Journal of Thrombosis and Haemostasis, **2**: 2156–2161

ORIGINAL ARTICLE

Risk factors for venous thrombosis in medical inpatients: validation of a thrombosis risk score

N. A. ZAKAI, J. WRIGHT and M. CUSHMAN
Department of Medicine, University of Vermont College of Medicine and Fletcher Allen Health Care, Burlington, VT, USA

To cite this article: Zakai NA, Wright J, Cushman M. Risk factors for venous thrombosis in medical inpatients: validation of a thrombosis risk score. *J Thromb Haemost* 2004; **2**: 2156–61.

Summary. *Background/objectives:* The occurrence of and risk factors for venous thrombosis (VT) complicating hospital admission in unselected medical inpatients have not been widely studied. *Patients and methods:* In a 400-bed teaching hospital we identified all cases of VT complicating hospital admission between September 2000 and September 2002 using discharge codes and chart review. Controls were randomly selected adult inpatients frequency matched to cases for medical service. *Results:* The incidence of VT complicating hospital admission was 7.6 per 1000 admissions. On average, VT was diagnosed on the fifth hospital day. The median age of the 65 cases and 123 controls was 68 years and 45% were men. Cases had a 4-fold higher death rate than controls [95% confidence interval (CI) 1.9, 8.8]. At admission, trauma within 3 months, leg edema, pneumonia, platelet count $> 350 \times 10^3$ mm^{-3} and certain cancers were associated with risk of VT. Age, body mass index, and acute myocardial infarction were not associated with VT risk. One of three published VT risk models was able to risk stratify patients and was associated with a 2.6-fold increased risk of VT (95% CI 1.3, 5.5). Use of VT prophylaxis did not differ in cases and controls; prophylaxis was used $< 1/3$ of hospital days in 52% of patients. *Conclusions:* VT was common among medical inpatients. Of the risk factors identified, elevated platelet count has not been previously reported. Only one of three published risk scores was associated with risk of inpatient VT. Future study should improve upon risk prediction models for in-hospital VT among medical patients.

Keywords: deep vein thrombosis, pulmonary embolus, risk factors, venous thrombosis.

Correspondence: M. Cushman, 208 South Park Drive, Suite 2, Colchester, VT 05446, USA.
Tel.: +1 802 656 8968; fax: +1 802 656 8965; e-mail: mary.cushman@uvm.edu

Received 31 March 2004, accepted 21 July 2004

Introduction

The occurrence of and risk factors for venous thrombosis (VT) complicating hospital admission in unselected medical inpatients have not been widely studied. Up to 21.5% of VT occur following non-surgical hospital admissions [1]. Given an annual incidence of VT of 200 000 cases per year in the USA [2], an estimated 40 000 cases of VT complicate non-surgical admissions in the USA per year. There is a strong need to define clearly the scope of the problem, develop a validated risk stratification model for medical inpatients, and encourage routine use of VT prophylaxis among at-risk medical inpatients.

Data from both autopsy studies and placebo groups in randomized trials of heparin prophylaxis suggest VT is a major cause of morbidity and mortality among medical inpatients. In an autopsy study, pulmonary embolus (PE) was the main cause of death in 10% of hospital autopsies, with only 24% of these having had surgery related to their last illness. Furthermore, VT was suspected prior to death in only 4.5% of these patients [3]. In another autopsy study, where the autopsy rate was 45%, 2.5% of deaths among medical patients had PE as the proximate cause [4]. In a meta-analysis of over 15 000 patients enrolled in trials assessing any form of subcutaneous heparin vs. placebo, the rate of clinically recognized and silent deep vein thrombosis (DVT) was 19% and clinical PE was 1% [5]. Although these findings are compelling, patient selection criteria in these studies were varied and may not represent general medical inpatients.

Several trials and consensus statements support the efficacy of VT prophylaxis among medical inpatients [6–15]. However, knowledge of which patients are at highest risk of in-hospital VT, and the widespread application of thromboprophylaxis in at-risk patients are suboptimal [7,15]. Other than intensive care unit (ICU) admission, risk factors for VT among acutely ill medical inpatients are assumed to be similar to those for outpatient VT. Three prediction models for development of inpatient VT have been proposed, but these have not been validated by other investigators [16–18]. None of these risk models determined the actual occurrence of VT among medical patients, nor did they study the risk factors for in-hospital VT in medical inpatients. We studied risk factors for in-hospital VT and attempted to validate three prediction models.

Methods

Subjects

We undertook a case control study of VT among medical patients admitted to Fletcher Allen Health Care Hospital (a 400-bed teaching hospital of the University of Vermont, Burlington, VT, USA). The project was approved by the institutional review committee of the University of Vermont.

From 1 September 2000 to 31 August 2002 we identified all cases of VT diagnosed after admission among patients at least 18 years old with hospital stays ≥48 h on the medical services (general medicine, cardiology, nephrology, hematology/oncology, and the ICU). Hospital ICD-9 codes for VT (415, 415.11, 415.19, 451, 451.0, 451.11, 451.19, 451.2, 451.81, 453, and 453.9) were used to select charts for review and cases were validated using information in the chart. Exclusion criteria were VT on admission, inpatient at the time of review, thrombosis in a location other than the deep veins of the legs or arms, or coding error. DVT was validated based on positive compression ultrasonography or autopsy. PE was validated based on a positive pulmonary angiogram or spiral computed tomography, high probability ventilation/perfusion scanning, or autopsy.

From among all hospitalized adults with stays of ≥48 h between 1 September 2000 and 31 August 2002, without an ICD-9 code for thrombosis, we randomly selected 150 controls frequency matched to cases by admitting service (though not by ICU admission status). Exclusion criteria during review were inpatient status at time of review, coding error (VT occurred or patient was not on a medical service), or chart unavailability.

A standard form was used to gather the medical history, presenting illness, physical exam findings, and laboratory values for each case and control. Using admission data, VT risk for each patient was evaluated using the published risk stratification models proposed by Arcelus, Lutz, and THRIFT [16–18]. The Arcelus model was based on adding risk factors in a table and the Lutz model was based on plotting 'acute' and 'basic' risk factors on two axes to determine risk. The THRIFT consensus group stratified surgical patients into three groups based on medical conditions and number of thrombosis risk factors. Use of VT prophylaxis was recorded for cases and controls. Information concerning the VT event was recorded for the cases. Adequate VT prophylaxis was defined as administration of at least 10 000 U unfractionated heparin per day, subcutaneous low-molecular-weight heparin, warfarin with an International Normalized Ratio of 2.0 or greater for another indication, or intermittent pneumatic compression devices.

Data analysis

Data was analyzed using SPSS software (SPSS Inc., Chicago, IL, USA). The incidence of in-hospital diagnosed VT was calculated by considering all admissions of ≥48 h as the denominator for the time period of the study. Means or frequencies of potential VT risk factors between cases and controls were compared using *t*-tests or ANOVA as appropriate. Logistic regression was used to calculated crude and adjusted odds ratios for VT for potential risk factors. We selected variables for inclusion in the final multivariate model that had an odds ratio (OR) of ≥2.0 in univariate analysis. Use of VT prophylaxis was included in the final model to adjust for potential confounding introduced by its use.

Results

Of 303 admissions identified by ICD-9 codes as having VT, 193 had VT on admission and were excluded, 65 were validated as VT complicating medical admission, 16 had thrombosis in other locations, 15 were incorrectly coded, and 14 charts were unavailable for review. Among 65 cases, 36 (55%) had PE, 45 (69%) had DVT and 16 (25%) were diagnosed with both. Of patients with diagnosed DVT, nine (20%) involved the upper extremity; two of these (22%) had PE. No systematic screening for PE was undertaken for patients with DVT, and *vice versa*. Of 150 controls selected, 123 charts were available for review and met eligibility criteria as controls. Table 1 shows the distribution of in-hospital VT by service. Of cases, 80% (52/65) were on the general medicine service, 12% on cardiology and lower numbers on nephrology and hematology/oncology. The overall incidence rate of in-hospital VT was 7.6 per 1000 medicine admissions, with the highest rate on the general medicine service at 13.0 per 1000 admissions. On average, the VT event occurred on median day 5 of hospitalization (interquartile range 4–10 days).

Table 2 shows baseline characteristics of cases and controls on admission, the death rate, and length of hospital stay. The age range was 18–96 years and 45% of patients were men. Age and body mass index (BMI) were not greater among cases compared with controls. Cases were 4-fold more likely to die than controls [OR 4.0, 95% confidence interval (CI) 1.9, 8.8] and had a longer length of stay. Of the 21 deaths among cases, eight (38%) were thought to be due to PE by their physicians (two of these were due to hemorrhage on anticoagulation) and an additional two (9%) cases with DVT died of sudden cardiovascular cause without investigation for PE. Thus, 10 of 65 (15%) of cases may have died due to thrombosis.

Table 3 shows the percentages of cases and controls with previously published risk factors for VT at the time of

Table 1 Number and incidence rate of venous thrombosis (VT) by medical service*

Medical service	Number of VT (%)	Number of admissions (%)	Incidence rate of VT per 1000 admissions (95% CI)
All	65 (100.0)	8529 (100.0)	7.6 (5.8, 9.5)
Medicine	52 (80.0)	3985 (46.7)	13.0 (9.5, 16.6)
Nephrology	3 (4.6)	316 (3.8)	9.5 (0, 20.2)
Oncology	2 (3.1)	750 (8.8)	2.7 (0, 6.4)
Cardiology	8 (12.3)	3478 (40.7)	2.3 (0.7, 3.9)

*Includes hospital stays of ≥48 h.

admission, and the unadjusted OR of VT for each factor. Of these factors, temperature ≥38.0 °C, leg edema, immobility ≥72 h before or after admission, pneumonia, cellulitis, and platelet count $> 350 \times 10^3$ mm^{-3} were significantly associated with increased risk of in-hospital VT. Trauma within 3 months, lung disease noted on admission, postmenopausal estrogen therapy, central venous access in the past 30 days, sepsis, and non-use of VT prophylaxis were associated with VT, but did not reach statistical significance. While ~20% of patients were admitted to the ICU, this frequency did not differ between cases and controls. Active cancer within the past year was not related to risk of VT; however, brain, breast, gastrointestinal and genitourinary cancers were more commonly observed among cases than controls and each was associated with a ~2-fold increased risk of VT. Taken together as a group, presence of any of these cancers was associated with a 2-fold increased risk of VT (95% CI 0.7, 5.7). Obesity was not associated with risk of VT, even if a higher cut point was used (BMI > 40 kg m^{-2}; data not shown). Adjustment for use of VT prophylaxis did not materially alter any of the null associations of individual risk factors with VT (data not shown).

In multivariate analysis (Table 3), a history of trauma within 3 months, leg edema, pneumonia, platelet count $> 350 \times 10^3$ mm^{-3}, and use of VT prophylaxis for > 2/3 of hospital days were significantly associated with occurrence of VT. Presence of primary brain, breast, genitourinary or gastrointestinal cancer was associated with a 2.8-fold higher

Table 2 Patient characteristics, mortality, and length of hospital stay

Characteristics*	Cases ($n = 65$)	Controls ($n = 123$)	*P*-value
Age (years)	68 (55–77)	68 (47–68)	0.61
Percent male	41.5%	47.2%	0.46
Body mass index (kg m^{-2})†	28.8 ± 7.8	27.6 ± 8.3	0.75
Hematocrit (%)	36.1 ± 5.8	35.6 ± 6.6	0.19
White blood count ($\times 10^3$ mm^{-3})	11.0 (7.7–13.8)	9.1 (7.0–13.1)	0.32
Platelet count ($\times 10^3$ mm^{-3})	298 ± 159	253 ± 115	0.04
Mortality	32.3% ($n = 21$)	10.6% ($n = 13$)	< 0.0001
Length of stay (days)	16 (10–28)	6 (4–10)	< 0.0001

*Mean ± SD, median (interquartile range) or frequency. †Available in 47 cases, 105 controls.

Table 3 Frequency of categorical risk factors in cases and controls, with crude and adjusted odds ratios (OR) of venous thrombosis (VT)

Risk factor	Cases ($n = 65$)	Controls ($n = 123$)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Age ≥ 74†	36.9%	31.7%	1.3 (0.7, 2.4)	
Trauma last 3 months	7.7%	1.6%	5.0 (0.9, 26.8)	7.9 (1.1, 54.9)
History of VT	6.2%	7.3%	0.8 (0.2–2.8)	
Active cancer past year	24.6%	21.1%	1.2 (0.6–2.5)	
Primary brain, breast, gastrointestinal, or genitourinary cancer	12.3%	6.5%	2.0 (0.7, 5.7)	2.8 (0.8, 9.5)
Other cancer	12.3%	14.6%	0.8 (0.3, 2.0)	
Myocardial infarction in last 3 months	10.8%	8.9%	1.2 (0.5, 3.3)	
Congestive heart failure	24.6%	29.3%	0.8 (0.4, 1.6)	
Chronic lung disease	41.5%	32.5%	1.5 (0.8, 2.7)	
Chronic renal failure	20.0%	24.4%	0.8 (0.4, 1.6)	
Dialysis	4.6%	7.3%	0.6 (0.2, 3.3)	
Diabetes	30.8%	37.4%	0.7 (0.4, 1.4)	
Postmenopausal estrogen use‡	12.5%	4.1%	2.9 (0.8, 10.9)	
Admission temperature > 38 °C	27.7%	13.8%	2.4 (1.1, 5.0)	1.9 (0.8, 4.5)
Body mass index > 30 kg m^{-2}§	34.0%	31.4%	1.1 (0.5, 6.6)	
Leg edema on admission	33.8%	13.8%	3.2 (1.5, 6.6)	3.0 (1.2, 7.3)
Immobility > 72 h¶	52.3%	30.1%	2.5 (1.4, 4.7)	2.0 (0.8, 4.6)
Bacterial infection				
Cellulitis	10.8%	3.3%	3.6 (1.0, 12.8)	2.5 (0.6–11.3)
Pneumonia	40.0%	21.1%	2.5 (1.3, 4.8)	2.7 (1.2–5.8)
Sepsis	10.8%	5.7%	2.0 (0.7, 6.0)	1.3 (0.3–4.7)
Other	9.2%	15.4%	0.6 (0.2, 1.5)	
Platelet count $> 350 \times 10^3$ mm^{-3}**	32.3%	16.3%	2.5 (1.3, 4.8)	3.1 (1.4–7.0)
ICU admission††	23.1%	20.3%	1.2 (0.6, 2.4)	
Venous catheter past 30 days	26.2%	16.3%	1.8 (0.9, 3.8)	
Paresis of limb	9.2%	8.1%	1.1 (0.4, 3.3)	
Use of VT prophylaxis‡‡				
< 1/3 of days	50.8%	54.5%	1.0 (Reference)	1.0 (Reference)
1/3–2/3 of days	15.4%	8.1%	1.0 (0.5, 2.0)	1.1 (0.3, 3.4)
> 2/3 of days	33.8%	37.4%	2.1 (0.8, 5.8)	0.4 (0.2, 0.9)

*Variables not significant in univariate models were not included, and had trivial influence on the final multivariate model. †Top tertile. ‡Women only; a separate multivariate analysis was not performed due to small sample size. §Available in 47 cases, 105 controls. ¶Assessed after admission. **Top quartile. ††Cardiac and medical patients. ‡‡Prophylaxis rate reported before VT event for cases.

Table 4 Percentage of participants with high risk score and validation of risk stratification models

Model	Cases	Controls	OR for VT (95% CI)	Adjusted OR for VT (95% CI)*
Arcelus [17]	70%	56%	2.4 (1.3, 4.5)	2.6 (1.3, 5.5)
Lutz [18]	58%	54%	1.2 (0.7, 2.2)	0.9 (0.5, 2.0)
THRIFT [16]	20%	12%	1.8 (0.8, 4.1)	1.3 (0.6, 3.2)

*Adjusted for use of venous thrombosis (VT) prophylaxis (< 1/3 of days, 1/3–2/3 of days, and > 2/3 of days).

risk of VT, but this was not statistically significant (95% CI 0.8, 9.5). Inclusion of other risk factors associated with VT in univariate analysis (OR ≥ 2.0), whether or not these associations were statistically significant, did not alter the results of this final model.

Use of VT prophylaxis was low, and did not differ significantly between cases and controls (Table 3). No prophylaxis was given in 41% of cases and 53% of controls ($P = 0.14$). Adequate VT prophylaxis was given 100% of the time in 23% of cases and 27% of controls ($P = 0.7$). However, with adjustment for other factors, administration of VT prophylaxis for > 2/3 of hospital days was associated with an adjusted OR of thrombosis of 0.4 (95% CI 0.2, 0.9) compared with use < 1/3 of hospital days. In the final multivariate model shown in Table 3, exclusion of use of prophylaxis as a covariate tended to lessen the associations of other risk factors with VT. Factors listed in Table 3 that were associated with use of VT prophylaxis for > 2/3 of the hospital days were history of central intravenous catheter (OR 2.5, 95% CI 1.2, 5.2), history of VT (OR 4.4, 95% CI 1.3, 15.0), ICU admission (OR 2.1, 95% CI 1.0, 4.2), history of congestive heart failure (OR 2.8, 95% CI 1.5, 5.4), immobility ≥ 72 h (OR 4.6, 95% CI 2.4, 8.6), and leg edema on admission (OR 3.2, 95% CI 1.6, 6.9). If VT prophylaxis was mentioned in the admission note, patients were 3.5 times more likely to receive VT prophylaxis for > 2/3 of the days (95% CI 1.8, 6.9). VT prophylaxis for > 2/3 of the days was more likely to be given to those with a high risk score by the models proposed by Arcelus (OR 4.6, 95% CI 2.4, 8.8) and Lutz (OR 8.0, 95% CI 3.8, 16.9) while a high score for the model proposed by the THRIFT consensus group was not associated with increased prophylaxis use (OR 1.7, 95% CI 0.7, 3.7).

Table 4 shows the percent of patients classified as high risk at the time of admission using the published risk scores, and the OR of VT associated with a high score [16–18]. A classification of high risk according to the scoring system of Arcelus and colleagues [17] was observed in 70% of cases and 56% of controls, and was associated with an OR for VT of 2.6 (95% CI 1.3, 5.5) after adjusting for VT prophylaxis use. The Lutz model [18] identified ~55% of cases and controls as high risk and this classification was not associated with risk of VT (OR 0.9, 95% CI 0.5, 2.0). The THRIFT model [16] identified 20% of VT cases as high risk while it classified 12% of controls as high risk. A high risk score with this model was associated with a 1.3-fold increased risk of VT (95% CI 0.6, 3.2).

Discussion

At a single university hospital, symptomatic VT complicated 7.6 per 1000 unselected medical admissions, occurring on median day 5 of hospitalization. Patients with VT complicating admission were 4-fold more likely to die than those without VT. Trauma within 3 months, platelet count $> 350 \times 10^3$ mm^{-3}, leg edema, pneumonia, and certain cancers were associated with increased risk of VT complicating admission among medical patients. Three published risk models for in-hospital VT were assessed, and one appeared potentially useful among medical inpatients. The frequency of use of VT prophylaxis was poor among medical inpatients studied here; however, patients at high risk by the Arcelus and Lutz risk models were more likely than those at low or moderate risk to receive adequate VT prophylaxis, despite lack of use of a prediction model in practice [17,18].

It is difficult to compare our finding of a rate of 7.6 VT per 1000 medical admissions with previously reported data based on the selection factors and screening for VT used in other studies. Among the general non-hospitalized adult population the incidence rate of VT is estimated as approximately one to two cases per 1000 per year [1,19]. In our study there was no systematic screening for VT and the work-up was initiated based on clinical suspicion. In a meta-analysis by Mismetti *et al.* the rates of DVT and PE among hospitalized medical patients were 19% and 1%, respectively [5], though the trials included in the analysis selected patients at high risk who were screened for asymptomatic VT. While asymptomatic VT is a good surrogate for testing interventions to prevent thrombosis, the long-term clinical sequelae of asymptomatic thrombosis are not clear. In one study only 6% of DVTs among medical patients were symptomatic [20]. In a series of 400 autopsies, PE was not suspected in life in 19 of 21 medical patients who died of PE, and eight of 21 died without warning [4].

The current standard of care for VT prophylaxis among medical inpatients is unclear, relying on consensus statements based upon older studies [12,15]. Knowledge of VT incidence rates in hospitalized patients is critical to understanding the potential benefit of prophylaxis. One group suggested that, assuming a 60% reduction in VT with prophylaxis and a 2% incidence of major adverse events for heparin prophylaxis, a 3.3% incidence of VT would be needed to justify prophylaxis [5]. The incidence of clinical VT in the general medicine service in this study was lower overall, at 1.3%, but among those at high predicted risk by the Arcelus model, the OR of VT was 2.6, which would yield an incidence sufficient to provide overall benefit for prophylaxis. However, for other groups in this study such as cardiology patients, based on an OR of 2.6 for those at high predicted risk, benefits do not seem as apparent. Thus, there is a need for improved risk prediction models.

Some established risk factors for VT in general, such as older age, obesity, cancer in general, and stroke were not

associated with VT in this study of medical inpatients. While it is possible that these factors are not important determinants of VT in medical inpatients, there are several alternative explanations for these findings. Insufficient power was a problem for some analyses, especially for BMI, which was not available for all patients. It is possible that the older age of the studied group contributed to a lack of association of age and VT. In addition, one-third of patients were below age 57 years, and of these 50% of the cases were admitted to the medical ICU, compared with 13% of cases older than 57. This suggests that younger hospitalized patients in our study were sicker, and thus at high risk of VT, diluting any observable association of age with VT. In relation to obesity, in one study the average BMI of VT patients was 29 kg m^{-2} [21] and in another 38% of outpatient VT patients had a BMI > 30 kg m^{-2} [22]. Given the high average BMI of our control group of medical inpatients, an association of BMI with VT might be difficult to detect. As we matched cases and controls for admission service (i.e. oncology and cardiology), these risk factors could not be assessed. However, taking all hospital admissions into account, the incidence rate of VT in these services was not higher than in the general medicine service. We could not adequately assess acute stroke in this study since a separate neurology service cared for most stroke patients and they were not included in this analysis.

Even though the multivariate analysis suggested that recent trauma, pneumonia, leg edema, and elevated platelet count were independently associated with in-hospital VT among medical patients, it is likely that not all these factors are causal. Some may represent factors in similar causal pathways to VT (such as elevated platelet count due to infection or cancer). Elevated platelet count as a risk marker for VT has not been previously reported in the general population [23]. In general, platelet function is not thought to play a prominent etiological role in VT [24]. In one study of heparin prophylaxis among medical patients a platelet count $> 500 \times 10^3$ mm^{-3} was used to help identify a high-risk group for venous thrombosis [25] though it was not assessed as a risk factor, and it is unclear why this was selected as a criterion. Two small older studies linked elevated platelet count to VT among surgical patients; however, a 1997 review of VT in surgical patients reported no association [26–28]. It is possible that higher platelet counts reflect increased inflammation as an etiological factor for VT (although white blood cell count was not associated with VT) or that platelet function might be involved in pathogenesis in hospitalized patients. Further confirmation of this finding is warranted. Leg edema can have a variety of causes (congestive heart failure, venous insufficiency, infection, or even DVT) and consequences (decreased mobility) which may promote thrombosis. Further, risk factors occurring prior to hospitalization (e.g. trauma) might not be as accurately assessed as risk factors measured on admission (e.g. leg edema, platelet count), diluting relationships of the former with VT [29]. Because of measurement error in ascertaining clinical information before admission, the estimated risks associated with these variables are probably underestimates. Factors recorded on admission were probably measured with less error, so risk associations for these factors are easier to detect.

Use of VT prophylaxis in this study was poor, but was associated with reduced risk of VT, in accordance with results from many trials [5]. There were no procedures in place at the time of the study to encourage use of prophylaxis among medical inpatients. Regardless, patients ranked as high risk by any of the risk stratification models were more likely to have been administered VT prophylaxis than those ranked as low or medium risk. Several risk factors for thrombosis were associated with increased use of VT prophylaxis; however, known risk factors such as presence of cancer, age, and obesity did not predict VT prophylaxis use. Data from this study cannot fully discern what factors physicians considered when prescribing VT prophylaxis.

The main limitations of this study are that it was a retrospective case–control study with a relatively small number of cases, and data were derived from chart review. Chart reviewers were not blinded to case or control status. The small number of cases makes it difficult to evaluate less common but well-established risk factors (such as estrogen use or presence of a central venous catheter) or to evaluate interactions among risk factors. Some cases may have been missed, as case identification relied on ICD-9 discharge coding, although coding has been reported to miss few cases [2]. It is likely that we did not detect some fatal PE due to relatively low autopsy rates for medical inpatients at our institution during this period (113 autopsies among 742 deaths). Matching controls to cases by service added validity to the study in some regards, but made it difficult to evaluate some risk factors such as the presence of cancer. Cases were more likely than controls to die in hospital and had a longer hospital stay. It might be concluded that the higher death rate and longer hospital stay were due to factors other than occurrence of VT, limiting our ability to draw conclusions about risk factors for VT comparing cases with controls. However, cases and controls were well matched for age, and chronic diseases. Further, we required cases and controls to be hospitalized for at least 48 h as an inclusion criterion, so controls were not 'hospitalized well' patients. Among cases, the VT event occurred on median hospital day 5, 1 day prior to the median length of hospitalization among controls. Given the case group did not appear to have more comorbid conditions than the control group, the timing of the VT event, and the 15% death rate from apparent PE among cases, it is likely that VT, rather than other factors present at admission, contributed to higher mortality and length of stay in cases.

In conclusion, we evaluated risk factors for VT complicating medical admission in unselected medical inpatients and gained insight into the incidence rate of this problem. We were able to validate a model for VT risk prediction among medical inpatients. Future areas of research include prospective validation of a VT risk model and further studies of the risk factors for VT in medical inpatients.

Acknowledgements

We appreciate the technical assistance of M. Gianni, Measurement Specialist, and D. Howard, Systems Manager for the Patient Oriented Research Unit, both at Fletcher Allen Health Care.

References

1 Heit JA, O'Fallon WM, Petterson TM, Lohse CM, Silverstein MD, Mohr DN, Melton LJ 3rd. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. *Arch Intern Med* 2002; **162**: 1245–8.

2 Cushman M, Tsai AW, Heckbert SR, White RH, Rosamond WD, Enright P, Folsom AR. Deep vein thrombosis and pulmonary embolism in two cohorts. the Longitudinal Investigation of Thromboembolism Etiology (LITE). *Am J Med* 2004; **117**: 19–25.

3 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.

4 Baglin TP, White K, Charles A. Fatal pulmonary embolism in hospitalised medical patients. *J Clin Pathol* 1997; **50**: 609–10.

5 Mismetti P, Laporte-Simitsidis S, Tardy B, Cucherat M, Buchmuller A, Juillard-Delsart D, Decousus H. 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.

6 Bergmann JF, Elkharrat D. Prevention of venous thromboembolic risk in non-surgical patients. *Haemostasis* 1996; **26** (Suppl. 2): 16–23.

7 Bergmann JF, Mouly S. Thromboprophylaxis in medical patients: focus on France. *Semin Thromb Hemost* 2002; **28** (Suppl. 3): 51–5.

8 Bick RL. Proficient and cost-effective approaches for the prevention and treatment of venous thrombosis and thromboembolism. *Drugs* 2000; **60**: 575–95.

9 Cohen AT, Zaw HM, Alikhan R. Benefits of deep-vein thrombosis prophylaxis in the nonsurgical patient: The MEDENOX Trial. *Semin Hematol* 2001; **38** (2 Suppl. 5): 31–8.

10 Davidson BL. Risk assessment and prophylaxis of venous thromboembolism in acutely and/or critically ill patients. *Haemostasis* 2000; **30** (Suppl. 2): 77–81.

11 Gallus AS, Nurmohammed M, Kearon C, Prins M. Thromboprophylaxis in non-surgical patients: who, when and how? *Haemostasis* 1998; **28** (Suppl. 3): 71–82.

12 Haas SK. Venous thromboembolic risk and its prevention in hospitalized medical patients. *Semin Thromb Hemost* 2002; **28**: 577–84.

13 Haas S. Risk of deep venous thrombosis in medical patients. *Curr Hematol Rep* 2002; **1**: 85–6.

14 Jacobs LG. Prophylactic anticoagulation for venous thromboembolic disease in geriatric patients. *J Am Geriatr Soc* 2003; **51**: 1472–8.

15 Michota FA. Venous thromboembolism prophylaxis in the medically ill patient. *Clin Chest Med* 2003; **24**: 93–101.

16 Thromboembolic Risk Factors (THRIFT) Consensus Group. Risk of and prophylaxis for venous thromboembolism in hospital patients. *Br Med J* 1992; **305**: 567–74.

17 Arcelus JI, Candocia S, Traverso CI, Fabrega F, Caprini JA, Hasty JH. Venous thromboembolism prophylaxis and risk assessment in medical patients. *Semin Thromb Hemost* 1991; **17** (Suppl. 3): 313–8.

18 Lutz L. Venous thromboembolism in internal medicine: risk assessment and pharmaceutical prophylaxis. *Die Med Welt* 2002; **53**: 231–4.

19 White RH. The epidemiology of venous thromboembolism. *Circulation* 2003; **107** (23 Suppl. 1): I4–8.

20 Samama MM, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Nguyen H, Olsson CG, Turpie AG, Weisslinger N. 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.

21 Cushman M, Folsom AR, Wang L, Aleksic N, Rosamond WD, Tracy RP, Heckbert SR. Fibrin fragment D-dimer and the risk of future venous thrombosis. *Blood* 2003; **101**: 1243–8.

22 Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Forcier A. The prevalence of risk factors for venous thromboembolism among hospital patients. *Arch Intern Med* 1992; **152**: 1660–4.

23 Tsai AW, Cushman M, Rosamond WD, Heckbert SR, Tracy RP, Aleksic N, Folsom AR. Coagulation factors, inflammation markers, and venous thromboembolism: the Longitudinal Investigation of Thromboembolism Etiology (LITE). *Am J Med* 2002; **113**: 636–42.

24 Kroegel C, Reissig A. Principle mechanisms underlying venous thromboembolism: epidemiology, risk factors, pathophysiology and pathogenesis. *Respiration* 2003; **70**: 7–30.

25 Dahan R, Houlbert D, Caulin C, Cuzin E, Viltart C, Woler M, Segestraa JM. Prevention of deep vein thrombosis in elderly medical in-patients by a low molecular weight heparin: a randomized double-blind trial. *Haemostasis* 1986; **16**: 159–64.

26 Sherry S. Interrelationships between platelets and coagulation in the pathogenesis of venous thrombosis. *S Afr Med J* 1976; **50**: 425–7.

27 Daniel S, O'Brien JR, John JA. Platelets in the prediction of thrombotic risk. *Atherosclerosis* 1982; **45**: 91–9.

28 Lowe GD. Prediction of postoperative venous thrombosis using haemostasis tests. *Int J Clin Lab Res* 1997; **27**: 153–7.

29 Phillips AN, Smith GD. How independent are 'independent' effects? Relative risk estimation when correlated exposures are measured imprecisely. *J Clin Epidemiol* 1991; **44**: 1223–31.