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ORIGINAL ARTICLE

Safety and feasibility study of holmium laser enucleation of the prostate (HOLEP) on patients receiving dual antiplatelet therapy (DAPT)

Jie Sun[1] · An Shi[1] · Zhen Tong[1] · Wei Xue[1]

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Abstract

Objective To evaluate the safety and feasibility of Holmium laser enucleation of the prostate (HoLEP) in patients receiving dual antiplatelet therapy (DAPT).

Methods From March 2013 to August 2016, we retrospectively analyzed 1124 benign prostatic hyperplasia (BPH) patients undergoing HoLEP and divided into four groups: 56 cases receiving DAPT therapy (group A); 72 patients treated with continuous single antiplatelet (AP) therapy (group B); 41 patients treated with single AP therapy but intermittent during preoperative time (group C) and 955 cases had no AP therapy (group D). Patients' baseline characteristics, 1-year clinical outcomes, rates of postoperative bleeding and complications were presented in this study.

Results All patients received successful operations and no severe postoperative complications occurred. Only one patient in Group D required transfusion. The enucleation time and catheterization time for the DAPT patients were the longest among four groups ($p < 0.001$, respectively). The overall complications rates within 30 days were 23.2% (13/56) in Group A, 27.8% (20/72) in Group B, 19.5% (8/41) in Group C, and 27.0% (258/955) in Group D, respectively ($p = 0.678$). By the 12 months, the international prostate symptom scores (IPSS), quality of life scores (QOL) and residual urine volume (RUV) in all groups have been significantly improved.

Conclusion HoLEP in patients receiving DAPT after coronary artery stunting showed similar results to those achieved in patients receiving single AP therapy or non-AP therapy. It can be a good option, which the urologists can offer to those patients with symptomatic benign prostatic hyperplasia refractory to medical treatment.

Keywords Benign prostate hyperplasia · Lower urinary tract symptoms · Holmium laser enucleation of the prostate · Dual antiplatelet therapy

Abbreviation

BPH	Benign prostatic hyperplasia
HoLEP	Holmium laser enucleation of the prostate
TURP	Transurethral resection of the prostate
PVP	Photoselective vaporization of the prostate
CABG	Coronary artery bypass grafts
DAPT	Dual antiplatelet treatment
PSA	Prostate-specific antigen
TRUS	Transrectal ultrasonography
PVR	Post-void residual urine

Jie Sun and An Shi authors contributed fully and equally to this work.

✉ Wei Xue
xwrenji@126.com

[1] Department of Urology, Renji Hospital affiliated to Shanghai Jiao Tong University, Medical School, No 160, PuJian Road, Pudong New District, Shanghai 201200, China

Introduction

Benign prostate hyperplasia (BPH) is the main etiology of lower urinary tract symptoms (LUTS) in elderly men [1]. It is inevitable as the risk of comorbidities grows exponentially with age. With the great advances in coronary stents, the diffusion of percutaneous interventions has been more popular than coronary artery bypass grafts (CABG) [2]. Urologists usually have to face the problem of operating on patients with dual antiplatelet treatment (DAPT). DAPT following an acute coronary syndrome or after placement of coronary stents, is considered to be superior to aspirin alone for prevention of acute thrombotic events [3]. Continuous DAPT

was proved to decrease the incidence of myocardial infarction, ischemic stroke and other cardiovascular events [4].

Transurethral resection of the prostate (TURP) has been the "Gold Standard" treatment of BPH for many decades. As technology has evolved in the past few years, the rate of alternative minimal invasive surgical therapies (MISTs) has increased [5]. Since first introduced in 1998, the holmium laser enucleation of the prostate (HoLEP) has shown similar postoperative outcomes compare with TURP and open prostatectomy, which has become a new standard method for the treatment of BPH/LUTS, especially in large volume prostate [6, 7]. The holmium laser is a pulsed solid-state laser with a wavelength of 2.1 μm. This wavelength is strongly absorbed by water, making its safety use in an aqueous environment [8]. Compared with TURP, the advantages of HoLEP include the reduced intraoperative bleeding risks and perioperative morbidity [9]. Based on the previous study that presented the safety and efficacy of HoLEP in men receiving single antiplatelet or anticoagulation therapy [10], we did not stop DAPT when caring out HoLEP. To validate this approach, we designed this retrospective study to evaluate the safety and feasibility of HoLEP in patients receiving DAPT.

Patients and methods

Institutional Review Board approval was obtained for the present retrospective study. This is a consecutive series of patients undergoing HoLEP in Renji Hospital affiliated to Shanghai JiaoTong University, School of Medicine by the same two experienced surgeons (having performed > 40 cases) from March 2013 to August 2016. Patients taking daily aspirin 100 mg + clopidogrel 75 mg were defined under DAPT. In our study, patients were categorized into four groups: 56 cases receiving DAPT therapy (group A); 72 patients treated with continuous single antiplatelet (AP) therapy (group B); 41 patients treated with single AP therapy but intermittent during preoperative time (group C) and 955 cases had no AP therapy (group D). Patients in group C were defined by stopping the single AP therapy preoperatively more than 3 days and restarting 1 week after the operation. 12 patients taking oral anticoagulants were excluded from the study. Treatment indications for HoLEP were in accordance with the clinical practice guidelines [11]. We excluded the patients with prostate cancer by digital rectal examination (DRE) combined with prostate-specific antigen (PSA) test or prostate biopsy. Preoperative variables included medical history, symptom index score, transrectal ultrasonography (TRUS), post-void residual urine (PVR), uroflowmetry, and serum PSA. Operation time and enucleated weight were also recorded. Patients were evaluated at 1, 6 and 12 months, postoperatively. The postoperative pathologic results were recorded if malignant neoplasm was present. Postoperative complications were also recorded during the follow-up visit. All complications were graded according to the Clavien–Dindo classification [12].

All the patients received the general anesthesia. Then operation was performed by a 550-μm end-firing laser fiber (SlimLine, Lumenis Ltd, Yokneam, Israel) engaged with a 100 W Holmium neodymium:yttrium-aluminum-garnet laser (VersaPulse Power-Suite, Lumenis Ltd). Saline was used as washing fluid, and a Storz 26F(Karl Storz GmbH&Co., Tuttlingen, Germany) continuous flow resectoscope with a laser bridge was used for all these surgeries. The surgical procedure has been previously described [13]. The voiding trial was taken on postoperative day 1 and patients were discharged when they met standardized criteria.

Statistical methods

Statistical analysis was performed using the Statistical Package for Social Sciences, version 22.0(IBM Corp., Armonk, NY). Continuous variables were described as means and standard deviation or as median value plus interquartile range (according to distribution). Continuous variables were analyzed using a Student *t* test, Mann–Whitney *U* test and one-way analysis of variance (ANOVA). Categorical variables were analyzed by the Chi-square and ANOVA test. All statistical tests were two sided, and the statistical significance was set at $p < 0.05$.

Results

The basic clinical characteristics of patients were shown in Table 1. These four cohorts were similar in terms of age, preoperative PSA and preoperative functional evaluation. The enucleated time was longer in Group A compared with another three groups ($p < 0.01$). The duration of continuous bladder irrigation was the longest in Group A with a median of 18 h. There was no significant difference in morcellation time, enucleated weight and length of hospital stays among four groups. The hemoglobin changes after operation in Group A also showed no difference compared with other three groups. The occurrence of postoperative complications is given in Table 2. The overall complication rates within 30 days were 23.2% (13/56) in Group A, 27.8% (20/72) in Group B, 19.5% (8/41) in Group C, and 27.0% (258/955) in Group D, respectively ($p = 0.678$). Majority of adverse events were transient and mild, which was similar in all groups. The rate of bleeding caused bladder tamponade in Group A was rare (1/56, 1.8%). Clinical outcomes at the postoperative 1-, 6- and 12-month follow-up are summarized in Fig. 1. IPSS, PVR and the maximum flow rate (Qmax) in all groups have significantly taken a favorable turn.

Table 1 Basic clinical characteristics and intraoperative outcomes

	Group A	Group B	Group C	Group D	*p* value
Number	56	72	41	955	
Age (years old)	72.4 ± 7.9	69.7 ± 8.2	70.8 ± 6.7	71.6 ± 8.3	0.187[a]
Prostate volume (mL)	77.7 ± 31.8	75.8 ± 40.1	67.5 ± 27.1	73.8 ± 35.7	0.541[a]
Preoperative IPSS	26.5 ± 3.7	26.1 ± 4.1	24.9 ± 3.5	26.3 ± 4.1	0.441[a]
Preoperative Qmax (mL/sec)	7.3 (5.3,9.2)	7.1 (4.8,9.5)	6.8 (5.1,9.6)	7.3 (5.3,9.6)	0.919[b]
Preoperative PSA (ng/mL)	4.9 (2.6,7.4)	5.5 (3.5,11.7)	6.4 (3.6,10.5)	6.9 (3.6,11.5)	0.024[b]
Enucleation time (min)	56.9 ± 19.1	47.0 ± 14.5	39.8 ± 19.6	38.5 ± 17.9	0.000[a]
Morcellation time (min)	10.6 ± 5.7	11.8 ± 7.2	13.6 ± 9.1	10.8 ± 8.5	0.091[a]
Enucleated weight (g)	37 (26,50)	46.5 (32,62)	38 (30,56)	39.5 (24,57)	0.053[b]
Hemoglobin change (g/L)	10.6 ± 7.3	9.7 ± 6.2	10.2 ± 8.5	9.8 ± 7.1	0.560[a]
Duration of continuous bladder irrigation (hrs)	18 (15,20)	13 (8,16)	13 (8,15)	12 (8,14)	0.000[b]
Length of hospital stays (d)	1.3 ± 0.6	1.3 ± 0.7	1.4 ± 0.8	1.3 ± 0.8	0.465[a]
Incidental prostate carcinoma	0	1	0	11	

Group A: patients treated with continued DAPT therapy during perioperative time; Group B: patients treated with continuous single AP therapy during perioperative time; Group C: patients treated with intermittent single AP therapy; Group D: patients had no AP therapy

[a]One-way ANOVA test

[b]Kruskal–Wallis test

Table 2 Postoperative complications during 1-month follow-up

	Clavien–Dindo grade	Group A	Group B	Group C	Group D	*p* value
Blood transfusion	II	0	0	0	1	/
Bladder tamponade	III	1	0	0	3	0.322
Recatheterization	II	2	2	0	31	0.824
Irritative symptoms	II	4	6	4	103	0.854
Stress urinary incontinence	I	4	7	3	67	0.803
Urinary tract infection	II	1	2	0	28	0.931
Urinary stricture	III	0	1	1	17	0.815
Bladder neck contracture	III	1	2	0	8	0.206
Total sum/total patients		13/10	20/15	8/7	258/236	0.678

Discussion

Due to the accelerating growth of aging population, the high BPH/LUTS prevalence is a significant financial and medical burden to patients and society. At the same time, concerns have raised that patients with obligatory DAPT after drug-eluding coronary after stunting are becoming more prevalent. Conventional TURP is contraindicated in these patients owing to its increased severe bleeding risks [14]. Several studies demonstrated the increased risks of transfusion and postoperative bleeding in TURP cohort receiving continuing AC/AP therapy [15, 16]. The oral anticoagulant drug affects TURP outcomes including longer hospital stays and higher rates of bleeding, blood transfusion and hematuria events. Previous studies have demonstrated superior clinical outcomes in HoLEP when compared to TURP [17, 18]. On the other hand, photoselective vaporization of the prostate (PVP) has been reported with great effect on patients receiving AC therapy [19, 20]. Compared with PVP, HoLEP showed similar effectiveness at improving urinary parameters and especially suitable for large volume prostate [21]. The safety and efficacy of HoLEP in men receiving single antiplatelet or anticoagulation therapy were also demonstrated in several reports. Bishop reported their retrospective review on 52 patients receiving antithrombotic therapy at the time of HoLEP compared with 73 non-antithrombotic patients [22]. The operation time, resection efficiency and clinical outcomes showed no difference between two cohorts. The rate of blood transfusion was 7.7% in antithrombotic group compared with 0 in the non-antithrombotic group ($p = 0.028$). EI Tayeb et al. studied 116 patients who took continuous and intermittent AC/AP therapy underwent

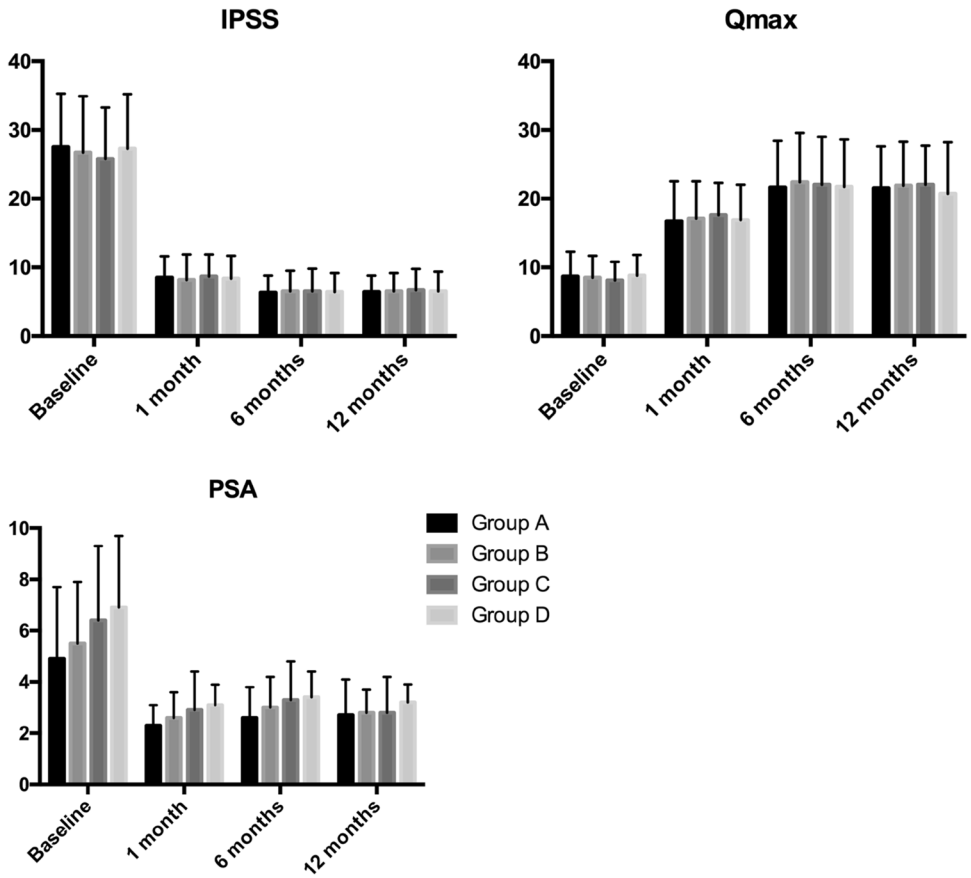

Fig. 1 Clinical outcomes at the postoperative 1-, 6- and 12-month follow-up (IPSS, Qmax, PSA)

HoLEP [10]. The transfusion rates were 3.5% for AC patients and 1.6% for the non-AC group, which showed no significant difference. Compared with non-AC group, the hospitalization time and duration of continuous bladder irrigation were longer in AC group (27.8 h vs. 24 h, 15 h vs. 13.5 h; $p < 0.001$, respectively). There were also no differences in enucleation time, catheterization time and transfusion rate between continuous AC/AP patients and intermittent AC/AP group.

Meanwhile, with the accelerating number of coronary artery disease (CAD) patient treated with drug-eluting stents, how to guide the decision-making on DAPT patients undergoing BPH surgery is pretty much the agenda for urologists. A prolonged DAPT use was recommended to reduce mortality and stent thrombosis [23, 24]. Thus, discontinuation of DAPT or reduced to single AC therapy may increase the risk of cardiovascular events in those high-risk patients. Our study is the first to our knowledge to evaluate the safety and postoperative results of HoLEP in DAPT patients.

Here, we retrospectively studied 56 patients receiving DAPT and compared this group with other three cohorts including single AP therapy (continuous or intermittent) and common non-antiplatelet therapy group. One of the possible DAPT drawbacks may consist in the prolonged operation time, which was also demonstrated in our study. Both group A and group B needed longer enucleation time compared with group C and D. Patients taking DAPT undergone the longest enucleation time with a mean value of 56.9 ± 19.1 min, owing to the need for meticulous hemostasis. The prolonged duration of bladder irrigation in group A was also associated with the anticipated need for postoperative surveillance. It did not mean the increased bleeding risks in those DAPT patients. The hemoglobin changes postoperatively and hospital stays showed no significant difference among four groups, which may directly and indirectly reveal the continuous use of DAPT might not be associated with the increased risk of bleeding. The Clavien–Dindo classification of postoperative complications was used in the current study. Overall, 13 surgery-related complications occurred in DAPT patients, all of which were transient and mild. Only one patient suffered bladder tamponade and treated under cystoscopy instantly. The rate of complications showed no significantly different among all groups. All patients in our study showed a favorable improvement in the functional outcomes after the operation.

The limitations of the present study include the heterogeneity of the series and the nature of retrospect. The results may only reflect a single center experience and a possible selection bias may have existed in this study. The data from

multicenter is further needed to generalize the findings of this study.

Conclusion

HoLEP in patients receiving DAPT after coronary artery stunting showed similar results to those achieved in patients receiving single AP therapy or non-AP therapy. It can be a good choice, which the urologists can offer to those patients with symptomatic benign prostatic hyperplasia refractory to medical treatment.

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Authors' contributions SJ: Project development and manuscript writing. SA: Data collection and analysis, and manuscript writing. TZ: Data collection and management. XW: Project development and manuscript editing.

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Compliance with ethical standards

Ethics statement Institutional Review Board approval of Renji Hospital affiliated to Shanghai JiaoTong University, Medical school was obtained for the retrospective study and patient written informed consent was obtained.

Consent to publish All of the details can be published and consent for publication was not required for this study.

Availability of data and materials The datasets during the current study were available from the corresponding author on reasonable request.

Conflict of interest The authors declare that they have no competing interests.

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