Failure of Anticoagulant Thromboprophylaxis: Risk Factors in Medical-Surgical Critically Ill Patients*

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Objectives: To identify risk factors for failure of anticoagulant thromboprophylaxis in critically ill patients in the ICU.

Design: Multivariable regression analysis of thrombosis predictors from a randomized thromboprophylaxis trial.

Setting: Sixty-seven medical-surgical ICUs in six countries.

Patients: Three thousand seven hundred forty-six medical-surgical critically ill patients.

Interventions: All patients received anticoagulant thromboprophylaxis with low-molecular-weight heparin or unfractionated heparin at standard doses.

Measurements and Main Results: Independent predictors for venous thromboembolism, proximal leg deep vein thrombosis, and pulmonary embolism developing during critical illness were assessed. A total of 289 patients (7.7%) developed venous thromboembolism. Predictors of thromboprophylaxis failure as measured by development of venous thromboembolism included a personal or family history of venous thromboembolism (hazard ratio, 1.64; 95% CI, 1.03–2.59; $p = 0.04$) and body mass index (hazard ratio, 1.18 per 10-point increase; 95% CI, 1.04–1.35; $p = 0.01$). Increasing body mass index was also a predictor for developing proximal leg deep vein thrombosis (hazard ratio, 1.25; 95% CI, 1.06–1.46; $p = 0.007$), which occurred in 182 patients (4.9%). Pulmonary embolism occurred in 47 patients (1.3%) and was associated with body mass index (hazard ratio, 1.37; 95% CI, 1.02–1.83; $p = 0.035$) and vasopressor use (hazard ratio, 1.84; 95% CI, 1.01–3.35; $p = 0.046$). Low-molecular-weight heparin (in comparison to unfractionated heparin) thromboprophylaxis lowered pulmonary embolism risk (hazard ratio, 0.51; 95% CI, 0.27–0.95; $p = 0.034$) while statin use in the preceding week lowered the risk of proximal leg deep vein thrombosis (hazard ratio, 0.46; 95% CI, 0.27–0.77; $p = 0.004$).

Conclusions: Failure of standard thromboprophylaxis using low-molecular-weight heparin or unfractionated heparin is more likely in ICU patients with elevated body mass index, those with a personal or family history of venous thromboembolism, and those receiving vasopressors. Alternate management or incremental risk reduction strategies may be needed in such patients. (*Crit Care Med* 2015; 43:401–410)

Key Words: anticoagulant; critically ill; heparin; intensive care unit; low-molecular-weight heparin; thromboprophylaxis

Critical illness increases the risk of venous thromboembolism (VTE) (1) secondary to immobility and concomitant proinflammatory and prothrombotic conditions (2). Despite use of anticoagulant thromboprophylaxis, VTE occurs in up to 7.7% of critically ill patients (3). Identifying independent predictors of VTE in patients receiving thromboprophylaxis in the ICU could help to identify patients who may need alternate strategies for thromboprophylaxis and expedite diagnosis in patients with suspected VTE.

In critically ill patients, studies using multivariable analyses have identified a personal or family history of VTE (4, 5), illness severity (6), duration of central venous catheter placement (7), D-dimer levels (8), end-stage renal failure, vasopressors, and platelet transfusion during critical illness (5) as predictors of VTE. A history of deep vein thrombosis (DVT), male sex, and platelet transfusion are independent risk factors for pulmonary embolism (PE) in medical ICU patients (9). In noncritically ill patients, medications that are commonly used in the ICU such as erythropoietin-stimulating agents (ESAs) (10) and statins (11) may influence the risk of VTE. However, comparing VTE risk factors across these studies is limited due to differences in case-mix, risk factors considered, and whether thromboprophylaxis was consistently used in the patients studied. Further, outcomes also differ based on whether VTE was detected by screening or based on signs and symptoms. Our objective was to determine the risk factors that predict for failure of standard thromboprophylaxis in critically ill patients using data from a large randomized thromboprophylaxis trial (3).

MATERIALS AND METHODS

Study Design

PROphylaxis for ThromboEmbolism in Critical care Trial was a multicenter randomized blinded trial comparing subcutaneous low-molecular-weight heparin (LMWH) (dalteparin) 5,000 IU daily with unfractionated heparin (UFH) 5,000 IU twice daily for thromboprophylaxis in 3,746 medical-surgical critically ill patients in 67 centers (ClinicalTrials.gov NCT00182143). The protocol (12) and outcomes are reported elsewhere (3). The study was approved by the research ethics committee at each study center (**Appendix 1**). Patients 18 years old or older and weighing greater than or equal to 45 kg were enrolled if they were expected to be in ICU for greater than or equal to 72 hours. Exclusion criteria were a contraindication to heparin, need for therapeutic heparin, and ICU admission diagnosis immediately following trauma or cardiac surgery, orthopedic surgery, or neurosurgery. We prospectively collected factors that could influence VTE risk using standardized definitions in the ICU. Demographic and clinical characteristics were

recorded at baseline, and key events and exposures in the ICU were recorded daily.

Definitions

We defined VTE as DVT at any site or PE diagnosed greater than or equal to 72 hours after ICU admission. VTE was defined as clinically suspected if the patient had objectively confirmed DVT or PE following investigation prompted by signs and/or symptoms compatible with VTE in contrast to an incidental VTE which was identified by a test to diagnose another condition or DVT diagnosed by screening ultrasound. Proximal leg DVT was defined as thrombosis occurring anywhere between the common femoral vein and calf trifurcation and included clinically suspected and incidental DVT. We analyzed only thrombotic events and risk factors occurring in the ICU. Screening was conducted using twice-weekly compression ultrasound performed by technologists with study-specific training and then interpreted by radiologists. All outcomes were adjudicated blinded to study drug, in duplicate (DVT) or quadruplicate (PE) as described previously (3).

Statistical Analysis

We present categorical data as counts and proportions with 95% CIs and continuous data as mean (SD) or median (interquartile range [IQR]) if data were skewed. We used Cox regression to first determine the independent risk factors for VTE. The Cox model assesses the effect of each risk factor on the hazard of VTE over time, adjusted for other factors, censoring due to death, ICU discharge, or occurrence of the outcome of interest (13). We tested the assumption of proportional hazards by evaluating the interaction of hazard with time for each variable.

The following baseline variables were used in the regression: age (10-yr increase), Acute Physiology and Chronic Health Evaluation (APACHE) II score (10-point increase) (14), body mass index (BMI) (10-point increase), medical versus surgical admitting diagnosis, chronic end-stage renal failure, cancer, pre-ICU hospitalization for more or less than 1 week, personal or family history of VTE, and treatment allocation (LMWH or UFH). We examined the effect of the following time-dependent interventions preceding the diagnosis of all VTE or proximal leg DVT: mechanical ventilation; inotropes or vasopressors; renal replacement therapy; central venous catheter insertion; RBC, platelet, or plasma transfusion within the preceding 3 days; and use of acetylsalicylic acid, ESAs, and statins in the preceding 7 days. For the outcomes of PE and clinically suspected VTE, fewer candidate risk factors were considered to avoid overfitting the model (15): APACHE II score (10-point increase) (14), BMI (10-point increase), personal or family history of VTE, and LMWH or UFH. We report hazard ratios (HRs) and 95% CIs. p values less than 0.05 were considered significant.

In sensitivity analyses, we added heparin-induced thrombocytopenia (HIT) diagnosed by a central serotonin-release assay (SRA) (16) to the regression models. HIT testing was performed for clinically suspected HIT and in patients with a platelet count of less than 50×10^9/L, had a 50% decrease in platelet count, or VTE. However, testing for HIT performed exclusively because of VTE was not included in this sensitivity analysis of risk factors for the development of VTE. HIT testing was performed in 763 of 3,746 patients (20.4%) and those without testing were considered negative.

RESULTS

All VTE

Among 3,746 patients, 289 (7.7%) developed an incident VTE during their ICU stay despite anticoagulant thromboprophylaxis (**Table 1**). All patients in the study received anticoagulant thromboprophylaxis; doses of either LMWH or UFH were administered on 96.7% of study days. The median duration of exposure to anticoagulant thromboprophylaxis was 7 days (IQR, 4–12 d). A personal or family history of VTE was independently associated with an increased risk of VTE (HR, 1.64; 95% CI, 1.03–2.59; $p = 0.04$) (**Table 2**). Overall, 20 of these 289 patients (6.9%) had a personal (17) or family (2) VTE history. The risk of VTE was also associated with increased BMI (HR, 1.18 for every 10-point increase; 95% CI, 1.04–1.35; $p = 0.01$).

Proximal Leg DVT

Proximal leg DVT developed in 182 patients (4.9%). Higher BMI was associated with an increased risk (HR, 1.25 for every 10-point increase; 95% CI, 1.06–1.46; $p = 0.007$) (Table 2). Statin treatment in the preceding week was associated with a lower risk (HR, 0.46; 95% CI, 0.27–0.77; $p = 0.004$). The most commonly administered statins were atorvastatin (median daily dose reported 40 mg) (64.6%), simvastatin (40 mg) (19.6%), and rosuvastatin (10 mg) (11.5%).

PE

PE was diagnosed in 47 patients (1.3%). Increased BMI (HR, 1.37; 95% CI, 1.02–1.83; $p = 0.035$) and use of inotropes or vasopressors (HR, 1.84; 95% CI, 1.01–3.35; $p = 0.046$) were independently associated with a higher risk of thromboprophylaxis failure and development of PE (**Table 3**). A total of 2,050 patients received inotropes or vasopressors over 9,389 days. The three most common agents were norepinephrine (7,479 d; 79.7%), phenylephrine (1,123 d; 12.0%), and vasopressin (1,025 d; 10.9%). Compared with UFH, LMWH thromboprophylaxis was associated with a lower risk of PE (HR, 0.51; 95% CI, 0.27–0.95; $p = 0.034$).

Clinically Suspected VTE

Clinically suspected VTE developed in 73 patients (1.9%); independent predictors of this outcome included cancer (HR, 2.34; 95% CI, 1.27–4.30; $p = 0.007$) and vasopressor/inotrope use (HR, 1.69; 95% CI, 1.04–2.76; $p = 0.034$) (**Table 4**).

Sensitivity Analysis: HIT

Seventeen patients (0.5%) developed HIT. In a sensitivity analysis, we added HIT into the previous models. None of the significant thrombosis risk factors changed in the original models. However, HIT was an additional independent predictor of

TABLE 1. Detailed Description of Patients in This Study

Patient Characteristics	Patients, *n* (%)
Baseline characteristics, *n* (%)	
Low-molecular-weight heparin as randomized	1,873 (50.0)
Age, mean (SD)	61.4 (16.5)
Body mass index, mean (SD)	28.3 (7.7)
Acute Physiology and Chronic Health Evaluation II, mean (SD)	21.5 (7.8)
Medical admission	3,046 (81.3)
Female sex	1,614 (43.3)
End-stage renal disease	118 (3.2)
Personal/family history of venous thromboembolism	120 (3.2)
Cancer	150 (4.0)
Hospitalized for 1 wk previously	730 (19.6)
Admitting diagnosis, *n* (%)	
Respiratory	1,701 (45.6)
Sepsis	549 (14.7)
Gastrointestinal	520 (14.0)
Cardiovascular	336 (9.0)
Neurologic	229 (6.1)
Renal	65 (1.7)
Metabolic	144 (3.9)
Other—surgical	118 (3.2)
Other—medical	65 (1.7)
Baseline advanced life support, *n* (%)	
Mechanical ventilation	3,358 (90.2)
Vasopressors or inotropes	1,677 (45.0)
Renal replacement therapy	226 (6.1)
Central venous catheter	3,119 (83.8)
Other interventions, *n* (%)	
RBC transfusion	1,227 (32.9)
Platelet transfusion	113 (3.0)
Acetylsalicylic acid or thienopyridine	1,244 (33.4)
Erythropoietin	105 (2.8)
Statin	762 (20.5)

In this table, we present characteristics of 3,746 medical-surgical ICU patients included in this study. Mechanical ventilation refers to ventilation with an endotracheal tube. Cancer is defined as lymphoma, metastatic cancer, leukemia, multiple myeloma, active malignancy, or history of malignancy. Thienopyridine is defined as ticlopidine or clopidogrel.

VTE (HR, 3.58; 95% CI, 1.13–11.32; $p = 0.030$) and proximal leg DVT (HR, 4.61; 95% CI, 1.45–14.69; $p = 0.010$), but not PE (HR, 5.98; 95% CI, 0.80–44.54; $p = 0.081$).

DISCUSSION

In this cohort of medical-surgical critically ill patients receiving standard doses of anticoagulant thromboprophylaxis, we documented that increased BMI was independently associated with failure of thromboprophylaxis and the development of both VTE and proximal leg DVT. The relative risk of VTE was increased approximately 20% for every 10-point increase in BMI. Personal or family history of VTE was also associated with thromboprophylaxis failure, with a 60% increase in risk of VTE. Treatment with inotropes/vasopressors was associated with a greater risk of PE and, along with cancer, was associated with symptomatic (clinically suspected) VTE. Statin use in the preceding week was associated with a 50% lower risk of proximal leg DVT, and LMWH was similarly associated with a 50% lower risk of PE compared with UFH.

This analysis was performed in a population of critically ill patients who received anticoagulant thromboprophylaxis in doses considered standard of care. Our findings highlight the need to consider alternate or incremental approaches to thromboprophylaxis in critically ill patients with increased BMI or a personal or family history of VTE and in those patients receiving inotropes or vasopressors while in the ICU.

The finding of BMI as an independent risk factor for VTE, proximal leg DVT, and PE is consistent with prior reports in noncritically populations. In a meta-analysis of observational studies, obesity was associated with an odds ratio (OR) for VTE of 2.33 (18). Similar results were found in a prospective Danish study of over 56,000 patients in which BMI and other anthropometric measures of obesity (body weight, waist and hip circumference) were all associated with increased VTE risk (17). Studies suggest that weight-based heparin dosing is superior to standard heparin treatment of DVT (19) and fixed dose oral anticoagulants may have reduced efficacy in patients with increased BMI (20–22). Failure of thromboprophylaxis in obese patients due to systematic underdosing of antithrombotic agents may potentially be addressed using weight-based dosing regimens (23). Observational studies examining weight-based dosing of LMWH have been too small to examine the effect on clinical outcomes of thrombosis and bleeding, but have demonstrated that peak anti-Xa levels in the prophylactic range can be achieved and suggest that weight-based dosing may be effective and safe (24–27).

Our results are also consistent with data in noncritically ill populations that suggest increased VTE risk in patients who have a family history of VTE. In a Swedish database linkage study, the standardized prevalence ratios for VTE in patients who had a history of VTE in one sibling ranged from 2.08 to 4.77 depending on patient age, but the ratio increased to 51.87 with two affected siblings (28). Critically ill patients with a personal or family history of VTE may benefit from a more aggressive thromboprophylactic approach, with consideration for a combination of pharmacologic and mechanical thromboprophylaxis.

TABLE 2. Independent Risk factors for Thromboprophylaxis Failure: Venous Thromboembolism and Proximal Leg Deep Vein Thrombosis Acquired During Critical Illness

Possible Risk Factors	VTE Hazard Ratio (95% CI)	*p*	Proximal Leg Deep Vein Thrombosis Hazard Ratio (95% CI)	*p*
Baseline factors				
Low-molecular-weight heparin vs unfractionated heparin as randomized	0.85 (0.67–1.08)	0.19	0.88 (0.65–1.19)	0.40
Age (10-yr increase)	0.94 (0.87–1.02)	0.14	0.97 (0.87–1.07)	0.54
Acute Physiology and Chronic Health Evaluation II (10-point increase)	1.02 (0.86–1.20)	0.82	1.07 (0.87–1.32)	0.54
Medical admission	0.87 (0.65–1.18)	0.38	1.22 (0.80–1.85)	0.36
End-stage renal disease	1.04 (0.45–2.40)	0.93	1.50 (0.62–3.65)	0.37
Personal/family history of VTE	1.64 (1.03–2.59)	0.04	1.69 (0.95–2.98)	0.07
Body mass index (10-point increase)	1.18 (1.04–1.35)	0.01	1.25 (1.06–1.46)	0.007
Cancer	1.19 (0.82–1.74)	0.36	0.80 (0.46–1.39)	0.42
Hospitalized for 1 wk	1.15 (0.88–1.52)	0.31	1.38 (0.98–1.93)	0.06
Time-dependent factors				
Mechanical ventilation	1.06 (0.71–1.59)	0.78	1.15 (0.67–1.95)	0.62
Vasopressors or inotropes	1.14 (0.87–1.49)	0.34	1.16 (0.83–1.63)	0.39
Renal replacement therapy	1.01 (0.69–1.47)	0.96	1.18 (0.76–1.84)	0.47
Central venous catheter	1.36 (0.86–2.15)	0.18	1.15 (0.66–2.02)	0.62
RBC transfusion	0.95 (0.70–1.30)	0.77	1.02 (0.69–1.49)	0.94
Platelet transfusion	1.44 (0.58–3.57)	0.43	2.14 (0.85–5.37)	0.11
Acetylsalicylic acid or thienopyridine	1.10 (0.82–1.46)	0.53	1.33 (0.94–1.89)	0.11
Erythropoietin-stimulating agents	0.54 (0.19–1.57)	0.26	0.17 (0.02–1.28)	0.09
Statin	0.76 (0.52–1.09)	0.14	0.46 (0.27–0.77)	0.004

VTE = venous thromboembolism.

In this table, we show risk factors for VTE and proximal leg deep vein thrombosis (DVT) developing in the ICU, as determined by multivariable Cox regression analysis. VTE is defined as a DVT in any location or pulmonary embolism. Mechanical ventilation refers to ventilation with an endotracheal tube. Thienopyridine is defined as ticlopidine or clopidogrel.

Inotrope/vasopressor use has previously been identified as a risk factor for thromboprophylaxis failure in the ICU (5). Vasopressors result in decreased peripheral circulation and potentially may result in suboptimal bioavailability and inadequate anticoagulant activity, as measured by lower anti-Xa levels in patients receiving vasopressors compared with those who are not (29). Analogous to patients with increased BMI, vasopressor use may result in systematic underdosing of anticoagulant thromboprophylaxis and higher heparin doses or a different mode of administration may be required. Targeting a specific subgroup of critically ill patients at higher VTE risk using alternate strategies has not been studied to date.

By contrast, statin treatment during critical illness was associated with an approximate 50% lower relative risk of DVT after adjusting for other confounders. A meta-analysis of observational studies found lower VTE rates in non-ICU patients receiving statins (OR for VTE, 0.67; 95% CI, 0.53–0.84) (30). In a trial of 17,802 persons whose C-reactive protein levels were greater than or equal to 2.0 mg/L, patients randomized to rosuvastatin compared with placebo were less likely to develop symptomatic VTE (HR, 0.57; 95% CI, 0.37–0.86; $p = 0.007$) (11). Although the association of statins with reduced VTE risk is consistent with data in other settings, whether this association is causal and whether statins interact with anticoagulant prophylaxis warrants further investigation.

In this study, we did not confirm the impact of previously identified VTE risk factors such as APACHE II score (6), perhaps because events following ICU admission more strongly influence thrombotic risk. In a study of 197 critically ill patients, we found that neither hypercoagulability tests nor D-dimer levels predictive or diagnostic of DVT (31). Identification of a risk factor in regression analyses is unlikely if the factor has a

TABLE 3. Independent Risk Factors for Thromboprophylaxis Failure: Pulmonary Embolism Acquired During Critical Illness

Possible Risk Factors	Pulmonary Embolism Hazard Ratio (95% CI)	*p*
Baseline factors		
Low-molecular-weight heparin vs unfractionated heparin as randomized	0.51 (0.27–0.95)	0.034
Acute Physiology and Chronic Health Evaluation II (10-point increase)	0.78 (0.52–1.16)	0.214
Personal/family history of venous thromboembolism	1.36 (0.42–4.40)	0.607
Body mass index (10-point increase)	1.37 (1.02–1.83)	0.035
Time-dependent factors		
Vasopressors or inotropes	1.84 (1.01–3.35)	0.046

In this table, we show risk factors for pulmonary embolism developing in the ICU, as determined by multivariable Cox regression analysis. Mechanical ventilation refers to ventilation with an endotracheal tube. Thienopyridine is defined as ticlopidine or clopidogrel.

TABLE 4. Risk Factors for Incident Clinically Suspected Venous Thromboembolism in the ICU

Possible Risk Factors	Clinically Suspected VTE Hazard Ratio (95% CI)	*p*
Baseline characteristics		
Low-molecular-weight heparin vs unfractionated heparin as randomized	0.69 (0.43–1.12)	0.136
Acute Physiology and Chronic Health Evaluation II (10-point increase)	0.86 (0.63–1.18)	0.361
Personal/family history of VTE	1.78 (0.76–4.16)	0.181
Body mass index (10-point increase)	1.24 (0.97–1.60)	0.088
Cancer	2.34 (1.27–4.30)	0.007
In hospital for > 1 wk or more prior to randomization	0.68 (0.37–1.25)	0.218
Time-dependent factors		
Vasopressors or inotropes	1.69 (1.04–2.76)	0.034

VTE = venous thromboembolism.

In this table, we show risk factors for 73 incident clinically suspected VTEs as determined by multivariable Cox regression analysis. VTE is defined as any leg or nonleg deep vein thrombosis or pulmonary embolism.

very high or low prevalence. We documented no relationship of VTE with central venous catheters, perhaps because of the high prevalence (87%) of central venous catheter use. Other studies in which almost all patients had a central venous catheter found no association with leg DVT (5, 6). We previously analyzed nonleg vein thromboses (superficial or deep, proximal or distal), including abdominal and upper extremity DVT in this population (32). Nonleg thromboses were more likely in patients with cancer and were associated with an increased risk of PE, but not ICU mortality. We found no association with ESAs or platelet transfusion with VTE; however, only 104 (2.8%) and 111 (3.0%) of patients received these interventions, respectively.

We found that HIT was associated with VTE after adjusting for other independent factors despite the low frequency of HIT (0.5%). The diagnosis of HIT often follows VTE, but our analysis assessed HIT diagnosed due to clinical suspicion for HIT, confirmed on central SRA testing. Earlier studies have documented the strong association of HIT with VTE following orthopedic surgery (relative risk, 11.6; 95% CI, 6.4–20.8) (33, 34). This study is unique in identifying an independent association between HIT and VTE in critically ill patients.

There are several implications of these findings. First, knowledge of factors predisposing to failure of thromboprophylaxis and the development of VTE in the ICU setting can help increase awareness of this complication of critical illness. This

can potentially result in more timely diagnosis and treatment of VTE when it develops, which could decrease associated morbidity and mortality. Finally, risk-stratification data may tailor thromboprophylaxis based on individual risk factors, using more aggressive strategies in patients at higher risk including higher doses, alternate anticoagulants, or combination of pharmacologic and mechanical thromboprophylaxis (1).

Our study has several limitations. Data on personal or family history of VTE may have been unreliable or underreported. We did not measure mobility using patient or institutional factors (e.g., frailty, sedation depth, nurse-to-patient ratio, and physiotherapist sessions). Instead, we used surrogates of immobility as VTE risk factors, such as illness severity, BMI, and advanced life support, which often limit rehabilitation in critical illness. Our primary outcome represents the composite thrombotic burden of VTE, including proximal leg DVT diagnosed by twice-weekly ultrasonography, given the inaccuracy of the physical examination at detecting lower limb DVT in the ICU (35). Patient follow-up was limited to the duration of hospitalization while in the ICU and consequently our analyses did not account for any VTE events or risk factors occurring post-ICU discharge. Last, we used dalteparin at the approved prophylactic dose of 5,000 IU SC daily. It is generally assumed that prophylactic doses of subcutaneous dalteparin and other LMWHs (e.g., enoxaparin 30 mg bid [used most commonly in North America] or 40 mg daily [used most commonly in Europe] and tinzaparin 4,500 IU daily or 50 IU/kg daily) are equivalent, but this is based only on indirect comparisons without robust endpoint assessments; no direct comparisons across LMWHs at these prophylactic doses examining patient-important outcomes have been performed, particularly in critically ill patients (36).

Strengths of this study include the largest number of patients and VTE events to examine predictors of VTE and failure of thromboprophylaxis in the medical-surgical population. All patients in this study received anticoagulant thromboprophylaxis (97% of ICU days) in contrast to previous studies in which omission of thromboprophylaxis may have influenced the results. The number of events is a major determinant of the power of regression analysis to identify risk factors for an outcome. The sample size for this study suggests that our findings are more robust than studies with fewer events, fewer patients, and less rigorous analytic approaches that do not address confounding. We considered all patient information by allowing for censoring due to death or discharge and testing the assumption of nonproportional hazards. To avoid spurious associations, we avoided overfitting regression models (15). We analyzed emerging VTE risk factors such as ESAs and statins. Our multicenter enrollment suggests that the results are generalizable to similar populations.

CONCLUSIONS

We found that despite use of anticoagulant thromboprophylaxis at standard doses, thromboprophylaxis is more likely to fail in patients who have a personal or family history of VTE and in those with increased BMI. Patients who receive inotropes/vasopressors are at increased risk of PE. Statin and LMWH use appears to be protective, with lower risks of proximal leg DVT and PE, respectively. Knowledge of the factors predisposing to thromboprophylaxis failure and to VTE during critical illness may help clinicians to risk stratify patients and guide appropriate thromboprophylaxis. In addition, awareness of the strongest risk factors may hasten diagnosis and treatment that could help to reduce VTE-associated morbidity and mortality.

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