The clinical value of holmium laser enucleation of the prostate in octogenarians

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Abstract

Objectives: With holmium laser enucleation of the prostate (HoLEP) a size-independent method for surgical treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic obstruction (BPO) has been introduced. HoLEP offers durable long-term results with reduced perioperative morbidity. As the risk of disease progression increases with age, the main goals, when offering surgery to an elderly population, are reducing perioperative morbidity and preserving quality of life (QoL). We therefore analyzed the impact of age on outcomes and perioperative morbidity in patients undergoing HoLEP for LUTS at our tertiary referral center.

Methods: We retrospectively collected data of 487 patients who underwent HoLEP for LUTS secondary to BPO between 2018 and 2019. Patients were divided into group 1 (<70 years), group 2 (70-79 years), and group 3 (≥80 years). Perioperative parameters, safety, and short-term functional outcomes were assessed and analyzed.

Results: Perioperative Clavien-Dindo grade ≥II complications were seen in 4.1% of patients (20/487). There was no difference in perioperative complications between all age groups (P = .176). Functional outcome was assessed 30 days post surgery. There was significant improvement in median International Prostate Symptom Score of 14, 10, and 8 points for groups 1, 2, and 3 (P < .001), respectively, with constant improvement of median QoL of 3 points for all groups. Median maximum flow rate (Qmax) showed significant improvement of 14.5, 10.5, and 13 mL/s for groups 1 to 3 (P = .467), respectively.

Conclusion: HoLEP offers acceptable perioperative complication rates even in the oldest patient cohort (≥80 years). Therefore, HoLEP is a safe and efficient option even in oldest patients.

KEYWORDS
age, benign prostatic enlargement, BPH, elderly, holmium laser enucleation of the prostate, LUTS
1 | INTRODUCTION

Transurethral resection of the prostate (TURP) has been considered as the surgical standard treatment for lower urinary tract symptoms (LUTS) secondary to benign prostatic obstruction (BPO). In 1996, holmium laser enucleation of the prostate (HoLEP) was introduced by Gilling et al and has since become one of the most scrutinized forms of surgical intervention for BPO.1,2 When comparing HoLEP to TURP, HoLEP has been accepted as at least equal in efficacy and even superior regarding perioperative morbidity.3-5 HoLEP is independent of prostate size, and its effectiveness in relief of LUTS is comparable to open prostatectomy (OP) with less blood loss, shorter catheterization time and hospital stay.6-7 As the benefits associated with HoLEP seem durable in long-term follow-up, it has even been considered the “new gold standard” for surgical intervention in LUTS secondary to BPO.4,8

The risk of progression of LUTS increases with age. During the last century, life expectancy in Western civilizations has been steadily increasing. By 2040, one in four Americans will be over the age of 65, most likely leading to a higher incidence of LUTS secondary to BPO.9,10 When offering surgical treatment to patients, the risk of developing complications is related to patients’ health status, which generally worsens with age.11 The main goals when offering surgery to an elderly population are reducing perioperative morbidity and mortality and preserving quality of life (QoL).

We therefore analyzed the impact of age stratification on outcomes and perioperative morbidity and mortality of patients undergoing HoLEP for LUTS/BPO. We especially focused on feasibility of HoLEP in the oldest patient cohort (>80 years of age) and aimed to analyze safety and efficacy.

2 | MATERIALS AND METHODS

2.1 | Patient population and study design

In our tertiary referral center, 513 patients underwent consecutive HoLEP for LUTS secondary to BPO between July 2018 and December 2019. A computerized database containing clinical and pathological information, as well as perioperative data and follow-up information, was used for this study. We retrospectively analyzed this database and included patients according to the aforementioned criteria. We identified 487 patients, for whom all the information was available, and subdivided them into three age groups. HoLEP for LUTS/BPO was indicated in accordance with the current European Association of Urology (EAU) guidelines on management of nonneurogenic male LUTS.12

Only two experienced surgeons performed all HoLEP. We used the VersaPulse 100W Holmium Laser (Lumenis Ltd, Yokneam, Israel) with a frequency of 53 Hz and a power setting of 1.2 kJ. Morcellation was performed using a mechanical tissue morcellator (Piranh; Richard Wolf, Knittlingen, Germany). According to our standard protocol, a 24F three-way foley catheter was inserted after surgery and followed by 12 hours of continuous bladder irrigation with normal saline.

Patients were stratified into three age groups. Group 1 included patients aged <70 years (n = 208), group 2 included patients aged 70 to 79 years (n = 164), and group 3 included only patients aged 80 and above (n = 115).

Clinical and pathological information as well as perioperative data were used to describe the cohorts. Perioperative complications were analyzed in all age groups. They were defined as any adverse event within 30 days of surgery. Complications were classified using the Clavien-Dindo scale.13-15

2.2 | Statistical analysis

Statistical analysis was performed using SPSS V25.0 software (SPSS Inc, Chicago, Illinois). Results are given as median and interquartile range (IQR) for continuous variables and as percentage for categoric variables. Univariate analyses were performed using Fisher’s exact test and Mann-Whitney U test for categorical variables and t test continuous variables, respectively. All reported P values were two sided and considered statistically significant if P < .05.

3 | RESULTS

3.1 | Patient characteristics

Table 1 displays the demographic parameters of patient groups 1, 2, and 3. In total, 487 patients underwent HoLEP for LUTS secondary to BPO. Patient characteristics were comparable between all three cohorts (Table 1). Obviously, the median age was significantly different in all three groups with a median of 64 (IQR 59-67), 74 (IQR 72-76), and 82 years (IQR 80-85) for groups 1 to 3, respectively (P < .001). Preoperative hemoglobin levels were statistically different between all groups with a median of 15.0 (IQR 14.2-15.8), 14.6 (IQR 13.7-15.2), and 13.7 g/dL (IQR 12.6-14.4) for groups 1 to 3, respectively (P < .001 for group 3 vs group 1 and P < .03 for group 3 vs group 2). Preoperative assessment of an American Society of Anesthesiologists (ASA) score ≥III was significantly higher in group 3 compared to the younger patient groups, with 65.2% in group 3, and 28.7% and 24.9% for groups 2 and 1, respectively (P < .001). However, groups 1, 2, and 3 showed no statistically significant difference in body mass index, preoperative International Prostate Symptom Score (IPSS), QoL, maximum flow rate (Qmax), postvoid residual (PVR), total prostate-specific antigen (PSA), PSA density, prostate volume (PV), or the rate of an indwelling urinary catheter prior to surgery.

3.2 | Perioperative assessment and functional outcomes

The analysis of the perioperative outcomes showed no difference in surgery time. The median tissue retrieval percentage was significantly different in groups 1 and 2 vs group 3 with 73.2% (IQR 65.5-80) and 73.3% (IQR 62.5-81) vs 81.3% (IQR 77.8-100), respectively (P < .001).
The median weights of resected tissue were significantly different in group 1 vs group 3 with 55 g (IQR 40-77.8) and 78 g (IQR 55-105), respectively (P < .02), with no difference for group 2 with 62.5 g (IQR 42-87.5, P = .182). There was no statistically significant difference in the overall median hemoglobin drop between the three groups (P = .505).

Four weeks after surgical treatment LUTS improved in all three patient cohorts. The median IPSS significantly decreased by 14 (IQR 7-17.5), 10 (IQR 4-16), and 8 points (0-17.8) for groups 1 to 3, respectively (P < .001). There was significant improvement in QoL of three points, with no statistically significant difference between all groups (P = .63). The early functional outcomes 4 weeks after surgery showed a nonsignificant difference for group 3 with 13.0 mL/s (IQR 8.5-17) vs groups 1 and 2 with 14.5 mL/s (IQR 9-26) and 10.5 mL/s (IQR 5-16), respectively (P = .467). A median PVR reduction of 80 (IQR 30-155.5), 63.5, (15.5-157.5), and 100 mL (40-165) was observed for groups 1 to 3, respectively (P = .566). There was no difference between the three groups in catheterization time or duration of hospital stay (P = .467 for both).

### TABLE 1  Demographic parameters

| Variables             | Group 1 (<70) (n = 208) | Group 2 (70-79) (n = 164) | Group 3 (≥80) (n = 115) | P value |
|-----------------------|--------------------------|---------------------------|-------------------------|---------|
| Age (y)               | Median 64                | 74                        | 82                      | <.001   |
|                       | IQR 59-67                 | 72-76                     | 80-85                   |         |
| BMI                   | Median 25.6               | 25                        | 25.3                    | .696    |
|                       | IQR 24-27.7               | 23-27                     | 22.6-26.4               |         |
| IPSS                  | Median 20                 | 18                        | 18                      | .130    |
|                       | IQR 15-25                 | 14-23                     | 14-25.8                 |         |
| QoL                   | Median 4                  | 4                         | 4                       | .998    |
|                       | IQR 3-5                   | 3-5                       | 4-5                     |         |
| Q_max (mL/s)          | Median 10                 | 10                        | 9.5                     | .664    |
|                       | IQR 7.5-14                | 7-13.8                    | 7.3-12                  |         |
| PVR (mL)              | Median 90                 | 77                        | 105                     | .570    |
|                       | IQR 40-160                | 20-180                    | 40-175                  |         |
| Hb (g/dL)             | Median 15*                | 14.6**                    | 13.7                    | <.001   |
|                       | IQR 14.2-15.8             | 13.7-15.2                 | 12.6-14.4               | <.03    |
| Total PSA (ng/mL)     | Median 6                  | 6.2                       | 5.1                     | .821    |
|                       | IQR 3.2-12.4              | 3-11.6                    | 3.2-11.3                |         |
| PSA density (ng/mL/cc)| Median 0.08               | 0.07                      | 0.07                    | .139    |
|                       | IQR 0.05-0.14             | 0.04-0.12                 | 0.04-0.11               |         |
| Prostate volume (cc)  | Median 75.5               | 85                        | 90                      | .124    |
|                       | IQR 60-100                | 60-120                    | 60-115                  |         |
| score ≥III vs <III (%)| 24.9% (51)                | 28.7% (46)                | 65.2% (75)              | <.001   |
| IDC                   | 33.5% (69)                | 33.5% (55)                | 47.8% (55)              | .372    |

Note: Bold values indicate statistically significant P values (P < .05).

Abbreviations: American Society of Anesthesiologists; BMI, body mass index; Hb, hemoglobin; IDC, indwelling urinary catheter; IPSS, International Prostate Symptom Score; IQR, interquartile range; PSA, prostate-specific antigen; PVR, postvoid residual urine; Q_max, peak urinary flow rate; QoL, quality of life.

*P < .001; **P < .03.
In total, 20 (20/487, 4.1%) patients of the entire cohort experienced at least one perioperative complication. In groups 1, 2, and 3, five (2.4%), ten (6.0%), and five (4.3%) patients, respectively, had at least one perioperative complication. There was no significant difference between all three groups ($P = .176$). The groups did not differ in the severity of their perioperative complications described by the Clavien-Dindo score in Table 3 either as we divided complications into minor (Clavien I) and major complications (Clavien II-V) ($P = .299$), requiring an intervention. Complications seen are listed in detail in Table 3. Grade I complications involved hematuria and blood clot retention with prolonged bedside bladder irrigation and clot evacuation ($n = 2$). Only one patient suffered from a grade II complication and was dismissed with indwelling suprapubic catheter for postoperative bladder training. Grade III complications mainly consisted of persistent hematuria ($n = 8$), requiring operative coagulation, and urethral obstruction due to a tissue flap ($n = 5$), requiring urethral resection of the tissue flap. One patient with significantly enlarged prostate with a large median lobe close to his ureteral ostia ($PV = 60$ cc) experienced an intraoperative injury to his right ureteral ostium and required a double J-stent placement, which could be removed 3 months after surgery in an outpatient procedure. Only one patient experienced a life-threatening grade IV complication due to postoperative aspiration pneumonia and was admitted to our intensive care unit.

### Table 2  Perioperative and clinical outcomes 4 weeks after surgery

| Variables                   | Group 1 (<70) (n = 208) | Group 2 (70-79) (n = 164) | Group 3 (≥80) (n = 115) | $P$ values |
|-----------------------------|-------------------------|---------------------------|-------------------------|------------|
| Surgery time (min)          | Median 75               | 87.5                      | 93                      | .909       |
|                             | IQR 58-109              | 66.8-118                  | 57-116                  |            |
| Resected tissue (g)         | Median 55*              | 62.5**                    | 78                      | <.020      |
|                             | IQR 40-77.8             | 42-87.5                   | 55-105                  | .182       |
| Resected tissue (%)         | Median 73.2             | 73.3                      | 81.3                    | <.001      |
|                             | IQR 65.5-80             | 62.5-81                   | 77.8-100                |            |
| Δ IPSS                      | Median 14               | 10                        | 8                       | <.001      |
|                             | IQR 7-17.5              | 4-16                      | 0-17.8                  |            |
| Δ QoL                       | Median 3                | 3                         | 3                       | .630       |
|                             | IQR 2-4                 | 2-4                       | 1.8-4                   |            |
| Δ $Q_{\text{max}}$ (mL/s)   | Median 14.5             | 10.5                      | 13                      | .467       |
|                             | IQR 9-26                | 5-16                      | 8.5-17                  |            |
| Δ PVR (mL)                  | Median 80               | 63.5                      | 100                     | .566       |
|                             | IQR 30-155.5            | 15.5-157.5                | 40-165                  |            |
| Δ Hb (g/dL)                 | Median 1.0              | 1.0                       | 1.0                     | .505       |
|                             | IQR 0.5-1.7             | 0.5-1.8                   | 0.7-2.2                 |            |
| Catheterization time (d)    | Median 2.0              | 2.0                       | 2.0                     | .467       |
|                             | IQR 2.0-2.0             | 2.0-2.0                   | 1.5-2.5                 |            |
| Hospitalization time (d)    | Median 3.0              | 3.0                       | 3.0                     | .467       |
|                             | IQR 3.0-3.0             | 3.0-3.0                   | 2.5-3.5                 |            |

Note: Bold values indicate statistically significant $P$ values ($P < .05$).

Abbreviations: Hb, hemoglobin; IPSS, International Prostate Symptom Score; IQR, interquartile range; PVR, postvoid residual urine; $Q_{\text{max}}$, peak urinary flow rate; QoL, quality of life.

* $P < .020$; ** $P < .182$. 

### 3.3  Perioperative complications

In total, 20 (20/487, 4.1%) patients of the entire cohort experienced at least one perioperative complication. In groups 1, 2, and 3, five (2.4%), ten (6.0%), and five (4.3%) patients, respectively, had at least one perioperative complication. There was no significant difference between all three groups ($P = .176$). The groups did not differ in the severity of their perioperative complications described by the Clavien-Dindo score in Table 3 either as we divided complications into minor (Clavien I) and major complications (Clavien II-V) ($P = .299$), requiring an intervention. Complications seen are listed in detail in Table 3. Grade I complications involved hematuria and blood clot retention with prolonged bedside bladder irrigation and clot evacuation ($n = 2$). Only one patient suffered from a grade II complication and was dismissed with indwelling suprapubic catheter for postoperative bladder training. Grade III complications mainly consisted of persistent hematuria ($n = 8$), requiring operative coagulation, and urethral obstruction due to a tissue flap ($n = 5$), requiring urethral resection of the tissue flap. One patient with significantly enlarged prostate with a large median lobe close to his ureteral ostia ($PV = 60$ cc) experienced an intraoperative injury to his right ureteral ostium and required a double J-stent placement, which could be removed 3 months after surgery in an outpatient procedure. Only one patient experienced a life-threatening grade IV complication due to postoperative aspiration pneumonia and was admitted to our intensive care unit.
3.4 | Antiplatelet medication

As antiplatelet medication is very common in the aging population, we summarized the use of time-released Aspirin (acetylsalicylic acid 100 mg, Leverkusen, Germany), clopidogrel (P2Y12 inhibitors), new oral anticoagulants (NOAC; apixaban, rivaroxaban; factor Xa inhibitors), and warfarin stratified by age group (Table 4). Time-released Aspirin was not discontinued in any case. Clopidogrel and NOAC were discontinued according to their respective medication half-life: Clopidogrel was discontinued 7 to 10 days prior to HoLEP, and NOAC were discontinued 48 to 72 hours prior to HoLEP. Warfarin was bridged perioperatively with low-molecular-weight heparin. No statistical difference could be detected between all groups, although a trend could be detected for group 3 (25; 21.7%) vs groups 1 (19; 9.1%) and 2 (22; 13.4%) for use of time-released Aspirin ($P = .09$).

4 | DISCUSSION

Bothersome LUTS affect considerably QoL in the elderly male population. LUTS secondary to BPO is age dependent and present in at least 40% of 50- to 60-year-old men and in about 80% of 80-year-old men. More than half of those affected will become symptomatic.12,16 As demographic changes will lead to a more aged population in Western countries, incidence of advanced-age LUTS will rise. Although many centers have shown that HoLEP for LUTS/BPO is feasible, the influence of age on functional outcomes and perioperative morbidity and mortality is of great importance in an ever-aging population.4,17 When comparing different transurethral procedures for the treatment of LUTS, only HoLEP shows results similar to OP.6,18 When being left with the choice of offering invasive OP to a frail population, in which increased morbidity and mortality can easily outweigh the benefit of surgical therapy, the
importance of offering minimally invasive and functionally equivalent techniques becomes self-evident. Therefore, we defined, assessed, and compared the selected groups of patients undergoing HoLEP for BPO: group 1 (<70 years) with 208 patients, group 2 (70-79 years) with 164 patients, vs group 3 (≥80 years) with 115 patients.

In our high-volume tertiary referral center, we analyzed patients’ age at time of HoLEP and their respective perioperative complications und postoperative outcomes. It is accepted that HoLEP is associated with high functional efficacy, low perioperative morbidity, and even lower mortality compared with TURP or OP. Frail older patients often present with various comorbidities, such as anemia. Our patient cohorts are highly comparable. They only significantly differed in preoperative hemoglobin value and score ≥III in the oldest patient cohort. Recently, Steinmeyer et al could show that anemia is present in a striking 20.83% of patients above the age of 80, while frailty depicted by the score is well documented in an elderly population with various comorbidities. However, there was no need for perioperative blood transfusion. This corresponds well to the data gathered on the perioperative safety profile of performing HoLEP in octogenarians by Mmeje et al. Also, postoperative drop in hemoglobin value showed no statistically significant difference between all age groups in our study population.

All patients in our study cohort showed significant improvement in functional outcomes after HoLEP. Patients in group 1 had the greatest improvement in postoperative IPSS and Qmax (Table 2). Although the association between a patient’s geriatric status and functional outcome after minimally invasive prostate resection remains controversial, the prevalence of detrusor underactivity increases with age and is thereby contrasted in a decline of bladder outlet obstruction and therefore may explain the less pronounced effect on the older patient cohorts. Patients aged 80 years and over had the highest absolute and relative prevalence of detrusor underactivity as well as functional outcomes in elderly patients undergoing HoLEP. HoLEP for LUTS/BPO can be offered as viable treatment option even in oldest patients. There are no limitations to using HoLEP in an elderly patient cohort. The modest initial improvement in Qmax and IPSS in the oldest patient cohort may be due to prolonged recovery of the patients’ detrusor. The oldest patients usually suffer from LUTS secondary to BPO for an extended period of time, and therefore detrusor contractility may need to be assessed over a longer follow-up period. However, Elshal et al could show no significant difference in short-term (30 days) postoperative functional outcomes compared to follow-up after 1 year. Furthermore, QoL did not differ significantly between the age groups and was similarly improved after HoLEP.

The Clavien-Dindo classification (CDC) is most commonly used for reporting and defining perioperative complications and has been modified for reporting complications following TURP by Mamoulakis et al. In our study cohort, overall 20 patients (20/487, 4.1%) suffered from a postoperative complication according to the CDC (I-IV) (Table 3). Compared to the results by Mamoulakis et al, where overall CDC rate was 15.7%, our population had very modest perioperative complications. Most of our complications were CDC grade III (14/20, 56.3%), with surgical reintervention after removing the catheter, while macrohematuria was rare (8/487; 1.6%). There was only one CDC grade IV complication due to life-threatening aspiration pneumonia, accounting for a 0.2% rate of all complications in our patient cohort. This again corresponds well with the complication rate of 0.7% for CDC grade IV reported by Elshal et al. There was no statistical difference for use of antiplatelet medication and postoperative complication rates, corresponding well with the findings by our research group comparing HoLEP to TURP in a matched-pair analysis of bleeding complications under various antithrombotic regimens (Table 4). There was no CDC grade V in our patient cohort within the first 30 days of surgery. This is in contrast to the data reported by Jorgensen et al. They retrospectively analyzed 249 patients aged >80 years, who underwent TURP for BPO, and found a 30-day mortality rate of 11.6% with 7 patients dying within the first week after surgery. In our present study, there were no deaths associated to the surgical procedure. This may be due to the fact that HoLEP was performed by a small number of high-volume experienced surgeons. Also, the advantages of HoLEP include using physiologic saline as an irrigant. We found no life-threatening transurethral resection (TUR) syndrome in our patient cohort.

Based on our data, we could show that, regardless of patients’ age, HoLEP is not only an effective but also safe surgical treatment option in LUTS secondary to BPO.

The limitations to our study surely include its retrospective design. We did not include patients undergoing other laser treatment options or TURP for LUTS/BPO in our study. There also was a smaller proportion of patients in our ≥80-years-of-age group than in the other groups, which naturally limits the power of our analysis. Being a tertiary referral center brings with it the problem of following up the patient at home, preventing the complete collection of data for more cases. A longer follow-up is required for complete appraisal of functional outcomes and the safety profile. However, we could show that there are no limitations to using HoLEP in an elderly patient cohort with exceptionally low morbidity and nonexistent perioperative mortality. When offering HoLEP as a treatment option in LUTS/BPO, one should consider offering it at even an earlier stage of the disease as younger patients may profit from increased functional results.

CONCLUSION

In light of increasing life expectancy in Western nations, we sought to evaluate the impact of age on perioperative morbidity and mortality as well as functional outcomes in elderly patients undergoing HoLEP for LUTS/BPO. HoLEP provides a favorable safety profile even in the oldest patient cohort (≥80 years). Therefore, HoLEP for LUTS/BPO can be offered as viable treatment option even in oldest patients.

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AUTHOR CONTRIBUTIONS

Alexander Tamalunas: project development, data collection and analysis, manuscript writing. Thilo Westhofen: data collection and
management, data analysis. Melanie Schott: data collection and management, data analysis. Patrick Keller: data collection and management, data analysis. Michael Atzler: data collection and management. Christian G. Stief: project development. Giuseppe Magistro: project development, data collection and analysis, manuscript writing.

CONFLICT OF INTEREST

The authors have not received any financial grants and declare that they have no industrial links or affiliations.

STATEMENT OF ETHICS

All human subjects provided written informed consent with guarantees of confidentiality. In lieu of an ethical review board, the authors state that this article does not contain any studies with human participants performed by any of the authors. Our research was carried out in accordance with the Declaration of Helsinki of the World Medical Association, and informed consent was obtained from all patients. All data were collected and analyzed anonymously.

DATA AVAILABILITY STATEMENT

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

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