TABLE E-1 Clinical Studies of Thromboprophylaxis Following Spine Trauma in Patients with and without Spinal Cord Injury*

	Number of Patients				Prevalence of Deep-Vein Thrombosis		Prevalence of Pulmonary Embolism			
Study, Year	SCI	No SCI	Thromboprophylaxis Methods	Study Design (Class of Evidence)	SCI	No SCI	SCI	No SCI	Prevalence of Bleeding Complications	Conclusions of Study
Deep et al.[63], 2001	130	146	Enoxaparin plus early mobilization plus antithrombotic stockings	Retrospective (III)	1.5%	0%	0%	0.7%	0%	In addition to physical and mechanical methods, low-molecular-weight heparin is effective for prophylaxis against venous thromboembolism
Knudson et al.[64], 1996	25	16	Low-molecular-weight heparin plus optimal mechanical (sequential or arteriovenous impulse compression device)	Randomized controlled trial (II)	8% (2 patients, both with mechanical prophylaxis only)	0%	0%	0%	0%	Low-molecular-weight heparin is safe and effective for patients with spinal trauma
Myllynen et al.[4], 1985	23	14	No prophylaxis	Case series (III)	64%	0%	8.7%	0%	Not reported	Prophylaxis is justified in all cases of acute spinal cord injury
Harris et al.[65], 1996	66	39	Enoxaparin 30 mg/12 hr	Retrospective (III)	0%	0%	0%	0%	10.5%	Low-molecular-weight heparin is a safe and effective agent for thromboprophylaxis
Geerts et al.[3], 1994	26	40	No prophylaxis	Case series (IV)	80%	50%	Not clarified	Not clarified	0%	Spinal cord injury is a risk factor for venous thromboembolism

*SCI = spinal cord injury.

TABLE E-2 Clinical Studies Showing Effect of Mechanical Prophylaxis in Patients with Acute Spinal Cord Injury

Study, Year	Number of Patients	Thromboprophylaxis Methods (No. of Patients)	Duration of Thromboprophylaxis	Study Design (Class of Evidence)	Prevalence of Deep-Vein Thrombosis	Prevalence of Pulmonary Embolism	Prevalence of Bleeding Complications	Conclusions
Aito et al.[30], 2002	99 (started early, within 72 hr after injury)	Low-molecular-weight heparin + early mobilization + permanently dressed gradient elastic stockings + external sequential pneumatic compression (99)	4 wk	Cohort (III)	2%	0%	Not reported	Prophylactic treatment should start early (<72 hr) after injury
Winemiller et al.[66], 1999	428	Sequential compression device (sequential compression device)/gradient compression stockings + heparin (428)	6 wk	Retrospective series (IV)	19.6%	0%	Not reported	Effectiveness of heparin greatest the first 14 days after injury, whereas sequential compression device/gradient compression stockings continues for 6 weeks
Spinal Cord Injury Thromboprophylaxis Investigators[29], 2003	107	Low-dose unfractionated heparin + intermittent pressure compression (49), enoxaparin (58)	2 wk	Randomized controlled trial (I)	63.3% in low-dose unfractionated heparin + intermittent pressure compression group, 65.5% in enoxaparin group	18.4% in low-dose unfractionated heparin + intermittent pressure compression group, 5.2% in enoxaparin group	5.3% in low-dose unfractionated heparin + intermittent pressure compression group, 2.6% in enoxaparin group	Safety and efficacy similar for low-dose unfractionated heparin + intermittent pressure compression or enoxaparin
Merli et al.[19], 1988	48	Placebo (17), low-dose unfractionated heparin (16), low-dose unfractionated heparin + electrical stimulation (15)	4 wk	Randomized controlled trial (I)	47% in placebo group, 50% in low-dose unfractionated	0	Not reported	The use of electric stimulation + low-dose heparin decreased the prevalence of deep-

					heparin group, 7% in low-dose unfractionated heparin + electrical stimulation group			vein thrombosis
Green et al.[13], 1982	27	External pneumatic calf compression (15), external pneumatic calf compression + aspirin + dipyridamole (12)	4 wk	Randomized controlled trial (II)	40% in external pneumatic calf compression group, 25% in external pneumatic calf compression + aspirin + dipyridamole group	0	3.6% (1 case needed transfusion) in external pneumatic calf compression + aspirin + dipyridamole group	Prophylaxis with external pneumatic calf compression significantly and safely reduces risk of deep-vein thrombosis, especially with antiplatelet therapy

TABLE E-3 Clinical Studies in Which Vitamin K Antagonists Were Used as Thromboprophylaxis for Patients with Spinal Cord Injury

Study, Year	Number of Patients	Thromboprophylaxis Methods (Number of Patients)	Study Design (Class of Evidence)	Prevalence of Deep-Vein Thrombosis	Prevalence of Pulmonary Embolism	Prevalence of Bleeding Complications	Conclusions
Silver and Moulton[49], 1970	77	Anticoagulated (phenindione) (35), non-anticoagulated (42)	Retrospective (III)	5% (anticoagulated), 25% (non-anticoagulated)	0% (anticoagulated), 14.3% (non-anticoagulated)	Not reported	Anticoagulant therapy in patients with spinal cord injury offers advantages in prevention of pulmonary embolism
Silver[55], 1974	100	Anticoagulated (either warfarin or phenindione) (68), non-anticoagulated (32)	Cohort (III)	5% (anticoagulated), 25% (non-anticoagulated)	2% (anticoagulated), 12.5% (non-anticoagulated)	8% (anticoagulated), 9.3% (non-anticoagulated)	Anticoagulation prevents deep-vein thrombosis and pulmonary embolism
El Masri and Silver[48], 1981	102	Anticoagulated (either warfarin or phenindione) (66), non-anticoagulated (36)	Cohort (III)	0%	52.7% (non-anticoagulated)	0%	Anticoagulation prevents pulmonary embolism
Hachen[46], 1974	120	Heparin 10,000 subcutaneously/12h for 3 weeks followed by warfarin (76), warfarin (44)	Cohort (III)	6.8% (heparin-warfarin), 21% (warfarin)	0% (heparin-warfarin), 6.5% (warfarin)	4.5% (heparin-warfarin), 5.3% (warfarin)	Heparin plus warfarin is more effective than warfarin alone in patients with acute spinal cord injury
Thumbikat et al.[50], 2002	173	Heparin 5000 subcutaneously/12h followed by warfarin (101), enoxaparin 20 mg (40), enoxaparin 40 mg (32). All patients received stockings	Retrospective (III)	2% (heparin-warfarin), 11.1% (enoxaparin, both groups)	2% (heparin-warfarin), 6.9% (enoxaparin, both groups)	8% (heparin-warfarin), 4.1% (enoxaparin, both groups)	Heparin plus warfarin is more effective than low-molecular-weight heparin

TABLE E-4 Characteristics of Randomized Controlled Trials Included in the Systematic Review and Characteristics of Patients Involved in Studies Comparing Low-Molecular-Weight Heparin and Unfractionated Heparin Following Acute Spinal Cord Injury

Study, Year	Number of Positive Internal Validity Criteria	Number of Patients	Age* *(yr)*	Tetraplegia *(no. of patients)*	Paraplegia *(no. of patients)*	Complete Neurologic Injury *(% of patients)*	Start of Treatment from Spinal Cord Injury *(d)*	Duration of Treatment and Follow-up*	Pharmacologic Prophylaxis†
Frisbie and Sasahara[32], 1981									
Unfractionated heparin	6	15	28 ± 12	11	4	100% had severe neurologic injury	2 ± 1	60 d	Heparin 5000 IU/12 hr
Control	6	17	27 ± 11	13	4	100% had severe neurologic injury	2 ± 2	60 d	0
Green et al.[35], 1988									
Unfractionated heparin (fixed dose)	7	29	28.9 ± 15.7	24	11	100%	≤3	12 wk	Heparin 5000 IU /12 hr
Unfractionated heparin (adjusted dose)	7	29	34.3 ± 16.2	26	14	100%	≤3	12 wk	Heparin dose based on PTT/12 hr
Green et al.[36], 1990									
Unfractionated heparin	6	19	31.4 ± 15.5	13	8	100%	≤3	40 ± 19 d	Heparin 5000 IU/8hr
Low-molecular-weight heparin	6	16	28.3 ± 11.8	10	10	100%	≤3	47 ± 16 d	Logiparin (3500 IU)/24 hr
Lohmann et al.[39], 2001									
Unfractionated heparin	6	80	34.7 ± 16.6	33	53	66.1%	≤4	41.5 ± 17.1 d	Heparin 7500 IU/12 hr
Low-molecular-weight heparin	6	86	35.4 ± 16.8	33	57	61.7%	≤5	42.9 ± 17.0 d	Dalteparin 5000 IU/24 hr
Spinal Cord Injury Thromboprophylaxis Investigators[28,29], 2003									
Unfractionated heparin	6	80	34.0 ±	32	18	65.0%	≤3	48 d	Unfractionated heparin 5000

			16.5						IU/8 hr
Low-molecular-weight heparin	6	59	30.5 ± 13.2	34	15	71.2%	≤3	48 d	Enoxaparin 30 mg/12 hr for 2 wk and enoxaparin 40 mg/24 hr for 6 wk

*The values are given as the mean and the standard deviation (where listed). †IU = international unit, and PTT = partial thromboplastin time.

TABLE E-5 Outcomes of Randomized Controlled Trials Included in the Systematic Review of Studies Comparing Low-Molecular-Weight Heparin and Unfractionated Heparin in Patients with Acute Spinal Cord Injury

Study, Year	No. of Cases of Deep-Vein Thrombosis	No. of Cases of Pulmonary Embolism	No. of Cases of Bleeding	No. of Cases of Other Events
Frisbie and Sasahara[32], 1981				
Unfractionated heparin	1 (6.7%)	0	0	0
Control	1 (5.9%)	0	0	0
Green et al.[35], 1988				
Unfractionated heparin (fixed dose)	6 (20.7%)	3 (10.3%)	0	0
Unfractionated heparin (adjusted dose)	2 (6.9%)	0	7 (24%)	0
Green et al.[36], 1990				
Unfractionated heparin	3 (15.8%)	2 (10.5%)	2 (10.5%)	0
Low-molecular-weight heparin	0	0	0	1 leg discomfort, unproved deep-vein thrombosis (6.25%)
Lohmann et al.[39], 2001				
Unfractionated heparin	10 (11.6%)	2 (2.33%)	0	2 thrombocytopenia (2.33%), 1 death (1.16%)
Low-molecular-weight heparin	5 (6.25%)	1 (1.25%)	0	0
Spinal Cord Injury Thromboprophylaxis Investigators[28,29], 2003				
Unfractionated heparin	11 (18.3%)	2 (3.3%)	2 (2.4%)	2 death (3.3%)
Low-molecular-weight heparin	4 (6.8%)	1 (1.7%)	1 (1.7%)	2 death (3.3%)

TABLE E-6 Clinical Studies of Thromboprophylaxis Starting Time in Patients with Acute Spinal Cord Injury

Study, Year	Number of Patients	Thromboprophylaxis Methods	Duration	Study Design (Class of Evidence)	Prevalence of Venous Thromboembolism
Gündüz et al.[67], 1993	12 early, 18 late	Heparin + passive range of motion	12 wk	Case series (IV)	33.3% (early), 66.6% (late)
Aito et al.[30], 2002	99 early, 176 late	Low-molecular-weight heparin + early mobilization + permanently dressed gradient elastic stockings + external sequential pneumatic compression	4 wk	Cohort (III)	2% (early), 26% (late)

TABLE E-7 List of Vitamin K Antagonists

Substance	Category
Acenocoumarol	Coumarin
Fluindione	Indanedione
Phenindione	Indanedione
Phenprocoumon	Coumarin
Warfarin	Coumarin

TABLE E-8 List of Commercially Available Low-Molecular-Weight Heparins

Drug	Commercial Name
Ardeparin, Ardeparin Sodium	Normiflo
Bemiparin, Bemiparin Sodium	Ivor
Certoparin, Certoparin Sodium	Sandoparin
Dalteparin, Dalteparin Sodium	Fragmin
Enoxaparin, Enoxaparin Sodium	Lovenox
Nadroparin, Nadroparin Calcium	Fraxiparine
Parnaparin, Parnaparin Sodium	Tromboparin
Reviparin, Reviparin Sodium	Clivarin
Tinzaparin, Tinzaparin Sodium	Innohep