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Concept and design: All authors.

Acquisition, analysis, or interpretation of data: Pottegård, Pedersen, Schmidt, Gaist.

Drafting of the manuscript: Pottegård, Pedersen, Gaist.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Pottegård.

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Administrative, technical, or material support: Pottegård.

Supervision: Pedersen, Schmidt, Friis, Gaist.

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LESS IS MORE

Use of Venous Thromboembolism Prophylaxis in Hospitalized Patients

National guidelines recommend objective risk stratification for venous thromboembolism (VTE) in hospitalized medical patients. The Padua Prediction Score risk assessment model is recommended to categorize patients as high or low risk. The Michigan Hospital Medicine Safety Consortium (HMS), a state-wide quality collaborative aimed at preventing adverse events in hospitalized medical patients, collects detailed data on VTE risk factors, prophylactic treatment, and outcomes. Using data from the HMS, we sought to determine whether patients in this cohort were receiving appropriate VTE prophylaxis.

Methods | Patients admitted to a non-intensive care medicine unit for 2 or more days were eligible for inclusion; data were collected through a standardized process at each hospital. Using the Padua Prediction Score risk assessment model, we categorized patients on admission as low or high risk for VTE events. For high-risk patients, contraindications to pharmacologic prophylaxis were assessed. Excessive VTE prophylaxis was defined as pharmacologic or mechanical prophylaxis for low-risk patients, pharmacologic prophylaxis for high-risk patients with a contraindication to anticoagulation, and the combination of pharmacologic and mechanical prophylaxis in all cases. Underuse of VTE prophylaxis was defined as no pharmacologic prophylaxis in high-risk patients without a contraindication to anticoagulation and no prophylaxis (pharmacologic or mechanical) in high-risk patients with a contraindication to anticoagulation. Appropriate pharmacologic prophylaxis included any of the following on day 1 and/or day 2 of the index hospitalization: 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. The HMS-defined contraindications include any of the following: bleeding present upon hospital admission; intracranial hemorrhage within the past year; other hemorrhage within the last 6 months; coagulopathy, hemophilia, or other significant bleeding disorder; and platelet levels lower than 50 × 10⁹/L (to convert to × 10⁹ per liter, multiply by 1.0). Hospitals were rank ordered according to rates of excess VTE prophylaxis across low- and high-risk patients and rates of underuse of VTE prophylaxis in high-risk patients. Rank of hospital excess use and underuse of VTE prophylaxis were compared using a Pearson correlation coefficient.

Excessive VTE prophylaxis was assessed using descriptive variables. Odds ratios, 95% CIs, and P values for excess prophylaxis were calculated using logistic generalized estimating equation models, accounting for hospital clustering. Findings were considered significant at P < .05. Because the purpose of the HMS is to measure and improve the quality of existing medical practice, this project received a “not regulated” status by the University of Michigan Medical School institutional review board.

Results | Between January 1, 2015, and December 21, 2016, data were collected on 44,775 eligible patients across 52 Michigan hospitals. Mean (SD) patient age was 64.7 (18.4) years; 24,742 (55.3%) were women. The mean (SD) length of hospital stay was 4.4 (4.6) days (median, 3.0 days). Of the eligible patients, 32,549 were assessed as low-risk for VTE, whereas 1804 were at high risk with a contraindication for pharmacologic prophylaxis and 10,422 were at high risk without a contraindication for pharmacologic prophylaxis.
Excess prophylaxis was used in 25,367 low-risk patients (77.9%), 3,366 high-risk patients (32.3%) without a contraindication to prophylaxis, and 485 high-risk patients (26.9%) with a contraindication to pharmacologic prophylaxis (Table). The oddsofreceivingexcessprophylaxisforlow-vshigh-riskpatientswas3.26(95%CI,2.36-4.51;P<.001).The rate of excess VTE prophylaxis varied between hospitals, with rates rangingfrom8.2%to84.6%inhigh-riskpatients(mean[SD],32.8%[21.4%]) and from 15.5% to 99.6% in low-risk patients (mean [SD], 79.7% [19.8%]) (Figure).

In the 12,226 high-risk patients, VTE prophylaxis was underused in 2,693 individuals (22.0%) and was more prevalent in those without a contraindication to pharmacologic prophylaxis (2,467 [23.7%] vs 226 [12.5%]; P < .001). As with low-risk patients, rates of VTE prophylaxis underuse in high-risk patients varied by hospital (range, 4.6%-62.1%; mean [SD], 21.3% [11.7%]) (Figure). Hospitals with higher rates of excessive VTE prophylaxis had lower rates of prophylaxis underuse in high-risk patients (Pearson correlation coefficient, −0.48; 95% CI, −0.66 to −0.23; P < .001).

Discussion | In this study, anticoagulant use among low-risk patients (18,584 [57.1%]) was the most important contributor to excess use of VTE prophylaxis. Excess use of mechanical VTE prophylaxis (almost exclusively sequential compression devices) was common among both low-risk patients (15,417 [47.4%]) and high-risk patients without a contraindication to anticoagulation (3,366 [32.3%]). When combining low- and high-risk patients, the total rate of excessive VTE prophylaxis was 65.3%.

The 22.0% rate of underuse of VTE prophylaxis was significantly lower than the 65.3% rate of excessive prophylaxis and is lower than the rates of underuse previously described in medical patients.4 Efforts aimed at improving VTE prophylaxis at local, regional, and national levels have been suc-

Table. Excess Prophylaxis Use by Risk Class in 44,775 Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Excess Prophylaxis, No. (%)</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Mechanical</td>
<td>Pharmacologic</td>
</tr>
<tr>
<td>Padua Prediction Score category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk (n = 32,549)</td>
<td>25,367 (77.9)</td>
<td>6,783 (20.8)</td>
<td>9,950 (30.6)</td>
</tr>
<tr>
<td>High risk (n = 12,226)</td>
<td>3,851 (31.5)</td>
<td>NA</td>
<td>221 (1.8)</td>
</tr>
<tr>
<td>With contraindications (n = 1,804)</td>
<td>485 (26.9)</td>
<td>NA</td>
<td>221 (12.3)</td>
</tr>
<tr>
<td>Without contraindications (n = 10,422)</td>
<td>3,366 (32.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; OR, odds ratio.

* Padua risk score elements: active cancer, prior venous thromboembolism, reduced mobility, known thrombophilia, recent trauma and/or surgery, age 70 y or older, heart and/or respiratory failure, acute myocardial infarction or ischemic stroke, acute infection and/or rheumatologic disorder, body mass index 30 or higher (calculated as weight in kilograms divided by height in meters squared), and hormonal treatment. High risk, 4 points or more; low risk, less than 4 points.

b Contraindications to pharmacologic prophylaxis. The Hospital Medicine Safety Consortium–defined contraindications include any of the following: bleeding present upon hospital admission; intracranial hemorrhage within the past year; other hemorrhage within the last 6 mo; coagulopathy, hemophilia, or other significant bleeding disorder; platelet level lower than 50 × 10^9/μL (to convert to × 10^9 per liter, multiply by 1.0).

Excess prophylaxis was used in 25,367 low-risk patients (77.9%), 3,366 high-risk patients (32.3%) without a contraindication to prophylaxis, and 485 high-risk patients (26.9%) with a contraindication to pharmacologic prophylaxis (Table). The odds of receiving excess prophylaxis for low- vs high-risk patients was 3.26 (95% CI, 2.36-4.51; P < .001). The rate of excess VTE prophylaxis varied between hospitals, with rates ranging from 8.2% to 84.6% in high-risk patients (mean [SD], 32.8% [21.4%]) and from 15.5% to 99.6% in low-risk patients (mean [SD], 79.7% [19.8%]) (Figure).

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The 22.0% rate of underuse of VTE prophylaxis was significantly lower than the 65.3% rate of excessive prophylaxis and is lower than the rates of underuse previously described in medical patients.4 Efforts aimed at improving VTE prophylaxis at local, regional, and national levels have been suc-
cessful. However, most interventions have focused on increasing overall rates of prophylaxis rather than overall appropriateness. Although overall rates have improved, the unintended consequence may be excess administration of VTE prophylaxis among low-risk patients.

The major drawback to pharmacologic overprophylaxis is major bleeding. Patient discomfort, potential risk of falls and impaired mobility with mechanical prophylaxis, medication cost, and risk for heparin-induced thrombocytopenia are additional concerns.

Limitations of this study include its observational design subject to inherent biases. Furthermore, this analysis did not incorporate VTE events, so it is unknown whether 1 specific VTE prophylaxis strategy was superior to another.

After years of promoting aggressive VTE prophylaxis strategies for hospitalized patients, renewed effort to scale back—or “deimplement”—this practice in low-risk patients may be necessary. Discontinuing conventional practices, however, can be difficult, even in the presence of newer compelling data.

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Study concept and design: Grant, Chopra, Flanders.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Grant, Chopra, Flanders.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Grant, Conlon, Chopra.

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Study supervision: Flanders.

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HEALTH CARE POLICY AND LAW

Diversity of Participants in the 340B Drug Pricing Program for US Hospitals

The 340B program was initiated in 1992 by the US Congress to allow participating hospitals to generate additional revenue by purchasing certain drugs used for outpatient care at an approximately 22% discount while charging payers the full price.1,2 The program was designed to support hospitals caring for uninsured patients and low-income patients with Medicare and Medicaid coverage, allowing the hospitals to reach “more eligible patients” and provide “more comprehensive services.”2,3 Although the 340B program was initially targeted to a select group of hospitals, participation has swelled, owing to expanded eligibility in 2004 and 2010 and the program’s popularity.1

Effective January 2018, the Centers for Medicare & Medicaid Services reduced Medicare reimbursement to physicians administering discounted drugs acquired by most 340B hospital participants.3 Opponents of reform contend that 340B revenues finance safety-net services,4 whereas supporters contend that most participants do not direct revenue back to safety-net care.5 We examined how uncompensated care, provision of low-profit services, and financial stability differed between nonprofit and public hospital 340B participants and nonparticipants in 2015.

Methods | We linked data from 1224 general acute care nonprofit and public hospitals from the Healthcare Cost Report Information System to 660 hospitals participating in the 340B program from the Health Resource & Services Administration’s provider list in 2015. Our sample was limited to urban hospitals with 100 or more beds that were not affected by eligibility expansions. The sample included nonprofit and public general acute-care hospitals that were not the target of direct eligibility expansions of 340B in 2010 or of indirect eligibility expansions of 340B eligibility through changes to the disproportionate-share hospital percentage adjustment in 2004. The sample excluded 115 hospitals that began participating in the program before 2015 but were no longer participating in 2015, 44 hospitals with missing data on the outcomes, and 21 observations representing more or less than 1 year. Owing to the use of publicly available data, the institutional review board of Vanderbilt University determined that the study was exempt from the need for review.

We compared 340B hospital participants with those that never participated with respect to their patient populations and US Census Bureau–reported community characteristics. We further divided participants into cohorts based on the date when they first registered for the program. We examined differences in uncompensated care, provision of low-profit services, and financial services from the hospitals’ cost reports using multivariable ordinary least-squares regressions with