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Electronic Alerts to Prevent Venous Thromboembolism among Hospitalized Patients

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ABSTRACT

BACKGROUND

Prophylaxis against deep-vein thrombosis in hospitalized patients remains underused. We hypothesized that the use of a computer-alert program to encourage prophylaxis might reduce the frequency of deep-vein thrombosis among high-risk hospitalized patients.

METHODS

We developed a computer program linked to the patient database to identify consecutive hospitalized patients at risk for deep-vein thrombosis in the absence of prophylaxis. The program used medical-record numbers to randomly assign 1255 eligible patients to an intervention group, in which the responsible physician was alerted to a patient's risk of deep-vein thrombosis, and 1251 patients to a control group, in which no alert was issued. The physician was required to acknowledge the alert and could then withhold or order prophylaxis, including graduated compression stockings, pneumatic compression boots, unfractionated heparin, low-molecular-weight heparin, or warfarin. The primary end point was clinically diagnosed, objectively confirmed deep-vein thrombosis or pulmonary embolism at 90 days.

RESULTS

More patients in the intervention group than in the control group received mechanical prophylaxis (10.0 percent vs. 1.5 percent, $P < 0.001$) or pharmacologic prophylaxis (23.6 percent vs. 13.0 percent, $P < 0.001$). The primary end point occurred in 61 patients (4.9 percent) in the intervention group, as compared with 103 (8.2 percent) in the control group; the Kaplan–Meier estimates of the likelihood of freedom from deep-vein thrombosis or pulmonary embolism at 90 days were 94.1 percent (95 percent confidence interval, 92.5 to 95.4 percent) and 90.6 percent (95 percent confidence interval, 88.7 to 92.2 percent), respectively ($P < 0.001$). The computer alert reduced the risk of deep-vein thrombosis or pulmonary embolism at 90 days by 41 percent (hazard ratio, 0.59; 95 percent confidence interval, 0.43 to 0.81; $P = 0.001$).

CONCLUSIONS

The institution of a computer-alert program increased physicians' use of prophylaxis and markedly reduced the rates of deep-vein thrombosis and pulmonary embolism among hospitalized patients at risk.

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DESPITE THE EXISTENCE OF DETAILED European¹ and North American² consensus guidelines, the use of prophylaxis against venous thromboembolism continues to be spotty. Randomized, controlled trials of hospitalized medical patients³⁻⁵ have shown that certain measures safely prevent venous thromboembolism, yet European^{6,7} and North American⁸⁻¹⁰ surveys show persistent underuse of prophylaxis. In a registry of 5451 consecutive patients with ultrasonographically confirmed deep-vein thrombosis at 183 U.S. institutions,¹⁰ only 42 percent of inpatients had received prophylaxis within 30 days before deep-vein thrombosis developed. Although approaches involving continuing medical education¹¹ and computerized electronic alerts^{12,13} can increase physicians' use of prophylaxis against venous thromboembolism, it is not known whether the use of an electronic alert system can actually reduce the rate of deep-vein thrombosis.

Brigham and Women's Hospital in Boston has made concerted efforts to increase physicians' awareness of risk factors for venous thromboembolism and their understanding of the effectiveness of prevention strategies. Frequent educational programs that focus on the necessity of venous thromboembolism prophylaxis are convened. The order-entry system is programmed to suggest prophylaxis if an order for bed rest is entered. Nevertheless, a two-year audit found that prophylaxis was used in only 52 percent of patients in whom deep-vein thrombosis developed while they were hospitalized for other reasons.¹⁴ Therefore, as a quality-improvement initiative, we undertook a randomized, controlled study of 2506 hospitalized patients to evaluate a strategy of issuing or withholding electronic alerts to physicians whose patients were not receiving prophylaxis against deep-vein thrombosis.

METHODS

STUDY DESIGN

We developed a computer program to identify consecutive hospitalized patients at increased risk for venous thromboembolism. The program was linked to the patient database (Partners Information Systems) of Brigham and Women's Hospital. The study was approved by the human research committee of Partners HealthCare System. The requirement for informed consent was waived.

From September 2000 to January 2004, we identified 2506 consecutive hospitalized patients from

medical and surgical services who were at least 18 years of age and who were at increased risk for venous thromboembolism. Patients from the Department of Neurology, the Newborn Service, and the Neonatal Intensive Care Unit were excluded, as were patients receiving mechanical or pharmacologic prophylaxis.

The principal investigator (Dr. Goldhaber) designed the study, edited the manuscript, and vouches for the data and analyses. Drs. Koo, Quiroz, and Cooper gathered data. Dr. Kucher performed data analyses and drafted the manuscript.

IDENTIFICATION OF PATIENTS AT RISK FOR VENOUS THROMBOEMBOLISM

The computer program used eight common risk factors to determine each hospitalized patient's risk profile for venous thromboembolism. Each risk factor was weighted according to a point scale: the major risk factors of cancer, prior venous thromboembolism, and hypercoagulability were assigned a score of 3; the intermediate risk factor of major surgery was assigned a score of 2; and the minor risk factors of advanced age, obesity, bed rest, and the use of hormone-replacement therapy or oral contraceptives were assigned a score of 1. An increased risk of venous thromboembolism was defined as a cumulative risk score of at least 4, so that patients who had at least one major risk factor and at least one intermediate risk factor or minor risk factor were eligible for the study. In the absence of a major risk factor, patients who had at least one intermediate risk factor and at least two minor risk factors were also eligible. Daily screening of the computer-alert program permitted us to identify and enroll patients who initially had a venous thromboembolism risk score of less than 4 but whose score increased to 4 or higher during hospitalization.

The program used current lists of inpatient diagnoses to identify patients with the following types of cancer: cervical, colon, lung, ovarian, prostate, rectal, renal, thyroid, uterine, pancreatic, liver, stomach, brain, esophageal, and head and neck, as well as sarcoma and melanoma. In addition, the admitting diagnoses were screened for cancer coded according to the *International Classification of Diseases, 9th Revision (ICD-9)*, as codes 149.0 to 172.99 and 174.0 to 209.99. Inpatient and outpatient records were checked to identify patients with a personal history of deep-vein thrombosis or pulmonary embolism, as well as those with a history of venous

thromboembolism, as indicated by ICD-9 codes 415.1, 415.19, 453.8, 453.9, and 671.31 to 671.50.

Hypercoagulable states were identified on the basis of laboratory test results, including the presence of factor V Leiden, lupus anticoagulant, and anticardiolipin antibodies, in the database. Major surgery was defined as any surgery lasting more than 60 minutes. Bed rest was defined as an active order for bed rest that was not related to surgery. Advanced age was defined as an age of more than 70 years. If data on weight and height were available, the program calculated the body-mass index (the weight in kilograms divided by the square of the height in meters). Obesity was defined as a body-mass index of more than 29. If weight and height data were not available, inpatient and outpatient records were screened for a diagnosis of obesity and for the ICD-9 code for obesity (278.0). Ongoing use of hormone-replacement therapy or oral contraceptives was identified by reviewing patients' active medications.

SCREENING FOR VENOUS THROMBOEMBOLISM PROPHYLAXIS

If the cumulative risk score for venous thromboembolism was at least 4, the computer program reviewed orders to identify the ongoing use of mechanical or pharmacologic prophylactic measures. Electronic orders were searched for mechanical prophylactic measures, including the use of graduated-compression stockings or intermittent pneumatic-compression boots. Lists of active medications were screened for the presence of prophylactic pharmacologic measures, including the use of unfractionated heparin, enoxaparin, dalteparin, danaparoid, hirudin, or warfarin. Of 13,922 patients with a risk score for venous thromboembolism of at least 4, 11,416 (82.0 percent) had received mechanical or pharmacologic prophylaxis a priori and 2506 (18.0 percent) had not received it.

RANDOMIZATION AND ELECTRONIC ALERTS

Patients with even medical-record numbers were assigned to the intervention group, and those with odd medical-record numbers were assigned to the control group, without further stratification. Among the 2506 eligible patients, 1255 were assigned to the intervention group, in which the responsible physician received one electronic alert about the risk of venous thromboembolism, and 1251 to the control group, in which no alert was issued. Overall, 120 physicians were responsible for the study

patients: 104 physicians were assigned to a median of 12 patients in the intervention group (range, 2 to 19), and 102 physicians to a median of 13 patients in the control group (range, 2 to 18). Thirty-four physicians (28.3 percent) were assigned to treat only patients in one group: 18 to the intervention group alone and 16 to the control group alone. Physicians responsible for patients in the control group were not aware that these patients were being followed for clinical events.

Each responsible physician had to acknowledge the computer alert and could then withhold prophylaxis or, on the same computer screen, order prophylaxis with options that included graduated-compression stockings, intermittent pneumatic-compression boots, unfractionated heparin, low-molecular-weight heparin, or warfarin. In addition, the computer-alert screen was linked to the hospital's venous-thromboembolism-prevention guidelines, which provided drug regimens for various indications according to published consensus guidelines.² Guidelines for the prevention of venous thromboembolism were also available for patients in the control group, but no specific prompt was provided to use them.

FOLLOW-UP

We conducted a 90-day follow-up of all study patients, reviewing their medical records in the patient database of Brigham and Women's Hospital. Clinical events were identified with the use of information from the index hospitalization, subsequent hospitalizations, and office visits, including discharge summaries, physician's notes, blood-test results, vascular-laboratory reports, nuclear-medicine reports, and radiology reports. In addition, the Social Security Death Index was used to identify patients who died during the 90-day period.

Overall, 2361 patients (94.2 percent) had follow-up data beyond the index hospitalization, and 145 patients (5.8 percent) were lost to follow-up. Of the patients lost to follow-up, 78 were in the intervention group and 67 were in the control group ($P=0.39$). A total of 2007 patients (80.1 percent) had outpatient visits, and 1008 (40.2 percent) were rehospitalized during the 90 days after randomization.

DATA COLLECTION AND STUDY END POINTS

The primary end point was clinically diagnosed deep-vein thrombosis or pulmonary embolism at 90 days. For patients with more than one event,

only the first event was counted. Safety end points included total mortality at 30 days and the rate of hemorrhagic events at 90 days. We defined major bleeding as intracranial, intraocular, retroperitoneal, or pericardial bleeding, or bleeding that required surgical intervention or that resulted in a hemoglobin loss of more than 3 g per deciliter.¹⁵

Deep-vein thrombosis was diagnosed if there was ultrasonographic evidence of the loss of vein compressibility or evidence of a filling defect on conventional contrast venography.¹⁶ Pulmonary embolism was diagnosed on the basis of findings on ventilation–perfusion scanning,¹⁷ computed tomography of the chest with contrast medium,¹⁸ or conventional pulmonary angiography.¹⁹ Events clinically suspected to be related to venous thromboembolism without objective confirmation of the diagnosis were not counted. Three investigators who were unaware of patients' group assignments adjudicated all end points.

STATISTICAL ANALYSIS

We initially estimated that we would need to enroll 1400 patients for the study to have a statistical power of 90 percent (two-sided alpha of 5 percent), given an estimated 50 percent rate of use of prophylaxis against venous thromboembolism in the intervention group, a 10 percent rate of the primary end point in the control group, and an odds ratio of 0.50 for the primary end point in the intervention group as compared with the control group. After 700 patients had been enrolled, the protocol was modified to increase the sample size to 2500 patients, because the rate of use of prophylaxis against venous thromboembolism in the intervention group was lower than expected. At that time, no clinical end-point data had been obtained. An interim analysis of efficacy and safety undertaken after approximately half the expected information was obtained indicated that the predefined boundaries for early stopping had not been crossed, on the basis of the O'Brien–Fleming spending function according to the method of Lan and DeMets.²⁰

We used Wilcoxon rank-sum tests to compare the distributions of continuous variables between groups and chi-square tests or Fisher's exact tests to compare categorical variables. The primary analysis was performed with the use of Greenwood's formula for the difference between the intervention group and the control group in the Kaplan–Meier estimates of freedom from deep-vein thrombosis or pulmonary embolism on day 90. The log-rank

test was used to estimate the cumulative probability of the primary end point in the intervention and control groups. We used the proportional-hazards model to estimate the relative hazard of clinical end points associated with the computer alert and obtained 95 percent confidence intervals from this model. We also used the proportional-hazards model to evaluate the effect of the computer alert on the primary end point in clinically important subgroups. In addition, we assessed the effect of the computer alert in subgroups by including a term for the interaction between group assignment and each clinical factor. All reported P values are two-sided.

RESULTS

CHARACTERISTICS OF THE PATIENTS

The intervention and control groups were well balanced with respect to baseline characteristics (Table 1). Overall, 52.9 percent were women, and 47.1 percent were men. Almost two thirds had a risk score for venous thromboembolism of 4; 37.2 percent had a risk score ranging from 5 to 8. Overall, 434 of the patients (17.3 percent) had undergone surgery or had trauma. The remaining 2072 (82.7 percent) had been hospitalized for other reasons. The most common coexisting conditions were cancer (in 79.7 percent), hypertension (in 34.4 percent), and infection (in 30.3 percent); 20.3 percent had prior venous thromboembolism.

PROPHYLAXIS AGAINST VENOUS THROMBOEMBOLISM

Prophylactic measures were ordered for 421 of the 1255 patients in the intervention group (33.5 percent) and 182 of the 1251 patients in the control group (14.5 percent, $P < 0.001$). The intervention group had higher rates of use of both mechanical prophylaxis (10.0 percent vs. 1.5 percent, $P < 0.001$) and pharmacologic prophylaxis (23.6 percent vs. 13.0 percent, $P < 0.001$) than the control group (Table 2). The difference in the use of prophylaxis between the groups was mainly driven by increased use of graduated-compression stockings, intermittent pneumatic-compression boots, and subcutaneous unfractionated heparin in the intervention group.

Patients who received prophylaxis were older than those who did not receive prophylaxis (mean [\pm SD] age, 66 ± 15 vs. 59 ± 17 years; $P < 0.001$), and they had a lower rate of cancer (70.7 percent vs.

82.6 percent, $P<0.001$) and higher frequencies of congestive heart failure (16.6 percent vs. 8.8 percent, $P<0.001$), coronary artery disease (21.6 percent vs. 15.1 percent, $P<0.001$), chronic lung disease (15.3 percent vs. 11.5 percent, $P=0.01$), prior venous thromboembolism (32.8 percent vs. 16.3 percent, $P<0.001$), hypertension (39.3 percent vs. 32.9 percent, $P=0.004$), and recent surgery or trauma (37.3 percent vs. 14.2 percent, $P<0.001$). These covariates were predictive of the use of prophylaxis in both the intervention and control groups.

END POINTS

Efficacy

The primary end point of deep-vein thrombosis or pulmonary embolism at 90 days occurred in 61 patients in the intervention group (4.9 percent), as compared with 103 patients in the control group (8.2 percent); the Kaplan–Meier estimates of the absence of venous thromboembolism at 90 days were 94.1 percent (95 percent confidence interval, 92.5 to 95.4 percent) and 90.6 percent (95 percent confidence interval, 88.7 to 92.2 percent), respectively ($P<0.001$) (Fig. 1). The computer alert reduced the risk of venous thromboembolism at 90 days by 41 percent (hazard ratio, 0.59; 95 percent confidence interval, 0.43 to 0.81; $P=0.001$). The computer alert was similarly effective in reducing the rates of deep-vein thrombosis of the legs and pulmonary embolism (Table 3).

The electronic alert also reduced the rates of venous thromboembolism at 90 days in clinically important subgroups (Table 4). Proportional-hazards models did not reveal any significant interaction between the effect of the computer alert and any subgroup.

At 90 days, venous thromboembolism had occurred in 31 of 603 patients who received prophylaxis (5.1 percent), as compared with 133 of 1903 patients who did not receive prophylaxis (7.0 percent); the Kaplan–Meier estimates of the absence of venous thromboembolism at 90 days were 93.6 percent (95 percent confidence interval, 91.0 to 95.5 percent) and 92.0 percent (95 percent confidence interval, 90.5 to 93.2 percent), respectively ($P=0.08$). In the intervention group, venous thromboembolism occurred in 20 of 421 patients who received prophylaxis (4.8 percent), as compared with 41 of 834 who did not receive prophylaxis (4.9 percent); the Kaplan–Meier estimates of the absence of venous thromboembolism at 90 days were 94.3 percent (95 percent confidence interval, 92.3 to

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Intervention Group (N=1255)	Control Group (N=1251)
Female sex — no. (%)	672 (53.5)	654 (52.3)
Age — yr		
Median	63	62
Range	18–99	18–97
Age \geq 75 years — no. (%)	279 (22.2)	292 (23.3)
Risk score for venous thromboembolism — no. (%)†		
4	792 (63.1)	782 (62.5)
5	327 (26.1)	321 (25.7)
6	110 (8.8)	117 (9.4)
7	22 (1.8)	23 (1.8)
8	4 (0.3)	8 (0.6)
Cancer — no. (%)	1010 (80.5)	988 (79.0)
Lymphoma	270 (21.5)	249 (19.9)
Genitourinary	166 (13.2)	145 (11.6)
Acute leukemia	159 (12.7)	168 (13.4)
Gastrointestinal	129 (10.3)	153 (12.2)
Breast	103 (8.2)	107 (8.6)
Lung	93 (7.4)	91 (7.3)
Sarcoma	23 (1.8)	36 (2.9)
Melanoma	16 (1.3)	12 (1.0)
Head and neck	14 (1.1)	6 (0.5)
Mesothelioma	13 (1.0)	8 (0.6)
Brain (primary)	3 (0.2)	4 (0.3)
Other	21 (1.7)	9 (0.7)
Hypertension — no. (%)	403 (32.1)	459 (36.7)
Infection within previous 30 days — no. (%)	390 (31.1)	370 (29.6)
Prior venous thromboembolism — no. (%)	253 (20.2)	255 (20.4)
Coronary artery disease — no. (%)	212 (16.9)	205 (16.4)
Diabetes mellitus — no. (%)	171 (13.6)	187 (14.9)
Chronic lung disease — no. (%)	160 (12.7)	151 (12.1)
Congestive heart failure — no. (%)	152 (12.1)	116 (9.3)
Renal insufficiency — no. (%)	144 (11.5)	151 (12.1)
Major surgery or trauma within previous 30 days — no. (%)	227 (18.1)	207 (16.5)
Breast surgery	61 (4.9)	62 (5.0)
Genitourinary surgery	51 (4.1)	34 (2.7)
Abdominal surgery	35 (2.8)	45 (3.6)
Orthopedic surgery	26 (2.1)	21 (1.7)
Thoracic surgery	16 (1.3)	15 (1.2)
Cardiovascular surgery	15 (1.2)	7 (0.6)
Reconstructive surgery	12 (1.0)	11 (0.9)
Neurosurgery	5 (0.4)	7 (0.6)
Ear, nose, and throat surgery	2 (0.2)	3 (0.2)
Other surgery	4 (0.3)	2 (0.2)

* Because of rounding, not all percentages within a category sum to their respective total percentages.

† Higher scores indicate greater risk.

95.3 percent) and 93.8 percent (95 percent confidence interval, 90.6 to 96.0 percent), respectively (P=0.82). In the control group, venous thromboembolism occurred in 11 of 182 patients who received prophylaxis (6.0 percent), as compared with 91 of 1069 patients who did not receive prophylaxis (8.5 percent), and the respective Kaplan–Meier estimates were 93.1 percent (95 percent confidence interval, 87.8 to 96.1 percent) and 90.2 percent (95 percent confidence interval, 88.1 to 91.9 percent) (P=0.23).

Safety

The overall rate of death was 13.2 percent at 30 days and 22.4 percent at 90 days, with no significant

difference between the groups (Table 3). There was no increase in the rate of major or minor hemorrhage at 30 days in the intervention group.

DISCUSSION

The computer program facilitated the identification of hospitalized patients at increased risk for venous thromboembolism in the absence of prophylaxis, more than doubling the rate of orders for prophylaxis (from 14.5 percent to 33.5 percent), and reduced the overall rate of venous thromboembolism at 90 days by 41 percent, without an increase in bleeding or mortality rates. The reduction in clinically diagnosed and objectively confirmed venous thromboembolism was due mainly to a decreased frequency of pulmonary embolism and proximal-leg deep-vein thrombosis.

Our study population consisted mostly of medical patients (82.7 percent) who were severely ill; there was a high prevalence of cancer (79.7 percent) and a three-month mortality rate that exceeded 20 percent. The rate of deep-vein thrombosis of the upper extremities was high among patients with cancer and most likely due to the frequent use of chemotherapy through central venous catheters.²¹ The prophylaxis rate in the intervention group was low (33.5 percent) in this ill population; many may have had conditions precluding the use of pharmacologic prophylaxis, but there is no obvious explanation for the failure to order mechanical prophylaxis, such as graduated-compression stockings or intermittent pneumatic-compression boots. Although we did not track contraindications to prophylaxis, they were probably evenly distributed between the intervention and control groups owing to the randomized design of the trial.

The computer alert was effective in patients with a wide spectrum of major risk factors for venous thromboembolism, such as advanced age, prior venous thromboembolism, and cancer. The computer alert was similarly efficacious in reducing the rate of the primary end point in patients with a risk score for venous thromboembolism of 4 and those with higher risk scores. However, the use of prophylaxis against venous thromboembolism has not significantly reduced the overall mortality rate in any major study of prevention of venous thromboembolism among hospitalized medical patients,^{3-5,22,23} including ours; none were adequately powered to investigate the effect of prophylaxis against venous thromboembolism on overall mortality.

Table 2. Prophylactic Measures against Venous Thromboembolism.

Measure	Intervention Group (N=1255)	Control Group (N=1251)	P Value
	<i>no. of patients (%)</i>		
Mechanical	125 (10.0)	19 (1.5)	<0.001
Compression stockings	52 (4.1)	7 (0.6)	<0.001
Pneumatic boots	73 (5.8)	12 (1.0)	<0.001
Pharmacologic	296 (23.6)	163 (13.0)	<0.001
Unfractionated heparin	213 (17.0)	81 (6.5)	<0.001
Warfarin	28 (2.2)	41 (3.3)	0.11
Enoxaparin	55 (4.4)	41 (3.3)	0.18

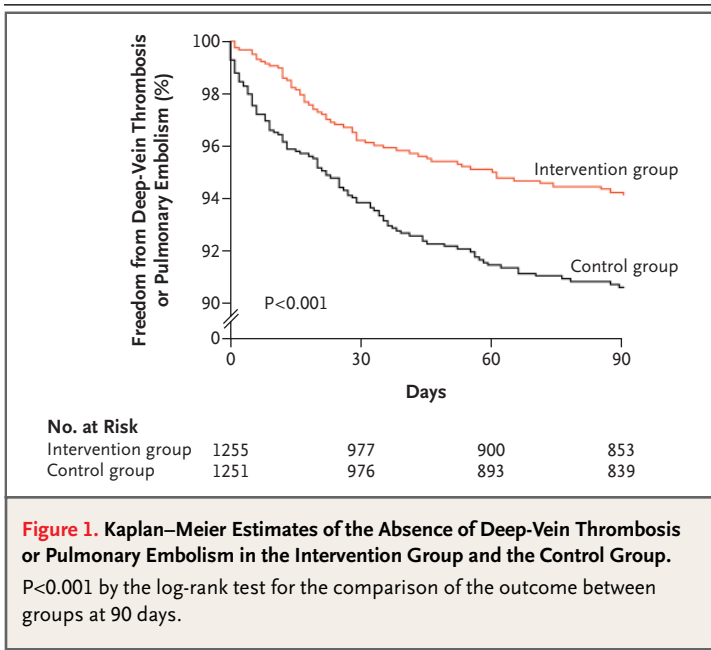


Figure 1. Kaplan–Meier Estimates of the Absence of Deep-Vein Thrombosis or Pulmonary Embolism in the Intervention Group and the Control Group.

P<0.001 by the log-rank test for the comparison of the outcome between groups at 90 days.

In our study, the reduction in events related to venous thromboembolism may be explained only partly by increased use of prophylaxis. Assignment to the intervention group itself decreased such events through day 90: for patients in this group, the computer alert itself may have increased the physicians' awareness of a high-risk situation, even though they did not administer mechanical or pharmacologic prophylaxis. Our study design did not allow the assessment of additional preventive measures, such as early ambulation or physiotherapy, that may have decreased the rate of venous thromboembolism among patients in the intervention group. In addition, the fact that physicians treating patients in the intervention group were aware that their patients were monitored may have further affected the rate of venous thromboembolism. However, since the use of prophylaxis was not randomized but was up to the individual physician, it may not be appropriate to compare patients who received prophylaxis with those who did not receive prophylaxis. Therefore, the results of analyses of the study groups according to prophylaxis status must be interpreted with caution.

We cannot rule out the possibility of diagnostic bias, since the administration of prophylaxis was not blinded and testing for venous thromboembolism was not routinely performed. It is therefore possible that physicians were more likely to order an imaging test for patients with symptoms who had not received prophylaxis than for those who had received prophylaxis. On the other hand, testing may not have been performed in symptomatic patients with limited life expectancy or contraindications to anticoagulation therapy, even if prophylaxis was not administered.

Because of the high rate of use of prophylaxis among the 13,922 patients with a risk score for venous thromboembolism of at least 4, the overall effect of the computer program was weak. The rate of use of prophylaxis among these patients might have increased from 84.6 percent without the computer-alert program to 88.0 percent if computer reminders had been issued for all 2506 eligible patients. The study intervention involved physicians, but randomization involved patients. Therefore, we were not able to assess whether physicians had an effect on the use of prophylaxis and rate of events related to venous thromboembolism. Since most physicians treated both intervention and control patients, it is likely that receiving computer reminders for patients in the intervention group also affected

Table 3. Study End Points.

End Point	Intervention Group (N=1255) <i>no. of patients (%)</i>	Control Group (N=1251) <i>no. of patients (%)</i>	Hazard Ratio (95% CI)*	P Value
Venous thromboembolism				
At 30 days	41 (3.3)	71 (5.7)	0.58 (0.39–0.85)	0.004
At 90 days	61 (4.9)	103 (8.2)	0.59 (0.43–0.81)	0.001
Pulmonary embolism				
At 30 days	10 (0.8)	21 (1.7)	0.48 (0.22–1.01)	0.05
At 90 days	14 (1.1)	35 (2.8)	0.40 (0.21–0.74)	0.004
Proximal-leg deep-vein thrombosis				
At 30 days	8 (0.6)	17 (1.4)	0.47 (0.20–1.09)	0.08
At 90 days	10 (0.8)	23 (1.8)	0.47 (0.20–1.09)	0.08
Distal-leg deep-vein thrombosis				
At 30 days	3 (0.2)	8 (0.6)	0.37 (0.10–1.41)	0.15
At 90 days	5 (0.4)	12 (1.0)	0.42 (0.15–1.18)	0.10
Deep-vein thrombosis of the arms†				
At 30 days	20 (1.6)	25 (2.0)	0.80 (0.44–1.44)	0.46
At 90 days	32 (2.5)	33 (2.6)	0.97 (0.60–1.58)	0.90
Death				
At 30 days	174 (13.9)	157 (12.5)	1.07 (0.86–1.32)	0.56
At 90 days	282 (22.5)	279 (22.3)	0.97 (0.82–1.15)	0.74
Major hemorrhage				
At 30 days	19 (1.5)	19 (1.5)	0.95 (0.50–1.80)	0.87
Minor hemorrhage				
At 30 days	81 (6.5)	88 (7.0)	0.88 (0.65–1.20)	0.43

* CI denotes confidence interval.

† Among the 65 patients with deep-vein thrombosis of the arms at 90 days, 51 (78.5 percent) received chemotherapy through a central venous catheter or portal with a catheter.

physicians' use of prophylaxis in some patients in the control group.

Computer-based clinical decision-making systems may be less effective for the management of chronic disease than they are for the management of acute disease,²⁴ but they appear to be particularly useful for preventive care and dosing regimens in hospitals.²⁵⁻²⁹ In a randomized, controlled trial of 6371 hospitalized patients,¹² the use of computerized reminders increased orders for unfractionated heparin from 18.9 percent in the control group to 32.2 percent in the intervention group. In a French orthopedic-surgery department, the use of electron-

Table 4. Hazard Ratios for the Primary End Point at 90 Days in Clinically Important Subgroups.

Primary End Point	Intervention Group	Control Group	Hazard Ratio (95% CI)*	P Value for Interaction†
	<i>no./total no. (%)</i>			
Risk score for venous thromboembolism				0.22
4	29/792 (3.7)	59/782 (7.5)	0.49 (0.31–0.76)	
>4	32/463 (6.9)	44/469 (9.4)	0.73 (0.46–1.15)	
Sex				0.93
Male	33/583 (5.7)	56/597 (9.4)	0.59 (0.38–0.91)	
Female	28/672 (4.2)	47/654 (7.2)	0.57 (0.36–0.91)	
Age				0.24
<75 yr	52/976 (5.3)	79/959 (8.2)	0.63 (0.45–0.90)	
≥75 yr	9/279 (3.2)	24/292 (8.2)	0.38 (0.18–0.82)	
Cancer				0.22
Present	55/1010 (5.4)	84/988 (8.5)	0.63 (0.45–0.88)	
Absent	6/245 (2.4)	19/263 (7.2)	0.33 (0.13–0.83)	
Major surgery or trauma				0.22
Present	10/227 (4.4)	9/207 (4.3)	1.00 (0.41–2.47)	
Absent	51/1028 (5.0)	94/1044 (9.0)	0.55 (0.41–0.78)	
Prior venous thromboembolism				0.37
Present	18/253 (7.1)	25/255 (9.8)	0.75 (0.41–1.37)	
Absent	43/1002 (4.3)	78/996 (7.8)	0.54 (0.37–0.79)	

* CI denotes confidence interval.

† The null hypothesis is that there are no significant differences between subgroups.

ic reminders increased compliance with guidelines for the prevention of venous thromboembolism from 82.8 percent in the control group to 94.9 percent in the intervention group.¹³ These two studies, however, did not analyze outcomes among the patients. Thus, our data — taken together with these two prior studies — support the use of a computer-generated alert to reduce clinical events among hospitalized patients at increased risk for venous thromboembolism.

Key elements in making the study software work were the availability of a full and integrated database, which allowed us to gather the data needed to determine each patient's risk score for venous thromboembolism; a robust, rule-based alerting system capable of being triggered in a variety of ways; and an existing and well-accepted notification system with which our physicians were already fa-

miliar. Our design may be useful at other institutions; however, it may require modification, because other hospitals may use different computer languages and database layouts, may not have an integrated data system, and may use different terms to identify patients who are at high risk in the absence of prophylaxis.

Our results suggest that hospitals with adequate information-systems resources should consider implementing electronic alerts to increase physicians' awareness of the risk of venous thromboembolism, to increase the use of prophylaxis, and to reduce the rates of deep-vein thrombosis and pulmonary embolism.

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