Evaluation of Holmium Laser Enucleation of the Prostate Learning Curves with and without a Structured Training Programme

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Key Words
Benign prostatic hyperplasia • Learning curve • Holmium laser enucleation of the prostate • Lower urinary tract symptoms

Abstract

Background/Aims: To evaluate perioperative parameters, early functional outcomes, and the safety profile of holmium laser enucleation of the prostate learning curves with and without mentoring. Methods: The learning curves of 2 surgeons of their first 100 consecutive patients treated with holmium laser enucleation of the prostate were retrospectively analyzed. We analyzed demographic parameters, clinical outcomes, adverse events, and the progress during each learning experience. Results: The only statistically significant differences between the two learning curves were found for operation time (138.2 ± 60.7 vs. 98.2 ± 37.7 min; p < 0.001) in favor of the supervised approach, the total weight of resected prostatic tissue (81.5 ± 50.5 vs. 65.0 ± 6.7 g; p < 0.001) with more tissue removal by the surgeon without guidance, and the perioperative hemoglobin drop (1.9 ± 1.4 vs. 1.1 ± 1.0 g/dl; p < 0.001) in favor of the learning curve with a training programme. In multivariate logistic regression, the time factor was independently associated with a higher drop in hemoglobin levels (OR 1.015; 95% CI 1.000–1.023; p = 0.001). The improvements of clinical outcomes as determined by International Prostate Symptom Score, quality of life, peak urinary flow rate and postvoid residual volume were comparable. After the first 50 procedures the mean operation time significantly improved from 147 to 107.5 minutes for the learning curve without supervision (p < 0.001), whereas the surgical time was consistent throughout the 100 cases with a mentoring programme. The overall incidence of treatment-related adverse events was significantly higher without the training programme (16 vs. 5%; p = 0.008). Conclusions: Our study clearly showed the benefits of a structured training programme to overcome the steep learning curve.

Introduction

Holmium laser enucleation of the prostate (HoLEP) has become more than just a household name in the repertoire of surgical treatment options for male lower urinary tract symptoms (LUTS) due to benign prostatic obstruction (BPO). Its efficacy and safety are well doc-
HoLEP has become an integral part of international guideline recommendations [4]. In this rapidly advancing field of treatment modalities, HoLEP has more and more gained the top position, and some even consider it the new gold standard [5–8]. Compared to standard procedures such as transurethral resection of the prostate (TURP) or open prostatectomy, HoLEP was shown to be at least equally effective and durable, but with obvious advantages including shorter hospital stay, reduced bleeding complications, and shorter catheterization time [9, 10]. The initial economic burden for the technical equipment is significant, but the favourable safety profile, affordable low-power systems, and available reusable fibres make it a cost-effective investment. Indeed, taking all the positive aspects into account, HoLEP deserves to be considered the new gold standard. But, why is it still not the most commonly used technique?

One of the main obstacles to overcome is the notorious learning curve. Although urologists may be well experienced with standard transurethral procedures such as TURP, they are hesitant to venture upon the new technique. The perception is that HoLEP is a challenging and tough procedure to learn. Surgeons might be concerned in harming the patient during the first steps.

The main objective of the current study was to evaluate perioperative parameters, the early functional outcomes, and the treatment-related complications recorded for the learning curves of the first 100 consecutive HoLEP patients. One surgeon started without any guidance or assistance, while the other passed through a curriculum under supervision.

**Material and Methods**

**Study Design and Surgical Procedures**

In the current study the learning curves of 2 surgeons were evaluated. Both surgeons were well experienced with endoscopic procedures, performing more than 150 TURPs per year. At our institute the first 100 consecutive patients undergoing surgical treatment of LUTS due to BPO of each surgeon were retrospectively analyzed. Surgeon 1 (P.W.) learned the HoLEP procedure without any mentoring and after completing his first 400 interventions, he trained surgeon 2 (G.M.). The first 100 patients treated by surgeon 1 were enrolled from May 2015 until January 2016 and the first 100 consecutive cases of surgeon 2 were treated from January 2017 until August 2017. The three-lobe technique was always conducted. The curriculum (fig. 1) developed for training consisted of 50 interventions based on 3 steps, always under supervision of the experienced surgeon. Surgeon 2 started with 10 cases of the middle lobe preparation (step 1), followed by 20 interventions including the lateral lobe enucleation (step 2), and finally, 20 further surgeries training the ventro-apical dissection of the adenoma (step 3). Surgeon 2 performed all morcellations starting from the very first case. After surgeon 2 had finished the learning objective of each step, surgeon 1 completed the procedure. After the first 50 procedures, surgeon 2 performed independently in all following cases. In that way, the progress and benefits made through the training process may be considered more conclusive.

![Structured training programme used in the study.](image)
of 53 Hz and a power setting of 1.2 kJ. Morcellation was carried out using the Piranha morcellator system (Richard Wolf GmbH, Knittlingen, Germany). Both participating surgeons used the same equipment.

### Parameters

The early functional outcomes after 4 weeks were compared to the preoperative levels. We evaluated prostate volume (PV; ml) determined by transrectal ultrasound (TRUS), International Prostate Symptom Score (IPSS), quality of life (QoL), peak urinary flow rate (Qmax; ml/s), postvoid residual urine volume (PVR; ml), complete surgical time (min), resected prostate weight (g), resected tissue relative to preoperative PV measured by TRUS (%), and hemoglobin loss (g/dl). The short-term LUTS improvements and functional outcomes were determined 4 weeks after surgery, whereas the perioperative technical parameters were measured in the operating room directly after surgery. The drop in hemoglobin levels was studied 24 hours after the intervention. The tissue retrieval percentage (%) was defined as the proportion of removed tissue relative to the PV as determined by TRUS prior to surgery. The total mean operation time was defined as the start of the procedure to completion by the placement of the catheter after surgery. Demographic parameters included age, body mass index (BMI), and total serum prostate-specific-antigen (PSA; ng/ml; Elecsys® Assay, Roche Diagnostics GmbH, Mannheim, Germany). Treatment-related adverse events (AE) were classified according to the Clavien-Dindo classification [11].

### Statistical Analysis

The first 100 consecutive HoLEP patients of surgeon 1 and 2 were retrospectively evaluated. For descriptive statistics, continuous variables were presented as the mean ± SD, and categorical variables were presented as percentages or absolute numbers. Univariate analysis were performed using the Fisher’s exact test, t test, and Mann-Whitney U test for categorical variables and continuous variables, respectively. Normal distribution of variables was determined with the Shapiro-Wilk test. A Spearman’s rank-order correlation test was run to determine the relationship between outcomes. Multivariate logistic regression analysis was performed on perioperative parameters to identify potential predictors associated with elevated blood loss. A p-value < 0.05 was considered statistically significant. All calculations were carried out using SPSS Statistics software, version 25.0 (SPSS, Chicago, IL, USA).

### Results

#### Baseline Characteristics

We retrospectively reviewed the charts of the first 100 patients of each surgeon. Patient baseline characteristics are displayed in table 1. The 2 cohorts were comparable. The mean PV for surgeon 1 was 97.4 ± 36.0 ml (range

### Table 1. Baseline characteristics

| Variables                  | Surgeon 1 (n = 100) | Surgeon 2 (n = 100) | p    |
|----------------------------|---------------------|---------------------|------|
| Age, years                 | 71.9 (6.5)          | 69.1 (8.3)          | 0.076|
| Mean (SD)                  | 56–87               | 48–86               |      |
| Range                      | 27.9 (4.2)          | 26.4 (3.6)          | 0.108|
| BMI, kg/m²                 | 20.4–39.9           | 19.9–37.3           |      |
| Mean (SD)                  | 19.2 (6.9)          | 17.8 (6.7)          | 0.261|
| Range                      | 3–35                | 2–32                |      |
| IPSS                       | 3.6 (1.3)           | 3.6 (1.6)           | 0.297|
| Mean (SD)                  | 0–6                 | 0–6                 |      |
| PV, ml                     | 97.4 (36.0)         | 90.6 (31.2)         | 0.361|
| Mean (SD)                  | 40–207              | 40–200              |      |
| Total PSA, ng/ml           | 8.7 (7.9)           | 7.8 (6.7)           | 0.533|
| Mean (SD)                  | 0.8–35.4            | 0.4–36.9            |      |
| Qmax, ml/s                 | 13.6 (10.2)         | 12.5 (6.8)          | 0.861|
| Mean (SD)                  | 1–50                | 3–36                |      |
| PVR, ml                    | 113.9 (112.9)       | 115.3 (133.7)       | 0.685|
| Mean (SD)                  | 0–600               | 0–700               |      |

### Table 2. Peri- and post-operative outcome parameters

| Clinical Outcomes          | Surgeon 1 (n = 100) | Surgeon 2 (n = 100) | p    |
|----------------------------|---------------------|---------------------|------|
| IPSS                       | 8.3 (8.2)           | 10.0 (8.4)          | 0.261|
| Mean (SD)                  | 13–30               | 8–27                |      |
| Range                      | 2.2 (2.1)           | 2.8 (3.6)           | 0.119|
| QoL                        | 2–6                 | 1–6                 |      |
| Resected tissue, g         | 81.5 (33.8)         | 65.0 (6.7)          | <0.001*|
| Mean (SD)                  | 24–215              | 14–151              |      |
| Resected tissue, %         | 81.2 (50.5)         | 83.0 (50.0)         | 0.281|
| Mean (SD)                  | 15.6–337.5          | 11.6–337.5          |      |
| Time, min                  | 138.2 (60.7)        | 98.2 (37.7)         | <0.001*|
| Mean (SD)                  | 52–323              | 49–315              |      |
| Hemoglobin drop, g/dl      | 1.9 (1.4)           | 1.1 (1.0)           | <0.001*|
| Mean (SD)                  | 0.3–6.5             | 1.6–4.5             |      |
| Qmax, ml/s                 | 9.6 (15.3)          | 13.1 (10.1)         | 0.334|
| Mean (SD)                  | 27–43               | 2–33                |      |
| PVR, ml                    | 102.2 (114.4)       | 102.3 (129.7)       | 0.654|
| Mean (SD)                  | 50–600              | 70–600              |      |

*p < 0.05.
40–207 ml) and the mean PV of the patient group treated by surgeon 2 was 90.6 ± 31.2 ml (range 40–200 ml) (p > 0.05). The means for patient age were 71.9 ± 6.5 years (range 56–87 years) and 69.1 ± 8.3 years (range 48–86 years), and the mean BMI in the 2 cohorts were 27.9 ± 4.2 kg/m² (range 20.4–39.87 kg/m²) and 26.4 ± 3.6 kg/m² (range 19.9–37.33 kg/m²), respectively (both; p > 0.05). The means for IPSS were 19.2 ± 6.9 (range 3–35) and 17.8 ± 6.7 (range 2–32) and the means for QoL were 3.6 ± 1.3 (range 0–6) and 3.6 ± 1.6 (range 0–6), respectively (both; p > 0.05). No significant difference was found for preoperative functional parameters including Qmax (13.6 ± 10.2 vs. 12.5 ± 6.8 ml/s) and PVR (113.9 ± 112.9 vs. 115 ± 133.7 ml) (both; p > 0.05). The means for total PSA were 8.7 ± 7.9 ng/ml (range 0.8–35.4 ng/ml) and 7.8 ± 6.7 ng/ml (range 0.4–36.9 ng/ml), respectively (both; p > 0.05).

**Learning Curves with and without Mentoring**

Perioperative and functional postoperative outcomes of the first 100 cases of each surgeon were evaluated and compared (table 2). The total mean operation time was significantly longer for surgeon 1 with 138.2 ± 60.7 min (range 52–323 min) compared to the duration of 98.2 ± 37.7 min (range 49–315 min) for surgeon 2 (p < 0.001). With the mean of 81.5 ± 50.5 g (range 24–215 g) surgeon 1 removed more prostatic tissue than surgeon 2 (mean 65.0 ± 6.7 g; range 14–151 g) (p < 0.001). But, when the percentage of the resected tissue was analyzed in relation to the preoperative PV, no statistically significant difference was observed. The tissue retrieval percentage was 81.2 ± 50.5 and 83.0 ± 50%, respectively (p > 0.05). After the intervention, the hemoglobin levels were measured to evaluate the blood loss during intervention. Patients treated by surgeon 1 showed a mean loss of 1.9 ±
1.4 g/dl (range 0.3–6.5 g/dl), whereas the learning curve with mentoring revealed a significantly reduced loss of 1.1 ± 1.0 g/dl (range 1.6–4.5 g/dl) (p < 0.001). We ran a Spearman’s rank-order correlation test to determine the relationship between surgical time and blood loss. There was a weak, positive correlation, which was of statistical significance (rs = 0.205, p = 0.004). In multivariate logistic regression, we analyzed the association of resected prostate tissue and surgery time with the blood loss. Only the time factor was independently associated with a higher drop in hemoglobin (OR 1.015; 95% CI 1.000–1.023; p = 0.001).

The early functional outcomes were evaluated 4 weeks after treatment. This included improvements in IPSS, QoL, Qmax, and PVR. No significant differences could be identified between the 2 cohorts in the direct comparison. IPSS was reduced by 8.3 ± 8.2 (range 13–30) and 10.0 ± 8.4 (range 8–27), respectively (p > 0.05). QoL improved in the patient group of surgeon 1 by 2.2 ± 2.1 (range 2–6) and for surgeon 2 by 2.8 ± 3.6 (range 1–6) (p > 0.05). Qmax increased by 9.6 ± 15.3 ml/s (range 27–43 ml/s) and 13.1 ± 10.1 ml/s (range 2–33 ml/s), respectively (p > 0.05). The reductions of PVR were 102.2 ± 114.4 ml (range 50–600 ml) for surgeon 1 and 102.3 ± 129.7 ml (range 70–600 ml) for the surgeon under supervision (p > 0.05).

**Progress During the Learning Curve with and without Mentoring**

Next, our objective was to investigate the progress between the 2 approaches. We analyzed the first 50 patients and the second 50 patients treated by each surgeon for their differences in perioperative and functional outcomes (fig. 2–4). The learning curve without mentoring

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**Fig. 3.** Progress during the learning curve with structured training programme for the first and second 50 cases.
revealed only a significant longer operation time in the beginning (fig. 2). The median surgery time was 147 min (IQR 112.75–205 min) compared to 107.5 min (IQR 79.25–126 min) (p < 0.001). Median changes in IPSS (6.0 vs. 8.0), QoL (2.0 vs. 2.0), desobstruction rate (82.8 vs. 77.25%), blood loss (1.9 vs. 1.7 g/dl), Qmax (7.5 vs. 8.0 ml/s) and PVR (76.5 vs. 78.5 ml) were not significantly different for the first and second parts (all; p > 0.05).

Surgeon 2 who underwent a structured curriculum was consistent throughout his learning curve. All investigated parameters showed no relevant changes between the first 50 and the last 50 patients (fig. 3). The mean changes of IPSS (8.5 vs. 10.0), QoL (3.0 vs. 3.0), operation time (81.0 vs. 95.0 min), enucleation rate (66.4 vs. 62.5 %), hemoglobin drop (0.8 vs. 1.0 g/dl), Qmax (11.5 vs. 11.0 ml/s), and PVR (60.0 vs. 60.0 ml) were comparable (all; p > 0.05). The temporal progress based on total surgical time showed that surgeon 1 reached a plateau phase around the 50th case, whereas surgeon 2 was consistent throughout his first 100 surgeries (fig. 4).

**Adverse Events**

The overall incidence of treatment-related AE was significantly different between the 2 groups. The safety assessment demonstrated fewer complications for the trained surgeon with an incidence of 5% compared to 16% for surgeon 1 (p = 0.008) (table 3). It is important to stress that 13 out of 16 (81%) and 3 out of 5 (60%) AE were Clavien-Dindo grade ≥ 2 for surgeon 1 and 2, respectively. Especially Clavien-Dindo 3 AE occurred more frequently for the surgeon without mentorship (8 vs. 1%; p = 0.035). The complications requiring intervention included urinary retention (n = 3), clot retention (n = 2), bleeding (n = 2) and 1 case of an early urethral stricture. Most of these complications were observed in the first 50 consecutive cases in each group. No significant difference of incidence between the surgeons was
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Table 3. Overall treatment related AEs according to the Clavien-Dindo classification without (surgeon 1) and with training programme (surgeon 2)

| Clinical Outcomes | Surgeon 1 (n = 100) | Surgeon 2 (n = 100) | p |
|-------------------|---------------------|---------------------|---|
| Overall AEs, n (%)| 16 (16%)            | 5 (5%)              | 0.008* |
| Clavien-Dindo I, n (%)| 3 (3%)             | 2 (2%)              | 1.000 |
| Urinary retention | 1                   | 2                   | 0.621 |
| Macrohematuria    | 1                   | 0                   | 1.000 |
| Bladder injury    | 1                   | 0                   | 1.000 |
| Clavien-Dindo II, n (%)| 3 (3%)           | 1 (1%)              | 0.621 |
| Clot retention    | 3                   | 1                   | 0.621 |
| Clavien-Dindo III, n (%)| 8 (8%)          | 1 (1%)              | 0.035* |
| Clavien-Dindo IIIa| 0                   | 0                   | 0.035* |
| Clavien-Dindo IIIb| 8                   | 1                   | 0.246 |
| Urinary retention | 3                   | 0                   | 0.498 |
| Clot retention    | 2                   | 0                   | 1.000 |
| Bleeding          | 2                   | 0                   | 1.000 |
| Urethral stricture| 1                   | 1                   | 1.000 |
| Clavien-Dindo IV, n (%)| 2 (2%)         | 1 (1%)              | 1.000 |
| Urosepsis         | 1                   | 1                   | 1.000 |
| Circulatory failure| 1                   | 0                   | 1.000 |

*p < 0.05.

identified for their first and second 50 cases (table 4). Strikingly, after completing the training programme no AE were recorded for surgeon 2.

Discussion

The role of HoLEP among the treatment modalities for male LUTS due to BPO is beyond any controversy due to the plethora of positive clinical studies. It is on its way to becoming the new reference method for prostates of any size [6]. Nevertheless, there is still a considerable reservation among urologists to introduce this procedure owing to the prevailing experience made in some clinical studies. The HoLEP learning curve is known to be steep and even advanced expertise in the field of transurethral procedures will not prevent a prolonged operation time and the difficulties of the first enucleation attempts [3, 9, 10, 12–14]. Evaluations of the HoLEP learning curve suggest 20–30 cases with mentoring and about 50 cases without proper instructions to become comfortable with the technique [3]. The efficiency rates for enucleation and morcellation were reported to reach a plateau after the first 50 procedures [13, 14]. This was also confirmed by the results of the current analysis. However, in our series we additionally demonstrated that undergoing a structured training programme, perioperative parameters including the duration of the intervention can be maintained on a constant level. Especially safety issues that are associated with HoLEP can be reduced to a minimum from the very beginning of the learning process. This is a welcome prospective when venturing on a new surgical technique.

In a multicentre prospective analysis of the learning progress 3 out of 9 participating institutions abandoned HoLEP because of complications [15]. Reasons for unsuccessful interventions comprised a prolonged operation time, conversion to TURP, incomplete morcellation, a significant distress level of the surgeon, or technical difficulties during the procedure. The most severe Ho-LEP-specific complication that might occur during the first step is bladder injury during morcellation. Short-term complications including acute urinary retention, catheterization, clot retention, short-term re-intervention, postoperative urinary tract infections, storage symptoms, and urethral strictures are not significantly different compared to TURP. As mentioned above, a better hemostatic control, a shorter hospital stay, and a shorter catheterization time are associated with HoLEP in comparison to TURP or open prostatectomy [9].

In the current study, perioperative relevant differences between the 2 surgeons were identified as operation time and the drop in hemoglobin levels. With a mean time of 138.2 min, the surgeon without assistance needed about 40% more time for the complete intervention than the surgeon under supervision. But after the first 50 procedures the median operation time significantly improved from 147 to 107.5 min for the next 50 cases, whereas with a mentoring programme the surgical time was consistent throughout the 100 cases. Completion of about 50 cases was required to reach a plateau phase in terms of surgical time. A significant drop of 1.9 g/dl in hemoglobin levels was also observed for the learning curve without supervision, which exceeded the mean blood loss of 1.1 g/dl determined for the surgeon with a proper instructor. Both observations suggest that a prolonged operation time leads to an increasing blood loss. This correlation was statistically confirmed, but on this small scale it may not be considered clinically relevant. Thus, none of the patients included in this analysis received a blood transfusion. The short-term functional assessment including IPSS, QoL, Qmax, and PVR clearly demonstrated that the clinical outcome was comparable between the two learning curves. This was also confirmed for the progress during both learning curves for the first 50 cases and the second 50 cases. This is an important finding. An
A structured training programme. Despite a steeper learning experience without proper instructions, the functional outcomes were equally improved. However, a favorable safety profile can only be preserved with a clearly defined patient selection is needed. One major limitation of this analysis is that we present only short-term outcomes. The long-term evaluation is still ongoing. Another limitation is that we do not present efficiency rates for enucleation and morcellation, as is standard in a learning curve analysis. The reason for this omission is that the times for enucleation and morcellation were not documented for the first learning curve. Here, the overall incidence was 5% for the first 100 consecutive cases and no relevant AE was recorded after 50 completed procedures.

Certain limitations of this study need to be acknowledged. Obviously, this is a retrospective, single-centre analysis evaluating the learning curves of 2 surgeons. The presented 3-step programme and the number of cases for each learning unit were determined according to the experience made by the first surgeon, who started HoLEP in our department without supervision. We believe that it should be widely useful and generally applicable, but the validation of this training programme was not the scope of this analysis. Of course, other forms of a curriculum will definitely work as well. To answer the question about the most efficacious training programme, a prospective study design including more surgeons, various approaches, and a clearly defined patient selection is needed. One major limitation of this analysis is that we present only short-term outcomes. The long-term evaluation is still ongoing. Another limitation is that we do not present efficiency rates for enucleation and morcellation, as is standard in a learning curve analysis. The reason for this omission is that the times for enucleation and morcellation were not documented for the first learning curve. Obviously, these parameters will provide a more profound and detailed analysis. But the observation that the enucleation efficiency rates become better over time was confirmed in almost every study investigating the HoLEP learning curve, and this is also suggested by our results, which recorded the complete procedure. Finally, comorbidities and medications of enrolled patients were not part of our analysis. This additional information might reveal the potential impact of both aspects on relevant learning curve outcomes such as the drop of hemoglobin during surgery.

Here, our main objective was to identify the true benefits of a structured training programme. Despite a steeper learning experience without proper instructions, the functional outcomes were equally improved. However, a favorable safety profile can only be preserved with a structured training programme.
Conclusions

HoLEP has the potential to be considered the new gold standard, as its safety and efficacy are well documented. The notorious learning curve associated with HoLEP is still one of the main reasons for the considerable reservation among urologists to learn the technique. Our study clearly speaks in favor of a mentoring programme to overcome the steep learning curve.

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