Safety of Surgery in Benign Prostatic Hyperplasia Patients on Antiplatelet or Anticoagulant Therapy: A Systematic Review and Meta-Analysis

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Purpose: The management strategies of anticoagulant (AC) or antiplatelet (AP) therapy in the preoperative period of benign prostatic hyperplasia (BPH) is still controversial. Therefore, a meta-analysis to systematically evaluate the surgical safety for BPH patients on AC or AP therapy was performed.

Materials and Methods: The protocol for the review is available on PROSPERO (CRD42018105800). A literature search was performed by using MEDLINE, Web of Science, PubMed, Cochrane library, and Embase. Summarized odds ratios (OR), mean difference (MD) and 95% confidence intervals (CI) were used to assess the difference in outcomes.

Results: We identified 13 trials with a total of 3767 patients. An intragroup significant difference was found in bleeding complications and blood transfusions when undergoing transurethral resection of the prostate (TURP). For laser surgery, the intragroup significant difference was found in the result of blood transfusion. Bridging therapy would not cause a higher risk of bleeding complications and blood transfusion during the perioperative period. Besides, no difference existed in operation time, catheterization time, hospitalization, and thromboembolic events.

Conclusion: Patients with BPH on perioperative AC/AP therapy would have a risk of postoperative hemorrhage after TURP or laser treatments. To reduce the risk of hemorrhage, bridging therapy could be a good choice.

Keyword: Transurethral resection of prostate (TURP); Laser treatment; Benign prostatic hyperplasia (BPH); Anticoagulant; Antiplatelet

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a disease common in men over 50 years of age. Up to 50% of men in their sixth decade suffer from BPH, and the corresponding rate was increased with age[(1)] The men troubled by lower urinary tract symptoms need drug treatment or surgical intervention. For pharmacological treatment, α1-adrenoceptor antagonists like tamsulosin can effectively improve lower urinary tract symptoms.[(2)] Nevertheless, α1-adrenoceptor antagonist cannot prevent the occurrence of urinary retention or the need for surgery. Transurethral resection of the prostate (TURP) has been the gold standard for the surgical management of BPH in recent decades. However, morbidity followed with TURP is still concerned, especially bleeding requiring blood transfusion and late postoperative bleeding.[(3)] With an aging population and a high incidence of cardiovascular disease, the number of patients requiring anticoagulant (AC) or antiplatelet (AP) therapy is steadily growing.[(4)] With an increasing elderly population requiring surgical procedures for BPH treatment and long-term use of anticoagulants, the management strategies of AC/AP therapy in the preoperative period remain controversial. Some surgeons prefer to discontinue AC/AP therapy and replaced low molecular weight heparin (LMWH) in advance of surgery, whereas others continue AC/AP therapy perioperatively.

Recently, a number of laser techniques have emerged as alternatives to TURP including the holmium yttrium aluminum garnet neodymium (Ho:YAG), thulium laser, and potassium titanyl phosphate (KTP, also known as the Greenlight), offering new options for patients with BPH. These laser surgeries present the advantage of hemostasis comparing with TURP and have been an effective tool for BPH.[(5-8)] All types of lasers are considered suitable and safe for patients taking anticoagulants in the recommendation of European Association of Urology (EAU) guidelines for the treatment of BPH. Furthermore, EAU guidelines on the surgical treatment of BPH nominated that 532-nm laser vaporization should be considered in patients receiving anticoagulant medication or for those with a high cardiovascular risk.[(9)] However, the EAU guidelines did not mention whether preoperative anticoagulant therapy should be

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Table 1. Characteristics and quality evaluation of including studies.

Study	Country	Study period	Design	No. of patients AC/AP	Control	Age AC/AP	Control	Comparability	Study quality
Ala-Opas et al. 1995	Finland	May. 1993 to Feb. 1994	CCT	40	42	69 (53-85)	75 (64-86)	①④⑥	4 (NOS)
Dotan et al. 2002	America	Nov. 1997 to Feb. 2001	CCT	20	20	N/A	N/A	①③④⑤	6 (NOS)
Nielsen et al. 2000	Denmark	1996 to 1998	RCT	26	27	70 (66-74)	69 (65-76)	①②③④⑤⑥	3 (Jadad)
Descazeaud et al. 2011	France	Jan. 2007 to Dec. 2008	CCT	55	406	75 ± 14.14	71 ± 14.14	②③④⑤⑥	6 (NOS)
Taylor et al. 2011	Australia	Jan. 2008 to Jun. 2009	CCT	7	91	69 ± 6.37	71 ± 8.56	①④	6 (NOS)
Ong et al. 2015	Australia	Jan. 2011 to Dec. 2013	CCT	32	166	N/A	N/A	①④⑤⑥	6 (NOS)
Tyson et al. 2009	England	May. 2002 to Sep. 2007	CCT	25	37	69.4 ± 7.2	65.2 ± 8.7	①③⑤	5 (NOS)
Tayeb et al. 2016	America	1999 to 2014	CCT	30	1558	N/A	N/A	②③④⑤	7 (NOS)
Ruszat et al. 2006	Switzerland	Sep. 2002 to Jan. 2006	CCT	71	92	72 ± 9	68 ± 9	②③⑤	7 (NOS)
Knapp et al. 2017	Australia	Jul. 2010 to Dec. 2016	CCT	59	272	74.9 ± 10.3	67.6 ± 9	①②③⑤	6 (NOS)
Piotrowicz et al. 2017	Poland	2009 to 2012	CCT	65	44	68.3 ± 6.63	66.9 ± 6.5	②③⑤	6 (NOS)
Eken et al. 2018	Turkey	Nov. 2012 to Oct. 2016	CCT	59	174	74.8±9.1	69.2±5.5	①	5 (NOS)
Meskawi et al. 2018	Canada	2011 to 2016	CCT	87	274	70±7.48	66±9.62	①②③④	7 (NOS)

①bleeding complications ②operation time ③catheterization time ④blood transfusion ⑤hospitalization ⑥Thromboembolic events. RCT: randomized controlled trials, CCT: case control trials, AC: anticoagulant, AP: antiplatelet, N/A: not available, NOS: Newcastle–Ottawa Scale, Jadad: Jadad scale. Values are presented as mean ± standard deviation or mean (range).

withdrawn regardless of whether traditional TURP or advanced laser technology is selected. Similarly, the National Institute for Health and Care Excellence (NICE) guidelines did not specify the perioperative management of patients under AC/AP therapy.[10]
Therefore, we performed this meta-analysis based on the current evidence to assess the safety of surgery in BPH patients on AC/AP therapy. Our goal was to derive an evidence-based recommendation for clinical practice.

MATERIALS AND METHODS

Literature search

The present meta-analysis was performed in accordance with the Preferred Reporting Item for systematic Reviews and Meta-Analysis (PRISMA) guidelines. The protocol for the review was available on PROSPERO (CRD42018105800; https://www.crd.york.ac.uk/prospero/). The studies were identified by a literature search of MEDLINE, Web of Science, PubMed, Cochrane library and Embase database articles published up to July 2019. Separate searches were completed using the following search terms: benign prostatic hyperplasia, BPH, transurethral resection of the prostate, TURP, holmium laser enucleation of the prostate, HoLEP, photoselective vaporization of the prostate, PVP, thulium vaporesection of the prostate, ThuVARP, laser therapy, anticoagulants, antiplatelet, aspirin, warfarin, Coumadin and clopidogrel. The detailed retrieval strategy was listed in S1 file. In addition, a manual search was also performed in the references from the included studies and databases like EMBASE. No temporal, regional, publication status, or language restrictions were applied.

Inclusion and exclusion criteria

Literature searching, study examinations, data extractions, study quality assessment and statistical analyses were conducted by two authors (JH and YH) independently. Disagreement was resolved through consultation with the third author (TZ). Eligibility criteria for the included studies were defined base on the PICOS principles: (1) Participants (P): Patients having a series of symptoms of urinary obstruction, with clinical and laboratory evidence suggesting enlarged prostate and necessitating surgical treatment. (2) Interventions (I) and comparisons (C): Exploring the safety of surgery in BPH patients on AC/AP therapy compared with the patients who do not need AC/AP therapy. (3) Outcomes (O): Including at least one of the predefined outcome measurements. (4) Study design (S): randomized controlled trials (RCTs), case-control studies or cohort studies with relative data could be used directly or indirectly. In contrast, studies were excluded if the inclusion criteria were not met or the relevant data could not be extracted in the appropriate format and obtaining the data from the authors. Additionally, studies as conference proceedings, reviews, case reports, abstracts, and unpublished studies were excluded from this study.

Procedures

Patients on AC/AP therapy during the surgery for BPH constituted AC/AP group, and patients who do not need AC/AP therapy formed the control group. The following variables from each study were recorded independently by two reviewers: first author name; publication year; study period; research design type; AC/AP type; total number of patients enrolled; PSA (prostate-specific antigen level); IPSS (international prostate symptom score); maximum urinary flow; prostate volume; weight of resected tissue; and age of patients. In addition, the following outcome measures were extracted: operative time, bleeding complications, thromboembolic events, blood transfusion, length of hospital stay, and catheterization time. Bleeding complication is a combined concept described in the included studies. Several studies directly defined bleeding complication as an extended period of bladder irrigation (3 or more days postoperatively), clot retention or persistent hematuria necessitating recatheterization.[11-13] While two only record incidents of persistent hematuria,[14,15] and the other one record incidents of extended period of bladder irrigation.[16] Thromboembolic events, as included studies described, was defined as pulmonary embolism, deep venous thrombosis, acute coronary syndromes, and cerebrovascular events like stroke.[12, 17-19] Outcome of bleeding complication and blood transfusion, assessing the degree of hemorrhage, were the key parameters evaluating the safety of the surgery for BPH patients with AC/AP therapy. Discrepancies were resolved through consultation with the third author.

Table 2. Perioperative parameters of each selected studies.

Study	Surgery type	Prostate volume (ml)		Weight of resected tissue (g)		Preoperative PSA (ng/ml)		Preoperative IPSS		Preoperative maximum urinary flow (ml/s)		AC/AP type	Perioperative management of AC/AP therapy
		AC/AP	Control	AC/AP	Control	AC/AP	Control	AC/AP	Control	AC/AP	Control		
Ala-Opas et al. 1995	TURP	N/A	N/A	30 (7-70)	28 (5-80)	N/A	N/A	N/A	N/A	9 (4.2-19)	9.6 (4.6-16.8)	AC	AC continued
Dotan et al. 2002	TURP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Type of AC/AP was not counted separately	AC/AP withdrawal + LMWH
Nielsen et al. 2000	TURP	N/A	N/A	37 (27-64)	30 (16-50)	N/A	N/A	N/A	N/A	N/A	N/A	AP	AP continued
Descazeaud et al. 2011	TURP	58.5	49	30.5	21.7	3.8	4.6	17.6	20.5	5.8	8.3	AC	AC withdrawal + LMWH
Taylor et al. 2011	TURP	N/A	N/A	17	25	N/A	N/A	N/A	N/A	N/A	N/A	AP	AP continued
Ong et al. 2015	TURP	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	AP	AP continued
Tyson et al. 2009	HoLEP	50.3 ± 16.7	49.9 ± 20.6	N/A	N/A	3.9 (2.2)	4.4 (3.9)	16.5 (8.7)	23.5 (6.7)	N/A	N/A	AC	AC continued
Tayeb et al. 2016	HoLEP	N/A	N/A	55.5 (1-206)	68 (0.2-532.2)	5.5	5.2	N/A	N/A	N/A	N/A	AP	AP continued
Ruszat et al. 2006	PVP	58 ± 31	71 ± 39	N/A	N/A	3.4 (2.7)	4.6 (4.2)	N/A	N/A	N/A	N/A	AP	AP continued
Knapp et al. 2017	PVP	90.8 ± 58.7	79.1 ± 47	N/A	N/A	5.6 (6.2)	6.2 (8.0)	17.8 (6.9)	20(7.1)	N/A	N/A	AC	AC continued
Piotrowicz et al. 2017	PVP	66.3 ± 6.63	66.9 ± 6.5	N/A	N/A	2.55 (1.25)	2.68 (1.42)	24.7 (4.58)	25.19 (4.11)	9.78 (2.99)	9.42 (2.73)	Type of AC/AP was not counted separately	AC/AP withdrawal + LMWH
Eken et al. 2018	PVP	61.5 ± 20.7	54.8 ± 16.9	N/A	N/A	3.3 (2.8)	3 (2.4)	22.5 (7.6)	21.6 (5.3)	7.9 (2.2)	8.3 (3.1)	Type of AC/AP was not counted separately	AC/AP withdrawal + LMWH
Meskawi et al. 2018	PVP	71 ± 29.63	76 ± 29.63	N/A	N/A	3.8	7.6	N/A	N/A	N/A	N/A	AP	AP continued

AC: anticoagulant, AP: antiplatelet, PSA: prostate-specific antigen level, IPSS: international prostate symptom score, HoLEP: holmium laser enucleation of the prostate, TURP: transurethral resection of the prostate, PVP: photoselective vaporization of the prostate, LMWH: low molecular weight heparin, N/A: not available, Values are presented as mean ± standard deviation or mean (range).

Evaluations

The quality of the randomized controlled trials (RCT) included in this systematic review was assessed independently by two reviewers by using the Jadad scale score,[20] which ranges from 0 to 5 points; a higher score indicates a better quality of the research. The Jadad score evaluates studies based upon their randomization, blinding, and descriptions of participant withdrawals and dropouts. A study with a Jadad score of 3 points or more was considered to be a relatively high-quality study. The Newcastle-Ottawa scale (NOS) was used to assess the quality of case-control trials included in this meta-analysis.[21] The review scores range from 0 to 9 points for each trial. Scores between 0 and 4 implied a low-quality study, while those between 5 and 9 implied a high-quality study. Discrepancies were resolved through consultation with the third author.

Statistical analysis

Odds ratios (OR) were used for binary outcomes with 95% confidence intervals (CI), and mean difference (MD) or standardized mean difference was used for continuous variables with 95% CI. Pooled estimates were calculated using a fixed-effects model[22] if no heterogeneity was presented; otherwise, a random-effects model[23] was used. The overall effect was determined by the Z-effect, and $p < .05$ was considered to be statistically significant. The Cochrane X2-test and Inconsistency (I^2) were used to assess the heterogeneity among studies.[24,25] $P < .1$ indicated the presence of heterogeneity, and $I^2 < 50\%$ indicated that the level of heterogeneity was acceptable. Sensitivity analysis was performed using a single item removal method. The funnel plot was used to assess the publication bias. All tests were performed using Review Manager Software (Revman 5.3, Cochrane Collaboration, Oxford, English).

RESULTS

Study characteristics

The search protocol and its results are shown in **Figure 1**. The initial search identified 383 potentially relevant studies. Additionally, 33 studies were available by manual search with references. Then 181 duplicates were detected and excluded by NoteExpress. After screening of studies titles and abstract, 39 potentially relevant studies needed further assessment for eligibility. Among them, 9 studies were excluded for no control

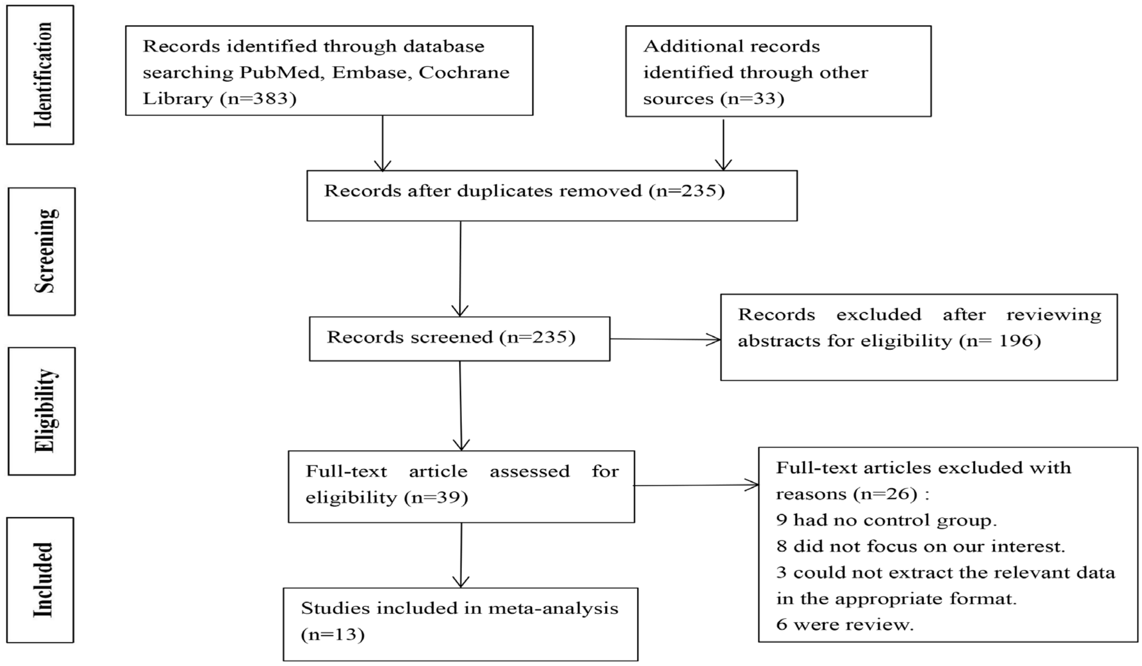

Figure 1. Meta-analysis flowchart.

group; 8 studies were excluded for irrelevant topics; 3 studies were excluded for failure to extract the primary data assessing the safety of surgery; and 6 for being reviews. At the end, 13 eligible studies(11-19, 26-29) including 3767 patients (564 on AC/AP and 3203 control) were included in the subsequent meta-analysis according to our predefined selection criteria.

The 13 studies included one RCT and twelve case-control trials. No prospective cohort study that met the inclusion criteria was found (**Table 1**). The methodological quality of the included non-randomized studies was mostly granted a score between 5 and 7, while the RCT got 3 points on the Jadad scale.

AC agent reported included coumadin and pradaxa, and AP agent reported included aspirin, clopidogrel, ticlopidine and dipyridamole. Of BPH patients on AC/AP, seven included studies evaluated the surgical safety of perioperative AP therapy, and three included studies evaluated the surgical safety of perioperative AC therapy. Three included studies did not record the use of AC and AP agent separately when assessing the safety of surgery. AC/AP therapy was continued during the perioperative period in nine studies, while AC/AP therapy was withdrawn and replaced with low molecular weight heparin in four studies (**Table 2**).

Preoperative measurement of prostate size and the weight of the resected prostate during operation of each study were summarized in **Table 2**. Five studies reported weight of resected tissue, and seven studies reported preoperative measurement of prostate volume rather than weight of resected tissue. One study reported both preoperative measurement of prostate volume and weight of resected tissue. Preoperative PSA, IPSS, and maximum urinary flow in each study were also described in **Table 2**.

Bleeding complications

Figure 2A presents the comparison of the cases of bleeding complications between the AC/AP group and the control group. As the heterogeneity was low among these studies (P = .17, I^2 = 31%), a fixed-effects model was applied for meta-analysis and showed that perioperative AC/AP therapy would lead to a higher risk of bleeding complications compared with the control group (95% CI: 1.32–4.13, OR = 2.33, P = .004) (Figure 2A). The funnel plot showed no publication bias (Figure S1A). Subgroup analysis was conducted on account of surgical type, AC/AP type, and management of AC/AP therapy. The subgroup meta-analysis result showed that patients in TURP treatment for BPH would have a higher risk of bleeding complication in AC/AP group (OR = 2.58, P = .005, **Table S1**). However, for laser surgical treatment for BPH, including holmium laser enucleation of the prostate (HoLEP) and photoselective vaporization of the prostate (PVP), the risk of bleeding complications in the AC/AP group was similar to the control group (OR = 1.70, P = .36, **Table S1**). The subgroup meta-analysis result also showed that perioperative AP therapy would increase the risk of bleeding complication (OR = 2.65, P =.004, **Table S1**), while no significant difference between patients on perioperative AC therapy and controls (OR = 0.91, P = .92, **Table S1**). Besides, the analysis indicated no significance between AC/AP patients bridged with LMWH and controls (OR = 2.58, P = 0.24, **Table S1**). Continuing AC/AP therapy during surgery could led to increased risk of bleeding complication (OR = 2.29, P = .008, **Table S1**).

Blood transfusion

Eight studies were included in the forest plot of blood transfusion. As no heterogeneity existed among these studies (P = .89, I^2 = 0%, **Figure 2B**), a fixed effects model was applied for meta-analysis. The pooled result showed that perioperative AC/AP therapy would lead to a higher risk of blood transfusion compared with the control group (OR = 2.86, 95% CI: 1.50–5.45, P =

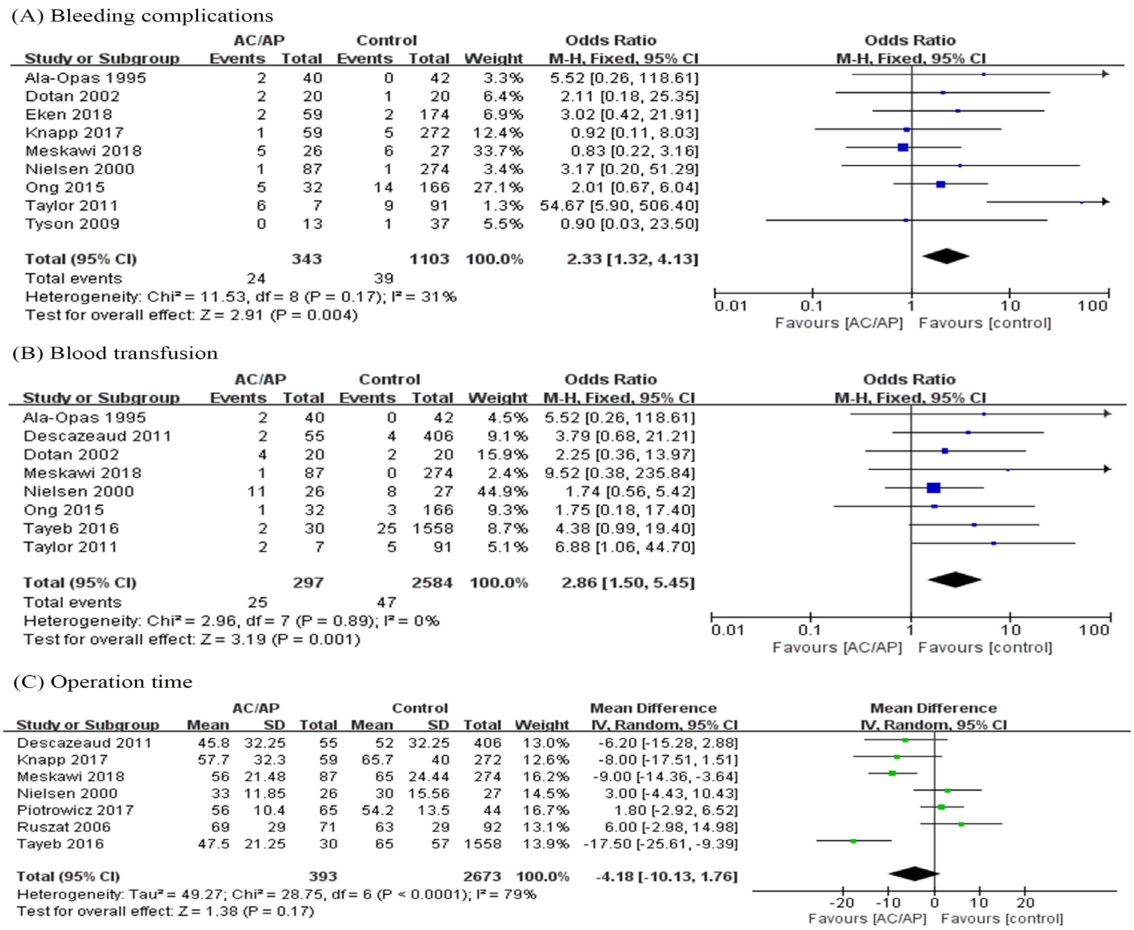

Figure 2 Forest plots and meta-analysis. (A) Bleeding complications, (B) blood transfusion, (C) operation time.

Figure 2. Forest plots and meta-analysis. **(A)** Bleeding complications, **(B)** blood transfusion, **(C)** operation time.

.001, **Figure 2B**). The funnel plot did not show obvious publication bias (**Figure S1B**). The subgroup analysis showed that both the patients undergoing laser surgical treatment and TURP need more blood transfusions (OR = 2.53, *P* = .01; OR = 5.47, *P* = .01, respectively, **Table S2**). Of AC/AP type, the subgroup analysis presented the transfusion rate of patients under AC therapy was similar to that of the control group (OR = 3.79, *P* = .13, **Table S2**), whereas the transfusion rate of patients under AP therapy was higher than the control group (OR = 2.76, *P* = .004, **Table S2**). Of perioperative administration of AC/AP therapy, the method that preoperative AC/AP therapy replaced with LMWH would not cause a higher risk of blood transfusion in BPH patients during the perioperative period (OR = 2.81, *P* = .12, **Table S2**). The patients who continued AC/AP therapy during perioperative period had a higher risk of blood transfusion compared with the control group (OR = 2.76, *P* = .004, **Table S2**).

Operation time

Seven studies were included in the forest plot of operation time. The pooled result showed no significant difference between the AC/AP group and control group (MD = -4.18 min, 95% CI: -10.13–1.76, *P* = .17, **Figure 2C**). The random effect model was applied because there was evidence of significant heterogeneity (*P* = .0001, I2 = 79%). The sensitivity analysis showed that heterogeneity originated from the studies of Tayeb et al(27) and Meskawi et al[29], probably due to the different size of resected prostate tissue (**Table 2**). The funnel plot showed no publication bias (**Figure S1C**). The subgroup analysis results based on surgical type, AC/AP type and management of AC/AP therapy all showed that no significant difference between the AC/AP group and control group, which were consistent with overall outcome (**Table S3**).

Catheterization time

Nine studies reported the catheterization time after surgery. Random effect was applied for analysis with significant heterogeneity ($P < .00001$, $I^2 = 95\%$). The pooled results showed that no significant difference between the AC/AP group and control group (MD = 0.26 day, 95% CI: -0.06–0.58, *P* = .11, **Figure 3A**). The sensitivity analysis suggested that heterogeneity being mainly from the study of Dotan et al[16]. Limited sample size from the study of Dotan et al, causing potential bias, may be the reason of the heterogeneity. After removal of study of Dotan et al, the pooled results still showed no significant difference between the AC/AP group and control group with mild heterogeneity (MD = 0.08 day, 95% CI: -0.08–0.25, $P = .33$, $I^2 = 35\%$). The subgroup analysis results account of surgical type, AC/AP type and management of AC/AP therapy was

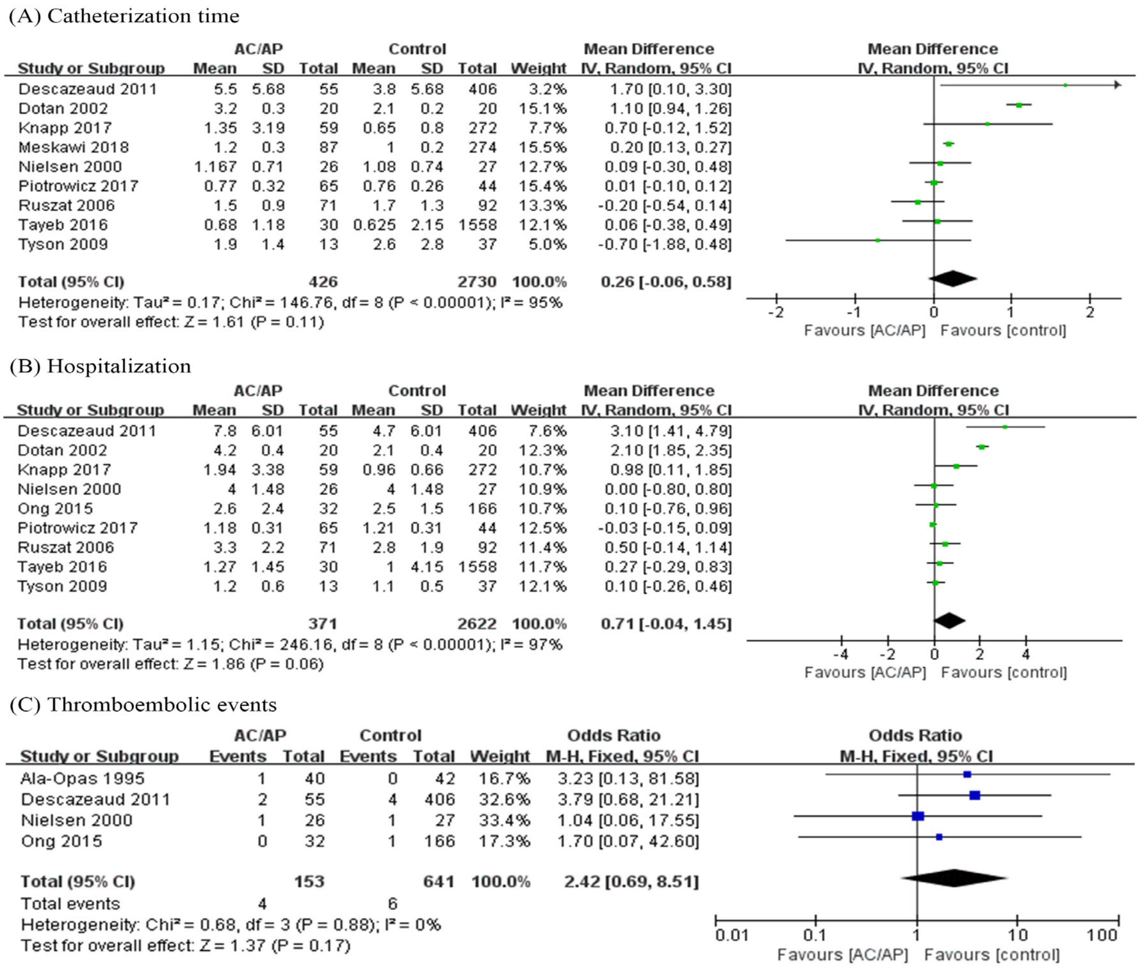

Figure 3. Forest plots and meta-analysis. **(A)** Catheterization time, **(B)** hospitalization, **(C)** thromboembolic events.

also conducted. The funnel plot did not show obvious publication bias (**Figure S1D**). The subgroup analysis revealed that patients on perioperative AP therapy would have a longer catheterization time (MD = 0.18 day, 95% CI: 0.11–0.24, $P < 0.00001$, **Table S4**), while perioperative AC therapy would not prolong the catheterization time (MD = 0.46 day, 95% CI: -0.16–0.24, P < 0.00001, **Table 4**). Meanwhile, the subgroup analysis of surgical type or management of AC/AP therapy showed that no significant difference between the AC/AP group and control group, which were consistent with overall outcome (**Table S4**).

Hospitalization

Nine studies reported the hospitalization time. The pooled meta-analysis result using a random effects model because of existence of significant heterogeneity among these studies ($P < 0.00001$, $I^2 = 97\%$) showed no significant difference between the AC/AP group and control group (MD = 0.71 day, 95% CI: -0.04–1.45, $P = .06$, **Figure 3B**). The sensitivity analysis showed that heterogeneity mainly originated from the study of Dotan et al and Descazeaud et al[16,17]. The sample size, study design, geographical area, and individual differences of patients were all likely responsible for the heterogeneity. The heterogeneity decreased substantially after remove the study of Dotan et al and Descazeaud et al (MD = 0.13 day, 95% CI: -0.07–0.34, $P = .20$, $^{I2} = 30\%$). The funnel plot did not show obvious publication bias (**Figure S1E**). The subgroup analysis results based on the surgical type and AC/AP type showed that no significant difference between the AC/AP group and the control group, which were consistent with the overall outcome (**Table S5**). Of perioperative management of AC/AP therapy, our subgroup analysis indicated that the patients who continued AC/AP therapy during perioperative period had longer hospitalization time compared with the control group (MD = 0.25, $P = .04$, **Table S5**), whereas the method that preoperative AC/AP therapy replaced with LMWH would not prolong hospitalization time (MD = 1.60, $P = .08$, **Table S5**).

Thromboembolic events

Four studies were included in the forest plot of thromboembolic events. All included studies were on TURP treatment group. A fix effects model was applied for analysis as no heterogeneity exist ($P = .88$, $I^2 = 0\%$, **Figure 3C**). The pooled results revealed that no significant difference between AC/AP group and control (OR = 2.42 , 95% CI: 0.69–8.51, $P = .17$, **Figure 3C**). The funnel plot did not give any indication of publication bias (**Figure S1F**). The subgroup results of AC/AP type and management of AC/AP therapy was also conducted. The results both showed that no significant difference between the AC/AP group and control group, which were consistent with overall outcome (**Table S6**).

DISCUSSION

TURP has been widely used for the treatment of BPH. However, the morbidity of patients after TURP is considerably high due to intraoperative and postoperative bleeding and electrolyte disorder. Due to the AC/AP therapy for atrial fibrillation, recurrent thromboembolic disease, or prosthetic heart valves, the risk of bleeding complications associated with surgery is higher in BPH patients;[30] however, discontinuation of AC/AP therapy before surgery may predispose patients to thromboembolism caused by the release of tissue thromboplastins.[31]

Various laser treatment options have been developed for BPH surgery for these patients on AC/AP therapy in recent years, such as PVP, Ho:YAG. These laser therapies seem to minimize bleeding during surgery.(32-35) Particularly in patients receiving AC/AP therapy, these laser treatments seem to have a favorable safety profile.[33,35,36] Both EAU guidelines and NICE guidelines recommend that laser treatment can be safely applied in patients who have an increased risk of bleeding. However, regarding the perioperative management of AC/AP therapy, the guidelines did not mention whether there is a need to discontinue or replace to LMWH.[9,10] Consequently, some surgeons discontinued AC/AP therapy and replaced LMWH in advance of surgery, whereas others continued AC/AP therapy perioperatively. Recently, Zheng and his colleagues conducted a meta-analysis to assess the efficacy and safety of PVP on high-risk patients including patients on anticoagulation.[37] However, their analysis did not conduct subgroup analysis for people on AC/AP therapy, and the management of perioperative AC/AP therapy still remained unsettled. Therefore, our meta-analysis, which synthesized all available evidence including TURP and other laser surgeries, should offer an objective verdict. A series of subgroup analyses based on surgical type, AC/AP type, and management of AC/AP therapy were conducted.

The present meta-analysis studied the safety profile of the surgery for BPH patients with AC/AP therapy. The incidence of bleeding complications and blood transfusions can represent a key parameter when evaluating the safety of the surgery for BPH patients with AC/AP therapy. Our subgroup analysis indicated that AC/AP therapy would have a higher risk of blood transfusion and bleeding complications when receiving TURP treatment for BPH. For the patients receiving laser surgical treatment for BPH, our result presented that continuing perioperative AC/AP therapy would increase blood transfusions, but would not have effects on the incidence of bleeding complications. Although the excellent hemostasis of laser surgery,[38,39] the laser treatment might still carry a risk of bleeding on patients receiving AC/AP therapy.

Besides, the subgroup meta-analysis result of bleeding complication, blood transfusion, and catheterization time on AC/AP type showed that the patients under perioperative AP therapy had a higher risk of postoperative bleeding than those who did not need anticoagulant or antiplatelet agent, which was in line with previous studies.[13,17] However, the subgroup analysis results indicated that perioperative AC therapy would not affect postoperative bleeding. The reason is probably because of limited sample size. Notably, AC therapy subgroup analysis showed all postoperative bleeding was related to laser treatment. For perioperative AC/AP management, the commonly used procedure in current practice included bridging treatment with LMWH and continued therapy. One of the main concerns about bridging treatment is that it might increase the risk of thromboembolic events. To settle this dilemma, the subgroup analysis of perioperative AC/AP management was also conducted. According to our result, the patients bridging with LMWH would not increase the incidence of bleeding complications, blood transfusion, and prolong hospitalization time, indicating that bridging treatment could effectively reduce the risk of severe hemorrhage requiring blood transfusion. Furtherly, our meta-analysis proved that the bridging treatment before surgery had no effect on thromboembolic events, which was consistent with the previous researches. Chakravarti et al.[40] managed anticoagulation for 11 patients undergoing TURP by stopping warfarin and bridging with heparin preoperatively. They observed only one blood transfusion, but mild bleeding occurred in 27% of the patients. Descazeaud et al.[41] also concluded that replacement by LMWH preoperatively is preferable for BPH patients under AC/AP therapy.

Among the studies for operation time and catheterization time, the synthesis of meta-analysis revealed a same effect between groups. These results suggest that application of AC/AP therapy during perioperative period would not affect the quality of surgery.

There are several limitations to our present study. First, most of the studies were case-control trials except for one RCT, which may cause potential bias in our results. In addition, because the use of anticoagulant and antiplatelet drugs in the included studies is not recorded in detail, comparison among antiplatelet drugs or anticoagulant drugs failed to be conducted. Comparison of different doses of AC/AP therapy failed to be performed, either. All included studies did not mention the threshold of transfusion, and the definition of bleeding complication varied among included studies, posing potential bias on the pooled results. In addition, although random-effect model was applied to some parameters with high heterogeneity, there might be some influence on the efficiency of our meta-analysis.

CONCLUSIONS

This meta-analysis has demonstrated that patients on perioperative AC/AP therapy would have a higher risk of hemorrhage in TURP for the treatment of BPH. Even for laser treatments, perioperative AC/AP therapy also have a risk of postoperative hemorrhage. To reduce the incidence of hemorrhage requiring transfusion, bridging treatment with LMWH could be a good choice. Due to the inherent limitations of the included studies, further large cohorts prospective, multi-center, and RCTs should be conducted to confirm our findings.

APPENDIX

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CONFLICT OF INTEREST

No conflict of interest exits in this study.

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