Hospital Performance for Pharmacologic Venous Thromboembolism Prophylaxis and Rate of Venous Thromboembolism
A Cohort Study

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**IMPORTANCE** Hospitalization for acute medical illness is associated with increased risk of venous thromboembolism (VTE). Although efforts designed to increase use of pharmacologic VTE prophylaxis are intended to reduce hospital-associated VTE, whether higher rates of prophylaxis reduce VTE in medical patients is unknown.

**OBJECTIVE** To examine the association between pharmacologic VTE prophylaxis rates and hospital-associated VTE.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective, multicenter cohort study conducted at 35 Michigan hospitals participating in a statewide quality collaborative from January 1, 2011, through September 13, 2012. Trained medical record abstractors at each hospital collected data from 31,260 general medical patients. Use of VTE prophylaxis on admission, VTE risk factors, and VTE events 90 days after hospital admission were recorded using a combination of medical record review and telephone follow-up. Hospitals were grouped into tertiles of performance based on rate of pharmacologic prophylaxis use on admission for at-risk patients.

**MAIN OUTCOMES AND MEASURES** Association between hospital performance and time to development of VTE within 90 days of hospital admission.

**RESULTS** A total of 14,563 of 20,794 patients (70.0%) eligible for pharmacologic prophylaxis received prophylaxis on admission. The rates of pharmacologic prophylaxis use at hospitals in the high-, moderate-, and low-performance tertiles were 85.8%, 72.6%, and 55.5%, respectively. A total of 226 VTE events occurred during 1,765,449 days of patient follow-up. Compared with patients at hospitals in the highest-performance tertile, the hazard of VTE in patients at hospitals in moderate-performance (hazard ratio, 1.10; 95% CI, 0.74-1.62) and low-performance (hazard ratio, 0.96; 95% CI, 0.63-1.45) tertiles did not differ after adjusting for potential confounders. Results remained robust when examining mechanical prophylaxis, prophylaxis use throughout the hospitalization, and subsequent inpatient stays after discharge from the index hospitalization.

**CONCLUSIONS AND RELEVANCE** The occurrence of 90-day VTE in medical patients after hospitalization is low. Patients who receive care at hospitals that have lower rates of pharmacologic prophylaxis do not have higher adjusted hazards of VTE, even after accounting for individual receipt of pharmacologic prophylaxis. Efforts to increase rates of pharmacologic VTE prophylaxis in hospitalized medical patients may not substantively reduce this adverse outcome.
Although pharmacologic venous thromboembolism (VTE) prophylaxis has been reported to reduce the incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE) in medical patients, rates of pharmacologic prophylaxis remain low in many US hospitals. As a result, numerous national quality improvement efforts have focused on improving pharmacologic VTE prophylaxis. The Joint Commission and the Centers for Medicare and Medicaid Services recently introduced a performance measure for VTE prophylaxis, which requires reporting the percentage of all medical patients who received prophylaxis or had documentation on why no prophylaxis was provided. The intended goal of this measure is to increase rates of appropriate prophylaxis in hospitalized patients.

Although local and regional efforts to increase pharmacologic prophylaxis rates have been associated with reductions in VTE, these programs have traditionally included populations at higher risk of this outcome, such as surgical and critically ill patients. Whether increasing rates of pharmacologic prophylaxis will result in decreased VTE events in general medical patients remains unknown.

The Michigan Hospital Medicine Safety (HMS) Consortium, a payer-funded regional quality collaborative with a goal of reducing adverse events in hospitalized medical patients, has been collecting detailed data, including patient demographics, VTE risk factors, VTE prevention strategies, and clinical outcomes, for patients in select hospitals across Michigan. Using data from the HMS Consortium, we sought to evaluate the association between rates of pharmacologic VTE prophylaxis and hospital-associated VTE in general medical patients in a diverse group of hospitals.

Methods

Study Setting and Participants

The HMS Consortium is a group of hospitals working to prevent adverse events in hospitalized medical patients in Michigan through creation of a data registry and sharing of best practices. Although participation is voluntary, each hospital receives payments for participating in the consortium and for data collection. Because the purpose of the HMS Consortium is to measure and improve the quality of existing care practices, this project received a “not regulated” status by the University of Michigan Medical School’s Institutional Review Board, and informed consent was not required.

Eligible patients include those admitted to a medicine service for 2 days or longer. Patients are not eligible for entry into the data registry if they meet any of the following criteria: (1) age younger than 18 years, (2) pregnant, (3) any surgical procedure during the admission, (4) direct admission to an intensive care unit, (5) direct admission for palliative care, (6) diagnosis of VTE in the 6 months before admission, (7) admitted for presumed VTE, (8) admitted under observation status, and (9) readmitted within 90 days of discharge from an admission included in the registry. Otherwise eligible study patients entered into the data registry were excluded from this particular analysis if any of the following applied: receiving systemic anticoagulation for any reason, contraindications to pharmacologic prophylaxis, and/or at low risk for VTE (Caprini score <2) given low inherent risk for VTE.

Clinical data on patients are collected through a standardized process at each hospital using dedicated, trained medical record abstractors. Patients discharged from each participating hospital are sampled on an 8-day rolling cycle to avert bias in selecting cases for review. Data on the first 18 eligible patients discharged during each cycle are collected. Follow-up data are collected by medical record review and direct telephone follow-up at 90 days after 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 serves as the HMS Consortium coordinating center.

Ascertainment of Outcomes

The primary outcome of interest was clinically diagnosed, image-confirmed, hospital-associated VTE, including proximal upper- or lower-extremity DVT and PE. The VTE events that occurred during the index hospitalization must have occurred on the third day of the hospital stay or later to be attributable to the facility. The diagnosis of DVT required confirmation via Doppler ultrasonography or venography, whereas PE required confirmation via computed tomography, ventilation perfusion scan, or pulmonary angiography. The VTE events identified solely by telephone follow-up were included if patients reported a diagnosis of an acute VTE and treatment consistent with acute VTE. The VTE outcomes were assessed until 90 days from the date of hospital admission. Patients transferred to an intensive care unit or palliative care and those who died during follow-up were censored. However, the VTE events that contributed to death or were the reason for transfer to the intensive care unit were captured. Patients who were alive and free of VTE occurrence at 90 days after admission were right-censored. Medical record review at 90 days was completed in 20,691 (100%) of eligible patients discharged alive, including those discharged to home and post-acute care settings, at every hospital. Among the 19,026 patients eligible for telephone follow-up, successful telephone follow-up was completed for 10,667 patients (56.1%). Rates of telephone follow-up did not differ among the hospital performance tertiles.

Hospital Performance Metrics

Hospital performance for VTE prophylaxis was based on the mean rate of administration of acceptable pharmacologic prophylaxis on day 1 or 2 of hospitalization in eligible patients. The HMS Consortium deemed the following pharmacologic prophylaxis regimens as acceptable: heparin, 5000 U twice daily; heparin, 5000 U 3 times daily; heparin, 7500 U 3 times daily (for morbid obesity); enoxaparin, 40 mg/d; enoxaparin, 30 mg/d (for creatinine clearance <30 mL/min); enoxaparin, 30 mg twice daily; dalteparin, 5000 U daily; or fondaparinux, 2.5 mg/d.

Covariates of Interest

Detailed data on patient demographics, medical history, physical examination findings, laboratory, and medication use were collected, including those needed to calculate the Caprini risk score. Patients were deemed at risk for VTE if their Caprini...
score was 2 or higher. Contraindications to pharmacologic prophylaxis included gastrointestinal or genitourinary bleeding within the last 6 months; high-bleeding-risk procedure (eg, liver or renal biopsy); thrombocytopenia (platelet count <50 × 10⁹/μL [to convert to ×10⁹/L, multiply by 1]); heparin-induced thrombocytopenia; coagulopathy (hemophilia, prothrombin time >18 seconds, or international normalized ratio >2); intracranial bleeding within the last year; hypersensitivity to unfractionated or low-molecular-weight heparin; severe head, spinal cord, or extremity trauma within the 24 hours before admission; or intracranial lesion, neoplasm, and/or monitoring device. Admissions to a hospital within 90 days from a patient entering the study were identified.

Statistical Analysis

Hospitals were aggregated into performance tertiles based on their respective rates of pharmacologic prophylaxis on admission. Differences in patient and hospital characteristics among the performance tertiles (relative to the high-performance hospitals) were assessed via χ² tests for categorical variables or t tests for continuous variables.

Cox proportional hazards regression models, with γ-shared frailty by hospital (to account for potential clustering effects within each of the 35 hospitals), were fit to assess whether risk-adjusted hazards of VTE differed by performance tertile. The proportional hazards assumption across performance groups was assessed via the global test based on Schoenfeld residuals.

Our primary outcome was time to VTE from index hospitalization admission. We also examined time to death as a secondary outcome. Models included contextual-level dummy variables for performance tertile for each patient, and the high-performance hospitals group was set as the referent group. Additional covariates were included in the adjustment model if differences were detected between the moderate- and/or low-performance hospitals relative to the high-performance hospitals group. The final model was also adjusted for the following patient-level covariates: age, sex, race, length of stay, history of cancer, central venous catheter use at the time of admission or during hospitalization, and receipt of pharmacologic prophylaxis on day 1 and/or day 2 of the index hospitalization.

Additional Cox proportional hazards regression models specified a priori were fit during sensitivity analyses. In addition to the covariates included in the main models, sensitivity analysis 1 adjusted for whether the patient had mechanical prophylaxis ordered on day 1 and/or day 2 of the index hospitalization. Sensitivity analysis 2 included the same covariates as the main models; however, VTEs that occurred after a postdischarge inpatient stay (including post–acute care settings) were recoded as nonevents. Sensitivity analysis 3 was limited to those patients with complete longitudinal pharmacologic prophylaxis administration information throughout the index hospitalization. The covariates in sensitivity analysis 3 were identical to the main models; however, acceptable patient-level receipt of pharmacologic prophylaxis was made more robust and defined as 80% or more of hospital-days with appropriate administration of pharmacologic prophylaxis: 1 of 1 dose for daily regimens, 2 of 2 doses for twice daily regimens, or 2 of 3 doses for 3 times daily regimens. All analyses were performed in Stata statistical software, version 13.0 (StataCorp).

Results

Data on 31 260 eligible patients were collected from January 1, 2011, through September 13, 2012, from 35 hospitals. A total of 10 466 patients were excluded as ineligible for pharmacologic prophylaxis (Figure 1). Of 20 794 patients included in the analy-
sis, 14,563 (70.0%) received pharmacologic prophylaxis on admission. The mean pharmacologic prophylaxis rate for each hospital, aggregated by performance tertile, is presented in Figure 2.

Selected patient and hospital characteristics by performance group are given in Table 1. The mean age was 65.9 years, and 11,815 (56.8%) were female. Patients were predominantly white, were insured by Medicare, and had a median length of stay of 4 days. A total of 6,877 patients had a length of stay of 5 days or longer. Relative to the high-performance hospitals, patients in moderate- and/or low-performance hospitals were more likely to be white, less likely to have a history of cancer, and had more mechanical prophylaxis ordered on admission. Caprini scores among patients receiving pharmacologic prophylaxis on admission did not differ by performance group.

The 20,794 patients contributed a total of 176,449 patient-days of follow-up (Figure 1). A total of 1,223 patients were censored because of death, whereas 425 patients were censored because of transfer to intensive or palliative care. Of the 226 VTEs that occurred during the observation period, 88 (38.9%) were PEs and 138 (61.1%) were DVTs. Only 34 of the 226 VTEs (15.0%) occurred during the index hospitalization. Of the 192 VTEs occurring after discharge, 31 (16.1%) were identified via telephone follow-up. The percentage of VTEs identified by telephone follow-up did not differ by performance group. A total of 166 patients (73.5%) who experienced a VTE event received pharmacologic prophylaxis on admission.

Table 2 gives the incidence rates of VTE and death by performance group. A statistically significant difference in the incidence of post-

Figure 2. Pharmacologic Prophylaxis on Admission Stratified by Hospital Venous Thromboembolism Prophylaxis Performance in 35 Hospitals

Table 1. Select Patient and Hospital Characteristics Stratified by Hospital VTE Prophylaxis Performance*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High-Performance Hospitals (n = 5,514)</th>
<th>Moderate-Performance Hospitals (n = 7,897)</th>
<th>Low-Performance Hospitals (n = 7,383)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>5,514</td>
<td>7,897</td>
<td>7,383</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>66.7 (17.8)</td>
<td>64.5 (17.5) b</td>
<td>67.0 (17.6) b</td>
</tr>
<tr>
<td>Female sex</td>
<td>3,118 (56.5)</td>
<td>4,329 (54.8)</td>
<td>4,368 (59.2) b</td>
</tr>
<tr>
<td>White race</td>
<td>3,867 (70.1)</td>
<td>6,396 (81.0) b</td>
<td>5,865 (79.4) b</td>
</tr>
<tr>
<td>Length of stay, mean/median, d</td>
<td>4.3/3.0</td>
<td>4.5/3.0</td>
<td>4.5/4.0 b</td>
</tr>
<tr>
<td>Caprini score, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>5.75 (2.42)</td>
<td>5.54 (2.51) b</td>
<td>5.61 (2.48) b</td>
</tr>
<tr>
<td>Patients receiving pharmacologic prophylaxis</td>
<td>5.84 (2.49)</td>
<td>5.81 (2.44) b</td>
<td>5.96 (2.44) b</td>
</tr>
<tr>
<td>History of cancer</td>
<td>1,231 (22.3)</td>
<td>1,686 (21.4)</td>
<td>1,417 (19.1) b</td>
</tr>
<tr>
<td>Prior VTE</td>
<td>304 (5.51)</td>
<td>449 (5.69)</td>
<td>386 (5.23)</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>12 (0.22)</td>
<td>29 (0.37)</td>
<td>9 (0.12)</td>
</tr>
<tr>
<td>Central venous catheter during admission</td>
<td>618 (11.2)</td>
<td>994 (12.6) b</td>
<td>804 (10.9)</td>
</tr>
<tr>
<td>Pharmacologic prophylaxis on admission</td>
<td>4,729 (85.8)</td>
<td>5,734 (72.6) b</td>
<td>4,100 (55.5) b</td>
</tr>
<tr>
<td>Mechanical prophylaxis ordered on admission</td>
<td>1,137 (20.6)</td>
<td>2,859 (36.2) b</td>
<td>2,429 (32.9) b</td>
</tr>
<tr>
<td>Pharmacologic and/or mechanical prophylaxis</td>
<td>5,054 (91.7)</td>
<td>6,645 (84.2) b</td>
<td>5,233 (70.9) b</td>
</tr>
<tr>
<td>Major bleeding*</td>
<td>9 (0.32)</td>
<td>12 (0.30) b</td>
<td>7 (0.26)</td>
</tr>
<tr>
<td>No. of hospitals</td>
<td>11</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Bed size, mean (SD)</td>
<td>384.7 (333.4)</td>
<td>387.8 (215.9)</td>
<td>324.0 (98.7)</td>
</tr>
<tr>
<td>Teaching status</td>
<td>7 (66.7)</td>
<td>8 (66.7) b</td>
<td>7 (58.3) b</td>
</tr>
</tbody>
</table>

Abbreviation: VTE, venous thromboembolism.
* Data are presented as number (percentage) unless otherwise indicated.
** Statistically significant difference compared with high-performance hospitals (P < .05).
* Major bleeding only among those receiving pharmacologic prophylaxis on admission. Major bleeding during hospitalization among those receiving pharmacologic prophylaxis was captured and defined as presumed bleeding with a decrease in hemoglobin of 3 g/dL or more (to convert to grams per liter, multiply by 10) or bleeding that required 2 U or more of packed red blood cells.
discharge VTE was detected between the moderate- and low-performance hospitals (P = .04); however, there was no difference in overall VTE incidence by performance group. Incidence of death did not differ by performance group.

The risk-adjusted hazards of VTE are given in Table 3. A length of stay of 5 days or longer was associated with a 2-fold increase in the hazard of VTE (hazard ratio [HR], 2.07; 95% CI, 1.58-2.71). History of cancer was associated with a 53% increased hazard (HR, 1.53; 95% CI, 1.14-2.03), and central venous catheters were associated with a nearly 3-fold increase in the hazard of VTE (HR, 2.86; 95% CI, 2.11-3.87). The hazard of VTE did not differ by receipt of pharmacologic prophylaxis on admission (HR, 1.09; 95% CI, 0.80-1.48).

Hazards of VTE were proportional across performance groups (P = .13). Relative to high-performance hospitals, hazards of VTE at 90 days were not significantly different in the moderate-performance (HR, 1.10; 95% CI, 0.74-1.62) or low-performance (HR, 0.96; 95% CI, 0.63-1.45) hospitals, suggesting that hospital performance was not associated with risk of subsequent VTE. In addition, on modeling hospital performance as a continuous variable, increasing hospital performance was not significantly associated with the risk-adjusted hazard of VTE (HR, 1.00; 95% CI, 0.99-1.01). The Kaplan-Meier survival estimates by performance group are illustrated in Figure 3. Survivor functions did not differ by performance group (Wilcoxon test for equality, P = .42).

**Sensitivity Analyses**

The risk-adjusted hazard of VTE did not differ by performance group, even after additional adjustment for mechanistic prophylaxis ordered on admission (eTable 1 in the Supplement). A total of 103 of the 226 VTE events occurred in patients after a subsequent, postdischarge inpatient stay. On reclassifying these as nonevents, the risk-adjusted hazard of VTE also did not vary by performance group (eTable 2 in the Supplement). A total of 16298 patients had complete data on pharmacologic prophylaxis administration throughout the hospital stay. On defining patient-level acceptable prophylaxis as receipt of appropriate pharmacologic prophylaxis for more than 80% of hospital-days, the risk-adjusted hazard of VTE again did not differ by performance group (eTable 3 in the Supplement).

**Discussion**

In this study of more than 20 000 patients at 35 Michigan hospitals, we observed that the rate of 90-day hospital-associated VTE for general medical patients is low. Furthermore, patients who received care at hospitals with lower rates of pharmacologic prophylaxis use on admission did not have higher adjusted hazards of clinical VTE. These results were robust to sensitivity analyses that account for mechanical prophylaxis ordered on admission, adherence to prophylaxis throughout the hospitalization, and consideration of subsequent inpatient stays that occur after discharge but before the diagnosis of VTE. Collectively, our findings imply that efforts to broadly increase rates of pharmacologic prophylaxis in noncritically ill general medical patients may not yield significant reductions in hospital-associated DVT or PE.

Although lower than in studies that use routine screening techniques, the frequency of hospital-associated VTE observed in our study is consistent with reports that describe clinically diagnosed or symptomatic VTE in medical patients. Because standard clinical practice does not include screening for VTE events and the clinical importance of asymptomatic VTE remains debatable, our focus on symptomatic or clinically diagnosed VTE is important and relevant. In a retrospective cohort study of medical patients discharged from 370 acute care hospitals, hospital-associated VTE was clinically diagnosed in 0.4% of patients at 30 days after discharge. However, the 30% pharmacologic prophylaxis rate reported in that study is substantially lower than ours. A systematic review of randomized clinical trials that evaluated the effect of pharmacologic DVT prophylaxis in medical and stroke pa-

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**Table 2. Incidence of VTE and Death (per 10 000 Patient-Days) Stratified by Hospital VTE Prophylaxis Performance**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Patients</th>
<th>High-Performance Hospitals (n = 5514)</th>
<th>Moderate-Performance Hospitals (n = 7897)</th>
<th>Low-Performance Hospitals (n = 7383)</th>
<th>Total (N = 20 794)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTEs during index hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>226</td>
<td>1.27</td>
<td>1.42</td>
<td>1.15</td>
<td>1.28</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>88</td>
<td>0.43</td>
<td>0.61</td>
<td>0.43</td>
<td>0.50</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>138</td>
<td>0.84</td>
<td>0.81</td>
<td>0.72</td>
<td>0.78</td>
</tr>
<tr>
<td>All VTEs at 90 days after admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1260</td>
<td>7.29</td>
<td>7.23</td>
<td>6.92</td>
<td>7.14</td>
</tr>
</tbody>
</table>

Abbreviation: VTE, venous thromboembolism.

* Statistically significant difference in incidence detected on pairwise comparison within row. Unless noted, no other significant differences in incidence rates between performance groups were detected.

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patients reported symptomatic DVT rates of 0.21% to 0.97% at 120 days after randomization depending on setting and prophylaxis use. Rates of PE were also low and varied from 0.53% to 1.1%. Despite similar rates of VTE, direct comparisons between our findings and the published literature are difficult given varying inclusion criteria, duration of follow-up, and differing methods of outcome ascertainment.

Why might higher rates of prophylaxis fail to be associated with reduced rates of hospital-associated VTE in general medical patients? Although several investigators have reported reduced rates of VTE through increased use of pharmacologic prophylaxis, many of these studies include populations with higher baseline risk of VTE, such as surgical patients, intensive care unit patients, or patients with cancer. A recent report describing use of a clinical decision support intervention at a 3-hospital system found a significant increase in pharmacologic prophylaxis use for all patients, but a reduction in VTE was only found in the subset of surgical patients. However, another report that evaluated the effect of hospital performance on the Surgical Care Improvement Project VTE measure failed to find an association between prophylaxis rates and VTE outcomes. Although other studies that included medical patients have found a significant benefit of improving prophylaxis rates, they have methodologic limitations that prevent a full understanding of the population studied or have focused only on in-hospital outcomes, potentially missing many postdischarge events.

In addition, although randomized clinical trials have revealed the benefit of pharmacologic prophylaxis in medical patients, the population cared for on an average general medicine ward differs from patients enrolled in clinical trials in important ways. For example, the median length of stay for patients in our study was 4 days, whereas the lengths of stay for patients enrolled in large VTE prophylaxis trials routinely exceed 1 week. Furthermore, the duration of prophylaxis in efficacy trials varies from 6 to 10 days, yet most guidelines suggest discontinuing prophylaxis at hospital discharge—a practice that is common in US hospitals. Thus, in real-world settings, patients actually receive relatively short courses of prophylaxis. These truncated courses of prophylaxis may not provide as much clinical benefit, as suggested by the fact that 73.5% of patients ultimately diagnosed as having VTE received pharmacologic prophylaxis on admission in this study and that 85.0% of events occurred after discharge from the initial hospitalization. Finally, patients in trials are often carefully selected because they are known to be at high risk of VTE and are thus more likely to benefit from prophylaxis. Correspondingly, recent clinical practice guidelines emphasize strategies to more carefully select patients who may benefit from pharmacologic prophylaxis. Despite this, many VTE prevention experts and improvement toolkits (such as those endorsed by the Agency for Healthcare Research and Quality) argue that most medical patients have 1 or more risk factors for VTE and therefore up to 95% of hospitalized patients may warrant prophylaxis. Our study questions the wisdom of this approach and suggests that analyses dedicated to general medical patients are warranted before such sweeping policy changes.

Our study has several important limitations. First, low rates of VTE may have limited our ability to show benefit for higher

Table 3. Risk of Venous Thromboembolism by Patient and Hospital Characteristics

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 years</td>
<td>1.34 (1.01-1.77)</td>
<td>.04</td>
</tr>
<tr>
<td>Length of stay ≥5 days</td>
<td>2.07 (1.58-2.71)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patient receipt of pharmacologic prophylaxis on admission</td>
<td>1.09 (0.80-1.48)</td>
<td>.58</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.53 (1.14-2.03)</td>
<td>.004</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td>2.86 (2.11-3.87)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.92 (0.71-1.20)</td>
<td>.56</td>
</tr>
<tr>
<td>White race</td>
<td>1.04 (0.75-1.46)</td>
<td>.81</td>
</tr>
<tr>
<td>Moderate-performance hospitals†</td>
<td>1.10 (0.74-1.62)</td>
<td>.65</td>
</tr>
<tr>
<td>Low-performance hospitals†</td>
<td>0.96 (0.63-1.45)</td>
<td>.84</td>
</tr>
</tbody>
</table>

† Referent group was high-performance hospitals. A Cox proportional hazards regression model with γ-shared frailty was fit to account for potential clustered effects within each of the 35 hospitals. The total number of venous thromboembolisms (failures) was 226.

Figure 3. Kaplan-Meier Survival Curve Showing Estimates of Venous Thromboembolism (VTE)-Free Survival by Hospital VTE Prophylaxis Performance

Numbers in parentheses represent the number of VTE events within each performance group that occur at each time point. For example, 5514 patients were in the high-performance hospitals, and 12 had VTEs between admission and 15 days after admission. The numbers preceding the parentheses represent the number of patients remaining at risk of VTE for each time point reflected on the x-axis. This still-at-risk number accounts for censorship due to having a VTE, death, and transfers to intensive care unit or palliative care.
rates of VTE prophylaxis. However, because we evaluated the effect of prophylaxis in more than 20,000 patients, any benefit from higher rates of pharmacologic prophylaxis is likely to be small and not clinically meaningful. Second, a recent study suggested that surveillance bias may limit the validity of VTE rate comparisons among hospitals. Although this remains a potential concern, it is most relevant for the diagnosis of events during hospitalization; because 192 of our VTE events (85.0%) occurred after hospital discharge, surveillance bias is unlikely to substantially affect our findings. Third, because we did not standardize the process for risk-assessing patients at each hospital, we do not know whether health care professionals at hospitals in the low-performance tertile were better at identifying at-risk patients or used a system that improved identification of particularly high-risk patients. However, this limitation is mitigated by our analytic approach in which we used a Caprini score greater than 2 to define patients who were at risk for VTE and by the observation that mean Caprini scores did not differ by hospital performance tertile in patients receiving prophylaxis. Although the criterion standard for risk assessment in medical patients is unknown, the Caprini score is linearly correlated with risk of VTE in surgical and medical patients. Finally, although all patients had complete medical record review at 90 days after discharge, telephone follow-up to identify events without documentation in the medical record averaged only 56.1%. Although it is possible that some VTE events after discharge were missed, the rate of telephone follow-up did not differ among the performance tertiles.

These limitations notwithstanding, our study has notable strengths. We report real-world data from a large group of diverse hospitals and evaluated the impact of VTE prophylaxis rates in settings generalizable to most US hospitals. Our data were collected in a standard fashion by trained medical record abstractors with audits to ensure reliability, and we used clinically meaningful outcomes with VTE events until 90 days after hospital admission. To our knowledge, this is the first large-scale study that has assessed patient- and hospital-level VTE prophylaxis rates and outcomes for a population of this nature in such detail. Finally, the inclusion of several sensitivity analyses (including more stringent definitions of appropriate prophylaxis) that corroborate our results strengthens the validity of our findings.

Our study has substantial implications for efforts to reduce rates of hospital-associated VTE. First, because rates of VTE at 90 days in noncritically ill, general medical patients are low, strategies to increase overall VTE performance may not result in a meaningful effect. Performance measures or quality improvement efforts that indiscriminately target all patients with any risk factor may result in overprophylaxis, producing an unintended increase in harms associated with such treatment (eg, bleeding, patient discomfort, and cost) without the benefit of VTE reduction. Second, our findings suggest that efforts to better identify subsets of general medical patients at sufficient risk for VTE to warrant pharmacologic prophylaxis are needed. Correspondingly, approaches to avoid pharmacologic prophylaxis and its attendant risks in patients who are at otherwise low risk of this outcome are necessary.

Conclusions

Continued efforts to increase prophylaxis rates in medical patients without nuanced risk targeting may not lead to reductions in hospital-associated VTE. A new paradigm that incorporates a tailored, evidence-based, pragmatic approach to VTE prevention in hospitalized general medical patients is needed.

REFERENCES


ARTICLE INFORMATION

Accepted for Publication: June 6, 2014.
Published Online: August 18, 2014.

Author Contributions: Drs Flanders and Greene had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Flanders, Greene, Paje, Lee, Barron, Share, Bernstein.
Acquisition, analysis, or interpretation of data: Flanders, Greene, Grant, Kaatz, Paje, Barron, Chopra, Bernstein.
Drafting of the manuscript: Flanders, Greene, Lee, Barron, Chopra.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Greene, Barron, Chopra.
Obtained funding: Flanders, Share.
Administrative, technical, or material support: Flanders, Paje, Lee, Barron, Share, Bernstein.
Study supervision: Flanders, Grant, Bernstein.
Conflict of Interest Disclosures: Dr Flanders reports receiving compensation for consultancies for the Institute for Healthcare Improvement and the Society of Hospital Medicine; royalties from Wiley Publishing; honoraria for various talks at hospitals as a visiting professor; grants from the Centers for Disease Control and Prevention Foundation, Blue Cross Blue Shield of Michigan, Michigan Health and Hospital Association, and the Agency for Healthcare Research and Quality; and compensation for expert witness testimony. Dr Chopra reports receiving grant support from Blue Cross Blue Shield of Michigan. Dr Grant reports receiving royalties from Wiley Publishing and compensation for expert witness testimony. Dr Kaatz reports receiving compensation for consultancies for Boehringer Ingelheim, Daiichi Sankyo, Janssen, and Bristol-Meyers Squibb. Dr Paje reports receiving compensation for a consultancy for Rush University Medical Center. Dr Barron reports receiving support for travel for this study from Spectrum Health Hospital. Dr Bernstein reports receiving compensation as a consultant for Blue Care Network and the Michigan Department of Community Health, honoraria for various talks, and grants from Blue Cross Blue Shield of Michigan, Michigan Health and Hospital Association, Department of Veterans Affairs, National Institutes of Health, and the Agency for Healthcare Research and Quality. No other disclosures were reported.
Funding/Support: This study was supported through funding from Blue Cross Blue Shield of Michigan.
Role of the Funder/Sponsor: Blue Cross Blue Shield of Michigan supported data collection at each participating site and funded the data coordinating center but had no role in study concept, interpretation of findings, or preparation, review, or final approval of the manuscript.
Previous Presentations: The general overview and results of this study were presented at the Society of General Internal Medicine Annual Meeting; April 26, 2013, Denver, Colorado; and Society of Hospital Medicine Annual Meeting; May 17, 2013, National Harbor, Maryland.
Additional Contributions: Andrew Hickner, MSI, and Latoya Kuhn, MPH, proofread the manuscript and assisted with the submission process.
 Venous Thromboembolism

Research  Original Investigation


