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CLINICAL AND CANCER-RELATED PREDICTORS FOR VENOUS THROMBOEMBOLISM IN CANCER PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: The accurate detection of cancer-associated venous thromboembolism (VTE) can avoid unnecessary diagnostic imaging or laboratory tests. Objective: We sought to determine clinical and cancer-related risk factors of VTE that can be used as predictors for oncology patients presenting to the emergency department (ED) with suspected VTE. Methods: We retrospectively analyzed all consecutive patients who presented with suspicion of VTE to The University of Texas MD Anderson Cancer Center ED between January 1, 2009, and January 1, 2013. Logistic regression models were used to identify risk factors that were associated with VTE. The ability of these factors to predict VTE was externally validated using a second cohort of patients who presented to King Hussein Cancer Center ED between January 1, 2009, and January 1, 2016. Results: Cancer-related covariates associated with the occurrence of VTE were high-risk cancer type (odds ratio [OR] 3.64 [95% confidence interval {CI} 2.37–5.60], $p < 0.001$), presentation within 6 months of the cancer diagnosis (OR 1.92 [95% CI 1.62–2.28], $p < 0.001$), active cancer (OR 1.35 [95% CI 1.10–1.65], $p = 0.003$), advanced stage (OR 1.40 [95% CI 1.01–1.94], $p = 0.044$), and the presence of brain metastasis (OR 1.73 [95% CI 1.32–2.27], $p < 0.001$). When combined, these factors along with other clinical factors showed high prediction performance for VTE in the external validation cohort. Conclusions: Cancer risk group, presentation within 6 months of cancer diagnosis, active and advanced cancer, and the presence of brain metastases along with other related clinical factors can be used to predict VTE in patients with cancer presenting to the ED.**

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INTRODUCTION

Cancer-associated venous thromboembolism (VTE) has an annual incidence of 1 in 200 (1). The high mortality rate of VTE makes it a leading cause of death among patients with cancer, and its high morbidity rate causes consequential economic burden (2–4). VTE events may be related to the cancer, a side effect of cancer therapy, or associated with other comorbidities. Many cancer patients with VTE present to the emergency department (ED) for care. Therefore, timely and accurate detection of VTE in the ED has enormous clinical significance and may improve patient management and clinical outcomes.

Studies have shown an increased risk for VTE in patients with various types of cancer (5,6). Several scoring systems for the evaluation of suspected VTE have already been established for patients in the general population. This includes the Wells score, the Geneva score, and the revised Geneva score. In addition, guidelines including the American College of Physicians guideline use these validated scores in combination with other tools, such as the PE Rule Out Criteria and D-dimer as a risk stratification tool in the evaluation of pulmonary embolism (PE) (7–11). Others, including the Khorana scoring system, assessed clinical and laboratory parameters and built predictive models to identify cancer patients who have an increased risk for developing VTE (12–15).

Because VTE occurs more often in patients with cancer than in those without an underlying malignancy, patients with cancer have a higher pretest probability for VTE than do patients without cancer; in addition, the diagnostic strategy used for cancer patients is different (1,16). D-dimer has lower predictive values in patients with cancer, especially among patients with leukemia and lymphoma (16–18). Furthermore, the ability of this clotting biomarker to detect VTEs in cancer patients varies significantly among different cancer types (17). Therefore, predictors that help diagnose VTEs in patients with cancer in an urgent/emergent care setting are needed to guide the optimal use of diagnostic laboratory and imaging studies.

In the current study, we analyzed and identified predictive clinical and cancer-related factors in patients with cancer who were suspected to have VTE who visited our ED. We then validated these predictors in a different cohort of patients with cancer from another institution.

MATERIALS AND METHODS

Study Participants and Data Collection

Two cancer patient cohorts were investigated. For the first, all consecutive patients who visited the ED of The University of Texas MD Anderson Cancer Center in Houston, Texas, USA, between January 1, 2009, and January 1, 2013, and who had D-dimer laboratory results, were identified by querying billing and laboratory databases. This patient cohort was used to identify VTE predictive factors. In the same way, we identified a second cohort of consecutive patients with cancer who visited the ED of King Hussein Cancer Center in Amman, Jordan, between January 1, 2009, and January 1, 2016. This patient cohort was used to externally validate the VTE predictors determined from the MD Anderson cohort. Exclusion criteria for both cohorts were 1) age <18 years; 2) no cancer diagnosis; 3) no follow-up records during the ED visit or within 30 days of the visit; 4) missing emergency physician notes; and 5) arterial thrombosis or VTE other than lower limb deep venous thrombosis and PE.

At MD Anderson, potential participants were identified using the electronic medical record system. Patient demographics, cancer information, morbidities, vital signs, and clinical variables that are known to be associated with thrombosis (including a history of VTE, immobilization, surgery or fractures within 30 days before presentation) were collected. The presence or absence of VTE was determined by reviewing the imaging reports. The presence of VTE as the outcome of interest was defined as an incidence of acute lower limb deep venous thrombosis or acute PE during the ED visit (i.e., ≤72 h before or after presentation) or within the 30-day follow-up period, found on an appropriate diagnostic imaging study (lower extremity Doppler ultrasound, chest computed tomography with intravenous contrast, or radionuclide ventilation/perfusion scans). Questionable radiologic results were further reviewed by a board-certified thoracic radiologist and classified as either positive or negative. Collaborators at King Hussein cancer center used a similar workflow.

This study was approved by the institutional review boards of MD Anderson and King Hussein cancer centers; both granted waivers of informed consent.

Predictor Derivation and Validation

We identified VTE predictors using the MD Anderson cohort. Variables included in the development phase were clinical variables that have been previously shown to be associated with VTE, as well as other cancer-

related clinical factors. Immobility was defined as motionlessness for ≥3 days within the 4 weeks preceding ED presentation. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Hypoxemia was defined as partial pressure of oxygen <60 mm Hg with arterial blood gas or oxygen saturation <95%. Advanced cancer stage was defined as solid tumors with American Joint Committee on Cancer anatomic stage/prognostic groups of stage IV, brain and spinal cord tumors with World Health Organization grade IV, or hematologic malignancies in relapsed or refractory phases. Time from cancer diagnosis was calculated from the time of confirmed pathologic diagnosis to the time of ED presentation.

Univariate analysis was performed to determine the association between each variable and VTE. Significance was appraised using the χ^2 test for categorical variables and the Student *t* or Wilcoxon-Mann-Whitney tests for continuous variables where appropriate. Cancer types were analyzed using multiple logistic regression controlled for cancer stage and were simplified by combining groups with similar adjusted odds ratios (AORs). Race/ethnicity was analyzed using multiple logistic regression controlling for cancer type, stratifying the race groups according to their AORs. Continuous variables were categorized using a cutoff point according to levels previously used in patients with cancer (19,20). Statistically significant clinical variables from the univariate analyses were further analyzed using a multiple logistic regression model. The Hosmer-Lemeshow goodness-of-fit statistic was used to evaluate the calibration of the model. The prediction performance of the model was assessed using receiver operating characteristic analysis calculating the area under the curve. External validation of the performance of the predictive factors was done using the King Hussein cohort. Receiver operating characteristic/area under the curve analysis followed by the DeLong test were used to identify statistically significant differences between the derivation (MD Anderson) cohort and the external validation (King Hussein) cohort. Two-tailed p values < 0.05 were considered statistically significant.

All statistical analyses were performed using R software (v 3.5.1; The R Foundation, http://www.r-project.org).

RESULTS

Patient Characteristics and VTE Prevalence

Of the eligible patients initially identified in the MD Anderson cohort (4432 patients) and the King Hussein cohort (551 patients), 4145 patients and 508 patients, respectively, were included in the analysis once exclusion criteria were applied (Figure 1). Table 1 shows the general characteristics of the patients in each cohort. The prevalence of VTE was 23.1% (958/4145 patients) in the MD Anderson cohort and 21.7% (110/508 patients) in the King Hussein cohort cohort. Of the patients with VTE in the MD Anderson cohort, 47.3% (453/958) had a PE, 32.2% (308/958) had lower limb deep venous thrombosis, and 20.6% (197/958) had both (Figure 1).

Clinical and Cancer-Related Predictors for Cancer-Associated VTE

Cancer types were categorized into 4 risk groups according to their AORs, after controlling for cancer stage: very high risk (AOR >3), high risk (AOR 2–3), intermediate risk (AOR 1–2), and low risk (AOR <1). Brain and spinal cord cancer and gastric cancer represented the very high-risk group, having the highest AORs (4.21 and 3.81, respectively). The high-risk group included pancreatic, urinary bladder, and cervical, ovarian, and other gynecologic (excluding endometrial) cancers; the intermediate-risk group comprised lung, endometrial, esophageal, testicular, prostate, rectal, and hepatobiliary cancers, along with multiple myeloma, sarcoma, melanoma, and metastatic cancer of unknown primary origin; and the low-risk group included kidney, breast, colon, and head and neck cancers, along with lymphoma, mesothelioma, and leukemia (Table 2). As for race/ethnicity, white race had a significantly higher AOR than other races or ethnicities (1.67 [95% confidence interval {CI} 1.11–2.61], $p = 0.029$) after controlling for cancer type; therefore, race was grouped into white and nonwhite for the multivariable analysis (Supplemental Table S1).

Among the other 26 clinical variables screened, 14 variables were associated with the occurrence of VTE in univariate analysis (Table 3). Missing values were rare; time from cancer diagnosis had the most missing values (7/4145, 0.2%). Weight and height were among the variables most significantly associated with VTE, but these variables were excluded from subsequent analysis to prevent multicollinearity with BMI. The remaining 12 significant variables (chest pain, shortness of breath, unilateral limb swelling, unilateral limb pain, hypoxemia, heart rate, systolic blood pressure, BMI, previous VTE, immobility, time from cancer diagnosis, and brain metastasis), along with 5 common clinical variables (age, race, Charlson comorbidity index, cancer stage, and cancer type risk group), were included in the multivariable analysis.

In the multivariable analysis, cancer type risk groups showed good discrimination compared with the reference (low-risk group); the very high-risk group VTE rate was almost fourfold higher than in the low-risk group (AOR 3.64 [95% CI 2.37–5.60], $p < 0.001$; Table 4). Other cancer-related covariates associated with the occurrence

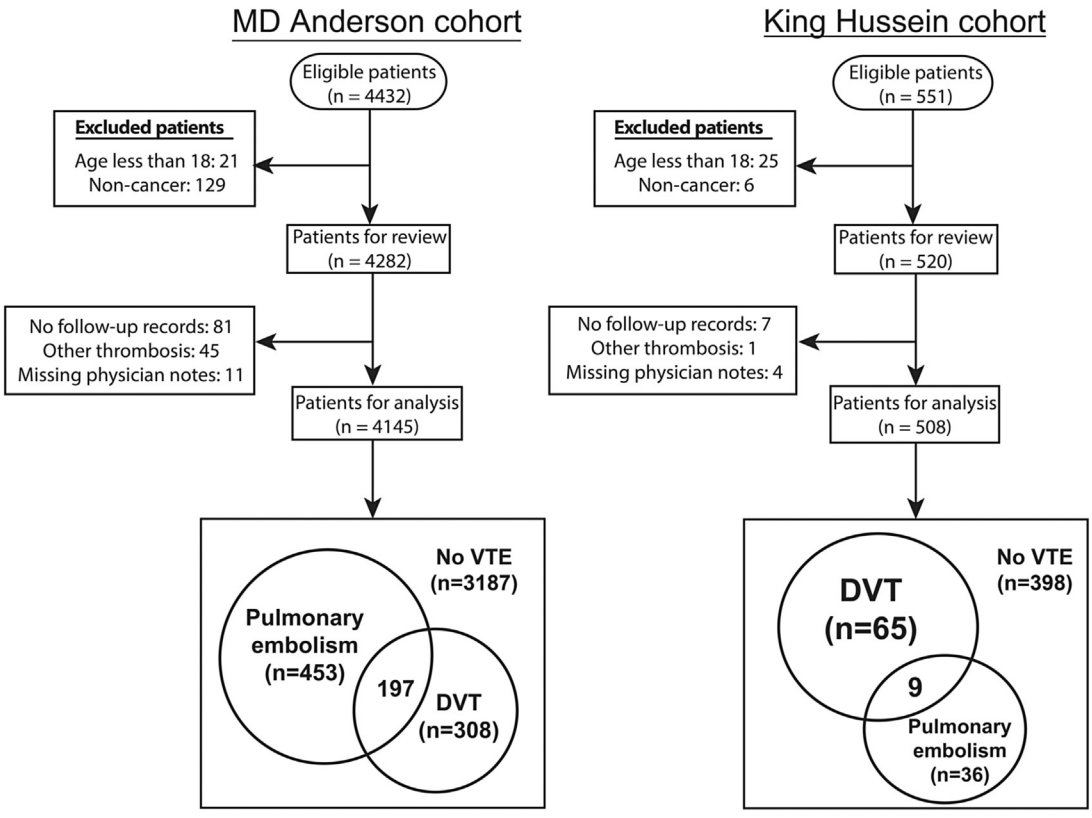

Figure 1. Exclusion criteria used to determine study eligibility for MD Anderson and King Hussein cohorts. DVT = deep venous thrombosis; VTE = venous thromboembolism.

of VTE were presentation within 6 months of the cancer diagnosis (AOR 1.92 [95% CI 1.62–2.28], $p < 0.001$), active cancer (AOR 1.35 [95% CI 1.10–1.65], $p = 0.003$), advanced stage (AOR 1.40 [95% CI 1.01–1.94], $p = 0.044$), and the presence of brain metastasis (AOR 1.73 [95% CI 1.32–2.27], $p < 0.001$; Table 4). As for clinical factors, previous VTE, higher BMI, immobility, and presenting with tachycardia, hypoxemia, or unilateral lower limb swelling or pain were all predictors of VTE (Table 4).

The model showed good calibration in the Hosmer-Lemeshow goodness-of-fit test ($p = 0.903$), indicating no evidence of poor fit. The receiving operating characteristic analysis of the model yielded an area under the curve of 0.74 (95% CI 0.72–0.76). The area under the curve for the King Hussein cohort was 0.78 (95% CI 0.72–0.83), which was not significantly different from the 0.74 area under the curve in the MD Anderson cohort ($p = 0.164$; Figure 2).

DISCUSSION

Using data from a comprehensive cancer center, we identified cancer-related and clinical risk factors for VTE in patients with cancer presenting to the ED. Specifically, our model showed that cancer type, VTE within 6 months of diagnosis, active and advanced cancer, and the presence of brain metastases can be used to predict VTE in patients with cancer with suspected VTE presenting to the ED. VTE as the outcome of interest was identified by well-established diagnostic criteria and verified by follow-up within 30 days of ED presentation. Having 958 VTE events fulfilled the accepted rule that ≥10 outcome events are included for each predictor in the derivation model. The model showed high prediction performance for VTE and was also validated externally by data from a cancer center in a different country.

There is currently no validated clinical decision scoring system specific for patients with cancer that can help in the evaluation of these patients for suspected PE. The Wells and Geneva scores are validated clinical decision rules for evaluating patients with suspected PE in emergency/acute care of the general population but are not specifically for patients with cancer. The Khorana score is a helpful tool in patients with cancer, but it is a risk assessment model for identifying patients who are underoing active chemotherapy with a high risk of developing VTE during or after their chemotherapy treatment, to guide the decision for prophylactic anticoagulation. The Khorana score is not for the evaluation of patients

Table 1. Characteristics of the Patients Included in Each Cohort

Characteristic	Patients					
	MD Anderson			King Hussein		
	No VTE	VTE	*p* Value	No VTE	VTE	*p* Value
Total, n	3187	958		398	110	
Median age, years (range)	60 (18–101)	61 (18–92)	0.128	54 (19–88)	58 (18–84)	0.035*
Sex, n (%)						
Female	1660 (52.1)	462 (48.2)	0.036*	203 (51.0)	64 (58.2)	0.182
Male	1527 (47.9)	496 (51.8)		195 (49.0)	46 (41.8)	
Race/ethnicity, n (%)						
White	2026 (63.6)	641 (66.9)	0.208	398 (100.0)	110 (100.0)	N/A
Black	524 (16.4)	153 (16.0)		0 (0.0)	0 (0.0)	
Hispanic	425 (13.3)	112 (11.7)		0 (0.0)	0 (0.0)	
Asian	133 (4.2)	28 (2.9)		0 (0.0)	0 (0.0)	
Other	79 (2.5)	24 (2.5)		0 (0.0)	0 (0.0)	
Median CCI (range)	6 (2–16)	6 (2–14)	0.004*	8 (2–19)	8 (2–15)	0.068
Cancer stage, n (%)						
Undetermined	20 (0.6)	7 (0.7)	<0.001*	43 (10.8)	10 (9.1)	0.104
I	170 (5.3)	36 (3.8)		21 (5.3)	8 (7.3)	
II	234 (7.3)	44 (4.6)		18 (4.5)	5 (4.5)	
III	340 (10.7)	100 (10.4)		14 (3.5)	7 (6.4)	
IV	1689 (53.0)	583 (60.9)		196 (49.2)	64 (58.2)	
Nonsolid	734 (23.0)	188 (19.6)		106 (26.6)	16 (14.5)	
Cancer type, n (%)						
Gastrointestinal	344 (10.8)	148 (15.4)	<0.001*	74 (18.6)	30 (27.3)	<0.001*
Chest	717 (22.5)	218 (22.8)		36 (9.0)	15 (13.6)	
Hematologic	738 (23.2)	189 (19.7)		115 (28.9)	16 (14.5)	
Genitourinary	333 (10.4)	125 (13.0)		53 (13.3)	18 (16.4)	
Brain and spinal cord	31 (1.0)	31 (3.2)		7 (1.8)	10 (9.1)	
Other	1024 (32.1)	247 (25.8)		113 (28.4)	21 (19.1)	

CCI = Charlson comorbidity index; N/A = not applicable; VTE = venous thromboembolism.
* Statistically significant ($p < 0.05$).

with suspected PE, and this score is unsuitable for the ED. Here, we have shown for the first time that cancer-related factors can be combined with clinical factors to predict VTE in patients with cancer who are seeking emergency care. These predictors can be further used in the development of a VTE-predicting scoring system unique for the emergency care cancer population. Such a system could be used in the ED to guide the diagnostic evaluation of VTE, avoiding unnecessary diagnostic imaging studies, laboratory workups, or both.

It has been known for >150 years that cancer and thrombosis are linked (21). Not only is the risk of thrombosis higher in patients with various malignancies, but unprovoked thrombosis can also be considered an early sign of cancer (6,22,23). Several studies have successfully established a correlation between thrombosis and clinical, laboratory, and cancer parameters (12,13,19,20). However, a model that can predict the risk for VTE in patients with any type of cancer is needed. Wells et al. and Le Gal et al. established clinical prediction rules to help with the accurate diagnosis of VTE in the general population; both systems assign points for the existence of active cancer (7,8). Several groups, including the Wells et al. group, tested the usefulness of these scores in patients with cancer, with or without the combination of D-dimer levels, and concluded that these scores had a lower clinical utility for excluding VTE in patients with cancer (24–26). This can be explained by the fact that those with active malignant conditions were assigned the same point values for active cancer regardless of the patient's cancer type, stage, or other cancer-related factors. As a result, a significant knowledge gap about the performance of these scores in patients with cancer continues to exist. Using the large MD Anderson cohort, we identified cancer-related and clinical predictors for VTE in patients with cancer, and these factors could be used to develop a more accurate cancer-specific scoring system.

Malignant cells can produce procoagulant and proinflammatory modulators that activate vascular cells and cause direct adhesion of malignant cells to normal cells, resulting in thrombus formation (27). These biological factors, along with patient clinical factors, explain why patients with cancer have an increased risk for VTE and highlight the importance of a prediction scoring system solely for the cancer population that incorporates disease-related factors. Among these factors, cancer site, cancer stage, metastatic site, and time from cancer diagnosis were significant cancer-related predictors for

Table 2. Cancer Type Risk Group Stratification for Venous Thromboembolism

Cancer Type	Adjusted OR* (95% CI)	Final Risk Group
Brain and spinal cord	4.21 (2.25–7.97)	Very high
Gastric	3.81 (1.97–7.40)	Very high
Cervical	2.73 (1.31–5.60)	High
Pancreatic	2.46 (1.36–4.47)	High
Ovarian	2.27 (1.28–4.05)	High
Other gynecologic	2.26 (0.57–7.74)	High
Bladder	2.12 (0.94–4.62)	High
Rectal	1.84 (0.84–3.90)	Intermediate
Esophageal	1.66 (0.93–2.97)	Intermediate
Metastatic of unknown primary	1.53 (0.77–2.97)	Intermediate
Testicular	1.47 (0.39–4.57)	Intermediate
Endometrial	1.37 (0.67–2.73)	Intermediate
Lung	1.26 (0.84–1.93)	Intermediate
Prostate	1.22 (0.63–2.30)	Intermediate
Sarcoma	1.22 (0.76–2.00)	Intermediate
Skin melanoma	1.19 (0.65–2.15)	Intermediate
Hepatobiliary	1.17 (0.56–2.35)	Intermediate
Multiple myeloma	1.04 (0.05–7.61)	Intermediate
Kidney	0.96 (0.51–1.75)	Low
Breast	0.93 (0.60–1.46)	Low
Colon	0.93 (0.51–1.68)	Low
Lymphoma	0.90 (0.04–6.39)	Low
Mesothelioma	0.89 (0.34–2.11)	Low
Head and neck	0.87 (0.50–1.51)	Low
Leukemia	0.80 (0.04–5.80)	Low

CI = confidence interval; OR = odds ratio.
* ORs adjusted for cancer stage.

Table 3. Univariate Analysis for the Association of Clinical Risk Factors with Venous Thromboembolism

Variable Name	OR (95% CI)	*p* Value
Demographics and anthropometrics		
Age, years	1.00 (1.00–1.01)	0.075
Race		
Nonwhite	Reference	
White	1.16 (1.00–1.35)	0.059
Sex		
Female	Reference	
Male	1.17 (1.01–1.35)	0.036*
Height, cm	1.01 (1.01–1.02)	<0.001*
Weight, kg	1.01 (1.01–1.01)	<0.001*
BMI, kg/m^2	1.02 (1.01–1.03)	<0.001*
BMI category		
<25 kg/m^2	Reference	
25–<30 kg/m^2	1.35 (1.16–1.58)	<0.001*
≥30 kg/m^2	1.59 (1.15–2.18)	0.004*
Vital signs		
Systolic blood pressure, mm Hg	0.99 (0.99–1.00)	0.003*
Diastolic blood pressure, mm Hg	1.00 (0.99–1.00)	0.405
Heart rate >90 beats/min	1.26 (1.08–1.46)	0.003*
Respiratory rate	1.02 (0.99–1.04)	0.238
Temperature, C°	0.98 (0.88–1.06)	0.629
Hypoxemia	1.52 (1.24–1.85)	<0.001*
Signs and symptoms		
Shortness of breath	0.91 (0.78–1.05)	0.208
Chest pain	0.71 (0.61–0.82)	<0.001*
Hemoptysis	0.71 (0.49–1.01)	0.062
Unilateral limb swelling	2.95 (2.39–3.63)	<0.001*
Unilateral limb pain	2.37 (1.87–2.99)	<0.001*
Bilateral limb swelling	1.04 (0.66–1.61)	0.852
Bilateral limb pain	0.80 (0.34–1.66)	0.583
Clinical factors		
Previous venous thromboembolism	3.94 (3.33–4.65)	<0.001*
Charlson comorbidity index	1.05 (1.02–1.08)	0.003*
Immobilization	1.77 (1.32–2.34)	<0.001*
Surgery	1.10 (0.83–1.43)	0.506
Fractures	1.43 (0.50–3.57)	0.466
Atrial fibrillation	1.03 (0.80–1.32)	0.800
Cancer-related factors		
Cancer type risk group		
Low	Reference	
Intermediate	1.36 (1.16–1.59)	<0.001*
High	2.42 (1.83–3.18)	<0.001*
Very high	4.14 (2.82–6.06)	<0.001*
Cancer stage		
Local	Reference	
Advanced	1.64 (1.29–2.11)	<0.001*
Liquid/hematologic	1.25 (0.95–1.66)	0.122
Active cancer	1.48 (1.27–1.74)	<0.001*
Time from cancer diagnosis, months	1.00 (0.99–1.00)	<0.001*
Brain metastasis	1.52 (1.20–1.93)	<0.001*
Lung metastasis	0.85 (0.70–1.04)	0.113
Liver metastasis	1.13 (0.94–1.36)	0.194

BMI = body mass index; CI = confidence interval; OR = odds ratio.
* Statistically significant ($p < 0.05$).

VTE in our model. We found that brain and spinal cord cancer and gastric cancer were associated with a very high risk for VTE and that pancreatic, urinary bladder, and gynecologic cancers (excluding endometrial cancer) were associated with a high risk for VTE, corroborating previous reports (2,5,6,28,29).

In addition, similar to previous studies, we found that patients with distant metastases or advanced cancer had an increased risk for VTE (2,30,31). Chew et al. showed that the incidence of VTE is highest within the first year after a cancer diagnosis, especially in patients with advanced cancer, and others have shown that the risk is highest within the first 3–6 months after the diagnosis (2,19,31,32). We found that patients who had their cancer diagnosis ≤6 months before ED presentation had an AOR of 1.92 ($p < 0.001$), concurring with previous studies. One novel finding in our study was that brain metastasis was associated with a significantly higher risk for VTE compared with other metastatic sites (i.e., lung or liver), suggesting that both primary and metastatic brain tumors are of clinical importance in patients with cancer who are suspected to have VTE.

Previous VTE, immobility, and obesity are known common risk factors associated with thrombosis, and our study substantiated these factors (13,30,33). We stratified patients by BMI into <25 kg/m^2, 25–30 kg/m^2, and ≥30 kg/m^2 categories to examine VTE risk. We found that patients with a BMI 25–30 kg/m^2 and those with BMI >30 kg/m^2 had AORs of 1.36 (95% CI 1.14–1.61) and 1.83 (95% CI 1.27–2.61), respectively, for VTE compared with patients with a BMI <25 kg/m^2.

Racial/ethnic differences in VTE risk have also been reported. Chew et al. showed that racial differences in

Table 4. Clinical and Cancer-Related Predictors for Venous Thromboembolism in Patients with Cancer

Variable	AOR (95% CI)	*p* Value
Age	1.00 (1.00–1.01)	0.174
Race		
Nonwhite	Reference	
White	1.18 (0.99–1.4)	0.062
Sex		
Female	Reference	
Male	1.12 (0.95–1.33)	0.168
BMI		
<25 kg/m^2	Reference	
25–<30 kg/m^2	1.36 (1.14–1.61)	<0.001*
≥30 kg/m^2	1.83 (1.27–2.61)	<0.001*
Systolic blood pressure <90 mm Hg	1.13 (0.73–1.71)	0.588
Heart rate >90 beats/min	1.38 (1.17–1.64)	<0.001*
Hypoxemia	1.42 (1.13–1.78)	0.003*
Chest pain	0.89 (0.75–1.05)	0.176
Hemoptysis	0.78 (0.52–1.14)	0.207
Unilateral lower limb swelling	2.47 (1.90–3.20)	<0.001*
Unilateral lower limb pain	1.65 (1.22–2.21)	<0.001*
Previous venous thromboembolism	4.33 (3.60–5.20)	<0.001*
Charlson comorbidity index	0.97 (0.92–1.02)	0.266
Immobility	1.40 (1.01–1.93)	0.039*
Cancer type risk group		
Low	Reference	
Intermediate	1.24 (1.03–1.50)	0.027*
High	2.55 (1.86–3.50)	<0.001*
Very high	3.64 (2.37–5.60)	<0.001*
Cancer stage		
Local	Reference	
Advanced	1.40 (1.01–1.94)	0.044*
Liquid/hematologic	1.29 (0.93–1.8)	0.124
Active cancer	1.35 (1.10–1.65)	0.003*
Time from cancer diagnosis <6 months	1.92 (1.62–2.28)	<0.001*
Brain metastasis	1.73 (1.32–2.27)	<0.001*

AOR = adjusted odds ratio; BMI = body mass index; CI = confidence interval.
* Statistically significant ($p < 0.05$).

VTE risk depend mainly on the cancer type, with the lowest risk observed among Asian-Pacific Islanders (2). We also found that Asian patients had the lowest risk (and thus used that group as our reference), while white patients were at higher risk than other racial and ethnic categories in our cohort.

We also found that heart rate and unilateral limb swelling or pain were significant predictors of VTE. This is consistent with the findings of Wells et al. and Le Gal et al. (7,8). Hypoxemia, a known sign associated with PE that mainly reflects ventilation-to-perfusion mismatch, also was also a significant predictor of VTE (34).

Limitations

Certain biases and limitations accompanied our study. Not all patients presenting to the ED were included in the analysis. Specifically, only those who had D-dimer results were included. Although this is an unavoidable limitation given the retrospective nature of the dataset and may have introduced selection bias, we used this exclusion criterion because D-dimer is on the diagnostic panels for the evaluation of chest pain, shortness of breath, or limb swelling. Most ED patients had D-dimer ordered for the evaluation of these symptoms. Also, this made it possible to include all signs and symptoms in the analysis without preselection using particular signs or symptoms as study inclusion criteria.

CONCLUSION

In summary, we identified cancer-related and clinical predictors of VTE in patients with cancer who presented to the ED. We successfully validated the predictive ability of these variables externally. A future prospective study can be helpful to assess these predictors and combine them in a clinical prediction scoring system, similar to the Wells and Geneva scores, that can be safely used to improve the use of imaging and other work-up of suspected VTE in patients with cancer.

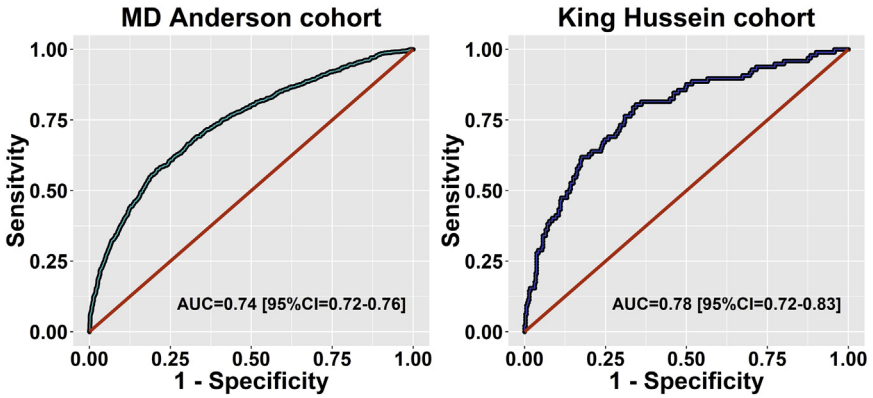

Figure 2. Receiver operating characteristic analysis. Cancer-related and clinical factors for the prediction of venous thromboembolism did not differ between the MD Anderson and King Hussein cohorts ($p = 0.164$). AUC = area under the curve; CI = confidence interval.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jemermed.2020.03.039.

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ARTICLE SUMMARY

1. Why is this topic important?

Accurate and early detection of cancer-associated venous thromboembolism including pulmonary embolisms can avoid unnecessary diagnostic imaging or laboratory tests.

2. What does this study attempt to show?

In this study, we sought to determine cancer-related risk factors of venous thromboembolism in patients with cancer that can be combined with common clinical risk factors and used as predictors for cancer-associated venous thromboembolism.

3. What are the key findings?

Cancer risk group, presentation within 6 months of cancer diagnosis, active and advanced cancer, and the presence of brain metastases along with other related clinical factors can be used to predict venous thromboembolism in cancer patients presenting to the emergency department.

4. How is patient care impacted?

Using both cancer-related and common clinical factors to predict the presence of thrombosis in patients with cancer who present with suspected venous thromboembolism can help in identifying the need for diagnostic imaging or laboratory tests and prompt accurate and early detection of these thrombotic events.