Venous thromboembolism prophylaxis in a general hospital*

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Abstract
Objective: To evaluate the use of venous thromboembolism (VTE) prophylaxis in a general hospital. Methods: A cross-sectional cohort study at the Hospital Nossa Senhora da Conceição, located in the city of Porto Alegre, Brazil, involving a random sample of patients admitted between October of 2008 and February of 2009. We included patients over 18 years of age and hospitalized for more than 48 h. The exclusion criteria were anticoagulant use, pregnancy, puerperium, and a history of thromboembolic disease. The adequacy of prophylaxis was evaluated in accordance with a protocol created by the Hospital and principally based on the American College of Chest Physicians guidelines, eighth edition. Results: We included 262 patients. The mean age was 59.1 ± 16.6 years. The most common risk factors were immobilization (in 70.6%), infection (in 44.3%), cancer (in 27.5%), obesity (in 23.3%), and major surgery (in 14.1%). The risk of VTE was classified as high and moderate in 143 (54.6%) and 117 (44.7%) of the patients, respectively. Overall, 46.2% of the patients received adequate prophylaxis, 25% of those with ≥ three risk factors for VTE and 18% of those with cancer, the differences between these last two groups and their counterparts (patients with < three risk factors and those without cancer) being statistically significant (p < 0.001 for both). Conclusions: Our data reveal that nearly all patients at our hospital were at risk for VTE, and that less than half received adequate VTE prophylaxis, which is in agreement with the literature. It is surprising that inadequate prophylaxis is more common in high-risk patients.

Keywords: Venous thromboembolism/prevention and control; Venous thrombosis/prevention and control; Heparin.

Resumo
Objetivo: Avaliar a prática de profilaxia para tromboembolia venosa (TEV) em pacientes em um hospital geral. Métodos: Estudo de coorte transversal conduzido no Hospital Nossa Senhora da Conceição, localizado na cidade de Porto Alegre (RS), com uma amostra constituída de pacientes internados selecionados randomicamente entre outubro de 2008 e fevereiro de 2009. Foram incluídos pacientes maiores de 18 anos e internados por mais de 48 h. Os critérios de exclusão foram pacientes em uso de anticoagulantes, história de doença tromboembólica, gestação e puerpério. A adequação da profilaxia foi avaliada seguindo as recomendações de um protocolo criado pela instituição e tendo como base principal a diretriz da American College of Chest Physician, oitava edição. Resultados: Foram incluídos 262 pacientes com média de idade de 59,1 ± 16,6 anos. Os fatores de risco mais comuns foram immobilização (70,6%), infecção (44,3%), câncer (27,5%), obesidade (23,3%) e cirurgia maior (14,1%). Na avaliação do nível de risco para TEV, 143 (54,6%) e 117 pacientes (44,7%), respectivamente, foram classificados como de risco alto e moderado. No geral, 46,2% dos pacientes tiveram profilaxia adequada, assim como 25% dos pacientes com três ou mais fatores de risco e 18% dos pacientes com câncer, e houve diferenças estatisticamente significativas entre esses grupos quando comparados àqueles com menos de três fatores de risco e sem câncer (p < 0,001 para ambos). Conclusões: Os dados demonstram que quase a totalidade dos pacientes do hospital estava em risco para TEV e que menos da metade deles recebeu profilaxia adequada, dados esses semelhantes aos da literatura. A inadequação da profilaxia é surpreendentemente maior em pacientes de alto risco.

Descritores: Tromboembolia venosa/prevención y control; Trombose venosa/prevenção e controle; Heparina.
Introduction

Venous thromboembolism (VTE), which combines two related conditions—deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE)—is the leading and most commonly unrecognized cause of morbidity and mortality in hospitalized patients. In addition, PTE is considered the leading preventable cause of in-hospital death.

The current incidence of VTE without prophylaxis is unknown, because of the difficulty in assembling a control/placebo group. Therefore, early studies that relied on the analysis of a population receiving no prophylaxis are still used as reference sources. In this context, the incidence of nosocomial VTE is estimated to be approximately 10–40% among medical and surgical patients, reaching 75% in patients with acute stroke and in those undergoing hip surgery. Although VTE is frequently associated with trauma and surgery, most cases occur in medical patients, of whom 50–70% have symptomatic PTE and 70% have fatal PTE.

Nearly all hospitalized patients have at least one risk factor for VTE, and approximately 40% have three or more. Among medical patients, the most common risk factors are congestive heart failure (in 25–31%), severe acute respiratory disease (in 24–53%), infection (in 20–54%), and obesity (in 27–53%). Other important factors include the hospitalization itself, which is considered an independent risk factor and can increase the risk of VTE by eight times, and cancer, which can increase this risk by six times. Among cancer patients, VTE is one of the most common complications, patients who are hospitalized and patients who are receiving chemotherapy being at higher risk, as are post-surgical patients.

Regarding surgical patients, there is, in addition to clinical risk of VTE, the risk related to the type of surgery these patients are undergoing. This becomes important because surgical risk of venous thromboembolic events is low in outpatient procedures and minimally invasive procedures, whereas it is higher in major surgical procedures. The classification of the type of procedure (minor or major surgery) to which the patient will be exposed is the key to the stratification of surgical risk of VTE. The first study on major and minor surgery was published in 1917, major surgery being defined as all procedures requiring general anesthesia, involving the opening of large cavities, involving risk of severe hemorrhage, or involving patients at risk of death (emergency surgery). Currently, there are video-assisted procedures and closed procedures (laparoscopy, thoracoscopy, mediastinoscopy, arthroscopy, transurethral surgery, transvaginal surgery, etc.) For the purposes of VTE risk assessment, these procedures are considered to have a profile similar to that of minor surgery. In a review article, there is a recommendation that prophylaxis of patients undergoing laparoscopic surgery be focused only on the clinical risk status of each patient. However, abdominal laparoscopic procedures lasting more than one hour are associated with a state of hypercoagulability that is as intense as is that of open surgery, resulting in a hypothetically higher risk of VTE.

Cancer patients undergoing surgical procedures have a two times higher risk of DVT and a three times higher risk of PTE than do patients without cancer undergoing similar procedures.

There is evidence that primary prophylaxis substantially reduces the incidence of VTE without increasing the risk of major bleeding. In one meta-analysis, the use of prophylaxis with unfractionated heparin (UFH) in medical inpatients reduced the number of cases of fatal PTE by 64%, that of symptomatic PTE by 58%, and that of symptomatic DVT by 53%. The results are even more relevant in surgical patients, the number of cases of fatal PTE being reduced by 70%, that of symptomatic PTE being reduced by 58–71%, and that of DVT being reduced by 75–79%. However, a prospective study of 2,373 patients undergoing cancer surgery showed that VTE was the leading cause of death within the first 30 postoperative days, despite the fact that prophylaxis was used in 82% of the patients. Since 1977, there has been strong evidence of the particular importance of thromboprophylaxis in this last situation.

In addition to the arguments previously cited, routine use of VTE prophylaxis reduces overall expenditures.

Over the last decade, a number of guidelines have been published in order to increase compliance with prophylactic measures and to perfect prophylactic strategies.
recently, a review of the recommendations of the American College of Chest Physicians (ACCP) proposed a more aggressive approach, especially regarding hospitalized cancer patients, cancer patients with multiple risk factors for VTE, or patients falling into both categories.\(^7\)

The objective of the present study was to evaluate the use of VTE prophylaxis in a general hospital in Brazil.

**Methods**

This was a cross-sectional cohort study at the Hospital Nossa Senhora da Conceição, which is located in the city of Porto Alegre, Brazil, and is the largest general hospital in the southern region of the country. This hospital, which is affiliated with the Brazilian National Ministry of Health and provides treatment only via the Brazilian Unified Health Care System, is a teaching hospital with 750 adult inpatient beds available for use in a number of medical and surgical specialties, except for orthopedics and neurosurgery.

The study involved a random sample of 262 patients admitted to the medical and surgical wards, including the ICU, of the Hospital Nossa Senhora da Conceição between October of 2008 and February of 2009. Randomization was performed by drawing bed numbers, and the number of beds used in each specialty was determined considering the proportionality between the number of beds used in the specialty and the total number of beds available in the hospital. The inclusion criteria were being over 18 years of age and having been hospitalized for more than 48 h in any of the specialty wards, whereas the exclusion criteria were anticoagulant use because of other medical conditions, pregnancy, puerperium, and a history of established thromboembolic disease.

The collection of data related to the selected patients and the evaluation of the use of prophylaxis were performed at a single time point by reviewing patient charts and prescription forms. We did not set a specific time point for data collection during the hospital stay. Data collection was performed by residents in internal medicine, who were previously trained in the appropriate techniques. In addition, the physicians responsible for prescribing to patients were not informed of the study. The main variables studied were age, gender, serum creatinine levels, risk factors for VTE, contraindications to the use of heparin, type of surgery, and type of anesthesia, as well as type of prophylaxis prescribed and dose prescribed.

The following risk factors were considered: immobilization (more than half a day confined to bed or chair, excluding sleep hours, for more than 3 days); use of oral contraceptives or hormone replacement therapy; stroke; cancer; use of a central venous catheter; inflammatory bowel disease; myeloproliferative disease; severe lung disease (abnormal pulmonary function test results or abnormal blood gas analysis results, or a combination of the two, in patients with respiratory failure, decompensated COPD, pulmonary hypertension, or interstitial lung disease); acute coronary syndrome; congestive heart failure; infection (pneumonia, sepsis, abdominal infection, pyelonephritis, or complicated skin infection); ICU admission; obesity (body mass index \(\geq 30\) kg/m\(^2\)); limb paralysis or paresis; chemotherapy; radiotherapy; nephrotic syndrome; and a history of VTE or thrombophilia.

The following contraindications were evaluated: active bleeding; active peptic ulcer disease; a history of heparin-induced thrombocytopenia; allergy to heparin; coagulopathy, defined as thrombocytopenia (platelet count < 50,000/L) or a prolonged prothrombin time (international normalized ratio > 1.5); recent hemorrhagic stroke; uncontrolled hypertension (arterial pressure > 200/120 mmHg); proliferative retinopathy; and liver failure.

The institution created a hospital protocol to guide the prescription of VTE prophylaxis (Chart 1). The protocol, mainly based on the ACCP guidelines,\(^7\) eighth edition, and also on the review of some articles pertaining to each specialty, was created through meetings with the team of internal medicine physicians and physicians practicing other specialties of the hospital.

The patients were stratified by risk of VTE (low, moderate, and high), and the prescription to each patient was considered adequate or inadequate on the basis of whether or not it followed the protocol.

In the analysis of the results, we determined descriptive measures for the prevalence of risk factors and the frequency of the use of VTE
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Table 2 shows the methods used for VTE prophylaxis. This evaluation revealed that low-molecular-weight heparin (LMWH) was not prescribed for VTE prophylaxis.

When we analyzed the adequacy of prophylaxis in relation to the protocol created for the hospital, we found that 141 patients (53.8%) received inadequate prophylaxis and 121 patients (46.2%) received adequate prophylaxis.

Results

The sample consisted of 262 patients, 137 (52.3%) of whom were male. The mean age was 59.1 ± 16.6 years.

Table 1 shows the most common risk factors for VTE among the hospitalized patients, chief among which were immobilization (in 70.6%), infection (in 44.3%), cancer (in 27.5%), obesity (in 23.3%), and major surgery (in 14.1%).

The major specialties responsible for patient care were as follows: internal medicine (22.1%); general surgery (13.4%); urology (7.6%); infectology (7.3%); gynecology (6.5%); pulmonology (6.5%); and vascular surgery (6.1%). Of the sample as a whole, 21.4% were post-surgical patients and 78.6% were medical patients.

The risk of VTE was classified as high in 143 patients (54.6%), as moderate in 117 patients (44.7%), and as low in only 2 patients (0.8%).

Table 1 - Risk factors.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Immobilization</td>
<td>185 (70.6)</td>
</tr>
<tr>
<td>Infection</td>
<td>116 (44.3)</td>
</tr>
<tr>
<td>Cancer</td>
<td>72 (27.5)</td>
</tr>
<tr>
<td>Obesity</td>
<td>61 (23.3)</td>
</tr>
<tr>
<td>Major surgery</td>
<td>37 (14.1)</td>
</tr>
<tr>
<td>Use of a central venous catheter</td>
<td>35 (13.4)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>22 (8.4)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>21 (8.0)</td>
</tr>
<tr>
<td>Limb paralysis/paresis</td>
<td>21 (8.0)</td>
</tr>
<tr>
<td>Severe lung disease</td>
<td>20 (7.6)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>16 (6.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>13 (5.0)</td>
</tr>
<tr>
<td>Chemotherapy/radiotherapy</td>
<td>7 (2.7)</td>
</tr>
<tr>
<td>Myeloproliferative disease</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>Use of oral contraceptives/ hormone replacement therapy</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>History of venous thromboembolism</td>
<td>3 (1.1)</td>
</tr>
</tbody>
</table>

GCS: graded compression stockings; IPC: intermittent pneumatic compression; DVT: deep vein thrombosis; and PTE: pulmonary thromboembolism.
considering patient risk level and the presence of contraindications (Table 3).

The analysis of the adequacy of prophylaxis with stratification by patient type (medical patients vs. post-surgical patients) revealed no statistically significant differences ($p = 0.27$). The prescription was considered adequate in 91 medical patients (44.2%) and in 30 post-surgical patients (53.6%).

Less than 9.5% of the patients had contraindications to the use of heparin for VTE prophylaxis. The major contraindications found in the sample were active bleeding (in 5.0%) and coagulopathy (in 3.8%). In the group of patients with contraindications, 44.0% received incorrect prescription of prophylactic measures.

The illness severity profile of the patients was assessed by analysis of the number of risk factors for VTE. Only 4% had no risk factors, whereas more than 40% had three or more risk factors. Of the patients with multiple risk factors, considered to be at high risk, 75% received inadequate VTE prophylaxis, as classified by the protocol of the institution, compared with 39.9% of the patients with less than three risk factors ($p < 0.001$; Table 4). The proportion of patients whose prophylaxis prescription was considered inadequate was higher among the cancer patients. Although cancer patients are currently recognized as high-risk patients, heparin for VTE prophylaxis was prescribed appropriately in only 18% of the cancer patients in the sample, this difference being considered statistically significant when these patients were compared with the patients without cancer ($p < 0.01$; Table 4).

### Discussion

The process of evaluating the prescription pattern and the rates of VTE prophylaxis adequacy at the hospital began in 2008, particularly after the release of the eighth edition of the ACCP consensus on VTE prevention in June of the same year, with the creation of a protocol for the hospital. In our study, we observed that 53.8% of the prescriptions of VTE prophylaxis were inadequate, as assessed by the institutional protocol. Most patients were high risk (54.6%), and approximately 75% of them were considered to receive inadequate VTE prophylaxis. Of the cancer patients—who are, by definition, high risk—82% were prescribed heparin for VTE prophylaxis inadequately.

Despite all evidence available in the literature, VTE prophylaxis is not widely practiced. International data show that most hospitalized patients are at risk for VTE and that only about half of these patients receive some type of prophylaxis. The use of VTE prophylaxis ranges from 3% to 70% in medical patients and from 0.2% to 92% in surgical patients among the various countries studied.

According to agencies that promote quality and safety in health care, the adequate use of thromboprophylaxis is considered an indicator of quality of hospital care. Although, for many years, there have been studies showing that the use of prophylaxis reduces morbidity and mortality in hospitalized patients, there are still a large number of reports that this intervention is underutilized in hospitals. In Brazil, reports evaluating the rate of use of prophylactic measures are scarce. Evaluations performed in general hospitals, university hospitals, or private hospitals report rates that fall far short of ideal, reaching values as low as 2.1%. The best results reported are those of rates that do not reach 50% in ward patients and 60% in ICU patients.

The low importance given to VTE prophylaxis might be attributable to the devaluation of VTE as a clinical entity, because VTE has a nonspecific clinical presentation and objective diagnosis is difficult. Perhaps the main reason for the limited use of preventive measures for VTE is the fear of bleeding, especially in the postoperative period. Our data reveal that less than 10% of the patients had contraindications to the use of prophylaxis.
thromboprophylaxis, which does not explain the rates of inadequacy found in our study.

The use of pharmacological prophylaxis in low-risk patients or in patients with contraindications could be more risky than beneficial. Our data reveal that there was a very small number of low-risk patients, negatively affecting the analysis of these data at our hospital. Among the 25 patients who had contraindications to the use of pharmacological prophylaxis, 11 (44%) were receiving inadequate prophylaxis, as assessed by the protocol.

At the Hospital Nossa Senhora da Conceição, UFH and a LMWH (enoxaparin) are available for VTE prophylaxis. Our study shows that, among the 197 patients who were prescribed heparin for thromboprophylaxis, 195 used UFH and only 2 (1%) used other types of pharmacological prophylaxis. The use of enoxaparin is controlled at the institution because of its higher cost. It is also of note that the hospital does not treat patients requiring orthopedic surgery, trauma surgery, or neurosurgery, which explains the option of not using LMWH.

Regarding the UFH dose, there is insufficient evidence to recommend the dose schedule of 5,000 IU three times a day over the dose schedule of 5,000 IU twice a day, because these two regimens have never been directly compared in medical or surgical patients. In a meta-analysis including 7,978 medical patients, the rate of thromboembolic events was lower, but not statistically so, in the group receiving 5,000 IU of heparin three times a day than in the group receiving 5,000 IU of heparin twice a day. In that study, the risk of major bleeding was higher with the dose of 5,000 IU three times a day than in the group receiving 5,000 IU of heparin twice a day. In our study, the rates of inadequacy found in our study.

The current literature recommends the use of prophylaxis with 5,000 IU of UFH three times a day in patients at high risk for thromboembolism, as well as in patients with multiple risk factors or cancer patients. The adoption of this recommendation in a hospital setting with high-risk patients is likely to have reduced the adequacy of the use of prophylaxis. In view of these findings, we should define, on the basis of the most recent evidence, new strategies to improve outcomes, and this adds to the challenge a large hospital faces in maintaining its practices and processes up-to-date.

Because of the large number of patients receiving inadequate prophylaxis at our hospital, a finding that is consistent with those of previous studies, it becomes necessary to implement effective measures to improve these rates.

One group of authors published a study evaluating VTE prophylaxis prescription in which physicians received electronic alerts about risk factors for VTE. That study showed that the rate of thromboprophylaxis was better in the study group than in the control group (33.5% vs. 14.5%, p < 0.0001) and that there was a 41% reduction in the rates of symptomatic DVT and symptomatic PTE (relative risk = 0.59; 95% CI: 0.43-0.81; p < 0.001).

According to the latest ACCP guidelines, all hospitals should take an active role in developing and implementing VTE prevention measures. Passive strategies, such as distributing educational materials or offering isolated educational events, are measures associated with poor compliance and are not recommended as an exclusive strategy. Active measures should include the use of computerized systems, periodic audits, and feedback on the functioning of the implemented measures.
The protocol created for the Hospital Nossa Senhora da Conceição and used for judging the adequacy of prophylaxis was the initial step toward the implementation of a strategy to improve these data. This strategy includes the use of electronic prescriptions to aid patient risk assessment, as well as frequent meetings and audits involving the teams.

References


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