Deep Vein Thrombosis in Elderly Patients Hospitalized in Subacute Care Facilities

A Multicenter Cross-sectional Study of Risk Factors, Prophylaxis, and Prevalence

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Background: The efficacy of venous thromboembolism prophylaxis has not been established, to our knowledge, in elderly patients hospitalized in subacute care facilities.

Objectives: To describe risk factors and physician practices in the prevention of venous thromboembolism and to estimate the prevalence of deep vein thrombosis.

Methods: A multicenter cross-sectional study was conducted in the subacute care departments of 36 French hospitals. The study population included 852 inpatients older than 64 years. Systematic ultrasound examination was performed by angiologists.

Results: Of the 852 inpatients, 178 (20.9%; 95% confidence interval [CI], 18.2%-23.8%) had 3 or more risk factors other than age, while 144 patients (16.9%; 95% CI, 14.4%-19.6%) had none. The rate of prophylactic anticoagulant treatment was 56.1%, ranging from 20.0% to 86.9%, depending on the department. In multivariate analysis, prophylaxis use was associated with acute immobilization (odds ratio [OR], 4.17; 95% CI, 2.48-7.01), chronic immobilization (OR, 3.19; 95% CI, 2.22-4.60), major surgical procedure (OR, 6.81; 95% CI, 4.26-10.88), and congestive heart failure (OR, 1.65; 95% CI, 1.02-2.67). Prophylaxis use was low in patients who had cancer (OR, 0.49; 95% CI, 0.29-0.84) or myocardial infarction (OR, 0.39; 95% CI, 0.14-1.00). It was not significantly associated with paralytic stroke or history of venous thromboembolism. Deep vein thrombosis was detected in 135 patients (15.8%; 95% CI, 13.4%-18.5%): 50 (5.9%; 95% CI, 4.4%-7.7%) had proximal vein thrombosis and 85 (10.0%; 95% CI, 8.0%-12.2%) had calf vein thrombosis.

Conclusions: The prevalence of deep venous thrombosis is high in these patients, despite wide use of prophylaxis. Further prospective studies assessing the clinical benefit of extended duration prophylaxis are needed in elderly patients hospitalized in subacute care settings.

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VENOUS THROMBOEMBOLISM is a common clinical problem among hospitalized patients. The clinical silence of deep vein thrombosis and the potential mortality of pulmonary embolism make prevention the most suitable response to this disease. The rationale for thromboprophylaxis with surgical patients has been extensively established by many randomized clinical trials. There are also sufficient data to make recommendations on prophylaxis for various conditions such as myocardial infarction and ischemic stroke, as well as prophylaxis for critical care patients and patients with cancer. Moreover, the efficacy of prophylaxis for nonselected medical patients has been recently assessed. In contrast, rigorous scientific data providing evidence of the efficacy of prophylaxis in patients hospitalized in subacute care settings are currently lacking, although these patients often have a combination of risk factors such as bed rest and age over 64 years. Subacute care settings are medical, rehabilitation, and skilled nursing services for inpatients who are not in the acute phase of an illness but who require a level of care higher than that provided in long-term care. In France, there are 1.6 subacute beds per 1000 inhabitants. The mean length of stay was 31.0 days in 1999. Patients are admitted into subacute care settings after discharge from acute care hospitals. Transition of elderly patients through subacute care settings are similar to those observed in the United States. Risk factors for venous thromboembolism among these patients have not been clearly described, except for major surgical procedures and stroke. Recommendations of ve-
nous thromboprophylaxis developed for acute care inpatients cannot be extended to this patient population.

To address the relative paucity of data on this growing population and before proposing clinical trials, a multicenter epidemiological study in subacute care facilities was carried out. We tried to estimate the prevalence of the risk factors of deep vein thrombosis in these patients, to describe physician practices in prophylaxis, and to estimate the prevalence of deep vein thrombosis detected by systematic ultrasound examination.

## METHODS

### STUDY DESIGN

A multicenter cross-sectional study was conducted in the subacute care departments of 36 hospitals evenly distributed throughout metropolitan France. Twelve of these departments were located in teaching hospitals. If there were more than 1 subacute care department in a hospital, one was randomly selected to maximize geographical diversity. For each patient, data on risk factors and prophylactic treatment were gathered and a systematic ultrasound examination was performed by a qualified angiologist.

### PATIENTS

The study population included hospitalized patients older than 64 years who were present on the day of the study in each selected department. Patients were excluded if they had a diagnosis of deep vein thrombosis or pulmonary embolism at admission or if they required long-term anticoagulant therapy because of atrial fibrillation, prosthetic heart valve, stroke, or atherosclerosis. The study was designed to enroll a sample of at least 800 patients, which was considered large enough to estimate the true proportion of prophylaxis for venous thromboembolism, with a 95% confidence interval of at most ±3.3%.

### DATA COLLECTION

Data were collected by independent physicians who were given standardized instructions on definitions and data collection techniques. They completed a data abstract form on the basis of medical records, nurses’ notes, and physicians’ orders. The data included sociodemographic characteristics, predefined risk factors for venous thromboembolism, concurrent treatment, contraindication to the use of anticoagulants, duration and modality of prophylaxis, and major adverse effects of prophylaxis. The risk factors assessed were derived from the literature. They included the following chronic or permanent factors: history of venous thromboembolism, current cancer, hereditary or acquired hypercoagulable state, chronic respiratory failure, congestive heart failure, hormone therapy (estrogen therapy, antiandrogen, and tamoxifen), varicos veins, current or previous paralytic stroke that remained symptomatic, history of myocardial infarction, inflammatory systemic disease, and chronic immobilization (defined as confinement to bed or to bed and armchair for more than 30 days). Transient risk factors included an orthopedic surgical procedure within the previous 6 weeks, other major surgical procedures within the previous 4 weeks, acute infectious disease within the previous 2 weeks, and acute immobilization for less than 30 days.

Patients were considered to be receiving prophylactic anticoagulant treatment if they were given unfractionated or low-molecular-weight heparin or warfarin sodium. Low-dose and high-dose low-molecular-weight heparin were both considered as an effective method of prophylaxis, since there were no evidence-based data on lack of efficacy of low-dose heparin in these patients. Patients who received aspirin or platelet aggregation inhibitors or used elastic stocking compression alone were considered as having received no prophylactic treatment. The previous major adverse effects of thromboprophylaxis (bleeding complications, thrombocytopenia, and local cutaneous hypersensitivity) that had occurred from the admission to the day of the study were recorded.

Several department characteristics were gathered: location in teaching hospital, rehabilitation vs skilled nursing care orientation, availability of ultrasound examination, and implementation of local venous thromboprophylaxis guidelines.

### ULTRASOUND EXAMINATION

Ultrasound examination was performed by experienced angiologists who were unaware of both risk factors and prophylaxis. Venous compression ultrasonography was performed as described previously, using 3- to 7.5-MHz transducers. All deep veins of the lower limbs were examined from the calf to the inferior vena cava. Incompressible thrombi of an anteroposterior diameter equal to or greater than 5 mm were considered positive. In patients with positive test results, anticoagulant treatment was recommended. Additional cases of symptomatic deep vein thrombosis or pulmonary embolism that had occurred within the 2 days following the day of the study were gathered.

### STATISTICAL ANALYSIS

The rate of prophylaxis for thromboembolism was calculated for all eligible patients and estimated by using the exact 95% confidence interval. The association between patients’ risk factors and the use of prophylaxis for thromboembolism was assessed using the crude odds ratio (OR) and was tested by using the χ² or Fisher exact test, when appropriate. The relationship between the rate of prophylaxis and the number of risk factors per patient was tested using χ² for trend. The association between department-related characteristics and rate of prophylaxis was tested using the Kruskal-Wallis rank sum test. Multivariate analysis was performed using random effect logistic models to account for the nonindependence of a department’s patient observations resulting from clustering. We assumed that the mean rate of prophylaxis use varies randomly between departments and covariates have the same effect among departments. Therefore, we entered the department as a random effect and all other covariates as fixed effects. Models were developed with both forward and backward selection procedures of patient characteristics associated with prophylaxis, with cutoffs of P<.15 for inclusion and P<.20 for exclusion. Variables with more than 2 categories were introduced using dummy variables. Statistical analyses were performed using the Stata 6.0 software (Stata Corporation, College Station, Tex). The study protocol was approved by the ethics committee for medical research (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Amiens, France), and written informed consent was obtained from each patient or a family member.

### RESULTS

#### STUDY POPULATION

A total of 957 patients were hospitalized on the day of the study in the 36 selected departments. Of these, 105 patients (11.0%) were excluded for the following reasons: diagnosis of pulmonary embolism or deep vein thrombosis present at admission in 40 cases (4.2%), long-term anticoagulant therapy in 61 cases (6.4%) (heart dis-
PREVALENCE OF RISK FACTORS

Other than age, the 3 most common risk factors were chronic or acute immobilization (48.2%; 95% confidence interval [CI], 44.8%-51.6%), major surgical procedure (22.2%; 95% CI, 19.4%-25.1%), and varicose veins (16.1%, 95% CI, 13.7%-18.7%) (Table 1). Overall, 178 patients (20.9%; 95% CI, 18.2%-23.8%) combined 3 or more risk factors, while 144 patients (16.9%; 95% CI, 14.4%-19.6%) presented no risk factors (Table 1).

USE OF PROPHYLACTIC ANTIAGGULANT TREATMENT

At the time of the study, 478 patients (56.1%; 95% CI, 52.7%-59.5%) received prophylaxis: 261 patients received high-dose low-molecular-weight heparin (30.6%; 95% CI, 27.5%-33.8%); 207, low-dose low-molecular-weight heparin (24.3%; 95% CI, 21.4%-27.3%); 6, unfractionated heparin (0.7%; 95% CI, 0.2%-1.5%); and 4, warfarin (0.5%; 95% CI, 0.1%-1.2%). On the day of the study, the mean duration of unfractionated heparin or low-molecular-weight heparin use was 33.8 days (median, 25 days; range, 1-268 days). A total of 17 patients (2.0%; 95% CI, 1.2%-3.2%) had a contraindication for the use of anticoagulants. Seventy-eight patients (9.1%) who received heparin, 24 patients (2.8%) who received platelet aggregation inhibitors, and 76 patients (8.9%) who used elastic compression stockings alone were considered not to be receiving prophylactic anticoagulant treatment.

In univariate analysis, the use of prophylactic anticoagulant treatment was significantly associated with acute and chronic immobilization, a major surgical procedure, current cancer, and acute infectious disease (Table 2). Overall, the use of prophylaxis increased significantly with the number of risk factors for venous thromboembolism (Figure 1). The rate of prophylaxis by department ranged from 20.0% to 86.9%. Prophylaxis use did not differ significantly depending on implementation of local guidelines, location in a teaching hospital, availability of ultrasound examination within 24 hours, or rehabilitation orientation.

In multivariate analysis, there was a significant department effect in the use of prophylaxis, supported by the variance of the intercept estimated at 0.49 (95% CI, 0.25-0.99; P=.04). Independent factors associated with

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Table 1. Patient Characteristics and Risk Factors*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>Prophylaxis, %</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
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<tr>
<td>No. of risk factors</td>
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<tr>
<td>0</td>
<td>169</td>
<td>16.9</td>
<td>1.00 (Reference)</td>
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<td>1</td>
<td>311</td>
<td>31.1</td>
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<td>≥3</td>
<td>311</td>
<td>31.1</td>
<td>1.00 (Reference)</td>
<td></td>
</tr>
</tbody>
</table>

*Values are percentage (95% confidence interval) unless otherwise specified.
†Not exclusive items.

Table 2. Univariate Analysis of Characteristics Associated With Prophylactic Anticoagulant Treatment*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>Prophylaxis, %</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
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<td>Major surgical procedure</td>
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<td></td>
<td></td>
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<tr>
<td>No</td>
<td>663</td>
<td>48.4</td>
<td>1.00 (Reference)</td>
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<td>Yes</td>
<td>189</td>
<td>83.1</td>
<td>5.23 (3.41-8.02)</td>
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<td>Immobilization</td>
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<td></td>
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<td>1.00 (Reference)</td>
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<td>Yes</td>
<td>127</td>
<td>74.8</td>
<td>3.48 (2.21-5.49)</td>
<td>&lt;.01</td>
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<td>History of venous thromboembolism</td>
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<td>No</td>
<td>284</td>
<td>63.4</td>
<td>1.90 (1.49-2.77)</td>
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<td>Yes</td>
<td>33.3</td>
<td>36.7</td>
<td>0.74 (0.55-1.00)</td>
<td>.06</td>
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<td>Acute infectious disease</td>
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<td>No</td>
<td>774</td>
<td>54.6</td>
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<td>Yes</td>
<td>78</td>
<td>70.5</td>
<td>1.98 (1.19-3.30)</td>
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<td>Congestive heart failure</td>
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<td>117</td>
<td>63.2</td>
<td>1.41 (0.94-2.11)</td>
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<td>826</td>
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<td>Yes</td>
<td>26</td>
<td>38.5</td>
<td>0.48 (0.21-1.07)</td>
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<td>Current cancer</td>
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<td>1.00 (Reference)</td>
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<tr>
<td>Yes</td>
<td>83</td>
<td>41.0</td>
<td>0.51 (0.32-0.81)</td>
<td>&lt;.01</td>
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</tbody>
</table>

Abbreviation: CI, confidence interval.
*Only characteristics with P<.15 are reported.
PREVALENCE OF DEEP VEIN THROMBOSIS

Deep vein thrombosis was detected by ultrasound examination in 135 patients (15.8%; 95% CI, 13.4%-18.5%): 50 patients (5.9%; 95% CI, 4.4%-7.7%) had proximal deep vein thrombosis, 55 (6.4%; 95% CI, 4.9%-8.3%) had isolated sural deep vein thrombosis, and 30 (3.5%, 95% CI, 2.4%-5.0%) had isolated muscular vein thrombosis. Bilateral thrombosis was found in 22 patients: 7 patients had proximal deep vein thrombosis and 15 patients had calf venous thrombosis. Of the 135 patients who had deep vein thrombosis detected by ultrasound examination, 34 (25.2%) also had clinical symptoms a posteriori. No additional case of symptomatic venous thrombosis nor pulmonary embolism was reported on either the day of the study or the following 2 days. The prevalence of deep vein thrombosis was significantly higher for patients who received no prophylaxis (20.8%; 95% CI, 16.3%-25.9%) than for patients who used elastic compression stockings alone (17.1%; 95% CI, 9.4%-27.5%), for patients who received anticoagulant alone (13.8%, 95% CI, 10.1%-18.1%), and for patients who received both elastic compression stockings and anticoagulant (10.4%; 95% CI, 6.3%-15.9%) ($\chi^2$ for trend=10.4; $P<.01$).

Among patients who did not use prophylactic anticoagulant treatment, the prevalence of systematically detected deep vein thrombosis was significantly increased in those who were acutely immobilized (OR, 2.59; 95% CI, 1.15-5.86) or had paralytic stroke (OR, 2.29; 95% CI, 1.07-4.87). When considering only symptomatic deep vein thrombosis, the results were comparable for patients acutely immobilized (odds ratio, 3.11; 95% CI, 0.58-16.72) or patients having paralytic stroke (OR, 6.12; 95% CI, 1.81-20.81). The rate of deep vein thrombosis remained significantly increased in patients who were acutely immobilized (odds ratio, 2.11; 95% CI, 1.03-4.30), despite use of prophylactic heparin treatment. It should be noted that only 6 (35%) of 17 recently bedridden patients who had deep vein thrombosis despite prophylactic treatment received high-dose low-molecular-weight heparin compared with 52 (67%) of those 78 patients who did not have deep vein thrombosis ($P=.03$).

ADVERSE EFFECTS OF THROMBOPROPHYLAXIS

No major adverse effect occurred on the day of the study. However, major adverse effects from the anticoagulant had occurred in 15 patients before the day of the study: bleeding complications in 9 cases and thrombocytopenia in 6 cases. In the 9 cases of previous bleeding, 2 patients received low-molecular-weight heparin on the day of the study and 3 used elastic compression stockings alone. In the 6 cases of previous thrombocytopenia, 1 patient received warfarin and 2 used elastic compression stockings alone. No current or previous case of local cutaneous hypersensitivity was reported.

We found a high prevalence of systematically detected deep vein thrombosis (over 15%) among patients hos-
Physicians seemed to be aware of this risk of venous thromboembolism, since 56% of patients received prophylactic anticoagulant treatment. Indeed, patients who presented common risk factors for venous thromboembolism (major surgical procedure, immobilization, acute infectious disease, and/or congestive heart failure) were more likely to receive prophylactic anticoagulant treatment. In addition, physicians were aware of the cumulative effects of risk factors, which has been evidenced in various epidemiologic studies. These findings are consistent with those of a previous study carried out in short-stay hospitals in Massachusetts. These authors have also reported a nonsignificant decrease in the rate of prophylaxis in patients who had cancer. Fear of bleeding complications and cases of end-stage cancer patients may explain this finding. Our study also highlighted wide hospital-to-hospital variations in the rate of prophylaxis (range, 20.0%-86.9%), which remained consistent after adjusting for independent risk factors in multivariate analysis. Such variations in practices are currently observed in situations characterized by both a lack of consensus and a high degree of uncertainty in medical decisions.

On the day of the study, the patients received an average of 33.8 days of prophylactic anticoagulant treatment. However, the clinical benefit of extending prophylaxis for a few weeks after discharge from an acute care hospital remains unproven. It is currently recommended to base the decision to prolong prophylaxis on individual patient risks. Considering the results of the present study, further prospective trials assessing the effect of prolonging prophylaxis should be planned. Special attention should be paid to immobilized patients in whom a significantly increased rate of deep vein thrombosis was detected. Our findings also contribute several important clarifications on the appropriateness of physician practices in prophylaxis against venous thromboembolism in several subgroups of patients for whom there are sufficient data suggesting efficacy of prolonged prophylaxis. Prophylactic anticoagulant treatment was ordered in 83% of patients who had undergone a recent major surgical procedure. When addressing the rate of deep vein thrombosis, previous studies support the benefit of extended-duration thromboprophylaxis after total hip or knee replacement and after surgery for cancer. However, the clinical benefit of extended-duration thromboprophylaxis on fatal or nonfatal pulmonary embolism remains unproven. Consequently, some authors recommend taking the decision of extended prophylaxis when additional risk factors such as old age, varicose veins, previous thromboembolism, or lack of full weight-bearing capability are present. In our study, 75% of patients who had undergone a major surgical procedure presented at least 1 additional risk factor other than age.

Use of prophylactic anticoagulant treatment was not significantly increased in patients who presented with paralytic stroke. Despite a lack of scientific evidence, presence of ongoing risk factors such as paresis, bedrest, or congestive heart failure may justify extended therapy in stroke patients. Paralytic stroke was associated in our study with a 2-fold increase in systematically detected deep vein thrombosis in the group of patients receiving no extended prophylaxis, whereas this association was not found in recipients of thromboprophylaxis. There is a need for improving physician practice in this subgroup of patients. Finally, our findings suggest that use of elastic compression stockings, which appeared to be an effective mechanical method of prophylaxis either alone or in combination with an anticoagulant, should be extended in subacute care settings.

The present study has several limitations. It is now acknowledged that observational surveys of professional practices may contribute to changing these practices. To reduce this potential bias, physicians were informed of the date of the study only 2 days in advance. In addition, physicians' orders from the previous 2 weeks were examined to check for changes in prophylaxis. Ultrasound examination is the most common screening test used in epidemiological studies because of its noninvasive nature. Venography, which remains the reference method of diagnosing deep vein thrombosis, could not be proposed in symptomless elderly patients because of potential adverse effects. The accuracy of ultrasound examination for screening deep vein thrombosis in symptom-free surgical patients remains controversial. Nevertheless, both sensitivity and specificity of venous compression ultrasonography performed by experienced and qualified angiologists have been recently shown to be satisfactory for detecting deep vein thrombosis in asymptomatic medical patients. Even if the lack of sensitivity of ultrasound examination were real, the statistical power of our study might be reduced but without clinical relevance, since most of the undetected thrombi would probably be small and not symptomatic. Deep vein thrombosis that is not associated with clinical symptoms has been questioned as a reliable surrogate for clinical venous thromboembolism, while it remains largely assessed in clinical trials. A recent meta-analysis of surgical high-risk groups found no evidence of mortality benefit or reduction in the rate of pulmonary embolism for extended prophylactic treatment. However, this meta-analysis lacked statistical power to provide precise estimates of treatment effect for these outcomes. In addition, the authors reported that the treatment effect for fatal or nonfatal pulmonary embolism was consistent, while nonsignificant, with that seen for deep vein thrombosis, suggesting that a similar reduction for these outcomes might be expected. Indeed, deep vein thrombosis and pulmonary embolism are clinical manifestations of the same underlying disease process. In addition, the rate of systematically detected symptomatic deep vein thrombosis in our study was paralleled by a similar increase in symptomatic deep vein thrombosis across risk factors, as shown in previous studies.

The high prevalence of deep vein thrombosis reported in the present study shows that venous thromboembolism is a common clinical problem in patients hospitalized in subacute care facilities. Given the current lack...
of scientific evidence, the variations in physician practices evidenced in our study highlight the urgent need for further prospective studies assessing the benefit of extended-duration prophylaxis in various subgroups of nonsurgical patients hospitalized in these settings.

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