Incidence, risk factors, and the role of anticoagulation therapy in venous thromboembolism following radical cystectomy

Randall Bissette¹, Maxwell Sandberg²*, Stephen Tranchina², Kimberly Waggener², Madeline Snipes², Emily Ye³, Jabrina Simmons⁴, John Strobel⁵, Ashok Hemal², Alejandro Rodriguez², Ronald Davis III²

¹Virginia Tech Carilion School of Medicine, Roanoke, Virginia, 24016 United States ²Department of Urology, Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, 27157 United States ³Wake Forest University School of Medicine, Winston-Salem, North Carolina, 27101 United States ⁴Northeast Ohio Medical University, Rootstown, Ohio, 44272 United States ⁵Indiana University School of Medicine, Indianapolis, Indiana, 46202 United States

Abstract

Background: Radical cystectomy (RC) for bladder cancer is associated with substantial postoperative complications. Among these complications, venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is particularly notable for its morbidity. Efforts to reduce VTE have been largely revolving around extended thromboprophylaxis (ETP) after discharge, typically with injectable heparins, and, more recently, with oral anticoagulants. **Objective:** The purpose of this study was to quantify the incidence of VTE within 90 days following RC and to identify risk factors associated with its development. **Methods:** We conducted a retrospective review of all patients who underwent RC for bladder cancer at our institution between 2012 and 2024, documenting instances of postoperative VTE. Data on demographics, anticoagulation therapy, surgical approach, and hospitalization were collected and analyzed. **Results:** A total of 372 patients received RC for bladder cancer during the study. Of them, 12 patients (3.2%) developed VTE at some point after surgery. The mediant time to VTE occurrence was between 31 and 90 days post-discharge. A higher rate of VTE was observed immediately following RC in patients who underwent surgery before 2018 (p = 0.021), the year in which enhanced recovery after surgery (ERAS) protocols were implemented. Demographic factors and operation-related variables did not influence the VTE rate (p > 0.05). Kaplan–Meier analysis revealed that cancer-specific survival was significantly lower in patients who developed VTE after RC compared to those who did not (p < 0.001). **Conclusion:** These findings underscored the importance of interventions such as ETP and ERAS protocols in reducing the incidence of VTE following RC for bladder cancer.

Keywords: Anticoagulation, Deep vein thrombosis, Direct oral anticoagulants, Enhanced recovery after surgery, Pulmonary embolism, Radical cystectomy, Venous thromboembolism

1. INTRODUCTION

Radical cystectomy (RC) is considered the gold standard for the treatment of muscle-invasive bladder cancer or highrisk non-muscle-invasive bladder cancer. Despite advances in surgical technique, various urinary diversion options, and the use of minimally invasive robotic methods, cystectomy remains associated with substantial morbidity and mortality. Morbidity can be categorized as early, related to the surgery itself, and late, related to urinary diversion [1]. Common early complications include gastrointestinal dysfunction, infections, and wound-related issues [2], while late complications related to diversion can include urinary tract infection, loss of renal function, calculi formation, and bowel obstruction [3].

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is

one of the most serious complications in the perioperative period. The incidence of symptomatic VTE following RC

*Corresponding author: Maxwell Sandberg (mlsandbe@wakehealth.edu)

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Received: 26 September 2024; Revision received: 18 October 2024; Accepted: 31 October 2024; Published: 06 December 2024

How to cite this article: Bissette R, Sandberg M, Tranchina S, *et al.* Incidence, risk factors, and the role of anticoagulation therapy in venous thromboembolism following radical cystectomy. *Bladder.* 2024;11(4):e21200020. DOI: 10.14440/ bladder.2024.0041

has been reported to range from 3% to 12% [4-13]. VTE can occur as early as postoperative day one but may also develop well after surgery, with some studies reporting VTE as late as postoperative day 91 [5]. These complications are particularly concerning because between 46% and 58% of VTE events following cystectomy occur after discharge, making timely intervention difficult [4,9,12,14]. A recent study demonstrated that PE was responsible for 6% of 90-day postoperative mortality following RC [15]. Although the exact mortality rate for patients with VTE after RC is unknown, the overall morbidity associated with VTE is wellestablished in other surgical fields. For example, the 30-day postoperative mortality rate was significantly higher for patients with VTE following general, vascular, and orthopedic surgeries [16]. While VTE is not unique to RC in urological oncology, cystectomy has been shown to be an independent risk factor for VTE when compared to radical nephrectomy or prostatectomy [10]. Among urological surgeries, RC is consistently associated with the highest postoperative VTE rate [8,17]. VTE risk is traditionally attributed to "Virchow's Triad," which consists of vascular stasis, a hypercoagulable state, and endothelial damage. Patients undergoing RC may experience malignancy-induced hypercoagulability and venous stasis, particularly in the lower extremities, during the prolonged duration of the operation. Risk factors for VTE following RC include a prior history of VTE, higher body mass index (BMI), congestive heart failure, chronic obstructive pulmonary disease (COPD), non-organ-confined disease or positive surgical margins, older age, female gender, sarcopenia, and preoperative thrombocytosis. Non-patientrelated risk factors involve operative duration, estimated blood loss, perioperative blood transfusion, type of urinary diversion, and length of hospitalization [4,5,7,8,14,18-23].

Various pharmaceutical regimens have been implemented to mitigate the risk of VTE after RC. Historically, inpatient postoperative prophylaxis has been the mainstay. In the 2010s, extended thromboprophylaxis (ETP) using heparins or lowmolecular-weight heparin (LMWH) emerged as an effective method for VTE reduction [12,24]. The evidence for ETP favors a duration of 28 - 30 days postoperatively, with notable benefits in reducing postoperative VTE [12,25-29]. Despite this evidence, practices vary across institutions and among clinicians. In a 2020 survey of academic urologists, 97% reported utilizing inpatient VTE prophylaxis, while 80% used ETP [30]. Of those using ETP, 96% employed enoxaparin, and only 3% used oral formulations. More recent efforts have focused on improving ETP through alternative medication formulations, specifically direct oral anticoagulants (DOACs) in place of injectable heparin derivatives. A 2021 retrospective analysis of 66 patients who underwent RC with ETP found that those treated with DOACs had similar rates of VTE and bleeding events to those treated with enoxaparin [31].

A 2022 study reported the initial experience with the DOAC apixaban for ETP after RC in a cohort of 72 patients [32], with no symptomatic VTE or major bleeding events recorded. Another 2022 retrospective study of 101 patients who received ETP after RC assessed a single institution's switch from enoxaparin to apixaban or rivaroxaban [33] and found no significant difference in the VTE rate. In this cohort, none of the 46 patients in the DOAC group developed VTE. Most recently, a 2023 study examining a prospectively implemented protocol showed a 1.6% VTE rate with apixaban ETP compared to a 3.2% rate with enoxaparin, with no statistically significant difference [34]. These studies suggest that DOACs may have similar efficacy to LMWH for VTE prophylaxis following RC, but larger studies are needed for confirmation.

The primary goal of this study was to quantify the incidence of VTE within 90 days following RC and identify risk factors associated with the development of VTE. The secondary objective was to evaluate the effect of anticoagulant medications on the development of VTE after RC.

2. MATERIALS AND METHODS

2.1. Methods

This study was a retrospective analysis of all patients who underwent RC for bladder cancer at our institution from 2012 to 2024. Patients who received cystectomy for conditions other than bladder cancer were excluded from the analysis. Demographic characteristics of the study population were recorded, including age at surgery, gender, BMI, and the Charlson Comorbidity Index. Perioperative and post-operative variables recorded included the surgical approach (open or robotic), operative time, length of hospital stay, complications, anticoagulation agent administered after surgery, and the anticoagulation agent prescribed at discharge. VTE complications were noted in the immediate postoperative period according to the Clavien-Dindo grading system [35-37], and at 30 days and 31 – 90 days after discharge from RC. VTE complications were classified as DVT (either proximal or distal) and/or PE (pulmonary artery or its branches) based on the location of the thrombus. Confirmation of VTE was acquired by imaging, such as Doppler ultrasound and/or computerized tomography angiography. Before 2018, postoperative management was determined by the surgeon's preference. Starting in 2018, all patients were managed according to an institutional enhanced recovery after surgery (ERAS) protocol. This protocol included the administration of a bowel stimulating agent (alvimopan) beginning preoperatively, immediately before RC, and continuing until the return of bowel function (ROBF) postoperatively. In addition, inpatient anticoagulation was provided with either LMWH or heparin until discharge. Upon discharge, patients were continued on LMWH, heparin, apixaban,

or occasionally home antiplatelet medications (aspirin and clopidogrel) to ensure a cumulative total of 28 days of anticoagulation prophylaxis postoperatively (including inpatient days). Standard dosing regimens were as follows: 40 mg of LMWH subcutaneously daily, 5000 units of heparin subcutaneously every 8 h, 2.5 mg of apixaban orally twice daily, and home dosage of aspirin or clopidogrel as prescribed before RC. Patients with contraindications to postoperative anticoagulation were excluded from the analysis. In addition, patients on chronic anticoagulation for atrial fibrillation or a prior VTE before RC were excluded.

2.2. Statistical analysis

The primary statistical analysis aimed to identify risk factors for DVT and/or PE after RC. We compared patients who developed DVT and/or PE postoperatively with those who did not, using independent samples t-test, chi-squared test, and Kaplan-Meier survival analysis with log-rank test. In addition, subgroup analysis was performed based on several accepted risk factors for VTE, including nonorgan-confined disease, operative duration, perioperative blood transfusion, and hospitalization duration, as reported in the current literature [4,5,7,8,14,18-23]. This analysis used the Chi-squared test, with operative duration and hospitalization duration categorized into quartiles. Variables with p < 0.1 and/or clinical relevance were selected for further analysis, and a binary logistic regression was conducted, with VTE occurrence (anytime postoperatively) as the outcome, ensuring no collinearity between variables.

For secondary statistical analysis, the prevalence of DVT and/or PE after RC was compared based on the anticoagulation agent administered while inpatient and at discharge, using independent samples *t*-test and Chi-squared test. In addition, the incidence of VTE was compared between patients who underwent RC before 2018 (<2018) and those who underwent surgery in or after 2018 (<2018) to assess the impact of the ERAS protocol on VTE incidence. All statistical analyses were performed using SPSS Statistics Version 28 (IBM, US).

3. RESULTS

3.1. VTE rates and timing

A total of 372 patients who underwent RC for bladder cancer were included in the study. In the immediate postoperative period, before discharge from the hospital, four patients (1.1%) experienced VTE. Within 30 days of discharge from RC, five patients (1.3%) developed VTE, and within 31 – 90 days of discharge, three patients (0.8%) experienced VTE. In total, 12 patients (3.2%) developed VTE at any point during the study, and these patients constituted the comparative group for both primary and secondary analyses. The median time to VTE identification was between 31 and 90 days after discharge. There was a significant association between the occurrence of VTE immediately after RC and the year of surgery, with patients undergoing RC before 2018 exhibiting a higher rate of VTE (p = 0.021) in the immediate postoperative period. No significant differences in VTE incidence were observed when comparing the years before 2018 (<2018) to those in or after 2018 (<2018) for the 30-day, 31 – 90-day, and overall postoperative periods (p > 0.05).

3.2. Risk factors and survival

The primary analysis compared patient variables to identify potential risk factors for VTE following RC (Table 1). Age at surgery was similar between patients who developed VTE (mean age 68 years) and those who did not (mean age 67 years) (p > 0.05). The proportion of females was not significantly different between those who developed VTE (n = 3; 25%) and those who did not (n = 71; 20%). Race was also comparable between the two groups (p > 0.05). Rates of diabetes mellitus, coronary artery disease, and COPD were similar in both groups (p > 0.05). There was no significant difference in the incidence of VTE based on whether patients had bowel resection (0%) or not (n = 12, 3%) at the time of RC (p > 0.05). Tumor pathology, operative approach, and conduit type did not differ significantly between patients with and without VTE (p > 0.05). Operative time was similar in both groups, with a mean of 351 min for patients with VTE and 350 min for those without (p > 0.05). Length of stay was also comparable: patients with VTE had a mean of 6 days, while patients without VTE had a mean stay of 14 days (p > 0.05). Overall survival (OS) was similar between patients with VTE (mean of 10 months) and those without VTE (mean of 18 months) (p > 0.05). Cancer-specific survival (CSS) was lower in patients with VTE (mean of 4 months) compared to those without VTE (mean of 15 months) (p > 0.05). Kaplan-Meier analysis with log-rank testing revealed no significant difference in OS between the two groups (p > 0.05), but a significant difference was observed in CSS, with patients without VTE exhibiting better survival (Figure 1). Subgroup analysis demonstrated no significant association between VTE and operative time quartile (p = 0.550), perioperative blood transfusion (p = 0.579), length of stay quartile (p = 0.570), or non-organ-confined disease (p = 0.138). Binary logistic regression indicated that operative time, perioperative blood transfusion, length of stay, urinary diversion type, nonorgan-confined disease, COPD, and female gender were not significantly associated with VTE (Table 2).

3.3. Anticoagulation

Secondary analysis found no significant association between the choice of inpatient anticoagulant agent and the

Table 1. Risk factors for venous thromboembolism following radical cystectomy

Variable	No VTE (<i>n</i> =360)	VTE (<i>n</i> =12)	<i>p</i> -value	Confidence interval	
				Upper	Lower
Gender					
Male	289 (80)	9 (75)	0.652	-	-
Female	71 (20)	3 (25)		-	-
Race					
White	317 (88.1)	9 (75)	0.078	-	-
Black	33 (9.2)	2 (16.7)		-	-
Hispanic	3 (0.8)	0 (0)		-	-
Asian	2 (0.6)	1 (8.3)		-	-
Native American	4 (1.1)	0 (0)		-	-
Other	1 (0.3)	0 (0)		-	-
Diabetes					
Yes	277 (76.9)	9 (75)	0.875	-	-
No	83 (23.1)	3 (25)		-	-
CAD		- (-)			
Yes	295 (81.9)	9 (75)	0.54	-	-
No	65 (18.1)	3 (25)		-	-
COPD		- ()			
Yes	314 (87.2)	10 (83.3)	0.693	_	-
No	46 (12.8)	2 (16.7)	0.072	_	-
Bowel resection	10 (12.0)	= (10.7)			
Yes	350 (97.2)	12 (100)	0.558		_
No	10 (2.8)	0 (0)	0.550	_	_
Tumor pathology after cystectomy	10 (2.0)	0(0)			
T0	43 (11.9)	0 (0)	0.544	_	_
Ta	13 (3.6)	0 (0)	0.544	-	_
Tis	24 (6.7)	1 (8.3)			
T1	30 (8.3)	0 (0)		-	_
T2a	60 (16.7)	2 (16.7)		-	-
T2b	53 (14.7)	2 (16.7) 2 (16.7)		-	-
T3a	48 (13.3)	· /		-	-
T3b		2 (16.7)		-	-
	26 (7.2)	3 (25)		-	-
T4a	54 (15)	2 (16.7)		-	-
T4b Conduit	6 (1.7)	0 (0)		-	-
Conduit Used see duit	204 (01.7)	10 (02 2)	0.040		
Ileal conduit	294 (81.7)	10 (83.3)	0.949	-	-
Indiana pouch	1 (0.3)	0 (0)		-	-
Neobladder	8 (2.2)	0(0)		-	-
Cutaneous ureterostomy	47 (13.1)	2 (16.7)		-	-
Other	9 (2.5)	0 (0)		-	-
Approach		C (50)	0.647		
Open	204 (56.7)	6 (50)	0.647	-	-
Robotic	156 (43.3)	6 (50)	0.407	-	-
Mean Charlson comorbidity index (points)	5.31	4.83	0.406	-0.649	1.601
Mean overall survival (months)	18.3	9.86	0.255	-5.938	22.275
Mean length of stay (days)	14.26	6.42	0.817	-58.774	74.460
Mean age day of surgery (years)	66.64	67.92	0.658	-6.92051	4.37606
Mean procedure time (min)	350.6	349.18	0.961	-55.256	58.101
Mean cancer-specific survival (months)	14.77	4.2	0.107	-2.316	23.45

Notes: This table compares patients who did not develop venous thromboembolism versus those who did, at any point after radical cystectomy. A variety of potential risk factors were compared with the associated *p*-values. For categorical variables, the total number of patients is shown with the percentage in parentheses. For continuous variables, the mean is shown with the standard deviation in parentheses. Confidence intervals are provided where appropriate.

CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, VTE: Venous thromboembolism.

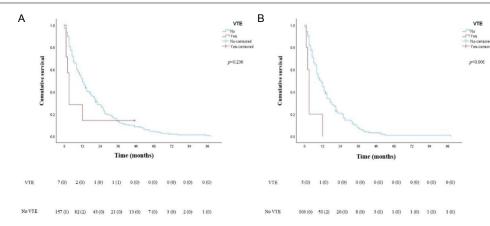


Figure 1. Kaplan–Meier survival analysis. (A) Overall survival in patients who did versus did not develop venous thromboembolism after radical cystectomy during the study window. (B) Cancer-specific survival in patients who did versus did not develop venous thromboembolism after radical cystectomy during the study period.

Notes: The y-axis represents the proportion of patients surviving at each time point. Time is shown on the x-axis. Number-at-risk tables with censored data are provided below each plot. Log-rank test *p*-values are also shown.

VTE: Venous thromboembolism.

Variable	В	S.E.	<i>p</i> -value	Exp (<i>B</i>)	CI	
					Upper	Lower
Gender	0.213	0.690	0.758	1.24	0.320	4.78
Operative time quartile	0.098	0.300	0.745	1.10	0.612	1.99
Length of stay quartile	0.243	0.300	0.417	1.28	0.709	2.30
Urinary diversion	-	-	0.997	-	-	-
Non-organ confined disease	0.815	0.603	0.177	2.26	0.692	7.37
Perioperative blood transfusion	-17.86	13097.42	0.999	0.001	0.001	-
COPD	0.367	0.812	0.651	1.44	0.294	7.09

Table 2. Binary logistic regression

Notes: This table presents a regression model with venous thromboembolism occurring at any time after radical cystectomy as the outcome. B is the unadjusted odds ratio, S.E. denotes the standard error, Exp (B) is the adjusted odds ratio, and CI refers to 95% confidence intervals. No significant associations were identified in the model.

COPD: Chronic obstructive pulmonary disease.

development of VTE during the initial hospital stay (p > 0.05) (Table 3). Similarly, the anticoagulant agent prescribed at discharge did not affect the incidence of VTE within 30 days of discharge, 31 - 90 days from discharge, or at any time after RC (p > 0.05).

4. DISCUSSION

In this study, we found that patients who developed VTE had worse CSS compared to those who did not develop VTE. This finding underscores the importance of VTE prevention in patients undergoing RC for bladder cancer. Prior studies have emphasized the mortality associated with VTE following major surgeries, including abdominal surgery, orthopedic, and cardiovascular procedures [16]. For instance, a large 2023 retrospective review of 14,362 patients who underwent RC found higher mortality in patients who developed VTE compared to those who did not [38]. However, their study was limited to in-hospital VTE events. In contrast, our study

supports these previous findings and extends the analysis beyond discharge, demonstrating a potential link between postoperative mortality and VTE following RC. The impact of VTE on CSS has been documented previously, although the exact mechanism remains unclear. An activated coagulation system may promote tumor spread by helping cancer cells evade the immune system. Hypercoagulability could also be a consequence of adverse tumor biology, potentially contributing to cancer progression. Prior research has established several risk factors for VTE following RC [4,5,7,8,14,18-23]. In our study, however, we did not identify any specific risk factors, even upon subgroup analysis. This lack of significant findings on risk factors may be attributed to the low event rate observed in our study. Nonetheless, these results complicate the development of targeted interventions, highlighting the need for further research in this area.

While we demonstrated the role of VTE in CSS, comorbidities and systemic preoperative factors also play a

Anticoagulant	Immediately post-operative		30 days post-operative		31 – 90 days post-operative			Ever?				
	No VTE (<i>n</i> =368)	VTE (<i>n</i> =4)	<i>p</i> -value	No VTE (<i>n</i> =367)	VTE (<i>n</i> =5)	<i>p</i> -value	No VTE (<i>n</i> =368)	VTE (<i>n</i> =3)	<i>p</i> -value	No VTE (n=360)	VTE (<i>n</i> =12)	<i>p</i> -value
Heparin	224 (60.9)	2 (50)	0.958	7 (1.9)	0 (0)	0.937	7 (1.9)	0 (0)	0.943	7 (1.9)	0 (0)	0.268
Low-molecular heparin	122 (33.2)	2 (50)		159 (43.3)	3 (60)		159 (43.2)	2 (66.7)		153 (42.5)	9 (75)	
Apixaban	2 (0.5)	0 (0)		10 (2.7)	0 (0)		10 (2.7)	0 (0)		10 (2.8)	0 (0)	
Other	3 (0.8)	0 (0)		15 (4.1)	0 (0)		15 (4.1)	0 (0)		15 (4.2)	0 (0)	
None	16 (4.3)	0 (0)		175 (47.7)	2 (40)		176 (47.8)	1 (33.3)		174 (48.3)	3 (25)	

 Table 3. Association between anticoagulation agent at discharge and venous thromboembolism

Notes: This table compares each anticoagulation agent prescribed at discharge with the incidence of venous thromboembolism to assess any significant associations. The total number of patients is shown with the percentage in parentheses. The analysis was conducted immediately after surgery, within 30 days of discharge, 31 - 90 days post-discharge, and any time after radical cystectomy (Ever?). Anticoagulant agents included heparin, low-molecular-weight heparin, apixaban, other anticoagulants, or no anticoagulation. No significant differences were found at any time points analyzed.

VTE: Venous thromboembolism.

crucial part in oncological outcomes. For example, elevated systemic immune-inflammation index (SII) has been associated with a higher risk of nodal invasion, advanced pT stage, and locally advanced disease in patients undergoing RC. Higher SII values have also been found to be linked to lower recurrence-free survival and OS [39]. Patients with heart valve replacement are at a greater risk for postoperative cardiac complications following RC [40], and those with paraplegia have been shown to experience significantly higher in-hospital morbidity following RC, with a four-fold increase [41]. In the context of our findings, we found that both postoperative complications and preoperative patient-specific factors heavily influence patient outcomes. Collectively, these findings underscore the need to integrate preoperative inflammatory markers with VTE prevention strategies to optimize outcomes, particularly in patients with multiple comorbidities.

One of the key challenges in addressing VTE after RC is timing. Approximately half of all VTE incidents occur after discharge [4,9,12,14], which complicates the course of care compared to inpatient VTE management. With a mean time to VTE of 31 – 90 days post-discharge, our findings are consistent with previously reported data, emphasizing the importance of both early and sustained VTE prevention following RC. This observation highlights the need for a comprehensive regimen of prophylaxis during the immediate and extended postoperative periods. Although studies have demonstrated the efficacy and safety of ETP for approximately 4 weeks, using either subcutaneous LMWH or DOACs, patient adherence remains suboptimal [30,42,43].

We also performed a chart review before and after our institution implemented the ERAS protocol in 2018. ERAS protocols, particularly following RC, have demonstrated significant benefits, including a faster ROBF, shorter length of hospital stay, lower readmission rates, and fewer overall complications [44,45]. The advantages of the ERAS protocol

that directly influence VTE after RC include reduced bed rest, early ambulation, and accelerated nutritional advancement to promote early ROBF, which enables quicker discharge. While the adoption of ETP has been inconsistent across institutions, likely due to challenges with patient adherence and concerns about bleeding risk, ERAS implementation and intraoperative VTE prophylaxis are becoming more standardized. These perioperative interventions are critical, especially in institutions where ETP is not routinely used. Beyond VTE and its impact on survival, other postoperative complications can negatively affect patient welfare. For example, within the ERAS framework, constipation and diarrhea are linked to reduced quality of life in patients following RC, particularly in frail individuals [46]. Our findings reinforce the patient benefits of these perioperative measures, with potential reductions in mortality related to VTE. However, they also highlight the need for comprehensive postoperative management pathways, beyond ERAS, that improve overall patient well-being and aim to reduce other complications as well.

Results from the present study are consistent with prior studies demonstrating similar efficacy between subcutaneous heparins and DOACs. Both ETP modalities have been studied retrospectively and, more recently, prospectively, with all results supporting a comparable risk of VTE following RC, regardless of the choice of ETP [31-34]. A recent systematic review of these studies affirmed similar efficacy in a meta-analysis of the combined data [47]. One potential advantage of DOACs over subcutaneous heparins is improved patient adherence, as the injectable route of heparins may be a barrier for some patients. This issue could be mitigated through oral medication. Surgical teams should feel comfortable prescribing either form of prophylaxis, and individualized regimens are appropriate, taking unique patient factors into account. Regarding the individualization of treatment, it remains unclear whether anticoagulation and antiplatelet

medications should be continued in patients already on these therapies, although this has been studied. An observational cohort study conducted in 2022 found that perioperative continuation of aspirin, oral anticoagulation with international normalized ratio of 2 - 2.5, or bridging with LMWH did not significantly affect blood loss or transfusion rates following RC [21].

While we are confident in the findings reported, we acknowledge several limitations in our analysis. The retrospective nature of this study inherently limits our ability to capture all relevant VTE events, as some may not have been documented in the medical record. Additionally, while prior studies have demonstrated risk factors for VTE, our sample size may have been insufficient to detect significant differences in some variables. Variability in the results could also be attributed to institution-specific protocols following surgery, patient demographics, differences in thromboprophylaxis regimens, and other known factors that influence VTE rates after RC. Moving forward, a prospective study comparing different durations and types of anticoagulation would strengthen the evidence from this retrospective analysis.

Our study was further restricted by the overall low VTE event rate. We observed a 3.2% VTE rate, whereas prior studies have reported rates ranging from 3% to 12% following RC [4-13]. This low incidence is likely multifactorial. The studies cited above spanned a wide range of years (2011 - 2021) and included data from both before and after the implementation of ETP and ERAS protocols. As a result, modern VTE incidence after RC may be closer to the lower end of this range, thanks to the adoption of ETP, ERAS, and other interventions. Our observed 3.2% VTE rate may be more reflective of contemporary risk. For example, a 2024 study involving 450 RC patients reported a VTE rate of 2.7% [48], suggesting that modern VTE risk may be declining due to the introduction of these newer protocols. Notably, our study captured data from a period during which both ETP and ERAS were implemented, contributing to the potential reduction in VTE rates. The present study was conducted at a suburban academic center with comprehensive inpatient and outpatient care following cystectomy. Given the unique institutional protocols and patient population, the results may not be directly generalizable to all settings. However, our study is relevant to modern academic centers that have the resources to implement such protocols. Furthermore, the discrepancy between our VTE rate and those reported in other studies may encourage institutions that have not yet adopted these protocols to consider their potential benefits. To obtain more definitive insights into the true VTE rate following RC with modern protocols, multi-institutional studies with

detailed analyses of ETP, ERAS, and associated risk factors are warranted.

5. CONCLUSION

VTE following RC is a serious complication that can significantly increase postoperative mortality. Patients who develop VTE may also experience higher cancer-related mortality. Prophylactic strategies, particularly those revolving around ERAS protocols and thromboprophylaxis, are essential in mitigating this risk. Future research is needed to better understand the causes, risk factors, morbidity, prevention, and management of VTE following RC.

ACKNOWLEDGMENTS

None.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Randall Bissette, Maxwell Sandberg Data Curation: Maxwell Sandberg Formal analysis: Maxwell Sandberg Investigation: Randall Bissette, Maxwell Sandberg, Stephen Tranchina, Kimberly Waggener, Madeline Snipes, Emily Ye, Jabrina Simmons, John Strobel Methodology: Randall Bissette, Maxwell Sandberg Project Administration: Maxwell Sandberg Resources: Ashok Hemal, Ronald Davis, Alejandro Rodriguez Software: Maxwell Sandberg Validation: Randall Bissette, Maxwell Sandberg, Ashok Hemal, Ronald Davis, Alejandro Rodriguez Visualization: Maxwell Sandberg, Alejandro Rodriguez Writing – original draft: Randall Bissette, Maxwell Sandberg Writing – review & editing: All authors

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research was approved by the Atrium Health Wake Forest Baptist Medical Center Institutional Review Board on 10/3/2023 under IRB00100649. Waiver of informed consent was granted by the IRB.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA

Data are available in de-identified format upon reasonable request to the corresponding author.

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