External validation of a risk assessment model for venous thromboembolism in the hospitalised acutely-ill medical patient (VTE-VALOURR)

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Summary

Venous thromboembolic (VTE) risk assessment remains an important issue in hospitalised, acutely-ill medical patients, and several VTE risk assessment models (RAM) have been proposed. The purpose of this large retrospective cohort study was to externally validate the IMPROVE RAM using a large database of three acute care hospitals. We studied 41,486 hospitalisations (28,744 unique patients) with 1,240 VTE hospitalisations (1,135 unique patients) in the VTE cohort and 40,246 VTE-free hospitalisations (27,609 unique patients) in the control cohort. After chart review, 139 unique VTE patients were identified and 278 randomly-selected matched patients in the control cohort. Seven independent VTE risk factors as part of the RAM in the derivation cohort were identified. In the validation cohort, the incidence of VTE was 0.20%; 95% confidence interval (CI) 0.18–0.22, 1.04%; 95%CI 0.88–1.25, and 4.15%; 95%CI 2.79–8.12 in the low, moderate, and high VTE risk groups, respectively, which compared to rates of 0.45%, 1.3%, and 4.74% in the three risk categories of the derivation cohort. For the derivation and validation cohorts, the total percentage of patients in low, moderate and high VTE risk occurred in 68.6% vs 63.3%, 24.8% vs 31.1%, and 6.5% vs 5.5%, respectively. Overall, the area under the receiver-operator characteristics curve for the validation cohort was 0.7731. In conclusion, the IMPROVE RAM can accurately identify medical patients at low, moderate, and high VTE risk. This will tailor future thromboprophylactic strategies in this population as well as identify particularly high VTE risk patients in whom multimodal or more intensive prophylaxis may be beneficial.

Keywords

Venous thromboembolism risk assessment, prevention, risk assessment models, hospitalised medical patients, validation

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Introduction

There are an estimated 8 million hospitalised acutely-ill medical patients in the United States (US) on an annual basis at risk of developing venous thromboembolism (VTE) (1, 2), while this number is likely even higher in the European Union (EU) (3, 4). The most recent international guideline and consensus statements have stressed the importance of proper use of risk assessment models (RAM) in this patient population to not only identify patients at risk of VTE, but also to ensure that over-prophylaxis for patients ***not*** at-risk is avoided (1). This is especially true in light of the most recent randomised controlled trials of extended thromboprophylaxis in hospitalised medical patients which have failed to show benefit/risk of pharmacologic thromboprophylaxis across a heterogenous group of these patients (5–7).

There have been multiple VTE RAMs in this patient population that have been derived by expert consensus or by regression analysis to identify patients at risk of developing VTE; however, the RAMs have either not been externally validated or validated to a limited degree (8–16). External validation provides evidence that the RAM can be used with reproducible accuracy in settings and populations other than those from which it was derived prior to widespread clinical use (17–19). The IMPROVE (International Medical Prevention Registry on Venous Thromboembolism) RAM was derived from a large international registry of 15,156 hospitalised acutely ill medical patients and consists of seven clinical risk factors that are associated with VTE risk in this population (1, 12, 20). Risk factors (i.e. predictors) in the model are given 1-3 points each, and points are added to achieve a final score which is then categorised into tiers of low, moderate or high risk for VTE. The objective of this study was to externally validate this VTE RAM in three acute care hospitals as part of a large healthcare system (19) and to determine its calibration and discrimination versus the original derivation cohort (21).

Methods

The derivation population has been previously described (12). Briefly, the seven VTE risk factors identified in the IMPROVE RAM can be associated with the acronym ImPACT-ILL including **Im**mobilisation ≥ 7 days, **P**revious VTE, **A**ge > 60 years, **C**ancer, Known **T**hrombophilia, **I**ntensive care / coronary care unit (ICU/CCU) stay, and **L**ower **L**imb paralysis using a point system of 1-3 points for each risk factor (►Table 1). A known thrombophilia was defined as an acquired or familial disorder of the haemostatic system that resulted in an increased risk of antithrombin deficiency, protein C and protein S deficiencies, resistance to activated protein C, prothrombin G20210A mutation, antiphospholipid syndrome, and factor V Leiden. A score of 0 to 1 placed patients at low VTE risk (symptomatic VTE rate of <1%), score of 2 to 3 at moderate VTE risk (VTE rate of 1 – 2 %), and a score of 4 or more at high VTE risk (VTE rate of > 4.8%). The risk threshold using American College of Chest Physician (ACCP) criteria warranting pharmacologic thromboprophylaxis was a score of 2 or more.

The external validation population (VTE-VALOURR) included all acutely-ill medical patients admitted to the hospital between January 1st 2005 and February 28th 2011. Patients were identified utilising the McMaster Transfusion Registry for Utilisation and Surveillance and Tracking (TRUST) database and International Classification of Diseases, 10th Revision, Clinical Modification Codes (ICD-10-CM) (see Online Appendix Tables A-D, available online at www.thrombosis-online.com). The study was approved by the McMaster Research Ethics Board and complied with all privacy rules and regulations. The TRUST database contains information from three acute care sites of Hamilton Health Sciences in Hamilton, Ontario, Canada (General, Juravinski, and McMaster Hospitals). It includes demographic variables on all hospitalised patients; primary and secondary diagnoses, procedures, length of stay (LOS), Intensive Care/Critical Care Unit (ICU/CCU) stay, and discharge status. The database also contains information extracted from the laboratory information system including all blood products transfused, and laboratory test results (e.g. complete blood counts, coagulation testing and serum creatinine.) For consistency, MDs and PharmDs were trained by the principal investigator (CEM) to minimise variability in chart abstraction. Discrimination was defined as a measure of how well the RAM can separate those who do and do not have VTE (21). If predicted values for VTE are all higher than VTE-free patients, the RAM will demonstrate good discrimination. Calibration is a measure of how well predicted probabilities of VTE in the derivation cohort agree with actual observed risk in the validation cohort. If the proportions of VTE match well, the RAM would show good calibration (21).

Inclusion and exclusion criteria of the derivation cohort have been previously described (12, 20). The inclusion criteria of the validation cohort assembled for this study were: age ≥18 years and admission for an acute medical illness with ≥3-day duration of hospitalisation. Patients were excluded if any of the following applied: anticoagulant or thrombolytic drug use at admission or within 48 hours (h) after admission; major surgery or trauma within three months before admission; admission for deep-vein thrombosis (DVT) or pulmonary embolism (PE) (or a diagnosis of either within 24 h of admission) unrelated to a previous hospital stay; and patient transfer from another facility for a stay ≥ 24 h to minimise confounding of care that occurred at other facilities. Coding in the Online Appendices (available online at www.thrombosis-online.com) was used in the TRUST database to include or exclude patients and also to initially identify VTE patients (►Figure 1).

The VTE population was defined as patients having an event beyond 24 h after their hospitalisation time or being admitted for a hospital-acquired VTE from a related hospitalisation within 92 days. Data for included and non-excluded patients from the TRUST database was imported into a secure Microsoft® Access database for chart review by an MD or PharmD. The exclusion criteria of treatment dose anticoagulation and transfer from a non-McMaster facility were applied at the chart level. In addition due to coding not being fully accurate, some patients were excluded at the chart level due to a record of a surgical procedure (Online Appendix C, available online at www.thrombosis-online.com) that occurred within the previous three months or during index hospitalisation. Chart reviews were performed to extract relevant study information and identify patients with VTE if patients met inclusion and exclusion criteria. All abstracted data was reviewed (CEM) and verified from the medical record after data abstraction by the initial abstractor.

After VTE patients were identified (N=139) and data was locked in the VTE cohort, a control cohort of random patients selected from VTE-free controls was created in a 2:1 distribution matched for gender, hospital and week of admission. In a similar fashion as the VTE cohort (►Figure 1), included patients were extracted from the TRUST database with relevant clinical information. MD and PharmD abstractors then reviewed the medical records of potentially qualified VTE-free controls using the same inclusion and exclusion criteria (i.e. except a hospital acquired VTE) until two matched controls were found for each VTE case. Reasons for ex-

Table 1: Adjusted Cox model for three-month VTE of the IMPROVE RAM: points assigned each patient characteristic: $Im_1P_3A_1C_2T_2$ I_1LL_2 (Immobilisation, Previous VTE, Age >60 years, Cancer, known Thrombophilia, ICU/CCU stay, and Lower Limb paralysis).

Patient characteristic	Hazard ratio (95% CI)	P-value	Points
Previous VTE	4.7 (3.0–7.2)	<0.001	3
Known thrombophilia	3.5 (1.1–11)	0.04	2
Lower limb paralysis	3.0 (1.6–5.7)	0.001	2
Cancer	2.8 (1.9–4.2)	<0.001	2
Immobilised ≥7 days [a]	1.9 (1.3–2.7)	0.001	1
ICU/CCU stay	1.8 (1.1–2.9)	0.01	1
Age >60 years	1.7 (1.1–2.6)	0.01	1

[a] Days immobile immediately prior to and during hospital admission. * Tiers: 0–1 Points = Low Risk Tier, 2–3 Points = Moderate Risk Tier, ≥ 4 points = High Risk Tier.

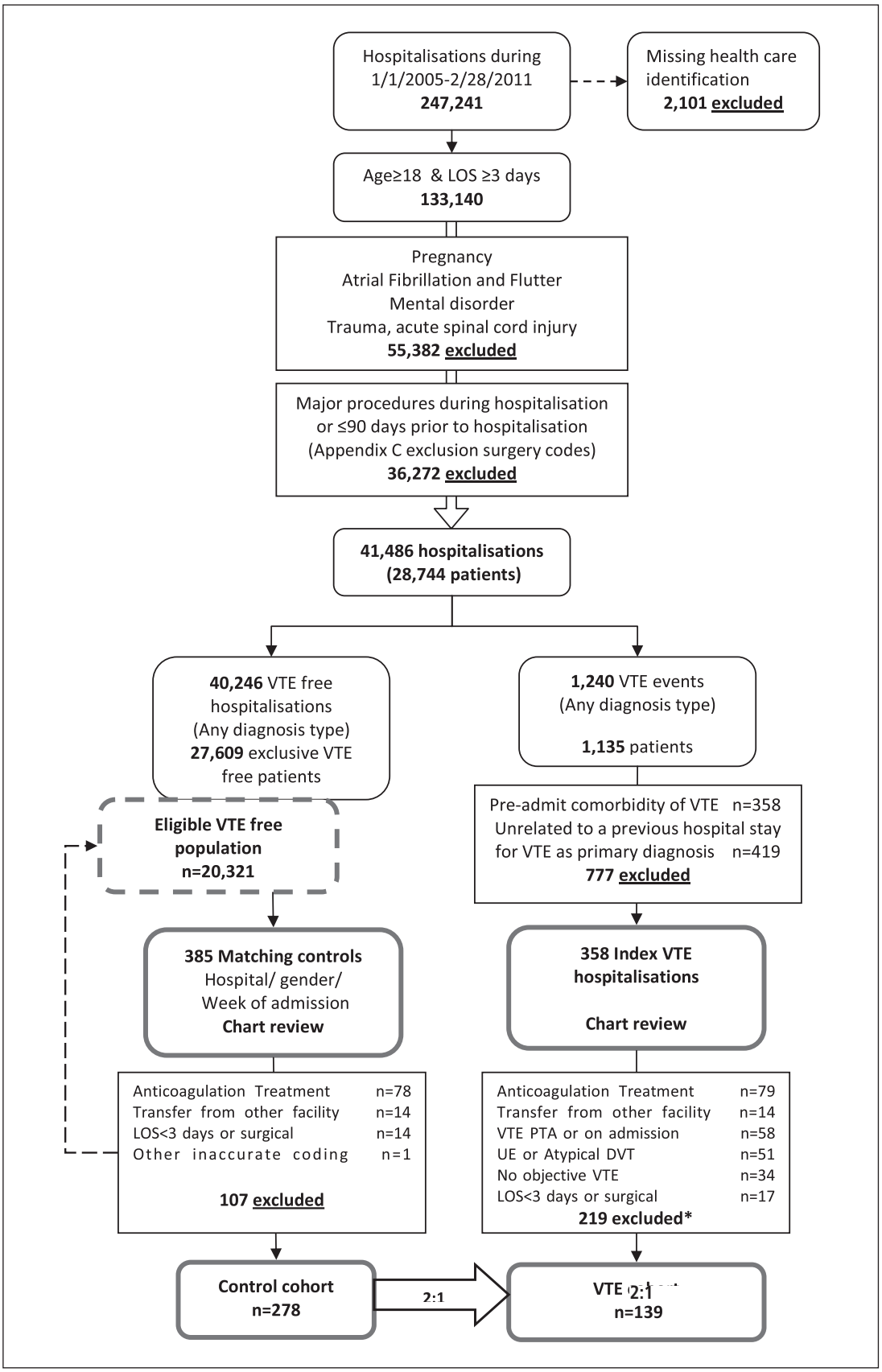

Figure 1: Study flow-chart of patients.
*Exclusions are not mutually exclusive.
DVT= deep vein thrombosis; LOS = length of stay; PTA = prior to admission; UE = upper extremity; VTE = venous thromboembolism.

Table 2: IMPROVE risk assessment model and distribution of risk factors in the VTE and VTE-free control cohorts (1).

VTE Risk Factor	Points*	Number (%) in the VTE Group n=139	Number (%) in the Control Group n=278	OR	p-value**
Previous VTE	3	21(15.1)	6(2.2)	8.07	<0.0001
Known Thrombophilia	2	8(5.8)	1(0.4)	16.92	0.0009*
Lower Limb Paralysis	2	12(8.6)	4(1.4)	6.47	0.0003
Current Cancer	2	70(50.4)	77(27.7)	2.65	<0.0001
Immobilization ≥ 7 Days	1	58(41.7)	23(8.3)	7.94	<0.0001
ICU / CCU Stay	1	18(12.9)	26(9.4)	1.44	0.2597
Age > 60 Years	1	101(72.7)	186(66.9)	1.31	0.2317

* Tiers: 0–1 Points = Low Risk Tier, 2–3 Points = Moderate Risk Tier, ≥ 4 points = High Risk Tier. **Fisher exact test.

clusion were recorded and data was abstracted into a duplicately structured Microsoft® Access database for comparison against the VTE cohort.

Outcomes were objectively verified VTE within 92 days from index admission as in the IMPROVE registry and the derivation study of the IMPROVE RAM (12, 20). VTE was defined as PE (i.e. verified by a positive pulmonary angiogram, spiral computed tomography, high probability ventilation / perfusion scan, or at autopsy) while lower extremity DVT was verified by compression ultrasonography, computed tomography, magnetic resonance imaging, or at autopsy. Included lower extremity DVT were proximal, distal, or both; however, upper extremity DVT and other atypical VTE were excluded (e.g. portal vein, renal vein, mesenteric vein thrombosis, etc.) due to different pathophysiologic mechanisms as compared to lower extremity DVT (22).

Statistical analysis

In order to calculate calibration versus the derivation cohort, exclusion criteria for the VTE-free cohort were evaluated by regarding the exclusion process through chart review for each VTE case as a negative binomial exercise. Exclusion rates (parameters of negative binomial distribution) were estimated separately for six hospital/gender stratum. The number of total eligible controls and VTE incidence were computed based on the estimation of exclusion rates, which allowed for an estimation of total patients in each cohort. Odds ratios (OR) were reported for individual risk factors. IMPROVE scores were computed and score distributions in the VTE and control cohort were compared using a proportional odds model. The predictive performance of IMPROVE score on VTE risk was examined by fitting a logistic regression model. Receiver-operator curves (ROC) were constructed by plotting the sensitivity of the score against the false positive rate to demonstrate the discriminant ability of the IMPROVE score in the validation population. In order to see whether VTE prophylaxis use confounded the correlation of score and the VTE event, the logistic model and ROC analysis were repeated by adjusting for use of any thromboprophylaxis or appropriate (i.e. type, dose and duration) thromboprophylaxis. Positive predictive value (PPV), negative predictive value (NPV), and positive and negative likelihood ratios (LR) were computed for different score cut-off points using estimated VTE rates. The probability of VTE at different IMPROVE scores tiers (low, moderate and high) was estimated for the stratified case control settings using overall VTE incidence. All analyses were performed using computer software (SAS 9.3, SAS Institute, Cary, NC, USA).

Results

Initially, 247,241 hospitalisations were available for assessment between January 1st 2005 and February 28th 2011 and 133,140 hospi-

Table 3: Distribution of risk scores.

	Number (%) in the VTE Group n=139	Number (%) in the Control Group n=278
IMPROVE Score		
0	5(3.6)	57(20.5)
1	21(15.1)	110(39.6)
2	25(18.0)	49(17.6)
3	41(29.5)	47(16.9)
4	25(18.0)	11(4.0)
5	10(7.2)	0(0.0)
6	8(5.8)	4(1.4)
7	4(2.9)	0(0.0)
IMPROVE Score tiers		
Low risk (0–1 points)	26(18.7)	167(60.1)
Moderate risk (2–3 points)	66(47.5)	96(34.5)
High risk (≥4 points)	47(33.8)	15(5.4)

talisations met inclusion criteria (►Figure 1). After exclusion criteria were applied, 41,486 hospitalisations (28,744 unique patients) with 1,240 VTE hospitalisations (1,135 unique patients) in the VTE cohort and 40,246 VTE-free hospitalisations (27,609 unique patients) in the control cohort remained. After chart review of included VTE patients, 139 unique VTE patients were identified and 385 randomly selected VTE-free control patients from the first admission of 27,609 patients were also evaluated, 107 were excluded resulting in 278 matched patients for the control cohort. For demographics, male sex percentage was the same at 48.9% in both the VTE and VTE-free control cohorts and mean age was higher in the VTE cohort as compared to the VTE-free control cohort although not significantly (68.4 years old vs 65.3 years old, p = 0.085). For VTE vs VTE-free cohorts, the risk factor distribution is shown in ►Table 2 with all seven risk factors occurring more frequently in the VTE group compared to controls: previous VTE (15.1% vs 2.2%), thrombophilia (5.8% vs 0.4%), lower limb paralysis (8.6% vs 1.4%), current cancer (50.4% vs 27.7%), immobilisation ≥ 7 days (41.7% vs 8.3%), ICU/CCU stay (12.9% vs 9.4%), and age > 60 years (72.7% vs 66.9%).

Distribution of risk scores is also depicted in ►Table 3. More VTE-free control patients had a lower score of 0 or 1 as compared to the VTE-cohort while scores of 2 were evenly distributed between the two cohorts. Scores of ≥ 3 were more commonly distributed in the VTE cohort. Distribution in the low, moderate and high-risk tiers was 18.7% vs 60.1%, 47.5% vs 35.5%, and 33.8% vs 5.4% in the VTE and VTE-free cohorts, respectively, and the VTE cohort demonstrated significantly higher risk scores (p<0.0001).

Statistical adjustment of control cohort

During the process of evaluating controls to obtain two controls per VTE case, 107 out of 385 randomly selected VTE-free control patients were excluded due to treatment dose anticoagulation (n=78), transfer from a non-McMaster facility (n=14), length of stay < 3 days or surgical procedures (n=14) and other inaccurate coding (n=1). Exclusion rates were estimated for six hospital/gender strata (range 15% – 35%) by regarding the selection process for each case as a negative binomial exercise. Following the methodology described of estimation of exclusion rates, the total eligible VTE-free population was estimated at 20,321 compared to the initial 27,609 controls. Thus, the total denominator utilised was 20,460 which included the 20,321 VTE-free population and the 139 VTE patients. Therefore, the estimation of the incidence of VTE in the validation population was 0.68% (139/20,460).

Calibration and discrimination

Comparing the IMPROVE derivation cohort to the VALOURR validation cohort, the incidence of VTE closely paralleled that of the original derivation cohort which demonstrated a low VTE risk group of 0.45%, moderate VTE risk group of 1.3%, and high VTE

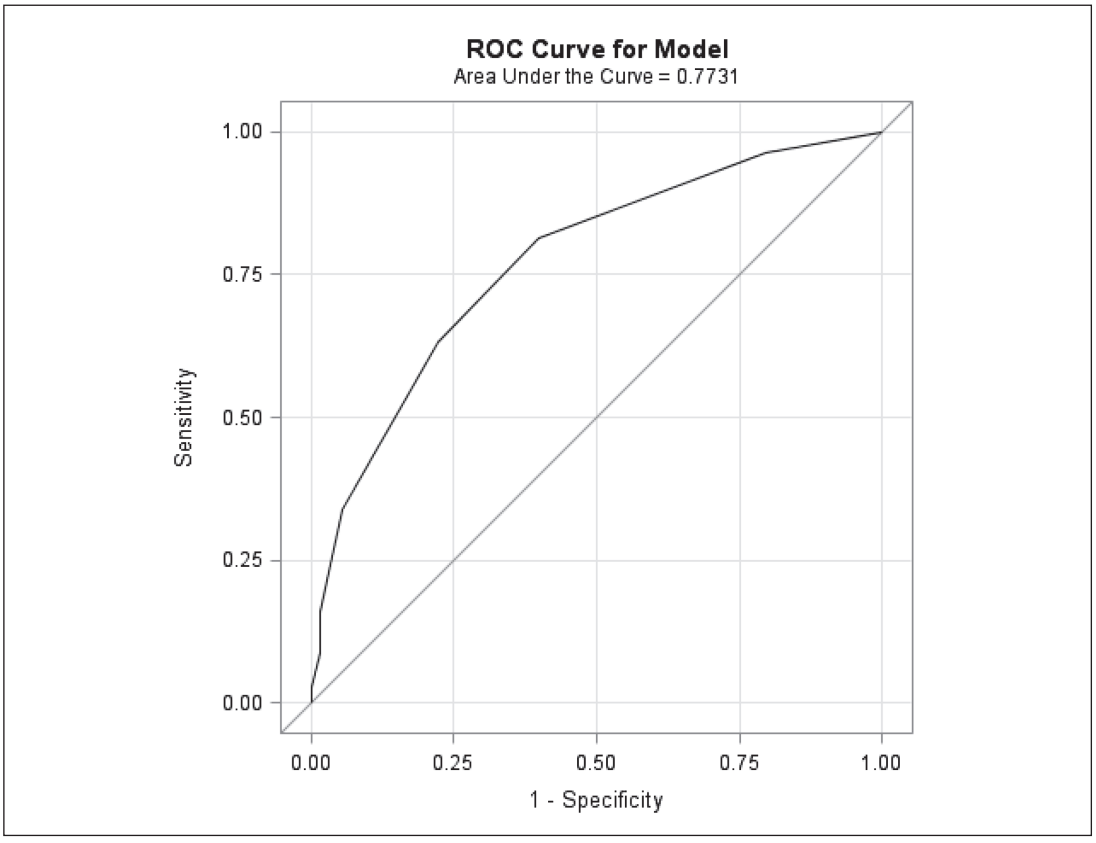

Figure 2: Discrimination of VTE-VALOURR vs IMPROVE score ROC curve.

Table 4: Calibration: VTE % in the IMPROVE (derivation) and VTE-VALOURR populations.

	Low (Score 0–1)	Moderate (Score 2–3)	High (Score ≥ 4)	TOTAL Population *	Moderate and High Risk Population
IMPROVE VTE Incidence	47 / 10379 (0.45%; total 68.6%)	49 / 3755 (1.3%; total 24.8%)	47 / 991 (4.74%; total 6.5%)	143 / 15125 (0.95%)	96 / 4746 (2 %)
VALOURR VTE Incidence	26 /12961 (0.20%; 95%CI 0.18–0.22; total 63.3%)	66 / 6366 (1.04%; 95%CI 0.88–1.25; total 31.1%)	47 / 1133 (4.15%; 95%CI 2.79–8.12; total 5.5%)	139 / 20460 (0.68 %)	113 / 7499 (1.51 %; 95% CI 1.31–1.78%)

* Low plus Moderate plus High Tiers. ** CI = Confidence Interval.

risk group of 4.74%. In the VALOURR validation group, incidence of VTE was 0.20% (95% confidence interval [CI] 0.18–0.22) in the low risk group, 1.04% (95%CI 0.88–1.25) in the moderate VTE risk group, and 4.15% (95%CI 2.79-8.12) in the high VTE risk group (►Table 4). For the derivation and validation cohorts, the total percentage of patients in low, moderate and high VTE risk tiers occurred in 68.6% vs 63.3%, 24.8% vs 31.1%, and 6.5% vs 5.5%, respectively. Discrimination of VTE-VALOURR vs IMPROVE Score and the ROC are depicted in ►Figure 2. Overall, the area under the ROC curve was 0.7731. Sensitivity and specificity, estimated PPV and NPV and positive and negative LRs by various score cutpoints are depicted in ►Table 5.

Effect of thromboprophylaxis

Logistic regression models with and without use of any thromboprophylaxis or appropriate thromboprophylaxis (i.e. appropriate type, dose, and duration of agent per ACCP) revealed no significant changes in the score estimate (Online Appendix E, available online at www.thrombosis-online.com). In addition, the area under the curve (AUC) did not appreciably change when adjusting for both use of any thromboprophylaxis and appropriate thromboprophylaxis (Online Appendix E, available online at www.thrombosis-online.com).

Discussion

To our knowledge, this is the first, large-scale, multicentre, external validation study of a RAM, the IMPROVE RAM, for VTE prevention in the acutely-ill hospitalised medical patient. The results of this external validation study demonstrate a level 2 validation of this VTE RAM, meaning that results can be used in various settings with confidence in their accuracy (19). This simple RAM utilised seven independent clinical risk factors that are evidence-derived, weighted, and easily obtainable during the course of a hospital admission in this patient population.

The derivation and validation cohorts exhibited good concordance of VTE risk distribution, with approximately two-thirds of patients classified as low VTE risk with a symptomatic VTE incidence of ~ 0.2 – 0.4%, approximately 25–30% of patients classified as moderate risk with a VTE incidence of ~1.0%, and approximately 5% of patients classified as high risk with a VTE incidence of greater than 4%. The validation cohort also displayed excellent

Table 5: Sensitivity, specificity, positive (PPV) and negative predictive values (NPV), and positive and negative likelihood ratios (LR) at various score cut-off points.

Score cut-off point	Prediction of VTE %	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
0	8.97%	100.00	0.00	0.69	--	1	--
1	17.18%	96.40	20.50	0.84	99.88	1.213	0.176
2	30.39%	81.29	60.07	1.40	99.78	2.036	0.312
3	47.89%	63.31	77.70	1.94	99.67	2.839	0.472
4	65.92%	33.81	94.60	4.19	99.51	6.261	0.700
5	80.28%	15.83	98.56	7.13	99.41	10.993	0.854
6	89.55%	8.63	98.56	4.02	99.36	5.993	0.927
7	94.75%	2.88	100.00	100.00	99.33	--	0.971

Spyropoulos AC, Anderson FA, Jr., Fitzgerald G, et al. Predictive and associative models to identify hospitalized medical patients at risk for VTE. Chest. 2011;140(3):706–14. Epub 2011/03/26.

discrimination characteristics of the VTE risk score compared to the derivation cohort, with an area under the ROC curve of 0.77 compared to the area under the ROC curve of 0.65 seen in the original derivation cohort (12). Lastly, the effect of any and appropriate thromboprophylaxis did not appreciably change the score estimate or AUC of the validation cohort.

Previous RAMs in the medical patient population have been derived mostly in populations with surgical or cancer patients and mostly with the use of expert consensus or with the use of validation cohorts in the same patient population. (11, 13, 14, 23) In this patient population, a recent multicentre validation study of the Padua VTE RAM revealed that a score of 4 or more was strongly associated with symptomatic VTE and VTE-related death at 90 days (24). However, unlike the Padua VTE RAM, all of the risk factors of the IMPROVE VTE RAM are evidence-derived and fewer in number (7 vs 11), which may enhance model utility. In addition, compared to the Padua VTE RAM which utilised a binary cut-off of 4 points to discriminate low vs high risk patient groups, the IMPROVE VTE RAM could discriminate a three-tiered VTE risk group model, placing patients into low, moderate, and high VTE risk categories which may be used to better tailor thromboprophylactic strategies. VTE RAMs should be derived appropriately, be externally validated, and have impact analyses conducted upon them to demonstrate that they can be used with reproducible accuracy and confidence in other settings to ensure appropriate patient care (25). The present validation study, with excellent discrimination and calibration characteristics, represents an important step in the potential widespread use of a simple, evidence-derived, VTE RAM in hospitalised, acutely-ill medical patients (17–19).

These findings have important clinical implications. With at least 8 million acutely-ill medical patients being at risk of VTE within the US and another 12 million estimated acutely-ill medical patients in the EU, risk assessment for VTE is of critical importance to not only identify patients at risk of VTE but also to ensure that overprophylaxis for patients ***not*** at-risk is avoided (1). With major bleed rates between 0.4% to 1.7% (26, 27), use of anticoagulant prophylaxis in patients at low VTE risk may pre-dispose them to adverse events such as bleeding and heparin induced thrombocytopenia which may outweigh the benefits of VTE risk reduction (28). As such, the IMPROVE VTE RAM suggests that approximately two-thirds of hospitalised medical patients are at low risk of VTE and efforts to promote widespread thromboprophylaxis without proper VTE risk assessment may expose a large amount of this population to unnecessary harm from bleeding. Conversely, approximately 5% of this population has very high risk of symptomatic VTE (>4%) that may benefit from multimodal or targeted approaches to thromboprophylaxis. Lastly, the seven independent clinical VTE risk factors of the present VTE RAM (previous VTE, known thrombophilia, lower limb paralysis, cancer, immobilisation ≥ 7 days, ICU/CCU stay, and age > 60 years) have been well-described in previous epidemiologic studies in this patient population and are simple and quick to implement in a hospitalised setting (29).

Strengths of the present study include a large, multi-centre, database of acute care hospitals in a setting different from the original derivation cohort population. Second, the number of VTE events in both the cases and controls were robust to assess calibration and discrimination of the model. Lastly, the use of ICD-10 coding provided more granularity than ICD-9 and likely allowed for the TRUST database to include and exclude patients more appropriately at a large scale. Limitations may include the retrospective design and the possibility that a small number of VTE events were missed due to the initial use of a database to identify patients. However, missing these events would likely bias the results towards improved calibration versus the original derivation cohort. A second limitation may be that the overall denominator was estimated due to the inability to abstract data from more than 27,000 patient medical records. However, these conservative estimates were based off the number of total eligible controls where VTE incidence was computed based on the estimation of exclusion rates, which allowed for an estimation of the total number of patients in each cohort. This appears to be confirmed by the lower rates of VTE than seen in the initial study, although the true denominator may have been lower than our estimation.

Conclusion

The VTE-VALOURR study is the first large-scale external validation of IMPROVE VTE RAM in the hospitalised acutely-ill medical patient. This also represents the first external validation of any appropriately evidence-derived RAM in this patient population. The derivation and validation cohorts showed good discrimination and calibration in a three-tiered RAM of low, moderate, and high VTE risk using seven well-established and easy-to-implement VTE risk factors in a weighted point system. This represents an important advance to the field of risk assessment in the acutely-ill medical patient and should help optimise medical care to this group by better assessing both patients at-risk for VTE and those at low VTE risk in order to better tailor thromboprophylactic strategies and minimise overprophylaxis. In addition, the IMPROVE RAM can identify particularly high VTE risk patient groups to target more intensive or multimodal thromboprophylactic strategies that can be assessed in future clinical trials. Additional prospective validation studies as well as impact analyses should be undertaken to further assess this RAM.

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Conflicts of interest

Alex Spyropoulos has served as a consultant for Boehringer Ingelheim, Johnson & Johnson (J&J), Eisai, Bayer, and Astellas and has served on advisory committees for Bristol-Myers Squibb, Boehr-

What is known about this topic?

- Risk assessment models (RAMs) should be validated prior to widespread clinical use.
- Few RAMs have been evidence-derived or validated in the acutely-ill hospitalised medical patient.

What does this paper add?

- This study externally validates one of the few evidence-derived RAMs in the acutely ill hospitalised medical patient.
- The IMPROVE VTE RAM is a simple, seven-risk factor model that may be utilised to stratify patients into high, moderate and low VTE risk categories.
- Use of this RAM may prevent overprophylaxis of low VTE risk patients and identify high-risk patients who may benefit from more intensive or multimodal thromboprophylaxis.

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