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Original Article

Venous Thromboembolism Chemoprophylaxis Within 24 Hours of Surgery for Spinal Cord Injury: Is It Safe and Effective?

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Objective: Current guidelines recommend initiation of venous thromboembolism (VTE) chemoprophylaxis within 72 hours of spinal cord injury (SCI). This study investigated the safety and efficacy of chemoprophylaxis within 24 hours of surgery for SCI.
Methods: A retrospective review of 97 consecutive patients who underwent surgery for acute traumatic SCI at a single level 1 trauma center from 2013–2018 was performed. VTE/postoperative bleeding rates during hospitalization, demographics, medical/surgical complications, drain output, length of stay, and disposition were obtained. Chi–square with odds ratios (ORs), 1-way analysis of variance, and logistic regression were performed to establish significant differences between groups.
Results: Seventy–nine patients were included, 49 received chemoprophylaxis within 24 hours and 20 within 24–72 hours. Cohort characteristics included an average age of 51.8 years, 77.2% male, 62.0% cervical, and 35.4% thoracic SCIs. Using the American Spinal Injury Association Impairment Scale (AIS), 39.2% were AIS-A injuries, 19.0% AIS-B, 25.3% AIS-C, and 16.5% AIS-D. Unfractionated heparin was administered in 88.6% of patients and 11.4% received low molecular weight heparin. Chemoprophylaxis within 24 hours of surgery was associated with a lower rate of VTE (6.1% vs. 35.0%; OR, 0.121; 95% confidence interval [CI], 0.027–0.535) and deep vein thrombosis (4.1% vs. 30.0%; OR, 0.099; 95% CI, 0.018–0.548) versus 24–72 hours. Pulmonary embolism rates were not significantly different (6.1% vs. 5.0%, p = 1.0). There were no postoperative bleeding complications and no significant difference in drain output between cohorts.
Conclusion: Early VTE chemoprophylaxis is effective with lower VTE rates when initiated within 24 hours of surgery for SCI and is safe with no observed postoperative bleeding complications.

Keywords: Spinal cord injuries, Venous thromboembolism, Heparin, Low molecular weight, Pulmonary embolism

INTRODUCTION

Spinal cord injury (SCI) is a devastating occurrence, affecting 54 individuals per million in the United State each year, and resulting in significant disability and mortality. Approximately 288,000 individuals live with SCI in the United States, with direct lifetime costs estimated between 1.15 to 4.89 million dollars.[1] This population is at high risk for secondary complications, especially venous thromboembolism (VTE), with an incidence greater than 50% when prophylaxis is not initiated.[2] While there is some risk of VTE in the subacute stage[3,4] and long term[5] time periods, the vast majority of VTE occur in the first 3 months following SCI.[6-8] Among major trauma patients, those with SCI have the highest risk of VTE,[2] which is historically the third most common cause of death in this group.[9] Notably, long-term mortality has not decreased in this population

over the past 3 decades.[10]

Anticoagulation with heparinoid chemoprophylaxis has been utilized as an effective strategy to safely decrease VTE in SCI patients[11-13] with both unfractionated heparin (UFH)[14-16] and low molecular weight heparin (LMWH)[8,17] being most studied, and at various doses.[18] Mechanical prophylaxis has been shown to augment the effect of chemical prophylaxis,[16,19,20] but prophylaxis with inferior vena cava (IVC) filters has been associated with higher rates of deep vein thrombosis (DVT) in acute SCI patients.[21]

While it is well-known that UFH is associated with a significantly increased risk of heparin-induced thrombocytopenia compared to LMWH, there is significant variation in the literature about whether there is higher safety and/or efficacy with LMWH,[22-25] UFH,[26,27] or whether they are equivalent.[12,19,28-34] Bleeding risk is a concern with chemoprophylaxis, especially in the postoperative state after major spinal surgery, and further so in the setting of SCI, given that a bleeding event can result in a worsened neurological injury.

Many studies have compared the efficacy of different types of chemoprophylaxis, but fewer have studied how the timing of prophylaxis affects clinical outcomes. There is some evidence in the literature that chemoprophylaxis closer to the time of injury is associated with lower rates of DVT and VTE.[11,16,17,23,24,35-38] Several systematic reviews have subsequently recommended for the strategy of chemoprophylaxis within 72 hours of SCI[13,19,32] including guidelines published by the American Association of Neurological Surgeons/Congress of Neurological Surgeons in 2013, which gave a level II recommendation.[19,35]

The purpose of this study is to investigate the effectiveness and safety of initiating early VTE chemoprophylaxis within 24 hours of SCI in a surgical cohort by comparing the outcomes of individuals who received chemoprophylaxis within 24 hours of injury to those between 24 and 72 hours, and after 72 hours. We hypothesize that individuals who receive prophylaxis within 24 hours of injury will have lower rates of VTE with an adequate safety profile.

MATERIALS AND METHODS

Ninety-seven patients underwent surgical intervention for acute traumatic SCI at a single level 1 trauma center from January 2013 to August 2018. Patients were separated into 3 cohorts based on the timing of how long after surgery chemical thromboprophylaxis was initiated: within 24 hours (early), 24–72 hours (standard), and after 72 hours (late). These cohorts were retrospectively reviewed for VTE rates, and postoperative bleeding complication rates during the acute hospitalization. VTE was defined as either a DVT or PE, or the simultaneous discovery of both in a single patient. Orthopaedic injuries were defined as any long-bone fracture. Other variables obtained included age, sex, race, American Spinal Injury Association (ASIA) score, injury level, surgery performed, type of chemoprophylaxis used, medical/surgical complications, hospital/intensive care unit (ICU) length of stay, drain output if a postoperative drain was utilized, and disposition status. Exclusion criteria included age less than 18 (n = 2), hypercoagulable gene mutation (n = 2), conus medullaris/cauda equina syndrome (n = 5), and those that did not receive anticoagulation (n = 9).

All patients received heparinoid chemoprophylaxis and had sequential compression devices applied. Institutional protocol dictated that acute SCI patients receive prophylaxis within 24 hours of surgery for SCI. However, the clinical decision to give early VTE chemoprophylaxis was left to the discretion of the surgeon and ICU providers. Possible reasons for delayed prophylaxis included: medical history (gastrointestinal bleeding, hemorrhagic stroke, renal/liver disease-induced or other coagulopathies, thrombocytopenia), daily aspirin use, patient refusal, temporary IVC filter placement, neurosurgical intervention, or hemodynamic instability from polytrauma.

Enoxaparin was the LMWH medication of choice and was administered at 40 mg subcutaneously daily, while low-dose UFH was administered at 5,000 U subcutaneously twice daily. Patients were deemed to have received anticoagulation within 24 hours if they received UFH or LMWH within 24 hours of surgery for SCI. Duplex ultrasound was performed if there was clinical suspicion for DVT/PE.[11,17,26,28,31,38] Routine duplex ultrasounds were not obtained due to the increased cost and resource utilization required for obtaining the study in all SCI patients. PE was confirmed with computed tomography angiography. Surgical drains were applied in all but 13 patients and left in situ for a median of 4 days (range, 2–9 days), Institutional Review Board approval was obtained for this study (UCLA IRB# 18-000760).

A power analysis was performed to ascertain what sample size would be required to detect a 25% difference in VTE and bleeding rates between groups. A 2-tailed analysis with $\alpha = 0.05$, power = 0.8, and an allocation ratio of 2:1 between the early and late groups resulted in a required sample size of 35 and 18, respectively. Chi-square test of homogeneity and 1-way analysis of variance were performed in order to establish significant differences between groups. Odds ratios (ORs) were calculated to

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Table 1. Demographic data by anticoagulation timing

Variable	< 24 Hours (n = 49)	24–72 Hours (n = 20)	> 72 Hours (n = 10)	p-value
Age (yr)	53.9 ± 18.1	50.3 ± 23.5	43.9 ± 22.9	> 0.330
Sex				
Male	39 (79.6)	17 (85.0)	5 (50.0)	0.080
Female	10 (20.4)	3 (15.0)	5 (50.0)	
Race				
White	23 (46.9)	10 (50.0)	4 (40.0)	0.984
Hispanic	9 (18.4)	3 (15.0)	3 (30.0)	
Asian	7 (14.3)	3 (15.0)	1 (10.0)	
Black	7 (14.3)	3 (15.0)	2 (20.0)	
Other	3 (6.1)	1 (5.0)	0 (0)	
Injury level				
Cervical	32 (65.3)	13 (65.0)	4 (40.0)	0.387
Thoracic	15 (30.6)	7 (35.0)	6 (60.0)	
Lumbar	2 (4.1)	0 (0)	0 (0)	
AIS score				
A	23 (46.9)	5 (25.0)	3 (30.0)	0.049
B	10 (20.4)	2 (10.0)	3 (30.0)	
C	12 (24.5)	5 (25.0)	3 (30.0)	
D	4 (8.2)	8 (40.0)	1 (10.0)	
Syndromes				
Central cord	11 (22.4)	2 (10.0)	0 (0)	0.145
Vertebral fractures				
Burst	4	4	0	0.320
Chance	2	0	1	
Teardrop	1	1	1	
Dislocation	6	2	3	
Dens	1	1	0	
Other	2	3	2	
Other injuries				
TBI	3 (6.1)	5 (25.0)	2 (20.0)	0.077
Orthopaedic injury	8 (16.3)	6 (30.0)	4 (40.0)	0.179
Injury mechanism				
Vehicle accident	16 (32.7)	9 (45.0)	4 (40.0)	0.779
Fall	18 (36.7)	7 (35.0)	4 (40.0)	
Recreation	7 (14.3)	1 (5.0)	0 (0)	
Fallen object	1 (2.0)	1 (5.0)	1 (10.0)	
Other	7 (14.3)	2 (10.0)	1 (10.0)	
Surgery				
Laminectomy/fusion	30 (61.2)	8 (40.0)	5 (50.0)	0.828
Fusion	9 (18.4)	5 (25.0)	2 (20.0)	
ACDF	7 (14.3)	5 (25.0)	2 (20.0)	
Laminectomy	3 (6.1)	2 (10.0)	1 (10.0)	
Time to surgery (hr)	23.7	29.1	28.4	> 0.838
Anticoagulant				
UFH	43 (87.8)	19 (95.0)	8 (80.0)	0.454
LMWH	6 (12.2)	1 (5.0)	2 (20.0)	
VTE diagnostic studies				
LE Doppler US	33 (67.3)	13 (65.0)	8 (80.0)	0.686
CTA chest	31 (63.3)	12 (60.0)	7 (70.0)	0.866
Surgical drain placed	40 (81.6)	16 (80.0)	10 (100)	0.319

Values are presented as mean ± standard deviation or number (%).
AIS, American Spinal Injury Association Impairment Scale; TBI, traumatic brain injury; ACDF, anterior cervical discectomy and fusion; UFH, unfractionated heparin; LMWH, low molecular weight heparin; LE, lower extremity; US, ultrasound; CTA, computed tomography angiography. p-values refer to a chi-square comparison between early, standard, and late anticoagulation timing groups. p-value for age refers to a 1-way analysis of variance calculation.

denote the magnitude of this difference. Binomial logistic regression was performed to determine associations with VTE rates and to control for possible confounding. Comparisons between groups and within groups were deemed statistically significant at the $p < 0.05$ threshold. Statistical analyses were performed using IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA).

RESULTS

Seventy-nine patients (77% male, 23% female) were identified for the study upon application of the exclusion criteria. Forty-nine patients received prophylaxis within 24 hours of surgery (early group), 20 patients between 24 and 72 hours of surgery (standard group), and 10 patients greater than 72 hours after surgery (late group). Of the patients who received chemoprophylaxis greater than 72 hours after surgery, 3 received it on day 4, 3 on day 5, and one each on days 8, 10, 12, and 14 after injury.

The average age of SCI patients in this study was 51.8 years (Table 1). White was 47%, and the remainder were otherwise evenly distributed between various ethnicities (14%–19%). Fall and vehicular accidents were the most common injury mechanisms (37%), followed by sports/recreation (10%). Sixty-two percent of SCI occurred at the cervical spine, 35% at the thoracic spine, and 3% at the lumbar spine. The ASIA Impairment Scale (AIS) classification for these injuries was 39% AIS-A, 19% AIS-B, 25% AIS-C, and 17% AIS-D. An associated orthopaedic injury was identified in 23% of patients and 13% had an associated traumatic brain injury (TBI). Laminectomy and posterior fusion was performed in 54.4% of patients, 20.3% underwent posterior fusion alone, 17.7% anterior cervical discectomy and fusion, and 7.6% had laminectomy alone (Table 1). Average time to surgery was around 24 hours from injury in each cohort and not significantly different between cohorts ($p > 0.84$). UFH was administered in 88.6% of patients with only 11.4% receiving LMWH. Screening lower extremity doppler ultrasound was performed and surgical drains were placed at similar rates among the 3 cohorts ($p = 0.69$ and $p = 0.32$, respectively).

The only variable that was significantly different between the

Table 2. Medical/surgical complications, length of stay, and disposition by anticoagulation timing

Variable	< 24 Hours (n = 49)	24–72 Hours (n = 20)	> 72 Hours (n = 10)	p-value
Medical complications				
PNA	19 (38.8)	8 (40.0)	4 (40.0)	0.994
UTI	6 (12.2)	5 (25.0)	4 (40.0)	0.091
Sepsis	6 (12.2)	1 (5.0)	1 (10.0)	0.664
ARDS	3 (6.1)	0 (0)	1 (10.0)	0.430
C. difficile	3 (6.1)	0 (0)	0 (0)	0.385
Surgical complications				
Infection	0 (0)	0 (0)	0 (0)	
Reoperation	0 (0)	0 (0)	1 (10.0)	0.030
Length of stay				
Hospital	17.3 ± 12.9	16.3 ± 10.0	27.4 ± 19.9	> 0.078
ICU	11.5 ± 11.2	8.8 ± 8.2	10.9 ± 6.1	> 0.561
Disposition				
Acute rehabilitation	22 (44.9)	8 (40.0)	5 (50.0)	0.838
SNF	11 (22.4)	3 (15.0)	4 (40.0)	
Acute care	5 (10.2)	2 (10.0)	1 (10.0)	
Home	5 (10.2)	4 (20.0)	0 (0)	
LTACH	2 (4.1)	2 (10.0)	0 (0)	
LTC	3 (6.1)	1 (5.0)	0 (0)	
Death	1 (2.0)	0 (0)	0 (0)	

PNA, pneumonia; UTI, urinary tract infection; ARDS, acute respiratory distress syndrome; *C. difficile, Clostridium difficile*; ICU, intensive care unit; SNF, skilled nursing facility; LTACH, long-term acute care hospital; LTC, long-term care hospital.

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groups was AIS score. Namely, the early chemoprophylaxis group had a higher proportion of AIS-A injuries (47%) and the standard group had a higher proportion of AIS-D injuries (40%). Overall, the early and standard chemoprophylaxis groups were more similar in demographic variables than either of those groups compared to the late chemoprophylaxis group. One exception was the early chemoprophylaxis group had nonsignificantly lower proportions of TBI and orthopaedic injuries than the other 2 chemoprophylaxis groups.

Medical complications were common in the study cohort, with nearly 40% of all patients having hospital stays complicated by pneumonia (Table 2). Urinary tract infection and sepsis were also common complications affecting 19% and 10% of patients, respectively. These complications were not significantly more likely in any of the groups. While there were no surgical site infections, there were 2 cases of wound dehiscence in the early chemoprophylaxis group that went on to heal with standard wound care and secondary intention. One patient in the late anticoagulation group required reoperation due to osteoporosis-induced hardware failure. There were no postoperative bleeding complications in the early, standard, or late chemoprophylaxis groups with no hematoma, seroma, or neurologic deterioration after chemoprophylaxis initiation (Table 3). There

Table 4. VTE and bleeding complication rates by type of anticoagulation

Variable	UFH (n = 70)	LMWH (n = 9)	Odds ratio (95% CI)	p-value
Thromboembolism				
DVT	9 (12.9)	0 (0)		0.587
PE	5 (7.1)	1 (11.1)		0.528
VTE	11 (15.7)*	1 (11.1)		1.000
Bleeding				
Hematoma	0 (0)	0 (0)		N/A
Seroma	0 (0)	0 (0)		N/A
Dehiscence	1 (1.4)	1 (11.1)		0.216
Drain output				
Total† (mL)	633	793		0.570
Average daily‡ (mL)	131	137		0.873
Drain duration (day)	4.23	5.00		0.228

Values are presented as number (%) unless otherwise indicated.
VTE, venous thromboembolism; UFH, unfractionated heparin; LMWH, low molecular weight heparin; CI, confidence interval; DVT, deep vein thrombosis; PE, pulmonary embolism.
13 Patients in the UFH group did not have drain output data available. *3 Patients had DVT and PE in the UFH group. †Sum of daily drain outputs during entire hospital stay averaged by number of patients. ‡Total drain output divided by number of days drain in place averaged by number of patients.

Table 3. VTE and bleeding complication rates by anticoagulation timing

Variable	< 24 Hours (n = 49)	24–72 Hours (n = 20)‡	> 24 Hours (n = 30)§	Odds ratio (95% CI)	p-value
Thromboembolism					
DVT	2 (4.1)	6 (30.0)	7 (23.3)	0.099 (0.018-0.548)	0.006‡
				0.140 (0.027-0.727)	0.009§
PE	3 (6.1)	1 (5.0)	3 (10.0)	-	1.000‡/0.668§
VTE	3 (6.1)*	7 (35.0)	9 (30.0)†	0.121 (0.027-0.535)	0.005‡
				0.152 (0.037-0.620)	0.008§
Bleeding					
Hematoma	0 (0)	0 (0)	0 (0)	-	N/A
Seroma	0 (0)	0 (0)	0 (0)	-	N/A
Dehiscence	2 (4.1)	0 (0)	0 (0)	-	1.000
Drain output					
Total‖ (mL)	592	888	751	-	0.336‡/0.460§
Average daily¶ (mL)	117	167	154	-	0.247‡/0.261§
Drain duration (day)	4.45	4.15	4.19	-	0.512‡/0.640§

Values are presented as number (%) unless otherwise indicated.
CI, confidence interval; DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; N/A, not applicable. VTE refers to either a DVT, PE, or the simultaneous discovery of both in a single patient. Drain output data was available for 40, 16, and 26 patients or the early, standard, and standard+late groups, respectively.
*2 Patients had DVT and PE in the early anticoagulation group. †1 patient had DVT and PE in the standard+late anticoagulation group. ‡Comparison of early vs. standard anticoagulation groups. §Comparison of early vs. standard+late anticoagulation groups. ‖Sum of daily drain outputs during entire hospital stay averaged by number of patients. ¶Total drain output divided by number of days drain in place averaged by number of patients.

Table 5. VTE and bleeding complication rates by AIS score

Variable	A (n = 31)	B (n = 9)	C (n = 20)	D (n = 13)	p-value
Thromboembolism					
DVT	3 (9.7)	1 (6.7)	3 (15.0)	2 (15.4)	0.829
PE	3 (9.7)	1 (6.7)	2 (10.0)	0 (0)	0.695
VTE	4 (12.9)*	1 (6.7)	5 (25.0)	2 (15.4)	0.481
Bleeding					
Hematoma	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Seroma	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Dehiscence	0 (0)	2 (13.3)	0 (0)	0 (0)	0.033

Values are presented as number (%).
VTE, venous thromboembolism; AIS, American Spinal Injury Association Impairment Scale; DVT, deep vein thrombosis; PE, pulmonary embolism; N/A, not applicable.
VTE refers to either a DVT, PE, or a simultaneous discovery of both in a single patient.
*1 Patient had DVT and PE in the AIS-A group.

was no significant difference in the rates of VTE, DVT, PE, or wound dehiscence between the UFH and LMWH groups (Table 4). Drain output, both average total output and average daily output, as well as the duration that drains were in place was not statistically different between the early, standard, or late groups, nor between UFH and LMWH (Tables 3, 4).

When comparing 69 SCI patients given chemoprophylaxis within 72 hours of surgery, the early group had lower rates of DVT (4.1% vs. 30.0%; OR, 0.099; p = 0.006), and VTE (6.1% vs. 35.0%; OR, 0.121; p = 0.005) as compared to the standard group (Table 3). Rates of PE were low in both cohorts and not significantly different between groups (6.1% vs. 5.0%, p = 1.0). There were no postoperative bleeding complications (hematoma or seroma) in the early or standard prophylaxis group. When combining the standard and late groups (all patients >24 hours) and compared to the early group, the same trends held, albeit to a lesser magnitude (Table 3). There were lower rates of DVT (4.1% vs. 23.3%; OR, 0.140; p = 0.009) and VTE (6.1% vs. 30.0%; OR, 0.152; p = 0.008) in the early chemoprophylaxis group, and rates of PE were similar (6.1% vs. 10.0%, p = 0.67). Prior studies have reported higher VTE rates with more severe AIS scores,[39] however in our study, each AIS group had similar rates of DVT (6.7%–15.4%, p = 0.83), PE (0%–10.0%, p = 0.70), and VTE (6.7%–25.0%, p = 0.48) (Table 5).

1. Regression Analysis for VTE Risk Factors

Binomial logistic regression was performed to determine whether AIS score, age, or concomitant orthopaedic injury confounded the association of early chemoprophylaxis with lower VTE rates (Table 6). The model was statistically significant ($\chi^2(4) = 10.2$, p = 0.037, Nagelkerke $R^2 = 0.212$), finding early chemoprophylaxis maintained a robust association with lower VTE rates (OR, 0.192; 95% confidence interval [CI], 0.044–0.832; p = 0.027) even after correcting for differences in the distributions of the remaining variables between the 2 chemoprophylaxis groups. Age (OR, 1.003; 95% CI, 0.964–1.044; p = 0.881), AIS (OR, 1.863; 95% CI, 0.371–9.357; p = 0.450, and orthopaedic injury (OR, 0.358; 95% CI, 0.076–1.686; p = 0.194) were not significant predictors. ASIA C or D injury, orthopaedic injury, and standard/late chemoprophylaxis were coded as the comparison group.

Table 6. Binomial logistic regression of VTE rates

Variable	B	SE	Odds ratio (95% CI)	p-value
Age	0.003	0.020	1.003 (0.964–1.044)	0.881
AIS score	0.622	0.823	1.863 (0.371–9.357)	0.450
Orthopaedic injury	-1.028	0.791	0.358 (0.076–1.686)	0.194
Heparin <24 hr	-1.649	0.748	0.192 (0.044–0.832)	0.027
Constant	-0.297	1.444	0.743 (N/A)	0.837

VTE, venous thromboembolism; B, log odds change coefficient; SE, standard error; CI, confidence interval; AIS, American Spinal Injury Association Impairment Scale; N/A, not applicable.
AIS Score: 0 = C or D, 1 = A or B. Orthopaedic Injury: 0 = yes, 1 = no. Heparin < 24 hr: 0 = no, 1 = yes.

DISCUSSION

Given the relatively high risk of VTE in SCI patients, the timing of chemoprophylaxis is an important clinical concern. However, evidence is limited in the scientific literature regarding the timing of chemical thromboprophylaxis for patients with acute SCI. This may be due to surgeons being concerned about the possibility of bleeding complications with chemoprophylaxis postoperatively.

1. VTE Rates in the Literature

The reported rate of VTE after acute SCI is highly variable in the literature and depends on whether VTE surveillance was utilized routinely (screening) or whether it was utilized when there was clinical suspicion (symptomatic VTE) as in our study. Our DVT rate of 30% is at the high end of the studies that evaluated for symptomatic VTE (9%–26%) and at the lower end of studies that used routine VTE surveillance (23%–63%).[8,26,28,31,33,36] Our rate is at the higher end for symptomatic VTE studies since 68% of our patients received a lower extremity doppler ultra-

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sound during their hospital admission. Many studies do not report the exact proportion of patients who were evaluated for symptomatic VTE, but it is possible that the surgeons at our institution had higher clinical suspicion for VTE than those at other institutions, thus potentially inadvertently detecting asymptomatic DVT, increasing our DVT rate.

2. Timing of Chemoprophylaxis

Several studies have demonstrated improved clinical outcomes when chemoprophylaxis is administered within 72 hours of SCI with reported VTE rates ranging from 0%–64.5% and bleeding rates of 2.5%–4.9%.[17,24,29,33] The higher rates of VTE reported by the SCI thromboprophylaxis investigators study may be due to their protocol incorporating routine surveillance with ultrasonography as opposed to our study which did so only when there was clinical suspicion.[36] Multiple studies in the literature have previously utilized clinical suspicion as the trigger to obtain the duplex ultrasound[11,17,26,28,31,38] and a recent systematic review found insufficient evidence to support the hypothesis that routine surveillance decreases VTE-associated morbidity/mortality.[34] Aito et al.[36] performed a direct comparison of 275 consecutive acute SCI patients and found a low rate of DVT in those who received LMWH within 72 hours of injury (2%), which was a significantly lower DVT rate than in those with delayed LMWH administration 8–28 days after injury (26%). Our overall VTE and bleeding rates for patients with chemoprophylaxis within 72 hours of injury were on the lower end of the range reported in the literature.

One prospective case series and 2 retrospective cohort studies report data for chemoprophylaxis within 48 hours of SCI/surgery. An early study by Merli et al.[16] reported a DVT rate of 5.3%, without mention of bleeding complications as a result of chemoprophylaxis. Chang et al.[11] reported that patients who received heparinoids and/or aspirin within 48 hours of injury had a 5% VTE rate, trending toward significantly lower than those who did not (9%), with a low bleeding rate (0.8%). In their study, the early prophylaxis group did have a lower proportion of patients who underwent surgery than the late group. Zeeshan et al.[37] examined a cohort of operative spine fracture patients and found that those who received heparinoid prophylaxis within 48 hours of surgery had a VTE rate of 3.0%, which was significantly lower than those who did not (12.2%), and had a bleeding rate of 1.3%.[37]

One other study in the literature describes a chemoprophylaxis regimen within 24 hours of SCI. In a prospective case series of 49 patients, DiGiorgio et al.[38] found that LMWH administered within 24 hours of SCI yielded a 10.2% VTE rate and 0% bleeding rate. Our study, with a very similar VTE prophylaxis protocol, had a 6.1% VTE rate and a 0% bleeding rate as well. However, several differences exist in our study population, including that our patients received almost exclusively UFH instead of LMWH, required longer average hospital and ICU stays (17.3 days vs. 15.9 days and 11.5 days vs. 8.6 days, respectively), all underwent surgery (100% vs. 82%), and were more likely to have had complete SCIs (47% vs. 18%), which may increase the VTE risk in our patient population.

VTE risk is likely higher within 24 hours of surgery for SCI because of venous stasis from immobility, endothelial vessel wall injury from surgery, and a hypercoagulable state associated with the trauma/concomitant injuries. In our study, 3 of 12 (25%) of our VTE-related complications occurred within 24–48 hours of surgery. Of those who received VTE prophylaxis between 24–72 hours after surgery, 2 of 7 (29%) had a VTE within 24–48 hours of surgery. In the literature, few studies delineate the exact timing of VTE, however those with routine surveillance typically did so around 1 week after surgery and those that evaluated for symptomatic VTE found they occurred on average 8–15 days after surgery/SCI.[8,26,28,31,33,36] These studies were unable to demonstrate a higher risk of VTE within 24 hours of surgery for SCI.

In our study, there were no differences between the early and standard chemoprophylaxis groups including sex, age, injury level, rate of TBI/concomitant orthopaedic injuries, injury mechanism, surgical method, or anticoagulant used. The one exception was that the proportion of AIS scores were significantly different between the 3 chemoprophylaxis timing groups, but this was not found to be a significant risk factor for VTE in our regression analysis. In terms of surgical complications, there was only one case of reoperation in the late prophylaxis group and 2 wound dehiscence events in the early chemoprophylaxis group.

3. Type of Chemoprophylaxis

Prior studies have demonstrated mixed results on whether UFH or LMWH is superior in terms of thrombosis or bleeding rates. Reported VTE rates for UFH and LMWH in the literature have ranged from 0%–63.3% and 6.9%–65.5%, respectively and reported bleeding rates have ranged from 0%–10% and 0%–4.2%, respectively.[24,26-29,31,33] Our institution utilized predominantly UFH coupled with mechanical prophylaxis due to the possible concern of increased bleeding risk associated with LMWH. Our data demonstrated overall efficacy and safety

with rates of VTE and bleeding on the lower end of those reported in the literature (15.7% and 0%).

4. Strengths

Our study closely reflects the demographics of the nationwide population of SCIs as compared to the National SCI Statistical Center database in terms of sex (77% vs. 78% male), ethnicity (47% vs. 61% Caucasian), and injury mechanism (37% vs. 38% vehicular accidents).[1] Our population was, however, somewhat older than the national average with a longer average hospitalization. Our study is the second to demonstrate the efficacy and safety of early chemoprophylaxis within 24 hours of surgery for SCI, and the first to directly compare it to another cohort that is within the current 72-hour standards over the same time period. This study is the first to demonstrate efficacy with the early chemoprophylaxis strategy utilizing UFH within 24 hours of surgery. As opposed to some prior studies, our data derives from a purely surgical cohort, which allows for the opportunity to decrease possible confounding that would arise from different rates of surgery between groups, a known VTE risk factor.

5. Limitations

This study is retrospective and thus subject to inherent bias. While almost all of the baseline characteristics and treatment variables were not significantly different between groups, AIS score proportions were significantly different between the early, standard and late groups. However, regression analysis showed that prophylaxis timing was the only variable that significantly contributed to the predictive model, and AIS score did not confound the association of early prophylaxis and lower VTE rates. There is also possible indication bias in our study in that patients with lower risk for adverse bleeding events or presumed more severe coagulopathy may have been preferentially selected for or against the early chemoprophylaxis regimen. In addition, given duplex ultrasound tests were only performed on symptomatic patients and may not sufficiently detect proximal DVTs our study may underreport the true rate of DVT in this population. Although, given equal proportions in each cohort received DVT surveillance the relative trends of this study would be expected to still hold true. Certainly larger, randomized clinical trials would be necessary to affirm the findings described in the present study. Additionally, while all patients received heparinoid prophylaxis, the group was not completely homogenous in that some patients received LMWH instead of UFH. Both timing and type of chemoprophylaxis could be investigated further using randomization in future studies. However, multiple studies have previously demonstrated that neither is superior with similar VTE/bleeding rates.

CONCLUSION

This study demonstrated that heparinoid chemoprophylaxis administered within 24 hours of surgery for SCI is more effective in lowering rates of VTE than when it is administered both between 24–72 hours from injury and after 72 hours from injury. The strategy is equally safe and may not increase the risk of hemorrhagic complications.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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