A systemic review and meta-analysis of the effects of perioperative anticoagulant and antiplatelet therapy on bleeding complications in robot-assisted prostatectomy

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Abstract. – OBJECTIVE: Robot-assisted prostatectomy is commonly performed for the management of prostate cancer. The literature has noted that prostate cancer patients are often prone to increased risk for thromboembolic complications. Normally, such situations call for long-term anticoagulant/antiplatelet therapy. However, the administration of these drugs is usually contraindicated prior to surgical intervention to limit intra- and post-operative hemorrhagic complications. Despite some recent evidence that continued administration of anticoagulant/antiplatelet drugs does not impact intra- and post-operative outcomes, no consensus in the literature exists concerning the influence of anticoagulant and antiplatelet drug administration on intra- and post-operative outcomes for robot-assisted prostatectomy.

Our aim is to evaluate the influence of perioperative administration of anticoagulant and antiplatelet drugs in patients undergoing robot-assisted prostatectomy in terms of bleeding complication incidence, blood transfusion rate, blood loss, and hospital stay duration.

MATERIALS AND METHODS: The academic literature was systematically searched according to the PRISMA guidelines across five databases (Web of Science, EMBASE, CENTRAL, Scopus, and MEDLINE). Through this, we conducted a random-effect meta-analysis to evaluate the influence of perioperative administration of anticoagulant and antiplatelet drugs in patients undergoing robot-assisted prostatectomy in terms of bleeding complication incidence, blood transfusion rate, blood loss, and hospital stay duration.

RESULTS: From 993 studies, eight eligible studies containing 2516 patients (mean age: 65.7 ± 3.6 years) were selected for inclusion. Meta-analysis revealed a higher bleeding complication prevalence for patients receiving anticoagulants (event rate: 10.6%) compared to those receiving antiplatelets (3.4%). We also noted longer hospital stay durations for anticoagulant

group patients (Hedge's g: -0.30) compared to antiplatelet group counterparts (g: -0.01).

CONCLUSIONS: The study provides preliminary evidence that anticoagulant drug administration results in higher bleeding complication incidence and longer hospital stay durations in patients undergoing robot-assisted prostatectomy relative to antiplatelet drug administration.

Key Words:

Prostatectomy, Minimal invasive surgery, Hemorrhage, Morbidity.

Introduction

According to the American Cancer Society, prostate cancer is primarily characterized as an adenocarcinoma of the prostate glands affecting mostly middle-aged men (≥ 65 years)^{1,2}. Prostate cancer is one of the most common malignancies amongst men^{3,4}, with recent epidemiological studies reporting high prevalence rates ranging from 7.1% to 25% in various regions across the world^{3,4}. The World Health Organization documents that 1.28 million deaths every year occur worldwide due to prostate cancer^{5,6}.

Prostate cancer arises from mutations in glandular cells found among peripheral basal cells⁷. This peripheral origin leads to rapid metastasis to the surrounding prostate tissue and lymphatic nodules⁸. In order to deal with localized malignancies, minimally invasive robot-assisted prostatectomy has been popularized in the recent literature⁹⁻¹¹. This approach has been shown to reduce intra- and post-operative morbidity, as well as overall mortality¹²⁻¹⁴. A meta-analysis by Novara et al (2012)¹⁵ reported that robot-assisted prostatectomy reduced blood loss and blood transfusion rates relative to retropubic radical prostatectomy. However, despite these benefits, this approach is difficult to employ for patients taking antiplatelet/anticoagulant drugs¹⁶⁻¹⁸.

Typically, middle-aged patients with a history of thromboembolism or those predisposed to high risks of thromboembolic events due to androgen deprivation therapy are managed using anticoagulant/antiplatelet therapy^{19,20}. However, prolonged administration of these drugs can increase the risk of hemorrhagic complications during surgery²¹⁻²³. Conventionally, robot-assisted prostatectomy is contraindicated for patients administered anticoagulant/antithrombotic drugs, and vice versa. Problematically, this leads to either increased morbidity and mortality for prostate cancer patients²⁴ or an increase in thromboembolic events²⁵. That said, contrary to conventional beliefs, continuing to administer antiplatelet/anticoagulant drugs but at lower dosages can limit adverse impacts during both intra- and post-operative phases¹⁶.

A few individual retrospective cohort studies^{17,18,26,27} have attempted to evaluate the comparative influences of perioperative administration of anticoagulants or antiplatelet drugs in patients undergoing robot-assisted prostatectomy in terms of intra- and post-operative outcomes. However, there is a lack of consensus in the existing literature on this topic, particularly concerning parameters such as blood loss and hospital stay duration. Some studies^{17,28} reported increased intraoperative blood loss with the perioperative administration of antiplatelet agents, while others^{27,29,30} noted the opposite. Likewise, some studies²⁶⁻³⁰ noted no effect or a reduction in overall hospital stay durations with the perioperative consumption of antiplatelet/anticoagulant drugs, other have reported the opposite phenomenon (Oshima et al¹⁸).

To the best of our knowledge, there has only been one systematic review and meta-analysis¹⁶ to date that has attempted to evaluate the influence of perioperative administration of antiplatelet drugs on intra- and post-operative outcomes in patients undergoing robot-assisted prostatectomy. However, this review did not include studies that had evaluated the influence of perioperative administration of anticoagulant drugs, nor did it incorporate all available published studies in their knowledge synthesis, such as^{18,26}.

We, therefore, in this systematic review and meta-analysis, attempt to bridge this existing gap in knowledge concerning the influence of the perioperative administration of anticoagulant and antiplatelet drugs in patients undergoing robot-assisted prostatectomy. Through this study, we aim to raise clinical awareness among urologists and surgeons across the world regarding potential prognostic outcomes affected by anticoagulant/ antiplatelet drug administration in patients undergoing robot-assisted prostatectomy.

Materials and Methods

This meta-analysis was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines³¹.

Search Strategy

We searched for studies published prior to December 2020 in five scientific databases (Web of Science, MEDLINE, CENTRAL, EMBASE, and Scopus). Searches were executed using a combination of MeSH keywords including "anticoagulants", "antiplatelets", "warfarin", "heparin", "aspirin", "robot-assisted prostatectomy", "bleeding complications", "blood loss", "blood transfusion", and "hospital stay". Furthermore, reference sections of included studies were manually scanned to identify additional relevant studies. The inclusion criteria were as follows:

- a) Studies evaluating the effects of perioperative administration of anticoagulants and antiplatelets in patients undergoing robot-assisted prostatectomy.
- b) Studies evaluating bleeding complications, blood loss, blood transfusion, and hospital stay duration in patients undergoing robot-assisted prostatectomy.
- c) Studies involving human participants.
- d) Case-control studies, prospective trials, or retrospective cohort trials.
- e) Studies published in peer-reviewed scientific journals.
- f) Studies published in English.

Screening was performed by two independent reviewers, with a third independent reviewer serving to arbitrate disputes.

Ouality Assessment

Risk of bias was appraised using Cochrane's risk of bias assessment tool for non-randomized controlled trials³². This tool evaluates outcomes for selective reporting, confounding bias, measurement of outcomes, and incomplete data availability as threats that can instigate instigating. Methodological quality was appraised by two independent reviewers, with a third independent reviewer serving to arbitrate disputes.

Data Analysis

A within-group meta-analysis was performed using Comprehensive Meta-Analysis software (CMA, version 2.0)³³ based on the random-effects model³⁴. The weighted effect size (Hedge's g) was calculated to determine the influence of antiplatelet and anticoagulant agent administration on blood loss and hospital stay duration in patients undergoing robot-assisted prostatectomy. We also analyzed adverse event rates in patients administered anticoagulant and antiplatelet agents to determine the prevalence of bleeding complications and blood transfusions in patients undergoing robot-assisted prostatectomy. We assessed heterogeneity amongst studies by computing I², with values between 0-25% considered indicative of negligible heterogeneity, 25%-75% indicative of moderate heterogeneity, and \geq 75% indicative of substantial heterogeneity³⁵. Publication bias was evaluated using Duval and Tweedy's trim and fill procedure (Duval and Tweedy, 2000)³⁶, which is characterized by the imputation of studies from either side of the plotted graph to identify any unbiased effect. The significance level for this study was determined to be 5%.

Results

The search across five academic databases provided a total of 980 candidate studies. Further 13 studies^{17,18,26-30,37} were identified by screening the reference sections of included studies. After applying inclusion criteria, eight studies^{17,18,26-30,37} remained, all of which were retrospective cohort studies (Figure 1). Study information is summarized in Table I.

Participant Information

The eight studies^{17,18,26-30,37} contained data on a total of 2516 patients. Among these, 48 received anticoagulant agents pre-operatively, 306 received antiplatelet agents pre-operatively, and 2162 patients received neither.

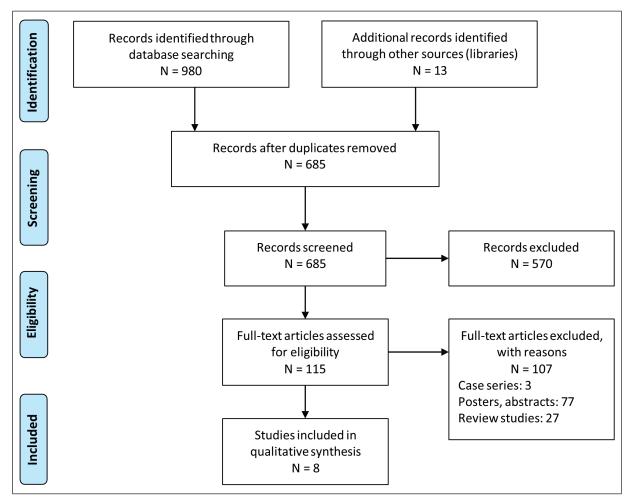
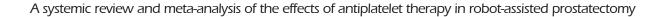


Figure 1. PRISMA flowchart.

Study	Country	Study type	Patients	Age (M ± S.D years)	Drugs	Bleeding complication events (n)	Hospital stay duration (days)	Blood loss (ml)	Blood transfusion events (n)
Kubota et al ²⁶	Japan	Retrospective Cohort Study	Anticoagulant: 31 Antiplatelet: 61 Control: 501	Anticoagulant: 71 Antiplatelet: 72 Control: 68	Anticoagulant: Warfarin, Clopidogrel, Direct Oral Anticoagulant Antiplatelet: Aspirin	Anticoagulant: 1 Antiplatelet: 0 Control: 2	Anticoagulant: 7 Antiplatelet: 7 Control: 7	Anticoagulant: 200 Antiplatelet: 175 Control: 165	Anticoagulant: 1 Antiplatelet: 0 Control: 2
Oshima et al ¹⁸	Japan	Retrospective Cohort Study	Anticoagulant: 17 Antiplatelet: 46 Control: 270	Anticoagulant: 70.8 ± 3.2 Antiplatelet: 69.8 ± 5.1 Control: 68.6 ± 6.0	Anticoagulant: Warfarin, Dabigatran Direct Oral Anticoagulant Antiplatelet: Aspirin, Clopidogrel, Cilostazol, Prasugrel	Anticoagulant: 4 Antiplatelet: 2 Control: 10	Anticoagulant: 8.6±2.6 Antiplatelet: 7.6±2.1 Control: 7.5±1.6	Anticoagulant: 130.9±137.9 Antiplatelet: 101.5±94.4 Control: 101.6±109.8	Anticoagulant: 0 Antiplatelet: 0 Control: 0
Tamhankar et al ³⁰	India	Retrospective Cohort Study	Antiplatelet: 31 Control: 85	Antiplatelet: 68±5.3 Control: 64.1±7.3	Antiplatelet: Aspirin	-	Antiplatelet: 2.2±0.5 Control: 2.1±0.3	Antiplatelet: 153.3±95.5 Control: 168.2±79	Antiplatelet: 0 Control: 0
Leyh-Bannurah et al ¹⁷	Germany	Retrospective Cohort Study	Antiplatelet: 19 Control: 381	Antiplatelet: 64 Control: 63	Antiplatelet: Aspirin	-	-	Antiplatelet: 250 Control: 193	Antiplatelet: 0 Control: 5
Mortezavi et al ²⁹	Zurich	Retrospective Cohort Study	Antiplatelet: 38 Control: 76	Antiplate let: 64.6±5.7 Control: 63.6±6.8	Antiplatelet: Aspirin	Antiplatelet: 0 Control: 0	Antiplatelet: 8±3 Control: 9±5	Antiplatelet: 271±172 Control: 345±282	Antiplatelet: 3 Control: 0
Parikh et al ²⁷	USA	Retrospective Cohort Study	Antiplatelet: 51 Control: 44	Antiplatelet: 59.8±5.8 Control:61.1±6.9	Antiplatelet: Aspirin	Antiplatelet: 0 Control: 0	Antiplatelet: 2 Control: 2	Antiplatelet: 100 Control: 175	Antiplatelet: 0 Control: 0
Nowfar et al ²⁸	USA	Retrospective Cohort Study	Antiplatelet: 6 Control: 236	Antiplatelet: 65±8 Control:62±7	Antiplatelet: Aspirin	-	Antiplatelet: 1.3±0.5 Control: 1.2±0.7	Antiplatelet: 180±84 Control: 156±91	Antiplatelet: 0 Control: 0
Binhas et al ³⁷	France	Prospective Cohort Study	Antiplatelet: 54 Control: 569	Antiplatelet: 65.3±5.7 Control:62.3±6.8	Antiplatelet: Aspirin	Antiplatelet: 3 Control: 19	Antiplatelet: 4 Control: 4	Antiplatelet: 450 Control: 450	Antiplatelet: 4 Control: 14

Table I. Summary of included studies.

Legends: M: Mean: S.D: Standard deviation.



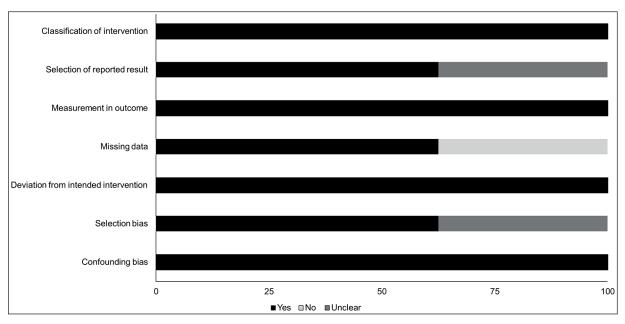


Figure 2. Bias risk for included studies according to the Cochrane risk of bias assessment.

Average patient age was 65.7 ± 3.6 years. The average age of patients receiving anticoagulants was 70.9 ± 0.14 years. The average age of patients receiving antiplatelets was 66.0 ± 3.7 years. The

Table II. Bias risk according to Cochrane's risk of bias assessment tool for randomized controlled trials.

Study	Confounding bias	Selection bias	Deviation from intended intervention	Missing data	Measurement in outcome	Selection of reported result	Classification of intervention
Kubota et ^{al26}	+	+	+	+	+	+	+
Oshima et al ¹⁸	+	+	+	+	+	+	+
Tamhankar et al ³⁰	+	?	+	-	+	?	+
Leyh-Bannurah et al ¹⁷	+	?	+	-	+	?	+
Mortezavi et al ²⁹	+	+	+	+	+	+	+
Parikh et al ²⁷	+	+	+	+	+	+	+
Nowfar et al ²⁸	+	?	+	-	+	?	+
Binhas et al ³⁷	+	+	+	+	+	+	+

average age of patients receiving neither was 64.0 ± 2.7 years.

Ouality Assessment for Non-Randomized Controlled Trials

Methodology bias risk analysis results are summarized in Table II and Figure 2. The overall risk of bias was found to be low in the included studies. We observed that missing data, selection of reported results, and selection bias were flagged within most of the included studies.

Publication Bias

We used Duval and Tweedy's trim and fill method to determine publication bias (Figure 3). The method observed that five studies^{17,18,27,30,37}.

were missing on the left side of the mean effect. The overall random effect models determined the point estimates and the 95% confidence intervals for all the combined studies as 0.03 (-0.07 to 0.14), using the trim and fill method the imputed point estimates were -0.05 (-0.17 to 0.06).

Meta-Analysis Report

Bleeding Complications

Anticoagulants

Two studies^{18,26} evaluated bleeding complication incidence in patients administered anticoagulant medications. We observed an event rate of 10.6% (95% CI: 1.4% to 50.6%, p=0.53, Figure 4) with no heterogeneity (I²: 0%).

Antiplatelets

Five studies^{18,26,27,29,37} evaluated bleeding complication incidence in patients administered antiplatelet medications. We observed an event rate of 3.4% (95% CI: 1.6% to 7.3%, p<0.01, Figure 5) with no heterogeneity (1²: 0%).

Blood Transfusion

Anticoagulants

Two studies^{18,26} evaluated blood transfusion complication incidence in patients administered anticoagulant medications. We observed an event rate of 3.1% (95% CI: 0.6% to 13.9%, p<0.01, Figure 6) with no heterogeneity (I²: 0%).

Antiplatelets

Eight studies^{17,18,26-30,37} evaluated blood transfusion complication incidence in patients administered antiplatelet medications. We observed an event rate of 4.8% (95% CI: 2.6% to 8.7%, p<0.01, (Figure 7) with no heterogeneity (1²: 0%).

Hospital Stay Duration

Anticoagulants

Two studies^{18,26} evaluated hospital stay duration for patients administered anticoagulant medications. We observed a *moderate* negative effect (Hedge's g: -0.30, 95% CI: -0.94 to 0.33, p=0.35, Figure 8) with no heterogeneity (I²: 0%).

Antiplatelets

Seven studies^{18,26-30,37} evaluated hospital stay duration for patients administered antiplatelet medications. We observed a *small* negative effect (Hedge's g: -0.01, 95% CI: -0.14 to -0.25, p=0.80, Figure 9) with no heterogeneity (I²: 0%).

Blood Loss

Anticoaqulants

Two studies^{18,26} evaluated blood loss amount in patients administered anticoagulant medications. We observed a *small* positive effect (Hedge's g: 0.04, 95% CI: -0.50 to 0.58, p=0.87, Figure 10) with no heterogeneity (I²: 0%).

Antiplatelets

Eight studies^{17,18,26-30,37} evaluated blood loss amount in patients administered antiplatelet medications. We observed a *small* negative effect (Hedge's g: -0.05, 95% CI: -0.26 to 0.15, p=0.59, Figure 11) with negligible heterogeneity (I²: 14.1%).

Discussion

We herein, for the first time, provide a comprehensive summarization of the effects of perioperative anticoagulant and antiplatelet drug administration for patients undergoing robot-assisted prostatectomy. Our analysis revealed increased incidence for bleeding complications, as well as increased hospital stay durations, for patients re-

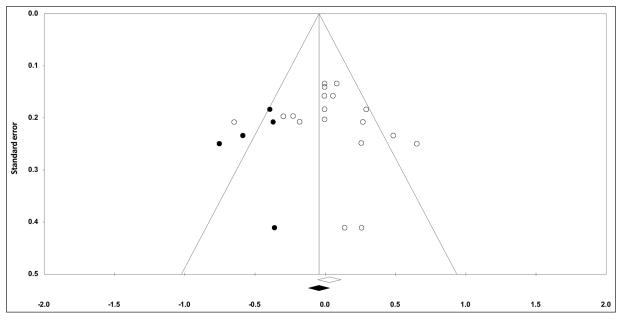


Figure 3. Publication bias was evaluated using Duval and Tweedy's trim and fill method.

Study name	,	Statistics	for each s	tudy	<u>_</u>	Event rat	e and 95	5% <u>CI</u>		
	Event rate	Lower limit	Upper limit	Z-Value	p-Value					
Kubota et al. (2020)	0.032	0.005	0.196	-3.346	0.001			-		
Oshima et al. (2020)	0.235	0.091	0.486	-2.061	0.039			-		
	0.106	0.014	0.506	-1.938	0.053					
						-1.00	-0.50	0.00	0.50	1.00

Figure 4. Forest plot for studies evaluating bleeding complication rates in patients receiving robot-assisted prostatectomy with anticoagulant drugs. The event rates are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative event rate represents a lower prevalence and a positive event rate represents a higher prevalence.

<u>Study name</u>		Statistics	for each s	_[Event rat	e and 95	5% <u>CI</u>			
	Event rate	Lower limit	Upper limit	Z-Value	p-Value					
Kubota et al. (2020)	0.008	0.001	0.116	-3.389	0.001					
Oshima et al. (2020)	0.043	0.011	0.158	-4.275	0.000					
Mortezavi et al. (2013)	0.013	0.001	0.175	-3.052	0.002			—		
Parikh et al. (2012)	0.010	0.001	0.136	-3.261	0.001					
Binhas et al. (2012)	0.056	0.018	0.159	-4.769	0.000					
	0.034	0.016	0.073	-8.319	0.000			•		
						-1.00	-0.50	0.00	0.50	1.00

Figure 5. Forest plot for studies evaluating bleeding complication rates in patients receiving robot-assisted prostatectomy with antiplatelet drugs. The event rates are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative event rate represents a lower prevalence and a positive event rate represents a higher prevalence.

<u>Study name</u>	<u>Statistics for each study</u> Event Lower Upper rate limit limit Z-Value					Ē	vent rate	e and 95	% CI	
				Z-Value	p-Value					
Kubota et al. (2020)	0.032	0.005	0.196	-3.346	0.001			–		
Oshima et al. (2020)	0.028	0.002	0.322	-2.479	0.013			•	-	
	0.031	0.006	0.139	-4.163	0.000					
						-1.00	-0.50	0.00	0.50	1

Figure 6. Forest plot for studies evaluating blood transfusion rates in patients receiving robot-assisted prostatectomy with anticoagulant drugs. The event rates are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative event rate represents a lower prevalence and a positive event rate represents a higher prevalence.

<u>Studyname</u>		Statistics	for each	study	Event rate and 95% CI					
	Event rate	Lower limit	Upper limit	Z-Value p-'	Value					
Kubota et al. (2020)	0.008	0.001	0.116	-3.389	0.001			∳		
Oshima et al. (2020)	0.011	0.001	0.149	-3.188	0.001			–		
Tamhankar et al. (2018)	0.016	0.001	0.206	-2.907	0.004			•		
Leyh-Bannurah et al. (2014)	0.025	0.002	0.298	-2.558	0.011			-	-	
Mortezavi et al. (2013)	0.079	0.026	0.218	-4.084	0.000					
Parikh et al. (2012)	0.010	0.001	0.136	-3.261	0.001			–		
Nowfar etal. (2012)	0.071	0.004	0.577	-1.748	0.081					
Binhas et al.(2012)	0.074	0.028	0.181	-4.861	0.000					
	0.048	0.026	0.087	-9.161	0.000			♦		
						-1.00	-0.50	0.00	0.50	1.00

Figure 7. Forest plot for studies evaluating blood transfusion rates in patients receiving robot-assisted prostatectomy with antiplatelet drugs. The event rates are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative event rate represents a lower prevalence and a positive event rate represents a higher prevalence.

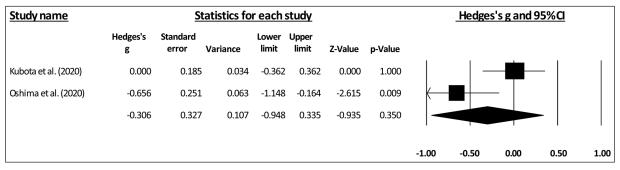


Figure 8. Forest plot for studies evaluating the influence of anticoagulant drugs on hospital stay duration in patients receiving robot-assisted prostatectomy. Weighted effect sizes (Hedge's g) are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents a longer duration in the group receiving anticoagulant drugs and a positive effect size represents a longer duration in the control group.

Study name		<u>St</u>	tatistics for e	ach study				Hedges's g and 95%Q					
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value p	-Value						
Kubota et al. (2020)	0.000	0.135	0.018	-0.265	0.265	0.000	1.000				-		
Oshima et al. (2020)	-0.059	0.159	0.025	-0.371	0.253	-0.373	0.709		-		.		
Tamhankar et al. (2018)	-0.273	0.209	0.044	-0.683	0.137	-1.306	0.191			∎			
Mortezavi et al. (2013)	0.224	0.198	0.039	-0.164	0.612	1.130	0.258				∎─┼─		
Parikh et al. (2012)	0.000	0.204	0.042	-0.400	0.400	0.000	1.000		_	#	_		
Nowfar et al. (2012)	-0.143	0.412	0.170	-0.951	0.665	-0.347	0.728	—					
Binhas et al. (2012)	0.000	0.142	0.020	-0.279	0.279	0.000	1.000				-		
	-0.017	0.067	0.005	-0.148	0.115	-0.250	0.803			\bullet			
								-1.00	-0.50	0.00	0.50	1.0	

Figure 9. Forest plot for studies evaluating the influence of antiplatelet drugs on hospital stay duration in patients receiving robot-assisted prostatectomy. Weighted effect sizes (Hedge's g) are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents a longer duration in the group receiving anticoagulant drugs and a positive effect size represents a longer duration in the control group.

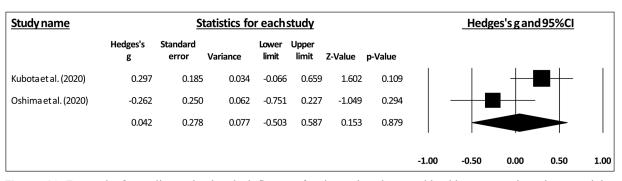


Figure 10. Forest plot for studies evaluating the influence of anticoagulant drugs on blood loss amount in patients receiving robot-assisted prostatectomy. Weighted effect sizes (Hedge's g) are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents larger blood loss in the control group and a positive effect size represents larger blood loss in the group receiving anticoagulant drugs.

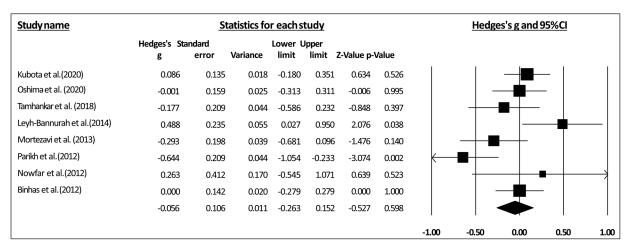


Figure 11. Forest plot for studies evaluating the influence of antiplatelet drugs on blood loss amount in patients receiving robot-assisted prostatectomy. Weighted effect sizes (Hedge's g) are presented as black boxes whereas 95% confidence intervals are presented as whiskers. A negative effect size represents larger blood loss in the control group and a positive effect size represents larger blood loss in the group receiving antiplatelet drugs.

ceiving anticoagulant drugs compared to those receiving antiplatelet drugs.

A higher predisposition for thromboembolic events is a common co-morbidity for prostate cancer patients³⁸⁻⁴⁰. Moreover, these events have been associated with poorer prognostic outcomes in terms of both short- and long-term morbidity and mortality³⁹. Thromboembolic event onset is believed to be caused as a result of a variety of factors, such as ongoing androgen deprivation therapy and co-existing co-morbidities such as dyslipidemia, diabetes, and increased fat mass quantity⁴¹⁻⁴³. Consequently, anticoagulant and/or antiplatelet drugs are commonly used to manage this increased risk^{44,45}. However, their administration complicates surgical management of prostate cancer, since these agents tend to augment intra- and post-operative morbidity and mortality⁴⁶.

As such, robot-assisted prostatectomy, the gold standard surgical approach for managing localized prostate cancer lesions^{47,48}, contraindicates the perioperative use of anticoagulant/antiplatelet drugs to prevent any associated hemorrhagic complications. Recent evidence also indicates that any attempt to abruptly stop the administration of anticoagulant/antiplatelet drugs prior to surgery can actually increase patient predisposition for thromboembolic and mortality related events (see rebound-hypercoagulability⁴⁹⁻⁵¹. Thus, the current consensus argues that perioperative anticoagulant and antiplatelet drug administration should persist during robot-assisted prostatectomy, but at lower dosages^{25,29,37}. Binhas et al (2012)³⁷ suggested that lowering aspirin dosage to 75 mg per day resulted in no difference in intra- or post-operative outcome for drug-treated patients undergoing robot-assisted prostatectomy relative to the control group.

Our analysis showed different outcomes for patients taking anticoagulants versus antiplatelets in terms of postoperative bleeding complication incidence. In a recent retrospective cohort trial, Oshima et al (2020)¹⁸ compared the effects of perioperative anticoagulant drug consumption of anticoagulant drugs with perioperative antiplatelet drug consumption. The authors reported increased incidence of grade 3 bleeding in the anticoagulant group (5.9%) relative to the antiplatelet (4.3%) and control groups (2.6%). Based on this, the authors suggested a "bridging therapy" where instead of halting oral anticoagulants 3 to 5 days pre-operation, they should instead be replaced with other anticoagulant drugs such as heparin. This, according to Oshima et al¹⁸, can potentially reduce the risk of perioperative bleeding and the development of thromboembolic adverse events.

Our present meta-analysis supports the findings of Oshima et al¹⁸ as we found that anticoagulant drug administration increased bleeding complication incidence (event rate: 10.2%) relative to antiplatelet drug administration (3.6%). However, we also noted that antiplatelet drug administration (4.8%), but not anticoagulant drug administration (3.1%), resulted in more blood transfusion events in patients undergoing robot-assisted prostatectomy.

We also looked at overall hospital stay duration as a factor for determining whether anticoagulant drugs and antiplatelet drugs should be administered. Here, the literature was divided. Oshima et al¹⁸ reported that patients administered anticoagulant drugs stayed in hospital longer (8.6 ± 2.6 days) than either those administered antiplatelet drugs (7.6 ± 2.1 days) or control group individuals (7.5 ± 1.6 days). However, Kubota et al²⁶ (2020) reported no difference in hospital stay duration between anticoagulant, antiplatelet, and control group patients.

Our meta-analysis supports the findings of Oshima et al¹⁸. Not only did we note that none of the included studies reported increased hospital stay durations for patients receiving antiplatelet drugs compared to control groups, but we also reported an overall longer hospital stay duration for patients given anticoagulant drugs (Hedge's g: -0.30) as compared to those receiving antiplatelet drugs (-g: 0.01).

These effects may be explained by how patients receiving anticoagulants presented increased intraoperative blood loss (g: 0.04) compared to antiplatelet group patients (g: -0.05).

Our study has several limitations. First and foremost, this study has not been pre-registered in a

systematic review repository such as PROSPERO York or the Joanna Briggs Institute. We understand that this could be of concern. However, we have made several attempts to register this review, but were thwarted by the current COVID-19 pandemic crisis which has extended registration times to greater than one year. Second, we did not report about the indications to the procedure that are controverse. This was mainly because of synthesis of evidence that had compiled and compared the efficacy of these drugs separately. Third, we do acknowledge that the paucity of data within the eligible included studies could bias our understanding of the situation. While we analyzed the influence of antiplatelet drugs among eight studies^{17,18,26-30,36}, we only found two studies^{18,26} that reported the influence of anticoagulant drugs, resulting further in a small sample size when it came to outcome evaluation. Therefore, the chances of incurring a type II error cannot be ruled out⁵¹. We strongly recommend conducting more studies to create a larger data pool in order to address these limitations.

Conclusions

Our review provides preliminary evidence concerning the influence of perioperative administration of anticoagulant and antiplatelet drugs in patients undergoing robot-assisted prostatectomy. We note that bleeding complication incidence and hospital stay duration are elevated in patients receiving anticoagulant drugs compared to those receiving antiplatelet drugs prior to undergoing robot-assisted prostatectomy. The findings from the present study can have implications in developing best practice guidelines for reducing intra- and post-operative complications with anticoagulant/ antiplatelet drug therapy in patients undergoing robot-assisted prostatectomy.

Ethical Clearance Not required.

Conflicts of Interest

The authors declare no conflicts of interest.

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Author Contribution Statement

Y.-J. NING conceived and designed the study; J. MENG and X.-P. WANG were involved in literature search and data collection; J. MENG and X.-P. WANG analyzed the data; Y.-J. NING wrote the paper; and Z.-X. WAN reviewed and edited the manuscript. All authors read and approved the final manuscript.

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