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Venous Thromboembolism Prophylaxis: Inadequate and Overprophylaxis When Comparing Perceived Versus Calculated Risk

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Abstract

Guidelines for venous thromboembolism (VTE) prophylaxis recommend appropriate risk stratification using risk estimation models as high risk or low risk followed by initiation of chemical or mechanical prophylaxis, respectively. We explored adherence to guidelines on the basis of the documentation of VTE prophylaxis. A retrospective medical record review of 437 consecutive adult patients (≥18 years) admitted to general medical wards under medicine service between January 1, 2015, and March 1, 2015, was performed. The primary outcome was appropriateness of risk stratification using the Padua Prediction Score. Secondary outcomes were appropriateness of type of prophylaxis (chemical vs mechanical) and cost-benefit analysis. We observed appropriate stratification based on the documented risk (compared with the calculated risk) in 54.9% of the patients (40.8% with low risk vs 72.1% with high risk; $P<.001$). Overall, 182 of 240 low-risk patients received unnecessary chemical prophylaxis, whereas 23 of 197 high-risk patients without contraindications for chemical prophylaxis received mechanical or no prophylaxis. No clinical VTE events were noted in the patients inappropriately assigned to mechanical or no prophylaxis. Also, 67.3% of patients with both low documented and low calculated risk and 74.5% of patients with low documented and high calculated risk received chemical prophylaxis, consistent with a tendency toward overtreatment. A total of 4068 annualized patient-days ($77,652/y) of inappropriate chemical prophylaxis were administered. In conclusion, estimation of the risk of VTE based on clinical impression was not congruent with the risk calculated using risk prediction models and was associated with a tendency toward overtreatment. These data support the inclusion of VTE risk calculators in electronic health record systems.

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Deep venous thrombosis and pulmonary embolism, together referred to as venous thromboembolism (VTE), are important causes of disability and death in hospitalized patients.[1] The incidence of VTE in hospitalized medical patients is approximated to be 1 in 1000 patients; however, current measurements underestimate the actual incidence of VTE due to the nonspecific symptoms that are often missed.[2,3] For many years, the American College of Chest Physicians (ACCP) has recommended VTE prophylaxis for medical patients in whom the benefits appear to outweigh the risks. In 2012, the ACCP recommended that patients hospitalized under medical services should undergo appropriate risk stratification followed by anticoagulant VTE prophylaxis in patients with high-risk features and without contraindications to anticoagulants.[4] In 2014, the Centers for Medicare & Medicaid Services introduced quality-based reimbursement based on the presence or absence of VTE prophylaxis documentation.[5] Following the introduction of quality-based reimbursement, an increasing rate of compliance with VTE prophylaxis (from 10% to 60%) has been observed.[6,7] We hypothesized that in low-risk patients with VTE, chemoprophylaxis is prescribed more often than mechanical prophylaxis. In this study, we examined the extent and appropriate use (type and dosage) of VTE prophylaxis in hospitalized medically ill patients in a large teaching hospital in Baltimore, Maryland.

TABLE 1. Padua Prediction Score[a,b]

Risk factor	Points
Active cancer[c]	3
Previous VTE (with the exclusion of superficial vein thrombosis)	3
Reduced mobility[d]	3
Already known thrombophilic condition[e]	3
Recent (≤1 mo) trauma and/or surgery	2
Elderly age (≥70 y)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI ≥30)	1
Ongoing hormonal treatment	1

[a]BMI = body mass index; VTE = venous thromboembolism.
[b]In the Padua Prediction Score risk assessment model, high risk of VTE is defined by a cumulative score of ≥4 points.
[c]Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 mo.
[d]Anticipated bed rest with bathroom privileges (either because of patient's limitations or on physician's order) for at least 3 d.
[e]Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome.

METHODS

We performed a retrospective medical record review of 500 consecutive adult patients (aged ≥18 years) admitted to general medical wards between January 1, 2015, and March 1, 2015. The exclusion criteria included admission to a nonmedical service; admission for pulmonary embolism or deep venous thrombosis; active bleeding or recent blood loss; anticoagulation therapy; presentation with systolic blood pressure of more than 200 mm Hg or diastolic blood pressure of more than 120 mm Hg; and pregnancy. After exclusion, a total of 437 patients were eligible for analysis. The individual patient's risk for VTE was calculated using the guideline-suggested Padua risk prediction model at the time of admission (Table 1).[8] The score was then compared with the documented risk of VTE in the electronic medical record. The documentation of patient risk was compulsory for every patient and was predominantly based on physicians' clinical judgment with the noncompulsory provision of a supportive tool (Padua prediction model) to assist in decision making. The medical record of each patient was then examined to determine whether pharmacologic (chemical) or mechanical VTE prophylaxis was ordered and received. The Medication Administration Record was used to check for prophylaxis received. This study was approved by the Institutional Review Board at Sinai Hospital of Baltimore.

Definitions

Appropriate risk stratification was a composite of low documented, low calculated risk with high documented, high calculated risk groups. Inappropriate risk stratification was a composite of low documented, high calculated risk with high documented, low calculated risk groups. The VTE prophylaxis was defined to include both pharmacological and mechanical means. The former category consisted of low-molecular-weight heparin, unfractionated heparin, and fondaparinux at prophylactic doses (dalteparin, ≤15,000 IU/d; enoxaparin, ≤40 mg/d; and fondaparinux, <5 mg/d, respectively). The mechanical measures included ambulation, graduated compression stockings, and intermittent pneumatic compression devices.

Primary and Secondary Outcomes

The primary end point was the appropriateness of risk stratification. The secondary end point was appropriateness of type of prophylaxis received. For a calculated Padua risk score of 4 or more, chemical prophylaxis (unless contraindicated) was considered appropriate, and for a score of less than 4, mechanical or no prophylaxis was considered appropriate. A cost-benefit analysis was conducted for inappropriate prophylaxis.

Statistical Analyses

Categorical variables are expressed as number (percentage) and continuous variables as mean ± SD, with $P \leq .05$ considered statistically significant. Fischer exact test was used for comparison of categorical variables. Student *t* test was used to compare normally distributed continuous variables, whereas a Wilcoxon rank sum test was used to compare continuous variables that were not normally distributed. Percent total agreement, percent positive agreement, and κ statistics were calculated to assess the agreement between physicians' perceived risk for VTE and calculated risk. IBM SPSS, version 22.0, was used to perform all statistical analyses.

RESULTS

Appropriate risk stratification based on electronic documentation was observed in only

TABLE 2. Baseline Demographic Characteristics According to the Documented and Calculated Risks[a,b]

Baseline demographic characteristic	Low documented, low calculated risk (n=98)	Low documented, high calculated risk (n=55)	High documented, low calculated risk (n=142)	High documented, high calculated risk (n=142)	*P*
Age (y), mean ± SD	66.0±19.2	68.6±17.6	64.5±19.0	68.1±18.2	.33
Age >70 y	31 (31.6)	38 (69.1)	46 (32.4)	88 (62.0)	<.001
Active cancer	0 (0.0)	8 (14.5)	3 (2.1)	40 (23.9)	<.001
Previous VTE	0 (0.0)	2 (3.6)	1 (0.7)	16 (11.3)	<.001
Reduced mobility	3 (3.1)	43 (78.2)	5 (3.5)	100 (70.4)	<.001
Acute myocardial infarction	1 (1.0)	2 (3.6)	5 (3.5)	4 (2.8)	.66
Heart failure exacerbation	9 (9.2)	5 (9.1)	24 (16.9)	29 (20.4)	.05
Acute stroke	1 (1.0)	1 (1.8)	1 (0.7)	2 (1.4)	.90
Acute infection	50 (51.0)	34 (61.8)	59 (41.6)	80 (56.3)	.02
Body mass index >30	35 (35.7)	19 (34.5)	55 (38.7)	33 (23.2)	.03
Calculated risk (Padua score), mean ± SD	1.5±1.0	5.1±1.2	1.7±1.0	5.3±1.5	<.001

[a]VTE = venous thromboembolism.
[b]Values represent No. (percentage) unless otherwise indicated.

54.9% of patients (40.8% with calculated low risk vs 72.1% with calculated high risk; *P*<.001) (Table 2). As shown in Table 3, the group with the overall appropriate risk stratification had a significantly higher proportion of patients with active cancer, previous VTE, reduced mobility, and a higher calculated risk of VTE compared with the group with inappropriate stratification. The patients with inappropriate risk stratification were observed to have significantly more obese patients (body mass index [BMI], >30 kg/m^2).

Appropriateness of Type of Prophylaxis

Of the 240 patients with a calculated low risk (by Padua score), 182 (75.8%) patients received unnecessary chemical prophylaxis. Twelve percent (23 of 197) of the patients at high risk (calculated by Padua score) and without contraindications for chemical prophylaxis received mechanical or no prophylaxis (21 and 2, respectively). No clinical VTE events were noted in this small group of patients. In addition, 66 of 98 (67.3%) patients with both low documented and low calculated risk and 41 of 55 (74.5%) patients with low documented and high calculated risk received chemical prophylaxis.

The actual calculated risk was compared with physician impression using standard observer agreement statistical techniques such as percent total agreement, percent

TABLE 3. Baseline Demographic Characteristics According to Appropriateness of Risk Stratification[a,b]

Baseline demographic characteristic	Appropriate stratification (n=240)	Inappropriate stratification (n=197)	*P*
Age (y), mean ± SD	67.2±18.6	65.6±18.7	.37
Age >70 y	119 (49.6)	84 (42.6)	.14
Active cancer	34 (14.2)	12 (5.9)	.003
Previous VTE	16 (6.7)	3 (1.5)	.008
Reduced mobility	103 (42.9)	48 (24.3)	<.001
Acute myocardial infarction	5 (2.1)	7 (3.6)	.35
Heart failure exacerbation	38 (15.8)	29 (14.7)	.74
Acute stroke	3 (1.2)	2 (1.0)	.81
Acute infection	130 (54.2)	93 (47.2)	.14
Body mass index >30	68 (28.3)	74 (37.6)	.04
Calculated risk (Padua score), mean ± SD	3.7±2.3	2.7±1.9	<.001

[a]VTE = venous thromboembolism.
[b]Values represent No. (percentage) unless otherwise indicated.

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positive agreement, and κ value. The percent total agreement was 55%; percent positive agreement was 42% and the κ value was 0.12 when comparing physician-perceived risk for VTE to the actual calculated risk. These statistical measures showed a weak agreement between physicians' impression and calculated risk for VTE prophylaxis.

A total of 1017 patient-days of inappropriate chemical prophylaxis were administered over a period of 3 months. The numbers of unnecessary subcutaneous injections were 2053, 312, and 10 for low-molecular-weight heparin, enoxaparin, and fondaparinux, respectively. The net drug cost of inappropriate prophylaxis was estimated to be $77,652/y ($19,413 over 3 months) without accounting for the additional costs related to drug administration.

DISCUSSION

Using the Padua risk score as a benchmark, we found that only 54.9% of patients admitted under a medical service underwent appropriate risk stratification. Of the patients with a calculated low risk, 76% received potentially unnecessary chemical prophylaxis, and 12% of patients at high risk and without contraindications for chemical prophylaxis received mechanical or no prophylaxis. Inappropriate prophylaxis had an annualized cost of $77,652 in addition to patients' discomfort and the additional cost associated with administration.

In agreement with previous studies, our data show that estimation of patients' risk of VTE based on clinical impression is not congruent with the risk calculated by prediction models.[9] The observed tendency toward overtreatment regardless of risk estimates supports the need for inclusion of VTE risk calculators with guideline-derived recommendations in electronic health records.

Since the introduction of the ACCP guidelines and the inclusion of the new measures quality-based reimbursements by the Centers for Medicare & Medicaid Services, there has been a rise in the rate of VTE prophylaxis.[5-7] However, the quality measure is based on the presence or absence of documentation and not on the appropriateness of VTE prophylaxis. Previous studies including the Prophylaxis in Medical Patients with Enoxaparin (MEDENOX) study (N=1102)[10] and the Arixtra for Thromboembolism Prevention in a Medical Indications Study (ARTEMIS) (N=849)[11] have shown a significant reduction in the incidence of VTE events with prophylactic use of enoxaparin (risk ratio, 0.37; 95% CI, 0.22-0.63; $P<.001$) and fondaparinux (relative risk reduction, 46.7%; 95% CI, 7.7%-69.3%; $P=.02$), respectively, in medically ill hospitalized patients. However, these studies did not use risk assessment models (RAMs). Instead, their inclusion criteria included parameters common with the Padua score including congestive heart failure (New York Heart Association class III or IV), acute respiratory failure (not requiring ventilatory support), acute infection without septic shock; acute rheumatic disorders, including acute lumbar pain or sciatica or vertebral compression (caused by osteoporosis or a tumor), acute arthritis of the legs, or an acute episode of rheumatoid arthritis in the legs; or an episode of inflammatory bowel disease. The additional risk factors were age more than 75 years, cancer, previous venous thromboembolism, obesity (BMI >30 for men and >28.6 for women), varicose veins, hormone therapy (antiandrogen or estrogen, except for postmenopausal hormone-replacement therapy), and chronic heart or respiratory failure.[10,11] The Padua score was proposed and subsequently validated in 1180 and 1080 patients, respectively, and has been suggested to be used as a RAM by the current ACCP guidelines.[4,8,12] A significant caveat in the existing RAMs are their low to mediocre C statistics (ranging from 0.56 to 0.62) as shown in a recent comparative analysis by Greene et al.[13,14] Because of a lack of large validated studies showing any single RAM to have good accuracy (including positive predictive value and negative predictive value) for prediction of subsequent VTE, one cannot determine whether the use of VTE prophylaxis would indeed reflect overprophylaxis. However, the central strength of the Padua model is its ease of use, which makes it a good starting tool for risk stratification.

In our study, we observed a high rate of inappropriate VTE prophylaxis leading to overtreating patients. Our study is in accordance with the results observed by Eijgenraam et al,[15] who showed a nonsignificant shift toward overtreatment after the introduction of a clinical decision support

tool for VTE risk assessment.[16] These findings were also reflected in a recent review by Bikdeli and Sharif-Kashani,[17] who showed that although many at-risk patients are underprophylaxed, there is increasing evidence to suggest overprophylaxis (ie, prescription of thromboprophylaxis in low-risk patients). We propose a need to shift focus from mere documentation of whether VTE prophylaxis was received to the institution of appropriate prophylaxis. This approach would not only save health care expenditure but also substantially reduce patient discomfort from the unnecessary institution of injections for VTE prophylaxis.

In addition, previous studies evaluating the utility of clinical decision support tools have shown mixed results.[6,15,18-20] Of note, the studies that showed a significant improvement in appropriate risk stratification with the introduction of clinical decision tools had an additional component of an extensive educational program[6,18,19] compared with those that did not.[15,20] Thus, we recommend that clinical decision tools be accompanied by extensive educational programs to reduce the inappropriate stratification and institution of VTE prophylaxis.

Our study has several limitations. First, this was an observational retrospective medical record review and hence lacks the merits of a randomized controlled trial. Second, the sample size of this pilot study was small with the inclusion of only 437 patients, and no follow-up VTE incidences were assessed. Third, this was an exploratory study and not designed or powered to detect a significant VTE event in patients who received mechanical prophylaxis when classified as high-risk patients. Fourth, although the Padua score might not be adequate to risk stratify complex patients (eg, an acutely ill patient with a BMI of >30, cardiac and respiratory failure, and ongoing hormone therapy; Padua score = 3), its ease of use makes it a good starting tool for risk stratification.

In addition, these results should be interpreted with caution because guidelines, albeit helpful, are to supplement rather than replace clinical judgment.

CONCLUSION

In agreement with previous studies, our data show that estimation of patients' risk of VTE based on clinical impression is not congruent with the risk calculated by prediction models. In addition, our observed tendency toward overtreatment regardless of risk estimates supports the need for the inclusion of VTE risk calculators with guideline-derived recommendations in electronic health records and the need to shift the focus from mere documentation to institution of appropriate prophylaxis.

Abbreviations and Acronyms: **ACCP** = American College of Chest Physicians; **BMI** = body mass index; **RAM** = risk assessment model; **VTE** = venous thromboembolism

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