A Cohort Study to Analyze the Risk of Venous Thromboembolism Mortality in Patients Admitted to the General Medicine Department, Tan Tock Seng Hospital, Singapore

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ABSTRACT

The purpose of this study was to assess the risk of venous thromboembolism (VTE) in patients admitted to the Tan Tock Seng Hospital (TTSH), Singapore during October and November 2009. The primary outcome assessed was mortality due to VTE, or development of deep vein thrombosis or pulmonary embolism (PE) within 3 months from the day of admission. Both univariate and multivariate analyses were performed for all-cause mortality and deaths associated with PE. Seven hundred twenty-one patients admitted to the 5th floor of the General Medicine Department, TTSH, during the 2 months were analyzed. There were 368 (51.04%) female patients and 353 (48.96%) male patients. As per race distribution, 566 (78.50%) patients were Chinese, 100 (13.86%) patients were Malaysians, 46 (6.38%) patients were Indians, and 9 (1.26%) were other races. Four hundred ninety-two (68.24%) were independent for activities of daily living (ADL) and 229 (31.76%) were dependent for all ADL. There were in all 42 deaths. There were definite PE deaths in 2 (4.76%) patients, probable PE deaths in 3 (7.14%) patients, and suspected PE deaths in 8 (19.05%) patients. Twenty (47.62%) deaths were due to pneumonia, 3 (7.14%) deaths were due to urinary tract infections, and 4 (9.52%) deaths were due to other infections. Two (4.76%) deaths were due to myocardial infarction. The risk of VTE was high in acutely ill patients admitted to the General Medicine Department, TTSH, Singapore. The factors that predispose patients to a very high risk are ADL dependence, acute heart failure, past history of VTE, or if they are clinically dehydrated and have acute renal failure. This warrants increased awareness and need for VTE prophylaxis.

KEYWORDS: Venous thromboembolism, mortality, Singapore, pulmonary embolism

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Deep vein thrombosis (DVT) and pulmonary embolism (PE) are responsible for significant morbidity and mortality in hospitalized patients.¹ In Caucasian populations, the incidence of DVT and PE is well documented and significant.² In contrast, DVT and PE are regarded rare in Asia.³ Prophylactic heparin for surgery was therefore not routine.⁴ More recent reports, however, indicate an increase in thromboembolic disease in Asians.⁵

AIM

Our aim was (1) to assess the risk of venous thromboembolism (VTE) in patients admitted to the 5th floor of the General Medicine Department of Tan Tock Seng Hospital (TTSH), Singapore and (2) to assess mortality due to VTE or PE.

METHODS

This study was an open-labeled cohort study in which data were analyzed for all admissions to the 5th floor of the General Medicine Department, TTSH, during October and November 2009. These patients were followed-up for 3 months for development of DVT or PE, or sudden death. Patients admitted to the 5th floor who did not belong to the General Medicine Department were excluded. A VTE questionnaire was filled out for all selected patients by a designated research coordinator after going through the case records, case notes, and talking to the patients by telephone. The questionnaire included date of admission, date of discharge, date of birth, sex, race, activities of daily living (ADL), assessment of medical comorbidities, and assessment of risk factors (Fig. 1).

In total, 721 patients were analyzed. The primary outcome assessed was various causes of mortality—mortality due to VTE, or development of DVT or PE within 3 months from the day of admission.

Deaths from PE were classified as definitive, probable, and suspected. Definitive death from PE was defined as evidence on computed tomography (CT) scan or autopsy diagnosis of PE death. Probable diagnosis was defined as Wells score >6 with evidence of malignancy and no other obvious cause of death such as infection or death from cardiac cause. Suspected death from PE was defined as Wells score >6 with no other obvious cause of death such as infection or cardiac cause. For each death in the hospital, records were traced for C-reactive protein (CRP), chest X-ray, total white cell counts, differential counts, urine routine analysis, urine cultures, blood cultures, electrocardiogram, and cardiac markers such as troponin I. Deaths were classified as infection due to urine, chest (pneumonia), or other causes; cardiac if there was evidence of myocardial infarction with raised troponin I, Wells

score <6 ; and PE definitive, probable, and suspected deaths.

Bleeding risk was assessed by Outpatient Bleeding Risk Index (OBRI), and patients were categorized into low, intermediate, and high risk. The approval of the ethics committee was obtained before the study. Hospital records were analyzed for all the patients, and a verbal consent was obtained for consultation over the telephone at 3 months. Statistical analysis was performed by descriptive statistics by using frequencies, means and standard deviations. Covariates associated with each of the primary outcomes were measured by using the logistic regression model. Both univariate and multivariate analyses were performed for all-cause mortality and deaths associated with PE. For the multivariate analysis, we included all significant variables identified in the univariate analysis in a sequential manner, using the likelihood ratio test. Data analysis was performed using Stata V10 (Stata Corp, College Station, TX), and the level of significance was set at 5%.

RESULTS

There were 368 (51.04%) female patients and 353 (48.96%) male patients. As per race distribution, 566 (78.50%) patients were Chinese, 100 (13.86%) patients were Malaysians, 46 (6.38%) patients were Indians, and 9 (1.26%) were other races. Four hundred ninety-two (68.24%) patients were ADL independent and 229 (31.76%) patients were ADL dependent. Twenty-two (3.05%) patients had no comorbidities and 699 (96.95%) patients had one or more comorbidities. There were no risk factors for acute DVT in 195 (27.05%) patients, and 526 (72.95%) patients had one or more risk factors for DVT. Bleeding risk was high in 97 (13.45%) patients, intermediate in 469 (65.05%) patients, and low in 155 (21.5%) patients (Table 1).

There were in all 42 deaths. There were definite PE deaths in 2 (4.76%) patients, probable PE deaths in 3 (7.14%) patients, and suspected PE deaths in 8 (19.05%) patients. Twenty (47.62%) deaths were due to pneumonia, 3 (7.14%) deaths were due to urinary tract infections, and 4 (9.52%) deaths were due to other infections. Two (4.76%) deaths were due to myocardial infarction.

The total deaths attributed to PE (definitive, probable, and suspected) was 13 of 721 (approx. 1.8%) patients analyzed; deaths due to myocardial infarction were 2 of 721 (0.28%) patients analyzed; and deaths due to infections were 27 of 721 (3.75%) patients analyzed.

We analyzed total deaths as well as deaths due to PE by both univariate and multivariate analyses. The factors that were significant both in univariate and multivariate analyses were ADL status, past history of VTE, and patients who had acute renal failure with dehydration. The results of univariate and multivariate

Tan Tock Seng HOSPITAL

Patient Study No.

Venous Thrombosis Embolism (VTE) Baseline Survey (please tick ☒ or write on the appropriate boxes)

INI	Patient Initial		
DOS	Date of survey	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	/ <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> / <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> (dd/mm/yyyy)
DOB	Date of birth	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	/ <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> / <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> (dd/mm/yyyy)
DOA	Date of admission	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	/ <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> / <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> (dd/mm/yyyy)
DODIS	Date of discharge	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	/ <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> / <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> (dd/mm/yyyy)
SEX	Sex	☐ Male (1) ☐ Female (2)	
RACE	Race	☐ Chinese (1) ☐ Malay (2) ☐ Indian (3) ☐ Others (4)	
WT	Patient's weight	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	. <div style="border: 1px solid black; width: 20px; height: 20px;"></div> kg
HT	Patient's height	<div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div> <div style="border: 1px solid black; width: 20px; height: 20px;"></div>	cm
ACUTE	Does the patient have reduced mobility?	☐ No (0) ☐ Yes (1)	
MED	Does the patient have one of the following medical illness/conditions? (may tick more than 1 choice)		
	☐ Acute heart failure (NYHA class III or IV) (1) ☐ Neurological disease (Stroke/ Advanced Parkinsonism/ Dementia/ Meningitis and Encephalitis) (2)		
	☐ Malignancy (3) ☐ Infection (Cellulitis) (4)		
	☐ NSTEMI / STEMI (5) ☐ Chronic renal disease, ESRF (6)		
	☐ Active rheumatological disease (7) ☐ Irritable bowel disease (8)		
	☐ Haematological diseases (Myelofibrosis/ Thrombocytosis and Polycythemia) (9) ☐ Endocrine/metabolic disease (DM/ Thyroid Disorder/ Cushing's Syndrome and Hyperlipidemia) (10)		
	☐ COPD (11) ☐ Gastrointestinal/hepatobiliary disease (Cholelithiasis/ Cholecystitis/ Cholangitis/ Hepatitis abscess/ liver cirrhosis) (12)		
RISK	Does the patient have one or more of the following risk factors? (may tick more than 1 choice)		
	☐ History of VTE (1) ☐ Post-menopausal hormone replacement (2)		
	☐ Thrombophilia (3) ☐ Varicose vein (4)		
	☐ Age > 60 years (5) ☐ Pregnancy (within 3 months) (6)		
	☐ Obesity (BMI above 30 as indicated in case-notes) (7) ☐ Nephrotic syndrome (8)		
	☐ Contraceptives (within 3months) (9) ☐ Central venous catheter (10)		
	☐ Dehydration (clinically mentioned dehydration or Acute Renal Failure) (12)		
THERPY	Was the patient put on any of the following therapy during admission?		
	☐ Any type of anticoagulant (1) ☐ Any form of mechanical thromboprophylaxis (2)		
	☐ Any type of antiplatelet (3)		

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Figure 1 Venous thrombosis embolism baseline survey questionnaire.

Tan Tock Seng HOSPITAL		Patient Study No. 	
Outpatient Bleeding Risk Index (please tick ☒ or write on the appropriate boxes)			
OBRI	This index considers (may tick more than 1 choice)	☐ Age > 65 years – 1 point (1) ☐ Prior stroke – 1 point (2) ☐ Prior GI bleed – 1 point (3) Any of four comorbidities – 1 point (4) • DM ☐ • chronic renal failure defined as creatinine clearance less than 30ml/min • Recent myocardial infarction (within 3 months) • Anemia (Hb < 8 g/dL)	
OBRIPT	OBRI (total no. of points)		(sum of the above points and max is 4) / if no risk put zero (0)
OBRIGP	OBRI stratifies patients into three risk groups	☐ Low risk – 0 (0) ☐ Intermediate risk – 1 or 2 (1) ☐ High risk – 3 or more (2)	
VTE Telephone Follow-up (Patient Outcome) at 1 Month			
TCU	Do you have any outpatient follow-up that is related to VTE in this one month?	☐ No (0)	☐ Yes (1)
PE	Do you have any readmission that is related to DVT or PE?	☐ No (0)	☐ Yes (1)
FAM	Family History of VTE	☐ No (0)	☐ Yes (1)
Survival status and cause of death			
DEATH	Any sudden death?	☐ No (0) skip DOD and INFO ☐ Yes, PE related (1) ☐ Yes, cardio related e.g. AMI and CCF (2) ☐ Yes, infection e.g. pneumonia and UTI (3) ☐ Yes, stroke (4) ☐ Yes others causes (5), specify ☐ Unknown (66)	
DOD	Date of death	 / / (dd/mm/yyyy)	
INFO	Death info obtained from	☐ Hospital data (1) ☐ Next of kin (2) ☐ Others (3)	

Figure 1 (Continued)

analyses for all mortality causes and PE deaths are shown in Tables 2–5.

DISCUSSION

DVT and PE are responsible for significant morbidity and mortality in hospitalized patients.¹ In Caucasian populations, the incidence of DVT and PE is well documented and significant. The National Institutes of Health Consensus Conference estimated that as many as 50,000 people die annually from PE in the United States, and 450,000 hospitalizations each year are associated with DVT.² In contrast, DVT and PE are considered rare in Asia.³ Prophylactic heparin for sur-

gery was therefore not routine.⁴ More recent reports, however, indicate an increase in thromboembolic disease in Asians.⁵ Rates of DVT from 2.7 to 19.3 per 10,000 hospital admissions were reported from Hong Kong, Malaysia, and Singapore between 1985 and 1998–2010. Likewise, a rising incidence of PE, from 1.1 to 2.8%, was found during autopsy studies over 15 years in Hong Kong Chinese.⁵ In a study done by Cheuk et al in a Chinese population in Hong Kong, information from 2000 to 2001 was retrieved from a centralized computer public health care database serving an ethnic Chinese population of 6.7 million and was analyzed. VTE was not as common in Chinese as in Caucasians.⁶ Ng and Lee noted DVT prevalence among hospitalized patients

Table 1 Demographic Data

Demographic Data	Actual Numbers	Percentage (%)
Total number of patients analyzed	721	100
Mean age in years (SD)	66.3 (18.5)	NA
Sex		
Male	353	48.96
Female	368	51.04
Race		
Chinese	566	78.72
Malaysian	100	13.91
Indian	46	6.40
Others	9	0.97
ADL		
Independent	492	68.24
Dependent	229	31.76
Risk factors for acute DVT		
None	195	27.05
One or more	526	72.95
Patient having one or more comorbidities	699	96.95
OBRI		
Low	155	21.5
Intermediate	469	65.05
High	97	13.45

ADL, activities of daily living; DVT, deep vein thrombosis; OBRI, Outpatient Bleeding Risk Index.

was 0.453%, a significant rise from reported rates of 0.079% and 0.158% in 1989–1990 and 1996–1997, respectively.⁷ Lee et al studied 388 cases of DVT. The frequency rate of acute DVT of 15.8 per 10,000 admissions is much higher than previously reported rates of 2.8 and 7.9 per 10,000 admissions in 1990 and 1992,

respectively. These findings confirmed the need for increased awareness of VTE in Asian populations and support the relevance of systematic studies of thrombosis risk and prophylaxis in Asia.⁸ Piovella et al performed a prospective epidemiological study in 19 centers across Asia in patients undergoing elective total hip replacement, total knee replacement, or hip fracture surgery. The rate of venographic thrombosis in the absence of thromboprophylaxis after major joint surgery in Asian patients is similar to that previously reported in patients in Western countries.⁹ Tan et al retrospectively reviewed 862 symptomatic patients referred to the vascular diagnostic laboratory in a hospital for suspected DVT over a 30-month period. Two hundred seventy-seven (32.1%) patients tested positive for DVT on duplex ultrasound. Thrombophilia and underlying malignancy were prominent risk factors among Asians.¹⁰ De Silva et al studied the risk of DVT in stroke patients. DVT was detected in 30% of patients at days 7 to 10 and in 45% of patients at days 25 to 30.¹¹ Ugaki et al analyzed the tolerance and efficacy of subcutaneous administration of a reduced 2500-unit, low-dose unfractionated heparin. The 2500 units of low-dose unfractionated heparin was given subcutaneously 2 hours preoperatively and again 12 hours postoperatively. Other standard methods of mechanical prophylaxis, including graduated compression stockings and intermittent pneumatic compression, were used. There were also no significant differences found in the perioperative bleeding complications between the two groups. However, three (3 of 55; 6%) of the patients in the no-heparin group suffered a symptomatic PE, although none was fatal. There was no onset of PE in the heparin prophylaxis group.¹² Leizorovicz studied the rate of postoperative asymptomatic DVT in Asian patients. In Asian patients, the incidence of asymptomatic and symptomatic VTE after major orthopedic surgery is high. These results suggest that

Table 2 Total Deaths for Univariate Analysis

Parameter	Odds Ratio	Confidence Interval	p Value
Age >60 years	1.047	1.023–1.071	<0.001
ADL dependent	4.746	2.447–9.205	<0.001
Heart failure	2.652	1.283–5.484	0.008
Malignancy	2.672	1.260–5.664	0.01
Dehydration/acute renal failure	6.355	3.311–12.194	<0.001

ADL, activities of daily living.

Table 3 Total Deaths for Multivariate Analysis

Parameter	Odds Ratio	Confidence Interval	p Value
Age >60 years	3.500	1.020–12.008	0.046
ADL dependent	3.286	1.633–6.612	0.001
Malignancy	6.677	2.21–20.13	0.001
Dehydration/acute renal failure	5.147	2.623–10.097	<0.001

ADL, activities of daily living.

Table 4 PE Deaths for Univariate Analysis

Parameter	Odds Ratio	Confidence Interval	p Value
ADL dependent	7.927	2.159–29.106	0.002
Heart failure	4.67	1.494–14.65	0.008
History of VTE	4.391	0.927–20.790	0.062
Dehydration/acute renal failure	8.989	2.946–27.431	<0.001
Malignancy	1.56	0.39–7.16	0.57

ADL, activities of daily living; VTE, venous thromboembolism.

Table 5 PE Deaths for Multivariate Analysis

Parameter	Odds Ratio	Confidence Interval	p Value
ADL dependent	9.56	2.041–44.77	0.004
History of VTE	102.629	7.190–1464.856	0.001
Dehydration/acute renal failure	8.377	2.533–27.705	<0.001

PE, pulmonary embolism; VTE, venous thromboembolism.

thromboprophylaxis should be considered in these patients.¹³

In spite of all the available data in Asians, DVT prophylaxis is not routinely given to acute medically ill patients admitted to the general medical wards in many centers across Asia and in Singapore.

In our study, 721 patients were admitted to our department over 2 months, and we followed them up to 3 months. There were 526 (72.95%) patients who had one or more risk factors for DVT. There were in total 42 deaths. There were definite PE deaths in 2 (4.76%) patients, probable PE deaths in 3 (7.14%) patients, and suspected PE deaths in 8 (19.05%) patients. The total number of deaths attributed to fatal PE (definitive, probable, and suspected) was 13 of 721 patients analyzed, which was around 1.8%. As per classification of level of risk (based on published data), the population of patients studied falls in the highest category. This could extrapolate into 4 to 10% of patients at risk of clinical PE, 10 to 20% of patients at risk of proximal vein thrombosis, and 40 to 80% at risk of calf vein thrombosis.^{14–16}

Our data as well as data in the Asian population suggest that mortality due to VTE is not uncommon in Asians compared with that in the West. As there is increased awareness now, we need to advocate VTE prophylaxis in this group of patients. As we did not perform Doppler scans, this study may underestimate the actual risk of VTE.

We analyzed total deaths as well as deaths due to PE by both univariate and multivariate analyses. The factors that were significant for deaths due to PE both in univariate and multivariate analyses were ADL status, past history of VTE, and patients who had acute renal failure with dehydration. To our surprise, malignancy was not statistically significant for deaths due to PE but was significant in all-cause death (Tables 2–5).

However, there are some limitations to this study. We classified diagnosis of PE as definite, probable, and suspected. The diagnosis of probable and suspected was based on Wells criteria and history of VTE.^{17,18} The patients were selected from the general wards on the 5th floor of TTSH and not from private wards. In our study, there were no diagnosed cases of symptomatic DVT. A similar finding was also observed in the ARTEMIS study in which cases of symptomatic DVT were not seen in either the fondaparinux group or the placebo group at the end of the study period.¹⁹

CONCLUSION

The risk of VTE was high in acutely ill patients admitted to the General Medicine Department, TTSH, Singapore. The factors that predisposed patients to a high risk were ADL dependence, acute heart failure, history of VTE, and clinical dehydration with acute renal failure. These data warrant increased awareness of VTE in high-risk patients and indicate the need for VTE prophylaxis.

REFERENCES

1. Cogo A, Bernardi E, Prandoni P, et al. Acquired risk factors for deep-vein thrombosis in symptomatic outpatients. *Arch Intern Med* 1994;154:164–168
2. Prevention of venous thrombosis and pulmonary embolism. NIH Consensus Development. *JAMA* 1986;256:744–749
3. Hwang WS. The rarity of pulmonary thromboembolism in Asians. *Singapore Med J* 1968;9:276–279
4. Tinckler LF. Absence of pulmonary embolism in Asians? *BMJ* 1964;i:502
5. Chau KY, Yuen ST, Ng TH, Ng WF. An autopsy study of pulmonary thromboembolism in Hong Kong Chinese. *Pathology* 1991;23:181–184

6. Cheuk BLY, Cheung GCY, Cheng SWK. Epidemiology of venous thromboembolism in a Chinese population. *Br J Surg* 2004;91:424–428
7. Ng HJ, Lee LH. Trends in prevalence of deep venous thrombosis among hospitalised patients in an Asian institution. *Thromb Haemost* 2009;101:1095–1099
8. Lee LH, Gu KQ, Heng D. Deep vein thrombosis is not rare in Asia—the Singapore General Hospital experience. *Ann Acad Med Singapore* 2002;31:761–764
9. Piovella F, Wang CJ, Lu H, et al; AIDA investigators. Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography. *J Thromb Haemost* 2005;3:2664–2670
10. Tan KK, Koh WP, Chao AK. Risk factors and presentation of deep venous thrombosis among Asian patients: a hospital-based case-control study in Singapore. *Ann Vasc Surg* 2007;21:490–495
11. De Silva DA, Pey HB, Wong MC, Chang HM, Chen CP. Deep vein thrombosis following ischemic stroke among Asians. *Cerebrovasc Dis* 2006;22:245–250
12. Ugaki H, Enomoto T, Fujiwara K, Kimura T, Kawasaki T. Safety and efficacy of lower-dose unfractionated heparin for prophylaxis of deep vein thrombosis and pulmonary embolism in an Asian population. *Blood Coagul Fibrinolysis* 2008;19:585–589
13. Leizorovicz A; SMART Venography Study Steering Committee. Epidemiology of post-operative venous thromboembolism in Asian patients. Results of the SMART venography study. *Haematologica* 2007;92:1194–1200
14. Clagett GP, Anderson FA Jr, Geerts W, et al. Prevention of venous thromboembolism. *Chest* 1998;114(5, Suppl):531S–560S
15. Nicolaides AN, Bergqvist D, Hull R, et al. Prevention of Venous Thromboembolism: International Consensus Statement (Guidelines According to Scientific Evidence). Nicosia, Cyprus: Med-Orion Publishing Company; 1997
16. Salzman EW, Hirsh J. Prevention of venous thromboembolism. In: Colman RW, Hirsh J, Marder VJ, et al, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 3rd ed. Philadelphia, PA: JB Lippincott; 1994:1332
17. Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA* 2006;295:199–207
18. Scarvelis D, Wells PS. Diagnosis and treatment of deep-vein thrombosis. *CMAJ* 2006;175:1087–1092
19. Cohen AT, Davidson BL, Gallus AS, et al; ARTEMIS Investigators. Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. *BMJ* 2006;332:325–329