CHEST

Validation of the International Medical Prevention Registry on Venous Thromboembolism Bleeding Risk Score

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BACKGROUND: Recent guidelines recommend assessing medical inpatients for bleeding risk prior to providing chemical prophylaxis for VTE. The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) bleeding risk score (BRS) was derived from a well-defined population of medical inpatients but it has not been validated externally. We sought to externally validate the IMPROVE BRS.

METHODS: We prospectively collected characteristics on admission and VTE prophylaxis data each hospital day for all patients admitted for a medical illness to the Walter Reed Army Medical Center over an 18-month period. We calculated the IMPROVE BRS for each patient using admission data and reviewed medical records to identify bleeding events.

RESULTS: From September 2009 through March 2011, 1,668 inpatients met the IMPROVE inclusion criteria. Bleeding events occurred during 45 separate admissions (2.7%); 31 events (1.9%) were major and 14 (0.8%) were nonmajor but clinically relevant. Two hundred fifty-six patients (20.7%) had an IMPROVE BRS $\geq$ 7.0. Kaplan-Meier curves showed a higher cumulative incidence of major ($P = .02$) and clinically important (major plus clinically relevant nonmajor) ($P = .06$) bleeding within 14 days in patients with an IMPROVE BRS $\geq$ 7.0. An IMPROVE BRS $\geq$ 7.0 was associated with major bleeding in Cox-regression analysis adjusted for administration of chemical prophylaxis (OR, 2.6; 95% CI, 1.1-5.9; $P = .03$); there was a trend toward a significant association with clinically important bleeding (OR, 1.9; 95% CI, 0.9-3.7; $P = .07$).

CONCLUSIONS: The IMPROVE BRS calculated at admission predicts major bleeding in medical inpatients. This model may help assess the relative risks of bleeding and VTE before chemoprophylaxis is administered. CHEST 2016; 149(2):372-379

KEY WORDS: antibiotic therapy; deep venous thrombosis; pulmonary embolism

ABBREVIATIONS: BRS = bleeding risk score; EMR = electronic medical record; ICD-9 = International Classification of Disease, Ninth Revision; IMPROVE = International Medical Prevention Registry on Venous Thromboembolism; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin

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VTE, which comprise DVT and pulmonary embolism, is a global public health problem.[1,2] Hospitalization for an acute medical illness is a recognized predisposing factor for VTE,[3,4] and hospital-acquired VTE causes a broad range of acute and chronic ill effects. Within the United States alone, VTE accounts for between 60,000 and 300,000 deaths each year, the majority of which occur in the hospital.[5-8] The cumulative cost of acute and chronic complications from thromboembolic disease likely exceeds $1.5 billion each year in the United States and accounts for 1% of overall health-care costs in the developed world.[4,9,10] Chemical thromboprophylaxis can prevent hospital-acquired VTE and is demonstrably cost effective when compared with no prophylaxis.[11]

Guidelines designed to address the public health burden associated with hospital-acquired VTE recommend patients be assessed for thrombosis and bleeding risk on admission to the hospital. Those with a favorable risk-benefit profile should have chemoprophylaxis administered.[12-15] However, data indicate that the majority of eligible inpatients do not receive chemoprophylaxis.[16-18] Physicians who purposely withhold chemoprophylaxis in eligible patients cite concern over bleeding risk as their rationale.[19]

Prospective assessment of bleeding risk features prominently in the most recent American College of Physicians and American College of Chest Physicians (CHEST) guidelines for the prevention of VTE, but the guideline authors have noted the absence of a validated risk-assessment tool.[13,20,21] The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) investigators have identified significant risk factors for bleeding in acutely ill hospitalized medical patients and have developed a bleeding risk score (BRS).[22] This score has yet to be validated externally, limiting its applicability.[23] We sought to validate the IMPROVE BRS in a large population of hospitalized patients. We also reviewed actual prophylaxis practice patterns and assessed the effects that various prophylactic regimens have on the risk of bleeding and the performance of the score. Finally, we used the IMPROVE VTE risk score[24] to assign a risk-benefit category to all patients in our cohort.

Materials and Methods

This study was part of a hospital-wide quality improvement initiative aimed at improving the safety and efficacy of VTE prophylaxis. The Department of Clinical Investigations at our hospital waived the need for formal submission to the institutional review board. The details of the project were presented to the quality improvement committee, and we were granted approval by that committee to collect our data.

To monitor prophylaxis rates, in September 2009 we began prospective collection of relevant demographic and clinical variables from consecutive adult patients (≥ 18 years old) admitted to the Walter Reed Army Medical Center. This hospital uses an electronic medical record (EMR) that allowed us to generate a daily report with all variables of interest downloaded into a spreadsheet (e-Appendix 1). We included patients on the general medical wards and in the ICUs. The patient was considered to have received chemoprophylaxis only if the nurse documented its administration in the EMR.

Because our goal for this study was to provide external validation for the IMPROVE BRS, we excluded all patients from the database who did not meet the inclusion criteria used by the IMPROVE investigators.[22] All patients were ≥ 18 years of age and were admitted to the hospital with a medical illness. Patients were excluded if they were admitted for bleeding or if they were receiving treatment-dose anticoagulation on admission or during the hospitalization.

We searched the inpatient and outpatient EMRs for new bleeding diagnoses that occurred during hospital stays and within 30 days of discharge. We used *International Classification of Disease, Ninth Revision* (ICD-9) codes (Table 1) from the inpatient and outpatient EMRs, free-text fields from the summary and discharge notes in the EMR, and a hematocrit drop > 6 points to identify patients who may have bled during admission. All bleeding events were confirmed by manual chart audit, and event characteristics were abstracted. Bleeds were defined as major or clinically relevant nonmajor using the criteria outlined by the IMPROVE investigators (e-Appendix 2) and the International Society on Thrombosis and Haemostasis guidelines.[25] Minor bleeding events were not assessed. The sum of major and clinically relevant nonmajor bleeding events is referred to as "clinically important" bleeds throughout this text.

Statistics

Means with SDs and medians with interquartile ranges are provided for normally and nonnormally distributed values, respectively. For univariate analyses, continuous normally and nonnormally distributed variables were compared using the independent Student *t* test and

TABLE 1] ICD-9 Coding for Bleeding Events

Code	Bleeding Event
578.0	Hematemesis, vomiting blood
578.1	Blood in stool
578.9	Hemorrhage of GI tract unspecified
459.0	Hemorrhage unspecified
430	Subarachnoid hemorrhage
431	Intracerebral hemorrhage
432.0	Nontraumatic extradural hemorrhage
432.1	Subdural hemorrhage
432.9	Unspecified intracranial hemorrhage

ICD-9 = *International Classification of Disease, Ninth Revision.*