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Assessment of venous thromboembolism risk and initiation of appropriate prophylaxis in psychiatric patients

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Abstract

Introduction: Venous thromboembolism (VTE) prophylaxis is not included among the measures for the Inpatient Psychiatric Facilities Quality Reporting Program. Evidence suggests that antipsychotic agents may be an independent risk factor for the development of VTE; therefore, development of a VTE risk stratification tool would improve the quality and safety of care for the psychiatric inpatient population. This study aims to develop clinically relevant criteria to assess VTE risk upon admission to an inpatient psychiatric hospital.

Methods: This retrospective, single-center cohort study enrolled patients in 2 cohorts from an inpatient psychiatric hospital. Patients in cohort I with new-onset VTE diagnosis during admission were identified through international classification of diseases 9 and 10 coding. Cohort II consisted of a random sample of 100 patients in a 3-month period. The percentage meeting criteria for prophylaxis in each cohort was assessed utilizing both the Padua Prediction Score and a modified score.

Results: In cohorts I and II, 66.7% and 14% of patients, respectively, met criteria for VTE prophylaxis utilizing the modified Padua Prediction Score. One patient received VTE prophylaxis in each cohort, and the median time to VTE diagnosis in cohort I was 42 days. In cohort I, the rate of VTE was 0.08% based on estimated discharges in the 26-month period. This is less than the annual rate of 1% to 2.4% for nursing homes or postacute rehabilitation facilities.

Discussion: We recommend the implementation of clinical decision support to prompt individualized reassessment of VTE risk when length of stay exceeds 30 days.

Keywords: venous thromboembolism, VTE, deep vein thrombosis, pulmonary embolism, antipsychotic, psychiatric, prophylaxis

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Introduction

Venous thromboembolism (VTE) carries a well-established correlation with increased morbidity and mortality across health care settings.[1] In the contemporary quality assessment for psychiatric inpatient facilities, VTE prophylaxis is not included among the core measures as it is for other acute care inpatient settings. To date, a consensus has yet to be reached regarding appropriate VTE risk assessments for patients admitted to a psychiatric inpatient facility.

The 2012 American College of Chest Physicians guidelines for the prevention of VTE in nonsurgical patients (CHEST Guidelines) recommend that acutely ill hospitalized medical patients at in increased risk of thrombosis receive VTE prophylaxis with a low molecular weight heparin, unfractionated heparin, or fondaparinux.[2] In contrast, VTE prophylaxis is not recommended for chronically ill or immobilized patients residing at home or a nursing facility. In order to stratify patients at greatest risk of VTE development, the CHEST guidelines utilize the Padua Prediction Score to assess cumulative risk by attributing points to patient-specific risk factors. Active cancer, previous VTE, reduced mobility, and a preexisting thrombophilic condition receive a 3-point designation, whereas recent trauma or surgery earns 2 points toward the total score. Risk factors earning 1 point include age 70 years or greater, heart or respiratory failure, acute myocardial infarction or ischemic stroke, acute infection or rheumatologic disorder, body mass index of 30 kg/m^2 or greater, and ongoing hormonal treatment. A patient earning 4 or more points is considered high risk, and, therefore, is a candidate for VTE prophylaxis.

Although psychiatric inpatients are often not acutely ill in a medical sense, evidence suggests that the presence of an antipsychotic in the medication regimen may be an independent risk factor for the development of VTE. A 2011 meta-analysis conducted by Zhang et al[3] investigated the association between antipsychotic use and VTE risk through analysis of 7 case-control studies. Exposure to an antipsychotic was found to be associated with increased risk of VTE (odds ratio [OR] 2.39; confidence interval [CI] 1.71-3.35), which remained consistent in pooled analyses by antipsychotic type. Low-potency antipsychotics carried an OR of 2.91 (CI 1.80-4.71), which was followed closely by atypical agents (OR 2.20, CI 1.5-1.67), conventional agents (OR 1.72, CI 1.31-2.24), and high-potency agents (OR 1.58, CI 1.5-1.67). To further corroborate these findings, Ishiguro et al[4] identified the highest risk of VTE development in the period immediately following antipsychotic initiation (OR 3.21, CI 1.64-6.29). In addition to antipsychotic therapy, comorbidities, such as dehydration with laboratory abnormalities and venous insufficiency, may further magnify VTE risk in the psychiatric inpatient population.[5,6]

Despite the growing body of evidence demonstrating increased VTE risk in psychiatric patients, research on guideline-driven implementation of thromboprophylaxis remains limited. In addition, initial VTE diagnosis may be more challenging in a psychiatric patient population due to communication barriers or misattribution of symptoms to a psychosomatic cause. In light of a perceived increase in VTE incidence at our facility, the development of a more sensitive VTE risk stratification tool for thromboprophylaxis would improve the quality and safety of care for the psychiatric inpatient population.

Methods

This retrospective, single-center, cohort study enrolled patients in 2 distinct cohorts. Cohort I consisted of patients diagnosed with a new-onset VTE during admission to the Medical University of South Carolina (MUSC) Institute of Psychiatry (IOP). Patients were identified through coding per the international classification of diseases 9th and 10th revisions during the time period spanning July 1, 2014, through August 31, 2016. Cohort II consisted of a random sample of 100 patients admitted to the MUSC IOP during the time period spanning May 1, 2016, through July 31, 2016.

All patients ≥18 years of age admitted to the MUSC IOP were eligible for study inclusion. Exclusion criteria consisted of the following: therapeutic anticoagulation on admission (warfarin, low molecular weight heparin, heparin, a novel anticoagulant agent, or fondaparinux), pregnant women, and patients readmitted during the time period of the study. Acute deep vein thrombosis/pulmonary embolism events were excluded from cohort II. Because this study was intended to improve the quality of patient care at MUSC, it was considered a quality improvement project and was, therefore, exempt from the institutional review board approval process.

The primary aim of this study was to develop clinically relevant criteria to assess the risk of VTE upon admission to the acute care inpatient units at the MUSC IOP. To accomplish this aim, a retrospective review was completed in 2 cohorts. Cohort I consisted of all new-onset VTE diagnoses to assess the proportion of these patients meeting established criteria for prophylaxis according to both the Padua Prediction Score utilized in the CHEST Guidelines as well as a modified Padua Prediction Score (Table 1). The development of the modified Padua Prediction Score accounted for VTE risk factors identified within the psychiatric patient population that are not included in the original Padua Prediction Score. The sensitivity of the Padua Prediction Score and a modified Padua Prediction Score were calculated for cohort I to determine their adequacy to predict risk of VTE in a population with known development of VTE. Cohort II consisted of a random sample of 100 patients who were assessed to determine the proportion of patients meeting established criteria for prophylaxis utilizing both the Padua Prediction Score as well as the aforementioned modified Padua Prediction Score. Of those patients meeting the criteria, the specificity of both the Padua Prediction Score and the modified Padua Prediction Score were calculated to determine their adequacy in excluding patients without known development of deep vein thrombosis. Contraindications to VTE prophylaxis were defined as active bleeding (hematoma, gastrointestinal bleed, or hemorrhage), platelet count <50, or lumbar

TABLE 1: Padua prediction score

Risk Factor	Points
Active cancer	3
Previous VTE (excluding superficial vein thrombosis)	3
Reduced mobility (paralysis, restraints ≥8 h, catatonia)	3
Preexisting thrombophilic condition (defects of antithrombin, protein C and S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome)	3
Recent trauma/surgery (≤1 mo)	2
Age ≥70 y	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection or rheumatologic disorder	1
Body mass index ≥30	1
Estrogen or testosterone hormonal treatment	1
Dehydration with laboratory abnormalities (BUN/serum creatinine >20)[a]	1
Varicose veins/venous insufficiency[a]	1
Treatment with an antipsychotic[a]	1
High risk: ≥4 points; low risk: <4 points	
Contraindications to VTE prophylaxis:	
Active bleeding (gastrointestinal, hematoma, hemorrhage)	
Platelet count <50 K/cmm^3	
Lumbar puncture/epidural/spinal anesthesia	

BUN = blood urea nitrogen; VTE = venous thromboembolism.

[a]Additional criteria included in modified score based on psychiatric risk factors.

puncture/epidural/spinal anesthesia within the previous 4 hours or next 12 hours.

Descriptive statistics and appropriate measures of central tendency were utilized to characterize all specific aims. In addition, the projected economic impact of prophylaxis implementation was assessed.

Results

Baseline characteristics in each cohort are depicted in Table 2. Notable variance between the cohorts include a greater median age (66.5 versus 42 years) and length of stay (90.5 versus 9 days) in cohort I. In cohorts I and II, 66.7% and 14% of patients, respectively, met criteria for VTE prophylaxis utilizing the modified Padua Prediction Score whereas 33.3% and 11%, respectively, met criteria utilizing the original Padua Prediction Score. Although 2 patients had a documented contraindication to VTE prophylaxis, 1 patient in each cohort received prophylaxis during admission at the IOP. Risk factors appearing in ≥15% of both cohorts include acute infection or rheumatologic disorder, obesity, and treatment with an antipsychotic agent. The 2 most prevalent risk factors in cohort I were treatment with an antipsychotic agent (100%) and reduced mobility (67%). Within cohort II, antipsychotic treatment was again one of the most prevalent risk factors (54%) along with a body mass index ≥30 kg/m^2 (30%). The median time to onset of VTE diagnosis in cohort I was 42 days (range: 16 to 94).

The sensitivity of the Padua Prediction Score to predict patents at high risk of VTE in cohort I was 33.3%, whereas the sensitivity of the modified Padua Prediction Score in cohort I was 66.7%. The specificity of the Padua Prediction Score to exclude patients not at high risk of developing a VTE in cohort II was 89%, and the specificity of the modified Padua Prediction Score in cohort II was 86%.

Discussion

Based on an estimated 7800 discharges from the IOP in the 26-month time period spanning cohort I, the rate of new-onset VTE was 0.08%. This is notably less than the reported annual rate of 1% to 2.4% for nursing homes or postacute rehabilitation facilities.[2] Although 14% of cohort II met the high-risk criteria per the modified Padua Prediction Score, no patients developed a VTE during admission. Given the sensitivity of the Padua Prediction Score and modified score in cohort I, it can be hypothesized that both the prediction score and the modified version would not yield a high positive predictive value in identifying psychiatric inpatients at high risk for VTE possibly because psychiatric patients are not admitted for an acute medical illness. The sensitivity and specificity values calculated in this study can be compared to those in the original assessment of the Padua Prediction Score in the medical patient population, which were found to be 94.6% and 62%, respectively.[7] Upon examination of patients in cohort I who developed a VTE during admission, the most significant differentiating factor when compared with cohort II was increased length of stay. Theoretically, increased hospital length of stay is inversely related to a patient's physical conditioning and ability to ambulate. Interestingly, a greater percentage of cohort I was considered high risk based on the modified criteria, suggesting that the addition of risk factors such as antipsychotic use, dehydration, and venous insufficiency may provide a tool more reflective of actual VTE risk in the psychiatric patient population; however, the sensitivity of the modified Padua Prediction Score in cohort I was only 66.7%. We are limited in the ability to draw definitive conclusions based on the small sample size (n = 6) in cohort I. Of note, no known significant staffing or unit modifications that may have affected the mobility of patients occurred between 2014 and 2016. Therefore, the difference in time frame between cohorts was not

TABLE 2: Baseline characteristics

Characteristic	Cohort I (n = 6)	Cohort II (n = 100)
Age, median (range), y	66.5 (51–78)	42 (18–83)
Weight, median (range), kg	68.3 (62.5–91.8)	77.1 (48.5–131.5)
Admission serum creatinine, median (range), mg/dL	0.9 (0.6–1.5)	0.9 (0.6–14.3)
Nursing unit, n (%)		
Senior care	5 (83.3)	25 (25)
General adult	1 (16.7)	50 (50)
Acute care	0 (0)	11 (11)
Addictions	0 (0)	14 (14)
Activity status, n (%)		
Independent	5 (83.3)	90 (90)
Assistive person/equipment	1 (16.7)	10 (10)
Length of stay median (range), d	90.5 (42–436)	9 (3–89)
Prior to admission location, n (%)		
Home	5 (83.3)	95 (95)
Long-term care facility	1 (16.7)	5 (5)
Disposition, n (%)		
Home	2 (33.3)	91 (91)
Long-term care facility	4 (66.7)	9 (9)
Clinical contraindication to venous thromboembolism prophylaxis, n (%)	0 (0)	2 (2)

thought to be a potential confounding factor. Given that the mean time to VTE development in cohort I was 42 days, we felt duration of admission to be a more effective clinical predictor of VTE risk in our psychiatric inpatient population.

According to a study conducted by Preblick et al,[8] the cost of inpatient VTE treatment for 7 days ranges from $1964.87 to $2347.60 based on acuity and requirement for an intensive care unit stay. For medically ill patients at moderate risk of VTE, the literature reports a number

TABLE 3: Economic and safety implications of prophylaxis[a]

	Subcutaneous Prophylaxis Agent	
	Heparin: 5000 units Q 8 h, $	Enoxaparin: 40 mg daily, $
Annual cost of prophylaxis		
High risk: Padua Prediction Score (11% of discharges with LOS ≥30 d)	13 854.46	12 205.12
High risk: Modified Padua Prediction Score (14% of discharges with LOS ≥30 d)	17 632.94	15 533.78
Venous thromboembolism inpatient treatment[8]	Cost per episode	
ED + floor	1964.87	
ED + floor + ICU	2347.60	
Nonvariceal upper gastrointestinal bleed[10]		
With complications	7262.95	
Without complications	4387.18	
Heparin-induced thrombocytopenia[11]		
Confirmed	4997.96	
Confirmed with thrombosis	37 319.89	

ED = emergency department; ICU = intensive care unit; LOS = length of stay.

[a]Cost (adjusted to 2017 US dollars) based on wholesale acquisition cost pricing and median LOS of 59.5 days in cohort II patients with LOS ≥30 days.

needed to treat of around 1000 in relation to pharmacologic prophylaxis.[9] The provision of VTE prophylaxis is also not without safety concerns, such as the development of heparin-induced thrombocytopenia (HIT) and major bleeding. The rate of HIT varies in the literature and between agents with unfractionated heparin carrying a higher incidence than low molecular weight heparins. The rate of HIT in studies examining nonsurgical patients receiving pharmacoprophylaxis with unfractionated heparin or a low-molecular weight heparin is estimated to range from 0.3% to 0.7%.[2] According the to the CHEST Guidelines, pharmacoprophylaxis in nonsurgical patients yields an increase in major bleeding events over the baseline risk (4 per 1000) of 1 event per 1000 patients treated.[2] The rates of HIT and major bleeding reported in the literature are the same or higher than the rate of VTE development in our population (cohort I), indicating that routine pharmacoprophylaxis may convey greater risk than the benefit provided to our population. However, given the differences in our population and the small sample size of cohort I, the ability to draw definitive conclusions may be limited. The estimated financial impact of prescribing VTE prophylaxis for the percentage of patients meeting high-risk criteria is provided in Table 3. Depending on the agent prescribed and dosing frequency, the annual cost for VTE prophylaxis based on the percentage of high-risk patients in cohort II ranges from $12 205.12 to $17 632.94. Given the low rate of VTE at the MUSC IOP, safety concerns outlined above, economic considerations illustrated by Table 3, and median time to onset of VTE in cohort I, we recommend the implementation of clinical decision support to prompt individualized reassessment of VTE risk when length of stay exceeds 30 days. Although the median time to VTE onset was 42 days, the establishment of a 30-day prompt would increase the feasibility of implementation. Despite our limited enrollment in cohort I, we believe this is the most clinically relevant VTE risk assessment criteria for a psychiatric inpatient facility with an inpatient population comparable to the MUSC IOP.

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