

## Intraoperative Blood Transfusion Is Associated With Increased Risk of Venous Thromboembolism After Radical Cystectomy

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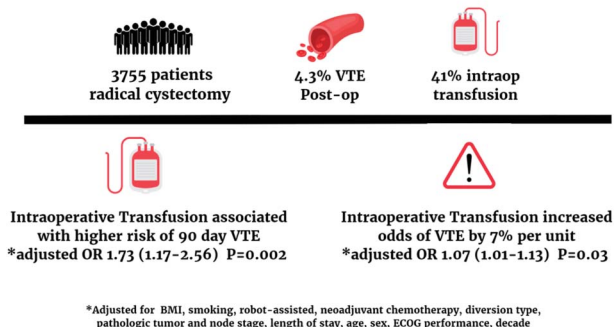
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**Study Need and Importance:** Venous thromboembolism (VTE) is a significant cause of morbidity and potential mortality after radical cystectomy, as well as the most expensive index complication. There is growing evidence that blood transfusions may increase the risk of postoperative venous thromboembolism; however, several important confounders—including tumor stage and receipt of neoadjuvant chemotherapy—have not been accounted for due to the inherent limitations of the data sets used previously. Therefore, our objective was to assess whether perioperative blood transfusion is associated with VTE following radical cystectomy after adjusting for disease-related characteristics.

**What We Found:** We identified 3,755 patients treated with radical cystectomy at Mayo Clinic, of whom 162 (4.3%) experienced a VTE within 90 days of surgery. Blood transfusion was studied as a 3-tiered variable: no transfusion, postoperative transfusion alone, or intraoperative with or without postoperative transfusion. Intraoperative with or without postoperative blood transfusion was associated with a significantly increased risk of VTE (adjusted OR 1.73, 95% CI 1.17-2.56,  $P = .002$ ) after multivariable adjustment. Moreover, each unit of blood transfused intraoperatively was associated with 7% higher odds of VTE (adjusted OR 1.07, 95% CI 1.01-1.13,  $P = .03$ ).

**Limitations:** This study is limited by its retrospective nature and potential for measurement bias as evaluation for VTE was based on clinical judgement.

### Is intraoperative blood transfusion associated with increased risk VTE?



**Figure.** Visual abstract of study. BMI indicates body mass index; ECOG, Eastern Cooperative Oncology Group; intraop, intraoperative; OR, odds ratio; post-op, postoperative; VTE, venous thromboembolism.

Additionally, although year of surgery was adjusted for, changes to institutional VTE prophylaxis over the study period may have influenced outcomes.

**Interpretation for Patient Care:** Efforts should be made to limit intraoperative transfusion through preoperative diagnosis and treatment of anemia, optimization of anticoagulant status, tranexamic acid infusion, and/or a robotic surgical approach when feasible. Surgeons should furthermore have a low index of suspicion to obtain diagnostic imaging and educate patients on the importance of VTE prophylaxis after intraoperative transfusion (see Figure).

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**Editor's Note:** This article is the second of 5 published in this issue for which Category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 647 and 648.

See Editorial on page 471.

**Purpose:** Our objective was to examine whether perioperative blood transfusion is associated with venous thromboembolism following radical cystectomy adjusting for both patient- and disease-related factors.

**Materials and Methods:** Patients who underwent radical cystectomy for bladder cancer from 1980-2020 were identified in the Mayo Clinic cystectomy registry. Blood transfusion during the initial postoperative hospitalization was analyzed as a 3-tiered variable: no transfusion, postoperative transfusion alone, or intraoperative with or without postoperative transfusion. The primary outcome was venous thromboembolism within 90 days of radical cystectomy. Associations between clinicopathological variables and 90-day venous thromboembolism were assessed using multivariable logistic regression, with transfusion analyzed as both a categorical and a continuous variable.

**Results:** A total of 3,755 radical cystectomy patients were identified, of whom 162 (4.3%) experienced a venous thromboembolism within 90 days of radical cystectomy. Overall, 2,112 patients (56%) received a median of 1 (IQR: 0-3) unit of blood transfusion, including 811 (38%) with intraoperative transfusion only, 572 (27%) with postoperative transfusion only, and 729 (35%) with intraoperative and postoperative transfusion. On multivariable analysis, intraoperative with or without postoperative blood transfusion was associated with a significantly increased risk of venous thromboembolism (adjusted OR 1.73, 95% CI 1.17-2.56,  $P = .002$ ). Moreover, when analyzed as a continuous variable, each unit of blood transfused intraoperatively was associated with 7% higher odds of venous thromboembolism (adjusted OR 1.07, 95% CI 1.01-1.13,  $P = .03$ ).

**Conclusions:** Intraoperative blood transfusion was significantly associated with venous thromboembolism within 90 days of radical cystectomy. To ensure optimal perioperative outcomes, continued effort to limit blood transfusion in radical cystectomy patients is warranted.

**Key Words:** cystectomy, venous thromboembolism, urinary bladder neoplasms

VENOUS thromboembolism (VTE) is a significant cause of morbidity and potential mortality after radical cystectomy (RC).<sup>1</sup> Rates of VTE after RC range from 2%-11%, and VTE is associated with the

highest costs of all index complications after RC.<sup>2-4</sup> Accordingly, significant effort has been aimed at decreasing the rates of VTE for patients undergoing RC, and VTE is increasingly

used as a quality indicator after RC.<sup>1</sup> However, the potential influence of perioperative blood transfusion on VTE development remains underexplored. Allogenic blood transfusion is known to stimulate the inflammatory cytokines and contribute to thrombosis, establishing a plausible biological rationale<sup>5-7</sup> whereby transfusion could increase VTE risk.

Several studies utilizing administrative data sets have associated perioperative blood transfusion with an increased risk of VTE in multiple surgical subspecialties,<sup>8,9</sup> however, due to inherent limitations of these data sets, authors have been unable to adjust for several important confounders—including tumor stage and neoadjuvant chemotherapy—that may modulate this association. Indeed, it is known that VTE risk is higher in patients with aggressive tumor biology and regional or metastatic spread.<sup>10</sup> Red blood cell (RBC) transfusion is also linked to increased risks of cancer recurrence, and disease-specific and all-cause mortality following RC.<sup>11,12</sup> Neoadjuvant chemotherapy, especially with platinum-based agents, is an additional risk factor for VTE.<sup>13,14</sup> Nevertheless, whether perioperative blood transfusion remains significantly associated with development of VTE after appropriate risk adjustment for disease related-factors remains undetermined.

Therefore, the objective of this study was to assess whether perioperative blood transfusion is associated with VTE following RC after adjusting for disease-related characteristics.

## METHODS

### Study Cohort

Following Institutional Review Board approval (IRB No. 21-007383), we reviewed the Mayo Clinic Cystectomy Registry to identify 3,755 patients treated with RC for bladder cancer between 1980 and 2020. Data are collected prospectively by a trained nurse abstractor. Lymphadenectomy at the time of RC was performed according to surgeon discretion. All pathological specimens were reviewed by a single urological pathologist for histological classification. Those with a known VTE prior to RC were excluded. Follow-up was calculated from date of RC to date of last known contact or death.

### Exposure and Outcomes

The exposure of interest was perioperative blood transfusion, which was defined as transfusion of allogenic red blood cells either intraoperatively during RC or during the initial postoperative hospitalization. To assess timing of perioperative transfusion, it was operationalized as a 3-tiered variable in accordance with prior literature: no transfusion, postoperative transfusion alone, or intraoperative with or without postoperative transfusion.<sup>15</sup> Transfusion with other blood products was not assessed. Indications for transfusion were not standardized and were based on discretion of the treating physicians.

The primary outcome was VTE within 90 days of RC. Diagnosis of VTE was inclusive of both deep vein thrombosis (DVT) and pulmonary embolism (PE). Assessment for VTE was based on symptomatic presentation and diagnosis

confirmed with conventional imaging that was standard at the time. Routine screening for VTE in asymptomatic patients was not performed, although VTEs identified incidentally on imaging done for other reasons were included. As part of database maintenance, available outside records are periodically reviewed by our nurse abstractor to capture 90-day outcomes that may have occurred outside of our hospital system, and follow-up questionnaires are routinely mailed to patients.

Perioperative VTE prophylaxis varied according to the institutional standard at the time, but generally consisted of sequential compression devices and subcutaneous unfractionated heparin while inpatient. In April 2013, we began using intraoperative tranexamic acid,<sup>16</sup> and in May 2014, we began prescribing outpatient extended duration VTE prophylaxis with enoxaparin 40 mg per day until postoperative day 28 in all patients without contraindications.<sup>17</sup>

### Statistical Analysis

Continuous variables are reported with medians and interquartile range (IQR), and categories with frequencies and percents. Baseline characteristics were compared using the Kruskal-Wallis test for continuous variables and the Chi-squared test for categorical variables. Associations between clinicopathological variables and 90-day VTE were assessed using multivariable logistic regression. Selection of variables for the multivariable models included all covariates with  $P < .2$  on univariate analysis, as well as variables deemed to have a clinical correlation with VTE based on prior literature and clinical reasoning. Patients with missing data were excluded from multivariable models. Intraoperative blood transfusion was analyzed separately as both a categorical and as a continuous variable. An interaction term between transfusion and decade of RC was added to each model.

Due to missing data in 40% of patients, number of lymph nodes removed and operative time were not included in the primary models. However, recognizing that extent of lymphadenectomy and operative time are potentially important confounders in developing a VTE, we performed a sensitivity analysis in the subset of patients for whom this information was known. For all analyses,  $P \leq .05$  was considered statistically significant. Statistical analysis was performed using SAS, version 9.4 (SAS Institute Inc, Cary, North Carolina).

## RESULTS

Between 1980-2020, we identified 3,755 patients with RC, of whom 162 (4.3%) experienced a VTE within 90 days of RC. The 162 VTE events included 89 (55%) patients with DVT, 54 (33%) with PE, and 19 (12%) with both DVT/PE. The median time from RC to VTE was 32 days (IQR 15-52). A total of 2,112 patients (56%) received a blood transfusion, of whom 1,540 (73%) patients received an intraoperative transfusion (811 intraoperative alone, 729 intraoperative and postoperative) and 572 (27%) patients received a postoperative transfusion only. Among those who received a transfusion, a median of 1 (range: 0-69, IQR: 0-3) unit was transfused. Transfusions were more common earlier in the series and were given to

**Table 1. Clinical Characteristics of Patients Under Study**

	No transfusion (n=1,643)	Intraoperative with/without postoperative transfusion (n=1,540)	Postoperative transfusion only (n=572)	P value
Age, median (IQR), y	67 (59-73)	69 (63-76)	69 (62-75)	<b>&lt; .001</b>
Sex, male, No. (%)	1,476 (90)	1,122 (73)	443 (77)	<b>&lt; .001</b>
ECOG performance status, No. (%)				.8
0	1,441 (88)	1,099 (71)	440 (77)	<b>&lt; .001</b>
1	168 (10)	297 (19)	113 (20)	
2+	34 (2.1)	144 (9.4)	19 (3.3)	
Cystectomy year, No. (%)				<b>&lt; .001</b>
1981-1990	128 (7.8)	556 (36)	96 (17)	
1991-2000	429 (26)	315 (20)	154 (27)	
2001-2010	524 (32)	440 (29)	187 (33)	
2011-2020	562 (34)	229 (15)	135 (24)	
BMI, median (IQR), kg/m <sup>2</sup>	28 (25-31)	27 (24-30)	27 (25-30)	<b>&lt; .001</b>
Smoking status, No. (%)				.2
Never	344 (21)	361 (23)	128 (22)	
Former	848 (52)	785 (51)	310 (54)	
Active	451 (27)	394 (26)	134 (23)	
Robot-assisted, No. (%)	177 (11)	14 (0.9)	16 (2.8)	<b>&lt; .001</b>
Lymph nodes, median (IQR), No. (n=2,822)	13 (7-22)	12 (5-20)	12 (6-20)	<b>&lt; .001</b>
Neoadjuvant chemotherapy, No. (%)	201 (12)	220 (14)	82 (14)	.2
Continent diversion, No. (%)	521 (32)	189 (12)	140 (25)	<b>&lt; .001</b>
Pathological T stage, No. (%)				<b>&lt; .001</b>
<pT2	890 (54)	674 (44)	284 (50)	
pT2	303 (19)	236 (15)	94 (16)	
pT3, pT4	450 (27)	630 (41)	194 (34)	
Pathological node positive, No. (%)	254 (16)	277 (18)	87 (15)	.1
Operative time, median (IQR), min (n=2,373)	295(248-349)	317(265-370)	303(260-364)	<b>&lt; .001</b>
Length of stay, median (IQR), d	8 (6-10)	10 (7-13)	9 (7-13)	<b>&lt; .001</b>

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range. Analyses performed using Kruskal-Wallis test for continuous variables and  $\chi^2$  test for categorical variables. Bolded values indicate statistical significance.

84% (652/780) of patients treated between 1980-1990 as compared to 39% (364/926) of patients treated from 2011-2020 ( $P < .001$ ). Median follow-up among those alive at last follow-up was 6.7 years (IQR 2.4-12.7). 90-day follow-up was available for 3,734 (99%) patients; of the 21 for whom this was not available, 20 died within 90 days of RC.

Table 1 summarizes clinical characteristics of our study cohort. Of the 162 patients who experienced a VTE, 65 (40%) had an intraoperative blood transfusion and 20 (12%) had a postoperative transfusion only. A comparison of clinical characteristics for the 162 patients who experienced a VTE, stratified by receipt of a blood transfusion, can be found in Supplementary Table 1 (<https://www.jurology.com>).

Among the 1,540 patients with an intraoperative blood transfusion, 77 (5.0%) developed a VTE; of the 572 patients with only postoperative transfusion, 20 (3.5%) had a VTE; and among the 1,643 patients without a transfusion, 65 (4.0%) had a VTE. After adjusting for age, sex, Eastern Cooperative Oncology Group performance status, cystectomy year, BMI, surgical approach, receipt of neoadjuvant chemotherapy, diversion type, length of stay, pathological tumor stage, and nodal stage, intraoperative with or without postoperative blood transfusion was associated with a significantly increased risk of VTE (adjusted OR 1.73, 95% CI 1.17-2.56,  $P = .002$ ; Table 2). The addition of an interaction term between cystectomy year and

intraoperative transfusion to the model was not statistically significant ( $P = .4$ ), indicating that the associations observed in Table 2 can be applied to the entire timeframe under study. When the number of units of blood transfused intraoperatively was further analyzed as a continuous variable, each unit of blood transfusion was significantly associated with increased odds of 90-day VTE (adjusted OR 1.07, 95% 1.01-1.13,  $P = .03$ ; Table 3). The addition of an interaction term between cystectomy year and number of intraoperative units transfused was not statistically significant ( $P = .5$ ).

Sensitivity analysis was performed in the subset of patients with available data on the total number of lymph nodes removed at RC and operative time ( $N = 2,215$ ), representing 59% of the overall cohort (Supplementary Table 2, <https://www.jurology.com>). Among these patients, 97 (4.4%) experienced a VTE within 90 days of RC. Patients with a VTE were observed to have a significantly higher number of lymph nodes removed at RC, with a median of 19 nodes removed (IQR 9-25) compared to 12 nodes (IQR 6-21) for those without a VTE ( $P < .001$ ). Operative time was significantly longer in patients who experienced a VTE, with a median 304 minutes (IQR 255-359) compared to 317 minutes (IQR 256-360;  $P = .005$ ). In a multivariable model including nodal yield and operative time as covariates, intraoperative with or without postoperative blood transfusion remained significantly associated with higher odds of a 90-day VTE (OR 1.90,

**Table 2. Multivariable Logistic Regression Model Evaluating Association Between Perioperative Blood Transfusion and Venous Thromboembolism Within 90 Days of Radical Cystectomy**

	Adjusted odds ratio (95% CI)	P value
Age	1.02 (1.00-1.04)	.056
Male sex	0.79 (0.52-1.18)	.25
ECOG performance status		
0	Ref.	
1	0.78 (0.48-1.27)	.6
2+	0.81 (0.39-1.69)	.8
Cystectomy decade		
1981-1990	Ref.	
1991-2000	1.35 (0.66-2.77)	.4
2001-2010	2.83 (1.50-5.32)	<b>.001</b>
2011-2020	4.10 (2.20-7.99)	<b>&lt; .001</b>
Body mass index	1.09 (1.06-1.12)	<b>&lt; .001</b>
Current or former smoker	1.01 (0.69-1.48)	> .9
Robot-assisted	0.85 (0.44-1.63)	.6
Neoadjuvant chemotherapy	1.27 (0.83-1.94)	.3
Continent diversion	1.51 (1.001-2.27)	.049
Pathological tumor stage		
<pT2	Ref.	
pT2	1.20 (0.74-1.94)	.9
pT3, pT4	1.40 (0.95-2.06)	.2
Pathological node positive	1.32 (0.88-2.01)	.18
Length of stay	1.00 (0.99-1.01)	.4
Blood transfusion		
No transfusion	Ref.	
Postoperative transfusion alone	0.92 (0.55-1.58)	.16
Intraoperative ± postoperative transfusion	1.73 (1.17-2.56)	<b>.002</b>

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; Ref., reference. Bolded values indicate statistical significance.

95% CI 1.16-3.12,  $P = .002$ ). Results of this model are summarized in Table 4.

**DISCUSSION**

In this single-institution cohort of patients undergoing RC for bladder cancer, we observed that receipt of an intraoperative blood transfusion was significantly associated with being diagnosed with a VTE within 90 days of surgery. Each unit of blood transfused intraoperatively was associated with 7% higher odds of a 90-day VTE, and this association remained statistically significant with a similar point estimate on sensitivity analysis including lymph node yield and operative time in the model. This is the first study to our knowledge to demonstrate a significant association between intraoperative transfusion and risk of VTE after RC when adjusting for disease-related variables including disease stage, presence of nodal metastases, and receipt of neoadjuvant chemotherapy, and suggests that intraoperative transfusion be considered in risk adjustment when assessing VTE as a quality metric after RC. Clinicians should also recognize that patients requiring intraoperative transfusion are at higher risk of VTE, and could consider screening ultrasound, better patient education on signs/symptoms of VTE, and use of extended duration VTE prophylaxis upon hospital discharge for these patients.

**Table 3. Multivariable Logistic Regression Model Evaluating Association Between Number of Units of Blood Transfused and Venous Thromboembolism Within 90 Days of Radical Cystectomy**

	Adjusted odds ratio (95% CI)	P value
Age	1.02(1.001-1.04)	<b>.044</b>
Male sex	0.75 (0.50-1.13)	.17
ECOG performance status		
0	Ref.	
1	0.78 (0.48-1.27)	.5
2+	0.87 (0.42-1.80)	> .9
Cystectomy decade		
1981-1990	Ref.	
1991-2000	1.15 (0.56-2.33)	.7
2001-2010	2.52 (1.35-4.72)	<b>.004</b>
2011-2020	3.49 (1.83-6.69)	<b>&lt; .001</b>
Body mass index	1.09 (1.06-1.12)	<b>&lt; .001</b>
Current or former smoker	1.00 (0.68-1.46)	> .9
Robot-assisted	0.76 (0.40-1.45)	.4
Neoadjuvant chemotherapy	1.36 (0.90-2.07)	.15
Continent diversion	1.42 (0.95-2.14)	.09
Pathological tumor stage		
<pT2	Ref.	
pT2	1.22 (0.75-1.97)	> .9
pT3, pT4	1.45 (0.99-2.14)	.14
Pathological node positive	1.33 (0.88-2.00)	.18
Length of stay	1.00 (1.00-1.01)	.4
Units of intraoperative blood transfused	1.07 (1.01-1.13)	<b>.03</b>

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; Ref., reference. Bolded values indicate statistical significance.

Several potential mechanisms may explain why perioperative RBC transfusion has been implicated as a risk factor for development of postoperative VTE.<sup>8</sup> RBCs play a critical role in physiological hemostasis via vessel wall adherence, platelet reactivity and margination, alterations in fibrin structure, and modulation of nitric oxide.<sup>18</sup> These effects are amplified by RBC membrane asymmetry that occurs as a result of enzymatic and oxidative injury during RBC storage, resulting in an undesirable exposure of procoagulant phospholipids at the time of transfusion.<sup>18</sup> Additionally, blood transfusion can stimulate the release of inflammatory cytokines that further potentiate prothrombotic events.<sup>7</sup> When considered in conjunction with previous observations that transfusion is associated with prolonged length of stay and an increased risk of cancer-specific mortality after RC, adopting a conservative approach toward blood transfusion for RC patients appears prudent.<sup>11,15</sup>

The year of cystectomy was a significant risk factor for VTE in our study, with VTE found to be more frequent in more recent decades. This is consistent with previous data which demonstrated an increase in incidence of VTE after major cancer surgery around year 2000,<sup>19</sup> and likely represents a measurement bias due to development of more sensitive diagnostic tests and higher index of clinical suspicion over time. However, this observation is in contrast to a recent series from 2011-2016 which demonstrated

**Table 4.** Multivariable Logistic Regression Model Evaluating Association Between Perioperative Blood Transfusion and Venous Thromboembolism Within 90 Days of Radical Cystectomy in the Subset of Patients With Known Operative Time and Lymph Node Yield

	Adjusted odds ratio (95% CI)	P value
Age	1.02 (1.00-1.04)	.11
ECOG performance status		
0	Ref.	
1	0.52 (0.26-1.09)	.07
2+	1.19 (0.53-2.71)	.3
Cystectomy decade		
1981-1990	Ref.	
1991-2000	0.77 (0.30-2.0)	.6
2001-2010	1.45 (0.60-3.51)	.4
2011-2020	1.98 (0.69-5.70)	.2
Body mass index	1.09 (1.06-1.13)	<b>&lt; .001</b>
Neoadjuvant chemotherapy	1.76 (0.98-3.14)	.3
Pathological tumor stage		
<pT2	Ref.	
pT2	1.26 (0.67-2.37)	<b>&gt; .9</b>
pT3, pT4	1.36 (0.81-2.27)	.19
Pathological node positive	1.11 (0.64-1.92)	.18
Number of lymph nodes removed	1.01 (0.99-1.03)	.31
Operative time	1.00 (1.00-1.004)	.061
Blood transfusion		
No transfusion	Ref.	
Postoperative transfusion alone	0.78 (0.37-1.63)	.10
Intraoperative ± postoperative transfusion	1.90 (1.16-3.12)	<b>.002</b>

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; Ref., reference.

Bolded values indicate statistical significance.

VTE rates after RC have significantly decreased over this more recent 5-year period.<sup>20</sup> This recent decrease is likely reflective of improved perioperative care pathways including early ambulation, and in-hospital and post-discharge VTE prophylaxis over the past decade.<sup>21</sup> The 40-year time period examined in the current study likely prevented us from discerning this more recent trend and likely explains these contrasting data.

BMI was also found to be significantly associated with VTE in RC patients, which is consistent with previous studies. Elevated BMI has been associated with suboptimal prophylactic anticoagulant dosing.<sup>22</sup> In a single-institution series, two-thirds of post-RC patients were found to have subtherapeutic anti-factor Xa levels after surgery, which was most pronounced among obese individuals. Obese patients are also predisposed to venous stasis, which incites activation of the endothelium and increases the risk of VTE.<sup>23</sup> This observation underscores the importance of prophylactic measures against VTE for obese patients undergoing RC.

This study is limited by its retrospective nature. Significant differences existed between patients with a VTE who did receive a blood transfusion compared to those with VTE who did not, including fewer robotic procedures, higher Eastern Cooperative Oncology Group score, and older age at surgery. Although these were adjusted

for in the multivariable models, other unmeasured confounders may persist between groups—including the presence of an indwelling port in patients who received neoadjuvant chemotherapy. Length of stay was used as a surrogate marker for ambulatory status and postoperative morbidity and adjusted for. However, other major complications that could have associations with VTE were not adjusted for due to lack of statistical power. Insufficient power similarly prevented us from separately analyzing drivers of early and late postoperative VTEs. Additionally, the retrospective nature prohibited standardized criteria for obtaining diagnostic testing for VTE. We acknowledge the likelihood of a detection bias, as postoperative complications may have increased rates of imaging and subsequent VTE diagnosis. Furthermore, we acknowledge that some of the events reported in this study could have been VTEs that were present preoperatively but were not detected until the postoperative period. The overall rate of blood transfusion was high in this series (60%), reflective of the time period studied, which may limit generalizability to other practice settings. The study period was long, during which changes to institutional VTE prophylaxis and RBC storage and preservation techniques evolved, which may have influenced the outcomes. Unfortunately, data regarding VTE prophylaxis used were unavailable, and despite the fact that all models were adjusted for cystectomy year we could not account for all potential variation in administration of VTE prophylaxis which may have confounded results, including differences in extended duration prophylaxis. Although outside records are reviewed by our nurse abstractor and follow-up questionnaires are routinely mailed to patients, we acknowledge that we may have failed to capture some VTE events that occurred outside of our hospital system, particularly during the earlier years of the study. Additionally, the percent of patients who received neoadjuvant chemotherapy in this series was low, likely reflective of temporal trends. Future study of an external cohort is necessary to validate the findings herein.

Nevertheless, despite these limitations, we present what is to our knowledge the first report to show a significant association between intraoperative blood transfusion and VTE after RC after adjusting for disease-related factors. This relationship was consistent when transfusion was modeled as either a categorical or continuous variable and is supported by a plausible biological rationale. These data support incorporating intraoperative blood transfusion in case mix adjustment when analyzing VTE as a postoperative quality metric and should remind surgeons to maintain a low threshold to obtain imaging for VTE after RC. Furthermore, these data suggest that surgeons strongly consider use of pharmacological VTE prophylaxis in patients with bleeding complications, a group in whom many clinicians may be otherwise reluctant to consider

this. Our findings emphasize the importance of efforts to limit need for intraoperative transfusions, including preoperative identification and correction of anemia, optimization of anticoagulant status, and selective use of evidence-based techniques including intraoperative cell salvage, tranexamic acid infusion, and/or a robotic surgical approach when appropriate.<sup>24-26</sup>

## CONCLUSIONS

Intraoperative blood transfusion was statistically significantly associated with VTE within 90 days of RC after adjusting for disease-related factors. Each unit of blood transfused was associated with higher odds of a VTE. Critical assessment of practices to decrease the risk of intraoperative transfusion represent important areas for future study.

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