

Blood Coagulation, Fibrinolysis and Cellular Haemostasis

Clinical presentation and time-course of postoperative venous thromboembolism: Results from the RIETE Registry

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Summary

There is little literature about the clinical presentation and time-course of postoperative venous thromboembolism (VTE) in different surgical procedures. RIETE is an ongoing, prospective registry of consecutive patients with objectively confirmed, symptomatic acute VTE. In this analysis, we analysed the baseline characteristics, thromboprophylaxis and therapeutic patterns, time-course, and three-month outcome of all patients with postoperative VTE. As of January 2006, there were 1,602 patients with postoperative VTE in RIETE: 393 (25%) after major orthopaedic surgery (145 elective hip arthroplasty, 126 knee arthroplasty, 122 hip fracture); 207 (13%) after cancer surgery; 1,002 (63%) after other procedures. The percentage of patients presenting with clinically overt pulmonary embolism (PE) (48%, 48%, and 50% respectively), the average time elapsed from surgery to VTE (22 ± 16 , 24 ± 16 , and 21 ± 15 days, respectively), and the three-

month incidence of fatal PE (1.3%, 1.4%, and 0.8%, respectively), fatal bleeding (0.8%, 1.0%, and 0.2%, respectively), or major bleeding (2.3%, 2.9%, and 2.8%, respectively) were similar in the three groups. However, the percentage of patients who had received thromboprophylaxis (96%, 76% and 52%, respectively), the duration of prophylaxis (17 ± 9.6 , 13 ± 8.9 , and 12 ± 11 days, respectively) and the mean daily doses of low-molecular-weight heparin ($4,252 \pm 1,016$, $3,260 \pm 1,141$, and $3,769 \pm 1,650$ IU, respectively), were significantly lower in those undergoing cancer surgery or other procedures. In conclusion, the clinical presentation, time-course, and three-month outcome of VTE was similar among the different subgroups of patients, but the use of prophylaxis in patients undergoing cancer surgery or other procedures was suboptimal.

Keywords

Venous thromboembolism, surgery

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Introduction

Venous thromboembolism (VTE) is a common complication in patients undergoing surgery (1). However, there is little information on the clinical presentation, time-course and outcome of symptomatic postoperative VTE. Most of what we know is based either on studies performed more than 20 years ago (2–4), on studies limited to patients undergoing major joint surgery (5–12), or on the findings of intervention prospective clinical trials on thromboprophylaxis that used objective diagnostic tests

to detect VTE before clinical signs had developed. There have not been comprehensive studies that have compared the clinical presentation and time-course of symptomatic VTE over a spectrum of different surgical procedures.

The RIETE (Registro Informatizado de la Enfermedad TromboEmbólica) initiative is an ongoing, international (Spain, France, Italy, Israel, Argentina), multicenter, prospective registry of consecutive patients presenting with symptomatic acute VTE confirmed by objective tests (13–15). The aim of the present study was to compare the baseline characteristics, prophylaxis

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Table 1: Baseline clinical characteristics, time-course and VTE characteristics of the 1,602 postoperative patients with VTE, according to the type of surgery.

	Major orthopaedic surgery	Cancer surgery	Other surgical procedures	OR (95% CI) orthopedic vs. cancer	OR (95% CI) orthopedic vs. other
Patients (n)	393	207	1002		
Clinical characteristics					
Gender (males)	109 (28%)	118 (57%)	500 (50%)	0.3 (0.2–0.4) [‡]	0.4 (0.3–0.5) [‡]
Age >65 years	329 (84%)	126 (61%)	453 (45%)	3.3 (2.2–4.9) [‡]	6.2 (4.6–8.4) [‡]
Body weight <70 kg	157 (40%)	89 (43%)	350 (35%)	0.8 (0.6–1.2)	1.2 (0.97–1.6)
Underlying diseases					
Creatinine levels >1.2 mg/dl	32 (8.1%)	20 (9.7%)	72 (7.2%)	0.8 (0.5–1.5)	1.1 (0.7–1.8)
Chronic lung disease	33 (8.4%)	12 (5.8%)	72 (7.2%)	1.5 (0.8–3.0)	1.2 (0.8–1.8)
Chronic heart failure	25 (6.4%)	4 (1.9%)	33 (3.3%)	3.4 (1.2–10) [*]	2.0 (1.2–3.4) [†]
Risk factors for VTE					
Cancer	21 (5.3%)	207 (100%)	162 (16%)	N/A	0.3 (0.2–0.5) [‡]
Prior VTE	29 (7.4%)	21 (10%)	98 (9.8%)	0.7 (0.4–1.3)	0.7 (0.5–1.1)
Time-course					
Time to VTE (days ± SD)	22 ± 16	24 ± 16	21 ± 15	p=NS	p=NS
VTE during the first 7 days	10 (2.5%)	4 (1.9%)	20 (2.0%)	1.3 (0.4–4.9)	1.3 (0.6–2.7)
VTE during the first 15 days	184 (47%)	85 (41%)	453 (45%)	1.3 (0.9–1.8)	1.1 (0.8–1.3)
VTE during the first month	279 (71%)	137 (66%)	759 (76%)	1.2 (0.9–1.8)	0.8 (0.6–1.0) [*]
VTE characteristics					
Symptomatic PE	187 (48%)	102 (49%)	498 (50%)	0.9 (0.7–1.3)	0.9 (0.7–1.2)
For patients with PE					
Heart rate <100 bpm	43 (24%)	33 (33%)	144 (30%)	0.6 (0.4–1.1)	0.7 (0.5–1.1)
SBP <100 mm Hg	14 (7.5%)	9 (8.8%)	38 (7.6%)	0.8 (0.3–2.0)	1.0 (0.5–1.9)
PO ₂ <60 mm Hg (N=609)	66 (45%)	34 (43%)	130 (34%)	1.1 (0.6–1.9)	1.6 (1.1–2.4) [*]
Sat O ₂ <90% (N=613)	41 (28%)	24 (29%)	90 (23%)	1.0 (0.5–1.7)	1.3 (0.8–2.0)
For patients with DVT					
Bilateral DVT	6 (2.9%)	8 (7.7%)	20 (4.0%)	0.4 (0.1–1.1)	0.7 (0.3–1.8)
Proximal DVT	145 (71%)	66 (84%)	351 (76%)	0.5 (0.2–0.9) [*]	0.8 (0.5–1.1)

Comparisons between groups: ^{*}p <0.05; [†]p <0.01; [‡]p <0.001. Abbreviations: VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep vein thrombosis; SD, standard deviation; bpm, beats per minute; SBP, systolic blood pressure; OR, odds ratio; CI, confidence intervals; N/A, not applicable. Major orthopaedic surgery: hip fracture repair, hip arthroplasty, knee arthroplasty.

patterns, time-course, VTE characteristics and three-month outcome of all patients who developed symptomatic postoperative deep vein thrombosis (DVT) or pulmonary embolism (PE).

Patients and methods

Patient entry criteria

Participating hospitals in the RIETE registry prospectively enrolled consecutive patients with symptomatic, acute DVT or PE confirmed by objective tests (i.e. compression ultrasonography, contrast venography, or computed tomography [CT] scan, for suspected DVT; helical CT scan, lung scintigraphy or pulmonary angiography, for suspected PE). All patients provided oral consent to their participation in the registry, according to the requirements of the ethics committee within each hospital.

Clinical definitions

Surgical patients were defined as those who had undergone an operation in the two months prior to VTE diagnosis. Proximal DVT was considered when occurring at the popliteal vein or above. In patients with acute respiratory symptoms suggesting PE the diagnosis was confirmed if they also had a positive helical CT scan, a high-probability ventilation-perfusion lung scintigraphy, a positive pulmonary angiography, visualization of thrombus on echocardiogram, or indeterminate-probability lung scan plus evidence of DVT in the lower limbs (by either compression ultrasonography or contrast venography). Fatal PE, in the absence of autopsy, was defined as death shortly after PE diagnosis, in the absence of any alternative cause of death. Fatal bleeding was defined as any death occurring shortly after a major bleeding episode. Bleeding complications were classified as

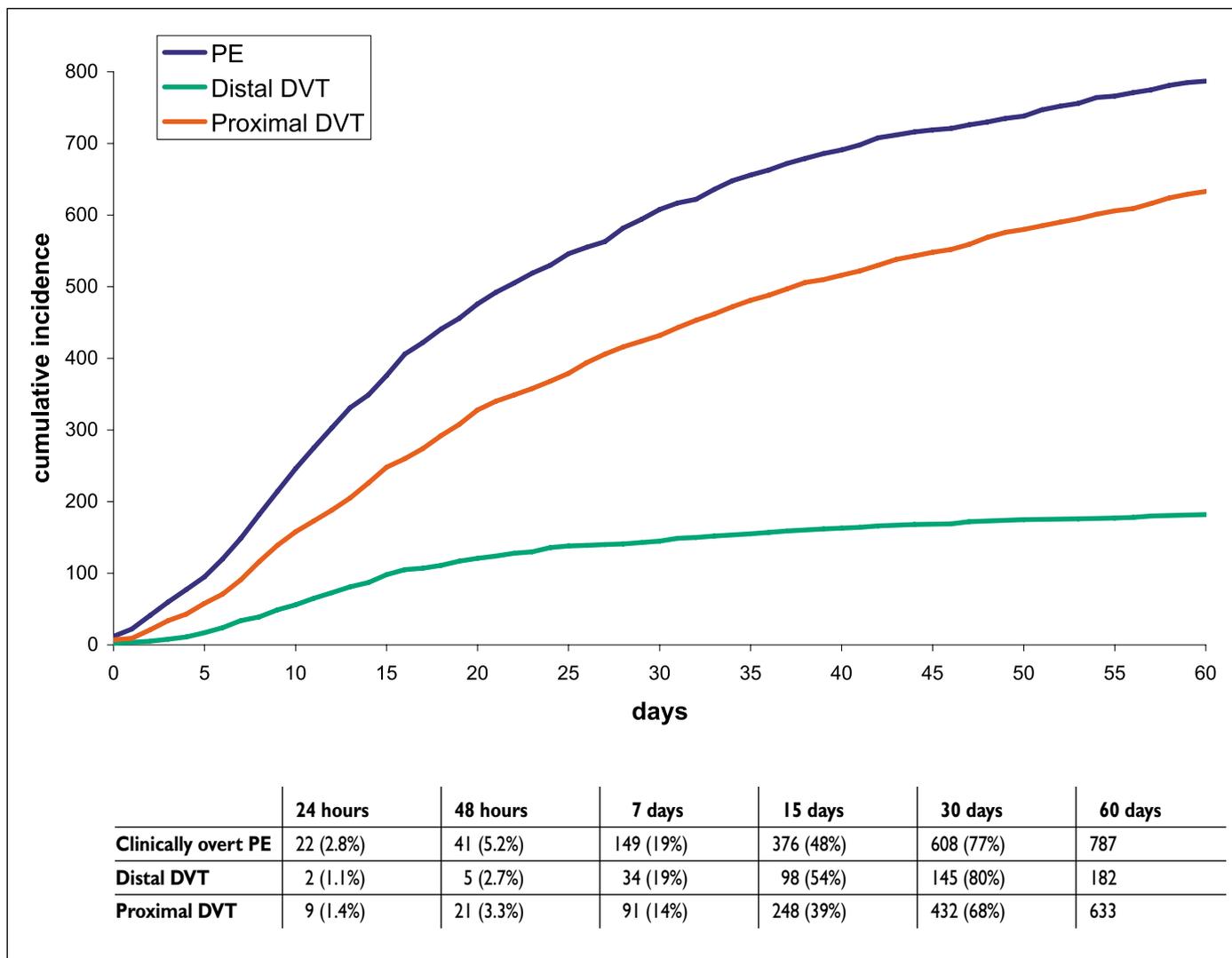


Figure 1: Cumulative number of patients with VTE after surgery, according to their clinical presentation. VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism.

‘major’ if they were overt and required a transfusion of two units of blood or more, or were retroperitoneal, spinal or intracranial.

Variables

The parameters recorded by the registry include details of each patient's baseline characteristics; type and date of surgery; clinical status including any coexisting or underlying conditions such as chronic heart or lung disease; creatinine levels; thromboprophylaxis received prior to VTE diagnosis and its duration; and the clinical characteristics of the VTE event. Patients received prophylaxis according to the clinical practice of each participating hospital and were not subject to any predetermined intervention. Data regarding prior VTE prophylaxis were obtained from medical records.

Follow-up

All patients were followed for at least three months after hospital discharge. During each visit, any signs or symptoms suggesting

recurrences of DVT or PE, or bleeding complications were noted. Each episode of clinically suspected recurrent DVT or PE was documented by repeat compression ultrasonography, venography, lung scanning, helical CT scan, or pulmonary angiography. Only objectively confirmed recurrent events are accepted. The causes of death were determined by the attending physicians.

Data collection

Data are recorded on to a computer-based case report form by a registry coordinator at each participating hospital and submitted to a centralized coordinating center through a secure website. The coordinators also ensure that eligible patients are consecutively enrolled. Patient identities remain confidential because they are identified by a unique number assigned by the study coordinating center, which is responsible for all data management. Study endpoints are adjudicated by the attending physicians, but in case of doubt they address the case report to the Adjudication

Table 2: Prophylaxis data, treatment options and three-month outcome in the 1,602 postoperative patients with VTE, according to the type of surgery.

	Major orthopaedic surgery	Cancer surgery	Other surgical procedures	OR (95% CI) orthopedic vs. cancer	OR (95% CI) orthopedic vs. other
Patients (n)	393	207	1002		
Prophylaxis					
Yes	376 (96%)	157 (76%)	525 (52%)	7.0 (3.9–13) [‡]	20 (12–33) [‡]
LMWH	364 (98%)	157 (100%)	504 (98%)	N/A	1.0 (0.3–2.8)
Mean daily dose (IU ± SD)	4252 ± 1016	3260 ± 1141	3769 ± 1650	<0.001	<0.001
Duration (days ± SD)	17 ± 9.6	13 ± 8.9	12 ± 11	<0.001	<0.001
Initial therapy					
LMWH	352 (90%)	192 (93%)	867 (87%)	0.7 (0.4–1.2)	1.1 (0.9–1.9)
UFH	40 (10%)	15 (7.2%)	121 (12%)	1.5 (0.8–2.7)	0.8 (0.6–1.2)
Inferior vena cava filter	4 (1.0%)	10 (4.8%)	31 (3.1%)	0.2 (0.1–0.7) [†]	0.3 (0.1–1.0) [*]
Long-term therapy					
Anti-vitamin K drugs	270 (72%)	84 (42%)	721 (74%)	3.5 (2.4–5.0) [‡]	0.9 (0.7–1.2)
LMWH	104 (28%)	115 (58%)	251 (26%)	0.3 (0.2–0.4) [‡]	1.1 (0.8–1.4)
3-month follow-up					
Major bleeding	9 (2.3%)	6 (2.9%)	28 (2.8%)	0.8 (0.3–2.3)	0.8 (0.4–1.7)
Fatal bleeding	3 (0.8%)	2 (1.0%)	2 (0.2%)	0.8 (0.1–4.8)	3.8 (0.6–23)
Recurrent DVT	5 (1.3%)	7 (3.4%)	15 (1.5%)	0.4 (0.1–1.2)	0.8 (0.3–2.3)
Recurrent PE	7 (1.8%)	5 (2.4%)	8 (0.8%)	0.7 (0.2–2.3)	2.3 (0.8–6.3)
Fatal initial PE	4 (1.0%)	2 (1.0%)	4 (0.4%)	1.1 (0.2–5.8)	2.6 (0.6–10)
Fatal recurrent PE	1 (0.3%)	1 (0.5%)	4 (0.4%)	0.5 (0.03–8.4)	0.6 (0.1–5.7)
Overall death	32 (8.1%)	30 (15%)	31 (3.1%)	0.5 (0.3–0.9) [*]	2.8 (1.7–4.6) [‡]

Comparisons between groups: ^{*}p <0.05; [†]p <0.01; [‡]p <0.001. Abbreviations: VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep vein thrombosis; SD, standard deviation; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; OR, odds ratio; CI, confidence intervals. Major orthopaedic surgery: hip fracture repair, hip arthroplasty, knee arthroplasty.

Committee of the RIETE Registry. Data quality is monitored and documented electronically to detect inconsistencies or errors, which are resolved by the local coordinators. Data quality is also monitored by periodic visits to participating hospitals, by contract research organizations, who compare the medical records with the data in the web, as in the case of most clinical trials. In the event of substantial or unjustifiable inconsistencies, patients enrolled from that center are not included in the database.

Statistical analysis

A commercial software package (SPSS version 12.0) was used to calculate odds ratios (ORs) and corresponding 95% confidence intervals (CIs), and a p-value <0.05 was considered to be statistically significant. Cox proportional hazards analysis was used to estimate the time-course of VTE after surgery.

Results

As of January 2006, 13,599 consecutive patients with symptomatic, acute VTE were enrolled at 124 participating centers. Of these, 1,602 (12%) were postoperative. The most common types of surgery were: hip fracture repair in 122 patients; hip arthroplasty 145; knee arthroplasty 126; other orthopaedic 191; cancer surgery 207; abdominopelvic for conditions other than cancer 397; neurosurgery 123; vascular 99; other 192.

roplasty 145; knee arthroplasty 126; other orthopaedic 191; cancer surgery 207; abdominopelvic for conditions other than cancer 397; neurosurgery 123; vascular 99; other 192.

Clinical presentation

Patients with VTE after major orthopaedic surgery (i.e. hip fracture or total hip or knee arthroplasty) were more commonly female, significantly older, and had more often chronic heart failure but less frequently cancer than those undergoing cancer surgery or other surgical procedures (Table 1). There were no differences between groups in the mean time elapsed from surgery to VTE (22 ± 16, 24 ± 16, and 21 ± 15 days, respectively), or the percentage of patients who developed VTE during the first 15 days after surgery (47%, 41% and 45%, respectively) was also similar. As for the clinical presentation of VTE, there were no differences in the percentage of patients with clinically overt PE (48%, 48%, and 50% respectively), or in the severity of the PE (expressed in terms of tachycardia, hypotension or hypoxemia). Among those with only DVT signs, patients undergoing cancer surgery had more often proximal DVT. However, clinically overt PE appeared significantly earlier (20 ± 15 vs. 24 ± 16 days; p <0.001) than proximal DVT, as shown in Figure 1.

Prophylaxis and therapy

Thromboprophylaxis was used in 1,058 (66%) patients, with a significantly higher use in those undergoing major orthopaedic surgery (96%) than in those undergoing cancer surgery (76%), or other procedures (52%), as shown in Table 2. The vast majority (97%) of patients with prophylaxis received low-molecular-weight heparin (LMWH). In 1,014 of the 1,058 patients (96%) who received prophylaxis there was information on its duration: those undergoing major orthopaedic surgery had received higher daily doses of LMWH and for longer than those in the other two groups. Overall, 478 (47%) patients had their VTE event diagnosed during prophylaxis, 536 (53%) after withdrawal. We have no data on mechanical prophylaxis. As for the use of anticoagulant therapy, most patients received LMWH as initial therapy, and then switched to long-term therapy with anti-vitamin K drugs, with the exception of cancer patients (who mostly received LMWH as long-term therapy).

Three-month outcome

There were no significant differences between groups in the incidence of recurrent VTE, major bleeding, fatal PE or fatal bleeding, the only exception being overall mortality (which was higher in cancer patients and those with major orthopedic surgery), as shown in Table 2.

Discussion

Our findings, obtained from a large prospective series of consecutive patients in the RIETE registry, reveal that two in every three (63%) postoperative VTE events occur after non-orthopaedic or cancer surgery, and that these patients were less likely to have received prophylaxis following surgery. This observation is of crucial importance because, while much attention has been paid to thromboprophylaxis post orthopaedic or cancer surgery, VTE after other surgical procedures constitutes a large proportion of the total burden of VTE in the community.

We also found that the clinical presentation of VTE, the severity of PE, the time course, and the three-month outcome were very similar among the three subgroups of patients, irrespective of the type of surgery. The proportion of patients presenting with clinically overt PE in our study was around 50% in all subgroups. Similar findings have been observed in patients undergoing major joint surgery (11), but after cancer surgery Agnelli et al. found most VTE patients (80%) to have PE (16). These differences may be attributed to the need for objective confirmation of PE diagnosis in both the RIETE registry and the study by Bjornara et al. (11). Interestingly, the rate of VTE recurrences or major bleeding complications during the three-month study period was also similar in the three surgical groups. This was rather unexpected, since orthopaedic patients were significantly older and more frequently had chronic heart failure.

Finally, our findings confirm that the use of thromboprophylaxis was suboptimal in many patients undergoing cancer surgery or other procedures. Interestingly, most cases (55%) of symptomatic postoperative VTE occurred beyond the first 15

days after surgery (again with no differences according to the type of surgery), and 53% of patients receiving prophylaxis had their VTE event diagnosed after withdrawal. These data, as well as those from others (11, 16–18), suggest the need for studies of extended VTE prophylaxis post surgery.

This study has a number of limitations. First, as an observational study, RIETE is not designed to answer questions regarding the relative efficacy and safety of different modalities of prophylaxis or therapy. Second, the use of prophylaxis following surgery was slightly higher than expected given findings from other community based studies, thus suggesting that it may be a result of some bias introduced by inclusion of hospitals with particular interest in VTE. Third, we do not know if the proportions of each type of surgery performed in RIETE hospitals mirror that of a typical community (for example if hospitals performing orthopaedic or cancer surgeries were under-represented in the RIETE registry). Finally, the study does not provide information concerning the number of procedures performed in the individual centres. This data would provide information concerning the incidence of VTE for each of the procedures and would have enhanced the relevance of the study. However, we included a large series of consecutive patients with symptomatic, objectively confirmed, acute VTE, after a spectrum of different urgent or elective surgical procedures. Our data are hypothesis-generating and provide feedback from real-world clinical situations.

In summary, the clinical presentation, time-course, and three-month outcome of VTE was similar among the different subgroups of patients, irrespectively of the type of surgery. However, the use of thromboprophylaxis in patients undergoing cancer surgery or other procedures was suboptimal. Our data suggest that the use of adequate thromboprophylaxis should be strongly encouraged for all postoperative patients.

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Appendix

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References

1. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the seventh ACCP Conference on antithrombotic and thrombolytic therapy. *Chest* 2004; 126: 338s-400s.
2. Scurr JH. How long after surgery does the risk of thromboembolism persist? *Acta Chir Scand* 1990; 556: 22-24.
3. Huber O, Bounameaux H, Borst F, et al. Postoperative pulmonary embolism after hospital discharge. An underestimated risk. *Arch Surg* 1992; 127: 310-313.
4. Dahl OE, Aspelin T, Arnesen H, et al. Increased activation of coagulation and formation of late deep venous thrombosis following discontinuation of thromboprophylaxis after hip replacement surgery. *Thromb Res* 1995; 80: 299-306.
5. Planes A, Vochelle N, Darmon JY, et al. Risk of deep venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet* 1996; 348: 224-228.
6. White RH, Romano PS, Zhou H, et al. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Arch Intern Med* 1998; 158: 1525-1531.
7. Phillips CB, Barrett JA, Losina E, et al. Incidence rates of dislocation, pulmonary embolism, and deep infection during the first six months after elective total hip replacement. *J Bone Joint Surg* 2003; 85-A: 20-26.
8. Dahl OE, Gudmundsen TE, Bjornara BT, et al. Risk of clinical pulmonary embolism after joint surgery in patients receiving low-molecular-weight heparin prophylaxis in hospital. A 10-year prospective register of 3,954 patients. *Acta Orthop Scand* 2003; 74: 299-304.
9. Howie C, Hughes H, Watts AC. Venous thromboembolism associated with hip and knee replacement over a ten-year period. A population-based study. *J Bone Joint Surg (Br)* 2005; 87-B: 1675-1680.
10. SooHoo NF, Zingmond DS, Lieberman JR, et al. Optimal timeframe for reporting short-term complication rates after total knee arthroplasty. *J Arthroplasty* 2006; 21: 705-711.
11. Bjornara BT, Gudmundsen TE, Dahl OE. Frequency and timing of clinical venous thromboembolism after major joint surgery. *J Bone Joint Surg (Br)* 2006; 88-B: 386-391.
12. Anand S, Buch K. Post-discharge symptomatic thromboembolic events in hip fracture patients. *Ann R Coll Surg Engl* 2007; 89: 517-520.
13. Arcelus JI, Monreal M, Caprini JA, et al. The management and outcome of acute venous thromboembolism: a prospective registry including 4011 patients. *J Vasc Surg* 2003; 38: 916-922.
14. Blanco-Molina A, Trujillo-Santos J, Criado J, et al. and the RIETE Investigators. Venous thromboembolism during pregnancy or postpartum: Findings from the RIETE Registry. *Thromb Haemost* 2007; 97: 186-190.
15. Falgà C, Capdevila JA, Soler S, et al. for the RIETE Investigators. Clinical outcome of patients with venous thromboembolism and renal insufficiency. Findings from the RIETE Registry. *Thromb Haemost* 2007; 98: 771-776.
16. Agnelli G, Bolis G, Capussotti L, et al. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery. The @RISTOS project. *Ann Surg* 2006; 243: 89-95.
17. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost* 2003; 90: 367-368.
18. Gangireddy C, Rectenwald JR, Upchurch GR, et al. Risk factors and clinical impact of postoperative symptomatic venous thromboembolism. *J Vasc Surg* 2007; 45: 335-341.