A Validation Study of a Retrospective Venous Thromboembolism Risk Scoring Method

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Objectives: Validate a retrospective venous thromboembolism (VTE) risk scoring method, which was developed at the University of Michigan Health System and based on the Caprini risk assessment model, and assess the confounding effects of VTE prophylaxis.

Background: Assessing patients for risk of VTE is essential to initiating appropriate prophylaxis and reducing the mortality and morbidity associated with deep vein thrombosis and pulmonary embolism.

Methods: VTE risk factors were identified for 8216 inpatients from the National Surgical Quality Improvement Program using the retrospective scoring method. Logistic regression was used to calculate odds ratios (OR) for VTE within 30 days after surgery for risk factors and risk level. A bivariate probit model estimated the effects of risk while controlling for adherence to prophylaxis guidelines.

Results: Distribution of the study population by risk level was highest, 52.1%; high, 36.5%; moderate, 10.4%; and low, 0.9%. Incidence of VTE within 30 days was overall 1.4%; by risk level: highest, 1.94%; high, 0.97%; moderate, 0.70%; low, 0%. Controlling for length of hospitalization (>2 d) and fiscal year, pregnancy or postpartum (OR = 8.3; 1.0–68, P < 0.05), recent sepsis (4.0; 1.4–10.9, P < 0.01), malignancy (2.3; 1.5–3.3, P < 0.01), history of VTE (2.1; 1.1–4.1, P < 0.05), and central venous access (1.8; 1.1–3.0, P < 0.05) were significantly associated with VTE. Risk level was significantly associated with VTE (1.9; 1.3–2.6, P < 0.01). The bivariate probit demonstrated significant correlation between the probability of VTE and lack of adherence to prophylaxis guidelines (ρ = 0.299, P = 0.013).

Conclusion: The retrospective risk scoring method is valid and supports use of individual patient assessment of risk for VTE within 30 days after surgery.


Venous thromboembolism (VTE), a disease which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common complication among hospitalized patients, where reported incidence ranges from 10% to 40% in medicine and general surgery populations in the absence of appropriate thromboprophylaxis. VTE results in significant mortality and morbidity; approximately 10% of hospital deaths are attributed to PE, and patients who do not die have an increased risk of postthrombotic syndrome, pulmonary hypertension, or recurrent thrombosis.¹

There is substantial evidence that primary thromboprophylaxis prevents VTE. According to the Agency for Healthcare Research and Policy, VTE prevention for at-risk patients presents the most significant opportunity to improve patient safety in hospitals among 79 patient safety practices because of its efficacy, cost-effectiveness, and benefit-risk ratio.² As a consequence, improvements in VTE prevention have been targeted by the Centers for Medicare and Medicaid Services, the National Quality Forum, and most recently, the Surgeon General of the United States.³⁻⁵

However, despite strong evidence that VTE prophylaxis reduces the incidence of DVT and PE, numerous studies show that prophylaxis is underutilized or inadequate for at-risk patients.⁶⁻⁸ Accurate assessment of patient VTE risk is critical to improving compliance with prophylaxis guidelines,⁷ but risk assessment can be complex because a variety of VTE risk factors must be considered, each risk factor confers a different relative risk, and the effect of multiple risk factors is cumulative.⁹⁻¹⁰

Several risk assessment models that stratify patients according to their risk of VTE have been published, the most notable being those developed by Caprini, Cohen, and Kucher.¹¹⁻¹³ These risk assessment models consist of a list of exposing risk factors (presenting illness or procedure) and predisposing risk factors (genetic and clinical characteristics), each with an assigned relative risk score.¹¹,¹³ The scores are summed to produce a cumulative score, which is used to classify the patient to 1 of 3 or 4 risk levels and determine the onset, intensity, type, and duration of prophylaxis. These models have been criticized for being cumbersome and because very few have been validated.¹¹,¹⁵ Consequently, the impact of the weight and interaction of individual risk factors on cumulative risk has not been tested.

As an alternative, the American College of Chest Physicians advocate a simpler approach, assigning risk according to the patient group to which an individual belongs. The patient group describes the primary reason the patient was hospitalized, such as major general surgery or major orthopedic surgery, and each was tested in randomized clinical trials of thromboprophylaxis. Though some patient-specific, predisposing risk factors may be considered, this method does not promote an individualized approach to risk assessment and thromboprophylaxis.¹

In 2005, the University of Michigan Health System (UMHS) adopted the Caprini risk assessment model¹¹ for medicine and surgery patients and prescribed a prophylaxis regimen for each risk level. To measure compliance with UMHS prophylaxis guidelines, we developed a retrospective VTE risk scoring method based on the Caprini model, which uses data from electronic sources, including hospital billing data, the operating room information system, and clinical data repository. A test of the reliability of this method was previously conducted.¹⁶ The goal of this study was to validate our scoring method.

An important step toward encouraging assessment of individual patient risk for VTE at UMHS and improving compliance with prophylaxis guidelines is to demonstrate the link between individual patient risk assigned by the Caprini model and VTE outcomes.¹⁷ The specific objectives of this study were to: (1) validate the
internally-developed retrospective VTE risk scoring method that is based on the Caprini risk assessment model for a population of general, vascular, and urologic surgery patients discharged from UMHS and (2) assess the confounding effects of provider adherence to UMHS VTE prophylaxis guidelines on the results of the validation study.

METHODS

A total of 8216 general, vascular, and urologic surgery inpatients from the UMHS National Surgical Quality Improvement (NSQIP) Program discharged between July 2001 and January 2008 were selected for study. The NSQIP is a program that measures and promotes improvement in surgical outcomes and is well-documented in the surgery literature. Nurses, who receive in-depth training to ensure data reliability, collect preoperative risk factors, operative variables, and 30-day postoperative mortality and morbidity outcomes, including VTE, in surgical patients.18

For 30-day VTE outcomes, nurses review patient medical records for evidence of a DVT or PE from diagnostic test results and physician notes. A DVT is noted when confirmed by duplex, venogram, or CT scan or evidence of treatment with anticoagulants or insertion of a vena cava filter. A PE is confirmed by V-Q scan, pulmonary arteriogram, or CT angiogram.

The Caprini risk assessment model was introduced at UMHS in 2005 to improve compliance with VTE prophylaxis guidelines for medical and surgery patients and uses a point-scoring system; the relative scores for individual risk factors are summed to produce a cumulative risk score that defines the patient’s risk level (low, moderate, high, or highest risk) and associated prophylaxis regimen (Fig. 1).

The VTE cumulative risk score and risk level was assigned to each patient in the study population using an internally-developed retrospective scoring method that is based on the Caprini model. Data for each VTE risk factor were obtained from electronic

![Figure 1. UMHS VTE patient risk assessment model and prophylaxis guidelines.](image-url)
sources. Hospital billing data were used to obtain patient age, ICD-9-CM diagnoses present at time of hospitalization or within a month or year prior to hospitalization, and ICD-9-CM procedures performed during the hospitalization. The operating room information system was used to define major and minor surgery based on surgical duration and the clinical data repository to calculate body mass index (BMI). Risk factors for each patient were scored and summed to determine the cumulative VTE risk and associated risk level. A test of the reliability of this retrospective scoring method was conducted for a population of 1470 general surgery inpatients whose VTE risk was prospectively assigned by physician assistants during the patients’ preoperative history and physical. The weighted kappa coefficient comparing these 2 approaches was 0.572 (0.525–0.618, P < 0.001), indicating acceptable agreement.16

A descriptive analysis of the percentage of the study population with each risk factor was conducted. Of the patients with each risk factor, the differences in the percentage who did and did not develop VTE were compared using a χ2 test. The distribution of the incidence rate of VTE by risk level and cumulative risk score and the significance of differences was reported using a χ2 test.

Logistic regression was used to calculate odds ratios for VTE of individual risk factors and of the 4 risk levels.19 The model is specified to include dichotomous risk factors as the explanatory variables, and the outcome variable of VTE. Odds ratios and the 95% confident intervals were reported. Ten risk factors whose coefficient estimates were insignificant due to small size (no more than 0.2% of the study sample), and which did not contribute to the model fit were excluded from the final model. A second logistic regression model was identified for the outcome of VTE regressed on 4 risk levels, as an ordinal categorical variable, coded 1 to 4 for low, moderate, high, and highest risk groups. Both models were tested for its fit using Hosmer-Lemeshow goodness-of-fit test, and c-statistic was reported for its discriminative power.

In both models, 2 control variables were included. Length of hospitalization of 2 days or longer was added to control for unobserved factors associated with short stays on VTE outcomes. Fiscal year was used to control for unobserved changes in clinical practice, medical record documentation, and ICD-9-CM diagnosis and procedure coding practices.

Because VTE prophylaxis protects patients from acquiring VTE, the rates of pharmacologic prophylaxis by risk level were reported and the confounding effects of adherence to UMHS prophylaxis guidelines were studied. Unfortunately, information about actual use of pharmacologic and mechanical prophylaxis were not readily available without manual abstraction of medication administration records and nursing notes, so drug orders and hospital billing codes for sequential compression devices that were available electronically were used instead. The percentage of the population that received pharmacologic prophylaxis and recommended prophylaxis by risk level was reported.

A control variable for VTE prophylaxis was not included in the regression models because of its correlation with the independent variable of risk category. VTE prophylaxis protects patients from acquiring VTE and, according to various studies, is more likely to be given to higher risk patients. Because of this simultaneous and opposite effect of prophylaxis and risk category on the probability of acquiring a VTE, a bivariate probit model was applied to estimate the effects of the risk level while accounting for provider adherence to UMHS prophylaxis guidelines.20–22 Finally, because it is difficult to interpret the magnitude of probit model coefficients, we calculated the marginal change in the probability of acquiring VTE associated with a change in the level of risk, after accounting for VTE prophylaxis.

The study was approved by the institutional review board of the University of Michigan Medical School.

RESULTS

Of the 8216 inpatients in the study population, 67% were general surgery, 16% were vascular surgery, and 17% were urologic surgery patients. Roughly, 88% of patients underwent a major surgical procedure, defined as an operation of more than 45 minutes in duration and 35% had a malignancy (Table 1).

The majority (52.1%) of the study population was classified to the highest risk level; 36.5% were classified as high-risk, 10.4% as moderate risk, and 0.9% as low risk.

The overall incidence of acquired VTE within 30 days was 1.44%. The incidence was associated with an increase in risk level; of the patients in the highest risk level, 1.94% acquired a VTE; of the high risk patients, 0.97%; moderate risk patients, 0.70%; and low-risk patients, 0%. The difference between high and highest risk levels was statistically significant (P < 0.001), but the difference between low and moderate and between moderate and high risk levels was not statistically significant (Fig. 2).

Further disaggregating the patients in the highest risk category, the growth in incidence of acquired VTE appears to accelerate according to their cumulative risk score (Fig. 3). The increase was statistically significant for cumulative risk scores of 7 to 8 and greater than 8.

The logistic regression identified recent pregnancy or postpartum (OR = 8.3; 1.0–68, P < 0.05), recent sepsis (4.0; 1.4–10.9, P < 0.01), malignancy (2.3; 1.5–3.3, P < 0.01), history of VTE (2.1; 1.1–4.1, P < 0.05), and central venous access (1.8; 1.3–3.0, P < 0.05) as significantly associated with VTE while age, varicose veins, and positive Factor V Leiden were marginally significant (P < 0.1). Both control variables, length of hospitalization of 2 days or longer and fiscal year, were significant (Table 2).

Controlling for length of hospitalization (≥2 d) and fiscal year, the 4 risk levels were significantly associated with the likelihood of acquiring a VTE within 30 days (1.9; 1.3–2.6, P < 0.01). With an increase in risk of 1 level, the odds of acquiring a VTE increased 90% (Table 3).

The percentage of patients for whom orders were written for pharmacologic prophylaxis increased with risk level, though the percentage of patients for whom orders for pharmacologic and/or mechanical prophylaxis that satisfied UMHS guidelines decreased as risk level increased (Table 4).

The bivariate probit model demonstrated that there was a significant correlation between the probability of acquiring VTE and lack of adherence to UMHS prophylaxis guidelines (ρ = 0.299, P = 0.013) (The positive value of ρ indicated that patients who did not receive recommended prophylaxis had higher probability of developing VTE within 30 days following surgery). However, a test of the significance of the protective effect of adherence to UMHS prophylaxis guidelines showed that it was not statistically significant.

After accounting for the effect of recommended prophylaxis, the estimated mean probability of acquiring VTE was 0.28% for moderate risk patients and 0.90% for high risk patients. The marginal effect of an increase in risk level from moderate to high on the mean probability of VTE was an increase of 0.37 percentage points (P < 0.0001); the marginal effect of an increase from high to highest risk was a growth of 0.90 percentage points (P < 0.0001).

DISCUSSION

This study demonstrates that the retrospective VTE risk scoring method based on the Caprini model is valid and underscores the importance of assessing individual patient risk for VTE. And, because the retrospective risk scoring method uses electronic
sources of data to assess patient risk rather than data collected through labor-intensive medical record abstraction, it is also an economical method. As such, the method can be the basis of a useful measure of adherence to VTE prophylaxis guidelines for general, vascular, and urologic surgery patients.

This retrospective cohort study tested a practical method of risk stratifying a large population of surgical inpatients. By contrast, prior evaluations of VTE risk assessment methods were conducted as small retrospective studies of VTE cases versus controls, where results were highly dependent on selection of adequate controls.15,17 Our findings validate the retrospective risk scoring method; the 4 VTE risk levels were predictors of VTE outcomes and increases in risk level and cumulative risk score were accompanied by increases in the incidence rate of VTE within 30 days after surgery.

The incidence of VTE within 30 days was 1.44% in this study, which was higher than the 0.64% reported in a study of predictors of VTE in NSQIP general and vascular surgery patients from 128 Veterans Affairs and private sector hospitals by Rogers et al.23 The higher incidence can be explained by the fact that this study includes only inpatients, whereas the other included both inpatients and outpatients.

An increase in incidence of VTE associated with an increase in risk was similarly reported by O’Shaughnessy et al who applied the risk assessment model from Kucher to 5692 patients from a database of patients with a suspected VTE where 33% had a

| TABLE 1. VTE Risk Factors of Study Population and Bivariate Analysis |
|--------------------------|--------------------------|--------------------------|--------------------------|
| Relative Risk Score | Pct Observed | Pct VTE | P |
| Age, <41 (not a risk factor) | — | 19.28% | 0.88% | — |
| Age, 41–60 | 1 | 39.59% | 1.41% |
| Age, 61–74 | 2 | 28.40% | 1.67% |
| Age, 75+ | 3 | 12.73% | 1.82% |
| Acute myocardial infarction* | 1 | 0.22% | 0.00% | 0.608 |
| Heart failure | 1 | 3.93% | 1.55% | 0.863 |
| Varicose veins | 1 | 0.11% | 11.11% | 0.015 |
| Obesity (BMI >25) | 1 | 24.71% | 1.63% | 0.409 |
| Inflammatory bowel disease | 1 | 2.98% | 1.22% | 0.777 |
| Sepsis (<1 mo) | 1 | 0.85% | 7.14% | <0.000 |
| COPD or abnormal pulmonary function | 1 | 7.57% | 1.77% | 0.469 |
| Severe lung disease, including pneumonia (<1 mo) | 1 | 0.68% | 3.57% | 0.178 |
| Oral contraceptives or hormone replacement therapy* | 1 | 0.00% | — |
| Pregnancy or postpartum (<1 mo) | 1 | 0.19% | 6.25% | 0.105 |
| Hx of unexpected stillborn infant, recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant* | 1 | 0.01% | 0.00% | 0.904 |
| Medical patient currently at bed rest† | 1 | — | — | — |
| Minor surgery planned | 1 | 5.66% | 1.94% | 0.352 |
| Swollen legs (current)† | 1 | — | — | — |
| Central venous access | 2 | 7.64% | 3.50% | <0.000 |
| Arthroscopic surgery* | 2 | 0.00% | — | — |
| Major surgery (>45 min) | 2 | 88.16% | 1.41% | 0.561 |
| Malignancy (present or previous) | 2 | 34.98% | 2.09% | 0.0003 |
| Laparoscopic procedure >45 min | 2 | 6.18% | 1.38% | 0.909 |
| Patient confined to bed (>72 h)† | 2 | — | — | — |
| Immobilizing plaster cast (<1 mo)† | 2 | — | — | — |
| History of DVT/PE | 3 | 3.47% | 4.21% | <0.000 |
| Positive Factor V Leiden; positive prothrombin G20210A; Positive Lupus anticoagulant | 3 | 0.56% | 6.52% | 0.004 |
| Other congenital or acquired thrombophilia* | 3 | 0.02% | 0.00% | 0.864 |
| Heparin-induced thrombocytopenia (HIT) | 3 | 0.13% | 9.09% | 0.033 |
| Family history of VTE† | 3 | — | — | — |
| Elevated anticardiolipin antibodies† | 3 | — | — | — |
| Stroke (<1 mo)* | 5 | 0.15% | 0.00% | 0.676 |
| Multiple trauma (<1 mo)* | 5 | 0.04% | 0.00% | 0.834 |
| Elective major lower extremity arthroplasty* | 5 | 0.01% | 100.00% | <0.000 |
| Hip, pelvis, or leg fracture (<1 mo)* | 5 | 0.00% | — | — |
| Acute spinal cord injury (paralysis) (<1 mo)* | 5 | 0.00% | — | — |

*Not included in the logistic regression of independent predictors of VTE.
†Not included in retrospective scoring method.
confirmed VTE and 67% did not.24 Although the percentage of patients with a VTE in both studies increased almost linearly with risk, our study exhibited greater specificity for patients classified as low risk (a cumulative risk score of 0 or 1). For low-risk patients, we reported a 0% incidence of VTE, whereas O’Shaughnessy et al identified 20% with confirmed VTE. The difference may be attributed to the Kucher risk assessment model, which is based on only 8 risk factors (compared with more than 30 risk factors in the Caprini model); patients classified as low risk may have had one or more risk factors that were not identified by the model.13

Our observation that the rate of acquired VTE within 30 days appeared to accelerate for patients within the highest risk level as cumulative risk score increased may be useful for identifying those who would benefit the most from long-term prophylaxis, but further study is needed of the relationship between the cumulative risk score and the length of time the patient continues to be at-risk.25,26

Although pharmacologic prophylaxis increased as patient risk increased, adherence to UMHS prophylaxis guidelines actually fell. The bivariate probit model showed that adherence to UMHS prophylaxis guidelines protected patients from VTE, but the effect was not statistically significant. This result may be due to the fact that we included the type and frequency but not the duration of prophylaxis in the model. Still, after adjusting for prophylaxis, the mean probability of VTE doubled when risk level increased from moderate to high and from high to highest.

Seruya et al stratified plastic surgery patients into VTE risk levels by applying the Caprini model preoperatively. Of 1156
patients, 120 (10%) were classified as highest risk. Despite a variety of prophylaxis measures, 9 of the 120 patients (7.5%) suffered a VTE. Because of their high postoperative incidence of VTE, highest risk patients may be candidates for extended out-of-hospital prophylaxis. In general, the study highlights the value of scoring to identify patients at-risk and of scoring patient populations that have not been studied with randomized clinical trials.  

The results of this study show that, controlling for length of hospitalization (≥2 d) and fiscal year, recent pregnancy or postpartum, recent sepsis, malignancy, history of VTE, and central venous access were associated with VTE. Age, varicose veins, and Factor V Leiden were marginally significant. These results are well-supported by the literature. Anderson and Spencer report that while major general surgery is a strong risk factor with an odds ratio of more than 10, other factors confer additional and substantial risk with odds ratios between 2 and 9, including arthroscopic knee surgery, central venous lines, chemotherapy, congestive heart failure or respiratory failure, hormones, malignancy, oral contraceptives, paralytic stroke, pregnancy postpartum, previous VTE, and thrombophilia. The weakest risk factors with odds ratios less than 2 were age, bed rest over 3 days, immobility due to casts, prolonged sitting, or long car or airplane rides, laparoscopic surgery, obesity, varicose veins, or antepartum pregnancy. Petralia and Kakkar, in a recent report on the status of VTE prophylaxis in general surgery patients, identified a long list of risk factors and highlighted the patient-related risk factors, malignant disease and its treatment, older age, history of VTE, increased BMI, varicose veins, and use of estrogens.  

Though identified in previous studies of factors associated with increased incidence of VTE, body mass index (BMI) >25, inflammatory bowel disease, chronic obstructive pulmonary disease, and heart failure in this study were not statistically significant in predicting VTE outcomes. However, it is possible that if BMI had been represented as 2 or 3 ordinal categories in the version of the Caprini model adopted by UMHS, patients with higher BMI might have been significantly associated with VTE. In addition, the odds ratios of some factors, notably pregnancy or postpartum, varicose veins, and sepsis, were higher than their assigned relative weight. The relative weights in the Caprini risk assessment model were established and revised based on results of randomized clinical trials reported in the literature over a period of 25 years, so updates that reflect our findings will only be made when corroborating evidences from other clinical trials and validation studies are published.  

The results of this study strongly support individual assessment of exposing and predisposing risk factors with relative weighting and application of a cumulative risk score and level.  

- Almost all patients in the study population underwent major surgery (88%) but a large portion had 1 or more predisposing risk factors—35% had a cancer diagnosis, 40% were age 61 or older, and 25% had a BMI of greater than 25. Although the percentage of patients with other predisposing risk factors was fairly small, several were significant predictors of VTE within 30 days after surgery and conferred substantial risk (pregnancy/postpartum, history of VTE, varicose veins, and Factor V Leiden).  
- The 4 VTE risk levels were significantly associated with the likelihood of acquiring a VTE. Incidence of VTE grew with an increase in risk level and appeared to accelerate in the highest risk level with an increase in cumulative risk score.  
- Stratification by risk level effectively discriminated patient risk and thromboprophylaxis; the majority of the study population was classified to the highest risk level (52.1%) with a recommendation of pharmacologic and mechanical prophylaxis and a small, but significant percentage, was classified to moderate (10.4%) or low risk (0.9%) levels with a recommendation of mechanical prophylaxis or no prophylaxis, respectively.  

This study has several limitations. First, it was conducted using a retrospective risk scoring method that cannot identify all patient risk factors. Although the reliability study showed that agreement between the retrospective scoring method and the PA reported risk level was acceptable, the PA reported results cannot be considered the gold standard. Still, the retrospective scoring model may underestimate the risk level and thromboprophylaxis for a minority of patients, roughly 5%.  

Second, this study was conducted at 1 academic medical center; a similar test of the retrospective scoring method and the association between VTE risk and outcomes should be conducted at other centers that participate in the NSQIP. A broader study would have the added benefit of enhancing the previous analysis of predictors of VTE from preoperative data collected for NSQIP by examining known VTE risk factors. But, such a study can only be accomplished if the data sources that are needed to apply the retrospective VTE risk scoring method are reliable.  

Third, VTE outcomes were reported for a period of 30-days post surgery, whereas studies have shown that the impact of hospitalization on development of VTE can exceed 30 days. In addition, the NSQIP model of reporting VTE outcomes may not identify perioperative DVTs that are clinically silent. So, the reported incidence of VTE in the study population may be understated.  

Ultimately, a multicenter study is needed to create and validate an individual prospective VTE scoring system for surgical patients, based on 90-day VTE outcomes. Finally, this study was conducted for general, vascular, and urologic surgery populations. Similar studies for other surgery and for medicine populations should be conducted to validate the risk scoring method and demonstrate the importance of individual risk assessment for a broader range of patients. After conducting such studies, the scoring method could be adopted as a very practical means to measure adherence to prophylaxis guidelines more broadly and fill the gap in current VTE measure sets promulgated by the Centers for Medicare and Medicaid Services and the National Quality Forum.  

In conclusion, an internally-developed UMHS retrospective VTE risk scoring system that is based on the Caprini risk assessment model, coupled with data about the patient length of hospitalization, produced a valid method for identifying patients at risk for DVT or PE within 30 days after surgery. This study demonstrates the importance of assessing individual patient VTE risk factors to determine overall risk and appropriate thromboprophylaxis. Finally, since the scoring method is based on readily available electronic data sources, it can be widely used to stratify patients by risk of VTE and provide the basis for a practical and economical means to measure and improve compliance with VTE prophylaxis guidelines.  

REFERENCES  

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