Holmium laser enucleation of prostate 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 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 the general population, with negative impact on quality of life due to 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 88–90% by 81 years of age. Urinary symptoms of urgency, nocturia, weak stream, intermittency, and incomplete emptying strongly correlate with age.[1-3]

Transurethral resection of the prostate (TURP) using the electrocautery loop has been used as the traditional 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 the management of BPH of different sizes. HoLEP rivals the success of the traditional TURP due to minimal blood loss, minimal postoperative complications, short lengths of stay, and low reoperation rate.[6,7] HoLEP has been associated with marked improvement in

KEY MESSAGES

- Our results showed that octogenarian and nonagenarian patients had longer operation time, higher need for blood transfusion, longer postoperative catheterization time, and higher readmission rates post-HoLEP.
- 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.

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 by reporting the perioperative and postoperative outcomes of HoLEP in this age group and comparing 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 nine years' experience with HoLEP. Patients were assigned to one of two groups according to their age, above or below 80 years. Patients with incomplete followup data up to one year were excluded.

Patient demographics, baseline preoperative characteristics, operative details, perioperative complications, postoperative outcomes at six weeks, three months, and one year followup, as well as the long-term followup complications were collected and compared between 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 followup 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 followup visits at six weeks, three months, and 12 months.

HoLEP protocol

Prostate volume was estimated in most of the patients before surgery through transabdominal or transrectal ultrasound or multiparametric magnetic resonance imaging for elevated prostate-specific antigen (PSA). Whenever possible, anticoagulants and antiplatelets, other than Aspirin®, were held 3–7 days before HoLEP. HoLEP was performed with holmium laser power setting of 2 J and frequency of 40 or 20 Hz. Lumenis MOSES™ technology was adopted as of 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 three days in the outpatient clinic. Earlier, patients were mostly discharged on a postoperative day 1, while in the last two years of the study period, same-day discharge was embraced in suitable patients, especially after the adoption of MOSES™ technology.

Statistical analysis

Data was analyzed using the commercially available SAS (Statistical Analysis Software) Version 9.4 (SAS Institute Inc., Cary, NC, U.S.). 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-squared 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 the two groups. Statistical significance is set at 0.05.

RESULTS

Among 1202 patients who underwent HoLEP during the study period, 112 patients (25 and 87 patients >80 and <80 years, respectively) were excluded for incomplete followup data; therefore, 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. Group B included 889 patients below 80 years old, with a median age of 70 years.

The patients in group A had significantly higher frailty score, higher ASA score, lower grip strength, lower body mass index (BMI), lower baseline hemoglobin level, and higher incidence of cardiovascular disease (CVD) and chronic anticoagulant use (Table 1). Sixteen (7.9%) and 28 (3.15%) patients in groups 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, and higher rates of failed hospital voiding trial and 30-day emergency room (ER) visits. The mean hospital stay in both groups A and group B were less than 1.5 days, with statistically longer hospital stays 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 Hb in group A since absolute decrease in Hb was similar. Readmission rate was 11.4% vs. 3.1% in groups 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 (IIIa) or general (IIIb) anesthesia, mainly for growth hematuria. Class IV complications were seen in a total of five patients with single or multi-organ failure due to sepsis.

To eliminate the effect of variation of antiplatelet/anticoagulant use rate during HoLEP, specific analysis of postoperative complications was performed after excluding the patients who used 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 in group B, respectively.

The postoperative outcome data at the three appointed followup periods (six weeks, three months, and one year) were statistically comparable in both groups regarding IPSS (p=0.37, 0.69, 0.13), QoL (0.47, 0.46, 0.12), postvoid residual (PVR)/incontinence (stress and/or urge) rates (p= 0.65, 0.77, 0.69), and serum PSA (0.07, 0.22, 0.47). Only median PVR was statistically higher in group A at the six-week followup (p=0.016), while it was comparable at the three-month and one-year encounters (p=0.68, 0.28, respectively) (Figure 1). With median followup of 19 and 17 months in groups A and B, respectively, the long-term followup (beyond one year) data showed comparable rates of urethral

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 hemoglobin, 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	

ASA: American Society of Anesthesiologists; BMI: body mass index; CVD: cardiovascular disease; DM: diabetes mellitus; IPSS: International Prostate Symptom Score; IQR: interquartile range; PSA: prostate-specific antigen; PSI: pounds per square inch.

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**
Hemoglobin 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**

CIC: clean intermittent catheterization; ER: emergency room; IQR: interquartile range; NA: sodium; SD: standard deviation.

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 postoperative day 1. On followup, median IPSS was 7 (4–11), 8 (6–16), and 6 (2–11), while urine incontinence was seen in seven, four, and two patients at six-week, three-month, and one-year followups, 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 QoL, particularly in elderly patients who are more susceptible to falls and infection.[14,15]

Mmeje et al 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 an age-stratified study, reported HoLEP results with 38 octogenarian patients, showing comparable overall morbidity and six-month functional outcomes in patients aged ≥80 years compared to the younger age groups. They reported prolonged operative time, higher enucleation weight, and prolonged hospital stay in the older age group; however, incidence of perioperative complication with Clavien-Dindo grade was 13.2%. At early followup, the older age group showed lower peak flow rate but similar QoL and PVR.[9]

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

The current study is the largest report for HoLEP in the octogenarian patients with complete followup 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 Clavien-Dindo grade II were 3.4%, almost close to the rates reported by Mmeje et al and Tamalunas et al, albeit higher than the complication rate reported by Piao et al and Heiman et al (13.2% and 10.8%, respectively).[9,10,16,17] Although the overall complication rate was higher in the older group, Clavien-Dindo >grade II complication rate was comparable to the 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 also reported higher overall complication rates in octogenarians,[9] whereas Heiman et al reported comparable overall complication rates in octogenarians and the younger age group.[17] We suggest 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 the 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

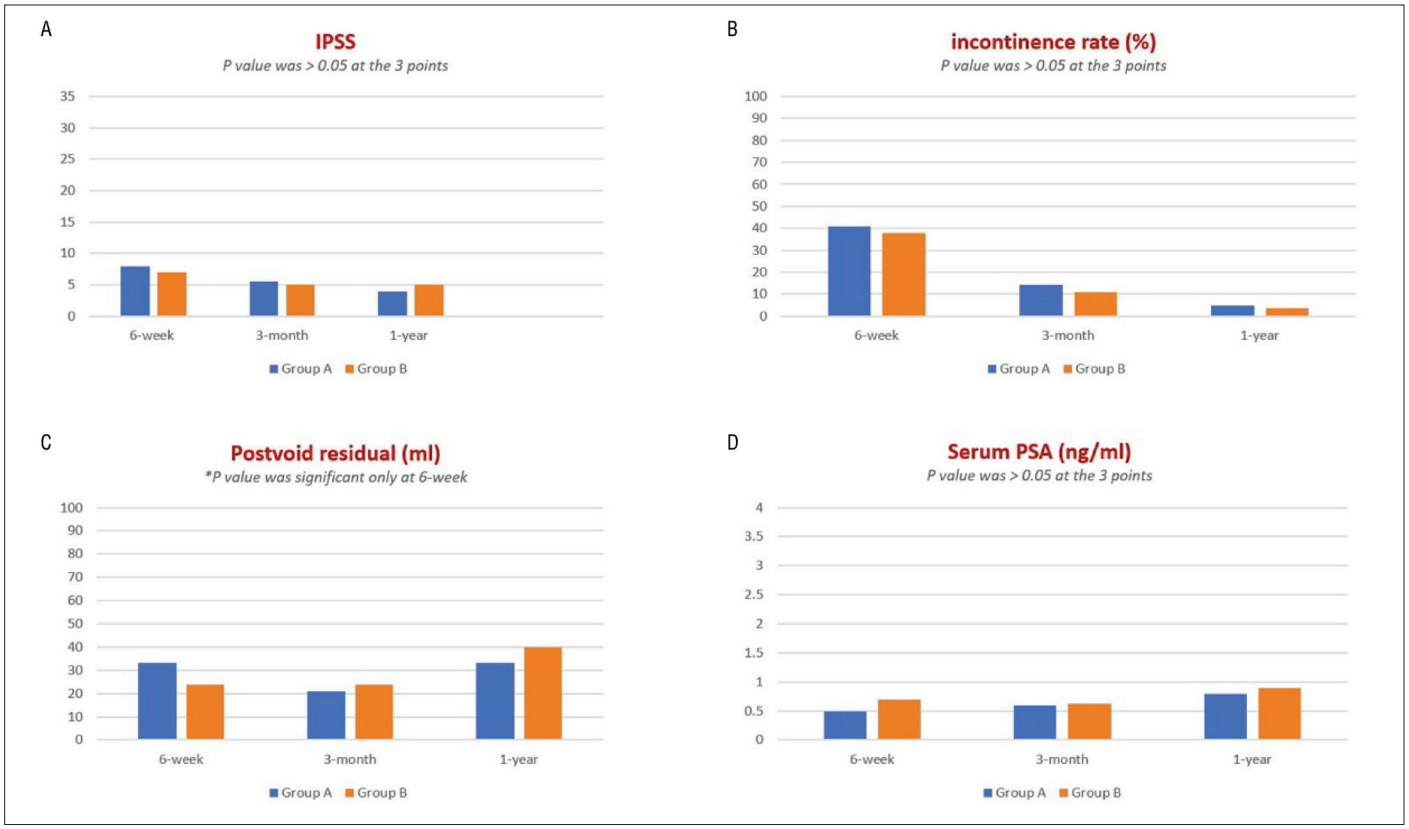

Figure 1. Comparison of (A) International Prostate Symptom Score; (B) incontinence rate; (C) postvoid residual; and (D) serum prostate-specific antigen (PSA) and in both age groups (group A>80 years, group B <80 years) at three followup occasions: 6 weeks, 3 months, 1 year.

evaluate surgical risk rather than 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 safe with the use of the continuous or intermittent anticoagulants or antiplatelets in multiple studies. This is of great value, specifically in geriatric age group, with high rates of CVD and anticoagulants use.[20] Although the older age group had higher rates of anticoagulant use in our study, the Hb 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 the general literature (0.8–5%).[21,22] The transfusion rate in group A was high (6.96%); however, Mmeje et al reported a higher transfusion of 11% in octogenarians.[10]

The followup data showed the great efficacy of HoLEP in the 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 six-week, three-month, and one-year followup, respectively. Interestingly, incontinence

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, n (%)	Urethral stricture	5 (2.48%)	15 (1.68%)	0.445
	Bladder neck contracture	1 (0.49%)	10 (1.12%)	0.421
	Long-term incontinence	7 (3.48)	18 (2.02%)	0.212

rates in the older group were comparable to those of the younger group at the three followup points. This may reflect the lesser effect of age and frailty on the incidence of incontinence compared to other factors that may be linked to incontinence, such as prostate volume, BMI, diabetes mellitus, and surgeon experience.[23]

Limitations

Limitations of the study include its retrospective nature, its origin from a single tertiary care center, where all surgeries were performed by a single experienced surgeon, and the small number of nonagenarian patients. Despite these limitations, the present study has some key strengths, such as the largest report of HoLEP in octogenarian patients, complete followup of at least one year, inclusion of multiple variables, and the use of frailty scores as indices of general status rather than just age.

CONCLUSIONS

HoLEP is a safe and very effective minimally invasive technique for the 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, most complications are minor, and postoperative functional outcomes are comparable to the younger age group.

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