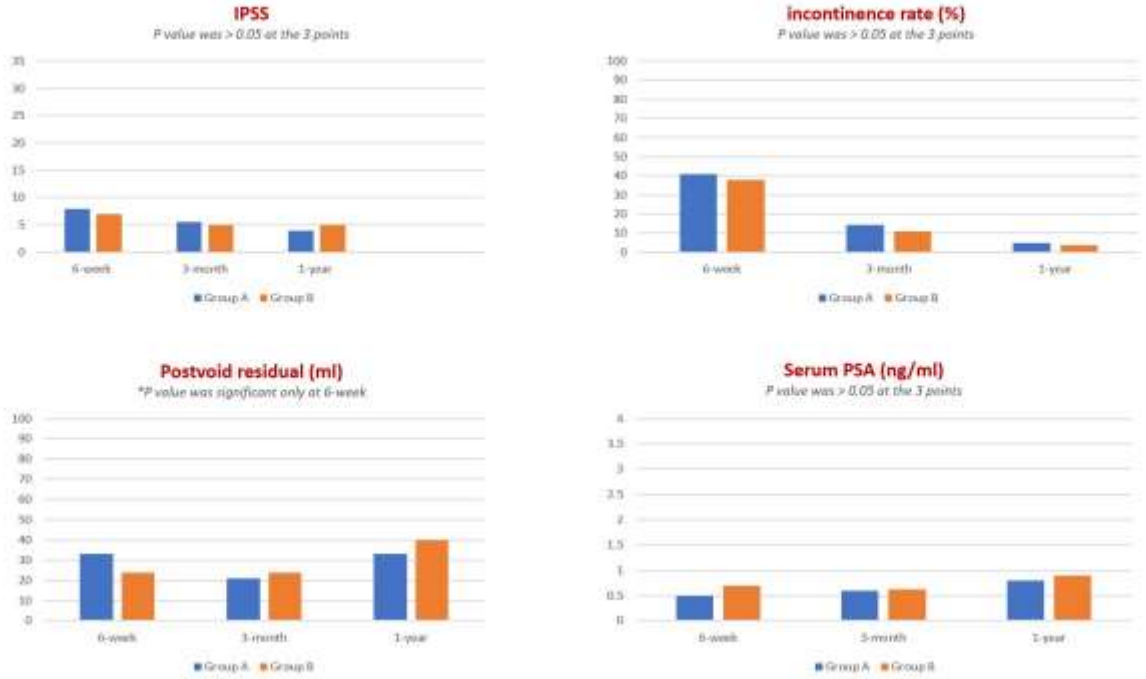

Table 1. Comparison of baseline characteristics of both group			
Variable	**Group A** (n=201)	**Group B** (n=889)	**p**
Age, median (IQR)	83.69 (81–86)	70 (64–74)	**0.0001**
BMI, median (IQR)	26.6 (23.9–29.9)	28.7 (25.8–32.3)	**0.0001**
PSA, median (IQR)	4 (1.7–7.8)	3.8 (1.8–6.8)	0.5893
Prostate volume, median (IQR)	80.5 (130–55)	91 (60–120)	0.3378
IPSS, median (IQR)	20 (14–26)	22 (16–27)	0.0740
Indwelling Catheter, n (%)	32 (15.9)	107 (12.03)	0.136
Preop Hb, gm/dl, median (IQR)	12.8 (11.8–14)	14.3 (13–15.2)	**0.0001**
CVD, n (%)	169 (84%)	614 (69%)	**0.0001**
DM, n (%)	56 (27.8%)	254 (28.5%)	0.7439

Anticoagulant use, n (%)		118 (58.7%)	342 (38.4%)	**0.0001**
Grip strength, PSI, median (IQR)		30 (26–36)	40 (32–46)	**0.0001**
ASA score, n (%)	1	5 (2.98%)	140 (15.7%)	**0.0001**
	2	76 (37.81%)	441 (49.6%)	
	3	91 (45.27%)	287 (32.2%)	
	4	29 (14.42%)	21 (2.4%)	
Frailty score, n (%)	0	81 (40.2%)	591 (66.4%)	**0.0001**
	1	86 (42.78%)	251 (28.2%)	
	2	27 (13.43%)	37 (4.16%)	
	3	5 (2.48%)	10 (1.12%)	
	4	2 (0.99%)	0	

Table 2. Perioperative outcome data

Variable	**Group A**	**Group B**	**p**
Operative time, minute, median (IQR)	55 (39–76)	50 (34–68)	**0.0241**
Specimen weight, g, median (IQR)	42 (22– 80)	45 (22–80)	0.9338
Prostate cancer pathology, n (%)	27 (13.43%)	104 (11.7%)	0.4947
Hospital stay, days, mean (SD)	1.34 (1.76)	1.04 (0.92)	**0.0042**
Catheter time, day, mean (SD)	2.18 (2.72)	1.61(2.52)	**0.0003**
Hb drop, g/dl, median (IQR)	1.4 (0.6–2.2)	1.2 (0.5– 2.1)	0.4695
Lowest Na, mg/dl, median (IQR)	138 (136–139)	138 (136–139)	0.5324
Blood transfusion, n (%)	14 (6.96%)	11(1.23 %)	**<0.0001**
Failed 1st voiding trial, n (%)	23 (11.44%)	56 (6.2%)	**0.0060**
Need for CIC, n (%)	15 (7.46)	44 (4.95)	0.155
30-day ER visit, n (%)	28 (13.9%)	65 (7.3%)	**0.0021**
30-day readmission, n (%)	23 (11.44%)	28 (3.14%)	**<0.0001**

Table 3. Comparison of 30-day Clavien-Dindo perioperative complication and long-term complications in both groups				
		Group A	**Group B**	**p**
30-day Clavien-Dindo complication grades, n (%)	I	19 (9.45%)	46 (5.17%)	**0.008**
	II	16 (7.96%)	21 (2.3%)	
	III a	1 (0.49%)	5 (0.56%)	
	III b	5 (2.48%)	6 (0.674%)	
	IV	1 (0.49%)	4 (0.449%)	
	V	0	1 (0.11)	
	Over grade II	7 (3.48%)	16 (1.79%)	0.133
	Overall	42 (20.89%)	83 (9.33%)	**0.001**
Long-term complications	Urethral stricture, n (%)	5 (2.48%)	15 (1.68%)	0.445
	Bladder neck contracture, n (%)	1 (0.49%)	10 (1.12%)	0.421
	Long-term incontinence, n (%)	7 (3.48)	18 (2.02%)	0.212