Holmium Laser Enucleation of the Prostate in Patients on Anticoagulant Therapy or With Bleeding Disorders

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Purpose: We evaluated the safety and efficacy of HoLEP in patients on anticoagulation with significant obstructive symptoms secondary to BPH refractory to medical therapy.

Materials and Methods: From May 1999 to October 2004, 83 patients with a mean age of 76.6 years who had symptomatic BPH and were on chronic oral anticoagulant therapy or had bleeding disorders underwent HoLEP. Mean preoperative prostate size estimated by transrectal ultrasound was 82.4 cc (range 25 to 222). A total of 14 patients underwent HoLEP without oral anticoagulant withdrawal, 34 underwent surgery with low molecular weight heparin substitution and 33 stopped anticoagulants before surgery, including 8 on antiplatelet therapy. All patients were assessed preoperatively, and 1, 3, 6 and 12 months after surgery.

Results: HoLEP was performed successfully in all patients with a mean enucleation time of 86.5 minutes (range 35 to 210). Mean morcellation time was 20.1 minutes (range 3 to 100). Peak urinary flow, post-void residual urine, International Prostate Symptom Score and quality of life score were significantly improved by 1 month after surgery and they continued to improve during subsequent followup. One patient required intraoperative platelet transfusion and 7 required blood transfusion early in the postoperative period due to hematuria coinciding with restarting oral anticoagulant therapy. Mean preoperative and postoperative hemoglobin was 13.5 (range 8.3 to 16.4) and 12.2 gm/dl (range 5.3 to15.4), respectively ($p < 0.0001$). There were no major operative or postoperative complications, or thromboembolic events.

Conclusions: HoLEP is a safe and effective therapeutic modality in patients on anticoagulation with symptomatic BPH refractory to medical therapy.

Key Words: prostate, prostatic hyperplasia, lasers, anticoagulants, urination disorders

LUTS secondary to BPH is a common condition in aging men with an overall prevalence of more than 50% in those older than 50 years.[1] Conventional TURP remains the gold standard treatment for symptomatic BPH. However, morbidity after TURP is still high, especially bleeding requiring blood transfusion (0.4% to 6.4%) and late postoperative bleeding (1.3% to 1.7%).[2,3] TURP is also associated with a perioperative hypercoagulability state with an overall 8% incidence of deep venous thrombosis after TURP.[4,5] Thus, TURP in patients with BPH on anticoagulant therapy is considered more hazardous and it is frequently avoided.

The most common indications for oral anticoagulant therapy are atrial fibrillation, recurrent thromboembolic disease and prosthetic heart valves.[6] Treating such cases with TURP when absolutely indicated adds an additional risk in comparison to routine cases. The risk of bleeding associated with surgery is higher due to anticoagulation and discontinuation of anticoagulant therapy before surgery increases the risk of thromboembolic events due to the release of tissue thromboplastins.[4] The cessation of anticoagulants for few days before surgery is sometimes feasible but early reinstitution of anticoagulation in the presence of hematuria is always fraught with more bleeding. In some instances anticoagulation cannot be safely stopped and surgery must be performed in patients fully on anticoagulation. Thus, treatment alternatives to TURP are required for treating patients with symptomatic BPH who are on chronic anticoagulation or who have bleeding disorders and are refractory to medical therapy for BPH.

HoLEP has been used to remove obstructive prostatic tissue with adequate hemostasis and it is described as an alternative to TURP for BPH. Bleeding complications after HoLEP are less likely than after TURP.[7] We evaluated the safety and efficacy of HoLEP in patients on anticoagulation with significant obstructive symptoms secondary to BPH that were refractory to medical therapy.

MATERIALS AND METHODS

A retrospective study was done in 83 patients with symptomatic BPH on chronic oral anticoagulant therapy who required surgical management and were referred for HoLEP. Surgery was done between May 1999 and October 2004. A total of 81 patients were on anticoagulant therapy for various indications (table 1). A bleeding disorder, namely hemophilia, was noted in 2 patients. Conservative medical

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TABLE 1. *Indications for oral anticoagulant therapy*

Indication*	No. Pts
Chronic atrial fibrillation	34
Prosthetic heart valves	14
Pacemaker	13
Myocardial infarction	11
Pulmonary embolism	11
Deep venous thrombosis	10
Congestive heart failure	7
Aortic aneurysm	2
Total	102

*More than 1 indication in some patients

TABLE 2. *Baseline characteristics in patients who underwent HoLEP*

	Mean (range)
Age	76.6 (55–94)
TRUS vol (cc)	82.4 (25–222)
No. surgery indications (%):	
LUTS refractory to medical treatment	40 (48.1)
Urinary retention	39 (47)
Hematuria	4 (4.9)
Preop Qmax (ml/sec)	7.7 (0–13)
Preop PVR (ml)	390 (21–2,000)
Preop I-PSS	20.1 (8–35)
Preop QOL	3.9 (1–6)

treatment for BPH failed to improve symptoms or patients were in urinary retention and repeat voiding trials with α-blocker therapy had failed.

Preoperative evaluation included physical examination with focused neurological examination and digital rectal examination, LUTS evaluation using I-PSS, free uroflowmetry in patients who were able to void, measurement of PVR volume using bladder scan, blood analysis, coagulation parameters, PSA determination and measurement of prostate volume using TRUS with TRUS guided biopsy when necessary. According to the indications for anticoagulant therapy and the degree of thromboembolic risk perioperative discontinuation of oral anticoagulant was based on cardiology consultation. In the majority of cases oral anticoagulant was stopped 5 days before surgery, and subcutaneous LMWH was started 24 hours after the discontinuation of oral anticoagulant and stopped 12 hours before surgery when INR decreased to less than 1.4. LMWH was restarted 12 hours after surgery and oral anticoagulation was resumed after the patients could receive medication. Hematuria frequently resolved on postoperative day 1. After INR increases to greater than 2 LMWH can be discontinued. A total of 14 patients underwent HoLEP without withdrawal of oral anticoagulants, 34 underwent surgery with LMWH substitution and 33 stopped anticoagulants before surgery, including 8 on antiplatelet therapy with clopidogrel bisulfate.

HoLEP was performed using an 80 to 100 W VersaPulse® Ho:YAG laser source , a 550 μm SlimLine™ 550 end firing fiber, a modified, continuous flow 26Fr resectoscope with a distal bridge, a 7Fr catheter through the proximal bridge to stabilize the laser fiber, continuous saline irrigation, a rigid indirect nephroscope, a tissue morcellator (Lumenis, Santa Clara, California) and a video system. All HoLEP procedures were performed by a single surgeon (MME), as previously described.[8–10] Furosemide was administered (20 mg per hour of enucleation intravenously), which almost always coincided with the end of enucleation to counteract any fluid absorption and enhance urine flow. Intermittent bladder irrigation was delivered through a Y-connector. On rare occasions if hematuria persisted despite intermittent irrigation, continuous irrigation was begun using a 3-way catheter. Routinely the catheter was removed the next morning. When the patient was able to void adequately, he was discharged from the hospital.

Followup evaluations after HoLEP were done in all patients at the visits at 1, 3 and 6 months, and 1 year. Mean Qmax, PVR, I-PSS and QOL score were compared before surgery and postoperatively using the paired Student t test with $p < 0.05$ considered significant.

RESULTS

A total of 83 patients on anticoagulation were included in this study, of whom 40 (48.1%) presented with symptomatic BPH refractory to medical treatment, 39 (47%) presented in urinary retention with failed repeat voiding trials without a catheter while on α-blocker therapy and 4 (4.9%) presented with hematuria. Table 2 lists the main baseline characteristics in all patients.

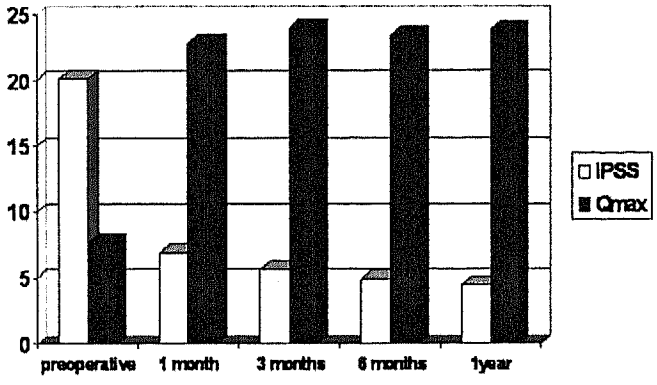
Mean preoperative INR just before surgery in all patients was 1.36 (range 0.9 to 2.4). Mean INR ± SD in patients on warfarin anticoagulation and in those on LMWH substitution was 2 ± 0.28 and 1.25 ± 0.17, respectively. The procedure was preceded by laser lithotripsy for bladder calculi in 8 patients (9.6%).

Mean enucleation time was 86.5 minutes and mean morcellation time was 20.1 minutes (table 3). In 2 patients morcellation was postponed to another session due to unclear vision in 1 and difficult morcellation due to tough prostatic tissues in 1. Mucosal bladder injury and capsular perforation were noted in 2 and 1 patients, respectively. Prolonged catheterization was required in these patients.

Continuous bladder irrigation was necessary for transient postoperative hematuria in 5 patients (5.3%). One patient had nonQ myocardial infarction and required intensive care unit admission for 5 days. One patient who did not stop antiplatelet therapy with clopidogrel bisulfate preoperatively required intraoperative platelet transfusion due to bleeding and morcellation was postponed due to poor visibility. Blood transfusions were required in 7 patients early postoperatively, mostly within 2 to 5 days after surgery, and the mean number of transfused blood units was 3.7 U (range 2 to 7). Persistent bleeding in 3 of those patients required cystoscopy and cauterization of bleeders. Five of these patients were placed on LMWH substitution and had hematuria early postoperatively, coinciding with restarting oral anticoagulants. One of 33 patients who stopped anticoagulant therapy preoperatively had bleeding 2 days after surgery and required 2 U blood transfusion. One of 14 patients on full anticoagulation had hematuria secondary to mucosal

TABLE 3. *Operative data*

	Mean (range)
Enucleation time (mins)	86.5 (35–210)
Morcellation time (mins)	20.1 (3–100)
Enucleated tissue wt (gm)	54.7 (6–245)
Total energy used (kJ)	198.7 (63–449)
Catheterization time (days)	2.2 (1–21)
Hospital stay (days)	2.5 (1–28)



Outcome measures from baseline to 12-month followup

bladder injury and required 3 U blood transfusion. Mean preoperative and postoperative hemoglobin was 13.5 (range 8.3 to 16.4) and 12.2 gm/dl (range 5.3 to15.4), respectively ($p < 0.0001$). Mean preoperative and postoperative serum sodium was 139.5 (range 133 to 145) and 138.7 mEq/dl (127 to 145), respectively ($p = 0.17$). Three patients had clot retention and required rehospitalization for cystoscopy and bladder irrigation within 2 weeks after surgery.

In 3 patients a trial of voiding after surgery failed and they required recatheterization for more than 1 day. However, the remaining patients were able to void adequately immediately after catheter removal the next morning. Two patients who presented in urinary retention were unable to void postoperatively and they were placed on clean intermittent catheterization. Qmax, PVR, I-PSS and QOL score were significantly improved by 1 month after surgery and continued to improve during subsequent followup (see figure). At 1 year postoperatively mean PVR had decreased from 390 (range 21to 2000) to 31.6 ml (range 0 to 160) ($p < 0.0001$) and Qmax had increased from 7.7 (range 0 to 13) to 23.9 ml per second (range 6 to 63) ($p = 0.006$). Mean I-PSS improved from 20.1 (range 8 to 35) to 4.4 (range 0 to13) ($p < 0.0001$) and QOL score improved from 3.9 (range 1 to 6) to 0.81 (range 0 to 3) ($p < 0.0001$).

The decrease in mean PSA was 82.7%, that is from 8.4 (range 0.59 to 92.7) to 1.45 ng/ml (range 0.12 to 10) 6 months postoperatively ($p < 0.0001$). Pathological examination of enucleated tissue revealed BPH in 76 patients, prostatic adenocarcinoma in 6 (6.3%) and high grade prostatic intraepithelial neoplasia in 1.

Seven patients (8.4%) had postoperative irritative symptoms and 5 (6%) had stress urinary incontinence, which resolved in all within 1 to 6 months, occasionally requiring anticholinergic therapy. Urinary tract infections developed in 3 patients and were treated with proper antibiotics. Bladder neck contracture and urethral stricture were noted in 2 patients (2.4%) 1 year after surgery (table 4). Bladder neck contracture was treated successfully with laser incision of the bladder neck and the stricture was easily dilated with the patient under local anesthesia.

DISCUSSION

Oral anticoagulants are frequently used to treat or prevent thromboembolic diseases in North America.[11] The number of patients requiring oral anticoagulant therapy is constantly increasing due to the growing percent of elderly individuals. The number of candidates presenting for prostatectomy who are on oral anticoagulant therapy is also increasing rapidly. This is further increased because of the fact that many patients presenting with LUTS are maintained on oral medication for many years, mainly α-blockers, with the result that surgery is required in older, more ill patients on anticoagulation with a larger prostate. This group of patients causes treatment problems when they are referred for standard TURP as surgical therapy for BPH. The risk of hemorrhage is higher and to interrupt anticoagulant therapy without substitution may place the patient at thromboembolic risk.[12]

Currently, as described by Gilling et al,[8] HoLEP seems to be an attractive alternative to conventional TURP. The Ho:YAG laser is a versatile, multifunction surgical laser that is now available at most urology centers. The holmium wavelength of 2,140 nm with a superficial penetration depth of 0.4 mm allows an almost bloodless field and a TURP-like cavity with excellent voiding results, short hospital stay and short catheterization time.[7]

In our study we noted a 210% improvement in mean Qmax from 7.7 to 23.9 ml per second, 92% decrease in PVR from 390 to 31.6 ml, 78% decrease in I-PSS from 20.1 to 4.4 and 79% improvement in QOL score from 3.9 to 0.81 at 1 year after surgery compared to preoperative values. There were no major operative or postoperative complications, or thromboembolic events. Seven patients required blood transfusion and 1 required intraoperative platelet transfusion. Two of 14 patients were on full anticoagulation, including 5 of 34 with LMWH substitution and 1 of 33 who stopped anticoagulant therapy before surgery. Blood transfusion was required in the early postoperative period, coinciding with the recommencement of oral anticoagulant therapy.

Parr et al reported on 12 patients who underwent standard TURP without withdrawal of oral anticoagulant therapy.[13] They noted a blood transfusion rate of more than 30% and half of the patients required fresh frozen plasma. In our study 2 of 14 patients (14.2%) on full anticoagulation required blood transfusion, including 1 who required intraoperative platelet transfusion and 1 with postoperative hematuria who required 2 U blood transfusion. Chakravarti and MacDermott reported the safety of TURP with brief anticoagulation interruption and full intravenous heparinization.[14] One of 11 patients required 3 U blood transfusion with a mean decrease in hemoglobin after TURP of 1.6 gm/dl and a mean hospital stay of 6.7 days. Dotan et al treated 20 patients with BPH using conventional TURP

TABLE 4. *Intraoperative and postoperative complications*

	No. (%)
Intraop:	
Bleeding requiring transfusion	1 (1.2)
Capsular perforation	1 (1.2)
Bladder injury	2 (2.4)
Myocardial infarction	1 (1.2)
Postop:	
Blood transfusion	7 (8.4)
Irritative symptoms	7 (8.4)
Stress incontinence	5 (6)
Urinary tract infection	3 (3.6)
Recatheterization	3 (3.6)
Clot retention	3 (3.6)
Bladder neck contracture	1 (1.2)
Urethral stricture	1 (1.2)

TABLE 5. *TURP and HoLEP in patients on anticoagulation*

	Parr et al[13]	Chakravarti and MacDermott[14]	Dotan et al[15]	Present Series
No. pts	12	11	20	83
No. anticoagulation:				
Full	12			14
Full heparinization		11		
LMWH			20	34
Stopped temporarily				33
Mean cc-preop prostate vol (range)	Not stated	23.2 (4–60)	Not stated	82.4 (25–222)
Mean gm resected tissue wt (range)	22 (6–41)	Not stated	26 (8–56)	54.7 (6–245)
No. postop bleeding	1	3	2	3
No. transfusion (%):	4 (33)	1 (9.1)	4. (20)	8 (9.6)
Full anticoagulation				2 (14.2)
LMWH				5 (14.7)
Stopped temporarily				1 (3)

with a change of oral anticoagulants to perioperative LMWH injection.[15] The blood transfusion rate was 20%, and catheterization time and hospital stay was 3.2 and 4.2 days, respectively. In the current study the transfusion rate in patients with LMWH substitution was 14.7% (5 of 34), which is lower than that reported by Dotan et al. The inclusion of 33 patients who stopped anticoagulant therapy before HoLEP in our cohort may have added a bias to the results in terms of perioperative bleeding and blood transfusion. However, even without the addition of these patients to our cohort the blood transfusion rate would be 14% (7 of 50), which is lower than transfusion rates after TURP in patients on anticoagulation (table 5).

Also, in our study catheterization time and hospital stay was less than in previous reports of TURP.[13–15] These reports were also based on small study population with smaller resected glands. The mean weight of resected tissue was 22 to 26 gm.

On the other hand, Nd:YAG laser ablation of the prostate has been reported to be a safe procedure in patients who are on full anticoagulation.[16] Bolton and Costello noted the safety of Nd:YAG ablation in 10 patients on full anticoagulation with a catheterization time of 1 day to 6 weeks.[17] The improvement in American Urological Association symptom score and Qmax was 67% and 68.7%, respectively. Kingston et al reported Nd:YAG ablation in 20 patients on continuous oral anticoagulant therapy and in 2 with bleeding disorders.[18] Three of 22 patients required postoperative blood transfusion, while 4 patients had mild hematuria requiring intervention. van Melick et al reported the safety of the contact Nd:YAG laser in 19 patients, and the safety of the combined contact and visual Nd:YAG laser in 11.[19] The men were on oral anticoagulant therapy with a mean catheterization time and hospital stay of 7.3 and 7 days, respectively. Holmium laser vaporization is usually indicated for smaller glands.

Recently Reich et al observed the safety and efficacy of KTP laser vaporization of the prostate in 66 patients at high risk, including 26 on oral anticoagulant therapy, of whom 11% required recatheterization and 3% required reoperation (TURP) within 4 weeks.[20] As for all laser vaporization procedures, KTP laser prostatectomy does not provide a tissue specimen for histopathological analysis and it is also best suited for smaller prostates.

Considering the high complication rate of TURP and modest clinical outcome with the high reoperation rate of various types of laser procedures in patients on anticoagulation, we consider that HoLEP is an effective alternative surgical treatment for BPH in this challenging group of patients. The advantages of HoLEP compared with TURP lie in the amount of blood loss, lack of transurethral syndrome, normal saline used as the irrigant and shorter convalescence. HoLEP provide the removal of obstructive prostatic tissues with an almost bloodless field, and immediate improvement in symptoms and flow rate with a short catheterization time and hospital stay. We would like to emphasize that performing prostatectomy in patients on anticoagulation is a challenge using whatever technique. The relative risk using the Ho:YAG laser is less than that of the alternatives.

CONCLUSIONS

HoLEP is relatively safe and effective procedure for treating patients on anticoagulation who have BPH refractory to pharmacotherapy. The excellent hemostatic properties of the holmium laser allow HoLEP to be a safer and effective alternative to conventional treatment in patients on anticoagulant therapy or with bleeding disorders with a lower incidence of bleeding requiring blood transfusion.

Abbreviations and Acronyms

BPH	=	benign prostatic hyperplasia
HoLEP	=	holmium laser prostate enucleation
INR	=	international normalized ratio
I-PSS	=	International Prostate Symptom Score
LMWH	=	low molecular weight heparin
LUTS	=	lower urinary tract symptoms
PSA	=	prostate specific antigen
PVR	=	post-void residual urine
Qmax	=	peak urinary flow rate
QOL	=	quality of life
TRUS	=	transrectal ultrasound
TURP	=	transurethral prostate resection

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