

## Quality of venous thromboembolism prophylaxis in a university hospital in Brazil

### *Qualidade das prescrições de profilaxia para tromboembolismo venoso em um hospital universitário no Brasil*

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**ABSTRACT:** *Objective:* Though recommended, prophylaxis for venous thromboembolism is not always correctly prescribed. In light of this fact, our objective is to evaluate the quality of medical prescriptions with regards to venous thromboembolism prophylaxis in a Brazilian teaching hospital. *Methods:* During a 30-day period, medical prescriptions to patients treated at the internal medicine ward, surgery ward and at the intensive care unit were assessed. Patients on anticoagulants for a non-prophylactic reason were excluded. This cross-sectional analysis evaluated the appropriateness of venous thromboembolism prophylaxis based on the 9th Guideline of the American College of Chest Physicians. *Results:* 358 prescriptions have been assessed, of which 65 were excluded. Out of the remaining 293 selected prescriptions, 106 (36.2%) were considered inaccurate. The main cause of inadequacy was underprescription, which was observed in 72 cases (67.9%). Surgery wards accounted for the majority of inaccurate prescriptions (48.72%) compared to internal medicine (35.11%) and critical care ones (26.2%) ( $p=0.0013$ ). *Conclusion:* Alarming rates of inadequate prescriptions regarding venous thromboembolism prophylaxis were found. Underprescription was the main cause of inadequacy. Surgery wards were responsible for most of the imprecision. Further interventions are required in order to improve this important and safe medical practice for hospitalized patients.

**Keywords:** Thrombosis/prevention & control; Venous thromboembolism/prevention & control; Disease prevention; Hospitalization; Prescriptions; Anticoagulants; Pulmonary embolism; Heparin.

**RESUMO:** *Objetivo:* Embora preconizada, a profilaxia para tromboembolismo venoso não é sempre corretamente prescrita. O objetivo deste estudo é avaliar o nível de adequação das prescrições de profilaxia para tromboembolismo venoso para pacientes internados em um hospital universitário. *Métodos:* Trata-se de um estudo analítico transversal no qual foram avaliadas prescrições para pacientes internados nas unidades clínicas, cirúrgicas e críticas de um hospital universitário durante 30 dias. Excluíram-se pacientes em uso de anticoagulantes para finalidade diferente da profilática. Os critérios de avaliação da profilaxia de tromboembolismo venoso basearam-se na 9ª Diretriz do *American College of Chest Physicians*. *Resultados:* 358 prescrições foram analisadas. 65 foram excluídas. Das 293 prescrições selecionadas, 106 (36,18%) foram consideradas incorretas. A subprescrição foi a principal causa de inadequação, observada em 72 casos (67,9%). Inadequações foram maiores nas unidades cirúrgicas (48,72%) do que nas clínicas (35,11%) e críticas (26,2%) ( $p = 0,0013$ ). *Conclusões:* Preocupantes taxas de inadequação da profilaxia para tromboembolismo venoso para pacientes internados foram encontradas, havendo predomínio da subprescrição. As maiores inadequações foram encontradas nas unidades cirúrgicas. Intervenções são necessárias para otimizar essa importante prática de segurança ao paciente hospitalizado.

**Descritores:** Trombose/prevenção & controle; Tromboembolia venosa/prevenção & controle; Prevenção de doenças; Hospitalização; Prescrições; Anticoagulantes; Embolia pulmonar; Heparina.

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**INTRODUCTION**

Being admitted to any hospital in the world can be risky. According to the World Health Organization, it is estimated that one in 10 patients suffer some type of harm during hospitalization, and it is said that half of those harms could have been avoided<sup>1</sup>. The venous thromboembolism (VTE) is one of those potential causes of damage in hospitalized patients.

The VTE is a condition resulted from a hypercoagulability state. It includes the deep vein thrombosis (DVT), usually in the pelvis and inferior limbs, and its feared complication, the pulmonary embolism (PE). It is a multifactorial disease originated from interactions between two main components: inherited or acquired thrombosis predisposing conditions, and a variety of known risk factors. The VTE is frequent, with similar incidence rates to stroke<sup>2</sup>. About 25% of VTE episodes are associated to hospitalizations<sup>3</sup> and 50 to 75% of those episodes occur inside a hospital<sup>4</sup>. It is estimated that this condition relates with 10% of inpatient death events<sup>5</sup>.

Beyond the high mortality rates, VTE is also related to complications development in hospitalized patients, which impacts on hospital expenses<sup>6</sup>. In a population-based study, the predicted average cost for patients with acute VTE related to a present or recent hospitalization was 2.5 times higher than the cost with oncologic patients, the control group<sup>7</sup>.

However, this undesirable scenario could be avoided. Several studies have shown that anticoagulants can reduce up to 63% of the relative risk for VTE occurrence during hospitalization<sup>8,9</sup>. Because of that, it has been considered the “number one practice in patient safety” by the Agency for Healthcare Research and Quality<sup>10</sup>.

Nevertheless, prophylactic prescription rates of anticoagulants in hospitals are still far from being considered adequate. Many Brazilian and international studies showed that pharmacological prophylaxis is usually underprescribed, resulting in a scenario where hospitalized patients are at risk for developing VTE<sup>11-13</sup>. Venous thromboembolism is still considered the main cause of avoidable death in hospitals<sup>14</sup>.

The objective of this study is to evaluate the adequacy of VTE prophylaxis prescription for patients admitted to a teaching hospital.

**METHODS**

This is a cross-sectional analytical study that evaluated the quality of VTE prophylaxis prescriptions of patients older than 18 years old who were hospitalized from 19/07/2017 to 19/08/2017 in either the internal medicine ward, the surgical ward or the intensive care unit from a

teaching hospital. Prescriptions of anticoagulants with a non-prophylactic purpose were excluded. Prescriptions of patients whose clinical conditions interfered in VTE prophylaxis indication were also excluded (those are listed in Results section).

The criteria for evaluation taken from the 9th edition of the Guideline for VTE Prophylaxis of the American College of Chest Physicians were adopted, which recommends anticoagulants prophylaxis for patients with high risk for VTE development. The Padua<sup>15</sup> and Caprini<sup>16</sup> scores were adopted to perform the risk stratification of clinical and surgical patients, respectively. When indicated, a VTE prescription was considered adequate if it was presented in any of the following posologies:

1) Low molecular weight heparin, 40 mg, subcutaneous, once daily.

2) Unfractionated heparin, 5000 IU, subcutaneous, twice daily or three times daily.

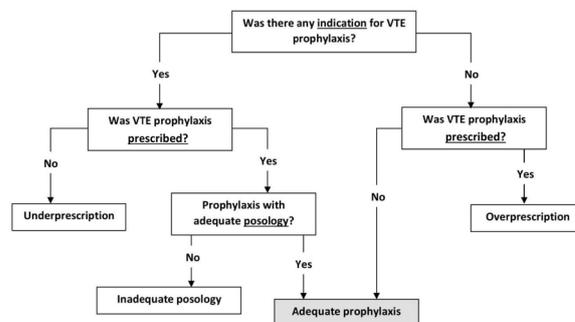
3) Fondaparinux, 2.5 mg, subcutaneous, once daily.

For chronic kidney disease patients, posology correction is recommended. In this case, prescriptions were considered adequate with the following posologies:

1) Low molecular weight heparin, 20 mg, subcutaneous, once daily.

2) Unfractionated heparin, 5000 IU, subcutaneous, twice daily or three times daily.

The prescriptions evaluation method is showed in Figure 1.



**Figure 1** – Prophylaxis prescriptions evaluation flowchart

The flowchart illustrates how the prescriptions for VTE prophylaxis were evaluated. When there was indication for prophylaxis but no prescription, underprescription was categorized. When there was indication and anticoagulant drug was prescribed, the analysis moves to a new stage, the posology evaluation. If the posology was incorrect, we categorized it as inadequate

posology; if correct, the prescription was considered an adequate prophylaxis. On the other hand, when there was no indication for prophylaxis, but anticoagulants were prescribed, overprescription was categorized; when not indicated and not prescribed, the prophylaxis was considered adequate.

This study was approved by the Research Ethics Committee of the Clinical Hospital of the Federal University of Paraná (Project number: 775445 | Approval number: 2.131.561 | Date of approval: June 22, 2017) and prior to the beginning of the daily data collection, the attending physician of each patient signed an informed consent form.

The collected data were stored in a Microsoft Excel spreadsheet. The adequacy level of prophylaxis

was determined according to the matchup between the current conduct and the recommended ones by the guidelines. Results obtained by qualitative variables were described by frequencies and percentages. For inference of association between two qualitative variables, the hi-square and Fisher's exact tests were performed. The considered statistical significance was 5%. Data were analyzed by R Core Team Software, version 3.4.0<sup>17</sup>.

**RESULTS**

In total, 358 VTE prophylactic prescriptions were analyzed (Table 1). Patients' mean age in the sample was 57.7 years (18 to 96, SD 16.7).

**Table 1.** Distribution of selected patients by inpatient unit

	INPATIENT UNIT			General
	Internal medicine	Surgery	Intensive care	
Number of prescriptions	170 (47.5%)	85 (23.7%)	103 (28.8%)	358 (100%)
Gender				
Men	74 (43.5%)	45 (52.9%)	55 (53.4%)	174 (48.6%)
Women	95 (55.9%)	40 (47.1%)	48 (46.6%)	183 (51.1%)
Transgender woman	1 (0.6%)	-	-	1 (0.3%)
Age (years)	60.0 ± 15.8	51.3 ± 16.6	59.3 ± 17.1	57.7 ± 16.7

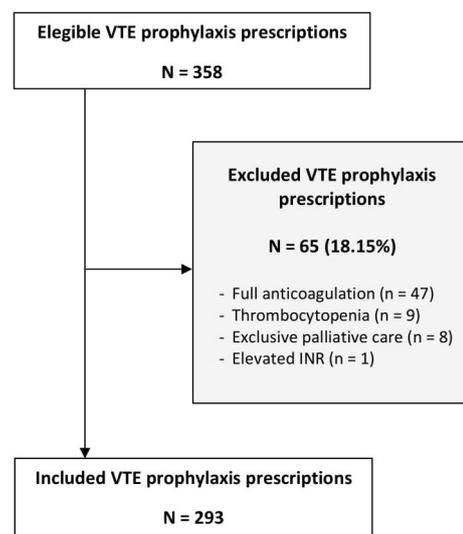
Sixty-five of the 358 analyzed prescriptions in this study had exclusion criteria (18.16%). The justifications for the exclusions are listed in Figure 2. Among the 47 patients under full anticoagulation, 19 had the diagnosis of venous thromboembolism.

A total of 358 prescriptions were elected for analysis, 65 of which were excluded. Therefore, 293 prescriptions were included in the study.

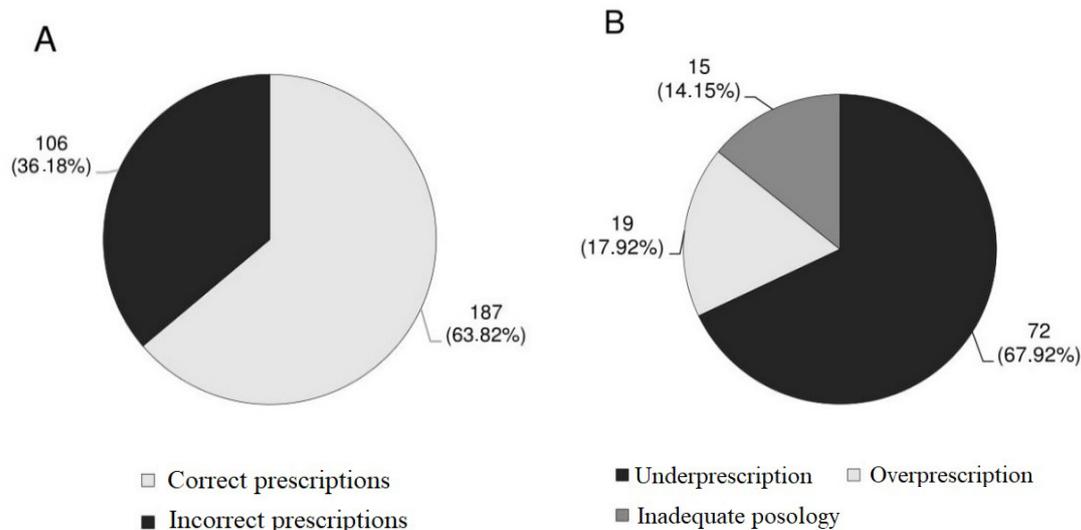
Figure 3 presents the results of the general analysis of VTE prophylaxis.

Prescriptions considered inappropriate due to incorrect posology (n = 15) had the following presentation: Enoxaparin 40 mg, once daily in chronic kidney disease patients (n = 8); Enoxaparin 20 mg, once daily in a patients without chronic kidney disease (n = 6); and Enoxaparin 40 mg twice daily (n = 1).

Among the analyzed units, the surgical ward presented the highest rates of inadequacy when prescribing VTE prophylaxis (48.72%; p = 0.0013) (Table 2).



**Figure 2.** Prescriptions included in and excluded from the study



**Figure 3** - General analysis of VTE prophylaxis. Graphic A illustrates the general distribution of adequacy levels of VTE prophylaxis prescriptions; graphic B presents the distribution of inadequacy causes among incorrect VTE prescriptions

**Table 2** – Analysis of VTE prophylactic prescriptions adequacy level according to inpatient unit

	INPATIENT UNIT			p-value
	Internal medicine	Surgery	Intensive care	
Correct prescriptions	85 (64.84%)	40 (51.28%)	62 (73.81%)	-
Incorrect prescriptions	46 (35.11%)	38 (48.72%)	22 (26.19%)	0.0013

Qui-squared test

The highest rate of incorrect prescriptions for VTE prophylaxis was found in surgical ward (48.72%), followed by internal medicine ward (35.11%), and the intensive care unit, which presented the lowest rate of incorrect prescriptions (26.19%).

In all units, underprescription was the major cause of inadequate prophylaxis, once again highlighting the surgical ward, which presented the highest underprescription rates among all units (94.74%,  $p < 0.001$ ) (Table 3).

**Table 3** – Cause of inadequacy of incorrect prescriptions according to inpatient unit

	CAUSE OF INADEQUACY		
	Overprescription	Underprescription	Inadequate posology
Internal medicine ward	16 (34.78%)	24 (52.17%)	6 (13.04%)
Surgery ward	1 (2.63%)	36 (94.74%)	1 (2.63%)
Intensive care unit	2 (9.09%)	12 (54.55%)	18 (36.36%)

Fisher's exact test;  $p < 0.001$

Among the causes of inadequacy of incorrect prescriptions for VTE prophylaxis, underprescription was the main cause in all three inpatient units studied. The surgical ward presented the highest underprescription rates (94.74%). The internal medicine ward presented the highest overprescription rates (34.78%). The intensive care unit presented the highest rates of inadequate posology (36.36%). Fisher's exact test,  $p$ -value  $< 0,001$ .

The internal medicine ward presented the highest

overprescription rates (34.78%,  $p < 0.001$ ), and the intensive care unit presented the highest rates of incorrect posology (36.36%,  $p < 0.001$ ).

## DISCUSSION

This study revealed inadequacies in venous thromboembolism prophylaxis prescriptions.

Among the analyzed prescriptions, 36,2% were considered inappropriate. Underprescription was the main reason for inadequacy (67,9%,  $p = 0,013$ ). Other similar studies performed in other locations have also found that the underuse of VTE prophylaxis was the main reason for inadequacy. A study performed in 4 hospitals in São Paulo, 3 of them teaching hospitals, showed that 20% of patients at high risk for VTE did not receive thromboprophylaxis. In Vitória-ES, also in a teaching hospital, inadequacy rate was slightly higher, at 47%<sup>11</sup>, and in a multicenter study conducted in 21 hospitals in 8 countries, this rate was even higher, reaching 60%<sup>13</sup>. Other studies have registered levels of up to 77%<sup>12, 19</sup>.

The highest inadequacy rate was found in surgical units (48.72%) when compared to clinics (35.11%) and critical care units (26.19%) ( $p = 0.013$ ). Amongst the incorrect prescriptions for surgical patients, 94.74% were due to underprescription ( $p < 0.01$ ). Similarly, subprescription was the main unconformity observed in critical units (54.44%) and also in clinic ones (52.17%) ( $p < 0.01$ ). In the latter, the overprescription rate was the highest found among all sectors (34.78%,  $p < 0.01$ ).

This significant difference between the inadequacy rates of VTE prophylaxis prescription in different types of hospitalization is unusual. In Vitória, 44% of surgical prescriptions were incorrect, while 48% of clinics prescriptions were as well. In the same study, no difference was registered between prophylaxis for patients admitted to the ward and those for critical units<sup>11</sup>. In contrast, in most studies in which there was a significant discrepancy between types of hospital admission, clinical patients were more likely not to receive adequate prophylaxis compared to surgical patients<sup>9,20</sup>. Deheinzeln et al.<sup>18</sup> revealed that surgical patients were more likely to receive adequate thromboprophylaxis compared to clinical patients in São Paulo hospitals (50% vs. 36%,  $p < 0.05$ ), as opposed to the present study.

The lowest index of inadequate prescriptions was found in critical units (26.19%,  $p = 0.013$ ). A possible explanation is that critical patients usually presents with a great number of risk factors for VTE, which may facilitate the identification of indications for thromboprophylaxis<sup>21</sup>. On the other hand, these sectors presented the highest frequency of inadequate prophylaxis dosage, despite the correct indication (36.36%,  $p < 0.01$ ).

The reasons why thromboprophylaxis in hospitalized patients is often underused are often discussed. The postulated hypotheses that may explain the prominent underprescription in this study include: the unawareness of medical professionals about the potential morbidity related to thromboembolic events, so that the risk of VTE is underestimated<sup>22</sup>; the confusion about appropriate prophylaxis for different risk levels<sup>20</sup>; the lack of familiarity or agreement of medical professionals with current guidelines, whose complexity may make it difficult to

adhere to their practices<sup>13,22</sup>; and the resident turnover as a limiting factor in training for proper prophylaxis practice. Moreover, a British study points out that some inexperienced doctors do not feel that VTE risk assessment is their responsibility<sup>23</sup>.

Another important reason for underutilization of prophylaxis is the overestimated risk of bleeding due to anticoagulants. It is common to fear the occurrence of hemorrhagic events in these cases<sup>24</sup>, since bleeding has a greater impact than thrombotic events. It leads to a desire to “do no harm” the patient, and may turn into omission of VTE prophylaxis. However, this argument is not justified, since the benefits resulting from the prevention of VTE outweighs the risk of bleeding with the prophylactic use of anticoagulants<sup>22</sup>.

There is also an economic reason. There is a cost-containment purpose used as a justification for not prescribing anticoagulants for patients at risk for VTE. This argument, however, is not supported, since it is proven to be more costly to treat VTE complications than to afford prophylactic anticoagulation<sup>25</sup>.

In addition, many studies have shown that the implementation of hospital protocols optimizes the safety and care of hospitalized patients. The use of the Padua score for risk stratification in a prospective study was associated with a higher appropriate rate of thromboprophylaxis<sup>15</sup>. It suggests that the lack of a hospital protocol, which could facilitate the assessment of the need for prescription prophylaxis, must have contributed to the prescriptions of the studied hospital being in disagreement with ACCP norms.

The lack of a protocol may also have favored overprescription episodes, which accounted for 17.92% of the incorrect prescriptions recorded, as well as those of posology errors (14.15%). These categories of inadequacy are supposed to be result of medical practice of “universal” prescription of anticoagulants for hospitalized patients, ultimately disregarding an individual risk analysis and other characteristics that would influence the choice of drug dosage.

Thus, some possible solutions to reduce VTE prophylaxis inadequacy rates are investments in educational measures for medical professionals, aiming at clarifying the risks of VTE in the hospitalized patient, as well as deconstructing misconceptions regarding the risks of use of anticoagulants. Also, the ACCP suggests the implementation of hospital protocols, which have already been shown to improve the use of prophylaxis and reduce VTE rates in hospitalized patients<sup>27,28</sup>.

In contrast, a study performed in Morocco showed that interventions did not result in a significant improvement in thromboprophylaxis. Actually, there was an increase in the rate of overprescription for VTE prophylaxis after the installation of hospital guidelines<sup>24</sup>.

This contradictory scenario reveals that VTE

prophylaxis remains a challenge to medical practice. Therefore, more targeted studies are needed to better understand which are the critical points that hinder the proper practice for VTE prophylaxis in each locality. Based on these results, interventions should be carried out.

A limitation of this study is the fact that the consent form was signed by the attending physicians prior to data collection, which may configure the so-called Hawthorne effect, which consists in a positive change in the conduct of the professional when he is aware that is being evaluated<sup>29</sup>. However, it is believed that this effect has been minimized, since the daily prescriptions had previously been registered by the physician when data for the research were collected. And even though this positive change of conduct had happen, the rates of inadequacy were alarming. This leads to the hypothesis that, without the Hawthorne effect, the rates of inadequacy could be even higher.

Therefore, we suggest future research using different methods in order to eliminate the Hawthorne

effect. Also, we reinforce the importance of local studies to better characterize the VTE prophylaxis scenario. Finally, we propose quality assessment of other important prophylaxis for inpatient safety, such as delirium and pressure ulcer prophylaxis.

## CONCLUSION

Alarming inadequacy rates of prescriptions for venous thromboembolism prophylaxis for hospitalized patients were found in a Brazilian teaching hospital. Underprescription was the major cause of inadequacy. It was in the surgical units in which the highest rates of incorrect prophylaxis were registered. Thus, effective interventions based on a specific analysis for each locality may be capable of adapting the prescriptions for venous thromboembolism prophylaxis. Maybe in the future, being admitted to any hospital can be safe.

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