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CLINICAL RESEARCH STUDY

Variability in the use of thromboprophylaxis and outcomes in critically ill medical patients

Krista L. Lentine, MD, MS,[a] Kara E. Flavin[b], Michael K. Gould, MD, MS[b,c]

[a]Department of Medicine, Center for Outcomes Research and Division of Nephrology, Saint Louis University School of Medicine, St. Louis, Mo; [b]Department of Medicine, Division of Pulmonary and Critical Care Medicine, VA Palo Alto Health Care System; [c]Department of Medicine, Division of Pulmonary and Critical Care Medicine, Stanford University School of Medicine, Stanford, Calif.

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ABSTRACT

PURPOSE: To describe practices for preventing venous thromboembolism in critically ill medical patients and to identify associations between prophylactic measures and survival.

METHODS: We reviewed the records of all medical admissions to the intensive care units of a university hospital and an affiliated Veterans Affairs hospital over a 1-year period. We recorded patients' demographic characteristics, risk factors for venous thromboembolism, methods of prophylaxis, and in-hospital deaths.

RESULTS: We identified 272 critically ill medical patients who received intensive care for at least 24 hours. Some form of prophylaxis was used in 205 patients (75%), including pharmacologic prophylaxis alone in 55 (20%), mechanical prophylaxis alone in 102 (38%), and both methods in 48 (18%). In-hospital mortality rates were 23% (24/103) for patients who received pharmacologic prophylaxis, and 36% (61/169) for those who received mechanical prophylaxis alone or no prophylaxis ($P = .03$). After adjusting for demographic characteristics, risk factors for thrombosis and severity of illness, the odds of death were 55% lower in patients who received pharmacologic prophylaxis (odds ratio [OR] = 0.45; 95% confidence interval (CI): 0.22 to 0.93; $P = .03$). Similar results were obtained in propensity-adjusted and propensity-stratified analyses. Use of mechanical prophylaxis was not associated with survival (OR = 0.88; 95% CI 0.44 to 1.77; $P = .73$).

CONCLUSION: In this cohort of critically ill medical patients, pharmacologic but not mechanical thromboprophylaxis was associated with reduced risk of in-hospital death. This hypothesis must be tested in randomized trials.

Venous thromboembolism, a common cause of preventable mortality among hospitalized patients,[1,2] is estimated to account directly or indirectly for 10% of all in-hospital deaths,[3,4] 75% of which occur in nonsurgical settings.[4] Critically ill patients often have one or more risk factors for thromboembolism, including prolonged stasis from bed rest, heart failure, advanced age, and vascular injury from indwelling central venous catheters.[5,6] Although the risk and predictors of thromboemobolic disease have been studied in critically ill surgical and mixed medical-surgical groups,[7-10] the epidemiology of

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Requests for reprints should be addressed to Krista L. Lentine, MD, Saint Louis University Center for Outcomes Research, Salus Center, 2nd Floor, 3545 Lafayette Avenue, St. Louis, MO 63104.

E-mail address: lentine.krista@stanfordalumni.org.

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this complication among critically ill medical patients has been described incompletely.

Thromboprophylaxis may be especially important in patients whose critical medical illness may result in inadequate cardiopulmonary reserve to tolerate even anatomically small pulmonary emboli. Despite the potential importance of the problem, recent guidelines note that little is known about the effectiveness of prophylaxis in this group.[1]

Lack of data from well-designed studies may contribute to variability in the use of thromboprophylaxis in medical intensive care units. Reported utilization rates vary from 33% in one medical intensive care unit[11] to a markedly higher rate of 86% among a cohort of critically ill medical-surgical patients after caregivers received intensive education on the use of prophylactic measures.[12]

Prompted by the limited evidence regarding the effectiveness of routine thromboprophylaxis in critically ill medical patients, we performed a retrospective longitudinal cohort study to describe variability in the use of prophylactic measures and to identify associations between thromboprophylaxis and survival.

Methods

After obtaining approval from the Stanford University Administrative Panel on Human Subjects in Medical Research, we reviewed the records of consecutive admissions to the medical intensive care unit at Stanford and an affiliated Veterans Affairs hospital. Critically ill medical patients in both teaching hospitals are cared for by critical care attending physicians and housestaff under a "closed unit" system.

Patient selection

We included patients who were admitted to the intensive care unit for management of a primary medical (nonsurgical) illness between January 1, 2000, and December 31, 2000. We excluded patients who were admitted with a diagnosis of deep venous thrombosis, pulmonary embolism, gastrointestinal bleeding, or end-stage liver disease, as well as patients who were treated with anticoagulants prior to admission. We also excluded patients who died or were discharged from the intensive care unit within 24 hours of admission, patients who were previously enrolled in the study during the same hospital stay, and patients who received therapeutic doses of anticoagulants after admission.

Data collection

An investigator (KEF) reviewed the hospital records of all medical intensive care unit admissions and abstracted relevant data from hospital charts, records of bedside computerized flow sheets, and computerized reports of radiographic studies.

Variable measurement and definitions

Baseline characteristics included age, sex, and study site. Variables necessary for calculation of the acute physiology and chronic health evaluation (APACHE) II score were recorded for each patient at the time of admission to the intensive care unit.[13] We also noted requirements for mechanical ventilation and for hemodynamic support with intravenous vasopressors as markers of the severity of illness. Clinical risk factors for venous thromboembolism included active smoking within the month preceding admission, recent surgery, prior history of venous thromboembolism, known hypercoagulable states, past or present history of malignancy, the nephrotic syndrome, myocardial infarction within the preceding month, chronic heart failure, and acute or chronic paresis.

Mechanical prophylaxis at the study sites was performed using the combination of elastic stockings and intermittent pneumatic compression. Pharmacologic prophylaxis consisted of low-dose subcutaneous unfractionated heparin 5000 units twice daily or less than therapeutic doses of a low-molecular-weight heparin preparation (0.5 mg/kg or less of enoxaparin). We recorded the time between admission to the intensive care unit and the implementation of prophylaxis.

The primary outcome measure was in-hospital mortality. Secondary outcomes included episodes of clinically suspected and confirmed venous thromboembolism, length of stay in the intensive care unit, and length of stay in the hospital. We assumed that deep venous thrombosis was suspected clinically when compression ultrasound of an upper or lower extremity was performed, and that pulmonary embolism was suspected clinically when ventilation-perfusion lung scanning, spiral computed tomographic angiography of the chest, or pulmonary angiography was performed. We assumed that venous thromboembolism was present when the results of one or more of these tests had positive or high probability results.

Statistical analysis

Continuous variables are reported as means and standard deviations, and categorical variables are reported as counts and proportions. Simple comparisons between groups were performed using the Student *t*-test for continuous variables and the chi-squared test or Fisher exact test for categorical variables. The time to death between groups was compared by the product-limit (Kaplan-Meier) method. For all analyses, statistical significance was defined as a P value $<.05$.

Multivariable logistic regression was used to estimate the risk of death (odds ratio [OR]; 95% confidence interval [CI]) associated with thromboprophylaxis after adjustment for demographic characteristics, markers of the severity of illness, and risk factors for venous thromboembolism. A matrix of