Level of concordance between two risk-assessment models for predicting venous thromboembolism in medical patients at admission

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ABSTRACT

Objectives To evaluate the level of concordance between the 2007 PRETEMED guidelines and the 2012 American College of Chest Physicians (ACCP) guidelines in medical patients at admission.

Methods A cross-sectional, observational and descriptive study was designed and included all adult medical patients admitted from an emergency department. Firstly, patients classified as low-moderate risk and high risk according to PRETEMED were compared to those classified by ACCP as low and high risk. Secondly, the same analysis was performed but this time low and moderate-high risk patients according to PRETEMED were compared to ACCP low and high risk patients. The level of concordance was calculated using the kappa concordance index. The study was approved by the Ethics Committee for Clinical Research of the hospital.

Results The analysis was performed with 207 patients; 53.1% were male and the median age was 75.3 years (minimum 18, maximum 100 years old). The most common diagnosis at admission was related to a respiratory disease (37.2%). The level of concordance was 0.59 (95% CI 0.48 to 0.70) when moderate risk patients were grouped with low-risk patients and 0.53 (95% CI 0.42 to 0.65) when moderate risk patients were grouped with high-risk patients.

Conclusions The level of concordance between both guides is moderate. It would be helpful to confirm whether the level of agreement improves when the patient's condition stabilises after several days of hospitalisation.

This lack of correlation between the degree of risk and the prophylaxis prescribed suggested that individual risk is not sufficiently valued, especially in medical patients who usually present, concomitantly, several risk factors for VTE.^{6 7}

For this reason, numerous scientific societies have developed models to assess individual risk of VTE such as the 2007 PRETEMED guidelines (one of the first international guidelines to provide a table of well-defined risk calculations) and the Padua Prediction Score, included in the ACCP 2012 guidelines.^{8 9} Both risk-assessment models are the most accepted models in Spain (see online supplementary appendix 1). However, given the different risk category classification for VTE between the two guides, the level of concordance was assessed.

The aim of this study was to evaluate the level of concordance between the 2007 PRETEMED guidelines and the 2012 ACCP guidelines in medical patients at admission.

METHODS

A cross-sectional, observational and descriptive study was designed and included all adult medical patients admitted from an emergency department (ED) during 7 days (between 20 November 2012 and 26 November 2012) at a 1400-bed tertiary care hospital.

Patients to whom anticoagulants were prescribed for therapeutic purposes, and patients admitted to the intensive care unit or maternity wards were excluded. Patients with contraindications for the prescription of pharmacological prophylaxis (hypersensitivity to the drug, background or suspected heparin-induced thrombocytopenia, active bleeding or increased risk of bleeding because of impaired haemostasis) were included in the study to assess their individual risk of VTE.

Variables collected

A database was designed and included the following information obtained from the ED medical record:

- Demographical data (age, gender and bodyweight)
- Diagnosis at admission
- Analytical parameters at admission (international normalised ratio (INR), prothrombin time (s), activated partial thromboplastin time

INTRODUCTION

Venous thromboembolism (VTE) is a frequent cause of preventable illness and death in hospitalised patients.^{1 2}

In 2008, the ENDORSE study, considered the largest study to address this issue, evaluated both the risk of VTE and the adequacy of thromboprophylaxis in 68 183 patients from 358 hospitals in 32 countries.^{3 4} This study revealed a large number of patients at high risk of VTE not receiving thromboprophylaxis according to the American College of Chest Physicians (ACCP) 2004 guidelines;⁵ it also showed that the use of preventive measures in surgical patients (58.5%) was more frequent than in medical patients (39.5%).

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(aPTT) (s), fibrinogen (mg/dL), and number of platelets ($\times 10^9/L$)

- Presence of risk factors for VTE (based on the PRETEMED guide): age >60 years; air travel >6 h; active inflammatory bowel disease; acute myocardial infarction (AMI); antidepressants; antipsychotics; aromatase inhibitors; bed rest >4 days; central venous catheter; chemotherapy; class III chronic heart failure (CHF); class IV CHF; chronic obstructive pulmonary disease (COPD) with severe decompensation; neoplasia; diabetes mellitus; hormonal contraceptives; hyperhomocysteinaemia; HIV; hormone replacement therapy; lower limb injury without surgery; myeloma with chemotherapy; nephrotic syndrome; obesity (body mass index (BMI) >28 kg/m²); paralysis of lower limbs; pregnancy/postpartum; deep vein thrombosis; prior superficial vein thrombosis; severe infection; smoking >35 cigarettes/day; stroke with lower limb paralysis; tamoxifen/raloxifen; thrombophilia; vasculitis (Beçhet/Wegener).
- Presence of risk factors for VTE (based on the Padua Prediction Score): active cancer; previous VTE; reduced mobility; already known thrombophilic condition; recent trauma and/or surgery (<1 month); being elderly (≥ 70 years); heart and/or respiratory failure; AMI or ischaemic stroke; obesity (BMI ≥ 30 mg/kg²); acute infections and/or rheumatological disorder; ongoing hormonal treatment.

Two experienced clinical pharmacists in VTE working in the ED were in charge of introducing the data into the database. The following sources of information were revised for each patient: electronic medical record (available on the hospital website), analytical results from the ModuLab programme, and in-hospital drug prescriptions, collected using the Prescriplant electronic prescribing software available on the hospital website.

VTE risk assessment

The individual risk of VTE was calculated based on the PRETEMED guide that classifies patients into low risk (if the score is equal to 1–3), moderate risk (if the score is equal to 4) and high risk (if the score is >4).

In addition, the individual risk was also assessed according to the criteria established by the ACCP 2012 guidelines. In this case, the guide classifies patients into two categories: low risk if the score is <4 and high risk if the score is ≥ 4 ⁷ (Table 1).

Level of concordance

The level of concordance between both guides was calculated. Firstly, patients classified as low-moderate risk and high risk according to PRETEMED were compared to those classified by ACCP as low and high risk. Secondly, the same analysis was performed but this time low and moderate-high risk patients according to PRETEMED were compared to ACCP low and high risk patients.

Table 1 Venous thromboembolism risk assessment according to PRETEMED and ACCP guidelines

Adjusted risk	PRETEMED 2007	ACCP 2012
Low	1–3	<4
Moderate	4	–
High	>4	≥ 4

ACCP, American College of Chest Physicians.

The study was approved by the Ethics Committee for Clinical Research of the hospital. No additional risk was observed and the informed consent was a non-compulsory requisite.

Statistical analysis

This was a descriptive study that utilised descriptive statistics only. Continuous, normally distributed variables were expressed as mean ($\pm$ SD) and non-normally distributed variables were expressed as median with IQR. Proportions were expressed as percentages with IQR.

The concordance assessment between both guides was calculated using the kappa (κ) concordance index.

All statistical analyses mentioned were performed using the statistical analysis package SPSS V.15.0. Chicago, SPSS Inc.

RESULTS

A total of 393 patients were examined and 186 of them were excluded as they did not fulfil inclusion criteria: nine patients (2.3%) were transferred to the intensive care unit, 83 (21.1%) to a maternity ward, six patients (1.5%) were terminally ill and only required supportive care, nine patients (2.5%) were diagnosed with acute VTE, 11 (2.8%) with acute coronary syndrome, six (1.5%) with ischaemic stroke, and 62 patients (15.8%) required chronic anticoagulation (six patients for pulmonary embolism, 10 patients for deep venous thrombosis, 45 for atrial fibrillation, and one had a prosthetic cardiac valve).

The final analysis was performed with 207 patients; 53.1% were male patients and the median age was 75.3 years (minimum 18, maximum 100 years old). The most common diagnosis at admission was related to a respiratory disease (37.2%). Bodyweight was not registered in the emergency medical record of any patient.

The characteristics of the study population are summarised in table 2.

Risk factors for VTE

The most prevalent risk factor in our study population regardless of which guide was used was infection, followed by being elderly. The third risk factor was diabetes mellitus (20.3%) in the PRETEMED guide and respiratory failure in the ACCP guidelines (47.8%). The complete list of risk factors is shown in table 2.

According to the recommendations of the PRETEMED guideline, 44% of the patients was at low risk of developing VTE, 16.4% at moderate risk, and 39.6% at high risk. Based on the ACCP guideline, 57% of the study population was at low risk and 43% at high risk.

Level of concordance

On the one hand, when low-moderate and high risk patients based on PRETEMED guidelines were compared to ACCP low risk or high risk patients, the level of concordance between both guides was 0.59 (95% CI 0.48 to 0.70).

On the other hand, when low and moderate-high risk patients according to PRETEMED were compared to ACCP low risk and high risk patients, the level of concordance between both guides was 0.53 (95% CI 0.42 to 0.65) (table 3).

DISCUSSION

The level of concordance between both guides is moderate. The number of factors included in each guide and the weight given to each factor differ one from the other.

There are a number of conflicting factors that could contribute to an increased risk of VTE according to the PRETEMED guide.

Table 2 Description of general characteristics

	N (%)
Demographical characteristics	
Gender (male)	110 (53.1)
Median age (years) (Q1–Q3)	75.3 (53.5–82.9)
Analytical parameters	
Platelets at admission ($\times 10^9/L$) $\pm$ SD	211.6 $\pm$ 100.2
INR at admission $\pm$ SD	1 $\pm$ 0.1
aPTT (s) $\pm$ SD	29.4 $\pm$ 5.5
Prothrombin time (s) $\pm$ SD	12.4 $\pm$ 7.7
Fibrinogen (mg/dL) $\pm$ SD	612.7 $\pm$ 192.0
Diagnosis at admission	
Respiratory disease	77 (37.2)
Others	39 (18.8)
Genitourinary disease	28 (13.5)
Gastroenterological disease	28 (13.5)
Signs and symptoms not associated with a clear disease	18 (8.7)
Cardiovascular disease	17 (8.2)
Risk factors for VTE according to PRETEMED	
Age >60 years	128 (61.8)
Air travel >6 h	0
Active inflammatory bowel disease	1 (0.5)
Acute myocardial infarction	0
Antidepressants	29 (14)
Antipsychotics	18 (8.7)
Aromatase inhibitors	0
Bed rest >4 days	34 (16.4)
Central venous catheter	0
Chemotherapy	6 (2.9)
Class III CHF	21 (10.1)
Class IV CHF	5 (2.4)
COPD with severe decompensation	22 (10.6)
Diabetes mellitus	42 (20.3)
Hormonal contraceptives	1 (0.5)
Hyperhomocysteinaemia	0
HIV	13 (6.3)
Hormone replacement therapy	0
Lower limb injury without surgery	1 (0.5)
Myeloma with chemotherapy	0
Neoplasia	28 (13.5)
Nephrotic syndrome	0
Obesity (BMI >28 kg/m ²)	26 (12.6)
Paralysis of lower limbs	0
Pregnancy/postpartum	0
Previous DVT	5 (2.4)
Prior SVT	0
Severe infection	131 (63.3)
Smoking >35 cigarettes/day	5 (2.4)
Stroke with lower limb paralysis	0
Tamoxifen/raloxifen	0
Thrombophilia	0
Vasculitis (Beçhet/Wegener)	0
Risk factors for VTE according to ACCP	
Active cancer	28 (13.5)
Previous VTE	5 (2.4)
Reduced mobility	34 (16.4)
Already known thrombophilic condition	0
Recent (≤ 1 month) trauma and/or surgery	25 (12.1)
Elderly age (≥ 70 years)	124 (59.9)
Respiratory failure	99 (47.8)
Heart failure	26 (12.6)

Continued

Table 2 Continued

	N (%)
Acute ischaemic stroke	3 (1.4)
Acute myocardial infarction	0
Acute infection	134 (64.7)
Rheumatological disorder	33 (15.9)
Obesity (BMI ≥ 30 kg/m ²)	26 (12.6)
Ongoing hormonal treatment	1 (0.5)

ACCP, American College of Chest Physicians; aPTT, activated partial thromboplastin time; BMI, body mass index; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; INR, international normalised ratio; SVT, superficial vein thrombosis; VTE, venous thromboembolism.

Firstly, COPD is given a score of 3 and it is a very common factor in our study population (10.6%). Some studies showed that patients with COPD have an increased risk of VTE, especially during acute exacerbations requiring hospitalisation.^{10–11} However, the ACCP scale does not contemplate this factor.

Secondly, the PRETEMED guide considers elderly patients who are above 60 years of age, but this threshold is higher in the ACCP scale (≥ 70 years).

Thirdly, a higher number of risk factors are included in the PRETEMED guide compared to the ACCP guideline (33 vs 14). However, the formula used by the PRETEMED guideline in order to calculate VTE risk can only be applied if the patient has at least one precipitating process or a process with adjusted weight ≥ 2 .

However, there are also several conflicting factors that could contribute to an increased risk of VTE according to the 2012 ACCP guide.⁹

- The final VTE risk score can be directly calculated and it does not depend on the existence of a specific process.
- Both guidelines consider infection as a risk factor for VTE. Nevertheless, in the case of the ACCP, the infection does not need to be severe.
- Common risk factors have a higher score in the ACCP than in the PRETEMED guide (eg, neoplasia and previous VTE have a risk score of 3, while in the PRETEMED scale, the score given to both of them is 2).
- Both guidelines consider trauma as a VTE risk factor. However, in the PRETEMED scale, trauma should only be considered if it affects lower limbs; in our study population, most traumas were cranioencephalic (24 cases).

Table 3 Level of concordance between the two risk-assessment models

	PRETEMED	
	Low-moderate risk N (%)	High risk N (%)
ACCP		
Low risk	101 (48.8)	17 (8.2)
High risk	24 (11.6)	65 (31.4)
	PRETEMED	
	Low risk N (%)	Moderate-high risk N (%)
ACCP		
Low risk	80 (38.6)	38 (18.4)
High risk	11 (5.3)	78 (37.7)

ACCP, American College of Chest Physicians.

In 2012, Gallardo *et al* published a study that evaluated the level of concordance between the PRETEMED and the 2004 ACCP guidelines.¹² In this case, the level of concordance was high ($\kappa=0.68$ and 0.81). One of the main reasons that could explain this discrepancy is related to the risk factor 'bed rest >4 days' which is given a high score in both guidelines. In the study of Gallardo *et al*, VTE risk assessment was performed at some point during the patient's period of hospitalisation, whereas in our study it was calculated at admission. For this reason, the factor 'bed rest' was present in 55.5% of the patients in their study compared to a 16.4% in our research.

Furthermore, Gallardo *et al*¹² pointed out that PRETEMED criteria overestimates VTE risk compared to the 2004 ACCP guideline due to the high number of risk factors considered (59.6% of patients were at high risk according to PRETEMED vs 50% based on ACCP). However, in our study, the ACCP scale classified more patients at high risk (43% vs 39.6%). Regardless of which guide was followed, a lower percentage of patients were classified as high risk because, as it has been mentioned above, the presence of 'bed rest' was not as common as in the Gallardo *et al*¹² study (the risk score given to 'bed rest' is 2 in the PRETEMED guide and 3 in the 2012 ACCP scale).

Both sets are widely distributed throughout our country, so one of the main questions that arise after analysing the data is: who is doing well? One possible cause for the lack of agreement is the fact that the 2012 ACCP guidelines focus on hospitalised patients, whereas PRETEMED was developed in order to take into account the ambulatory setting. Future studies should investigate which scale better identifies patients at risk.

Examples from the literature also show frequent discrepancies between clinical guidelines, for example, regarding the treatment of type 2 diabetes or lipid-lowering management.^{13 14} For this reason, in our opinion, the most important issues to be considered when selecting which recommendations to include in an institutional protocol are to evaluate the available evidence thoroughly and to have this evidence discussed by a broad panel of experts.

Regarding study limitations, the most frequent bias is the difficulty of validating the information obtained from medical records, as it may either be wrong or may not have been recorded. Furthermore, single-site case studies limit the ability to generalise the results. It would be preferable to experience

similar situations in other centres in order to confirm our finding or, alternatively, accept that we are dealing with an isolated incident in our institution.

In conclusion, the level of concordance between both guides is moderate. It would be helpful to confirm whether the level of agreement improves when the patient's condition stabilises after several days of hospitalisation.

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What this paper adds

What is already known on this subject

- Venous thromboembolism (VTE) is the most common preventable cause of hospital death.
- Adequate thromboprophylaxis has reduced the rate of hospital-acquired VTE.
- Models have been developed to assess individual risk of VTE.

What this study adds

- The level of concordance between two widely accepted VTE guides is moderate.