

Venous thromboembolism risk assessment in hospitalised patients: A new proposal

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OBJECTIVE: Cross-sectional studies have been conducted to evaluate the adequacy of prophylaxis for venous thromboembolism. However, these studies often evaluate prophylaxis on the data collection day, without analysing the prophylactic dose or duration and without reference to inappropriate use in patients without risk. A prospective, observational study was performed to assess the adequacy of prophylaxis in a general medicine ward of a university hospital.

METHOD: In the analysis, the use of the proper prophylactic dose at the correct time, the use in patients with contraindications, and the misuse in patients without risk of venous thromboembolism were considered.

RESULTS: A total of 245 patients were evaluated. Of these patients, 104 (42.4%) were considered to be at risk, and 82.7% either received adequate prophylaxis (i.e., the correct dose at the right time) or did not receive prophylaxis because it was contraindicated. Among the 141 patients who were not at risk, 81 (57.4%) incorrectly received prophylaxis, the majority (61/81) of whom presented with risk factors but did not demonstrate reduced mobility. Among the entire group, only 59.6% of patients were properly treated.

CONCLUSIONS: The evaluation of prophylaxis adequacy should consider not only whether the correct dose is administered at the correct time but also whether it is used in patients with contraindications and whether it is inappropriately administered to patients who are not at risk.

KEYWORDS: Deep Vein Thrombosis; Guidelines; Inpatients; Pulmonary Embolism; Prophylaxis.

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INTRODUCTION

Although venous thromboembolism (VTE) is the main preventable cause of death in hospitalised patients (1,2), VTE prophylaxis is still not routinely administered in most hospitals (3-6). There are numerous barriers to prophylaxis use, especially the natural resistance to change, fear of side effects, lack of effective institutional policies, and even lack of knowledge regarding the guidelines or difficulties in remembering the recommendations (7). Therefore, having a simple tool to aid in risk assessment and prophylaxis prescription is essential. However, various proposals from international societies indicate the lack of a universally accepted tool (8-11).

Studies assessing the adequacy of VTE prophylaxis are usually limited to an analysis of the number of patients at risk and the number who received prophylaxis (mechanical or drug) (3-6). Moreover, cross-sectional studies with data collected on a single day are common; however, these studies do not allow for an assessment of the adequacy of an anticoagulant dose or prophylaxis duration (4-6). In addition, patients not at risk for a VTE who received improper prophylaxis are not typically described in these studies (4-6).

The primary objective of this study was to evaluate the adequacy of VTE prophylaxis in a general medical ward and to present the results in a systematic manner, including the results of patients who were and were not at risk and details regarding why the use of prophylaxis was correct or incorrect.

METHODS

This prospective, observational study was conducted from October to December 2010 in a general practice ward of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, which is a university hospital

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and the biggest quaternary public hospital in Brazil. The personnel in the ward are divided into four groups, each consisting of second-year internal medicine residents, fifth-year medical students, and assistant teachers who regularly guide the team. Prescriptions are prepared by the second-year residents and checked by the assistant teachers during rounds. At the time of the study, there was no institutional protocol for or systematic training in VTE prophylaxis; therefore, the procedures varied according to the experience of the doctors working during that period. The study was approved by the local ethical committee, and because this study was observational in nature, informed consent was not required.

Assessment of VTE risk

The algorithm from the Brazilian Guidelines for VTE Prophylaxis in Hospitalised Patients was used to assess VTE risk (Figure 1). According to this algorithm, the patient is initially evaluated for reduced mobility and age >40 years. Reduced mobility is defined as an acute loss of mobility secondary to the cause of hospital admission that requires the patient to remain primarily lying down or sitting at the bedside for an estimated duration of at least 3 days. To be considered at risk for VTE, patients must be at least 40 years

of age; however, the doctor should consider the risk for each individual with significant risk factors for VTE, even if the patient is younger than 40 years of age. If the initial criteria are not met, the patient is not considered to be at risk and should have his or her health condition re-evaluated at least every 2 days. If the initial criteria are met, the presence of an additional risk factor related to VTE development is assessed. If there is at least one additional risk factor, the patient is considered to be at risk (Figure 1). If the patient is considered to be at risk for VTE, the contraindications for chemoprophylaxis are assessed. If the contraindication is absolute or if the doctor considers the risk of bleeding to be greater than the risk of thrombosis, the patient should receive mechanical prophylaxis; otherwise, chemoprophylaxis is indicated. The protocol was completed for each patient, and the data were extracted from the patient records during admission. The doctors responsible for patient care were not aware of the collected data.

Adequacy of prophylaxis

According to the Brazilian Guidelines, VTE prophylaxis for medical patients should be performed with unfractionated heparin (UFH) or low-molecular-weight heparin at high prophylactic doses (8). At the hospital utilised for this

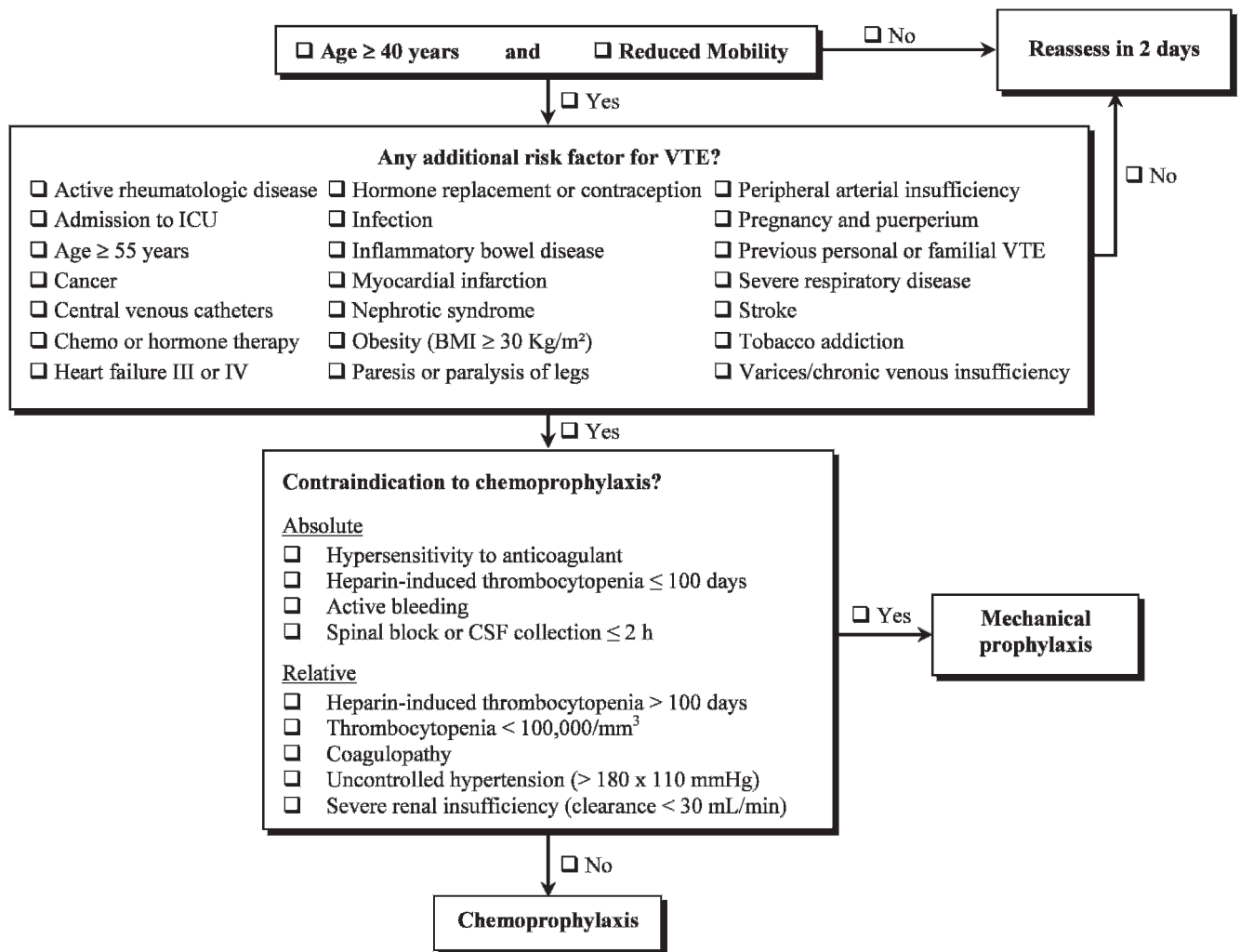


Figure 1 - Algorithm from the Brazilian Guidelines for VTE Prophylaxis in Hospitalised Patients.



study, only UFH and enoxaparin were available; the doses considered suitable were 5,000 U SC every 8 hours and 40 mg SC every 24 hours, respectively. For patients with a creatinine clearance of less than 30 mL/min, UFH 5000 U SC every 12 hours or enoxaparin 20 mg SC every 24 hours was considered to be appropriate (8). Prophylaxis was considered incorrect when the doses differed from these standards, when chemoprophylaxis was used in patients with an absolute contraindication, or when prophylaxis was not administered for 3 or more days during any period of hospitalisation.

The adequacy of prophylaxis and the development of deep vein thrombosis (DVT) or symptomatic pulmonary embolism (PE) were evaluated daily in each patient during the hospitalisation. Phone calls were performed at 30 and 90 days after discharge to identify VTE occurrence or death secondary to PE.

Statistical analyses

Because this study was observational with the primary objective of assessing the adequacy of prophylaxis according to the Brazilian Guidelines for Prevention of VTE, statistical analyses were not required. The patients who developed symptomatic VTE were identified. However, the study was not designed to compare rate of VTE development between patients who did or did not receive prophylaxis.

RESULTS

During the study, 248 patients were admitted to the hospital; 3 were admitted with existing thrombosis and were excluded from the analysis. Of the 245 remaining patients, 132 (53.9%) were female. The patient ages ranged from 13 to 91 years; the average age was 54.3 ± 19.2 years; and the average hospitalisation time was 18.8 ± 16.9 days (Table 1). A total of 104 (42.4%) of the 245 patients were considered to be at risk for VTE according to the Brazilian Guidelines. Most of the at-risk patients were female (57.7%), with an average age of 61.3 ± 15.3 years and an average hospitalisation time of 22.3 ± 18.4 days. In this group, the patients had an average of 2.9 ± 1.2 risk factors for VTE; 56.8% had 3 or more risk factors, and 8.7% had 5 or 6 additional risk factors (Table 1). The risk factors found most often were as follows: age 55 years or older (26.6%), infection (11.3%), cancer (11.0%), tobacco use (10.0%), heart failure (functional class III or IV; 7.3%), severe respiratory disease (6.0%), and nephrotic syndrome (5.3%; Table 2).

The analysis of prophylaxis adequacy showed that 86 of the 104 patients (82.7%) at risk for VTE were treated properly [i.e., they had no contraindications and received the correct dose of prophylactic drug (77/104; 74.0%) or had

Table 2 - Risk factors exhibited by patients considered to be at risk for VTE listed in descending order of frequency.

Risk factor	N	%
Age ≥ 55 years	80	26.6
Infection	34	11.3
Cancer	33	11.0
Smoking	30	10.0
Heart failure (functional class III or IV)	22	7.3
Severe respiratory disease	18	6.0
Nephrotic syndrome	16	5.3
Hospitalisation in the intensive care unit	15	5.0
Varicose veins and venous insufficiency	13	4.3
Previous or family history of VTE	9	3.0
Ischemic stroke	8	2.7
Central venous catheterisation	8	2.7
Acute myocardial infarction	4	1.3
Paresis or paralysis of the lower limbs	4	1.3
Active rheumatic disease	3	1.0
Chemotherapy or hormone therapy	2	0.7
Obesity	1	0.3
Arterial insufficiency	1	0.3

VTE, venous thromboembolism.

an absolute contraindication and were not given chemoprophylaxis (9/104; 8.7%; Table 3)]. Eighteen (17.3%) patients at risk for VTE did not receive the correct prophylaxis, either because heparin was not used in the absence of contraindications (14/104; 13.5%) or because chemoprophylaxis was used in the presence of an absolute contraindication (4/104; 3.8%; Table 3).

Among the 141 patients with no risk factors for VTE, the correct prophylaxis was used in 60 (42.6%) cases (Table 3). However, in 81 (57.4%) patients, chemoprophylaxis was used improperly. These patients were not considered to be at risk for VTE for the following reasons: no reduced mobility (68/141; 48.2%), no risk factors (6/141; 4.3%), or no reduced mobility or additional risk factors for VTE (7/141; 5.0%; Table 3). Considering all 245 patients, the prophylaxis was correct in 146 patients (59.6%) and incorrect in 99 (40.4%).

In 3 of the 245 patients (1.2%), VTE was detected at some point during the hospitalisation period or after discharge. Below is a brief description of each of these cases.

Patient 1 was a 57-year-old female with inactive systemic lupus erythematosus and a history of smoking. She was admitted with reduced mobility due to asthenia and weakness, which were attributed to depression at the end of her 10-day hospitalisation. Twenty days after discharge, she passed away from a PE diagnosed at another facility; an autopsy was not performed. Her risk factors included age ≥ 55 years and smoking history. During her hospitalisation,

Table 1 - Characteristics of the hospitalised patients according to VTE risk.

Characteristics	Total	With VTE Risk	Without VTE Risk
Number of patients, N (%)	245 (100.0%)	104 (42.4)	141 (57.6)
Females, N (%)	132 (53.9%)	60 (57.7)	72 (51.1)
Males, N (%)	113 (46.1)	44 (42.3)	69 (48.9)
Mean age in years (SD)	54.3 (19.2)	61.3 (15.3)	49.1 (20.2)
Mean days of hospitalisation (SD)	18.8 (16.9)	22.3 (18.4)	16.0 (15.2)
Mean number of RFs for VTE (SD)	2.2 (1.4)	2.9 (1.2)	1.7 (1.2)
3 or more RFs (%)	40.0	56.8	27.7
5 or 6 RFs (%)	3.7	8.7	0.0

VTE, venous thromboembolism; SD, standard deviation; RFs, risk factors.

**Table 3 - The adequacy of VTE prophylaxis according to the Brazilian Guidelines.**

Characteristic	Number	%
At risk for VTE	104	100.0
Correct prophylaxis	86	82.7
Pharmacological prophylaxis, no absolute contraindication and administered at the correct dose	77	74.0
With absolute contraindication and no pharmacological prophylaxis	9	8.7
Incorrect prophylaxis	18	17.3
Not performed and no contraindication was present	14	13.5
Incorrect dose	0	0.0
Performed despite an absolute contraindication	4	3.8
Not at risk for VTE	141	100.0
Correct prophylaxis (did not receive prophylaxis)	60	42.6
Incorrect prophylaxis (received prophylaxis)	81	57.4
No reduced mobility	68	48.2
Reduced mobility, but no risk factors	6	4.3
No reduced mobility and no risk factors	7	5.0
All patients	245	100.0
Correct prophylaxis	146	59.6
Incorrect prophylaxis	99	40.4

VTE, venous thromboembolism.

she was considered to be at risk for VTE and received prophylaxis with UFH 5000 U 3 times a day.

Patient 2 was a 62-year-old male admitted for lower limb paresis secondary to vitamin B₁₂ deficiency. He was considered to be at risk for VTE, received prophylaxis with UFH 5000 U 3 times a day for 7 days, was maintained without prophylaxis for 5 consecutive days, and then received prophylaxis with enoxaparin 40 mg daily for 5 days before being diagnosed with a DVT. His risk factors included age \geq 55 years and lower limbs paresis.

Patient 3 was a 19-year-old female with mental retardation. She was bedridden at home for 6 months with a history of extensive weight loss due to pulmonary tuberculosis that was diagnosed only on admission. In addition to tuberculosis, venous thrombosis of the subclavian and lower limbs was detected after admission, and whether these thromboses developed before or after admission was unclear. She did not meet the risk criteria for VTE due to being quite young and having chronically decreased mobility. She was adopted, so obtaining data regarding familial thrombosis was not possible. No investigation regarding the presence of thrombophilia was performed.

DISCUSSION

A total of 42.4% of the medical patients were at risk for VTE. This rate is similar to the value found in the ENDORSE study, which evaluated 68,183 patients admitted from 32 countries and found that 41.5% of the hospitalised medical patients were at risk for VTE (4).

The average length of hospitalisation in the present study was high (22.3 days), and the patients had multiple additional risk factors for VTE (an average of 2.9, and 56.8% had 3 or more risk factors). The rate of symptomatic events detected in the present study was 1.2%, which is similar to the values of 1.0 to 1.5% in the placebo groups from studies of prophylaxis in hospitalised medical patients (12,13).

Of the patients at risk for VTE, 82.7% correctly received prophylaxis. Compared with other studies, this rate is significantly high. In the ENDORSE study mentioned above, which evaluated prophylaxis in 32 countries, the rates of prophylaxis use were quite heterogeneous, with an average

rate of 50%, and only 2 countries reached adequacy rates close to 80% (Germany and Switzerland). Notably, the criteria used in ENDORSE were not as strict; prophylaxis was appropriate when the patient received any anticoagulant, regardless of the dose or duration of treatment (4). The high rate of adequate prophylaxis in patients at risk may be explained by the fact that the study was conducted in a university hospital, where the medical staff are concerned about patient safety, even though no institutional protocol for VTE prophylaxis was available at that time and the doctors had not received specific training for VTE prophylaxis. However, it is possible that this same concern resulted in excessive prophylaxis use in patients who were not at risk for VTE. Of the 141 patients who were not at risk, 81 (57.4%) incorrectly received prophylaxis, and most (68/81) were patients without reduced mobility.

Prophylaxis was correctly administered to 59.6% of the patients included in this study. We believe that this statistic is the best way to assess adequate prophylaxis administration, although this type of analysis is not commonly reported. In fact, in our review, we did not identify any study that included a similar analysis.

In conclusion, in a university hospital with patients of high complexity, 42.4% of the hospitalised patients were at risk for VTE, and the majority (82.7%) received the proper prophylaxis. However, more than half (57.4%) of the patients who were not at risk also received prophylaxis, which means that only 59.6% of the patients were properly treated. The analysis of adequate use of prophylaxis should consider not only the correct use of prophylaxis in patients at risk but also inadvertent use in patients who are not at risk.

AUTHOR CONTRIBUTIONS

Alckmin CA was involved in the study conception and design, data acquisition, analysis and interpretation, critical review, and final approval. Garcia MD was involved in data acquisition, analysis and interpretation, critical review, and final approval. Bricola SA and Martins MA were involved in the study conception and design, data analysis and interpretation, critical review, and final approval. Paiva EF and Lichtenstein A were involved in the study conception and design, data analysis and interpretation, drafting of the article, and final approval.



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