

DEEP VEIN THROMBOSIS AND THROMBOEMBOLISM IN PATIENTS WITH CERVICAL SPINAL CORD INJURIES

RECOMMENDATIONS

- Standards:
- Prophylactic treatment of thromboembolism in patients with severe motor deficits due to spinal cord injury is recommended.
 - The use of low molecular weight heparins, rotating beds, adjusted dose heparin, or a combination of modalities is recommended as a prophylactic treatment strategy.
 - Low dose heparin in combination with pneumatic compression stockings or electrical stimulation is recommended as a prophylactic treatment strategy.
- Guidelines:
- Low dose heparin therapy alone is not recommended as a prophylactic treatment strategy.
 - Oral anticoagulation alone is not recommended as a prophylactic treatment strategy.
- Options:
- Duplex Doppler ultrasound, impedance plethysmography, and venography are recommended for use as diagnostic tests for DVT in the spinal cord injured patient population.
 - A three-month duration of prophylactic treatment for DVT and PE is recommended.
 - Vena cava filters are recommended for patients who fail anticoagulation or who are not candidates for anticoagulation and/or mechanical devices.

RATIONALE

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are problems frequently encountered in patients who have sustained cervical spinal cord injuries. Several means of prophylaxis and treatment are available including anticoagulation, pneumatic compression devices, and vena cava filters. The purpose of this evidence-based medicine review is to evaluate the literature on the methods of prevention and identification of DVT and PE complications in patients following acute cervical spinal cord injury.

SEARCH CRITERIA

A National Library of Medicine computerized literature search from 1966 through 2001 was performed using Medical Subject Headings in combination with “spinal cord injury”: “deep venous thrombosis” “pulmonary embolism” and “thromboembolism.” The search was limited to human studies in the English language. This resulted in 129 citations. Duplicate references, reviews, letters, and tangential reports were discarded. Thirty-seven papers dealing with the prophylaxis or treatment of thromboembolic disease in adult spinal cord injured patients make up the basis for this guideline and are summarized in Evidentiary Table format. Supporting references included four evidence-based reviews published by various organizations concerned with thromboembolism prophylaxis and treatment in a variety of patient populations. Finally, several series dealing with thromboembolism in general trauma patients with results germane to a discussion of spinal cord injured patients are included in the bibliography as supporting documents.

SCIENTIFIC FOUNDATION

The incidence of thromboembolic complications in the untreated spinal cord injury (SCI) patient population is high. Depending upon injury severity, patient age, and the methods used to diagnose a thromboembolism, the incidence of thromboembolic events ranges from 7% to 100% in reported series of patients receiving either no prophylaxis or inadequate prophylaxis. (3,8,10,13,16,22,23,26,27,29,30,33,36)) Substantial morbidity and mortality has been associated with the occurrence of DVT and PE events in the SCI patient population. (6,11)

Prophylaxis

Prophylactic therapy has been shown to be effective for the prevention of DVT and PE. In a small randomized study, Becker et al demonstrated that the use of rotating beds during the first 10 days following SCI decreased the incidence of DVT. Four of five control patients were diagnosed with DVT (by fibrinogen screening) compared to one of ten treated patients. (2) The use of low dose heparin (5000 units given via subcutaneous injection twice or three times daily) has been described by several authors. (4,8,16,17,22,30,37) Hachen published the results of a retrospective historical comparison of low dose heparin versus oral anticoagulation in a group of 120 SCI patients. He found a lower incidence of thromboembolic events in the low dose heparin group compared to the oral anticoagulation group.(17) In 1977, Casas et al reported the results of a prospective assessment of low dose heparin in SCI patients. They administered heparin for a mean period of 66 days in 18 SCI patients and noted no thromboembolic events as detected by clinical examination.(4) Watson reported a lower incidence of thromboembolic events with the use of low dose heparin when compared to no prophylaxis in a retrospective historical cohort study.(37) Frisbie and Sasahara however, found that low dose heparin did not affect the incidence of DVT in a prospective study of 32 SCI patients compared to treatment with twice

daily physical therapy alone. These authors felt that the lack of effect was due to the very low incidence of DVT in their control group compared to other series because of the aggressive physical therapy paradigm employed in their patients. Although they performed venous occlusion plethysmography screening (VOP) with confirmatory venography weekly, the incidence of DVT was only 7% in both groups. (8) An identical observed frequency of DVT in both treatment groups cannot be explained by anything other than that the treatments were equivalent in this study. This incidence is substantially lower than that reported by two separate groups of investigators a decade later. In 1992, Kulkarni et al reported a much higher incidence of DVT (26%) and of PE (9%) in a group of 100 SCI patients prospectively treated with low-dose heparin.(22) In 1993, Gunduz et al reported a 53% incidence of DVT confirmed by venography in 31 patients they managed with SCI treated with low dose heparin.(16) In a study published in 1999, Powell et al noted that the incidence of DVT in 189 SCI patients receiving prophylaxis was significantly lower than that identified in SCI patients who did not receive prophylaxis, 4.1% vs. 16.4%. They found, in addition, that DVT in the prophylaxis group occurred in patients who received low dose heparin alone.(30)

Several studies have demonstrated that better prophylactic therapies than low dose heparin exist.(13,25,26) Green et al published a randomized controlled study comparing low dose versus adjusted dose heparin (dose adjusted to APTT 1.5 times normal) in SCI patients.(13) They found that patients treated with adjusted dose heparin had fewer thromboembolic events (7% versus 31%) during the course of their ten-week study, but had a higher incidence of bleeding complications. Merli et al in 1988 reported their findings of the additive protective effects of electrical stimulation in combination with low dose heparin, heparin alone, and placebo in 48 SCI patients treated for four weeks duration. In this Class I prospective,

randomized trial, they found that the heparin therapy alone group had a similar incidence of DVT compared to the placebo group. The combination of low dose heparin and electrical stimulation significantly decreased the incidence of DVT (one of fifteen patients compared to the other two treatment groups (eight of 16 low dose heparin alone and eight of 17 placebo, $p < 0.05$).(26) In 1992, this same group reported that heparin in combination with pneumatic stockings was equal to the effectiveness of heparin plus electrical stimulation. The heparin in combination with electrical stimulation group and the placebo group for this comparison were a historical cohort. This constitutes Class III evidence because the comparison group is a historical one. (25) Winemiller et al studied a large series of 428 SCI patients with a multivariate analysis and found that the use of pneumatic compression devices for six weeks duration was associated with a significant decrease in thromboembolic events (odds ratio of 0.5 (95% CI 0.28-0.90)).(40) Low dose heparin treatment seemed to have a protective effect as well, however the effect of heparin alone was not statistically significant.

Recently, low molecular weight heparins (LMWH) have been studied as prophylactic therapy for thromboembolism in SCI patients. Green et al treated a series of SCI patients with eight weeks of LMWH (tinzaparin) and compared the results with a historical cohort of patients treated with low dose or adjusted dose heparin.(12) They found that the use of LMWH compared favorably with the use of either heparin dosing regimen in terms of fewer thromboembolic events (16 of 79 in heparin group versus 7 of 68 in LMWH group, $p = 0.15$) and a significant decrease in bleeding complications (nine of 79 in heparin group versus one of 68 in LMWH group, $p = 0.04$).(12) More recently, Harris et al performed a retrospective study of LMWH (enoxaparin) administration in a series of 105 patients with spinal injuries. Forty of their 105 patients suffered neurologically complete injuries. No patient exhibited clinical or

ultrasound evidence of DVT and no patient suffered a PE treated with LMWH.(18) Roussi et al reported a 9% incidence of DVT in a study involving 69 SCI patients receiving LMWH, testimony to the fact that no prophylactic therapy is 100% effective.(32)

The use of inferior vena cava (IVC) filters as prophylactic devices for thromboembolism has been advocated.(19,20,31,39) Wilson et al placed caval filters in 15 SCI patients who were concurrently treated with either low dose heparin or pneumatic stockings. None suffered a PE during a one-year follow-up period. The one-year patency rate of the IVC was 81%.(39) These authors reported that their results are superior to those from a historical cohort of 111 patients treated without IVC filters. Seven of the cohort patients suffered a PE, however six of the seven were not receiving any prophylaxis at the time of their PE. The patient who was receiving DVT prophylaxis suffered a gunshot wound to the spine.(39) Khansarina and colleagues described a historical cohort study of 108 general trauma patients treated with prophylactic IVC filter placement. None of these patients suffered a PE. They compared this group to a historical cohort of 216 patients treated (apparently) with either low dose heparin or pneumatic compression devices prior to the use of IVC filters. Thirteen of these 216 suffered PE, nine were fatal. (20) The overall mortality of the filter group was lower than the control group, but this difference was not significant (16% vs. 22%).(20) Tola and colleagues have shown that percutaneous IVC filter placement in the ICU setting is as safe and is less costly than IVC filter placement in the operating room or the invasive radiology suite.(35) These authors suggest that IVC interruption is an effective means to prevent PE. Placement of filters is not without complications. Balshi et al, Kinney et al, and others have described distal migration, intraperitoneal erosion, and symptomatic IVC occlusion in patients with SCI treated with IVC filters.(1,15,21) Balshi et al have hypothesized that quadriplegic patients are at higher risk for

complications from IVC filter placement due to loss of abdominal muscle tone, as well as the use of the “quad cough” maneuver.(1) There has been no study performed to date comparing the use of prophylactic IVC filters to the use of modern methods of pharmacologic PE and DVT prophylaxis.

Duration of Prophylaxis

The vast majority of thromboembolic events appear to occur within the first 2-3 months following injury. Naso described his experience with four patients with PE in a group of 43 SCI patients. All four PE events were documented within three months injury. (28) Perkash et al reported an 18% incidence of thromboembolism in a series of 48 patients with acute spinal cord injury and two patients with transverse myelitis. Only one patient had a new onset PE three months after injury; two other patients had recurrent PE three months after injury due to existing DVT. (29) Lamb et al described a series of 287 SCI patients. The overall risk of thromboembolic events in their patient population was 10%. The vast majority of events occurred within the first six months following injury. Twenty-two of 28 events they documented occurred within the first three months of injury.(23) El Masri and colleagues reported 21 documented events of PE in a series of 102 spinal injured patients. Twenty of twenty-one events occurred within the first three months following SCI. A pulmonary embolism occurred in a patient with a history of PE whose therapeutic anticoagulation was discontinued for gallbladder surgery.(7) DeVivo et al found a 500-fold risk of dying from PE in the first month following SCI compared to age- and gender-matched non-injured patients. This risk decreased with time, however remained approximately 20 times greater than that for normative controls six months following injury.(6) McKinley et al studied chronic spinal injured patients in a rehabilitation center setting and found an incidence of DVT of 2.1% in the first year following injury. This

incidence dropped to between 0.5% and 1% per year thereafter.(24) Based upon these data, it is apparent that the great majority of thromboembolic events (DVT and PE) occur within three months of acute spinal injury. Although late thromboembolic events can occur, the risk of these events must be balanced against the cost and risks of indefinite anticoagulation. Prolonged prophylactic anticoagulation therapy is not without risk, and is associated with bleeding complications.(12,13) The vast majority of studies addressing prophylactic treatment for DVT and PE have utilized treatment courses of eight to 12 weeks duration with success. For these reasons, it is recommended that prophylactic treatment be continued for eight to 12 weeks in spinal cord injury patients without other major risk factors for DVT and PE (previous thromboembolic events, obesity, advanced age). Prophylactic treatment may be discontinued earlier in patients with useful motor function in the lower extremities, as these patients appear to be at less risk for DVT and PE. (11,27)

Diagnosis

The diagnosis of DVT in various studies has been made based on clinical criteria, Doppler ultrasound examination, venous occlusion plethysmography (VOP), venography, fibrinogen scanning or by D-Dimer measurement. (2-4,7-10,13,14,16,17,22,26-30,32,34,36-38,41) Although venography may be considered a “gold standard” examination for DVT, venography is not possible in all patients, is invasive, and expensive.(10) Gunduz and colleagues report a 10% incidence of adverse effects from venography including post-venographic phlebitis and allergic reactions.(16) Doppler ultrasound examination and VOP are both less invasive, less expensive, and more broadly applicable.(10,30) The sensitivity and specificity of these examinations when compared with venography has been generally reported

to range from 80% to 100%.⁽⁵⁾ Chu et al compared Doppler ultrasound and VOP with the clinical examination and found all three to agree 100% of the time in a small series of 21 patients. ⁽⁵⁾ Perkash and colleagues studied a series of 48 SCI patients with daily physical examinations and weekly VOP. They found that the sensitivity of the clinical examination compared to VOP was 89%. The specificity was 88%, the negative predictive value was 97%, and the positive predictive value was 62% in their study.⁽²⁹⁾ Other authors have described the increased sensitivity of fibrinogen scanning and the use of D-Dimer measurements for the diagnosis of DVT.^(32,34) Increased sensitivity is associated with decreased specificity. For example, Roussi et al reported 100% sensitivity and 100% negative predictive value with D-Dimer determinations compared to Doppler ultrasound and the clinical examination. However, the specificity of D-Dimer was only 34%, and the positive predictive value was only 13%.⁽³²⁾ Similarly, Todd et al found that fibrinogen scanning was positive in all 20 patients studied in a prospective fashion, yet the diagnosis of DVT was confirmed by another test in only half of the cases.⁽³⁴⁾ Overall, no single test is completely applicable, accurate, and sensitive for the detection of DVT in the SCI patient population. Furthermore, a substantial number of patients who suffer from PE are found to have negative lower extremity venograms.^(7,10) The Consortium for Spinal Cord Medicine has recommended the use of ultrasound for the study of patients with suspected DVT, and venography when clinical suspicion is strong and the ultrasound examination is negative.⁽¹¹⁾ Based upon the medical evidence available, these recommendations appear to be sound.

SUMMARY

Thromboembolic disease is a common occurrence in patients who have sustained a cervical spinal cord injury and is associated with significant morbidity. Class I medical evidence exists demonstrating the efficacy of several means of prophylaxis for the prevention of thromboembolic events. Therefore, patients with SCI should be treated with a regimen aimed at prophylaxis.

Although low dose heparin therapy has been reported to be effective as prophylaxis for thromboembolism in several Class III studies, other Class I, Class II, and Class III medical evidence indicates that better alternatives than low dose heparin therapy exist. These alternatives include the use of low molecular weight heparin, adjusted dose heparin, or anticoagulation in conjunction with pneumatic compression devices or electrical stimulation. Oral anticoagulation alone does not appear to be as effective as these other measures used for prophylaxis.

The incidence of thromboembolic events appears to decrease over time and the prolonged use of anticoagulant therapy is associated with a definite incidence of bleeding complications. There are multiple reports of the beneficial effects of the prophylaxis therapy for six to twelve weeks following spinal cord injury. Very few thromboembolic events occur beyond three months following injury. For these reasons, it is recommended that prophylactic therapy be discontinued after three months unless the patient is at high risk (previous thromboembolic events, obesity, advanced age). It is reasonable to discontinue therapy earlier in patients with retained lower extremity motor function after spinal cord injury, as the incidence of thromboembolic events in these patients is substantially lower than those patients with motor complete injuries.

Caval filters appear to be efficacious for the prevention of PE in SCI patients. The relative efficacy of caval filters versus prophylactic combination therapy with LMWH and pneumatic compression stockings has not been studied. Caval filters are associated with long-term complications in SCI patients, although these complications are relatively rare. Caval filters are recommended for SCI patients who have suffered thromboembolic events despite anticoagulation and for SCI patients with contraindications to anticoagulation and/or the use of pneumatic compression devices.

There are several methods available for the diagnosis of DVT. Venography is considered the “gold standard,” but is invasive, not applicable to all patients, and associated with intrinsic morbidity. Duplex Doppler ultrasound and venous occlusion plethysmography have been reported to have sensitivities of approximately 90% and are non-invasive. It is reasonable to use these non-invasive tests for the diagnosis of DVT and to reserve venography for the rare situation when clinical suspicion is high and the results of VOP and ultrasound testing are negative.

KEY ISSUES FOR FUTURE INVESTIGATION

Although thromboembolic events in the SCI patient are associated with significant morbidity, no study has demonstrated improved outcomes in SCI patients as a result of surveillance testing for them. A prospective study evaluating six-month outcomes in patients treated with prophylaxis with or without surveillance ultrasound imaging would be a substantial and potentially cost-saving contribution to the literature.

Caval filters appear to be effective in preventing PE and many institutions are using these devices as first-tier preventive therapy without trying other preventive measures. Caval filters

have not been compared to LMWH or combination therapy with anticoagulants and pneumatic compression devices for efficacy in the SCI patient population. As filters do appear to be associated with long-term morbidity in a fraction of SCI patients, a prospective study needs to be performed to establish whether the potential increase in protection against PE offsets the risks for long-term complications. A study comparing the use of vena caval filters prophylactically versus other modes of prevention with the use of filters placed only after failure of alternative methods should be instituted, including cost-effectiveness outcomes of each mode of prevention currently employed in spinal cord injured patients.

EVIDENTIARY TABLE

First Author Reference	Description of Study	Data Class	Conclusions
Chen et al, Arch Phys Med and Rehab, 1999	Large population of SCI pats (1649) studied from admission to rehab (mean 19 days) to discharge (mean 50 days). Incidence of DVT + PE declining over time but remains 6.1% despite prophylaxis.	Class III	DVT/PE still problems despite prophylaxis. (See McKinley for follow-up)
McKinley et al, Arch Phys Med Rehabil, 1999	Chronic SCI population studied. Incidence of DVT highest during first year (2.1%) but then drops off to 0.5-1% per year thereafter.	Class III	Risk of DVT/PE highest during first year following injury and then risk drops significantly.
Powell et al, Arch Phys Med Rehab, 1999	Incidence of DVT in SCI population (n=189) on transfer to rehab (dx with ultrasound) was 4.1% in group who received prophylaxis vs. 16.4% in group without prophylaxis. In prophylaxis group, DVTs only occurred in pts receiving heparin alone.	Class II	Prophylaxis decreases incidence of DVT in SCI population. Heparin alone was the least effective measure.
Roussi et al, Spinal Cord, 1999	6/67 (9%) of SCI patients developed DVT despite prophylaxis with LMWH. D-Dimer had 100% negative predictive value compared to duplex Doppler. (However, specificity only 34% and PPV 13%)	Class I for diagnostic test, class III otherwise	Incidence of DVT despite prophylaxis with LMWH still 9%. D-Dimer is sensitive but not specific test for DVT
Winemiller et al, Journal of Spinal Cord Medicine, 1999	Retrospective study of 428 SCI patients. TE occurred in 19.6%. Compression stockings and sequential compression devices lowered risk of TE. Effects of low dose heparin were seen in first 14 days but were not significant. TEs all occurred in first 150 days.	Class III	SCD and stockings reduce risk of thromboembolism. Low dose heparin may be effective in first 14 days following injury.
Tomaio et al, Journal of Spinal Cord Medicine, 1998	Enoxaprin (LMWH) vs heparin use for initial DVT treatment in group of 6 SCI patients.	Class III	Enoxaprin was cost effective alternative to IV heparin for initial treatment of DVT
Harris et al, Am J of Phys Med and Rehab, 1996	Retrospective study of enoxaparin (LMWH) in 105 SCI pts. (1/3 intact, 40 complete). No clinical DVT/PE in 105, no ultrasound evidence in 60.	Class III	Enoxaparin is safe and effective for DVT prophylaxis in the SCI patient.
Khansarina et al, Journal of Vascular Surgery, 1995	Retrospective historical cohort comparison of prophylactic PGF in 324 general trauma patients. PGF group had fewer PE than control group.	Class III	Greenfield filter safe and effective for PE prophylaxis in general trauma population
Geerts et al, New England Journal of Medicine, 1994	Prospective evaluation of 716 trauma patients (no prophylaxis) with VOP and venography. Incidence of DVT in SCI population (N=66) was 62%	Class III	DVT is very common in SCI patients if no prophylaxis used
Wilson et al, Neurosurgery, 1994	Inserted Caval filters in 15 SCI patients. None had DVT or PE in 1 year. Claims this result superior to historical controls (No evidence presented to support this claim). One-year patency rate was 81%.	Class III	Insertion of caval filters appears to be safe in SCI patients.

First Author Reference	Description of Study	Data Class	Conclusions
Green et al, Archives of Physical Medicine and Rehabilitation, 1994	Historical cohort comparison of LMWH and standard and adjusted dose heparin prophylaxis. Trauma patients treated with 8 week course of LMWH had fewer bleeding episodes ($p<0.05$) and thromboembolic complications ($p=0.15$) than those treated with heparin.	Class III	LMWH may be safer and more effective for prophylaxis than mini dose or adjusted dose heparin
Gunduz et al, Paraplegia, 1993	31 SCI patients on low dose heparin therapy underwent venography. Incidence of DVT was 53.3%	Class III	Incidence of DVT high in SCI patients despite low dose heparin (therapy started on rehab unit)
Burns et al, Journal of Trauma, 1993	Prospective assessment of DVT in high risk trauma patients with US. Found incidence of 21% (12/57) despite low dose heparin or pneumatic boots in 85%.	Class III	DVT is common despite use of low dose heparin or pneumatic boots.
Lamb et al, J Am Paraplegia Soc, 1993	287 chronically injured SCI patients followed. Overall incidence of thromboembolic events was 10%, vast majority of events in first 6 months	Class III	Prophylactic therapy not necessary beyond 6 months in SCI population
Kulkarni et al, Paraplegia, 1992	100 SCI patients prospectively treated with low dose heparin. 26% incidence of clinically detected DVT (9% PE) noted	Class III	DVT and PE incidence significant despite low dose sq heparin
Merli et al, Paraplegia, 1992	Heparin plus pneumatic stockings equal to historical controls of heparin plus stimulation and better than historical controls of heparin or placebo in SCI patients.	Class II	Low dose heparin plus pneumatic hose safe effective as DVT prophylaxis in SCI patients.
Waring and Karunas, Paraplegia, 1991	Large database (1419) of SCI patients. Incidence of DVT was 14.5%, PE 4.6%. Severity of injury was a predictor of DVT and age was a predictor of PE. No mention made of prophylactic measures.	Class III	DVT and PE are significant problems in SCI population. Age and injury severity need to be addressed in studies comparing treatment modalities.
Yelnik et al, Paraplegia, 1991	Prospective study of 127 SCI patients with phlebography. 29/127 had DVT on admission to rehab unit. Of 87 patients with initially negative studies, 12 developed DVT despite prophylaxis for up to 80 days.	Class III	Incidence of DVT in SCI population is high and high risk period extends to end of third month. Authors recommend periodic screening with phlebography.
Balshi et al, Journal of Vascular Surgery, 1989	Case series of 13 quadriplegic patients who had vena caval filters placed for DVT or PE. Abnormalities of the filter were detected in 5/11 patients who had follow-up X-rays. Two patients required laparotomy to remove filters, four had distal migration, and two had narrowing of diameter associated with caval occlusion. Nine of these 11 patients were treated with the "quad cough" technique.	Class III	Filter placement may be associated with significant long-term morbidity in the SCI population, particularly those requiring aggressive pulmonary toilet.

First Author Reference	Description of Study	Data Class	Conclusions
DeVivo et al, Arch Intern Med, 1989	Epidemiological study of causes of death for SCI patients. Highest ratios of actual to expected causes of death were for pneumonia, PE, and septicemia. The risk ratio for TE dropped significantly after the first month post injury but remained elevated at 6 months post injury.	Class III	TE is a significant problem for patients who survive SCI. Biggest period of risk is in first few months following injury, but risk continues even after 6 months.
Green et al, JAMA, 1988	RCT of Low dose vs. adjusted dose heparin in SCI patients. Rate of TE lower in adjusted dose group (7% vs 31%) (intent to treat p=ns), but also had higher rate of bleeding complications (7 of 29).	Class I	Adjusted dose heparin more effective than low dose heparin, bleeding more common in adjusted dose group.
Merli et al, Arch Phys Med Rehabil, 1988	Prospective randomized trial of placebo vs. mini dose heparin vs. heparin plus electrical stimulation in group of 48 SCI patients. Heparin group=placebo group at 50%, stim group significantly fewer DVT	Class I	Low dose heparin no better than placebo, heparin plus electrical stimulation much better for DVT prophylaxis in SCI patients.
Weingarden et al, Paraplegia, 1988	Retrospective review of 148 SCI patients. Ten had documented DVT or PE. Of six patients who had adequate records, all 6 had fever as a presenting sign, 4 had no other clinical signs recorded. All episodes occurred in first 12 weeks.	Class III	Fever may indicate thromboembolic disease in SCI patients.
Becker et al, Neurosurgery, 1987	Randomized trial of rotating versus non-rotating beds in the acute setting following SCI (10 days) N=15 Plethysmography and fibrinogen leg scans used	Class I	Rotating beds reduce the incidence of DVT during the first 10 days following SCI
Tator, Canadian Journal of Neurological Sciences, 1987	17% incidence of DVT in series of 208 SCI patients. Incidence was higher in operated patients (23%) compared to non operated (10%). Use of prophylaxis is not mentioned.	Class III	Patients requiring surgery may have higher incidence of DVT.
Chu et al, Archives of Physical Medicine and Rehabilitation, 1985	Comparison between doppler US, Venous occlusion plethysmography and clinical exam in SCI patients. All had sensitivity and specificity of 100% in small (n=21) series. Overall incidence 19%. (Class III because no gold standard used)	Class III	Doppler US, VOP, and clinical examination all good for diagnosis of DVT
Myllynen et al, Journal of Trauma, 1985	Compared incidence of DVT in immobilized spinal injured patients with and without paralysis. Those with paralysis had a 100% DVT incidence (fibrinogen scan) vs. 0% for patients immobilized following spinal fracture without paralysis.	Class III	Incidence of DVT is very high in SCI patients and is not totally dependent on immobilization.
El Masri and Silver, Paraplegia, 1981	Retrospective review of 102 patients with SCI. There were 21 episodes of PE in 19 patients. No patient with PE was adequately anticoagulated at the time of the PE (oral phenindione). Only 8/19 patients had evidence of DVT by exam or VOP.	Class III	The authors recommend prolonged treatment (up to 6 months) in patients with obesity or prior history of DVT.

First Author Reference	Description of Study	Data Class	Conclusions
Frisbie and Sasahara, Paraplegia, 1981	Small prospective controlled study of Low dose (5000 μ BID) heparin vs. Control group. No difference in incidence of DVT noted (only 7% in each group). Authors suggest protective effect of frequent physiotherapy.	Class II	No difference between low dose heparin and control groups in SCI patients receiving twice daily physiotherapy.
Perkash et al, Paraplegia, 1980	Treatment of 8 patients with thromboembolism discussed. Authors used heparin followed by coumadin with reasonable results	Class III	Anticoagulation is effective treatment for SCI patients with thromboembolism
Perkash et al, Paraplegia, 1978-9	Incidence of thromboembolism in 48 SCI patients was 18% Clinical exam sensitivity 89%, specificity 88%, NPV 97%, PPV 62% 1/3 of thromboembolic events occurred >12 weeks following injury	Class I for diagnostic tests, Class III otherwise	Clinical examination appears to be quite good for detection of DVT in subacute setting. Period of risk may extend beyond 12 weeks.
Watson, Paraplegia, 1978	Retrospective historical cohort study looking at low dose heparin vs. no prophylaxis.	Class III	Heparin group had fewer TE complications. No TE events after 3 months despite prophylaxis cessation at 3 months.
Casas et al, Paraplegia, 1977	Prospective assessment of low dose heparin in 18/21 patients with SCI (mean duration 66 days). No patient treated had symptomatic DVT or PE. No use of US/PG/venography	Class III	Low dose heparin may be useful for prevention of symptomatic DVT
Todd et al, Paraplegia, 1976	Used VOP, Fibrinogen scan and venography to study 20 SCI patients for 60 days. Fibrinogen scan was positive in all patients but was confirmed by another test in only half of the cases.	Class III	DVT is common in SCI population.
Hachen, Paraplegia, 1974	Cohort controlled trial of low-dose heparin (5000 μ t.i.d.) vs. oral warfarin in SCI patients. Heparin group had significantly fewer TE events.	Class II	Low dose SQ heparin better than oral warfarin for prophylaxis following acute SCI.
Naso, Arch Phys Med Rehab, 1974	PE occurred in 4/26 patients with acute (<3 months) SCI but none occurred in 17 patients with chronic (>3 months) SCI	Class III	SCI patients primarily at risk during first 3 months following injury.
Watson, Paraplegia, 1968	Incidence of thromboembolic complications per year ranges from 8-40% in same unit (no prophylaxis)	Class III	Thromboembolic complications are a significant problem and there is variability year to year despite identical treatment strategies.

REFERENCES:

1. Balshi JD, Cantelmo NL, Menzoian JO. Complications of caval interruption by Greenfield filter in quadriplegics. *Journal of Vascular Surgery* 9:558-62, 1989.
2. Becker D, Gonzalez M, Gentili A, Eismont F, Green B. Prevention of deep venous thrombosis in patients with acute spinal cord injuries: Use of rotating treatment tables. *Neurosurgery* 20:675-677, 1987.
3. Burns GA, Cohn SM, Frumento RJ, Degutis LC, Hammers L. Prospective ultrasound evaluation of venous thrombosis in high-risk trauma patients. *Journal of Trauma Injury Infection & Critical Care* 35:405-408, 1993.
4. Casas E, Sanchez M, Arias C, Masip J. Prophylaxis of venous thrombosis and pulmonary embolism in patients with acute traumatic spinal cord lesions. *Paraplegia* 15:209-214, 1978.
5. Chu D, Ahn J, Ragnarsson K, Helt J, Folcarelli P, Ramirez A. Deep venous thrombosis: diagnosis in spinal cord injured patients. *Archives of Physical Medicine and Rehabilitation* 66:365-368, 1985.
6. DeVivo MJ, Kartus PL, Stover SL, Rutt RD, Fine PR. Cause of death for patients with spinal cord injuries. *Archives of Internal Medicine* 149:1761-6, 1989.
7. El Masri WS, Silver JR. Prophylactic anticoagulant therapy in patients with spinal cord injury. *Paraplegia* 19:334-42, 1981.
8. Frisbie JH, Sasahara AA. Low dose heparin prophylaxis for deep venous thrombosis in acute spinal cord injury patients: a controlled study. *Paraplegia* 19:343-6, 1981.
9. Frisbie JH, Sharma GV. Pulmonary embolism manifesting as acute disturbances of behavior in patients with spinal cord injury. *Paraplegia* 32:570-2, 1994.

10. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. [see comments]. *New England Journal of Medicine* 331:1601-6, 1994.
11. Green D, Biddle A, Fahey V, et al. Prevention of thromboembolism in spinal cord injury. *Spinal Cord Medicine* 20:259-283, 1997.
12. Green D, Chen D, Chmiel JS, et al. Prevention of thromboembolism in spinal cord injury: role of low molecular weight heparin. *Archives of Physical Medicine & Rehabilitation* 75:290-2, 1994.
13. Green D, Lee MY, Ito VY, et al. Fixed- vs adjusted-dose heparin in the prophylaxis of thromboembolism in spinal cord injury. *JAMA* 260:1255-8, 1988.
14. Green D, Lee MY, Lim AC, et al. Prevention of thromboembolism after spinal cord injury using low-molecular-weight heparin. [see comments]. *Annals of Internal Medicine* 113:571-4, 1990.
15. Greenfield LJ. Does cervical spinal cord injury induce a higher incidence of complications after prophylactic Greenfield filter usage? [letter; comment]. *Journal of Vascular & Interventional Radiology* 8:719-20, 1997;.
16. Gunduz S, Ogur E, Mohur H, Somuncu I, Acjksoz E, Ustunsoz B. Deep vein thrombosis in spinal cord injured patients. *Paraplegia* 31:606-10, 1993.
17. Hachen HJ. Anticoagulant therapy in patients with spinal cord injury. *Paraplegia* 12:176-87, 1974.
18. Harris S, Chen D, Green D. Enoxaparin for thromboembolism prophylaxis in spinal injury. *American Journal of Physical Medicine and Rehabilitation* 75:326-7, 1996.

19. Jarrell BE, Posuniak E, Roberts J, Osterholm J, Cotler J, Ditunno J. A new method of management using the Kim-Ray Greenfield filter for deep venous thrombosis and pulmonary embolism in spinal cord injury. *Surgery, Gynecology & Obstetrics* 157:316-20, 1983.
20. Khansarinia S, Dennis JW, Veldenz HC, Butcher JL, Hartland L. Prophylactic Greenfield filter placement in selected high-risk trauma patients. *Journal of Vascular Surgery* 22:231-5, 1995.
21. Kinney TB, Rose SC, Valji K, Oglevie SB, Roberts AC. Does cervical spinal cord injury induce a higher incidence of complications after prophylactic Greenfield inferior vena cava filter usage? [see comments]. *Journal of Vascular & Interventional Radiology* 7:907-15, 1996.
22. Kulkarni JR, Burt AA, Tromans AT, Constable PD. Prophylactic low dose heparin anticoagulant therapy in patients with spinal cord injuries: a retrospective study. *Paraplegia* 30:169-72, 1992.
23. Lamb GC, Tomski MA, Kaufman J, Maiman DJ. Is chronic spinal cord injury associated with increased risk of venous thromboembolism? *Journal of the American Paraplegia Society* 16:153-6, 1993.
24. McKinley WO, Jackson AB, Cardenas DD, DeVivo MJ. Long-term medical complications after traumatic spinal cord injury: a regional model systems analysis. *Archives of Physical Medicine & Rehabilitation* 80:1402-10, 1999.
25. Merli G, Crabbe S, Doyle L, Ditunno J, Herbison G. Mechanical plus pharmacological prophylaxis for deep vein thrombosis in acute spinal cord injury. *Paraplegia* 30:558-62, 1992.

26. Merli G, Herbison G, Ditunno J, et al. Deep vein thrombosis: prophylaxis in acute spinal cord injured patients. *Archives of Physical Medicine and Rehabilitation* 69:661-5, 1988.
27. Myllynen P, Kammonen M, Rokkanen P, Bostman O, Lalla M, Laasonen E. Deep venous thrombosis and pulmonary embolism in patients with acute spinal cord injury: a comparison with nonparalyzed patients immobilized due to spinal fractures. *Journal of Trauma Injury Infection & Critical Care* 25:541-3, 1985.
28. Naso F. Pulmonary embolism in acute spinal cord injury. *Archives of Physical Medicine & Rehabilitation* 55:275-8, 1974;.
29. Perkash A, Prakash V, Perkash I. Experience with the management of thromboembolism in patients with spinal cord injury: Part I. Incidence, diagnosis and role of some risk factors. *Paraplegia* 16:322-31, 1978.
30. Powell M, Kirshblum S, O'Connor K. Duplex ultrasound screening for deep vein thrombosis in spinal cord injured patients at rehabilitation admission. *Archives of Physical Medicine and Rehabilitation* 80:1044-6, 1999.
31. Quirke TE, Ritota PC, Swan KG. Inferior vena caval filter use in U.S. trauma centers: a practitioner survey. *Journal of Trauma Injury Infection & Critical Care* 43:333-7, 1997.
32. Roussi J, Bentolila S, Boudaoud L, et al. Contribution of D-Dimer determination in the exclusion of deep venous thrombosis in spinal cord injury patients. *Spinal Cord* 37:548-552, 1999.
33. Tator C, Duncan E, Edmonds V, Andrews D. Comparison of surgical and medical management in 208 patients with acute spinal cord injury. *Canadian Journal of Neurological Sciences* 14:60-69, 1987.

34. Todd JW, Frisbie JH, Rossier AB, et al. Deep venous thrombosis in acute spinal cord injury: a comparison of 125I fibrinogen leg scanning, impedance plethysmography and venography. *Paraplegia* 14:50-7, 1976.
35. Tola JC, Holtzman R, Lottenberg L. Bedside placement of inferior vena cava filters in the intensive care unit. *American Surgeon* 65:833-7, 1999.
36. Waring WP, Karunas RS. Acute spinal cord injuries and the incidence of clinically occurring thromboembolic disease. *Paraplegia* 29:8-16, 1991.
37. Watson N. Anti-coagulant therapy in the prevention of venous thrombosis and pulmonary embolism in the spinal cord injury. *Paraplegia* 16:265-9, 1978.
38. Watson N. Venous thrombosis and pulmonary embolism in spinal cord injury. *Paraplegia* 6:113-21, 1968.
39. Wilson JT, Rogers FB, Wald SL, Shackford SR, Ricci MA. Prophylactic vena cava filter insertion in patients with traumatic spinal cord injury: preliminary results. *Neurosurgery* 35:234-9, 1994.
40. Winemiller MH, Stolp-Smith KA, Silverstein MD, Therneau TM. Prevention of venous thromboembolism in patients with spinal cord injury: effects of sequential pneumatic compression and heparin. *Journal of Spinal Cord Medicine* 22:182-91, 1999.
41. Yelnik A, Dizien O, Bussel B, et al. Systematic lower limb phlebography in acute spinal cord injury in 147 patients. *Paraplegia* 29:253-60, 1991.