BRIEF REPORTS

Pharmacological Thromboembolic Prophylaxis in a Medical Ward

Room for Improvement

Drahomir Aujesky, MD, Emmanuèle Guignard, PharmD, André Pannatier, PharmD, Jacques Cornuz, MD, MPH

To evaluate the adequacy of pharmacological thromboembolic prevention in the medical ward of a university hospital, we performed a retrospective study in 227 consecutive inpatients. The presence of risk factors, and type, length, and dose of pharmacological prevention were documented by chart review. Only 22% of the 153 risk patients received adequate prevention, whereas 38% of the patients at low risk were given pharmacological prophylaxis. The high prevalence of over- and undertreatment is an indicator of less than optimal care. Quality of care interventions, such as the development of local guidelines, might improve the appropriateness of pharmacological thromboembolic prophylaxis in medical inpatients.

KEY WORDS: **venous thromboembolism; pharmacological prevention; inpatients.**
J GEN INTERN MED 2002;17:788–791.

Venous thromboembolism is a frequent and potentially lethal complication in hospital patients. It has been reported in autopsy studies that up to 10% of deaths observed during hospital stay are related to pulmonary embolism and that 75% of these deaths occur in nonsurgical patients.[1–4] Although the risk of venous thromboembolism due to surgery is well-established and the benefit of antithromboembolic prophylaxis has been shown in surgical patients, the risk and prevention of venous thromboembolic disease is less well-studied in medical inpatients. In the recently published 6th American College of Chest Physicians Consensus Conference Guidelines on Antithrombotic Therapy, for example, prophylaxis in almost all surgical disciplines, such as orthopedics and neurosurgery, is extensively discussed; for medical patients, however, only relatively few recommendations are given.[5] Medical conditions in which pharmacological prevention of venous thromboembolism has proved to be effective are acute myocardial infarction, stroke, chest infection/respiratory insufficiency, heart failure, advanced cancer, and critically ill patients.[6–11] Pharmacological prophylaxis may also significantly reduce the incidence of thromboembolic events in medical inpatients with various other risk factors.[12,13]

According to the 1992 Thromboembolic Risk Factors (THRIFT) I Consensus Group recommendations, a risk profile followed by a risk-adapted antithrombotic prevention should be established for all hospital patients.[14] While low-risk patients (i.e., with minor medical illness) should be mobilized early and should not be given a pharmacological thromboembolic prophylaxis, risk patients with major medical illness such as myocardial infarction or stroke should receive low-dose unfractionated heparin (LDUFH) or low-molecular-weight heparin (LMWH) until hospital discharge or longer. In order to evaluate the need for quality of care interventions, such as the development of local guidelines, we performed a retrospective study examining pharmacological thromboembolic prevention in the general internal medicine ward of a Swiss tertiary care and community hospital.

METHODS

We retrospectively collected data on 368 consecutive patients admitted in the general internal medicine hospital ward of our 850-bed teaching and community hospital from May 1 to June 17, 1999. After exclusion of 53 patients receiving therapeutic anticoagulation, 45 patients having a contraindication to anticoagulation (active hemorrhage, thrombocytopenia $<50{,}000/mm^3$, coagulopathy, anatomical lesions), and 43 patients staying less than 96 hours, the final study population comprised 227 patients.

The following data were retrieved by chart review: age, sex, weight, length of hospitalization, principal reason for admission, and presence of risk factors (Table 1) for venous thromboembolism as identified by the THRIFT I Group Recommendations. We did not include other recognized risk factors such as immobility, varicosity, and obesity since documentation was less complete in our charts. We

Received from the Department of Internal Medicine (DA, JC), and the Department of Pharmacy (EG, AP), Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

Address correspondence and requests for reprints to Dr. Cornuz: Centre Hospitalier Universitaire Vaudois, Rue du Bugnon 46, 1011 Lausanne, Switzerland (e-mail: Jacques.Cornuz@chuv.hospvd.ch).

Table 1. Patient Characteristics and Risk Factors (*N* = 227)

Mean age, y ±SD	69 ± 17
Mean weight, kg ±SD	65 ± 15
Female, n (%)	126 (56)
Mean length of hospitalization, days ±SD	11 ± 5
Principal reason for admission, *n* (%)	
Heart disease	71 (31)
Respiratory diseases including pneumonia	49 (22)
Active cancer	29 (13)
Infections (pneumonia excluded)	26 (11)
Renal disease	7 (3)
Stroke/neurologic disease	6 (3)
Other	39 (17)
Risk factors (multiple entries possible), *n* (%)	
Chest infection/respiratory insufficiency	62 (27.3)
Symptomatic heart failure (≥NYHA II)	56 (24.7)
Active cancer	38 (16.7)
Acute myocardial infarction	10 (4.4)
Sepsis/bacteriemia	8 (3.5)
Paralysis (stroke, paraplegia, coma)	7 (3)
Previous venous thromboembolism	5 (2.2)
Inflammatory bowel disease	3 (1.3)
Hereditary thrombophilia	1 (0.4)
Nephrotic syndrome	1 (0.4)
Diabetic ketoacidosis	1 (0.4)

NYHA, New York Heart Association.

also recorded type (LDUFH or LMWH), dose, and duration of anticoagulation, and platelet counts.

All patients presenting 1 or more of the risk factors shown in Table 1 were classified into the elevated risk category. Patients with none of those risk factors were considered to be at low risk for venous thromboembolism. In compliance with the THRIFT I Group recommendations, pharmacological prophylaxis was considered to be adequate if 1) a patient of the elevated-risk category received anticoagulation until discharge, and 2) a low-risk patient received no pharmacological prophylaxis. Among the inadequately treated patients, those in the elevated-risk category who did not receive prophylactic anticoagulation or in whom the anticoagulation was not continued until discharge were considered to be undertreated. The presence of pharmacological prophylaxis in low-risk patients was defined as overtreatment. Monitoring of the platelet count was considered adequate if patients anticoagulated for ≥5 days had at least 1 platelet count between days 5 and 10 of prophylaxis.

Continuous variables are given as mean ± standard deviation or range. Categorical variables are expressed both in absolute values and as a percentage. Comparisons of mean age, weight, and sex distribution between the adequately and inadequately treated patients were performed by using the χ^2 statistic or the Student *t* test when appropriate. Logistic regression was used to express the likelihood of being inadequately treated. All statistical analyses were performed by means of a statistical computer program (STATA 7.0; Stata Corp., College Station, Tex).

RESULTS

The results of our analysis are summarized in Figure 1. Among the included 227 patients, 153 (67%) presented 1 or more of the risk factors listed in Table 1, primarily chest infection, symptomatic heart failure, and active cancer. Only 101 (66%) of 153 elevated-risk patients received prophylactic anticoagulation. This treatment was maintained in 33 (22%) patients until discharge. Thus, 120 (78%) of the risk patients were considered as undertreated according to the above-mentioned criteria. On the other hand, out of 74 patients with no risk factors, 28 (38%) received pharmacological antithrombotic prophylaxis and were considered as overtreated. Prophylaxis was adequate in 79 (35%) patients of the study population according to the above-mentioned criteria. By considering only the 5 best-documented risk factors (acute myocardial infarction, limb paralysis, chest infection/respiratory failure, heart failure, and cancer) as an indication for prophylaxis, the rate of adequately treated patients rose slightly to 38%. Neither univariate nor multivariate analysis (Table 2) showed an association between inadequate treatment and age, weight, and sex. However, inadequately treated patients tended to be older than adequately treated patients (mean age 69.4 vs 65.2 years, $P = .10$).

Prophylactic pharmacological anticoagulation was administered to 129 (57%) patients of the total study population at a given time. Subcutaneous injection of LMWH in a once-daily dose (Nadroparin, 1,900 to 7,600 IU) was by far the most common method of prophylaxis; only 1 patient received LDUFH. Among the 79 patients with a prophylaxis duration of ≥5 days, 65 (82%) had at least 1 platelet count between days 5 and 10 of anticoagulation.

DISCUSSION

Our study shows that 66% of the 153 patients at risk received pharmacological prophylaxis of variable length at a given time. Among these 153 patients, only 22% received

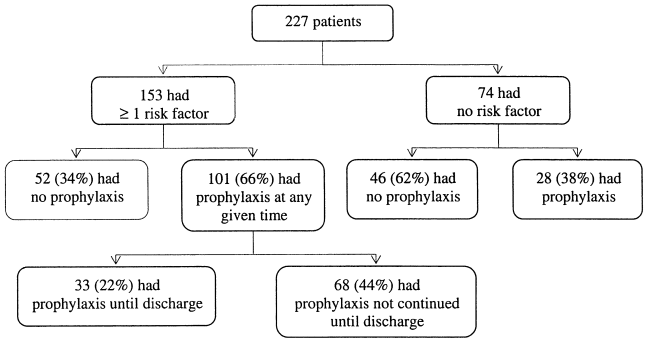

FIGURE 1. Pharmacological thromboembolic prophylaxis in 227 medical inpatients with and without thromboembolic risk factors.

Table 2. Influence of Age, Sex, and Weight on the Likelihood of Being Inadequately Treated

	Odds Ratio	95% Confidence Interval
Age (per 1-y increase)	0.99	0.97 to 1.00
Female	1.02	0.55 to 1.94
Weight (per 1-kg increase)	0.99	0.97 to 1.01

prophylaxis until discharge according to the THRIFT I recommendations. Although we fully recognize that it may be reasonable to stop prophylaxis prior to discharge when the acute illness is largely treated and the patient ambulatory, our data suggest that pharmacological prophylaxis is largely underused despite its proven effectiveness in preventing thromboembolic disease. The substantial number of anticoagulated patients whom we categorized as being low-risk might partly be explained by the presence of risk factors other than those we abstracted from the patient records.

Our results show that LMWHs had almost completely replaced LDUFH in thromboembolic prevention in our center in the year 1999. LMWHs have been proven to be at least as effective as LDUFH in the prevention of venous thromboembolism,[13] although the optimal prophylactic dosing regimen (fixed dose, weight-adjusted, or risk-adjusted) and duration of treatment for medical patients remain to be determined. To our knowledge, there are no studies comparing the cost-effectiveness of LMWH and LDUFH prophylaxis in medical patients, but LMWH has been shown to be more cost-effective than LDUFH in deep vein thrombosis prophylaxis after total hip replacement.[15] Complications associated with prophylactic LMWH are rare: less than 1% of patients suffer major bleeding (half of the rate observed with LDUFH).[13] Heparin-induced thrombocytopenia is also less common than with LDUFH.[16] Their good safety profile, their ease of use (once-daily subcutaneous injection), and the fact that there is no need for monitoring (with the exception of the platelet count) make LMWHs the pharmacological prophylaxis of choice for most medical patients.

A limitation of our study is the retrospective chart review: incomplete chart documentation did not allow the analysis of other important risk factors, such as immobilization. Further, it is a relatively small study of 227 patients in a single Swiss hospital. However, our 850-bed hospital has a double function as a tertiary care center and a community hospital, and we expect that similar results would have been seen in other places.

In fact, an underuse of prophylaxis among medical inpatients at risk was also reported in studies from the United States, New Zealand, and France, with a frequency of thromboembolic prevention ranging between 20% and 34%.[17–20]

The data of our study show that pharmacological thromboembolic prophylaxis is, despite its proven efficacy, largely underused among medical inpatients in our hospital. Furthermore, many patients with no major thromboembolic risk factors received pharmacological prophylaxis. The high prevalence of over- and undertreatment is an indicator of less than optimal care. Quality of care interventions, such as the development of local guidelines, might improve the appropriateness of pharmacological thromboembolic prophylaxis in medical inpatients.

REFERENCES

1. Rubinstein I, Murray D, Hoffstein V. Fatal pulmonary embolism in hospitalized patients: an autopsy study. Arch Intern Med. 1988;148:1425–6.
2. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis. J R Soc Med. 1989;82:203–5.
3. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. Chest. 1995;108:978–81.
4. Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death. The changing mortality in hospital patients. JAMA. 1986;225:2039–42.
5. Geerts WH, Heit JA, Clagett GP, et al. Prevention of venous thromboembolism. Chest. 2001;119:132S–75S.
6. Collins R, MacMahon S, Flather M, et al. Clinical effects of anticoagulant therapy in suspected acute myocardial infarction: systematic overview of randomised trials. BMJ. 1996;313:652–9.
7. Gubitz G, Counsell C, Sandercock P, Signorini D, eds. Anticoagulants for acute ischaemic stroke (Cochrane Review). In: The Cochrane Library, Issue 2. Oxford: Update Software; 2001.
8. Belch JJ, Lowe GDO, Ward AG, Forbes CD, Prentice CRM. Prevention of deep vein thrombosis in medical patients by low-dose heparin. Scott Med J. 1981;26:115–7.
9. Kleber FX, Witt C, Flosbach CW, Koppenhagen K, Vogel G. Study to compare the efficacy and safety of the LMWH enoxaparin and standard heparin in the prevention of thromboembolic events in medical patients with cardiopulmonary diseases. The PRINCE study group. Ann Hematol. 1998;76 (Suppl 1):269.
10. Levine M, Hirsh J, Gent M, et al. Double-blind randomised trial of very-low-dose warfarin for prevention of thromboembolism in stage IV breast cancer. Lancet. 1994;343:886–9.
11. Cade JF. High risk of the critically ill for venous thromboembolism. Crit Care Med. 1982;10:448–50.
12. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. N Engl J Med. 1999;341:793–800.
13. Mismetti P, Laporte-Simitsidis S, Tardy B, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomised clinical trials. Thromb Haemost. 2000;83:14–9.
14. Thromboembolic Risk Factors (THRIFT) Consensus Group. Risk of and prophylaxis for venous thromboembolism in hospital patients. BMJ. 1992;305:567–74.
15. Anderson DR, O'Brien BJ, Levine MN, Roberts R, Wells PS, Hirsh J. Efficacy and cost of low-molecular-weight heparin compared with standard heparin for the prevention of deep vein thrombosis after total hip arthroplasty. Ann Intern Med. 1993;119:1105–12.
16. Warkentin TE, Levine MN, Hirsh J, et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med. 1995;332:1330–5.

17. Anderson FA, Wheeler HB, Goldberg RJ, Hosmer DW, Forcier A, Patwardhan NA. Physician practices in the prevention of venous thromboembolism. Ann Intern Med. 1991;115:591–5.
18. Keane MG, Ingenito EP, Goldhaber SZ. Utilization of venous thromboembolism prophylaxis in the medical intensive care unit. Chest. 1994;106:13–4.
19. Egermayer P, Robis C, Town GI. Survey of the use of thromboprophylaxis for medical patients at Christchurch Hospital. N Z Med J. 1999;112:246–8.
20. Dh te R, Pellicer-Coeuret M, Belouet-Moreau C, Christoforov B, Vidal-Trecan G. Venous thromboembolism in medical inpatients: prophylaxis with low-weight heparin in a university hospital and prevalence of thromboembolic events. Clin Appl Thromb Hemost. 2001;7:16–20.