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ORIGINAL RESEARCH

Thromboelastography in Long-Term Antiplatelet Therapy for Patients Diagnosed with Benign Prostate Hyperplasia Undergoing Holmium Laser Enucleation of the Prostate: A Retrospective Study

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Objective: To compare low- vs high-power HoLEP effects on coagulation in patients on antiplatelet (AP) therapy via thromboelastography (TEG).

Methods: 210 patients was retrospectively analyzed and stratificated into three discrete groups, specifically: Group A (AP therapy, high-power HoLEP, n = 72); Group B (AP therapy, low-power HoLEP, n=73); Group C (no AP therapy, low-power HoLEP, n = 65). Baseline characteristics and coagulation profiles via TEG were compared. Univariate and multivariate analyses were conducted to identify independent risk factors associated with hematuria. Furthermore, parameters such as IPSS, Qmax, post-void residual volume V_2 and PSA levels were recorded during 1year follow-up.

Results: No differences in terms of baseline characteristics across all groups. Significant differences were observed in the duration of enucleation, morcellation, bladder irrigation, post-operative catheterization, length of hospital stay and the extent of hemoglobin reduction (F = 54.06, 8.54, 6.68, 9.24, 17.06, 5.97, $p < 0.05$). No differences were noted in postoperative hematuria, urine retention, transfusion rates, and SUI ($x_1^2 = 1.082$; $x_2^2 = 0.197$,; $x_3^2 = 3.981$;$x_4^2 = 0.816$, $p > 0.05$). Univariate and multivariate analyses revealed that prostate volume emerged as an independent risk factor for hematuria (OR 1.080, 95% CI: 1.007–1.158, p = 0.031). Clinical outcomes including Qmax, IPSS, V_2, and PSA demonstrated significant enhancement during 1 year follow-up.

Conclusion: Compared to HP-HoLEP, LP-HoLEP effectively reduces surgical and subsequent processing times, decreases hospital stay duration, and diminishes hemoglobin decline, offering a viable option without discontinuing AP therapy.

Keywords: anti-platelet therapy, BPH, high power, HoLEP, low power

Introduction

The prevalence of lower urinary tract symptoms attributed to benign prostatic hyperplasia (LUTS/BPH) is on the rise, particularly within the aging demographic.[1] This cohort of patients often presents with concomitant cardiovascular diseases, necessitating ongoing antiplatelet (AP) therapy.[2] Continuous administration of AP agents has demonstrated efficacy in reducing the incidence of cardiovascular events such as coronary heart disease, stroke, and venous thrombosis.[3,4] However, it poses a substantial risk for bleeding complications in the context of standard transurethral resection of the prostate (TURP).[5,6] Zheng et al confirmed that persistent use of antithrombotic medications significantly elevates the risk of bleeding, necessitating blood transfusion, bladder tamponade, and acute urine retention.[7] Consequently, addressing benign prostatic hyperplasia (BPH) in such patients poses a pertinent challenge for urologists, as discontinuation of AP therapy may heighten the risk of cardiovascular events. Meanwhile, prolonged lithotomy position can increase the probability of lower limb thrombosis.[8] Therefore, it is particularly important to find a reference standard for balancing the risk of bleeding and thrombosis.

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In recent years, thromboelastography (TEG) has been employed as a reference approach for assessing coagulation throughout all phases of clot formation and evaluating inherited bleeding disorders[9], especially for the long-term administration of oral anticoagulants in patients with coronary syndrome,[10] as well as for perioperative prevention of lower limb venous thrombosis in trauma patients.[11] Jan Hartmann employed thromboelastography for cardiovascular disease management in knowing individual reactivity at these stages when prescribing or when trying to assess risk of bleeding or thrombotic events.[12] Lin C et al has also used TEG to monitor the hemocoagulase effects of blood coagulation status in patients after thoracic surgery.[13] Therefore, incorporating TEG into clinical practice is of great significance in assessing the risk of bleeding and thrombosis in patients undergoing prostate hyperplasia surgery who are on antiplatelet therapy.

Holmium laser enucleation of the prostate (HoLEP) has emerged as a safe and effective intervention for BPH, and is particularly recommended for patients concurrently on AP medications.[14] Notably, transfusion rates in patients undergoing HoLEP while on AP therapy remain below 3%.[15] However, despite its proven efficacy, the widespread adoption of HoLEP faces hindrances due to its extended learning curve and the considerably higher cost of high-power holmium laser equipment, which is nearly three times that of low-power alternatives. Additionally, the technical challenges associated with high-power HoLEP (HP-HoLEP), including the risk of capsular perforation and reduced visibility, further limit its broader application.[16] In response to these challenges, the use of low-power holmium lasers has gained prominence. Studies conducted by Shah and Becker et al have affirmed the superiority of low-power holmium laser enucleation of the prostate (LP-HoLEP) in terms of hemostasis.[17,18] Minagawa demonstrated comparable safety and outcomes with the use of a low-power laser, providing the added benefit of reduced operative time, thus positioning it as a potential alternative treatment for BPH.[19]

Conventionally, the general recommendation has been to discontinue AP agents prior to surgery. While LP-HoLEP has demonstrated feasibility and safety in general, there is a lack of compelling evidence specific to patients requiring continuous AP therapy.[20] Building upon prior research establishing the safety and efficacy of LP-HoLEP, the objective of this study is to compare the results of low- and high-power HoLEP in patients undergoing continuous antiplatelet (AP) therapy through thromboelastography TEG evaluation.

Methods

Study Population

The analysis focused on patients with a medium-sized prostate (30–80 grams) who underwent HoLEP and were on aspirin/clopidogrel therapy. The analysis covered the period from March 2019 to March 2022 . For the purposes of this study, AP therapy was defined as the daily intake of aspirin/clopidogrel for a minimum duration of one year.[21] This study included a cohort of 220 patients, out of which 10 were lost to follow-up due to discontinuation of antiplatelet therapy before operation. Group A comprised 72 patients receiving AP therapy and undergoing high-power HoLEP; Group B included 73 patients on AP therapy undergoing low-power HoLEP; and Group C consisted of 65 patients not on AP therapy and undergoing low-power HoLEP. The coagulation status of the patients was evaluated using thromboelastography (TEG). The TEG tracings revealed prolonged R times, suggesting factor deficiency and/or the presence of heparin, and reduced maximum amplitude (MA), indicating defects in platelet function.[22,23] Clinical data, including age, hemoglobin (HB), prostate volume (V_1), International Prostate Symptom Score (IPSS), maximum urinary flow rate (Qmax), prostate-specific antigen (PSA), platelet count (PLT), MA, enucleation time, morcellation time, bladder irrigation, postoperative catheterization time (PCT), length of hospital stay (LOS) and hemoglobin drop (HBD), were collected for analysis.

All operations were performed under general anesthesia by an experienced surgeon (engaged in enucleation of prostate for 5 years and more than 200 cases have been enucleated). Inclusion criteria comprised of a medium-sized prostate, Qmax < 15 m/s, and IPSS >7. Exclusion criteria included the presence of bladder calculus, neurogenic bladder, and prostate cancer. Prostate weight and volume were examined using transrectal ultrasound scan (TRUS) and calculated using the formula—volume = upper and lower diameter x antero-posterior x left and right diameter x 0.52, weight = volume x 1.05). Patients underwent both LP-HoLEP (40 W, 1J x 40 Hz) and HP-HoLEP (100W, 2J x 50 Hz) procedures. A 550 µm laser fiber (SlimLine, Lumenis Ltd, Yokneam, Israel) was used with a 120 W Holmium neodymium: YAG laser (VersaPulse PowerSuite, Lumenis Ltd). Both procedures were conducted using a 26F continuous-flow laser resectoscope with a video system (Karl-Storz, Germany) and a mechanical tissue morcellator (DPM-3-A, Dahwa, China).

Statistical Analysis

SPSS version 22.0 was used for the execution of statistical analyses. Continuous variables were delineated as means ± standard deviation (SD) or as median values with interquartile range (IQR) based on their distribution. The Kruskal–Wallis test and one-way analysis of variance (ANOVA) were used for the analysis of continuous variables, while the chi-squared test was applied for categorical variables. Univariate and multivariate analyses were conducted to ascertain independent risk factors for hematuria. The association of categorical parameters was estimated with a 95% confidence interval. All statistical tests were two-sided, and a significance level of $p < 0.05$ was set.

Results

Table 1 presents a summary of the basic clinical data. There was no difference in terms of age, HB, V_1, IPSS, Qmax, PSA, PLT, MA among all groups. However, there were notable discrepancies in enucleation, morcellation, bladder irrigation, post-operative catheterization time, the LOS, and hemoglobin drop among all groups, with statistical significance (F=54.06, 8.54, 6.68, 9.24, 17.06, 5.97, $p < 0.05$). As indicated in Table 2, there were no discernible differences in postoperative hematuria, urine retention, the rate of transfusion, and stress urinary incontinence (x_2 = 1.082, p = 0.582; x_2 = 0.197, p = 0.906; x_2 = 3.981, p = 0.137; x_2 = 0.816, p = 0.665). Univariate and multivariate analyses, as presented in Table 3, revealed that prostate volume emerged as an independent risk factor for hematuria (odds ratio [OR] 1.080, 95% confidence interval [CI]: 1.007–1.158, p = 0.031 < 0.05) (Figure 1). The clinical outcomes including Qmax, IPSS, V_2, PSA were significantly enhanced during the 1-year follow-up (Figure 2).

Discussion

HoLEP has evolved as a well-established and minimally invasive alternative for patients undergoing AP therapy, particularly those with large prostates.[24,25] The feasibility and safety of HoLEP in patients on non-vitamin K antagonist oral anticoagulants (NOAC) or AP therapy have been demonstrated,[26,27] with patients exhibiting prostate sizes up to 105.8 ml, albeit with an increased risk of hematuria in cases of very large prostates.[10,28] Consequently, we opted for patients with medium-sized prostates as the focus of this study.

Table 1 Clinical Basic Data

Data	Group A (N=72)	Group B (N=73)	Group C (N=65)	P
Age y	69.5±7.4	67.8±5.9	68.5±5.3	0.256
HB g/L	130.6±8.4	132.2±7.2	127.5±8.8	0.197
V_1 ml	62.6±9.8	63.5±5.8	63.2±8.7	0.799
IPSS	22.4±3.7	23.6±4.2	22.0±3.8	0.064
Qmax	9.4±1.8	8.6±1.7	9.7±1.8	0.146
PSA ng/dL	3.0 (2.1–3.9)	3.2 (2.6–4.0)	3.1 (2.0–4.2)	0.072
PLT /L	208.9±29.3	204.0±28.2	201.1±18.3	0.202
MA mm	59.0 (48–68)	60.0 (46–72)	58.1 (49–69)	0.079
Enucleation min	68.3±11.2	58.7±6.3	51.6±10.3	0.000
Morcellaction min	13.1±3.2	13.6±2.8	11.8±3.1	0.002
Bladder irrigation h	40.6±8.7	36.6±11.8	33.3±.2	0.000
PCT d	3.0±0.7	2.7±0.6	2.3±0.6	0.000
LOS d	3.6±0.8	3.2±0.7	3.1±0.9	0.000
HBD g/L	7.6±1.8	7.0±2.0	6.5±1.7	0.003

Abbreviations: Values are presented as mean±standard deviations; PLT, platelet; $V_{1,}$ prostate volume; MA, the maximum degree of platelet aggregation in thrombus formation; PCT, postoperative catheterisation time ; LOS, length of hospital stay; HBD, Haemoglobin drop; Mann-Whitney rank sum test.

Table 2 Postoperative Complications

Complication	Group A (N=72)	Group B (N=73)	Group C (N=65)	P
Grade 1				
Urinary retention	5 (6.9)	2 (2.8)	3 (4.6)	0.492
SUI	4 (5.6)	3 (4.1)	5 (7.7)	0.662
Bladder spasm	8 (11.1)	7 (9.6)	6 (9.2)	0.925
Grade 2				
Capsular perforation	11 (15.3)	7 (9.6)	8 (12.3)	0.582
Urinary tract infections	9 (12.5)	6 (8.2)	7 (9.7)	0.699
Blood transfusion	3 (4.1)	2 (2.8)	0	0.137
Grade 3a				
Urethral stricture	2 (2.8)	0	1 (1.5)	0.242
Grade 3b				
Hematuria	7 (4.1)	6 (1.4)	5 (7.7)	0.906

Abbreviation: SUI, Stress urinary incontinence.

Table 3 Logistic Regression Models Predicting the Occurrence of Hematuria

	Univariate analysis			Multivariate analysis		
	OR	95%CI	P	OR	95%CI	P
Age	1.103	1.025–1.188	0.009	1.075	0.994–1.163	0.070
V_1	1.082	1.018–1.151	0.012	1.080	1.007–1.158	0.031
PLT	0.886	0.690–1.136	0.339	1.011	0.996–1.027	0.162
MA	0.937	0.864–1.016	0.113	0.920	0.840–1.006	0.068
LP Vs HP	0.527	0.206–1.346	0.180	0.641	0.225–1.823	0.404
WA /CA	1.708	0.651–4.481	0.277	1.403	0.493–3.989	0.525

Abbreviations: LP vs HP, LP-HoLEP vs HP-HoLEP; WA/CA, without Aspirin/clopidogrel/continuous Aspirin/clopidogrel; PLT, platelet; V_1, prostate volume; MA, the maximum degree of platelet aggregation in thrombus formation.

Initially, differences in preoperative characteristics between Group B and Group C were identified, highlighting the impact of Aspirin/clopidogrel intake on the surgical context. Subsequently, from our findings, we discovered that LP-HoLEP resulted in decreased enucleation, morcellation, bladder irrigation, postoperative catheterization duration, the length of hospital stays, and hemoglobin drop compared to HP-HoLEP. We attributed this superiority of LP-HoLEP to its efficacy in facilitating efficient vessel coagulation.[29]

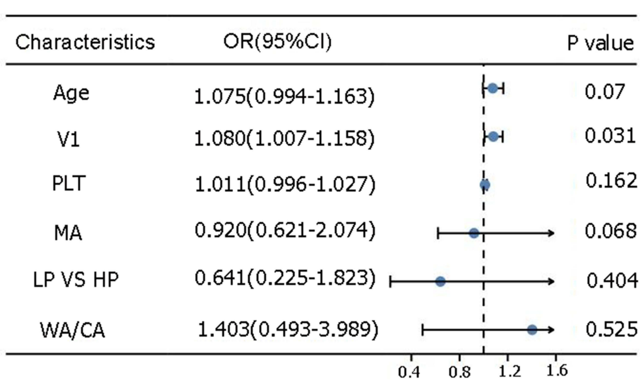

Figure 1 Forest plot about multivariate logistic regression analyses of factors related to hematuria V1, prostate volume. PLT, Platelet. MA, Maximum amplitude. LP vs HP, LP-HoLEP vs HP-HoLEP. WA/CA, without Aspirin/clopidogrel/continuous Aspirin/clopidogrel.

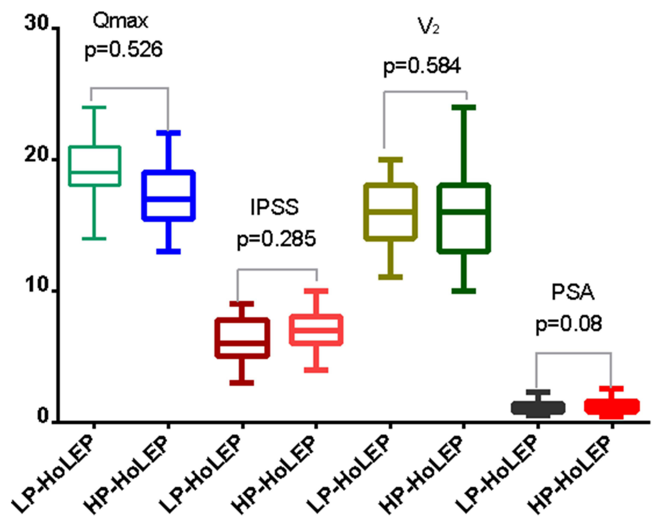

Figure 2 Clinical outcomes including Qmax, IPSS, V2, and PSA Qmax, maximum urinary flow rate. IPSS, International Prostate Symptom Score. V2, post-void residual volume. PSA, prostate-specific antigen.

Hematuria emerged as the most prevalent complication, particularly in patients with continuous AP therapy. Persistent or delayed postoperative bleeding, in some cases, correlated with a preoperative hypercoagulable state.[30] TEG was used to unveil coagulation defects challenging to detect through routine laboratory tests. Prior studies have associated a TEG MA value above 68 mm with an increased likelihood of postoperative thrombotic events.[31] In this study, no disparities in MA were observed among the groups, as antiplatelet therapy exhibited a low inhibitory rate on platelet aggregation. In this study, the MA values for all groups were below 68 mm, and the platelet counts remained within an acceptable range. This further demonstrates that Through the enhancement of the TEG examination, patients who are unsuitable for surgery due to long-term oral antiplatelet therapy can be identified and excluded. Simultaneously, there is no longer a need to discontinue antiplatelet medication in cases where platelet count and aggregation functions remain within normal parameters, as the approach now has greater support evidence.

Furthermore, there were no discernible differences in postoperative hematuria, hemorrhage, and transfusion rates, aligning with reported probabilities in the literature. Logistic regression models predicting hematuria revealed prostate volume as an independent risk factor associated with a higher complication rate. Consequently, we postulated that the thinner vessels of the medium-sized prostate could not be entirely excluded from the risk. Subsequently, 5-alpha reductase inhibitors (5-ARIs) were employed as a suitable and effective alternative treatment for men with refractory hematuria presumably due to prostatic bleeding.[32,33]

However, this study is not without limitations. It is a single-center study with a relatively short follow-up period, introducing inherent constraints. The patient population was limited to those on antiplatelet therapy medication with medium-sized prostates, inevitably introducing selection bias. Additionally, the study did not include information on the drug dose of aspirin/clopidogrel and other types of NOAC concerning postoperative bleeding complications.[34] Further and more detailed studies with great number of patients and a randomized asset should be made in future, based on overcoming limitations.

Conclusion

TEG holds potential utility in informing preoperative strategies, particularly in patients undergoing continuous AP therapy. In contrast to HP-HoLEP, LP-HoLEP demonstrated a capacity to mitigate enucleation requirements, morcellation procedures, bladder irrigation necessity, post-operative catheterization duration, length of hospitalization, and reductions in hemoglobin levels. LP-HoLEP presents a feasible option that may be advocated without interrupting AP therapy, particularly in cases where platelet count and aggregation functions remain within normal parameters. Preoperative management, particularly for patients undergoing continuous AP therapy, could benefit from the use of TEG as a guiding tool.

Abbreviations

BPH, Benign prostatic hyperplasia; TRUS, Transrectal ultrasound; LTUS, Lower urinary tract symptoms; HBD, Haemoglobin drop; HoLEP, Holmium laser enucleation of the prostate; PLT, Platelet; TURP, Transurethral resection of the prostate; MA, Maximum amplitude; LOS, Operative length of hospital stay; PCT, Post catheterisation time; Qmax, Maximum urinary flow rate; SUI, Stress urinary incontinence; NOAC, New oral anticoagulants.

Data Sharing Statement

The datasets during the current study were available from the corresponding author (Jian-Gang Chen) on reasonable request.

Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by The Affiliated Hospital 2 of Nantong University's ethics committee. The need for informed consent was waived by the ethics committee/Institutional Review Board of The Affiliated Hospital 2 of Nantong University, because of the retrospective nature of the study. The requirement of patient consent for inclusion was waived. Patient personal privacy and data confidentiality has been upheld.

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Disclosure

The authors declare that they have no competing interests.

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