ANTICOAGULATION IN SPINAL SURGERY. A CRITICAL REVIEW OF THE LITERATURE

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OBJECTIVE: To determine the natural incidence of thromboembolic complications and the effect of thromboprophylaxis associated with elective spinal surgery.

DATA SOURCES: A search of the MEDLINE database, using the key words anticoagulation, deep vein thrombosis (DVT) and spine, alone and in different combinations. Individual journals were also searched. Articles investigating the incidence or treatment (or both) of thromboembolism in elective spinal surgery were identified.

STUDY SELECTION: Studies describing elective spinal surgery. The type of surgery, days of recumbency, methods of thromboprophylaxis, study design, surveillance methods, rates of DVT and pulmonary embolism (PE), and type and rates of complications of thromboprophylaxis were determined.

DATA EXTRACTION: Single observer.

DATA SYNTHESIS: Only 15 studies were found. Most were of poor statistical quality: 5 were level IV quality (nonrandomized, historic controls), 8 were level V quality (no controls, cases series), 1 was a level III study (nonrandomized, contemporaneous controls) and 1 was a level II study (small randomized study, moderate to high risk of error). The raw incidence of thromboembolic complications derived from these studies was 7.1% (14.1%) (mean [and SD]). However, because of the poor quality of these studies, this figure is suspect.

CONCLUSIONS: The true incidence of thromboembolic complication in spinal surgery remains unknown. Recommendations for thromboprophylaxis cannot be made from the findings of these studies. There is a need for a well-designed, randomized controlled study to define the efficacy of thromboprophylaxis in elective spinal surgery.

OBJECTIF : Déterminer l'incidence naturelle des complications thrombo-emboliques et les effets de la thromboprophylaxie liés à une intervention chirurgicale élective à la colonne vertébrale.

SOURCES DE DONNÉES : Recherche effectuée dans la base de données MEDLINE au moyen des mots «anticoagulation», «deep vein thrombosis (DVT)» et «spine», seuls et combinés de diverses façons. On a aussi effectué des recherches dans certaines revues et trouvé des articles portant sur l'incidence ou le traitement (ou les deux) de la thrombo-embolie dans des cas d'intervention chirurgicale élective à la colonne vertébrale.

SÉLECTION D'ÉTUDES : Études décrivant une intervention chirurgicale élective à la colonne vertébrale. On a déterminé le type d'intervention chirurgicale, la durée du maintien en position couchée, les méthodes de thromboprophylaxie, la conception de l'étude, les méthodes de surveillance, les taux de thrombose veineuse profonde et d'embolie pulmonaire, ainsi que les types et les taux de complications de la thromboprophylaxie.

EXTRACTION DE DONNÉES : Observateur unique.

SYNTHÈSE DES DONNÉES : On n'a trouvé que 15 études, dont la qualité statistique était médiocre dans la plupart des cas : elle était de niveau IV (non randomisée, témoins historiques) dans 5 cas, de niveau V (aucun témoin, étude de cas) dans 8 cas, il y avait une étude de niveau III (non randomisée, témoins contemporains) et une autre de niveau II (étude randomisée d'envergure restreinte, risque d'erreur moyen à élevé). L'incidence brute de complications thrombo-emboliques dérivée de ces études s'est établie à 7,1 % (14,1 %) (moyenne [et ET]). À cause de la qualité médiocre de ces études, ces chiffres sont douteux.

CONCLUSIONS : L'incidence réelle des complications thrombo-emboliques en cas d'intervention chirurgicale à la colonne vertébrale demeure inconnue. On ne peut formuler de recommandation sur la thromboprophylaxie à partir des résultats de cette étude. Il faut procéder à une étude contrôlée randomisée bien conçue pour définir l'efficacité de la thromboprophylaxie dans les cas d'intervention chirurgicale élective à la colonne vertébrale.

Spinal surgery appears to have inherent risks for the formation of the thromboembolic complications of deep vein thrombosis (DVT) and pulmonary embolism (PE). Long operative time, thoracotomy, a retroperitoneal approach and a long periods of postoperative recumbency are just a few of the risk factors. Because of the clinically silent nature of thromboembolic complications, the use of thromboprophylaxis appears logical.[1,2] Surprisingly, there are only a few published studies addressing the issue of DVT, PE and prophylactic use of anticoagulating agents to prevent these complications in spinal surgery. Unfortunately, most of the studies are retrospective. The few studies that are prospective have deficiencies, so that the true incidence of thromboembolic complications in spinal surgery is unknown. The purpose of this review is to critically appraise the existing literature regarding thromboprophylaxis in elective spinal surgery.

Methods

A search of the literature through MEDLINE, using the key words anticoagulation, DVT and spine, alone and in different combinations, revealed only a few articles from 1965 to 1995. Recent editions of the following journals were also searched independently: *Spine*, *Journal of Bone and Joint Surgery* (American and British editions), *New England Journal of Medicine*, *Journal of the American Medical Association (JAMA)*, *Thrombosis and Haemostasis*, *Seminars in Thrombosis and Haemostasis* and the *Annals of Internal Medicine*. All articles on elective spinal surgery that dealt with DVT, PE and thromboprophylaxis were included. Data extracted from the articles included the type of surgery, days of recumbency, methods of thromboprophylaxis, design of the study, methods of surveillance, rates of DVT and PE, type and rates of complications of thromboprophylaxis. Fifteen articles were found (Table I[3–17]).

Results

Prothero, Parkes and Stinchfield[3] retrospectively studied complications after low-back fusion in 1000 patients during 2 time periods a decade apart. They did not report the use of anticoagulation prophylaxis nor their form of surveillance for thromboembolic complications. Between 1951 and 1953, they identified 21 patients (4.2%) who had thromboembolic disease. This early group had an average recumbency time of 18.5 days, the thromboembolism occurring on average 14 days after operation. Between 1959 and 1963, they identified 11 patients (2.2%) with thromboembolic disease. This later group had an average recumbency time of 10.5 days, the thromboembolism being detected on average 11 days after operation. In the authors' opinion the length of recumbency contributed to the difference in the rate of thromboembolic disease. However, this was a retrospective case series that did not have routine surveillance for thromboembolic complications. Thus, the incidence of clinically silent thrombosis and embolism cannot be inferred.

The results of the Harrington procedure for scoliosis was reported by Uden[4] in a retrospective study of 1229 patients treated between 1963 and 1976, based on reports from scoliosis centres in Denmark, Finland, Norway and Sweden. There was apparently no standardization of definitions, data-gathering, DVT surveillance or DVT prophylaxis. The average age of patients at the time of surgery from the different centres ranged from 14 to 18 years. All patients were restricted to bed for 3 to 5 weeks postoperatively.

Eight cases (0.79%) of symptomatic DVT were diagnosed and confirmed by contrast phlebography. Also, no cases of PE were reported. It is possible that the low incidence of DVT and PE in this study may be partially due to the young age of these patients. It is known that the occurrence of DVT and PE increases with age.[18] Because this was a retrospective, multicentre case series, there were many sources of potential bias. Uden suspected, therefore, that the true incidence of DVT was probably higher than the 6.5 per 1000 cases he found.

The Harrington procedure for scoliosis in 16 patients whose average age was 18 years, was also studied by Nillius and colleagues.[5] All patients were managed by bed rest for 3 to 4 weeks postoperatively. The purpose of their study was to investigate the possible occurrence of asymptomatic PE in this patient population and to evaluate a combined radionuclide phlebography and lung scanning method for diagnosing iliofemoral thrombi and PE. Three patients with symptoms of proximal vessel thrombosis were found to have iliac vein thrombosis, and 6 asymptomatic patients were found to have perfusion defects suggestive of PE. One patient had a ventilation-perfusion scan mismatch consistent with PE. The authors concluded that iliac vein thrombosis is an uncommon postoperative occurrence in the young scoliosis patient. This is supported by the work of Kniffin and associates[18] who reported that the rates of DVT and PE increase with age, thereby implying that the group in the study of Nillius and colleagues should have a low rate of DVT and PE. Also, the small number of subjects (16) in the latter study, which had not been validated for diagnosing iliofemoral thrombi and PE, was uncontrolled and did not account for other sources of DVT. Valid conclusions regarding

the natural incidence of DVT postoperatively in the patient with scoliosis cannot be made from this article.

A prospective study of DVT in 54 children (average age 13.5 years, range from 5.5 to 16.5 years) was reported by Leslie and associates.[6] The children had halo femoral traction for scoliosis before operation. The use of anticoagulation prophylaxis was not reported. The average length of recumbency was 28 days (range from 8 to 53 days). Bilateral ascending phlebography, performed on the lower limbs 2 days before operation, showed clinical evidence of thrombosis in 2 patients (3.7%) who also had abnormal venograms. It is possible, as in other studies,[4,5,18] that age played a role in the low DVT rates seen in this study.

The largest number of patients studied for thromboembolic complications in spinal surgery was reported by Miller, Young and Wang.[7] They published a retrospective review of 7986 patients who underwent 5966

Table I

Reported Thromboembolic (TE) Complication Rates Associated With Spinal Surgery

Series	TE rate, %	TE cases (n = 346)	Total cases (n = 11 912)	Level	Method of prophylaxis	Method of surveillance
Prothero, Parkes and Stinchfield, 1966[3]	4.2	21	1000	V	NR	NR
Uden, l979[4]	0.79	8	1220	V	NR	NR
Nillius et al, 1980[5]	56.25	9	16	IV	NR	Radionuclide phlebography
Leslie et al, 1981[6]	3.7	2	54	IV	NR	Ascending phlebography
Miller, Young and Wang, 1983[7]*	3.5	279	7986	V	NR	NR
Stolke, Sollmann and Seifert, 1989[8]	0.002	1	412	IV	NR	NR
West and Anderson, 1992[9]	14.0	6	41	V	CS + SCS	Colour duplex and Doppler ultrasonography
Ferree, 1993[10]	6.0	5	86	V	CS	Duplex ultrasonography
Ferree et al, 1993[11]	8.1	6	74	V	CS + PCS	Duplex ultrasonography
Ferree, 1994[12]	5.0	3	60	V	TEDs	Duplex ultrasonography
Smith et al, 1994[13]	0	0	317	IV	CS	Duplex and colour Doppler ultrasonography
Dearborn et al, 1995[14]†	3.4	4	116	V	Elastic stockings + SCS	Duplex ultrasonography
Nelson et al, 1995[15]†	0	0	117	IV	TEDs or TEDs + PCS	NR
Regan et al, 1995[16]†	1.2	1	84	III	SCS	Colour Doppler ultrasonography
Rokito, Schwartz and Neuwirth, 1996[17]	0.3	1	329	II	TEDs or GCS + PCS or GCS + low-dose coumarin	Duplex and Doppler ultrasonography
Mean (and standard deviation)	7.1 (14.1)	23 (70)	794 (2022)			

TE rate = deep venous thrombosis (DVT) + pulmonary embolism (PE) rate; TE cases = no. of DVT and PE cases reported; total cases = no. of spinal cases reported in DVT and PE studies; level = level of evidence, II = small randomized studies, uncertain results, moderate to high risk of error, III = nonrandomized, contemporaneous controls, IV = nonrandomized, historic controls, V = no controls, case series; NR = not reported; CS = compression stockings; SCS = sequential compression stockings; PCS = pneumatic compression stockings; TEDs = thigh-high antithrombo-embolic compression stockings; GCS = graduated compression stockings
*No. of cases of DVT and PE were not reported. The figures were calculated from others given in the article.
†Abstract

orthopedic operations over a 3-year period. Screening tests for thromboembolic complications were not routinely performed. They reported a single case of nonfatal pulmonary embolism and 3 cases of clinically evident DVT in cases of adult laminectomy or spinal fusion. However, they did not elaborate on the types (number of levels) of laminectomies, the use of instrumentation, the use of anticoagulation prophylaxis or the length of recumbency. Also, they did not report the total number of nontraumatic spinal procedures performed. However, they stated that their incidence of thromboembolic complications in this subgroup was 3.5%. Because this report was retrospective, with potential sources of biases in data gathering, this figure cannot be considered valid and possibly underestimates the true incidence of thromboembolic complications.

Intra- and postoperative complications in lumbar disc surgery were prospectively investigated by Stolke, Sollmann and Seiffert.[8] One case of fatal pulmonary embolism was reported among the 412 primary and 69 revision procedures studied. However, there was no report any anticoagulation prophylaxis, a control group, the length of recumbency, DVT surveillance, or the rate of silent or clinically evident DVT. Therefore, this low rate of thromboembolic complications may underestimate the natural rate of thromboembolic disease in this patient population.

The first report of the use of duplex Doppler imaging for thromboembolic surveillance in spinal surgery was by West and Anderson.[9] They investigated the incidence of DVT in major adult spinal surgery. Forty-one patients were studied prospectively with postoperative colour duplex Doppler imaging. The study included both elective surgery and trauma. All patients wore compression hose and sequential compression hose, although the differences, if any, between these groups were not factored into the analysis. Six patients (14%) were found to have lower extremity DVT, although location and propagation of the clot were not reported. Because the use of compression hose or sequential compression hose is an intervention and because a control group with neither compression nor sequential compression hose was not used, the natural incidence of thromboembolic events was not measured. It is possible that the true natural incidence of thromboembolic complications is higher than the 14% reported by West and Anderson.

Ferree's group demonstrated 3 different thromboembolic rates in 3 separate published reports. In 1993,[10] postoperative duplex ultrasonography demonstrated 5 (6%) cases of calf DVT among 86 patients who underwent lumbar and thoracic surgery. Only 1 of these 5 had proximal propagation on serial compression ultrasonography. Compression stockings were used as prophylaxis in all patients. Also in 1993,[11] duplex ultrasonography, demonstrated calf DVT in 4 of 74 patients who wore compression hose postoperatively. In this study also were 111 patients who wore intermittent pneumatic compression stockings postoperatively. This last group had no thromboembolic events. It was shown that intermittent pneumatic compression stockings significantly ($p < 0.05$) reduced the incidence of acute postoperative DVT when compared with compression stockings. A control group without anticoagulation prophylaxis was not used. In 1994,[12] 3 (5%) of 60 patients who had lumbar laminotomy and laminectomy were found by compression ultrasonography to have postoperative DVT. In all 3, the thrombi were distal to the knee. Thigh-high antithromboembolic (TED) compression stockings were used in all these patients. There was no control group. In all 3 studies, there was no control group without anticoagulation prophylaxis. Thus, the natural incidence of thromboembolic complications and the efficacy of compression stockings or intermittent pneumatic compression stockings cannot be measured.

A prospective study of 317 patients who had a spinal operation, including those with trauma, was reported by Smith and colleagues[13] Both anterior and posterior procedures were performed on 134 patients. However, no other information was given on the types of procedures performed. All patients wore compression stockings postoperatively. The average length of recumbency was not reported. Twelve patients were discharged before the fourth postoperative day. None of them had clinical evidence of DVT. Of the remaining patients, 126 (40%) were randomized for screening for asymptomatic thrombosis. The randomization method consisted of the ward clerk choosing a patient for screening depending on the availability of the ultrasound machine on the particular day. This pseudo-randomization procedure is fraught with selection bias, especially with respect to the clerk. Duplex ultrasonography with colour Doppler imaging was used as a screening technique. Smith and colleagues found no evidence of DVT in the patients studied. However, fatal PE developed in a patient who was not screened. The extremely low number of thromboembolic complications reported in this study may have been due to the inadequate randomization, incomplete screening of patients or because all patients wore compression stockings postoperatively (an intervention for thromboembolic complications).

Several recent abstracts have been published regarding DVT and PE in spinal surgery. Duplex ultrasonography was used by Dearborn and associates[14] to prospectively identify DVT in 116 adults. They detected only 1 asymptomatic DVT (0.9%). Three patients (2.6%) subsequently had symptomatic PE, implying that the ultrasonogram did not identify the DVT source before embolization. However, the timing of the ultrasonography was not standardized. Thus, the DVT and subsequent PE may have developed after the ultrasonography. Also, all patients wore elastic stockings and sequential compression boots just before surgery and postoperatively (prophylactic measuresfor of DVT and PE), thus confounding the screening results .

A randomized study of thigh-high TED stockings only versus TED hose and pneumatic compression stockings was published in an abstract by Nelson and colleagues.[15] One hundred and seventeen patients who underwent spinal fusion were randomized in the operating room to 1 of the 2 thromboprophylaxis arms. All of the patients wore the stockings until discharge. All patients were given 600 mg of buffered acetylsalicylic acid (ASA) twice daily. Neither inclusion nor exclusion criteria were defined. No patients were found to have DVT either clinically or by ultrasonography. This study does not shed any light on the natural incidence of DVT or PE in spinal surgery because TED stockings, pneumatic compression stockings and ASA are all are prophylactic treatments for DVT and PE.

A prospective study using Doppler ultrasonography for surveillance was reported by Regan and colleagues[16] in abstract form. The lower extremities of 86 patients who had undergone spinal surgery were scanned. Inclusion and exclusion criteria were not de-fined. Patients who were placed in the knee–chest position for surgery had sequential compression devices applied immediately after surgery and continued until discharge. Patients placed in the prone position for surgery wore sequential compression devices intraoperatively and postoperatively. The number of patients in each subgroup was not reported. All patients were also given ASA (650 mg twice daily) postoperatively. These authors reported only 1 case of DVT (1.2%) found by ultrasonography. The natural incidence of DVT and PE after spinal surgery remains unknown because this study used prophylactic treatment in the prevention of DVT and PE.

The most recent paper regarding DVT in spinal surgery is that by Rokito, Schwartz and Neuwirth.[17] They prospectively randomized spinal surgery patients to either graduated compression (TED) stockings only (group 1), graduated compression stockings and pneumatic compression stockings (group 2) or graduated compression stockings with low-dose coumadin (group 3). Of the 329 patients evaluated only 110 were randomized. The remaining 229 patients received TED stockings with or without pneumatic compression boots. Only randomized patients had duplex Doppler scanning of both lower extremities. All randomized patients were clinically asymptomatic, and all scans but 1, which was indeterminate, were normal. One of the nonrandomized patients had a clinically significant DVT. Rokito, Schwartz and Neuwirth reported their DVT rate as 0.3%. However, this study had several deficiencies that make this reported DVT rate suspect. The study was not blinded, having both patient and investigator bias. The actual number randomized to treatment groups was low, giving very low numbers in each treatment group: group 1 had 42 patients, group 2 had 33 patients, group 3 had 35 patients. This low number of patients subjects the study to a high probability of committing a type II error.[19] They included their nonrandomized patients, and thus a noncontrolled population, in their calculation, thus confounding the data. All patients in this study had some form of prophylactic treatment for DVT. Thus, because this study has several major deficiencies, the natural incidence of DVT and PE cannot be determined.

The raw average of thromboembolic complications calculated from these studies is 7.1% (14.1%) (mean [and standard deviation]). However, because of the poor statistical quality of the studies, this figure is not reliable.

Discussion

One of the major causes of death and morbidity among hospitalized patients is venous thromboembolism. In the United States, PE caused more than 100 000 deaths in this setting and contributed to another 100 000 deaths.[20,21] In Massachusetts, there is a reported in-hospital case-fatality rate of 12%.[22] However, this disease is clinically silent in the majority of cases. The diagnosis has been made only at autopsy in 70% to 80% of patients who die of PE.[18,23] Because of the low autopsy rate in both the US and Canada, the true incidence of PE and DVT is unknown. It is possibly higher than currently thought to be and has led some authors to believe that DVT may be the single most common cause of preventable death.[24,25]

Because of the clinically silent nature of DVT, prophylaxis for this disease is rational. Clinical diagnosis is insensitive and unreliable because there are few specific symptoms of both PE

and DVT.[2] The first manifestation may be death due to PE, thereby making reliance on clinical diagnosis and exposing at-risk patients to high risks of mortality unacceptable. Most deaths due to acute PE occur within 30 minutes of onset.[2] Thus, prophylaxis to prevent PE is much more rational than attempting to treat acute cases of PE.

There are only 15 published articles on thromboprophylaxis in spinal surgery. Of these, 5 are of level IV quality (nonrandomized, historic controls[26])[5,6,8,13,15] and 8 are of level V quality (no controls, case series[26]).[3,4,7,9–12,14] There was one level III abstract[16] (nonrandomized, contemporaneous controls[26]). However, in this study all patients were given some form of thromboprophylaxis, and the study had a small number of subjects. Their incidence of DVT in this report is undoubtedly after thromboprophylaxis and not reflective of the natural incidence of DVT. There was 1 level II quality article[17] (small randomized studies, uncertain results, moderate to high risk of error[26]). However, there was a high probability of a type II error in this study, making the conclusions suspect.[19]

From these 15 reports, it is obvious that the natural incidence of thromboembolic complications in spinal surgery is unknown. It appears that the rate of DVT and PE in spinal surgery is low, 7.1% (14.1%) (Table I[3–17]) and that some form of compression stockings are sufficient for thromboprophylaxis (Table I[3–17]). However, it is highly probable that all of these studies underestimated the true incidence of DVT and PE because all of them are faulted and because of the silent but deadly nature of this disease. The natural incidence of thromboembolic complications in elective spinal surgery cannot be determined from the current literature. Also, recommendations on the use of thromboprophylaxis cannot be made because of the lack of good scientific evidence.

The risk factors for thromboembolic complications after spinal surgery are also unknown. Furthermore, it is not known if prophylaxis to prevent DVT and PE is safe, clinically effective and cost-effective. Lower extremity DVT can lead to potentially fatal pulmonary emboli[21–23,25,27,28] and long-term hemodynamic and clinical sequelae affecting the lower extremity.[27–29] Current thromboprophylaxis in spinal surgery varies not only between institutions but also between surgeons within the same institutions. Because current thromboprophylaxis in spinal surgery is not based on good scientific evidence, there is an ethical impetus for conducting such a study.[30–37] For these reasons, there is a need to study the role of anticoagulation prophylaxis in spinal surgery in a properly designed, level I study: a randomized, double-blind, placebo-controlled study of anticoagulation in spinal surgery. It appears that PE and DVT are more prevalent in the elderly.[2,5] Perhaps a randomized controlled study on anticoagulation in spinal surgery should be directed toward elderly people. To the best of my knowledge, no such studies are currently being performed.

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