

Estimating Risk of Venous-Thromboembolic Events in Hospitalized Medical Patients: Comparison between 2008 and 2012 Guidelines

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ABSTRACT: **Background:** Prophylaxis for hospitalized venous-thromboembolic events (VTEs) is frequently underutilized, in part due to lack of a simple risk assessment model (RAM).

Objectives: To compare patient selection and administration of VTE prophylaxis according to the American College of Chest Physicians (ACCP) 2008 guidelines versus the newer 2012 guidelines, and assess the feasibility of developing simpler local RAMs.

Methods: We conducted a prospective assessment of VTE risk among 300 unselected consecutive patients admitted to a medical hospital ward, using the 2008 and 2012 ACCP guidelines. The frequency and relative weight of each risk factor in the 2012 ACCP guidelines were used to develop a local VTE RAM.

Results: VTE prophylaxis was indicated by the 2008 and 2012 ACCP guidelines in 40% and 42% of the cohort respectively, and was administered in 28% and 26% of eligible patients, respectively. Contraindication to VTE prophylaxis was found in 29% of patients according to both guidelines. In comparison to the 2008 guidelines, sensitivity and specificity of the 2012 guidelines were 96% and 88%, respectively. A local RAM based on the following concise score, comprising age, malignancy and immobility, correctly identified 99% of at-risk patients based on the 2012 guidelines, with a sensitivity and specificity of 98% and 95%, respectively.

Conclusions: Both guidelines performed to a similar degree and were poorly implemented in daily practice. A simplified RAM accurately identified the vast majority of these eligible patients. The development of local RAMs is feasible and may result in higher utilization rates.

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KEY WORDS: venous-thromboembolic events (VTE), prophylaxis, risk assessment model (RAM), guidelines

[3]. It is estimated that most VTEs among hospitalized patients can be prevented through administration of adequate prophylaxis. Nevertheless, adherence to VTE prophylaxis guidelines remains low, mainly due to lack of a simple-to-use, validated and universally accepted risk assessment model (RAM) [4-9]. Several scoring systems were previously suggested, albeit each with innate flaws, i.e., based on a specific population, lacking validation, or lacking universal acceptance [10-16].

The “Padua Score,” based on the pre-existing Kucher model, was developed and subsequently validated in one center as a scoring system for the assessment of VTE risk among hospitalized medical patients [14,17]. The score was implemented as part of the 2012 American College of Chest Physicians (ACCP) update on clinical practice guidelines for VTE prevention [18]. The Padua score, which is based on 11 risk factors, replaced the 2008 guidelines which recommended a 20 risk factor scoring system, developed locally by each hospital [19].

A separate, recently published study, aimed at developing a new RAM, had suggested a different set of risk factors and score cutoff compared to the 2012 guidelines [20]. Nonetheless, we chose to compare our results to the 2012 ACCP guidelines as they are widely recognized as the standard.

Whether or not the Padua score identifies the same population at risk as a local RAM is currently unknown. Accordingly, the intention was: (i) to compare the performance of the 2008 RAM score and the 2012 (Padua) scoring system among hospitalized medical patients, and (ii) to examine the feasibility of developing a concise VTE RAM based on the prevalence of the 2012 risk score components in our local patient population and measure its performance.

PATIENTS AND METHODS

We prospectively assessed 300 consecutive patients admitted to a single internal medical ward, with a five-bed respiratory unit, in a tertiary medical center. All data were extracted electronically using the Rabin Medical Center’s electronic medical records system which contains patient demographics

Venous-thromboembolic events (VTEs) cause substantial morbidity and mortality among hospitalized patients and are associated with a significant economic burden [1,2]. The prevalence of VTE is high and is foreseen to rise in the future

and hospitalization-related parameters. Immobilization was assessed by the treating physician and/or by a nurse within 24 hours of admission.

For each patient the indications for anticoagulation prophylactic therapy were assessed according to two risk assessment models: the hospital RAM based on the 2008 guidelines and the 2012 guidelines. Table 1 compares the indicative parameters between the two RAMs, while Table 2 compares contraindicative parameters.

VTE prophylaxis therapy was administered at the discretion of the treating physician using a standard dose of 40 mg (4000 units) enoxaparin sodium once daily. A dose of 20 mg (2000 units) was used in patients with a calculated glomerular filtration rate below 30 ml/min.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS software for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as the mean ± 1 standard deviation (SD) and categorical variables as percentages. Comparisons between the two groups were performed by Student’s *t*-test for continuous variables and the chi-square test for comparison of categorical values. All tests of significance were two-tailed, with a *P* value < 0.05 considered significant.

RESULTS

The medical ward we evaluated receives 3500 annual admissions. The major patient categories are cardiac (30%) and oncology (20%), the remainder comprising multiple subcategories including infections, hematology and pulmonology.

PATIENT CHARACTERISTICS

The average age of the cohort was 70 ± 16.6 years; males comprised 48%. The most frequent co-morbidities were hypertension and diabetes [Table 3].

INDICATIONS FOR AND UTILIZATION OF VTE PROPHYLAXIS

The incidence of scores indicative for VTE prophylaxis using the 2008 guidelines-based local hospital RAM and 2012 RAM were 40% and 42%, respectively. Both guidelines forecast 29% of the contraindications. The main contraindications for VTE prophylaxis were chronic anticoagulant treatment and acute or recent bleeding, which affected 19.3% and 9% of the patients, respectively. VTE prophylaxis was significantly underused. According to the local hospital RAM 28% of those eligible for treatment subsequently received prophylaxis, and an even lower 26% was based on the 2012 RAM. Using the 2008 guidelines-based local hospital RAM as a reference, the sensitivity and specificity of the 2012 ACCP guidelines to identify patients at increased risk for VTE were 96% and 88%, respectively.

Table 1. Risk factors according to the 2008 guidelines, 2008 guidelines-based local hospital RAM and the 2012 guidelines

2008 guidelines	2008 guidelines-based local hospital RAM	2012 guidelines
High risk: immobility + ≥ 1 risk factor	High risk ≥ 3 points	High risk ≥ 4 points
Immobility: a prerequisite status	Reduced mobility (1-3)	Reduced mobility (3)
Cancer/Cancer therapy	Active cancer (1)	Active cancer (3)
Previous VTE	Previous VTE (1)	Previous VTE (3)
Increasing age	Age > 70 (0.5)	Age > 70 (1)
Obesity	Obesity (0.5)	Obesity (1)
Inherited or acquired thrombophilia	Thrombophilic condition (0.5)	Thrombophilia (3)
Acute medical illness	Infection (1)	Acute infection/ rheumatologic disorder (1)
Surgery/Trauma	Sepsis (1)	Recent trauma/surgery (2)
Inflammatory bowel disease	Active rheumatologic disorder (1)	Hormonal treatment (1)
Nephrotic syndrome	Active inflammatory bowel disease (1)	Acute MI/stroke (1)
Lower extremity paresis	Nephrotic syndrome (1)	Heart/respiratory failure (1)
Oral contraceptives or hormone replacement therapy	Active neurologic disorder (1)	
Selective estrogen receptor modulators	Stroke (1)	
Pregnancy and the postpartum period	COPD exacerbation (1)	
Erythropoiesis-stimulating agents	Lung disease (1)	
Myeloproliferative disorders	Varicose veins (0.5)	
Paroxysmal nocturnal hemoglobinuria		
Central venous catheterization		
Venous compression		

The numbers in parentheses indicate the score
 VTE = venous thromboembolic event, COPD = chronic obstructive pulmonary disease, MI = myocardial infarction

Table 2. Contraindication for VTE prophylaxis according to 2008 guidelines-based local hospital RAM and the 2012 guidelines RAM

2008 guidelines-based local hospital RAM	2012 RAM
Active bleeding	Permanent anticoagulant treatment
Congenital/inherited bleeding disorder	Major bleeding
Heparin-induced thrombocytopenia	Platelet count ≤ 100,000
Heparin allergy	Creatinine clearance < 30 ml/min
Platelet count ≤ 50,000	
Excessive hypertension	
Active peptic disease	
Abnormal coagulation tests	
Permanent anticoagulant treatment	

RISK FACTORS FOR VTE

The most frequent risk factor was age over 70 years, noted in 59% of the patients. Fifty-eight percent of patients presented immobilization, 40% active infection and 16% malignant

Table 3. Patient characteristics and main diagnoses at discharge

Baseline characteristics	
Age (average \pm SD)	70 \pm 16.6
Male gender (%)	48
Co-morbidities (%)	
Hypertension	55.3
Diabetes	38.3
Dyslipidemia	33.3
Ischemic heart disease	30.3
Heart failure	20.3
Chronic renal failure	19
Atrial fibrillation	16.7
Malignancy	16
Stroke	15.7
Chronic obstructive pulmonary disease	14
Anemia	13.7
Transplant	3.3
Diagnoses at discharge (%)	
Infectious	39.3
Cardiovascular	25.7
Heart failure	14
Anemia	12
Pulmonary	11.7
Renal failure	8.7
Malignancy	6.7
Electrolyte disorder	6.3
Inflammatory	6
Mechanical ventilation	6
Stroke	6

disease. Analysis of the relative contribution of each of the risk factors for VTE, according to the 2012 ACCP guidelines (incidence and relative weight), revealed that only a few risk factors actually affect the scores, while others had minimal contribution. Among patients who had a score \geq 4 points, the most prevalent risk factor was immobilization, present in 92% of the patients. Of these, 72% were aged 70 or higher and 54% had a recent acute infection or rheumatologic disease. All factors are shown in Table 4.

Based on these results, we tested the sensitivity and specificity of a simplified risk score using the most influential factors. The new score was based on a three-factor calculation, with a 4-point threshold. Age \geq 70 years would account for 1 point, 3 points for immobilization and 3 points for malignancy. Overall, 99% of the patients identified by the 2012 ACCP score to be at increased risk for VTE were correctly classified by the simplified risk score, yielding a sensitivity of 98%, specificity of 95%, and positive and negative predictive values of 96% and 97% respectively.

DISCUSSION

The current study yielded two main results. The 2012 ACCP guidelines, and a comprehensive local RAM derived from the 2008 guidelines identified the same cohort at high risk of VTE. Secondly, a careful assessment of contributing risk factors among patients according to the 2012 ACCP guidelines allowed

Table 4. Prevalence of risk factors among patients with score \geq 4 according to the 2012 guidelines

Risk factor	Patients (%)
Reduced mobility	92
Age > 70	72
Acute infection/Rheumatologic disease	54
Heart/respiratory failure	38
Active cancer	25
Obesity	12
Acute MI/Stroke	9
Recent trauma/Surgery	7
Previous VTE	5
Thrombophilia	0
Hormonal treatment	0

MI = myocardial infarction, VTE = venous thromboembolic episode

us to develop a simple local 3-variable VTE RAM. When compared to the 2012 ACCP guidelines, this RAM correctly identified 99% of the cohort patients with a score of 4 or above.

The local three-variable RAM we created was based on the following model. This model suggests prescribing prophylaxis if the patient presents with any two of the following three risk factors: immobility, malignancy, or age > 70. Any of the following contraindications would prevent prescription: anticoagulant treatment, platelet count < 100,000, and recent bleeding.

Hospitalized patients with acute medical illness have an up to eightfold risk of VTE; such complications remain an important cause of in-hospital death [21]. The ACCP guidelines for prevention of VTE recommend daily administration of prophylactic therapy for those who are considered at high risk for VTE (Grade 1B) [18]. However, real-world adherence to VTE screening among hospitalized medical patients is poor, ranging between 27% and 33% [22,23]. In the current study, we noted a similar underutilization of VTE prophylaxis among eligible patients. In order to improve physicians' compliance with the guidelines, in 2012 the ACCP published an update on Clinical Practice Guidelines for VTE prevention introducing the Padua score. This simplified 11-variable score was aimed at replacing the 20-variable RAM score recommended in 2008. The current study found that the newly improved 2012 guideline utilization was as low as the more cumbersome 2008 derived RAM. Thus, a concern was raised whether the implementation of the 2012 ACCP guidelines would improve the rates of VTE prophylaxis at all [24]. In a hectic and high turnover setting such as an Israeli internal medicine ward, a locally based and simple RAM used as a preliminary screening tool may increase VTE prophylaxis.

No assessment was made of the utilization of a local VTE RAM on the frequency of VTE prophylaxis administration. Such a study may require an extended duration to assure natu-

ral implementation of the new score into daily practice. A prolonged study term may help to overcome biases created by the researchers' motivation to implement their new model.

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