CLINICAL RESEARCH STUDY

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Validation of Risk Assessment Models of Venous Thromboembolism in Hospitalized Medical Patients

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ABSTRACT

BACKGROUND: Patients hospitalized for acute medical illness are at increased risk for venous thromboembolism. Although risk assessment is recommended and several at-admission risk assessment models have been developed, these have not been adequately derived or externally validated. Therefore, an optimal approach to evaluate venous thromboembolism risk in medical patients is not known.

METHODS: We conducted an external validation study of existing venous thromboembolism risk assessment models using data collected on 63,548 hospitalized medical patients as part of the Michigan Hospital Medicine Safety (HMS) Consortium. For each patient, cumulative venous thromboembolism risk scores and risk categories were calculated. Cox regression models were used to quantify the association between venous thromboembolism events and assigned risk categories. Model discrimination was assessed using Harrell's C-index.

RESULTS: Venous thromboembolism incidence in hospitalized medical patients is low (1%). Although existing risk assessment models demonstrate good calibration (hazard ratios for "at-risk" range 2.97-3.59), model discrimination is generally poor for all risk assessment models (C-index range 0.58-0.64).

CONCLUSIONS: The performance of several existing risk assessment models for predicting venous thromboembolism among acutely ill, hospitalized medical patients at admission is limited. Given the low venous thromboembolism incidence in this nonsurgical patient population, careful consideration of how best to utilize existing venous thromboembolism risk assessment models is necessary, and further development and validation of novel venous thromboembolism risk assessment models for this patient population may be warranted.

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Identifying medical patients at increased risk for venous thromboembolism using an individualized approach is of increasing importance and is emphasized in available guidelines.[1] While several risk assessment models exist for venous thromboembolism in medical patients,[2-5] published risk assessment models have limited generalizability and validation.[6] Although a few recent studies have validated existing risk assessment models,[5,7,8] these validation efforts lacked external validation,[5] have had limited external validation,[9] or have had large-scale external validation with a risk assessment model that has limitations in predicting at-admission venous thromboembolism risk.[7,8] Additional large-scale, external validation studies are important to help confirm or refute the accuracy of available risk assessment models, especially during hospital admission and based on detailed clinical data, as the performance of existing risk assessment models has been moderate at best in this setting.

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The Michigan Hospital Medicine Safety Consortium (HMS) is a state-wide quality collaborative focused on preventing adverse events in hospitalized medical patients. The consortium collects detailed patient-level data on venous thromboembolism risk factors and outcomes. The aim of the present study was to externally validate several existing risk assessment models using the large HMS cohort to determine which risk assessment model optimally predicts venous thromboembolism in acutely ill, hospitalized, medical patients.

CLINICAL SIGNIFICANCE

- Several venous thromboembolism (VTE) risk assessment models (RAMs) have been developed, but lack external validation in hospitalized medical patients.
- VTE incidence in medical patients is low (1%).
- Results from an external validation study in a cohort of over 60,000 medical patients indicated poor model discrimination for VTE RAMs assessed.
- Existing VTE RAMs have limited utility in identifying the highest-risk subset of medical patients for whom pharmacologic prophylaxis is warranted.

METHODS

Study Setting and Participants

The setting and design of HMS have been previously described.[10] Although participation is voluntary, each hospital receives payments for participating in the consortium and for data collection.

Eligible patients included those admitted to a medicine service for 2 days or longer. Patients were excluded if they met any of the following criteria: 1) under the age of 18 years; 2) pregnant; 3) underwent any surgical procedure during the admission; 4) direct admission to an intensive care unit (ICU); 5) direct admission for end-of-life care; 6) diagnosis of venous thromboembolism in the 6 months prior to admission; 7) admitted for presumed venous thromboembolism; 8) admitted under observation status; 9) re-admitted within 90 days of discharge from an admission included in the registry; or 10) received systemic anticoagulation on day 1 or day 2 of the index hospitalization.

Detailed patient demographic, medical history, predefined risk factors for venous thromboembolism, and laboratory and medication data were collected through a standardized process using a trained medical record abstractor at each hospital. Patients discharged from each participating hospital were sampled on an 8-day rolling cycle to avert bias in selecting cases for review.[11] Data on the first 18 eligible cases discharged during each cycle were collected. Follow-up data were collected by medical record review and direct telephone follow-up at 90 days post-hospital discharge. Each hospital is audited on an annual basis by data quality coordinators to ensure completeness and accuracy of data abstraction. The University of Michigan is the HMS coordinating center.

Ascertainment of Outcomes

The primary outcome of interest was clinically diagnosed, image-confirmed hospital-associated venous thromboembolism, including proximal upper- or proximal lower-extremity deep vein thrombosis and pulmonary embolism. In order to be considered hospital acquired, venous thromboembolism events must have occurred on the third day after admission or later during an index hospitalization. The diagnosis of deep vein thrombosis was based on positive findings via compression Doppler ultrasound or venography, whereas pulmonary embolism was confirmed via computed tomography scan, ventilation perfusion scan, or pulmonary angiography. Venous thromboembolism outcomes were assessed out to 90 days from the date of index hospital admission. Patients transferred to an ICU or palliative care, and those who died during follow-up were censored; however, venous thromboembolism events that contributed to death or were the reason for transfer to the ICU were included. Patients who were alive and free of venous thromboembolism occurrence at 90 days following admission were right-censored. Telephone follow-up at 90 days was completed for 58% of patients. Medical record review at 90 days was completed for 100% of eligible patients.

Statistical Analysis

External Validation of Existing Risk Assessment Models. All eligible patients were included as an external validation sample for existing risk assessment models. Numerous risk factors thought to increase risk for venous thromboembolism as specified by each risk assessment model were assessed for all patients. Bivariable Cox regression was used to assess the independent associations between putative risk factors and 90-day venous thromboembolism. Cumulative risk scores based on the presence of individual risk factor associated weights for the Kucher,[3] Padua,[2] predictive IMPROVE,[4] and Intermountain[5] risk assessment models were calculated for each patient. In this manner, patients were assigned an "at-risk" status for each risk assessment model based on established cut points.[2-5] Cox regression models with gamma shared frailty by hospital were used to determine the hazards of developing venous thromboembolism for patients determined to be "at-risk" for each risk assessment model. Model discrimination was assessed via Harrell's C-index with 95% confidence intervals using the *somersd* package in Stata v.13 (StataCorp LP, College Station, Texas).[12,13] Calibration was assessed by comparing estimated incidence rates for both "low-risk" and "at-risk" groups for each of the existing risk assessment models. Event rates and hazard ratios for each of the represented scores across the scales of each risk assessment model were also investigated to assess calibration.