ORIGINIAL ARTICLE

Long-term sexual outcomes after holmium laser enucleation of the prostate: which patients could benefit the most?

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Assess rate and predictors of erectile function (EF) outcomes at long-term follow-up (FU) after holmium laser enucleation of the prostate (HoLEP). Cross-sectional analyses were performed on 135 patients with a mean FU of 12 years post HoLEP. Patients completed both a baseline and a FU International Index of Erectile Function (IIEF)-EF domain and the International Prostatic Symptoms Score (IPSS). Postoperative EF outcomes, including rate and predictors of EF improvement considering minimal clinically important differences (MCIDs) criteria, were assessed. Logistic regression models tested the association between predictors and EF. At a mean (median) FU of 152.1 (163) months, patients showed a significant decrease in the IIEF-EF score (P < 0.01) and significant IPSS improvement (P < 0.01). Overall, 50 (37%) patients worsened by at least one IIEF-EF category. Conversely, 23 (17%) patients reported an improvement in postoperative IIEF-EF score; 75 (55.6%) and 10 (7.4%) patients maintained and eventually improved their IIEF-EF category, respectively. Patients reporting a decrease in the postoperative IIEF-EF score were significantly older (P = 0.03) and showed a significantly larger mean FU (P < 0.01) than those reporting postoperative improvements of IIEF-EF. Nine (6.7%) patients showed significant EF improvement according to MCIDs criteria. Both higher IPSS scores (odds ratio (OR): 1.12; P = 0.02) and lower IIEF-EF (OR: 0.88; P < 0.01) at baseline, emerged as independent predictors of postoperative EF improvement. HoLEP was associated with a decrease in EF and a persistent amelioration of BPH-related urinary symptoms at long-term FU. Almost one third of patients worsened by at least one IIEF-EF category. However, a clinically meaningful EF improvement was observed in roughly 7% of the individuals. Patients with more severe preoperative urinary symptoms and ED benefited more from HoLEP in terms of EF.


INTRODUCTION

Erectile dysfunction (ED) and benign prostatic hyperplasia–related lower urinary tract symptoms (LUTS/BPH) are highly prevalent and comorbid conditions in middle-aged and elderly men. Data regarding the incidence of ED after surgery for LUTS/BPH has shown conflicting results. Trans-urethral resection of the prostate (TURP) is still considered the gold standard for BPH although the majority of these studies do not rely on validated instruments to assess erectile function (EF) outcomes. The literature suggests similar rates of postoperative ED in patients treated with HoLEP, TURP or open prostatectomy, although the majority of these studies do not rely on validated instruments to assess erectile function (EF) outcomes. Conversely, using the International Index of Erectile Function (IIEF), Briganti et al. showed a positive albeit not significant linear correlation between EF improvement and a concomitant postoperative LUTS amelioration in patients treated with either HoLEP or TURP.

We sought to assess (1) the rate of EF alteration at long-term follow-up (FU) after HoLEP using validated psychometric instruments, (2) clinically meaningful improvements in postoperative EF according to the minimal clinically important differences (MCIDs), defined as the smallest difference in the IIEF-EF domain score that patients perceived as beneficial) criteria and (3) potential clinical predictors associated with postoperative EF changes.

MATERIALS AND METHODS

These cross-sectional analyses were based on a cohort of 636 consecutive sexually active, heterosexual, Caucasian-Europeans with LUTS/BPH submitted to HoLEP at a single academic hospital, between January 2001 and June 2011. All surgical procedures were performed by one fully trained surgeon, according to the surgical technique previously described in detail. All subjects were preoperatively assessed with a thorough medical history; health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI) (categorized as 0 vs >1). We used the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM). Preoperative prostate volume was assessed via trans-rectal ultrasound evaluation.

Patients were stratified according to their educational status into a low-level educational group, which included patients with an elementary and/or secondary school education, and a high-level educational group, which consisted of men with a high school and/or university degree. Moreover, all patients completed a baseline IIEF-EF domain and International Prostate Symptom Score (IPSS).

From July to December 2012 all patients were re-assessed with a single outpatient clinic visit at a minimum FU of 12 months. Patients were invited to fill an IIEF and a IPSS targeting 4 week before the FU visit. All surveys were self-administered in a clinical setting. For the specific purposes of the study, all patients reporting to have used pro-erectile drugs in the last 4 weeks were excluded (125(19.6%)%). Similarly patients with incomplete baseline data or refusing to complete the FU survey are excluded from the analysis.
Clinical predictors of long-term post-HoLEP EF improvement or deterioration were identified using Spearman’s method. We used the IIEF-EF domain categories and 10 (7.4%) patients showed an improvement in IIEF-EF scores. Overall, 75 (55.6%) patients maintained the same baseline EF. Conversely, 23 (17%) patients worsened by at least one IIEF-EF category. Indeed, patients reporting a decrease in IIEF-EF scores were significantly older (68.7 (6.9) vs 65.3 (6.5) years; \(P=0.03\)) and those who underwent a redo-surgery during FU (10 (1.5%)) were excluded from the study. Overall, a total of 135 patients with complete baseline and FU data were included in the final analysis.

To provide a frame of reference for objectively interpreting ED severity, we used the IIEF-EF domain classification as proposed by Cappelleri et al.\(^{16}\) MCIDs were defined as 2, 5, and 7 for patients with mild, moderate, and severe preoperative ED, respectively; patients with mild to moderate ED were included in the moderate category.\(^{18}\)

Data collection followed the principles outlined in the Declaration of Helsinki; all patients signed an informed consent agreeing to supply their own anonymous information for this and future studies.

### Main outcome measures

The primary end point of the present study was to assess EF changes at long-term FU after HoLEP. Moreover, the rate of patients with clinically meaningful improvements in postoperative IIEF-EF according to the MCIDs criteria\(^{16}\) was also assessed. A secondary endpoint was to identify the clinical predictors of long-term post-HoLEP EF improvement or deterioration in the same cohort of patients.

### Statistical analysis

Clinical and sociodemographic characteristics of the patients are presented as means (medians; s.d.) and ranges. Descriptive statistics were used to analyze rates of pre- vs postoperative changes in IIEF-EF and IPSS. Differences in means and proportions were tested with the paired Student’s t-test, and the \(\chi^2\) test, respectively. Correlations were assessed using Spearman’s or Pearson’s method, whenever appropriate.

Univariable (UVA) and multivariable (MVA) linear and logistic regression models tested the association between predictors (for example, age, educational status, body mass index (BMI), CCI, preoperative IPSS and prostate volume) with EF improvement or deterioration at long-term FU. Statistical analyses were performed using SPSS statistical software, v 20.0 (IBM Corp, Armonk, NY, USA). All tests were two sided, with a significance level set at 0.05.

### RESULTS

Table 1 lists the socio-demographic and clinical characteristics of the entire cohort of patients. Preoperative and FU psychometric values are detailed in Table 2. Similarly, Table 2 also reports pre- and postoperative rates of ED severity according to Cappelleri’s classification criteria. At a mean FU of 152.1 months, patients showed a significant total IPSS improvement; a similar amelioration was observed for both storage and voiding symptoms (all \(P<0.01\)). A significant decrease in terms of mean IIEF-EF scores was observed at FU, with a mean delta of 3.9 (\(P<0.01\)). Fifty (37%) patients worsened by at least one IIEF-EF category. Conversely, 23 (17%) patients reported an improvement in postoperative IIEF-EF score. Overall, 75 (55.6%) patients maintained the same baseline IIEF-EF category, and 10 (7.4%) patients showed an improvement of at least one IIEF-EF category after surgery.

Age at survey was inversely correlated to IIEF-EF score at FU (\(r_\text{ho}: -0.25\); \(P<0.01\) (95% confidence interval (CI) \(-0.40, -0.086\)); indeed patients reporting a decrease in IIEF-EF scores were significantly older (68.7 (6.9) vs 65.3 (6.5) years; \(P=0.03\)) and showed a significantly longer mean FU (165.8 (86.4) vs 85.7 (82.4) months; \(P<0.01\)) compared to those reporting a postoperative improvement of IIEF-EF.

Table 2 also details IIEF-EF domain scores according to MCIDs criteria; overall, 9 (6.7%) patients had a postoperative MCID improvement of IIEF-EF.

At UVA, younger age, lower prostate volume, a higher preoperative IPSS score, and a lower baseline IIEF-EF score were positively associated with EF improvement after surgery (all \(P\leq 0.03\)) (Table 3). Similarly, at MVA, lower baseline IIEF-EF scores and higher baseline IPPS scores emerged as independent predictors of EF improvement at survey (all, \(P<0.03\)), whereas all other variables failed to predict improvement (Table 3).

### DISCUSSION

We tested long-term EF changes in a homogenous cohort of Caucasian-European men submitted to HoLEP for LUTS/BPH with a high-volume, fully trained surgeon. We found that long-term mean IIEF-EF scores were reduced after HoLEP, with up to 37% of patients reporting a worsening of their EF. Length of FU emerged as an independent predictor of this deterioration. Conversely, 17% of patients reported a long-term EF improvement, with nearly 7% of patients showing a clinically meaningful improvement of postoperative IIEF-EF. Patients with a significant improvement of IIEF-EF after HoLEP had a mean FU of almost 7 years. Of clinical importance, the higher the severity of baseline LUTS and ED, the greater the long-term postoperative IIEF-EF improvement.

Our interest was fueled by the existing controversies in terms of EF after surgery for LUTS/BPH.\(^5,9–12,20–22\) TURP is still considered the gold standard for the treatment of symptomatic BPH for prostates that do not exceed certain volumes.\(^5\) In this context, the multicenter American Urological Association Cooperative Study,
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Table 2. Preoperative and postoperative urinary symptoms and erectile function evaluation

<table>
<thead>
<tr>
<th></th>
<th>Preoperative assessment</th>
<th>Postoperative assessment</th>
<th>P-value* (95% CI)</th>
<th>Postoperative MCIDs improvements</th>
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<tbody>
<tr>
<td><strong>IPSS</strong></td>
<td></td>
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<tr>
<td>Mean (median; s.d.)</td>
<td>15.9 (16; 8.6)</td>
<td>5.4 (4; 5.4)</td>
<td>&lt; 0.01 (8.8–12.1)</td>
<td></td>
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<tr>
<td>Range</td>
<td>0–32</td>
<td>0–26</td>
<td></td>
<td></td>
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<tr>
<td>Storage symptoms</td>
<td></td>
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<tr>
<td>Mean (median; s.d.)</td>
<td>8.9 (8; 7.6)</td>
<td>3.3 (2; 3.5)</td>
<td>&lt; 0.01 (4.2–7)</td>
<td></td>
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<tr>
<td>Range</td>
<td>0–15</td>
<td>0–15</td>
<td></td>
<td></td>
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<tr>
<td>Voiding symptoms</td>
<td></td>
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<tr>
<td>Mean (median; s.d.)</td>
<td>10.6 (12; 5.4)</td>
<td>2.7 (1; 3.8)</td>
<td>&lt; 0.01 (6.7–9)</td>
<td></td>
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<tr>
<td>Range</td>
<td>0–20</td>
<td>0–18</td>
<td></td>
<td></td>
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<tr>
<td><strong>IIEF-EF score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean (median; s.d.)</td>
<td>23.1 (27; 8.8)</td>
<td>19.2 (23; 10.6)</td>
<td>&lt; 0.01 (2.4–5.4)</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0–30</td>
<td>0–30</td>
<td></td>
<td></td>
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<tr>
<td><strong>ED severity (N (%))</strong></td>
<td></td>
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</tr>
<tr>
<td>No ED</td>
<td>83 (61.5)</td>
<td>57 (42.2)</td>
<td>&lt; 0.01 (χ²: 9.3) (6.9, 31.1)</td>
<td></td>
</tr>
<tr>
<td>Mild ED</td>
<td>12 (8.9)</td>
<td>21 (15.6)</td>
<td>0.14 (χ²: 2.2) (−1.7, 15.1)</td>
<td>1 (0.7) 11 (8.6)</td>
</tr>
<tr>
<td>Mild-to-moderate ED</td>
<td>16 (11.9)</td>
<td>14 (10.4)</td>
<td>0.84 (χ²: 0.0) (−6.6, 9.6)</td>
<td>1 (0.7) 15 (11.1)</td>
</tr>
<tr>
<td>Moderate ED</td>
<td>8 (5.9)</td>
<td>7 (5.2)</td>
<td>0.99 (χ²: 0.0) (−5.5, 6.9)</td>
<td>2 (1.5) 6 (4.4)</td>
</tr>
<tr>
<td>Severe ED</td>
<td>16 (11.9)</td>
<td>36 (26.7)</td>
<td>&lt; 0.01 (χ²: 8.6) (4.9, 24.5)</td>
<td>5 (3.7) 11 (8.1)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ED, erectile dysfunction; IPSS, International Prostatic Symptom Score; IIEF-EF, International Index of Erectile Function-Erectile Function domain; MCIDs, minimal clinically important differences. *ED severity was categorized according to the classification suggested by Cappelleri et al.26 *P-value according to two-tailed independent t-test or the Mann-Whitney U-test, and the χ² tests, as indicated.

Table 3. Univariable (UVA) and multivariable (MVA) logistic regression models predicting either postoperative IIEF-EF improvement or deterioration

<table>
<thead>
<tr>
<th></th>
<th>IIEF-EF improvement</th>
<th>IIEF-EF deterioration</th>
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<tbody>
<tr>
<td></td>
<td>UVA</td>
<td>MVA</td>
</tr>
<tr>
<td></td>
<td>OR; P-value</td>
<td>OR; P-value</td>
</tr>
<tr>
<td>Age</td>
<td>0.92; 0.03</td>
<td>0.96; 0.40</td>
</tr>
<tr>
<td>BMI</td>
<td>1.08; 0.15</td>
<td>0.95; 0.64</td>
</tr>
<tr>
<td>CCI (0 vs ≥ 1)</td>
<td>1.42; 0.50</td>
<td>2.40; 0.25</td>
</tr>
<tr>
<td>Educational status (LL vs HL)</td>
<td>1.77; 0.49</td>
<td>2.7; 1.00</td>
</tr>
<tr>
<td>Length of FU</td>
<td></td>
<td></td>
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<tr>
<td>Baseline IIEF-EF</td>
<td>0.95; 0.03</td>
<td>0.88; &lt; 0.01</td>
</tr>
<tr>
<td>Baseline IPSS</td>
<td>1.08; &lt; 0.01</td>
<td>1.12; &lt; 0.01</td>
</tr>
<tr>
<td>Prostate volume</td>
<td>0.96; &lt; 0.01</td>
<td>0.13; 0.98</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; FU, follow-up; HL, high-level educational level; IIEF-EF, International Index of Erectile Function-Erectile Function domain; IPSS, International Prostatic Symptom Score; LL, low-level educational level; MVA, multivariable; OR, odds ratio; UVA, univariable.

based on data of 1000 men treated with TURP showed a postoperative ED rate of 13%.23 A review of 29 RCTs comparing TURP with less invasive approaches reported a 6.5% mean rate of post-TURP ED, but this data was not based on standardized questionnaires.24 Conversely, Leleifeld et al.9 did not report changes of sexual functioning in up to 84% of 670 patients at 9 months after either TURP, finasteride treatment, or watchful waiting. More recently, Choi et al.25 retrospectively evaluated IIEF-EF data from 108 patients treated with TURP and found no statistically significant decrease in terms of post- vs preoperative EF, with an IIEF-EF improvement in 14% of the patients. Dealing with theoretically less invasive methods, for instance Guo and Jin26 reported that patients with prostate volumes ≥ 70 ml had a worsening of the IIEF-5 score at 12 and 24 months after photoselective vaporization of the prostate (PVP), whereas Bruyere et al.4 reported that post-PVP sexual function was unchanged.

The results on sexual function outcomes assessed after HoLEP are not different from other BPH surgery series.2–5,15,20,27–29 In a prospective randomized trial with almost 7 years of FU, Gilling et al.4 reported that there was no significant difference in IIEF scores between patients submitted to TURP or HoLEP, although the analyses lacked a preoperative EF assessment. Similarly, Kuntz et al.15 found no differences in a cohort of 100 patients randomized to either TURP or HoLEP at a 12 months FU, with 11.2% and 10.5% of patients reporting decreases in potency after HoLEP and TURP, respectively.
To the best of our knowledge, we report for the first time real-life post-HoLEP long-term EF outcome data. One strength of this study is that the data originated from a single institute survey with a relatively large cohort of homogeneous, same-race patients for whom all surgical procedures and psychometric evaluations were performed using a consistent method. The major findings of the present study are that (1) mean IIEF-EF domain scores significantly decreased several months after HoLEP, although 63% of patients did not show a worsening of ED severity according to Cappelleri’s categories; (2) however, an improvement of EF was observed in 17% of patients with a mean FU of 7 years; (3) finally mean IPSS scores revealed no LUTS symptoms even after such a long FU.

From a naturalistic perspective, a deterioration of erectile functioning could be at least partially expected so long after surgery. In this context, we observed that patients with a worsened IIEF-EF were significantly older and had a longer mean FU. Conversely, such a significantly consistent lack of long-term storage/voiding symptoms clearly emerges as a clinical success, a finding which should be carefully considered in daily clinical practice.

As a further major finding, baseline severity of LUTS and ED emerged as independent predictors of long-term postoperative EF improvement. As a whole, these findings support the concept of potential sexual function improvements as the result of a satisfactory BPH/LUTS treatment. In this regard, a number of studies support a common ageing-related incidence of ED and LUTS/BPH.5,10,31 Recently Seftel et al. reviewed data from 23 epidemiologic studies correlating BPH/LUTS and ED, showing that one third of men >50 years complained of concomitant ED and LUTS/BPH.30 Therefore, although we certainly admit that a 12-year FU could not represent a correct time frame to assess postoperative EF, we could argue that a IIEF-EF score improvement even after such a long postoperative time frame may become even more clinically relevant.

MCIDs criteria were applied for the first time to identify patients who actually perceived a beneficial EF improvement.16 In this context, almost 7% of patients had a clinically meaningful EF improvement after surgery. A potential improvement in EF after surgery has been previously reported in literature;26,27 in a 6-month FU survey with a non-validated questionnaire which investigated libido, potency and sexual satisfaction, Jeong et al.5 reported a significant improvement in the number of early morning erections, a finding which the authors attributed to the concomitant amelioration of sleep quality due to the reduction of nocturia. Similarly, Meng et al.27 reported that HoLEP did improve the ability to have early morning erections in patients treated for LUTS/BPH. Moreover, in a cohort of 60 patients evaluated with the Male Sexual Health Questionnaire (MSHQ) 6 months after HoLEP, a significant improvement in sexual satisfaction was correlated with the improvement of LUTS after surgery,28 thus corroborating previous findings showing a postoperative IIEF-EF improvement, albeit non significant, with a positive linear correlation between the improvement of IPSS and QoL scores and EF findings.2

We examined baseline clinical variables potentially associated with an EF improvement; in the current series, the more severe the baseline LUTS, the more significant the increase in postoperative IIEF-EF domain scores. Even more clinically relevant, patients with the lowest baseline IIEF-EF scores achieved the highest scores postoperatively. The practical consequence of these results in the real-life setting would be that patients with the worst baseline clinical characteristics (that is, severe LUTS/BPH, and severe ED) would likely benefit most from HoLEP in terms of both LUTS resolution and EF improvement.

Our study is not devoid of limitations. First, although the study provides absolutely original results in showing that the severity of preoperative EF is significantly associated with long-term EF improvement in men undergoing HoLEP, the lack of dedicated prospective functional time-to-time assessment throughout the postoperative period could limit the significance of reported data. Similarly, although data collection was done in an adequate setting, it is not possible to completely eliminate the possibility that the authors’ expectations could have, in some way, influenced patient reports. Third, the number of patients included is likely too small to provide any conclusive answer in terms of the impact of BPH surgery on EF outcomes. Therefore, while the current findings may be representative of this cohort of same-race heterosexual men, they certainly deserve external validation with a larger independent sample. Fourth, this particular study lacks the observation of both EF and ejaculatory/organic outcomes at more points in time, data that would allow us to determine if the current findings are reliable and reproducible. Likewise, a penile doppler ultrasound assessment could have improved our findings to objectively interpreting erectile functioning both at baseline and over the FU period. Furthermore, our study lacks data on chronic medical therapy which could be potential predictors of changes in sexual functioning at long-term FU.

As a whole, these preliminary naturalistic data are useful for appropriately designing a longitudinal study whose findings would translate into knowledge that could be clinically applied to patient care and aid in decision making.

Our study confirmed that HoLEP for LUTS/BPH may be associated with a decrease in long-term postoperative EF at a long-term evaluation. Conversely, the current findings provide novel evidence showing that the severity of baseline LUTS and ED may account for a clinically meaningful improvement in long-term postoperative EF after HoLEP. Therefore, these results suggest that patients with severe LUTS, which could also negatively interfere with their sexual functioning, would probably benefit most from HoLEP in terms of clinically significant EF improvement, regardless of their age, even many years after BPH surgery. Additional prospective studies in larger population-based cohorts are certainly needed to confirm these results.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES


