PREDICTORS OF ENUCLEATION AND MORCELLATION TIME DURING HOLMIUM LASER ENUCLEATION OF THE PROSTATE

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Abstract

Objectives: To examine predictors of enucleation and morcellation time within a large cohort of men undergoing HoLEP for benign prostatic hypertrophy.

Methods: Pre-operative, peri-operative, and post-operative clinical characteristics were available from men treated with HoLEP between 1998 and 2013 at Indiana University Health Methodist Hospital. Stepwise linear regression was performed to determine clinical variables which are associated with enucleation and morcellation times.

Results: We identified 960 patients who underwent HoLEP. Average (range) enucleation time was 65.7 (11-245) minutes and morcellation time was 19.7 (3-260) minutes. History of anticoagulation was associated with a small decrease in enucleation time ($p=0.013$) while increasing HoLEP specimen weight was associated with increasing enucleation time ($p<0.001$). History of intermittent catheterization, urinary tract infections, presence of dense prostatic tissue (colloquially referred to as "beach balls"), and increasing specimen weight were associated with increasing morcellation time ($p<0.05$ each). Having HoLEP performed by a less experienced urologist was associated with longer enucleation and morcellation times.

Conclusions: Prostate volume is significantly associated with increased enucleation and morcellation times during HoLEP. Additionally, history of UTI and CIC are associated with modest increases in enucleation and morcellation times. Dense enucleated prostate tissue significantly impacts the ability to morcellate effectively. Increasing surgeon experience can significantly improve both enucleation and morcellation efficiency.

Introduction

Since its introduction in the late 1990s[1], holmium laser enucleation of the prostate (HoLEP) has increased in popularity for management of benign prostatic hyperplasia (BPH). Evidence suggests that HoLEP provides superior outcomes compared to TURP and open simple prostatectomy in men with BPH, regardless of prostate size[2-5]. Additionally, a recent study found that HoLEP is associated with decreased hospital costs compared to open prostatectomy.[6]

Performance and efficiency of HoLEP relies on two critical steps—transitional zone enucleation followed by tissue morcellation. Enucleation and morcellation times are dependent upon a number of factors including prostatic volume, as well as tissue quality. Because a steep learning curve and the potential for long operative times with HoLEP are common criticisms of the procedure, we sought to evaluate pre-HoLEP variables that may impact both enucleation and morcellation times during surgery.

Materials and methods

Patients, outcomes, and variables

After obtaining Institutional Review Board (IRB) approval (Protocol #1010002242), we conducted a retrospective cohort analysis using the prospectively collected IU Health Methodist Hospital database to identify patients who underwent HoLEP between 1998 and 2013. The primary outcomes of interest were enucleation and morcellation times. Variables included in the analysis were age, pre-HoLEP PSA, history of 5-alpha reductase inhibitor (5ARI) or alpha blocker therapy, history of urinary retention, history of recurrent urinary tract infections (UTI), history of anticoagulation, transrectal ultrasound (TRUS) prostate volume, final pathological HoLEP specimen weight (<30g, 30-100g, 100-150g, and >150g), presence of prostatic malignancy in HoLEP specimen, and surgeon experience (experienced vs. less experienced). The majority of surgeries were performed by a single experienced surgeon (JEL) who has performed over 2,000 HoLEP operations at IU Health Methodist Hospital. The remaining HoLEP cases were performed by six surgeons, all with less than 100 procedures on record at our hospital. Patients who did not have a recorded pre-HoLEP PSA, pertinent medical history details (variables included in the regression), pathologic details, and enucleation or morcellation times were excluded (n=560). There were no statistical differences in pre-operative PSA (when available) between the patients included in and excluded from the study.

Description of procedure

Using a 100 W Ho:YAG laser source, configured with a 550-nm end-fire laser fiber, the HoLEP procedure was performed as previously described[7]. A 28 F continuous-flow resectoscope (Karl Storz Endoscopy, Culver City, CA, USA) with a laser bridge housing a 7 F stabilizing catheter (Cook Urologic, Spencer, IN, USA) was used to enucleate the prostate. Normal saline was used as the irrigant in all cases. Briefly, the enucleation requires laser settings of 2 J and 40-50 Hz for the lateral lobes, 2 J and 20 Hz for the apical dissection, and 2 J and 20 Hz to divide the apical mucosal bridges.

Tissue morcellation was achieved using a Lumenis VersaCut™ tissue morcellator (Lumenis Ltd, Yokneam, Israel) introduced through a Storz nephroscope. Dual irrigation is used to keep the bladder full and to improve visualization. Irrigation was placed approximately 24-30 inches above the level of the bladder. Unusually tough prostatic tissue (termed "beach balls") may occasionally be encountered during enucleation which can prolong morcellation time.

Often these “beach balls” can be refractory to traditional morcellation techniques. When encountered, management options include removing pieces with grasping forceps, exchanging morcellation blades, and lasering into smaller pieces to facilitate engagement into the morcellator. As a last resort, a small cystotomy can be performed to remove residual tissue.

Statistical analyses

In order to identify potential predictors of enucleation time and morcellation time, separate forward and backward stepwise linear regression models were performed using $p<0.2$ as our criteria for model inclusion. All variables included in the descriptive analysis were included in the initial stepwise linear regression models and only variables that were identified as significant ($p<0.2$) were included in the final presented multiple linear regression models. *A priori* $p<0.05$ was set as the threshold for statistical significance for the final multiple linear regression models. All statistical analyses were performed using Stata version 13.0 (Statacorp, College Station, TX).

Results

Clinical pre-operative, peri-operative, and post-operative characteristics of our patient cohort are shown in Table 1. There were a total of 960 patients with an average age of 70 years. The majority of patients had a history of either 5ARI and/or alpha blocker therapy (79%). Twenty-six percent had urinary retention at the time of HoLEP (Table 1). Nearly 90% of HoLEPs were performed by a single surgeon. Mean enucleation time was 66 minutes while mean morcellation time was 20 minutes. Enucleation rates varied significantly between experienced and less experienced surgeons with enucleation rates of 1.46g/min (0.9) for experienced and 0.77g/min (0.6) for less experienced surgeons ($p<0.001$). Similar findings were observed for morcellation rate with 5.45g/min for experienced and 4.21g/min for less experienced surgeons ($p<0.001$). Of note, among cases where prostate "beach balls" were mentioned in the operative report (n=34, 3.5%), the average morcellation time was 51.4 minutes compared with 18.5 minutes in non-"beach ball" patients ($p<0.001$).

Enucleation time

Variables identified from the stepwise linear regression models as being associated with enucleation time included urinary retention, history of UTI, history of anticoagulation, HoLEP specimen weight, presence of "beach balls" in operative report, and surgeon experience (Table 2). In the final model, history of anticoagulation was associated with a five minute decrease in enucleation time ($p=0.024$). Less experienced surgeons had an estimated 21 minute increase in enucleation time ($p<0.001$). Compared with specimen weight of <30g, each progressive specimen weight category was associated with significant increases in enucleation time ranging from 18 to 40 minutes (Table 2).

Morcellation time

Variables identified from the stepwise linear regression models as being associated with morcellation time included history of 5ARI therapy, history of UTI, HoLEP specimen weight, presence of "beach balls", and experience of the surgeon (Table 3). In the final multiple linear regression model, history of UTI was associated with a significant increase in morcellation time by 2.5 minutes. Adjusting for the other covariates in the model, presence of "beach balls" conferred a 25 minute increase in morcellation time. Additionally, increasing HoLEP specimen weight conferred a 9-40 minute increase in morcellation time (Table 3).

Discussion

Considerable level one evidence has demonstrated the benefits of HoLEP over simple prostatectomy and TURP for the treatment of BPH in large glands[8-14]. Amongst established benefits of HoLEP are its long term, durable, and reproducible results that can be applied to any prostate gland size[12,15,16]. A frequently reported criticism of HoLEP is the length of the procedure, as well as the steep learning curve associated with surgical efficiency. Thus, understanding patient and tissue variables that may impact operative time may assist in patient counseling, scheduling of efficient OR time, and proper patient selection for surgeons in various stages of experience.

Enucleation involves complete removal of the transitional zone of the prostate using a holmium-YAG laser. This is not a vaporization procedure but rather the laser is used as a cutting tool. Enucleation time largely depends upon prostate size, configuration, and visualization. Similarly, morcellation time is impacted both by enucleation volume and visualization. As such, it is not surprising that HoLEP specimen weight was associated with significant increases in enucleation and morcellation time. Multiple previous studies have suggested this relationship with many further reporting that HoLEP operative efficiency increases with larger prostate volumes[17-20]. Interestingly, and in line with our findings, studies have suggested that as surgeons become more comfortable with performing HoLEP, the enucleation and morcellation time decreases[19]. Not unexpectedly, patients with “beach ball” enucleated tissue encountered during HoLEP had significantly longer morcellation times. Identifying factors contributing to the formation of these dense tissue pieces is worth investigation in future studies. Recently, the introduction of new morcellators (Wolf Piranha, Knittlingen, Germany) has greatly reduced this problem.

Elzayat et al examined the safety of HoLEP in chronically anticoagulated patients and found that HoLEP was a safe option for this patient population[21]. This is not surprising as the holmium-YAG laser effectively coagulates while enucleating the tissue[8]. We initially hypothesized that chronic anti-coagulation may worsen enucleation and/or morcellation times as this could negatively impact visualization during surgery.[21] Interestingly, our study found that a history of chronic anticoagulation was associated with a small but significant decrease in enucleation time. Although we are unable to explain this relationship, we speculate, because of anticipated concern regarding intra-operative bleeding, that this may actually reflect earlier participation by senior staff and thus decreased resident or fellow participation in the enucleation portion of the case.

The learning curve associated with HoLEP is often considered a disadvantage to the procedure despite studies suggesting that proficiency can be gained in as little as two dozen procedures[22,23]. Furthermore, studies have reported that there is little variation in operative efficiency between surgeons and that comparable times can be achieved[17,24]. We found that although there is a twenty minute increase in enucleation time associated with less experienced surgeons, there is minimal difference in morcellation time. Enucleation is the more time-consuming portion of HoLEP and we believe that efficiency likely improves with surgeon experience. Of note, the impact of tissue quality, i.e. prostatic “beach balls”, is an important determinant of time regardless of surgeon experience, although surgeon experience certainly diminishes the impact that difficult tissue has on overall operative times.

We examined whether recurrent UTI, chronic anticoagulation, and urinary retention (catheter or CIC leading up to surgery) would impact morcellation or enucleation time. We hypothesized that each of these might play a significant role because of their potential to impact prostatic tissue quality. Recent studies have evaluated the relationship between chronic prostatic inflammation with urinary retention and BPH progression with the finding that patients with chronic prostate inflammation have significantly higher risk of retention[25]. Recurrent UTI and chronic urinary catheterization can all hypothetically increase prostate inflammation, although studies examining this relationship have failed to demonstrate consistent findings[25,26]. Prostate inflammation impacts the histologic architecture, increasing gland volume and obliterates the natural plane between adenoma and prostate capsule which may result in a more complicated dissection during enucleation. Inflamed prostate tissue may also trigger increased bleeding or oozing while operating which may result in poorer visualization requiring increased time to achieve appropriate hemostasis during surgery. Furthermore, changes in gland volume and tissue quality may hinder morcellation as well, increasing surgical times in this select group of patients[25,26]. In our study, requiring a Foley at the time of HoLEP was not associated with increases in either enucleation or morcellation time. History of UTI, however, was associated with a modest increase in both surgical steps.

The impact of 5ARIs on prostatic tissue quality is not well understood but 5ARIs are known to affect the glandular to stromal ratio with an overall reduction in glandular tissue[27-28]. Therefore, hypothetically, long-term use of 5ARIs might increase the fibrous content of the prostate which could make enucleation and morcellation more difficult. We were surprised to find, therefore, that the use of 5ARI did not appear to affect our operative times. Sandfeldt et al reported a reduction in blood loss during transurethral resection of the prostate after 3 months of preoperative treatment with finasteride. However, in our experience, 5ARI use was not associated with any bleeding reduction during HoLEP[29]. Warner et al previously examined the impact of 5ARIs on HoLEP and reported that history of use does not impact HoLEP outcomes or operative time which is consistent with our findings[30]. Interestingly, in the current study we report that history of 5ARI was actually associated with a faster enucleation rate, although it did not reach statistical significance. Additionally, we observed shorter morcellation times in these patients. Whether these findings are related to random occurrence, reduced prostate volume associated with 5ARI use, or more senior participation during surgery remains unknown. In any event, there does not appear to be a clear relationship between 5ARI use and overall operative times during HoLEP.

This study is not devoid of limitations. It is retrospective in nature, although the data are collected in a prospective fashion. Additionally, complete preoperative data was not available for all patients and may have impacted results. As this study spans over a 15 year period, differences in patients and techniques may exist. Despite these limitations, this study is the first to examine how preoperative variables may impact enucleation and morcellation times in patients undergoing HoLEP for BPH.

Conclusions

HoLEP is an effective therapy for the management of BPH symptoms, particularly in men with large prostate glands. The duration of HoLEP is dependent upon prostate size, tissue quality, and surgeon's experience. A history of UTI is associated with an increase in operative time while anticoagulation is associated with a decrease in operative time. As surgeons gain proficiency and experience in performing HoLEP, enucleation and morcellation times decrease.

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Table 1. Characteristics of patients undergoing HoLEP

	Patients (n%)
Total patients	960
Age (years), mean (SD)	70.4 (8)
History of 5ARI use	323 (33.7)
History of alpha blocker use	696 (72.5)
Requiring Foley at time of HoLEP	250 (26.0)
History of UTI	393 (40.9)
History of anticoagulation	201 (20.9)
Pre-HoLEP PSA (ng/ml), mean (range)	8.1 (0.04-449.4)
TRUS weight (g), mean (SD) [a]	102.8 (51)
PSA density, mean (SD) [b]	0.10 (0.38)
Beach ball identified	34 (3.5)
Enucleation time (min), average (range)	65.7 (11-245)
Morcellation time (min), average (range)	19.7 (3-260)
HoLEP specimen weight (g)	
<30g	147 (15.3)
30-100g	499 (52.0)
100-150g	218 (22.7)
>150g	96 (10.0)
Enucleation rate (g/min), average (SD)	1.38 (0.9)
Morcellation rate (g/min), average (SD)	5.32 (2.8)
Presence of prostate cancer	84 (8.8)
Less experienced surgeon	107 (11.2)

[a] TRUS weight unavailable for 103/960
[b] PSA density unavailable for 125/960

Table 2. Predictors of enucleation time from multiple linear regression model

Characteristic	Coefficient (minutes)	95% CI	p-value
Requiring Foley at time of HoLEP	-3.49	-7.98-1.00	0.127
History of UTI	2.83	-0.71-6.38	0.117
History of anticoagulation	-4.93	-9.22- -0.64	0.024
HoLEP specimen weight			
<30g	Reference		
30-100g	17.86	12.85-22.87	<0.001
100-150g	31.55	25.76-37.33	<0.001
>150g	39.81	32.69-46.93	<0.001
Less experienced surgeon	20.86	15.28-26.44	<0.001
Beach ball present	-7.94	-17.38-1.50	0.099
Constant	43.76	39.00-48.52	<0.001

Interpretation of linear regression model: for a patient not requiring a Foley at time of HoLEP but with a history of UTI and anticoagulation, who had a HoLEP specimen weight of 125g, with HoLEP performed by an experienced surgeon, and no beach balls, the estimated enucleation time is 73.2 minutes (0+2.83-4.93+0+31.55+0+0+43.76=73.2). Negative coefficients represent decreases in estimated morcellation time.

Table 3. Predictors of morcellation time from multiple linear regression model

Characteristic	Coefficient (minutes)	95% CI	p-value
History of 5ARI	-1.28	-3.32-0.77	0.220
History of UTI	2.45	0.50-4.40	0.014
HoLEP specimen weight			
<30g	Reference		
30-100g	8.84	6.07-11.60	<0.001
100-150g	21.59	18.39-24.78	<0.001
>150g	39.71	35.77-43.65	<0.001
Less experienced surgeon	3.00	-0.08-6.08	0.056
Beach ball present	25.26	20.10-30.42	<0.001
Constant	4.47	1.83-7.10	0.001

Interpretation of linear regression model: for a patient with a history of 5ARI use, no history of UTI, HoLEP specimen weight of 125g, with HoLEP performed by a less experienced surgeon, and no beach balls present, the estimated morcellation time is 24.8 minutes (-1.28+0+21.59+ 3.0+0+4.47=24.8). Negative coefficients represent decreases in estimated enucleation time.