Caprini venous thromboembolism risk assessment permits selection for postdischarge prophylactic anticoagulation in patients with resectable lung cancer

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ABSTRACT

Objective: Postoperative venous thromboembolism (VTE) creates an 8-fold increase in mortality after lung resection. About one third of postoperative VTEs occur after discharge. The Caprini risk assessment model has been used by other specialties to calculate the risk of a VTE. Patients deemed high risk by the model are candidates for prophylactic anticoagulation after discharge, reducing the VTE risk by 60%. Our primary aims were to determine the frequency of VTE events and evaluate whether the Caprini model could risk-stratify patients.

Methods: Patients undergoing lung cancer resections during 2005 to 2013 were evaluated. Exclusion criteria were preoperative filter and therapeutic anticoagulation. A total of 232 patients were reviewed and Caprini scores calculated. Subjects were risk stratified into groups of low risk (0-4), moderate risk (5-8), and high risk (≥ 9). Occurrence of VTE events (deep vein thrombosis; pulmonary embolism) were identified by imaging.

Results: The 60-day VTE incidence was 5.2% (12 of 232); 33.3% occurred post-discharge ($n = 4$). Half (6 of 12) were pulmonary emboli, 1 of which caused a death, in an inpatient with a score of 16. The VTE incidence increased with Caprini score. Scores in the low, moderate, and high risk groups were associated with a VTE incidence of 0%, 1.7%, and 10.3%, respectively. With a high risk score cutoff of 9, the sensitivity, specificity, and accuracy are 83.3%, 60.5%, and 61.6%, respectively.

Conclusions: One third of VTE events occurred after discharge. Postoperative VTE incidence was correlated with increasing Caprini scores. Patients in the high risk group had an incidence of 10.3%. Elevated scores may warrant extended chemoprophylaxis for patients after discharge. (*J Thorac Cardiovasc Surg* 2016;151:37-44)

Risk category (score range)	Distribution of total cohort by risk category (n = 232)	# VTE patients (n = 12)	# no-VTE patients (n = 220)	VTE vs. no-VTE p-value	VTE incidence by risk category
Low (0-4)	16 (6.9%)	0 (0.0%)	16 (7.3%)	1.0	0.0%
Moderate (5-8)	119 (51.3%)	2 (1.7%)	117 (53.2%)	0.01	1.7%
High (9+)	97 (41.8%)	10 (10.3%)	87 (39.5%)	0.004	10.3%

Distribution of patients and overall venothromboembolism (VTE) incidence by risk category. Values are n (%), unless otherwise indicated. "VTE patients" had a VTE event; "No-VTE patients" did not have a VTE event.

Central Message

Postresection venothromboembolic events were correlated with high scores on a risk-assessment model for selecting extended prophylaxis.

Perspective

The risk of death from a postoperative VTE can reach 20% in some series of lung cancer patients. One third of the VTEs occur after discharge. Our study demonstrated the predictive ability of the Caprini risk-assessment model to allow risk stratification of patients after lung resection, for extended preventive anticoagulation after discharge in those at highest risk.

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Postoperative venous thromboembolism (VTE) after lung resection for cancer leads to a nearly 8-fold increase in mortality, higher than that reported after esophagectomy and major abdominal and pelvic operations.¹ Furthermore, as many as one third of postoperative VTE events occur after discharge, with risk persisting for >30 days.²⁻⁸ As a result, new strategies are necessary to identify patients who are at increased risk for perioperative VTE and may benefit from extended prophylaxis with agents such as low molecular weight heparin.

Abbreviations and Acronyms

CI	= confidence interval
DVT	= deep vein thrombosis
IQR	= interquartile range
LOS	= length of stay
OR	= odds ratio
PE	= pulmonary embolism
VTE	= venous thromboembolism

Multicenter trials in abdominal and pelvic cancer surgery, and within general and orthopedic surgical populations, demonstrate that extended courses of chemoprophylaxis with these heparin products, such as enoxaparin sodium, for as long as 30 postoperative days, can reduce VTE rates by as much as 60% without an increase in adverse bleeding events.^{3-5,9} Considering the costs, inconvenience, and potential side effects associated with prolonged prophylactic anticoagulation, the use of a VTE risk assessment tool might selectively apply this intervention to only those patients at high risk.

The Caprini VTE risk assessment model is an individualized risk screening tool that has been evaluated in multiple specialties, including general, vascular, and plastic surgery, as well as gynecologic oncology.^{6,10-13} The American College of Chest Physicians currently includes a modified Caprini model for VTE risk stratification among abdominal and pelvic cancer patients to identify candidates for prolonged prophylaxis although no guidelines have been developed for risk-based extended courses of chemoprophylaxis in thoracic surgery patients.¹⁴

The Caprini model is comprised of approximately 40 risk factors, including, but not limited to, duration of operation, personal or family history of VTE, body mass index ≥ 30 kg/m², and malignancy. A patient's risk factor score can be calculated throughout the hospitalization, but it is most important to determine it at the time of discharge. The total score is used to place individuals into 1 of 3 main risk categories: low (scores 0-4); moderate (5-8); and high (≥ 9). Although not yet widely adopted, a modified Caprini model is integrated into the electronic medical record at our institution, where the risk assessment protocol, in conjunction with early mobility measures, was shown to reduce postoperative VTE rates by as much as 80% for general and vascular surgical services.¹¹ With these services, moderate- and high-risk patients, respectively, are candidates for 10 and 30 days of total postoperative anticoagulant prophylaxis.

This risk assessment model has been implemented for our thoracic surgery patients only recently, and this article does not include patients managed per the model protocol. In this study, we sought to determine the 60-day incidence of postoperative VTE in patients who underwent lung cancer

resection. In addition, we calculated the Caprini scores for these patients, to determine whether the model could identify patients at high VTE risk who might benefit from an extended course of prophylaxis.

METHODS

This retrospective study was approved by the Boston University Medical Center Institutional Review Board. Patients who underwent segmentectomy, lobectomy, or pneumonectomy for lung cancers within the Division of Thoracic Surgery were identified between June 2005 and June 2013 (n = 309). Pertinent cases were selected based on current procedural terminology codes for open and minimally invasive operations, and all cases were included that matched International Classification of Diseases (9th edition) codes for non-small cell lung cancers and small cell lung cancers.

All included patients had evidence documenting at least 60-day follow-up and had received routine postoperative, prophylactic, subcutaneous, unfractionated heparin 3 times daily, and/or intermittent pneumatic compression during the hospitalization. Low molecular weight heparin was not used as inpatient prophylaxis. Patients were excluded based on presence of any of the following criteria: lost to follow-up or missing records (n = 42); deceased due to non-VTE causes before 60 days after surgery (n = 7); multiple operations after the first (n = 5); preoperative inferior vena cava filter placement (n = 6); and hospital discharge on therapeutic anticoagulation for indications not related to postoperative VTE (n = 17). A total of 232 patient records were subsequently analyzed.

The definition used for a VTE event was any pulmonary embolism (PE) or deep vein thrombosis (DVT) identified via clinical imaging studies (ie, computed tomography pulmonary angiogram or duplex ultrasound) and treated with therapeutic anticoagulation or inferior vena cava filter. Caprini risk factors were recorded based on the modified scoring system used at Boston Medical Center,¹¹ and patients were stratified into 1 of 3 risk categories: low (scores 0-4), moderate (5-8), and high (≥ 9). The last 2 categories are currently linked to recommendations for prophylaxis extending beyond discharge. Risk factors were included up until the date of a VTE (for inpatient VTE cases) or until the date of discharge (for outpatient VTE and patients without VTE). The 60-day VTE incidence was determined based on the number of identified VTEs with respect to the total included cohort.

Statistical comparison of patient samples of those who had, versus did not have, VTE was accomplished using the 2-sample *t* test, the Fisher exact test, the Wilcoxon rank sum test, and χ^2 analysis, as appropriate. Logistic regression models were used to assess the relationship between raw Caprini scores or risk categories and the probability of postoperative VTE. The following potential confounders in these models were assessed: baseline cohort characteristics, fiscal year of procedure, adherence to inpatient prophylaxis (subcutaneous, unfractionated heparin, and pneumatic compression boots). Hospital length of stay (LOS) was assessed as a potential covariate, because LOS has been associated with increased risk of VTE and has been evaluated in other risk assessment model validation studies.¹⁰ Significant confounders were included in adjusted logistic regressions. Regression models were assessed with C-statistics for test discrimination and the Hosmer-Lemeshow test for goodness of fit. Linear trends in odds ratios (ORs) were assessed using the Cochran-Mantel-Haenszel test.

Potential Caprini score thresholds were scrutinized for their predictive ability to isolate the high risk group as dichotomized variables with assessment of sensitivity, specificity, positive predictive value, negative predictive value, and C-statistics. This evaluation applied an ad hoc criterion for threshold selection (eg, matching to existing Caprini risk categories and maximization of C-statistic values), rather than an inferential one; thus, no adjustment for multiple testing was needed.

RESULTS

Incidence of Venous Thromboembolism and Hospital Length of Stay

The 60-day postoperative VTE incidence was 5.2% (12 of 232). One third of VTE events occurred after discharge, with an incidence of 1.7% within the total cohort (4 of 232). All 4 patients who had VTE after discharge (3 PE; 1 lower-extremity DVT) were symptomatic and were treated with therapeutic anticoagulation. Of the inpatient VTE events, 3 were PEs, accounting for 50% (6 of 12) of the total VTE complications. Two of the PEs affected main branch pulmonary arteries; 3 involved segmental pulmonary arteries. One patient was diagnosed at an outside hospital, with no specification of anatomic location.

All PEs were associated with clinical manifestations, ranging from shortness of breath, chest pain, and oxygen desaturation, to hypotension with the need for ventilatory support. Of the 5 patients with DVT diagnosed during the hospitalization, 1 had a presumed PE but was too clinically unstable to undergo a computed tomography pulmonary arteriogram. One patient died of a PE during the hospitalization, after a pneumonectomy.

The median time from operative day to VTE event was 10 days (14.5; interquartile range [IQR]: 4-37) (Table 1). For inpatient VTE events (n = 8), the median time to

VTE was 7 days (IQR 9, range 4-21), whereas the median time to VTE event in the outpatient VTE group (n = 4) was 20 days (IQR 13.5, range 12-37). The median LOS for VTE patients was 13.5 days (IQR 28). For inpatient events, the median LOS was 24.5 days (IQR 28, range 6-63) and for outpatient events, the median LOS was 12 days (IQR 4, range 7-15). Furthermore, the median interval between hospital discharge and VTE was 8 days in the outpatient VTE group (IQR 9.5).

The median hospital LOS in the VTE group was significantly different than in the no-VTE group ($P < .001$) (Table 2). Furthermore, a higher number of total hospital days was associated with an increased OR for VTE of 1.1 (95% confidence interval [CI] 1.05-1.18, $P < .001$). No significant differences were found between the VTE and the no-VTE groups based on gender, body mass index, histologic diagnosis, operation type, or prevalence of inpatient prophylaxis. Additionally, no significant difference was found between the number of open operations in the 2 groups, although 68.6% of no-VTE cases were open operations, versus 91.7% in the VTE group ($P = .11$).

Caprini Risk Assessment

The distributions of Caprini scores in the VTE and no-VTE groups were significantly different based on the

TABLE 1. Postoperative venous thromboembolism (VTE) cases (n = 12)

Patient #	Surgical procedure	VTE type	Time to VTE (d)	Total hospital LOS (d)	VTE symptoms	VTE location
Inpatient VTE event						
1	Open lobectomy	DVT	4	6	Swelling	Duplex ultrasound: gastrocnemius vein
2	Open pneumonectomy	PE	4	9	Hypotension; reintubation; death	Autopsy: large PE main branch PA Duplex ultrasound: common femoral, femoral, profunda femoral, and popliteal veins
3	VATS lobectomy	PE	5	32	Desaturation; reintubation	CTPA: segmental PA
4	Open lobectomy	PE	6	17	Desaturation; shortness of breath	CTPA: segmental PA
5	Open segmentectomy	DVT	8	10	Swelling	Duplex ultrasound: common femoral, superficial femoral, profunda femoral, and popliteal veins
6	Open lobectomy	DVT	8	43	Swelling	Duplex ultrasound: internal jugular and brachial veins
7	Open lobectomy	DVT	19	32	Shoulder pain	Duplex ultrasound: subclavian and axillary veins
8	Open lobectomy	DVT	21	64	Desaturation; hemodynamic instability; lower-extremity swelling	Duplex ultrasound: common femoral and internal jugular veins Echocardiogram: dilated, hypokinetic RV
Postdischarge VTE event						
9	Open lobectomy	PE	12	7	Desaturation	Unknown — outside hospital CTPA
10	Open lobectomy	PE	19	12	Chest pain	CTPA: distal main PA extending to upper and lower lobes
11	Open lobectomy	DVT	21	12	Swelling	Duplex ultrasound: common femoral vein
12	Open lobectomy	PE	37	15	Shortness of breath	CTPA: segmental PA

All patients were classified as high risk per the Caprini risk assessment, except for patients 1 and 12, who were classified as moderate risk. The time to VTE is measured from the day of surgery. The VTE diagnoses were verified through review of CTPA or duplex ultrasound results, except for patient 9, who had an outpatient VTE event at an outside hospital. For patient 8, PE was clinically suspected based on echocardiogram findings. VTE, Venous thromboembolism; LOS, length of stay; DVT, deep vein thrombosis; PE, pulmonary embolism; PA, pulmonary artery; VATS, video-assisted thoracoscopic surgery; CTPA, computed tomography pulmonary angiogram; RV, right ventricle.

TABLE 2. Baseline characteristics of lung resection cohort by VTE status

Baseline characteristic	No-VTE (n = 220)	VTE (n = 12)	P value
Age, mean (SD), (y)	64.36 (11.0)	63.83 (10.2)	.87
Gender			.1
Male	92 (41.8)	8 (66.6)	
Female	128 (58.2)	4 (33.3)	
Body mass index, mean (SD) (kg/m ²)	27.42 (7.02)	27.38 (5.05)	.98
Pathologic diagnosis			
Adenocarcinoma	120 (54.5)	7 (58.3)	1.0
Squamous cell carcinoma	58 (26.4)	4 (33.3)	.74
Small cell carcinoma	6 (2.7)	0 (0.0)	1.0
Other non–small cell carcinoma	36 (19.1)	1 (8.3)	.7
Extent of disease			
pN0	168 (76.4)	10 (83.3)	.7
pN1	30 (13.6)	1 (16.7)	1.0
pN2	18 (8.1)	0 (0.0)	.6
pM1	4 (1.8)	0 (0.0)	1.0
Procedure			
Lobectomy	186 (84.5)	10 (83.3)	.9
Pneumonectomy	16 (7.3)	1 (8.3)	1.0
Segmentectomy	18 (8.2)	1 (8.3)	1.0
Open procedure			
Thoracotomy	151 (68.6)	11 (91.7)	.11
Median length of stay (d) (IQR)	8 (6)	13.5 (22.3)	<.001
Inpatient VTE prophylaxis			
Routine pharmacologic	202 (91.8)	12 (100.0)	.61
Intermittent pneumatic compression	202 (91.8)	12 (100.0)	.61

Values are n (%), unless otherwise indicated. Other non–small cell carcinomas observed: bronchioloalveolar (no-VTE, n = 12); large cell carcinoma (no-VTE, n = 9); mixed or other (no-VTE, n = 15; VTE, n = 1). VTE, Venous thromboembolism; SD, standard deviation; IQR, interquartile range.

Wilcoxon rank sum test ($P < .001$). The net VTE incidence increased with higher Caprini scores (P for trend $< .001$). A higher Caprini score is associated with a higher OR for VTE of 1.5 (95% CI 1.19-1.78, $P < .001$). Adjusting for total LOS, a higher Caprini score is associated with an increased OR of VTE of 1.32 (95% CI 1.04-1.67, $P = .02$). C-statistics for the association between Caprini score and the probability of VTE were 0.78 and 0.84 in the unadjusted and total LOS-adjusted models, respectively, and Hosmer-Lemeshow goodness-of-fit tests were satisfied for both models (Table E1). Furthermore, a higher Caprini risk category was associated with an increased OR for

VTE of 7.02 (95% CI 1.55-31.7, $P = .01$) on univariate analysis. Adjusting for LOS, the OR for VTE is 3.86 (95% CI 0.78-19.0, $P = .01$).

Of the total cohort, 41.8% had scores in the high risk category; 51.3% had scores in the moderate risk category; and 6.9% had scores in the low risk category (Table 3). The overall VTE incidence in the high risk category was 10.3%, compared with 1.7% and 0.0% in the moderate- and low risk groups, respectively (P for trend = .004). In the VTE group, 83.3% were high risk, compared with 39.5% in the no-VTE group ($P = .004$). Of the 2 VTE cases in the moderate risk group, 1 was an inpatient with DVT identified on postoperative day 4; the other was a nonocclusive thrombus found adjacent to the lobectomy staple line, on postoperative day 37, characterized as a potential postsurgical thrombus.

Scrutinizing the high risk score cutoff of 9 (currently used at our institution on other surgery services) showed that the sensitivity was 83.3% (95% CI 58.3%-100%); specificity was 60.5% (95% CI 54.4%-67.3%); accuracy was 61.6%; and the C-statistic was 0.72. The positive predictive value was 10.3%, and the negative predictive value was 98.5%. The highest C-statistic value was 0.73, with a cutoff of 10 for the high risk group. The resultant sensitivity, with a cutoff of 10, was 75.0% (95% CI 50%-100%); specificity was 69.6% (95% CI 64.6%-76.4%); and accuracy was 69.8%. The resultant sensitivity with a cutoff of 7 to capture all events was 100.0% (95% CI 100%-100%), but the specificity was only 31.4% (95% CI 25%-37.3%), and accuracy was 34.9%. Similarly, with a score cutoff of 5, used in another published evaluation¹⁰ as “highest” risk, the sensitivity remained at 100% (95% CI 100%-100%); however, the specificity was only 7.2% (95% CI 4.1%-11.0%). The Caprini risk factors most closely associated with a VTE event in this cohort included postoperative sepsis, a history of VTE, serious acute lung disease (such as acute respiratory disease and pneumonia), as well as congestive heart failure, varicose veins, swollen legs, and central venous access (Table 4).

DISCUSSION

In this retrospective study of VTE risk stratification in lung resection for cancer, the postoperative VTE incidence was 5.2%, with one third of events occurring after discharge. This study establishes that higher Caprini risk

TABLE 3. Distribution of patients and VTE incidence by risk category

Risk category (score range)	Distribution of total cohort by risk category, n = 232	VTE patients by risk category, n = 12	No-VTE patients by risk category, n = 220	VTE vs no-VTE P value
Low (0-4)	16 (6.9)	0 (0.0)	16 (100.0)	1.0
Moderate (5-8)	119 (51.3)	2 (1.7)	117 (98.3)	.01
High (≥ 9)	97 (41.8)	10 (10.3)	87 (89.7)	.004

Values are n (%), unless otherwise indicated. “VTE patients” had a VTE event; “No-VTE patients” did not have a VTE event. VTE, Venous thromboembolism.

TABLE 4. Prevalence of Caprini risk factors by VTE status

Caprini risk factor	Caprini score	No-VTE (n = 220)	VTE (n = 12)	Fisher P value	Logistic P value
Age 40-59 (y)	1	66 (30.0)	2 (16.7)	.52	.33
Abnormal pulmonary function	1	107 (48.6)	6 (50)	1.0	.93
Acute myocardial infarction (<1 mo)	1	1 (0.5)	0	1.0	1.0
Body mass index ≥30 (kg/m ²)	1	64 (29.1)	4 (33.3)	.75	.75
Congestive heart failure (<1 mo)	1	3 (1.4)	2 (16.7)	.02	.005
History of inflammatory bowel disease	1	1 (0.5)	0	1.0	1.0
History of prior major surgery (<1 mo)	1	8 (3.6)	0	1.0	1.0
Complications of pregnancy*	1	1 (0.5)	0	1.0	1.0
Oral contraceptive use or HRT	1	6 (2.7)	0	1.0	1.0
Sepsis (<1 mo)	1	2 (0.9)	3 (25)	.001	<.001
Serious acute lung disease (<1 mo)	1	33 (15.0)	5 (41.7)	.03	.02
Swollen legs (current)	1	13 (5.9)	3 (25.0)	.04	.02
Varicose veins	1	23 (10.5)	4 (33.3)	.04	.03
Age 60-74 (y)	2	109 (49.5)	8 (58.3)	.37	.3
Central venous access	2	61 (27.8)	7 (58.3)	.04	.03
Confined to bed (>72 h)	2	22 (10.0)	2 (16.7)	.36	.5
Major open surgery (≥45 min)	2	151 (68.6)	11 (91.7)	.11	.13
Present cancer	2	220 (100)	12 (100)	1.0	1.0
Prior cancer, except nonmelanoma skin	2	50 (22.7)	3 (25)	1.0	.86
Age ≥75 (y)	3	41 (18.6)	2 (16.7)	1.0	.86
History of VTE	3	3 (1.4)	3 (25)	.002	<.001
Family history of VTE	3	3 (1.4)	1 (8.3)	.2	.12
Chemotherapy	3	27 (12.3)	2 (16.7)	.65	.66
Positive anticardiolipin antibody	3	1 (0.5)	0	1.0	1.0
Positive Lupus anticoagulant	3	1 (0.5)	0	1.0	1.0
Acute spinal cord injury (<1 mo)	5	1 (0.5)	0	1.0	1.0
Major surgery ≥6 h	5	1 (0.5)	1 (8.3)	.1	.04

Values are n (%), unless otherwise indicated. VTE, Venous thromboembolism; HRT, hormone replacement therapy. *History of unexplained stillborn infant, recurrent or spontaneous abortion (>3), premature birth with toxemia of pregnancy, or growth-restricted infant.

assessment model scores are correlated with an increased likelihood of VTE events, with an overall VTE incidence of 10.3% in the high risk group. The accurate identification of patients at risk for VTE, as well as the safety of prolonged prophylaxis and prevention of adverse bleeding events, both important aspects of this VTE prevention protocol. Thus, the current institutional high risk score cutoff of 9 seems to be adequate based on sensitivity and specificity for further validation in lung resection patients. In contrast, the score cutoff of 5, used in prior validation studies,^{10,12} resulted in an unacceptably low specificity in this study.

The high risk score cutoff of 9 was associated with a negative predictive value of 98.5%; thus, VTE risk stratification could potentially spare approximately 60% of postoperative lung resection patients from the potential side effects and costs associated with 30-day prophylaxis, tailoring this intervention to those who will likely benefit most. Additionally, the reported reduction in postoperative VTE, by 55%-60% with extended course low molecular weight heparin anticoagulant prophylaxis could result in a significant decrease in health care costs associated with the diagnosis and treatment of VTE complications, which can range from approximately \$11,000-\$17,000 per event,

with an additional 5%-14% risk of readmission for VTE recurrence.^{3,4,15}

Successful implementation of the Caprini risk assessment model, with associated prophylaxis recommendations, has already been demonstrated among general and vascular surgery patients at our institution, with high rates of provider adherence.¹¹ The model checklist is integrated into our electronic medical record system, and a patient's risk score is calculated by the care team before and after surgery, and modified as risk factors are acquired during the hospitalization. Risk score calculation is most crucial at the time of discharge, when decisions are made about extended courses of prophylaxis.

The American Society of Clinical Oncology, the European Society for Medical Oncology, and other groups currently recommend consideration of 7 to 10 days of total postoperative prophylaxis for cancer surgery patients.^{16,17} This recommendation is currently applied to moderate-risk patients receiving our general and vascular surgical services, based on Caprini score, with postdischarge anticoagulation prescribed to satisfy the prophylaxis duration. In our lung cancer surgical cohort, we identified a VTE incidence of 1.7% in the moderate risk group, which

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FIGURE 1. Proposed clinical application of the Caprini venous thromboembolism risk assessment model throughout the preoperative, postoperative, and hospital discharge phases for lung resection patients. DVT, Deep vein thrombosis; IVC, interior vena cava; VTE, venous thromboembolism; LMWH, low molecular weight heparin. *Integration into the electronic medical record recommended for access throughout perioperative period. †Enoxaparin 40mg daily or weight-based dosing. Assess bleeding risks prior to prescribing extended course anticoagulation. ‡Anticoagulation duration per ASCO recommendations¹⁵.

included an early inpatient DVT, and a late identification of a nonocclusive pulmonary arterial thrombus near the surgical staple line, which may have been an acute PE or a post-surgical clot. The current American College of Chest Physicians guidelines report that those at “low risk” for VTE have a postoperative rate of approximately 1.5%; they do not recommend anticoagulant prophylaxis for this risk group.¹⁴ Thus, the clinical impact of prescribing additional postdischarge prophylactic anticoagulation, in lung resection patients who are not considered high risk by Caprini score, is unclear and may benefit from prospective evaluation.

Longer hospitalizations have been shown to confer a 3.4- to 11.16-fold increased odds of VTE, compared with shorter (<1 week) hospitalizations.¹⁸ However, we found that 50% of VTE cases in our lung cancer resection cohort occurred ≤ 8 days postoperatively, which is the median total LOS in the no-VTE group. A prolonged median LOS was identified in this study, even in the no-VTE cohort. These findings likely reflect the characteristics and challenges faced by the patient population treated at our large safety net hospital. Delays in hospital discharge after surgery at safety-net hospitals are correlated with increased patient comorbidities and inadequate access to appropriate acute care facilities after hospital discharge.¹⁹ Nonetheless, most VTE patients had Caprini scores that put them in the high risk category, regardless of the interval between surgery and the VTE event; such categorization is supported by the observation that contributing Caprini risk factors were comprised largely of pertinent medical history (age, body mass index, cancer), and that acquired risk factors seemed to occur relatively early during the postoperative period.

This study demonstrated that symptomatic postoperative VTE events in lung resection patients were detected during hospitalization, despite inpatient prophylaxis. Three early postoperative PEs, resulting in 1 mortality

and 1 prolonged intubation for ventilatory support complicated by pneumonia, were associated with high risk Caprini scores (patients 2-4). In ambulatory lung cancer patients, VTE rates as high as 15% have been reported²⁰; thus, preoperative targeted duplex screening ultrasound in the high risk cohort, particularly when significant risk factors such as history of VTE are present, may permit early identification of occult DVT before symptoms are manifested.

Duplex ultrasound screening in asymptomatic patients has been associated with sensitivity and specificity of 61%-92%, and 97%, respectively.²¹ However, the accuracy of ultrasound screening in a risk-stratified cancer patient population has not been well studied. Lung resection patients who become high risk postoperatively, as a result of significant acquired risk factors such as sepsis and pneumonia, as well as high risk patients with an initial negative preoperative study or identified calf vein thrombosis, may benefit from 1 postoperative ultrasound when therapeutic anticoagulation indicated by test results could be initiated safely.²²

Clearly, targeted screening ultrasound in high risk lung resection patients requires prospective evaluation, and a proactive approach to occult VTE identification (Figure 1), throughout the perioperative period, may prove critical in preventing symptomatic VTE, particularly in pneumonectomy patients and other surgical patients who have borderline postoperative pulmonary reserve. Efforts may be conducted to minimize acquired Caprini VTE risk factors by removing unnecessary central vein catheters and ensuring early postoperative mobility. Additionally, elevated body mass index is a VTE risk factor, and evidence suggests that weight-based enoxaparin sodium therapy has improved efficacy compared with standard prophylactic doses, particularly in obese patients.^{9,23} Thus, the risk assessment model may be useful in identifying candidates for enhanced prophylaxis, both

during hospitalization and in high risk patients after discharge.

Reduction of VTE risk using the risk assessment model protocol may be improved with direct oral anticoagulants, such as rivaroxaban and argatroban. Rivaroxaban was approved by the US Food and Drug Administration in 2011, for postoperative VTE prevention in hip- and knee-replacement surgery, but its use is not well established among nonorthopedic patients.²⁴ The Regulation of Coagulation in Orthopedic Surgery to Prevent Deep Venous Thrombosis and Pulmonary Embolism 1, 2, and 3 randomized, double-blind, multicenter trials included a total of 9581 total hip and knee arthroplasty patients. The trials directly compared either enoxaparin sodium (a 40-mg daily injection) or rivaroxaban (10 mg daily) for ≤ 35 days (trials 1 and 2).^{25,26}

These studies demonstrated a relative risk reduction of as much as 88% for major VTE (including proximal DVT, nonfatal PE, and death from VTE) in favor of rivaroxaban. Although the difference was not statistically significant, the rate of bleeding with rivaroxaban was higher than it was with enoxaparin sodium in these trials; thus, it may be a caveat to the use of these oral agents, particularly in patients with renal impairment. Post hoc analyses of trials 1-3, just mentioned, report an overall more favorable risk-benefit outcome with rivaroxaban, compared with enoxaparin sodium, including a cost savings of $> \$500$ per patient.^{27,28}

Limitations of this analysis include the fact that the data collection was retrospective, leading to reliance on documentation and imaging studies to confirm VTEs, complex disease states such as sepsis, and inpatient prophylaxis. Total hospital LOS was assessed as a covariate in logistic regression models because LOS was significantly associated with the probability of VTE. However, usage of LOS as a covariate is limited, because some VTE events occurred prior to hospital discharge, and other postoperative factors may have contributed to total LOS. In addition, the study is limited by sample size and the small number of VTE cases for comparison. Furthermore, given that most cases were lobar resections, findings may not necessarily be extrapolated to sublobar resections or pneumonectomy patients. A few cases were excluded; thus, the VTE risks among patients undergoing resection of lung cancers may have been overestimated in this cohort.

This study is the first to demonstrate the ability of the Caprini risk assessment model to predict VTE in patients after resections of lung cancers. Integration of Caprini risk screening throughout the course of care has the potential to identify patients at greatest risk of developing VTE and can be linked to anticoagulation prophylaxis recommendations, which we are currently evaluating in a prospective quality-improvement study.

Conflict of Interest Statement

Dr Fernando reports consulting fees for CSA Medical and Galil Medical. All other authors have nothing to disclose with regard to commercial support.

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Key Words: lung cancer, postoperative care, embolism (venous)

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TABLE E1. Logistic regression models for Caprini score and Caprini risk category versus probability of VTE

Measure	Caprini score vs probability of VTE		Risk category vs probability of VTE	
	Univariate	Multivariate	Univariate	Multivariate
Caprini score	1.46 (1.19-1.78) <i>P</i> < .001	1.32 (1.04-1.67) <i>P</i> = .02	—	—
Risk category	—	—	7.02 (1.55-31.7) <i>P</i> = .01	3.86 (0.78-19.0) <i>P</i> = .1
Total LOS	—	1.08 (1.02-1.15) <i>P</i> = .01	—	1.09 (1.03-1.15) <i>P</i> = .002
C-statistic	0.78	0.84	0.73	0.82
Hosmer-Lemeshow*				
χ^2 /df	6.33/8	5.39/8	0.04/1	4.85/8
<i>P</i> value	.61	.72	.84	.77

Values in first 3 rows are OR (95% CI). Columns represent individual univariate or multivariate logistic regression models. *VTE*, Venous thromboembolism; *LOS*, length of stay; *df*, degrees of freedom. *Goodness-of-fit performance data, with specific covariates.

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