Eur Spine J (2004) 13 : 1–8
DOI 10.1007/s00586-003-0538-7

REVIEW

S. Brambilla
C. Ruosi
G. A. La Maida
S. Caserta

Prevention of venous thromboembolism in spinal surgery

Received: 8 October 2002
Revised: 14 January 2003
Accepted: 20 January 2003
Published online: 11 November 2003

S. Brambilla (✉) · G. A. La Maida
S. Caserta
Department of Spinal Surgery,
Gaetano Pini Orthopaedic Institute,
Milan, Italy
Fax: +39-02-58301443,
e-mail: brambilla@gpini.it

C. Ruosi
Department of Orthopaedics
and Traumatology,
"Federico II" University, Naples, Italy

S. Brambilla
Viale Beatrice d'Este 35,
20122 Milan, Italy

Abstract Deep vein thrombosis (DVT), and its most feared complication, pulmonary embolism (PE), still have a high incidence with high risk for patients' health. Proven prophylactic measures are available but are generally underused, and DVT is still considered the most common cause of preventable death among hospitalized patients. The rationale for prophylaxis of venous thromboembolism is based on the clinically silent nature of the disease, the relatively high prevalence among hospitalized patients and the potentially tragic consequences of a missed diagnosis. During the last 15–20 years, spine surgery has changed radically, developing into a well-defined area of specialist surgery, and some attention is now being given to DVT events in spine surgery. The incidence of DVT during spine surgery is not documented in the literature, because only case reports or retrospective studies are reported. It would therefore be very helpful to initiate a multicenter study in order to understand this problem better and to develop, if possible, some guidelines on prophylactic measures in spine surgery. In doing so, we need to consider each patient's pattern, any risk factors and every kind of surgical technique related to DVT, in order to improve the outcome of the patient and to reduce any medicolegal problems that could arise from a thrombotic complication or an epidural hematoma, with its high potential for irreversible consequences.

Keywords Deep vein thrombosis · Pulmonary embolism · Prophylaxis · Spinal surgery

Introduction

Pulmonary embolism (PE) represents one of the most frequent and dangerous complication in patients undergoing a surgical procedure [76, 81]. Approximately 500,000 cases of deep vein thrombosis (DVT) and PE occur in the United States each year. In about 20% of cases, the initial clinical manifestation of venous thromboembolism (VTE) is sudden death due to PE. Of those patients who suffer a massive PE, 70% die within the first hour of symptom onset [2, 64, 66].

Because patients with recent surgery have a 22-fold increased risk of postoperative VTE, a large research effort has been directed toward identifying the safest and most effective prophylaxis after surgery [44, 49].

Obviously, thromboembolic risk is not the same in all patients, and it can vary greatly depending on the kind of surgery. To appropriately target prophylaxis against thromboembolism, surgical procedures and patients at risk must first be identified and categorized into levels of risk [20, 40, 67] (Table 1).

The patients at greatest risk for VTE are those undergoing major lower extremity orthopedic surgery, and those who have experienced major trauma or spinal cord injury [6, 8, 10, 15, 19, 20, 24, 28, 30, 39, 44, 67, 84].

For instance, the incidence of DVT in patients who underwent hip and knee surgery without prophylaxis ranges

Table 1 Levels of thromboembolism risk in surgical patients without prophylaxis (modified from Clagett et al., Geerts et al., and Nicolaides et al. [19, 40, 67]) (*DVT* deep vein thrombosis, *PE* pulmonary embolism, *VTE* venous thromboembolism)

Level of risk	Calf DVT (%)	Proximal DVT (%)	Clinical PE (%)	Fatal PE (%)
Low risk: Minor surgery in patients aged <40 years with no additional risk factors	2	0.4	0.2	0.002
Moderate risk: Minor surgery in patients with additional risk factors; non-major surgery in patients aged 40–60 years with no additional risk factors; major surgery in patients <40 years with no additional risk factors	10–20	2–4	1–2	0.1–0.4
High risk: Non-major surgery in patients >60 years or with additional risk factors; major surgery in patients >40 years or with additional risk factors	20–40	4–8	2–4	0.4–1.0
Highest risk: Major surgery in patients >40 years plus prior VTE, cancer, or molecular hypercoagulable state; hip or knee arthroplasty, hip fracture surgery; major trauma; spinal cord injury	40–80	10–20	4–10	0.2–5

from 48 to 80% [6, 25, 46, 63, 65, 66, 80, 90, 94]. In a prospective study of 443 patients with major trauma who did not receive any thromboprophylaxis, the incidence of DVT, using routine bilateral contrast venography, was 58%. Among trauma subgroups, the expected high rates of DVT were seen in patients with lower extremity (69%) and spine (62%) fractures and in patients with major head injuries (54%) [39]. Other less invasive procedures, such as knee arthroscopy, also pose a risk [26].

For any kind of surgery, certain patient characteristics have been identified as risk factors for VTE. These include: increasing age; prolonged immobility; stroke or paralysis; previous VTE; cancer and its treatment [33, 54, 59]; trauma (especially fractures of the pelvis, hip, or leg); obesity; varicose veins; cardiac dysfunction; pregnancy; and oral contraceptive use or estrogen replacement therapy [19, 43]. These are often present in combination in a hospitalized population. For surgical patients, the incidence of VTE is affected by pre-existing factors and by factors related to the procedure itself [19, 20, 40, 64, 67, 79, 87].

It is therefore appropriate to perform a prophylaxis in surgical patients. Table 2 summarizes some advice regarding the risk of VTE.

Pharmacological prophylaxis to prevent thromboembolic events has become standard practice in high-risk patient groups. The gold standard is low-molecular-weight heparin (LMWH). The major advantages of LMWH are

Table 2 Regimens to prevent VTE (modified from the Sixth ACCP Consensus Conference on Antithrombotic Therapy, 2001 [40]) (*LMWH* low-molecular-weight heparin, *ES* elastic stockings, *IPC* intermittent pneumatic compression, *LDUH* low-dose unfractionated heparin)

Type of surgery	Recommended prophylaxis
Total hip replacement	LMWH 2.500–6.000 IU once daily starting 12 h preoperatively (Europe) or 12–24 h postoperatively (North America), or 4–6 h after surgery at half the usual high-risk dose and then continuing with the usual high-risk dose the following day; adjuvant prophylaxis with ES or IPC may provide additional efficacy, or adjusted-dose warfarin (INR target=2.5, range 2.0–3.0 started preoperatively or immediately after surgery)
Total knee replacement	LMWH as in total hip replacement or adjusted-dose warfarin (INR 2.0–3.0); optimal use of IPC is an alternative option
Hip fracture surgery	LMWH as in total hip replacement or adjusted-dose warfarin; the use of LDUH may be an alternative option
Elective neurosurgery	IPC (plus or minus ES); other options that may also be acceptable include LDUH and postoperative LMWH; the combination of LMWH and ES is more efficacious than ES alone
Intracranial surgery	IPC with or without ES; LDUH or postoperative LMWH (2.000–6.000 IU once daily 12–24 h after surgery) are acceptable alternatives (because of concerns about clinically important intracranial hemorrhage); the combination of physical (ES or IPC) and pharmacologic (LMWH or LDUH) prophylaxis modalities may be more effective than either modality alone in high-risk patients
Acute spinal cord injury	LMWH, ES and IPC might have benefit if used in combination with LMWH or LDUH or if anticoagulants are contraindicated early after injury
Elective spine surgery	No firm recommendations; it is reasonable to use ES alone, LDUH alone, or the combination of the two; intraoperative plus postoperative IPC may also be effective. For spine surgery patients with additional thromboembolic risk factors, prophylaxis with one of these options is suggested

improved efficacy and safety, longer half-life and reduced need for laboratory monitoring [71].

If these recommendations are well known for general orthopedic surgery, especially in elective hip and knee and trauma procedures, little has been published about the problem of DVT and it prophylaxis for spinal surgery.

Despite being generally considered as a sub-speciality of orthopedic or neuro-surgery, spine surgery has developed significantly over the last 20 years, to become an independent surgical speciality. It includes many surgical procedures for a variety of pathologies, and involves a highly heterogeneous class of patients. A careful analysis in terms of thromboembolic risks is therefore required in each individual case.

Three main variables need consideration:

1. Patient-related variables, such as age, gender (oral contraceptive use or hormonal substitutive therapy), bed rest, obesity and concomitant pathologies (hypertension, diabetes, varicose veins)
2. Disease-related variables, such as trauma, tumor, deformity, degenerative pathology, and finally
3. Surgery-related variables, such as approach (anterior, posterior, combined), positioning, instrumentation, operating time, and location (cervical, thoracic, lumbar spine)

There is no unique risk factor, because spinal surgery does not take one single form; it is therefore not possible to suggest a standardized thromboprophylaxis for spinal surgery, as can be done for hip and knee surgery. Moreover pharmacological prophylaxis has never met the approval of spine surgeons, due to the possibility of hemorrhagic complications [10, 16, 25, 32, 37, 47, 82, 85, 91, 92, 94].

For more on this subject, the interesting paper by Janku et al. published in 1996 [53] is worth a review. Janku and co-workers conducted a study into the practice of prevention of venous thromboembolism among orthopedic surgeons in the United States, based on a questionnaire mailed to 5000 randomly selected practising surgeons. They found that the low rate of incidence of venous thrombosis and the risks related to the use of anticoagulants, which can lead to hematoma and cauda equina syndrome in patients undergoing elective spinal surgery, appeared to discourage pharmacologic prophylaxis. Elective spinal procedures were carried out by 383 of the surgeons, each of whom estimated dealing with, on average, 37 such cases per year. Only 21% of surgeons used prophylaxis in all patients, a further 21% used it only in risk cases, and 58% of surgeons did not employ any kind of prophylaxis.

The figure of 58% using no kind of prophylaxis is high, considering that the onset of an epidural hematoma with its potentially tragic complications (not always reversible even after an immediate revision and decompression) or a deep hematoma with a consequent infection and hardware removal, represent a failure of treatment and a source of disability in the patient. Among those who did use some form of prophylaxis, the most frequent method was mechanical (elastic compressive stockings, intraoperative compressive pumps).

Up to now, no precise indications have been published relating to VTE prophylaxis in spinal surgery, with spine surgeons having to rely on generic recommendations from general orthopedic surgery and neurosurgery [1, 3, 13, 69, 77].

We performed a literature review concerning this topic in order to better understand and quantify the incidence of VTE and its prophylaxis in spinal surgery.

Literature review

Historically, the first contribution was published by Uden [88] in1979. Out of 1229 patients who underwent Harrington correction and fusion for idiopathic scoliosis, there were eight DVT cases (0.0065%), with one fatal PE, which occurred between the 12th and 34th postoperative day.

Subsequently three papers were published by Ferree and co-workers on a limited number of cases. In the first paper [36], 86 patients were studied with preoperative and postoperative ultrasonography of the lower extremities to identify acute DVT. Postoperative DVT developed in five of them (6%), and there were two decompressions (one breast cancer); one discectomy; one posterior fusion (previous thrombophlebitis); and one anterior fusion (oral contraceptive use). None of the patients developed symptoms of PE.

In the second paper [35], 185 posterior surgery patients were studied. Elastic compression stockings (ECS) were used for prophylaxis in 74 patients (ECS group); and intermittent pneumatic compression (IPC) was used in the remaining 111 patients (IPC group). The results were: three cases of DVT following laminectomy (4% of 84 total laminectomy patients; 8% of 40 ECS group laminectomy patients), and one case of DVT in the fusion group (1% of 101 total fusion patients; 3% of 34 ECS group fusion patients).

The last of the Ferree studies [34] reviewed 60 consecutive patients undergoing lumbar laminotomy for herniated disc (n=51) or laminectomy for spinal stenosis (n=9); compression stockings were the method of prophylaxis. Three patients (5%) developed postoperative calf DVT (ultrasonography detection); one was a 43-year-old man without risk factors in the herniated disc group; one was a 67-year-old woman (L4–S1 laminectomy for stenosis); and one was a 75-year-old woman (decompressive laminectomy) affected by breast cancer.

In the Dearborn et al. study [29], 318 major spinal reconstructive procedures, excluding discectomies and cervical spine cases, were considered. There were seven cases of PE, six of which occurred among 97 patients undergoing combined anterior and posterior spinal procedures (6.1%). Only one patient had a clinical PE after posterior procedure. The overall clinical PE rate in combined-ap-

proach patients was 6%, significantly greater than the rate in patients undergoing posterior surgery alone. PE occurred in two patients with negative ultrasound examinations, and none of the patients with PE had clinical signs or symptoms of DVT before embolization.

The higher risk of PE after combined anterior-posterior spinal fusions indicates that retraction and manipulation of the great vessels may lead to stasis or intimal damage that can predispose to clot formation.

A multicentric retrospective study of thromboembolic complications after lumbar disc surgery involving 16,656 patients from 50 French neurosurgical units was published in 1993 [31]. No prophylaxis was used in 62.2% of the patients; subcutaneous heparin was employed in 6% of patients, LMWH was used in 25.8% of patients, and in 6% oral anticoagulants were used. Two major groups were identified: group A (10,351 patients), without prophylaxis, and group B (6305 patients), with some kind of prophylaxis. There were 105 VTE complications (0.63% of all surgical patients), with 94 cases of DVT and 11 of PE. In group A there were 63/10,351 cases of DVT (0.609%) and 5/10,351 cases of PE (0.048%); in group B there were 31/6305 cases of DVT (0.492%) and 6/6305 cases of PE (0.095%).

Kozak and O'Brien [58], in a series of 69 simultaneous combined anterior (left-sided, retroperitoneal approach to the lower lumbar spine) and posterior fusions between January 1984 and November 1986 for primary low-back pain or persistence of pain following previous lumbar surgery, reported an incidence of 3/69 cases of DVT (4.34%) and 2/69 (2.89%) cases of nonfatal pulmonary embolism.

More recently, two papers coming from East Asia have been published. The first of these [70] concerned 110 patients who underwent posterior spinal surgery: 54 cervical; 7 thoracic; and 49 lumbar, without any type of prophylaxis.

No patients showed clinical signs of DVT or PE. However, 17 patients (15.5%) showed venographic evidence of DVT; 16 of these had distal thrombi, and only one had a proximal thrombus. DVT was venographically evident in 3 (5.6%) of the 54 patients who underwent cervical procedures, and in 13 (26.5%) of the 49 patients who underwent lumbar procedures.

In the study by Lee et al. [60], which was based on 313 patients, no specific anti-thrombotic prophylaxis was used in any patient before or after surgery. All patients were examined with duplex ultrasonography in both lower extremities between the 5th and 7th postoperative days, to ensure that any asymptomatic thrombi were not missed. Only one patient had a clinically symptomatic DVT; four patients were noted to have results compatible with DVT. The overall incidence of thrombotic complication without any form of prophylaxis was 1.3% (4/313) and the incidence of symptomatic DVT was 0.3% (1/313).

Smith et al. [83] studied 317 patients in whom prophylaxis was done with compressive stockings and sequential-pneumatic-compression thigh-length cuffs. Duplex ultrasonography was performed in 126 patients (40%) to screen for the presence of asymptomatic thrombosis.

DVT developed in 1 of the 126 patients who had been evaluated with duplex ultrasound, 16 days after the operation and 10 days after discharge, and in 1 of the 191 who had not been so evaluated,15 days after the operation, after discharge from the hospital. The operation in both patients had involved a left-sided, lateral, retroperitoneal exposure of the caudal lumbar and lumbosacral discs.

A fatal PE developed in one of the patients who had not been evaluated with ultrasound, 8 days after the operation (anterior decompression and arthrodesis with anterior instrumentation) for a severe burst fracture of the second lumbar vertebra.

Wood et al. [95] published in 1997 a study on 136 patients in whom a mechanical prophylaxis was used (thigh-high sequential-pneumatic-compression wraps or pneumatic foot-compression wraps).

Investigations using Doppler ultrasound revealed one ultrasound positivity in a 49-year-old woman who had undergone anterior spine T11–L3 fusion and posterior T4–L3 fusion on the 6th postoperative day, and one case of subclinical PE (3rd postoperative day) in a 33-year-old woman, who was a smoker and was obese, and had undergone a posterior L3–L5 fusion.

West and Anderson [93] carried out a prospective study on 41 adult patients (>18 years old) undergoing major spinal surgery using pedicular or segmental instrumentation (including six cases of anterior surgery): 14 operations were for spinal deformity; 16 for trauma; and 11 for degenerative spine disease.

No preoperative or intraoperative thrombotic prophylaxis was used. After surgery, all patients were placed in compression stockings until the patient was able to walk well. One day before discharge the patients underwent noninvasive testing to rule out DVT of the lower extremities (color Doppler). Six patients (14%) were found to have results compatible with DVT, of whom three were trauma patients (two paraplegic); two had been operated for spinal deformity; and one for degenerative spine disease. If we eliminate the two patients who had paraplegia secondary to trauma, the incidence of DVT changes to 4/39, or 9.8%.

Rokito et al. [78], in 370 major reconstructive spinal procedures on 329 patients, reported one case of DVT (0.3% of incidence) on the 16th day in a patient with high co-morbidity (obesity, diabetes, hypertension, bed rest, anterior retroperitoneal approach), in whom only mechanical prophylaxis was used.

Benz et al. [12] found an incidence of 1 case of PE in 68 patients operated on for decompression or decompression combined with fusion in patients aged over 70 years. One case of non-fatal PE in a 57-year-old woman affected by cauda equina tumor (neurinoma) at the L2 and L3 levels, who underwent tumor resection with L1–L5 postero-

Table 3 Literature review listed by type of study (*ECS* elastic compressive stockings, *PC* pneumatic compression)

References	No. of cases	Prophylaxis	Type of study
Uden [88]	1229	No	Retrospective
Benz et al. [12]	68	?	Retrospective
Ramirez and Thisted [74]	28,395	?	Retrospective
Desbordes et al. [31]	16,656	No (62.2%); pharmacologic (37.8%)	Retrospective
Smith et al. [83]	317	ECS; PC	Prospective, randomized, no control group
Rokito et al. [78]	329	ECS, PC, Coumadin	Prospective, partially randomized
Dearborn et al. [29]	318	ECS; PC	Prospective and retrospective
Wood et al. [95]	136	ECS; PC	Prospective, randomized
Ferree et al. [36]	86	ECS	Prospective
Ferree and Wright [35]	185	ECS; PC	Prospective
Ferree [34]	60	ECS	Prospective
Kozak and O'Brien [58]	69	?	Prospective
Oda et al. [70]	110	No	Prospective
Lee et al. [60]	313	No	Prospective
West and Anderson [93]	41	PC	Prospective
Knop et al. [57]	682	?	Prospective
Andreshak et al. [5]	159	PC	Prospective
Stolke et al. [86]	481	?	Prospective
Fujita et al. [38]	137	Only postop.	Prospective
Arai et al. [7]	–	–	Case report
Brown and Eismont [14]	–	–	Case report

lateral fusion and spinal instrumentation, was found in a report by Arai et al. [7].

Knop et al. [57] described three cases of fatal PE and six of DVT and non-fatal PE in a group of 682 patients who underwent surgical repair for thoracolumbar injuries.

Andreshak et al. [5] investigated 150 lumbar spine surgery procedures in which the patients were placed in intraoperative sequential-pneumatic-compression devices and divided into an obese and a non-obese group. In the obese group (55 patients), there was 1 case of fatal PE out of 55 procedures, which occurred in a 62-year-old man on the 3rd postoperative day; and there was 1 case of DVT in the non-obese group (95 patients).

Stolke et al. [86] reported 1 case of fatal PE in 412 primary surgeries and 69 reoperations in lumbar disc macro- and microsurgery.

Fujita et al. [38] studied 169 spinal fusions in adult patients of more than 60 years of age; there was 1 case of PE and 2 of DVT in 169 patients.

Brown and Eismont [14] reported 1 case of DVT in 98 patients undergoing anterior correction for scoliosis, while Ramirez and Thisted [74] found an incidence of pulmonary embolism of 0.1% among 28,395 patients undergoing lumbar discectomy. Patients undergoing lumbar discectomy are generally considered at low risk for thromboembolism [48].

Finally, four isolated cases of arterial thromboembolism were reported as a consequence of compression and occlusion of the common left iliac artery during anterior lumbar interbody fusion [45, 56, 61, 75].

Table 3 summarizes the most important studies found in the literature, divided by type of study. The gold standard for these types of studies, represented by a prospective, randomized, controlled study, is impossible because of ethical and health issues.

Conclusions

Prophylaxis for VTE is an area that has received intense study in certain contexts [27], but less than adequate coverage in others. A Scottish study documented fatal PE in surgical patients over a 1-year period: 56% of the patients who died of PE had not received prophylaxis, despite having major risk factors and with no contraindications to standard antithrombotic regimens [42].

The true incidence of thromboembolic complications in spinal surgery remains unknown [17]. The question is whether the incidence of DVT in spinal surgery is sufficient to consider any type of prophylaxis. Because insufficient data exist, it is not possible to suggest a standardized prophylactic regimen; elastic compression alone or combined with pharmacological prophylaxis seem both to be efficacious. For patients at risk, prophylaxis with both measures is strongly recommended [40].

Methods of prophylaxis include pharmacologic [10, 21, 22, 23, 37, 41, 62, 68, 73, 89], mechanical [9, 11, 92], and combinations of these. Anticoagulation has not gained wide acceptance by spinal surgeons: the possibility of epidural hematoma and catastrophic neurologic injury makes the

morbidity of anticoagulation potentially worse in spinal surgery patients than in total joint replacement patients.

Major bleeding was significantly increased with the preoperative regimen, but not with the postoperative regimen of LMWH. Recent studies revealed that LMWH beginning within 2 h preoperatively or 6 h postoperatively decrease the risk of venous thrombosis equally [1, 3, 47, 50, 51, 52, 55, 63, 72] and should be helpfully employed in spinal surgery.

We think that the problem of VTE and its prophylaxis should be more extensively investigated in controlled studies specifically for complex modern spinal surgery in order to formulate some guidelines for the sake of patient health and safety and to address surgeons' uncertainty in this matter.

References

1. Agnelli G (1999) Prevention of venous thromboembolism after neurosurgery. Thromb Haemost 82:925–930
2. Agnelli G, Sonaglia F (2000) Prevention of venous thromboembolism. Thromb Res 97:V49–V62
3. Agnelli G, Piovella F, Buoncristiani P, Severi P, Pini M, D'Angelo A, Beltrametti C, Damiani M, Andrioli GC, Pugliese R, Iorio A, Brambilla G (1998) Enoxaparin plus compression stockings compared with compression stockings alone in the prevention of venous thromboembolism after elective neurosurgery. N Engl J Med 339:80–85
4. Agnelli G, Mancini GB, Biagini D (2000) The rationale for long-term prophylaxis of venous thromboembolism. Orthopedics 23 [Suppl 6]:643–646
5. Andreshak TG, An HS, Hall J, Stein B (1997) Lumbar spine surgery in the obese patient. J Spinal Disord 10: 376–379
6. Ansari S, Warwick D, Ackroid CE (1997) Incidence of fatal pulmonary embolism after 1390 knee arthroplasties without routine prophylactic anticoagulation, except in high-risk cases. J Arthroplasty 12:599–602
7. Arai Y, Shitoto K, Muta T, Kurosawa H (1999) Pulmonary thromboembolism after spinal instrumentation surgery. J Orthop Sci 4:380–383
8. Arcelus JI, Caprini JA, Reyna JJ (2000) Finding the right fit: effective thrombosis risk stratification in orthopedic patients. Orthopedics 23 [Suppl 6]: 633–638
9. Asano H, Matsubara M, Suzuki K, Morita S, Shiinomiya K (2001) Prevention of pulmonary embolism by a foot sole pump. J Bone Joint Surg Br 83:1130–1132
10. Axelrod DA, Wakefield TW (2001) Future directions in antithrombotic therapy: emphasis on venous thromboembolism. J Am Coll Surg 192:641–651
11. Benko T, Cooke EA, McNally MA, Mollan RAB (2001) Graduated compression stockings. Knee length or thigh length? Clin Orthop 383:197–203
12. Benz RJ, Ibrahim ZG, Afshar P, Garfin SR (2001) Predicting complications in elderly patients undergoing lumbar decompression. Clin Orthop 384:116–121
13. Bostrom S, Holmgren E, Jonsson O, Lindberg S, Lindstrom B, Winso L, Zachrisson B (1986) Post-operative thromboembolism in neurosurgery. A study on the prophylactic effect of calf muscle stimulations plus Dextran compared to low-dose heparin. Acta Neurochir 80:83–89
14. Brown CA, Eismont FJ (1998) Complications in spinal fusion. Orthop Clin North Am 29:679–699
15. Buehler KO, D'Lima DD, Petersilge WJ (1999) Late deep venous thrombosis and delayed weightbearing after total hip arthroplasty. Clin Orthop 361: 123–130
16. Cain JE, Major MR, Lauerman WC, West JL, Wood KB, Fueredi GA (1995) The morbidity of heparin therapy after development of pulmonary embolus in patients undergoing thoracolumbar or lumbar spinal fusion. Spine 20:1600–1603
17. Catre MG (1997) Anticoagulation in spinal surgery. A critical review of the literature. Can J Surg 40:413–419
18. Chasan-Taber L, Stampfer MJ (1998) Epidemiology of oral contraceptives and cardiovascular disease. Ann Intern Med 128:467–477
19. Clagett GP, Anderson FA, Levine MN, Salzman EW, Wheeler HB (1992) Prevention of venous thromboembolism. Chest [Suppl] 102:391–407
20. Clagett GP, Anderson FA, Geerts W, Heit JA, Knudson M, Lieberman JR, Merli GJ, Wheeler HB (1998) Prevention of venous thromboembolism. Chest [Suppl] 114:531–560
21. Collins R, Scrimgeour A, Yusuf S (1988) Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin: overview of results of randomised trials in general, orthopaedic, and urologic surgery. N Engl J Med 318:1162–1173
22. Colwell CW (2001) Low molecular weight heparin prophylaxis in total knee arthroplasty. The answer. Clin Orthop 392:245–248
23. Comp PC, Spiro TE, Friedman RJ, Whitsett TL, Johnson GJ, Gardiner Jr GA, Landon GC, Jové M (2001) Prolonged Enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. J Bone Joint Surg Am 83:336–345
24. Consortium for Spinal Cord Medicine (1997) Prevention of thromboembolism in spinal cord injury. J Spinal Cord Med 20:259–283
25. Costantini S, Ashkenazi E, Shoshan Y, Israel Z, Umansky F (1992) Thoracic hematomyelia secondary to Coumadin anticoagulant therapy: a case report. Eur Neurol 32:109–111
26. Dahl OE, Gudmundsen TE, Haukeland L (2000) Late occurring clinical deep vein thrombosis in joint-operated patients. Acta Orthop Scand 71:47–50
27. Dahl OE, Bergqvist D, Cohen AT, Frostick SP, Hull RD (2001) Low-molecular-weight heparin as prophylaxis against thromboembolism after total hip replacement. The never-ending story? Acta Orthop Scand 72:198–204
28. De Vivo MJ, Krause JS, Lammertse DP (1999) Recent trends in mortality and causes of death among persons with spinal cord injury. Arch Phys Med Rehabil 80:1411–1419
29. Dearborn JT, Hu SS, Tribus CB, Bradford DS (1999) Thromboembolic complications after major thoracolumbar spine surgery. Spine 24:1471–1476
30. Decousus H, Marchal C, Bonnardot JP, Elias A (1992) Frequence de la maladie thromboembolique en fonction des types de chirurgie. Ann Fr Anesth Reanim 11:244–251
31. Desbordes JM, Mesz M, Maissin F, Bataille B, Guenot M (1993) Etude multicentrique retrospective de la prevention des complications thromboemboliques apres chirurgie discale lombaire. Neurochirurgie 39:178–181

32. Dunn AS, Schechter C, Gotlin A, Vomvolakis D, Jacobs E, Sacks HS, Coller B (2001) Outpatient treatment of deep venous thrombosis in diverse inner-city patients. Am J Med 110: 458–462
33. Falanga A, Rickles FR (1999) Pathophysiology of the thrombophilic state in the cancer patient. Semin Thromb Hemost 25:239–243
34. Ferree BA (1994) Deep venous thrombosis following lumbar laminotomy and laminectomy. Orthopedics 17:35–38
35. Ferree BA, Wright AM (1993) Deep venous thrombosis following posterior lumbar spinal surgery. Spine 18:1079–1082
36. Ferree BA, Stern PJ, Jolson RS, Roberts JM, Kahn A III (1993) Deep venous thrombosis after spinal surgery. Spine 18:315–319
37. Fitzgerald Jr RH, Spiro TE, Trowbridge AA, Gardiner Jr GA, Whitsett TL, O'Connell MB, Ohar JA, Young TR (2001) Prevention of venous thromboembolic disease following primary total knee arthroplasty. A randomized, multicenter, open-label, parallel-group comparison of enoxaparin and warfarin. J Bone Joint Surg Am 83:900–906
38. Fujita T, Kostuik JP, Huckell CB, Sieber AN (1998) Complications of spinal fusion in adult patients more than 60 years of age. Orthop Clin North Am 29:669–678
39. Geerts WH, Code KI, Jay RM (1994) A prospective study of VTE after major trauma. N Engl J Med 331:1601–1606
40. Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA, Wheeler HB (2001) Prevention of venous thromboembolism. Chest [Suppl] 119:132–175
41. Gillespie W, Murray D, Gregg PJ, Warwick D (2000) Prophylaxis against deep-vein thrombosis following total hip replacement: risks and benefits of prophylaxis against venous thromboembolism in orthopaedic surgery. J Bone Joint Surg Br 82:475–479
42. Gillies TE, Ruckley CV, Nixon SJ (1996) Still missing the boat with fatal pulmonary embolism. Br J Surg 83: 1394–1395
43. Grady D, Wenger NK, Herrington D, Khan S, Furberg C, Hunninghake D, Vittinghoff E, Hulley S (2000) Heart and Estrogen/Progestin Replacement Study Research Group. Postmenopausal hormone therapy increased risk for venous thromboembolic disease. Ann Intern Med 132:689–696
44. Haas S (2000) Deep vein thrombosis: beyond the operating table. Orthopedics 23 [Suppl 6]:629–632
45. Hackenberg L, Liljenqvist U, Halm H, Winkelmann W (2001) Occlusion of the left common iliac artery and consecutive thromboembolism of the left popliteal artery following anterior lumbar interbody fusion. J Spinal Disord 14:365–368
46. Haentjens P (2000) Venous thromboembolism after total hip arthroplasty. A review of incidence and prevention during hospitalisation and after hospital discharge. Acta Orthop Belg 66:1–8
47. Haentjens P, Lemaire R (2000) A pragmatic approach to prophylaxis of thromboembolic complications in orthopaedic surgery. Editions Scientifiques et Medicales Elsevier SAS (Paris), Surgical Techniques in Orthopaedics and Traumatology 55–010-D-30
48. Hamilton MG, Hull RD, Pineo GF (1994) Venous thromboembolism in neurosurgery and neurology patients: a review. Neurosurgery 34:280–296
49. Heit JA (2001) Low-molecular-weight heparin: the optimal duration of prophylaxis against postoperative venous thromboembolism after total hip or knee replacement. Thromb Res 101: V163–V173
50. Hull RD (2000) New insights into extended prophylaxis after orthopaedic surgery. The North American Fragmin Trial experience. Haemostasis 30 [Suppl 2]:95–100
51. Hull RD, Brant RF, Pineo GF (1999) Preoperative vs postoperative initiation of low molecular weight heparin prophylaxis against VTE in patients undergoing elective hip replacement. Arch Intern Med 159:137–141
52. Hull RD, Pineo GF, MaC Isaac S (2001) Low-molecular-weight heparin prophylaxis. Preoperative versus postoperative initiation in patients undergoing elective hip surgery. Thromb Res 101:V155–V162
53. Janku GV, Paiement GD, Green HD (1996) Prevention of venous thromboembolism in orthopaedics in the United States. Clin Orthop 325:313–321
54. Kakkar AK, Williamson RCN (1999) Prevention of VTE in cancer patients. Semin Thromb Hemost 25:239–243
55. Kearon C, Hirsch J (1995) Starting prophylaxis for VTE postoperatively. Arch Intern Med 155:366–372
56. Khazim R, Boos N, Webb JK (1998) Progressive thrombotic occlusion of the left common iliac artery after anterior lumbar interbody fusion. Eur Spine J 7:239–241
57. Knop C, Bastian L, Lange U, Oeser M, Zdiichavsky M, Blauth M (2002) Complications in surgical treatment of thoracolumbar injuries. Eur Spine J 11: 214–226
58. Kozak JA, O'Brien JP (1990) Simultaneous combined anterior and posterior fusion: an independent analysis of a treatment for disabled low-back pain patient. Spine 15:322–328
59. Lee AYY, Levine MN (1999) The thrombophilic state induced by therapeutic agents in the cancer patient. Semin Thromb Hemost 25:137–145
60. Lee HM, Suk KS, Moon SH, Kim DJ, Wang JM, Kim NH (2000) Deep vein thrombosis after major spinal surgery. Incidence in East Asian population. Spine 25:1827–1830
61. Marsicano J, Mirovsky Y, Remer S, Bloom N, Neuwirth M (1994) Thrombotic occlusion of the left common iliac artery after an anterior retroperitoneal approach to the lumbar spine. Spine 19:357–359
62. Matzsch T (2000) Thromboprophylaxis with low-molecular-weight heparin: economic considerations. Haemostasis 30 [Suppl 2]:141–145
63. Mollan R (2000) Deep venous thrombosis: prophylaxis and treatment. Editions Scientifiques et Medicales Elsevier SAS (Paris), Surgical Techniques in Orthopaedics and Traumatology, 55–010-D-10
64. Muntz JE (2000) Deep vein thrombosis and pulmonary embolism in the perioperative patient. Am J Managed Care 6 [Suppl 20]:1045–1052
65. Murray DW, Britton AR, Bulstrode CJK (1996) Thromboprophylaxis and death after total hip replacement. J Bone Joint Surg Br 78:863–870
66. National Institute of Health – Thrombosis and Embolism – Consensus Conference (1986) Prevention of venous thrombosis and pulmonary embolism. JAMA 256:744–749
67. Nicolaides AN, et al (1997) Prevention of venous thromboembolism. Int Angiol 16:3–38
68. Nurmohamed MT, Rosendaal FR, Buller HR, Dekker E, Hommes DW, Vandenbroucke JP, Briet E (1992) Low-molecular-weight heparin versus standard heparin in general and orthopaedic surgery: a meta-analysis. Lancet 340:152–156
69. Nurmohamed MT, van Riel AM, Henkes CMA, Koopman MMW, Que GTH, d'Azemar P, Buller HR, ten Cate JW, Hoek JA, van der Meer J, van der Heul C, Turpie AGG, Haley S, Sicurella J, Gent M (1996) Low molecular weight heparin and compression stockings in the prevention of venous thromboembolism in neurosurgery. Thromb Haemost 75:233–238
70. Oda T, Fuji T, Fujita S, Kanemitsu N (2000) Deep venous thrombosis after posterior spinal surgery. Spine 25: 2962–2967

71. O'Shaughnessy DF (2000) Low-molecular-weight heparins in the prophylaxis and treatment of thrombo-embolic disease. Hematology 4:373–380
72. Prestar FJ (1992) Prevention of thromboembolism complications with low molecular weight heparin in microneurosurgical lumbar intervertebral disk operations. Neurochirurgia 35:1–4
73. Pulmonary Embolism Prevention (PEP) Trial Collaborative Group (2000) Prevention of pulmonary embolism and deep vein thrombosis with low-dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet 355:1295–1302
74. Ramirez LF, Thisted R (1989) Complications and demographic characteristics of patients undergoing lumbar discectomy in community hospitals. Neurosurgery 25:226–231
75. Raskas DS, Delamarter RB (1997) Occlusion of the left iliac artery after retroperitoneal exposure of the spine. Clin Orthop 338:86–89
76. Rasmussen MS, Wille-Jorgensen P, Jorgensen LN (1995) Postoperative fatal pulmonary embolism in a general surgical department. Am J Surg 169: 214–216
77. Ravelli V, Marconi F, Lutzemberger L, Marini C, Di Ricco G, Genovesi M (1992) Il rischio di embolia polmonare in neurochirurgia. Minerva Anestesiol 58 [Suppl 1]:173–181
78. Rokito SE, Schwartz MC, Neuwirth MG (1996) Deep vein thrombosis after major reconstructive spinal surgery. Spine 21:853–859
79. Rosendaal FR (1999) Risk factor for venous thrombotic disease. Thromb Haemost 82:610–619
80. Salvati EA, Pellegrini VD, Sharrock NE, Lotke PA, Murray DW, Potter H (2000) Recent advances in venous thromboembolic prophylaxis during and after total hip replacement. J Bone Joint Surg Am 82:252–270
81. Scavarda D, Peruzzi P, Bazin A (1997) Hematomes extra-duraux rachidiens post-operatoires. Quatorze observations. Neurochirurgie 43:220–227
82. Silverstein MD, Heit JA, Mohr DN (1998) Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med 158:585–593
83. Smith MD, Bressler EL, Lonstein JE, Winter R, Pinto MR, Denis F (1994) Deep venous thrombosis and pulmonary embolism after major reconstructive operations on the spine. A prospective analysis of three hundred and seventeen patients. J Bone Joint Surg Am 76:980–985
84. Spain DA, Richardson JD, Polk HC, Bergamini TM, Wilson MA, Miller FB (1997) Venous thromboembolism in the high-risk trauma patient: do risks justify aggressive screening and prophylaxis? J Trauma 42:463–469
85. Spanier DE, Stambough JL (2000) Delayed postoperative epidural hematoma formation after heparinization in lumbar spinal surgery. J Spinal Disord 13:46–49
86. Stolke D, Sollmann WP, Seifert V (1989) Intra- and postoperative complications in lumbar disc surgery. Spine 14:56–59
87. Thromboembolic Risk Factors (THRIFT) Consensus Group (1992) Risk of and prophylaxis for VTE in hospital patients. BMJ 305:567–574
88. Uden A (1979) Thromboembolic complications following scoliosis surgery in Scandinavia. Acta Orthop Scand 50: 175–178
89. Warwick D, Bannister GC, Glew D, Mitchelmore A, Thornton M, Peters TJ, Brookes S (1995) Perioperative low-molecular-weight heparin. Is it effective and safe? J Bone Joint Surg Br 77:715–719
90. Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, Clement C, Robinson KS, Lewandowski B (1997) Value of assessment of pretest probability of deep-vein thrombosis in clinical management. Lancet 350: 1795–1798
91. Wen DY, Hall WA (1998) Complications of subcutaneous low-dose heparin therapy in neurosurgical patients. Surg Neurol 50:521–525
92. West JL (1998) Deep vein thrombosis in spinal surgery. Curr Opin Orthop 9: 43–47
93. West JL, Anderson LD (1992) Incidence of deep vein thrombosis in major adult spinal surgery. Spine [Suppl] 17: 254–257
94. Wisowski DK, Talarico R, Bacsanyii J, Botstein P (1998) Spinal and epidural hematoma and low-molecular-weight heparin. Letter to the editor. N Engl J Med 338:1774
95. Wood KB, Kos PB, Abnet JK, Ista C (1997) Prevention of deep-vein thrombosis after major spinal surgery: a comparison study of external devices. J Spinal Disord 10:209–214