

Risk Factor Model to Predict Venous Thromboembolism in Hospitalized Medical Patients

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BACKGROUND: The Joint Commission requires that all medical inpatients be assessed for venous thromboembolism (VTE) risk, but available risk stratification tools have never been validated.

METHODS: We conducted a retrospective cohort study of patients age ≥ 18 years, admitted to 374 US hospitals in 2004–2005, with a primary diagnosis of pneumonia, heart failure, chronic obstructive pulmonary disease (COPD), stroke, and urinary tract infection, and length of stay ≥ 3 days. Subjects were randomly assigned (80/20) to a derivation or validation set. We then assessed VTE (International Classification of Diseases, Ninth Revision [ICD-9] code plus diagnostic test plus treatment), patient demographics, 21 potential risk factors, and other comorbidities. We created a VTE risk stratification tool using multivariable regression modeling and applied it to the validation sample.

RESULTS: Of 242,738 patients, 612 (0.25%) patients fulfilled our criteria for VTE during hospitalization, and an additional 440 (0.18%) were readmitted for VTE within 30 days (overall incidence of 0.43%). In the multivariable model, age, sex, and 10 additional risk factors were associated with VTE. The strongest risk factors were inherited thrombophilia (OR 4.00), length of stay ≥ 6 days (OR 3.22), inflammatory bowel disease (OR 3.11), central venous catheter (OR 1.87), and cancer. In the validation set, the model had a c-statistic of 0.75 (95% CI 0.71, 0.78). Deciles of predicted risk ranged from 0.11% to 1.46% with observed risk over the same deciles from 0.17% to 1.81%.

CONCLUSIONS: The risk of symptomatic VTE in general medical patients is low. A risk factor model can identify those at sufficient risk to warrant pharmacologic prophylaxis. *Journal of Hospital Medicine* 2011;6:202–209. © 2011 Society of Hospital Medicine

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Venous thromboembolism (VTE) is a major source of morbidity and mortality for hospitalized patients. Among medical patients at the highest risk, as many as 15% can be expected to develop a VTE during their hospital stay^{1,2}; however, among general medical patients, the incidence of symptomatic VTE is less than 1%,¹ and potentially as low as 0.3%.³ Thromboprophylaxis with subcutaneous heparin reduces the risk of VTE by approximately 50%,⁴ and is therefore recommended for medical patients at high risk. However, heparin also increases the risk of bleeding and thrombocytopenia and thus should be avoided for patients at low risk of VTE. Consequently, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) recommends that all hospitalized medical patients receive a risk assessment for VTE.⁵

Certain disease states, including stroke, acute myocardial infarction, heart failure, respiratory disease, sepsis,

and cancer, have been associated with increased risk for VTE, and, based on the inclusion criteria of several randomized trials, current American College of Chest Physicians (ACCP) guidelines recommend thromboprophylaxis for patients hospitalized with these diagnoses.² However, evidence that these factors actually increase a patient's risk for VTE comes from studies of ambulatory patients and is often weak or conflicting. Existing risk-stratification tools,^{6,7} as well as the ACCP guidelines, have not been validated, and accordingly JCAHO does not specify how risk assessment should be conducted. In order to help clinicians better estimate the risk of VTE in medical patients and therefore to provide more targeted thromboprophylaxis, we examined a large cohort of patients with high-risk diagnoses and created a risk stratification model.

Methods

Setting and Patients

We identified a retrospective cohort of patients discharged between January 1, 2004 and June 30, 2005 from 374 acute care facilities in the US that participated in Premier's Perspective, a database developed for measuring quality and healthcare utilization. Participating hospitals represent all regions of the US, and are generally similar in composition to US hospitals; however, in comparison to information contained in the American Hospital Association annual survey, Perspective hospitals are more likely to be located in the South and in urban areas. Available data elements include those derived from the uniform billing 04 form, such as sociodemographic information about each patient, their International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, as well as hospital and physician information. This information is supplemented with a date-stamped log of all items and services billed to the patient or insurer, including diagnostic tests, medications, and other treatments. Permission to conduct the study was obtained from the Institutional Review Board at Baystate Medical Center.

We included all patients age ≥ 18 years at moderate-to-high risk of VTE according to the ACCP recommendations,⁸ based on a principal diagnosis of pneumonia, septicemia or respiratory failure with pneumonia, heart failure, chronic obstructive pulmonary disease (COPD), stroke, and urinary tract infection. Diagnoses were assessed using ICD-9-CM codes. Patients who were prescribed warfarin or therapeutic doses of heparin on hospital day 1 or 2, and those who received >1 therapeutic dose of heparin but otherwise did not fulfill criteria for VTE, were excluded because we could not evaluate whether they experienced a VTE event during hospitalization. We also excluded patients whose length of stay was <3 days, because our definition of hospital-acquired VTE required treatment begun on day 3 or later, and those with an indication for anticoagulation other than VTE (eg, prosthetic cardiac valve or atrial fibrillation), because we could not reliably distinguish treatment for VTE from treatment of the underlying condition.

Risk Factors

For each patient, we extracted age, gender, race/ethnicity, and insurance status, principal diagnosis, comorbidities, and specialty of the attending physician. Comorbidities were identified from ICD-9-CM secondary diagnosis codes and Diagnosis Related Groups using Healthcare Cost and Utilization Project Comorbidity Software, version 3.1, based on the work of Elixhauser et al.⁹ We also assessed risk factors which have been previously linked to VTE: paralysis, cancer (metastatic, solid tumor, and lymphoma), chemotherapy/radiation, prior VTE, use of estrogens and estrogen modulators, inflammatory bowel disease, nephrotic syndrome, myeloproliferative disorders, obesity, smoking, cen-

tral venous catheter, inherited or acquired thrombophilia, steroid use, mechanical ventilation, urinary catheter, decubitus ulcer, HMGco-A reductase inhibitors, restraints, diabetes, varicose veins, and length-of-stay ≥ 6 days. These additional comorbidities were defined based on the presence of specific ICD-9 codes, while use of HMG-co-A reductase inhibitors were identified from medication charge files. We also noted whether patients received anticoagulants, the dosages and days of administration, as well as intermittent pneumatic compression devices.

Identification of VTE

Because the presence of a secondary diagnosis of VTE in medical patients is not a reliable way of differentiating hospital-acquired VTE from those present at the time of admission,¹⁰ subjects were considered to have experienced a hospital-acquired VTE only if they underwent a diagnostic test for VTE (lower extremity ultrasound, venography, CT angiogram, ventilation-perfusion scan, or pulmonary angiogram) on hospital day 3 or later, received treatment for VTE for at least 50% of the remaining hospital stay, or until initiation of warfarin or appearance of a complication (eg, transfusion or treatment for heparin-induced thrombocytopenia) and were given a secondary diagnosis of VTE (ICD-9 diagnoses 453.4, 453.40, 453.41, 453.42, 453.8, 453.9, 415.1, 415.11, 415.19). We considered the following to be treatments for VTE: intravenous unfractionated heparin, >60 mg of enoxaparin, ≥ 7500 mg of dalteparin, or placement of an inferior vena cava filter. In addition, patients who were readmitted within 30 days of discharge with a primary diagnosis of VTE were also considered to have developed a VTE as a complication of their previous hospital stay.

Statistical Analysis

Univariate predictors of VTE were assessed using chi-square tests. We developed a multivariable logistic regression model for VTE on an 80% randomly selected subset of the eligible admissions (the derivation cohort) using all measured risk factors for VTE and selected interaction terms. Generalized estimating equations (GEE) models with a logit link (SAS PROC GENMOD) were used to account for the clustering of patients within hospitals. Initial models were stratified on VTE prophylaxis. Factors significant at $P < 0.05$ were retained. Parameter estimates derived from the model were used to compute individual VTE risk in the remaining 20% of the admissions (the validation cohort). Discrimination in the validation model was assessed by the c-statistic, as well as the expected/observed ratio. Both cohorts were categorized by decile of risk, based on the probability distribution in the derivation cohort, and observed VTE events compared to those predicted by the model. All analyses were performed using the Statistical Analysis System (version 9.1, SAS Institute, Inc., Cary, NC).

Role of the Funding Source

This study was supported by a Clinical Scientist Development Award from the Doris Duke Charitable Foundation. The funding source had no role in the study design, analysis, or interpretation of the data.

Results

Our sample contained 242,738 patients, 194,198 (80%) assigned to the derivation set and 48,540 (20%) to the validation set. Patient characteristics were similar in both sets (Supporting Information Appendix Table 1). Most patients were over age 65, 59% were female, and 64% were white (Table 1). The most common primary diagnoses were pneumonia (33%) and congestive heart failure (19%). The most common comorbidities were hypertension (50%), diabetes (31%), chronic pulmonary disease (30%), and anemia (20%). Most patients were cared for by internists (54%) or family practitioners (21%), and 30% received some form of anticoagulant VTE prophylaxis (Table 2). Of patients with an ICD-9 code for VTE during hospitalization, just over half lacked either diagnostic testing, treatment, or both, leaving 612 (0.25%) patients who fulfilled our criteria for VTE; an additional 440 (0.18%) were readmitted for VTE, for an overall incidence of 0.43%. Patients with a length of stay ≥ 6 days had an incidence of 0.79% vs 0.19% for patients with shorter stays.

Risk factors for VTE

A large number of patient and hospital factors were associated with the development of VTE (Table 1). Due to the large sample size, even weak associations appear highly statistically significant. Compared to patients without VTE, those with VTE were more likely to have received VTE prophylaxis (37% vs 30%, $P < 0.001$). However, models of patients receiving prophylaxis and of patients not receiving prophylaxis produced similar odds ratios for the various risk factors (Supporting Information Appendix Table 2); therefore, the final model includes both patients who did, and did not, receive VTE prophylaxis. In the multivariable model (Supporting Information Appendix Table 3), age, length of stay, gender, primary diagnosis, cancer, inflammatory bowel disease, obesity, central venous catheter, inherited thrombophilia, steroid use, mechanical ventilation, active chemotherapy, and urinary catheters were all associated with VTE (Table 3). The strongest risk factors were length of stay ≥ 6 days (OR 3.22, 95% CI 2.73, 3.79), central venous catheter (OR 1.87, 95% CI 1.52, 2.29), inflammatory bowel disease (OR 3.11, 95% CI 1.59, 6.08), and inherited thrombophilia (OR 4.00, 95% CI 0.98, 16.40). In addition, there were important interactions between age and cancer; cancer was a strong risk factor among younger patients, but is not as strong a risk factor among older patients (OR compared to young patients without cancer was 4.62 (95% CI 2.72, 7.87) for those age 18–49 years, and 3.64 (95% CI 2.52, 5.25) for those aged 50–64 years).

In the derivation set, the multivariable model produced deciles of mean predicted risk from 0.11% to 1.45%, while

mean observed risk over the same deciles ranged from 0.12% to 1.42% (Figure 1). Within the validation cohort, the observed rate of VTE was 0.46% (223 cases among 48,543 subjects). The expected rate according to the model was 0.43% (expected/observed ratio: 0.93 [95% CI 0.82, 1.06]). Model discrimination measured by the c-statistic in the validation set was 0.75 (95% CI 0.71, 0.78). The model produced deciles of mean predicted risk from 0.11% to 1.46%, with mean observed risk over the same deciles from 0.17% to 1.81%. Risk gradient was relatively flat across the first 6 deciles, began to rise at the seventh decile, and rose sharply in the highest one. Using a risk threshold of 1%, the model had a sensitivity of 28% and a specificity of 93%. In the validation set, this translated into a positive predictive value of 2.2% and a negative predictive value of 99.7%. Assuming that VTE prophylaxis has an efficacy of 50%, the number-needed-to-treat to prevent one VTE among high-risk patients (predicted risk $> 1\%$) would be 91. In contrast, providing prophylaxis to the entire validation sample would result in a number-needed-to-treat of 435. Using a lower treatment threshold of 0.4% produced a positive predictive value of 1% and a negative predictive value of 99.8%. At this threshold, the model would detect 73% of patients with VTE and the number-needed-to-treat to prevent one VTE would be 200.

Discussion

In a representative sample of 243,000 hospitalized medical patients with at least one major risk factor for VTE, we found that symptomatic VTE was an uncommon event, occurring in approximately 1 in 231 patients. We identified a number of factors that were associated with an increased risk of VTE, but many previously cited risk factors did not show an association in multivariable models. In particular, patients with a primary diagnosis of COPD appeared not to share the same high risk of VTE as patients with the other diagnoses we examined, a finding reported by others.¹¹ The risk model we developed accurately stratifies patients across a wide range of VTE probabilities, but even among those with the highest predicted rates, symptomatic VTE occurred in less than 2%.

VTE is often described as a frequent complication of hospitalization for medical illness and one of the most common potentially preventable causes of death. Indeed, rates of asymptomatic VTE have been demonstrated to be 3.7% to 26%.¹² Although some of these might have fatal consequences, most are distal vein thromboses and their significance is unknown. In contrast, symptomatic events are uncommon, with previous estimates among general medical patients in observational studies in the range of 0.3%³ to 0.8%,¹² similar to the rate observed in our study. Symptomatic event rates among control patients in landmark randomized trials have ranged from 0.86%¹³ to 2.3%,¹⁴ but these studies enrolled only very high-risk patients with more extended hospitalizations, and may involve follow-up periods of a month or more.

TABLE 1. Patient Characteristics and Their Association With Venous Thromboembolism (VTE)

Variable	Total		No VTE		VTE		P-Value
	N	%	N	%	N	%	
Total	242,738	100	241,686	100.0	1,052	100.0	
Demographics							
Age							0.20
18-49	31,065	12.8	30,952	12.8	113	10.7	
50-64	51,309	21.1	51,083	21.1	226	21.5	
65-74	51,230	21.1	50,993	21.1	237	22.5	
75+	109,134	45.0	108,658	45.0	476	45.2	
Female	142,910	58.9	142,330	58.9	580	55.1	0.01
Race/ethnicity							0.49
White	155,866	64.2	155,189	64.2	677	64.4	
Black	41,556	17.1	41,374	17.1	182	17.3	
Hispanic	9,809	4.0	9,776	4.0	33	3.1	
Other	35,507	14.6	35,347	14.6	160	15.2	
Marital status							0.28
Married/life partner	88,035	36.3	87,627	36.3	408	38.8	
Single	39,254	16.2	39,103	16.2	151	14.4	
Separated/divorced	23,492	9.7	23,394	9.7	98	9.3	
Widowed	58,669	24.2	58,426	24.2	243	23.1	
Other	33,288	13.7	33,136	13.7	152	14.4	
Admission characteristics							
Primary diagnosis							<0.001
Community-acquired pneumonia	81,171	33.4	80,792	33.4	379	36.0	
Septicemia	7,643	3.2	7,568	3.1	75	7.1	
Chronic obstructive pulmonary disease	35,116	14.5	35,027	14.5	89	8.5	
Respiratory failure	7,098	2.9	7,012	2.9	86	8.2	
Congestive heart failure	46,503	19.2	46,336	19.2	167	15.9	
Cardiovascular disease	33,044	13.6	32,931	13.6	113	10.7	
Urinary tract infection	32,163	13.3	32,020	13.2	143	13.6	
Insurance payer							0.93
Medicare traditional	157,609	64.9	156,927	64.9	682	64.8	
Medicare managed care	10,649	4.4	10,597	4.4	52	4.9	
Medicaid	17,796	7.3	17,720	7.3	76	7.2	
Private	44,858	18.5	44,665	18.5	193	18.3	
Self-pay/uninsured/other	11,826	4.9	11,777	4.9	49	4.7	
Admitted from skilled nursing facility	3,003	1.2	2,980	1.2	23	2.2	0.005
Risk factors							
Any VTE prophylaxis	72,558	29.9	72,164	29.9	394	37.5	<0.001
Length of stay \geq 6 days	99,463	41.0	98,680	40.8	783	74.4	<0.001
Paralysis	16,764	6.9	16,689	6.9	75	7.1	0.77
Metastatic cancer	5,013	2.1	4,928	2.0	85	8.1	<0.001
Solid tumor without metastasis	25,127	10.4	24,995	10.3	132	12.5	0.02
Lymphoma	3,026	1.2	2,995	1.2	31	2.9	<0.001
Cancer chemotherapy/radiation	1,254	0.5	1,231	0.5	23	2.2	<0.001
Prior venous thromboembolism	2,945	1.2	2,926	1.2	19	1.8	0.08
Estrogens	4,819	2.0	4,807	2.0	12	1.1	0.05
Estrogen modulators	2,102	0.9	2,091	0.9	11	1.0	0.53
Inflammatory bowel disease	814	0.3	803	0.3	11	1.0	<0.001
Nephrotic syndrome	520	0.2	517	0.2	3	0.3	0.62
Myeloproliferative disorder	1,983	0.8	1,973	0.8	10	1.0	0.63
Obesity	16,938	7.0	16,856	7.0	82	7.8	0.30
Smoking	35,386	14.6	35,284	14.6	102	9.7	<0.001
Central venous catheter	14,754	6.1	14,525	6.0	229	21.8	<0.001
Inherited or acquired thrombophilia	114	0.1	108	0.0	6	0.6	<0.001
Steroids	82,606	34.0	82,185	34.0	421	40.0	<0.001
Mechanical ventilation	13,347	5.5	13,167	5.4	180	17.1	<0.001
Urinary catheter	39,080	16.1	38,816	16.1	264	25.1	<0.001
Decubitus ulcer	6,829	2.8	6,776	2.8	53	5.0	<0.001
Statins use	57,282	23.6	57,068	23.6	214	20.3	0.01

TABLE 1. (Continued)

Variable	Total		No VTE		VTE		P-Value
	N	%	N	%	N	%	
Use of restraints	5,970	2.5	5,914	2.4	56	5.3	<0.001
Diabetes mellitus	75,103	30.9	74,799	30.9	304	28.9	0.15
Varicose veins	166	0.1	165	0.1	1	0.1	0.74
Comorbidities							
Hypertension	120,606	49.7	120,126	49.7	480	45.6	0.008
Congestive heart failure	18,900	7.8	18,793	7.8	107	10.2	0.004
Peripheral vascular disease	16,705	6.9	16,639	6.9	66	6.3	0.43
Valvular disease	13,683	5.6	13,628	5.6	55	5.2	0.56
Pulmonary circulation disease	5,530	2.3	5,492	2.3	38	3.6	0.004
Chronic pulmonary disease	72,028	29.7	71,698	29.7	330	31.4	0.23
Respiratory failure second diagnosis	13,027	5.4	12,893	5.3	134	12.7	<0.001
Rheumatoid arthritis/collagen vascular disease	7,090	2.9	7,050	2.9	40	3.8	0.09
Deficiency anemias	49,605	20.4	49,352	20.4	253	24.0	0.004
Weight loss	8,810	3.6	8,714	3.6	96	9.1	<0.001
Peptic ulcer disease × bleeding	4,736	2.0	4,723	2.0	13	1.2	0.09
Chronic blood loss anemia	2,354	1.0	2,338	1.0	16	1.5	0.07
Hypothyroidism	28,773	11.9	28,668	11.9	105	10.0	0.06
Renal failure	19,768	8.1	19,669	8.1	99	9.4	0.13
Liver disease	4,682	1.9	4,657	1.9	25	2.4	0.29
Other neurological disorders	33,094	13.6	32,905	13.6	189	18.0	<0.001
Psychoses	9,330	3.8	9,283	3.8	47	4.5	0.29
Depression	25,561	10.5	25,442	10.5	119	11.3	0.41
Alcohol abuse	7,756	3.2	7,727	3.2	29	2.8	0.42
Drug abuse	4,336	1.8	4,318	1.8	18	1.7	0.85
Acquired immune deficiency syndrome	1,048	0.4	1,045	0.4	3	0.3	0.47

TABLE 2. Venous Thromboembolism (VTE) Prophylaxis and Outcomes

Variable	Total		Derivation		Validation		P-Value
	N	%	N	%	N	%	
Total	242,738	100	194,198	100	48,540	100	
VTE prophylaxis							0.97
No prophylaxis	170,180	70.1	136,153	70.1	34,027	70.1	
Any prophylaxis	72,558	29.9	58,045	29.9	14,513	29.9	
Outcomes							
ICD-9 code for VTE	1,304	0.5	1,025	0.5	279	0.6	0.21
ICD-9 code + diagnostic test	989	0.4	777	0.4	212	0.4	0.26
ICD-9 code + diagnostic test + treatment for VTE	612	0.3	471	0.2	141	0.3	0.06
Readmission for VTE within 30 days	446	0.2	363	0.2	83	0.2	0.46
Total hospital-acquired VTE	1,052	0.4	829	0.4	223	0.5	0.33
In-hospital mortality	8,019	3.3	6,403	3.3	1,616	3.3	0.72
Any readmission within 30 days	28,664	11.8	22,885	11.8	5,779	11.9	0.46

Abbreviation: ICD-9, International Classification of Diseases, Ninth Revision.

Because it is unlikely that our diagnostic algorithm was 100% sensitive, and because 30% of our patients received chemoprophylaxis, it is probable that we have underestimated the true rate of VTE in our sample. Among the patients who received prophylaxis, the observed rate of VTE was 0.54%. If we assume that prophylaxis is 50% effective, then had these patients not received prophylaxis, their rate of VTE would have been 1.08% (vs 0.39% among those

patients who received no prophylaxis) and the overall rate of VTE for the sample would have been 0.60% ($1.08 \times 0.30 + 0.39 \times 0.70$). If we further assume that our algorithm was only 80% sensitive and 100% specific, the true underlying rate of symptomatic VTE could have been as high as 0.75%, still less than half that seen in randomized trials.

Prophylaxis with heparin has been shown to decrease the rate of both asymptomatic and symptomatic events, but

TABLE 3. Factors Associated Venous Thromboembolism (VTE) in Multivariable Model

Risk Factor	OR	95% CI
Any prophylaxis	0.98	(0.84, 1.14)
Female	0.85	(0.74, 0.98)
Length of stay ≥ 6 days	3.22	(2.73, 3.79)
Age*		
18-49 years	1	Referent
50-64 years	1.15	(0.86, 1.56)
>65 years	1.51	(1.17, 1.96)
Primary diagnosis		
Pneumonia	1	Referent
Chronic obstructive pulmonary disease	0.57	(0.44, 0.75)
Stroke	0.84	(0.66, 1.08)
Congestive heart failure	0.86	(0.70, 1.06)
Urinary tract infection	1.19	(0.95, 1.50)
Respiratory failure	1.15	(0.85, 1.55)
Septicemia	1.11	(0.82, 1.50)
Comorbidities		
Inflammatory bowel disease	3.11	(1.59, 6.08)
Obesity	1.28	(0.99, 1.66)
Inherited thrombophilia	4.00	(0.98, 16.40)
Cancer†		
18-49 years	4.62	(2.72, 7.87)
50-64 years	3.64	(2.52, 5.25)
>65 years	2.17	(1.61, 2.92)
Treatments		
Central venous catheter	1.87	(1.52, 2.29)
Mechanical ventilation	1.61	(1.27, 2.05)
Urinary catheter	1.17	(0.99, 1.38)
Chemotherapy	1.71	(1.03, 2.83)
Steroids	1.22	(1.04, 1.43)

*For patients without cancer.

† Comparison group is patients aged 18-49 years without cancer.

because of the low prevalence, the number-needed-to-treat to prevent one symptomatic pulmonary embolism has been estimated at 345, and prophylaxis has not been shown to affect all-cause mortality.^{4,15} At the same time, prophylaxis costs money, is uncomfortable, and carries a small risk of bleeding and heparin-induced thrombocytopenia. Given the generally low incidence of symptomatic VTE, it therefore makes sense to reserve prophylaxis for patients at higher risk of thromboembolism.

To decide whether prophylaxis is appropriate for a given patient, it is necessary to quantify the patient's risk and then apply an appropriate threshold for treatment. The National Quality Forum (NQF) recommends,¹⁶ and JCAHO has adopted, that a clinician must "evaluate each patient upon admission, and regularly thereafter, for the risk of developing DVT [deep vein thrombosis]/VTE." Until now, however, there has been no widely accepted, validated method to risk stratify medical patients. The ACCP recommendations cite just three studies of VTE risk factors in hospitalized medical patients.^{11,17,18} Together they examined 477 cases and 1197 controls, identifying congestive heart failure, pneumonia, cancer, and previous VTE as risk factors.

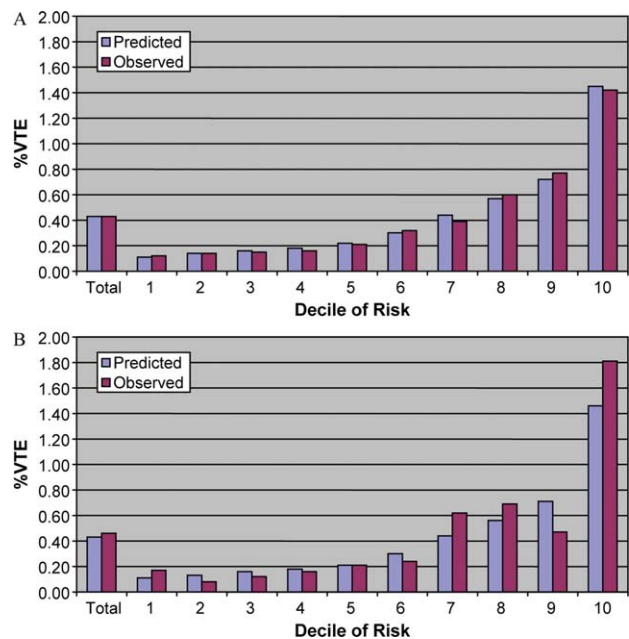


FIGURE 1. (A) Predicted vs observed venous thromboembolism (VTE) in derivation cohort. (B) Predicted vs observed VTE in validation cohort. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Predictive models based on these factors^{17,19-21} have not been subjected to validation or have performed poorly.¹⁸ Acknowledging this lack of standardized risk assessment, JCAHO leaves the means of assessment to individual hospitals. A quality improvement guide published by the Agency for Healthcare Research and Quality goes one step further, stating that "In a typical hospital, it is estimated that fewer than 5% of medical patients could be considered at low risk by most VTE risk stratification methods."²² The guide recommends near universal VTE prophylaxis.

In light of the JCAHO requirements, our model should be welcomed by hospitalists. Rather than assuming that all patients over 40 years of age are at high risk, our model will enable clinicians to risk stratify patients from a low of 0.1% to $>1.4\%$ (>10 -fold increase in risk). Moreover, the model was derived from more than 800 episodes of symptomatic VTE among almost 190,000 general medical patients and validated on almost 50,000 more. The observed patients were cared for in clinical practice at a nationally representative group of US hospitals, not in a highly selected clinical trial, increasing the generalizability of our findings. Finally, the model includes ten common risk factors that can easily be entered into decision support software or extracted automatically from the electronic medical record. Electronic reminder systems have already been shown to increase use of VTE prophylaxis, and prevent VTE, especially among cancer patients.²³

A more challenging task is defining the appropriate risk threshold to initiate VTE prophylaxis. The Thromboembolic Risk Factors (THRIFT) Consensus Group classified patients according to risk of proximal DVT as low ($<1\%$), moderate

(1%-10%), and high (>10%).²¹ They recommended heparin prophylaxis for all patients at moderate risk or higher. Although the patients included in our study all had a diagnosis that warranted prophylaxis according to the ACCP guidelines, using the THRIFT threshold for moderate-to-high risk, only 7% of our patients should have received prophylaxis. The recommendation not to offer heparin prophylaxis to patients with less than 1% chance of developing symptomatic VTE seems reasonable, given the large number-needed-to-treat, but formal decision analyses should be conducted to better define this threshold. Many hospitalists, however, may feel uncomfortable using the 1% threshold, because our model failed to identify almost three out of four patients who ultimately experienced symptomatic VTE. At that threshold, it would seem that hospital-acquired VTE is not a “preventable” complication in most medical patients, as others have pointed out.^{3,24} Alternatively, if the threshold were lowered to 0.4%, our model could reduce the use of prophylaxis by 60%, while still identifying three-fourths of all VTE cases. Further research is needed to know whether such a threshold is reasonable.

Our study has a number of important limitations. First, we relied on claims data, not chart review. We do not know for certain which patients experienced VTE, although our definition of VTE required diagnosis codes plus charges for both diagnosis and treatment. Moreover, our rates are similar to those observed in other trials where symptomatic events were confirmed. Second, about 30% of our patients received at least some VTE prophylaxis, and this may have prevented as many as half of the VTEs in that group. Without prophylaxis, rates might have been 20%–30% higher. Similarly, we could not detect patients who were diagnosed after discharge but not admitted to hospital. While we believe this number to be small, it would again increase the rate slightly. Third, we could not assess certain clinical circumstances that are not associated with hospital charges or diagnosis codes, especially prolonged bed rest. Other risk factors, such as the urinary catheter, were probably surrogate markers for immobilization rather than true risk factors. Fourth, we included length of stay in our prediction model. We did this because most randomized trials of VTE prophylaxis included only patients with an expected length of stay ≥ 6 days. Physicians’ estimates about probable length of stay may be less accurate than actual length of stay as a predictor of VTE. Moreover, the relationship may have been confounded if hospital-acquired VTE led to longer lengths of stay. We think this unlikely since many of the events were discovered on readmission. Fifth, we studied only patients carrying high-risk diagnoses, and therefore do not know the baseline risk for patients with less risky conditions, although it should be lower than what we observed. It seems probable that COPD, rather than being protective, as it appears in our model, actually represents the baseline risk for low-risk diagnoses. It should be noted that we did include a number of other high-risk diagnoses, such as cancer and inflammatory bowel disease, as secondary diagnoses. A larger, more

inclusive study should be conducted to validate our model in other populations. Finally, we cannot know who died of undiagnosed VTE, either in the hospital or after discharge. Such an outcome would be important, but those events are likely to be rare, and VTE prophylaxis has not been shown to affect mortality.

VTE remains a daunting problem in hospitalized medical patients. Although VTE is responsible for a large number of hospital deaths each year, identifying patients at high risk for clinically important VTE is challenging, and may contribute to the persistently low rates of VTE prophylaxis seen in hospitals.²⁵ Current efforts to treat nearly all patients are likely to lead to unnecessary cost, discomfort, and side effects. We present a simple logistic regression model that can easily identify patients at moderate-to-high risk (>1%) of developing symptomatic VTE. Future studies should focus on prospectively validating the model in a wider spectrum of medical illness, and better defining the appropriate risk cutoff for general prophylaxis.

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