

Effectiveness of a Guideline for Venous Thromboembolism Prophylaxis in Elderly Post-Acute Care Patients

A Multicenter Study With Systematic Ultrasonographic Examination

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Background: Thromboprophylaxis in elderly patients, including post-acute care patients, is at variance with scientific evidence. The purpose of this study was to determine whether a multifaceted intervention was followed by a decrease in deep venous thrombosis (DVT).

Methods: A prospective preintervention-postintervention study was conducted in 1373 patients (preintervention phase, n=709; postintervention phase, n=664), aged 65 years or older, enrolled in 33 hospital-based post-acute care facilities in France. An evidence-based guideline addressing pharmacologic and mechanical prophylaxis was implemented through a multifaceted intervention. The main outcome measure was any DVT diagnosed at routine comprehensive ultrasonography performed by registered angiologists.

Results: A DVT was found in 91 patients (12.8%) in the preintervention phase and in 52 patients (7.8%) in the postintervention phase ($P=.002$). The decrease in DVT involved the calf (7.1% vs 3.6%; $P=.005$) and the proxi-

mal venous segments (5.8% vs 4.2%; $P=.18$) and remained significant after adjusting for risk factors (adjusted odds ratio of any DVT, 0.58; 95% confidence interval, 0.39-0.86). Pharmacologic prophylaxis with either low-molecular-weight heparin at the high-risk dose, unfractionated heparin, and vitamin K antagonist was similar in the 2 study groups, whereas patients in the postintervention group were more likely to use graduated compression stockings (27.4% vs 34.6%; $P=.004$) and less likely to receive low-molecular-weight heparin at the low-risk dose (24.7% vs 18.5%; $P=.006$), which was not recommended by our guideline.

Conclusions: A multifaceted intervention addressing venous thromboembolism prophylaxis in post-acute care patients can be followed by a significant decrease in the rate of any DVT in elderly patients. More active interventions are needed to enforce compliance with evidence-based guidelines.

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ADVANCED AGE¹ AND HOSPITALIZATION² have been shown to be independent risk factors for deep venous thrombosis (DVT) and pulmonary embolism. The health burden associated with DVT is expected to grow dramatically during the next 30 years with the aging of the population.³ Randomized controlled trials have shown that pharmacologic prophylaxis can reduce DVT in elderly medical patients^{4,5} and in patients undergoing hip or knee replacement,⁶ cancer surgery,⁷ or other surgical procedures.⁸ There is also evidence that graduated compression stockings (GCS) can prevent DVT when properly used in surgical patients⁹ or in patients with specific medical conditions such as myocardial infarction.¹⁰ However, several studies demonstrate a gap between scientific evidence and clinical

practice in various settings,¹¹ including post-acute care facilities.¹² These facilities are used to ensure the transition between short hospital stays and home when patients require specialized care or rehabilitation services.¹³ Post-acute care patients often have multiple risk factors for DVT in addition to age.¹² In a multicenter cross-sectional study, DVT was found in 16% of post-acute care patients, with ultrasonography as a screening test.¹² In this study, the rate of anticoagulant-based prophylaxis ranged from 20% to 87% across departments, reflecting a high degree of uncertainty in the decision to use prophylaxis. As recommended,^{14,15} we have developed and implemented an evidence-based clinical practice guideline to provide clinicians with guidance on appropriate use of prophylactic treatment in post-acute care patients.¹⁶

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Group Information: A list of the participants in this study for the Association pour la Promotion de l'Angiologie Hospitalière is given at the end of this article.

The purpose of this study was to assess the effectiveness and safety of this clinical practice guideline on venous thromboembolism (VTE) prophylaxis in post-acute care patients. Using a preintervention-postintervention study design, we hypothesized that a multifaceted intervention to implement our guideline would be associated with more appropriate use of prophylaxis and a decreased rate of DVT without compromising patient safety.

METHODS

STUDY DESIGN

We conducted a prospective preintervention-postintervention study in 33 hospital-based post-acute care facilities in France. Of the participating facilities, 17 were located in teaching hospitals; 25 were skilled nursing facilities, and 8 were rehabilitation facilities. Inclusion criteria, data collection forms, and the ultrasonographic diagnostic procedure were similar for the 2 study phases. All enrolled patients provided written informed consent.

PRACTICE GUIDELINE

Our practice guideline for VTE prophylaxis in post-acute care patients was based on a systematic review of the literature and the results of a cross-sectional study and was developed using group consensus of expert panelists (listed in Bosson et al¹⁶). All recommendations were approved by physicians at participating post-acute care departments before implementation of the intervention. The guideline also was approved by the French Vascular Medicine Society and the French Geriatrics Society. In brief, the guideline recommended pharmacologic prophylaxis for up to 6 weeks after hip or knee replacement or other major surgical procedure; until discharge in patients with pulmonary embolism or proximal DVT within the previous 2 years; and for 1 week or longer, depending on the persistence of the risk factors, in patients with 2 or more risk factors such as recent immobility, VTE at other sites, hemiplegia, cancer, acute infectious disease, acute heart failure, acute respiratory failure, and myocardial infarction.¹⁶ Pharmacologic prophylaxis was recommended with either low-molecular-weight heparin (LMWH) at the usual high-risk dose (ie, dalteparin sodium, 5000 U/d; enoxaparin sodium, 4000 U/d; nadroparin calcium, 2850 U/d; and tinzaparin sodium, 4500 U/d), adjusted-dose vitamin K antagonist, or unfractionated heparin.¹⁶ Prophylaxis with LMWH at the low-risk dose was not recommended because there was no evidence that it performed better than placebo in preventing VTE in a broad spectrum of medical patients.¹⁷ Prophylaxis with unfractionated heparin, 5000 U per 12 hours, rather than LMWH was recommended in patients with creatinine clearance of 30 mL/min (0.50 mL/s) or less. We advocated the use of the Cockcroft-Gault equation for computing creatinine clearance.¹⁸ Our guideline also addressed mechanical prophylaxis including GCS use, early ambulation, and physical therapy. Graduated compression stockings (15-20 mm Hg) were recommended for use during daytime hours or longer, alone or in combination with pharmacologic prophylaxis, in immobilized patients until they recovered ambulation.¹⁶

STUDY INTERVENTION

We implemented a multifaceted intervention directed at physicians and nurses in every participating department. The intervention included an educational presentation, dissemination of educational material, and audit-feedback components.

A registered vascular medicine physician conducted a 1-hour on-site educational session for medical providers on VTE prophylaxis in the participating departments. The vascular medicine physician presented the clinical guideline, explained how to use it, and described its developmental process based on local physician practices. All medical providers were mailed baseline data on prophylaxis use and DVT prevalence in their departments, the practice guideline, supporting medical literature, and a plastic pocket card summarizing the guideline. Posters were displayed in nurse and physician offices. Depending on the facility, the preintervention enrollment was from April 3, 2001, to November 9, 2001, the intervention implementation from June 2, 2003, to November 28, 2003, and the postintervention enrollment from September 5, 2003 to April 15, 2004. All components of the intervention were completed at every study site 6 weeks before patient enrollment.

PARTICIPANTS

All patients 65 years or older who were hospitalized in the participating post-acute care departments were eligible. Patients were excluded from the study if they had a positive diagnosis of DVT or pulmonary embolism at admission or if they required long-term anticoagulant therapy with heparin or an oral anticoagulant agent because of atrial fibrillation, prosthetic heart valve, or any reason other than VTE prophylaxis.

DATA COLLECTION

Trained physicians independent of those in charge of the patients prospectively investigated transient and chronic risk factors for DVT (**Table 1**) and prophylaxis using a standardized data abstract form. For each patient, we retrospectively computed a DVT risk score using the risk factors and corresponding weights that composed the revised rule proposed by Wells et al.¹⁹ Data on prophylaxis with LMWH, unfractionated heparin, vitamin K antagonist, and GCS were investigated by reviewing physicians' orders and medical records. Compliance with GCS use was assessed by direct observation on the day compression ultrasonography was performed. We defined GCS users as patients who wore below-knee or thigh-high GCS during daytime hours or longer. Although we assessed stocking length, daily duration of use, and overall duration of use, we could not document correct sizing, application, and monitoring of GCS.

STUDY OUTCOMES

Our primary outcome was any DVT detected at routine ultrasonography on the day of a cross-sectional study. All patients underwent comprehensive compression ultrasonography performed by registered vascular medicine physicians (J.-L.B., M.-T.B., C.L.H., P.L.R., and M.-A.S.) who were unaware of both risk factors and thromboprophylaxis. As described,²⁰ all deep veins of the lower limbs were examined from the inguinal ligament to the malleolus using a 3- to 7.5-MHz transducer. Only incompressible veins with a thrombus 5 mm or larger in anteroposterior diameter were considered positive for DVT.²¹ Deep vein thromboses were categorized as proximal (thigh or popliteal segments) or distal (calf segments). Isolated muscular vein thromboses (ie, gastrocnemius or soleal vein thromboses) were not considered DVTs.

We also investigated secondary outcome measures, including major and minor bleeding and thrombocytopenia, to assess the safety of our intervention. Thrombocytopenia was defined as platelet count less than $100 \times 10^9/L$. Platelet count was ordered at the discretion of physicians in charge of the patients.

Table 1. Baseline Characteristics in Elderly Post-Acute Care Patients in the Preintervention and Postintervention Groups*

Characteristic	Preintervention (n = 709)	Postintervention (n = 664)	P Value
Age, median (IQR), y†	82 (77-88)	82 (77-89)	.22
Female sex‡	486 (69)	432 (65)	.20
Transient risk factors for venous thromboembolism			
Acute immobility <30 d	113 (15.9)	97 (14.6)	.49
Hip or knee replacement <6 wk	100 (14.1)	56 (8.4)	.001
Major surgery <4 wk	62 (8.7)	85 (12.8)	.01
Stroke <4 wk	10 (1.4)	16 (2.4)	.18
Acute respiratory failure or exacerbation of COPD	30 (4.2)	22 (3.3)	.37
NYHA class III or IV congestive heart failure	13 (1.8)	17 (2.6)	.36
Acute infectious disease	65 (9.2)	64 (9.6)	.77
Chronic risk factors for venous thromboembolism			
Prolonged immobility ≥30 d	221 (31.2)	242 (36.4)	.04
History of DVT or pulmonary embolism	82 (11.6)	55 (8.3)	.04
Hemiplegia ≥4 wk	64 (9.0)	49 (7.4)	.27
Cancer	70 (9.9)	97 (14.6)	.007
Chronic respiratory failure or COPD	29 (4.1)	57 (8.6)	.001
Chronic heart failure	87 (12.3)	135 (20.3)	<.001
Varicose veins	115 (16.2)	105 (15.8)	.84
Hormone therapy	8 (1.1)	17 (2.6)	.05
Inflammatory disorder‡	18 (2.5)	19 (2.9)	.71
History of myocardial infarction	24 (3.4)	43 (6.5)	.008
Obesity§	74 (10.4)	56 (8.4)	.21
Risk score for DVT			
0	198 (27.9)	192 (28.9)	.59
1	378 (53.3)	339 (51.1)	
2	120 (16.9)	119 (17.9)	
3	13 (1.8)	12 (1.8)	
4	0	2 (0.3)	

Abbreviations: COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; IQR, interquartile range; NYHA, New York Heart Association.

*Data are given as number (percentage) unless otherwise indicated.

†Data on age and sex were missing for 10 patients.

‡Inflammatory disorders included arthritis, connective tissue disease, and inflammatory bowel disease.

§Obesity was defined as body mass index (calculated as weight in kilograms divided by height in meters squared) of 30 or higher in men and 28.6 or higher in women.

||Computed using the following risk factors and corresponding weights that comprised the revised rule by Wells et al¹⁹: active cancer (+1); paralysis, paresis, or recent plaster immobilization of the lower extremities (+1); recently bedridden for 3 days or more or major surgery requiring general or regional anesthesia (+1); and previously documented DVT (+1).

SAMPLE SIZE

Based on the findings of a previous study,¹² we hypothesized that the prevalence of any DVT would be 15% in the preintervention phase. Assuming a power of 80% and a statistical significance level of .05, we estimated that 727 patients enrolled in each study phase would be enough to evidence a 30% relative reduction in the rate of any DVT (ie, from 15% in the preintervention phase to 10% in the postintervention phase).

STATISTICAL ANALYSIS

Categorical variables were expressed as frequencies and percentages, and continuous variables as median and interquartile range. Differences in baseline characteristics for patients in the preintervention and postintervention groups were compared using χ^2 or Fisher exact tests when appropriate for categorical variables and the Wilcoxon rank sum test for continuous variables. We estimated the odds ratio (OR) of any DVT and its associated 95% confidence interval for patients in the postintervention phase compared with those in the preintervention phase using univariable logistic regression. An OR lower than 1 meant that patients in the postintervention group were at decreased risk for any DVT. In multivariable analysis, we developed a logistic regression model adjusting for sex, age, tran-

sient and chronic risk factors, and post-acute care department characteristics. Ten patients with missing data for 1 covariate or more were excluded from multivariable analysis. We used a 2-level logistic regression model to account for patients clustering within post-acute care departments. $P \leq .05$ was considered statistically significant. Analyses were performed using STATA version 9.0 (StataCorp, College Station, Tex) and MLWin 2.0 (Institute of Education, London, England).

RESULTS

Of the 1804 patients screened for eligibility, 431 (23.9%) were excluded for the following reasons: long-term anticoagulant therapy with heparin or an oral anticoagulant agent for reasons other than VTE prophylaxis (136 patients), age younger than 65 years (135 patients), positive diagnosis of DVT or pulmonary embolism at hospital admission (81 patients), and refusal to participate (79 patients). Of eligible patients, 709 were enrolled in the preintervention phase and 664 were enrolled in the postintervention phase, with a median number of patients enrolled per department of 22 (interquartile range, 15-28) and 19 (interquartile range, 11-26), respectively ($P = .29$).

Table 2. Pharmacologic and Mechanical Prophylaxis Use in Elderly Post-Acute Care Patients in the Preintervention and Postintervention Groups

Prophylaxis	Preintervention (n = 709)	Postintervention (n = 664)	P Value
High-risk dose of LMWH*	224 (31.6)	203 (30.6)	.68
Low-risk dose of LMWH†	175 (24.7)	123 (18.5)	.006
Unfractionated heparin	6 (0.8)	7 (1.0)	.69
Vitamin K antagonist	3 (0.4)	5 (0.7)	.49
Graduated compression stockings	194 (27.4)	230 (34.6)	.004

Abbreviation: LMWH, low-molecular-weight heparin.

*Prophylaxis with LMWH at high-risk dose included dalteparin sodium, 5000 U/d; enoxaparin sodium, 4000 U/d; nadroparin calcium sodium, 2580 U/d; and tinzaparin sodium, 4500 U/d.

†Prophylaxis with LMWH at low-risk dose, including dalteparin sodium, 2500 U/d; enoxaparin sodium, 2000 U/d; nadroparin calcium sodium, 1900 U/d; and reviparin sodium, 1432 U/d, was not recommended by the study guideline.

The median age of the patients was 82 years (interquartile range, 77-88), and 66.9% of all patients were women. Patients in the postintervention group were more likely to have prolonged immobility, recent major surgery, cancer, chronic respiratory failure or chronic obstructive pulmonary disease, chronic heart failure, and history of myocardial infarction, whereas those in the preintervention group were more likely to have recent hip or knee replacement surgery and a history of VTE. Overall, the preintervention and postintervention patient groups had a comparable DVT risk score at hospital admission (Table 1).

The percentages of patients receiving pharmacologic prophylaxis with either LMWH at the high-risk dose, unfractionated heparin, or vitamin K antagonist were comparable for the preintervention and postintervention groups, whereas patients in the postintervention group were more likely to use GCS and less likely to receive LMWH at the low-risk dose, which was not recommended by our guideline (Table 2). The increased use of GCS was observed in patients in whom pharmacologic prophylaxis was not recommended (Table 3) but mechanical prophylaxis was recommended (Table 4) according to our guideline. The decrease in the use of LMWH at the low-risk dose involved patients in whom pharmacologic prophylaxis was not recommended (Table 3).

The median day on which patients underwent compression ultrasonography was not different for the preintervention and postintervention groups (21 vs 22; $P = .25$). Deep venous thrombosis was found in 91 patients (12.8%) in the preintervention group and in 52 (7.8%) in the postintervention group (OR, 0.58; 95% confidence interval, 0.40-0.83; $P = .002$). The decrease in thrombosis involved all venous segments of the lower limbs, although it was not significant for the proximal veins (Figure). In multivariable analysis, the decreased odds of DVT in patients in the postintervention group remained significant after adjusting for baseline patient and facility characteristics (adjusted OR, 0.58; 95% confidence interval, 0.39-0.86; $P = .007$). Considering safety outcomes, no major

bleeding was documented, and the rates of minor bleeding (0.7% vs 1.0%; $P = .49$) and thrombocytopenia (0.8% vs 0.1%; $P = .12$) were not different in the preintervention and postintervention groups, respectively.

COMMENT

In this prospective multicenter study, a multifaceted intervention designed to implement an evidence-based guideline addressing VTE prophylaxis after acute care was followed by a reduction in DVT without compromising patient safety. These findings are consistent with those of previous studies. In a clustered, randomized, controlled trial, Anderson et al²² demonstrated that a formal continuous medical education program increased the use of both pharmacologic and mechanical prophylaxis in inpatients who required acute care. However, the authors did not investigate whether their intervention was followed by a reduction in DVT. Using the same study design as in the present study, we previously reported a significant decrease in the rate of any DVT after the implementation of a multifaceted intervention directed at all medical providers involved in VTE prophylaxis in acutely ill medical inpatients.²⁰ Our findings are also supported by randomized controlled trials that demonstrated that multifaceted intervention can change professional practice and health care outcomes.²³

Changes in the prophylaxis means measured can only partly explain the decrease in the rate of DVT observed in our study. The most important change in prophylaxis consisted of an increased use of GCS, while the change in pharmacologic prophylaxis use was modest and not statistically significant. The apparent failure of our intervention to alter the rate of pharmacologic prophylaxis may have several potential explanations. First, the baseline rate of pharmacologic prophylaxis use (33% for all patients and 45% for patients in whom prophylaxis was recommended according to our guideline) was relatively high compared with previous studies,²⁴ and a more intensive intervention would have been necessary to further increase this rate. Second, physicians were likely reluctant to order pharmacologic prophylaxis in this setting because they feared patient bleeding.²⁵ Third, evidence of the efficacy of prolonged pharmacologic prophylaxis is lacking, although some studies indirectly suggest it may be necessary in medical inpatients at high risk.²⁶ Another important finding of our study was the significant decrease in the rate of prophylaxis with LMWH at the low-risk dose, which reflected physician compliance with our guideline. These observations together suggest that our multifaceted intervention not only altered the use of measured prophylaxis means but also improved physician and nurse awareness of patients at risk for VTE and eventually increased the use of additional prophylactic measures including early ambulation and physical therapy, which were addressed by our intervention but not investigated in our study.

Another finding was the low rate of hemorrhage observed in our study despite the advanced age of the patients. This finding confirms safety results from previous studies that included large numbers of elderly patients⁵

Table 3. Appropriateness of Prophylaxis Use in Elderly Post-Acute Care Patients in the Preintervention and Postintervention Groups*

Ordered Prophylaxis	Pharmacologic Prophylaxis					
	Recommended			Not Recommended		
	Preintervention (n = 254)	Postintervention (n = 209)	P Value	Preintervention (n = 455)	Postintervention (n = 455)	P Value
High-risk dose of LMWH†	112 (44.1)	91 (43.5)	.90	112 (24.6)	112 (24.6)	.99
Low-risk dose of LMWH‡	76 (29.9)	59 (28.2)	.69	99 (21.8)	64 (14.1)	.002
Unfractionated heparin	2 (0.8)	5 (2.4)	.25	4 (0.9)	2 (0.4)	.69
Vitamin K antagonist	0	2 (1.0)	.20	3 (0.7)	3 (0.7)	.99
Graduated compression stockings	93 (36.6)	92 (44.0)	.10	101 (22.2)	138 (30.3)	.005
Alone	37 (14.6)	40 (19.1)	.19	65 (14.3)	93 (20.4)	.01
In combination with pharmacologic prophylaxis	56 (22.0)	52 (24.9)	.47	36 (7.9)	45 (9.9)	.29

Abbreviation: LMWH, low-molecular-weight heparin.

*Data are given as number (percentage) of patients.

†Prophylaxis with LMWH at high-risk dose included dalteparin sodium, 5000 U/d; enoxaparin sodium, 4000 U/d; nadroparin calcium, 2580 U/d; and tinzaparin sodium, 4500 U/d.

‡Prophylaxis with LMWH at low-risk dose, including dalteparin sodium, 2500 U/d; enoxaparin sodium, 2000 U/d; nadroparin calcium, 1900 U/d; and rivarparin sodium, 1432 U/d, was not recommended by the study guideline.

Table 4. Appropriateness of Graduated Compression Stocking Use in Elderly Post-Acute Care Patients in the Preintervention and Postintervention Groups*

Graduated Compression Stocking Use	Preintervention	Postintervention	P Value
Recommended†	98/334 (29.3)	126/339 (37.2)	.03
Not recommended	96/375 (25.6)	104/325 (32.0)	.06
Total	194/709 (27.4)	230/664 (34.6)	.004

*Data are given as number of patients/total number of patients (percentage).

†Graduated compression stockings (15-20 mm Hg) were recommended for use during daytime hours or longer, alone or in combination with pharmacologic prophylaxis, in immobilized patients until they recovered ambulation.

and supports the idea that physicians may often overestimate the risk for bleeding in their patients and inappropriately withhold pharmacologic prophylaxis.²⁵

Our uncontrolled preintervention-postintervention study design has potential limitations. First, our intervention was not based on random assignment, and, therefore, our results may be confounded by other factors. Using the revised Wells rule, we showed that patients in the preintervention and postintervention groups were at comparable risk for DVT at hospital admission. Moreover, the decrease in the rate of DVT in the postintervention group remained significant after adjustment for risk factors in multivariable analysis. Although we cannot exclude hidden confounding factors, it was unlikely that they had more effect than our active multifaceted intervention. Second, a secular trend was unlikely to account for the decrease in DVT, inasmuch as several studies reported a striking upward trend in the rate of DVT during the past decade.³ Third, the decrease in DVT was mainly driven by a reduction in distal DVT, for which the diagnostic performance of compression ultrasonography is poorer than for proximal clots.²⁷ However, several studies reported much better diagnostic perfor-

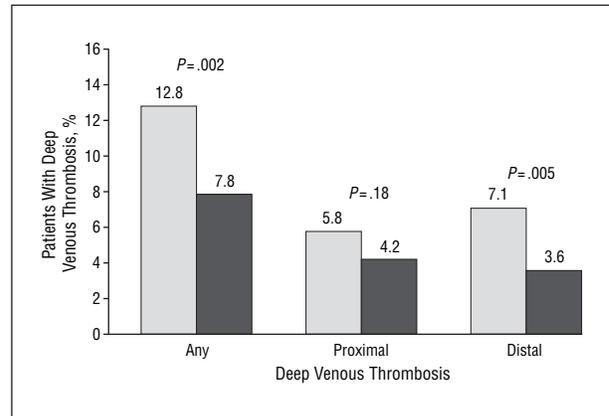


Figure. Prevalence of deep vein thrombosis detected at compression ultrasonography in elderly post-acute care patients enrolled in the preintervention phase (n=709; shaded bars) and postintervention phase (n=664; solid bars).

mance in patients with asymptomatic disease²⁸ when compression ultrasonography was performed by staff with substantial experience in ultrasonography and using a standardized examination procedure, as in our study. Even if the lack of sensitivity of compression ultrasonography were real in our study, it would not explain the decreased OR of DVT in patients in the postintervention group because the same diagnosis procedure was used in the 2 study phases. Fourth, the clinical significance of isolated distal DVT is controversial, although distal and proximal DVTs are likely 2 manifestations of the same underlying disease. There is evidence that DVT usually starts in the calf veins and may either resolve spontaneously or extend to the proximal veins.²⁹ As a result, most randomized controlled trials of thromboprophylaxis rely on a composite end point, combining proximal and distal DVTs,¹⁷ and published guidelines recommend treating patients with thrombosis confined to the deep veins of the calf with an anticoagulant agent for 3 months.³⁰ In our study, the decrease in the rate of isolated distal DVT in patients in the postintervention group was par-

alleled by a decrease in the rate of proximal DVT, suggesting that our intervention was effective in reducing the overall risk for DVT.

CONCLUSIONS

This multicenter study provides observational evidence that a multifaceted intervention directed at all medical providers can be followed by a decrease in DVT without compromising patient safety after acute care. More active strategies adapted to this setting should be developed and evaluated to enforce compliance with evidence-based guidelines.

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