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Venous thromboembolism prophylaxis in neurosurgical trauma patients

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ABSTRACT

Background: Venous thromboembolisms (VTEs) occur more frequently in patients with traumatic brain injuries (TBIs) and spinal cord injuries, yet the use of chemoprophylaxis is controversial. The purpose of this study was to investigate the relationship between the timing of chemical VTE prophylaxis initiation and the development of VTE events in these patients.

Methods: Prospective data were collected and retrospectively reviewed on 1425 patients sustaining TBIs or spinal injuries from 2010 to 2014. Patients were reviewed with respect to age, gender, injury severity score, Glasgow coma score, and mechanism of injury as well as timing of initiation of chemical VTE prophylaxis and presence or absence of VTE.

Results: Patients who developed a VTE had a significantly longer time to initiation of chemical VTE prophylaxis (6.7 ± 4.9 d *versus* 4.7 ± 4.9 d, $P < 0.001$) compared with those that did not develop a VTE. Also, for each 1 d increase in time to prophylaxis initiation, the odds of developing a VTE increased significantly (odds ratio = 1.055, $P < 0.001$). The combination subarachnoid hemorrhage/subdural hemorrhage group was started on VTE prophylaxis significantly later (8.3 ± 6.1 d *versus* 6.7 ± 3.9 d, $P < 0.01$) than the overall TBI group and had a higher incidence of VTE (14.4 *versus* 10.4%, P = NS). In contrast, patients sustaining isolated spinal injuries received chemical VTE prophylaxis significantly earlier (3.4 ± 4.2 d *versus* 6.7 ± 3.9 d, $P < 0.001$) and had a significant decrease in their VTE rate (4.4 *versus* 10.4%, $P < 0.0001$) compared with the overall TBI group.

Conclusions: Patients with VTEs had a significant delay in time to initiation of chemoprophylaxis compared with patients without VTEs. Patients sustaining a TBI had a 2-fold delay in initiation of chemoprophylaxis and an associated 2-fold increase in VTE events compared with patients who sustained spinal injuries. Of those patients who developed a TBI, patients who sustained a combination subarachnoid hemorrhage and/or subdural hemorrhage had a significant delay in initiation of chemoprophylaxis with a higher rate of VTE events.

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Introduction

Venous thromboembolisms (VTEs), comprised of deep venous thromboses (DVT) and pulmonary emboli (PE), are largely due to Virchow's triad of venous stasis, intimal injury, and a hypercoagulable state. Additional research has shown that the brain releases excess tissue factor from its vasculature after trauma leading to a procoagulant overflow.[1] It is therefore not surprising that trauma patients are at increased risk for the development of VTEs. A recent study by Gudipatia *et al.*[2] documented that trauma patients have up to a 1.8% incidence of VTE development compared to nontrauma patients who carry an incidence of 0.1-0.5%. Furthermore, certain traumatic subpopulations have even higher rates of VTE. For example, patients with traumatic brain injuries (TBIs) and traumatic spinal cord injuries (SCI) are noted to have VTE rates as high as 58%[3] and 60%,[4] respectively.

More than one-quarter million Americans sustain TBIs a year,[5] and these injuries have been identified as a significant risk factor for DVT development, independent of pharmacologic prophylaxis.[6,7] To prevent VTE events in the TBI population, many institution-based protocols have been designed to tailor such prophylaxis, yet the resulting data are often equivocal. Scudday *et al.* and Saadeh *et al.*[8,9] found that trauma patients with computed tomography (CT) evidence of brain hemorrhage treated with low-molecular-weight heparin (LMWH), such as enoxaparin, and a stable repeat head CT after 24 h have a statistical reduction in DVT. Levy *et al.*,[10] however, found that chemoprophylaxis exposure in patients with CT proven progression of intracranial bleed is a predictor of subsequent hemorrhage. Similar dilemmas of chemoprophylaxis initiation hold true for spinal trauma.[11]

SCI is an independent risk factor for DVT development.[12] A study by Christie *et al.*[13] documented a 500-fold increase risk of PE-related deaths relative to age- and gender-matched noninjured controls. Specifically, VTE is responsible for 9.7% of all deaths in the first year after SCI[14] and is largely due to a fear of rebleeding from the index injury, as seen with TBIs. For example, in a study by Arnold *et al.*,[15] SCI patients were started on chemical prophylaxis as late as 8 d while patients without those injuries were started on LMWH within 2.5 d because of the potential of rebleeding. In contrast, the review by Harris *et al.*[16] found that there was no evidence that continued administration of LMWH after spinal injury led to exacerbation of bleeding.

The purpose of this study was to investigate the relationship between the timing of chemical VTE prophylaxis initiation and the development of VTE events in patients with TBIs and spinal injuries. We hypothesized that there would be an increased incidence of VTE events when chemical prophylaxis initiation was delayed in these populations.

Methods

Prospective data were collected and retrospectively reviewed on 2128 patients sustaining traumatic neurosurgical injuries who were admitted to a rural level one trauma center over a 5-y period from 2010 to 2014. Our center's institutional review board approved this study and waived the need for patient consent. Patients were included in the study if they were older than 18 y had CT evidence of a neurologic injury to include any TBI or spinal fracture with or without cord compromise (SI) and who had received LMWH during their hospitalization. Any patients receiving unfractionated heparin were excluded. Patients were also excluded if they had an isolated concussion without CT evidence of brain injury. Date of initiation of LMWH was recorded prospectively by our trauma registrars, and any missed doses of LMWH administration were not accounted for. There were 1425 patients who met the inclusion criteria and comprised the study cohort. Patients were identified by age, gender, injury severity score (ISS), Glasgow coma score (GCS), and mechanism of injury. Baseline VTE calculations in the population according to a Caprini or Rogers score were not performed, thus we did not control for these possible confounders. In addition, overall TBI patients were further divided into subgroups to include subarachnoid hemorrhage (SAH), subdural hemorrhage (SDH), SAH/SDH, and any other brain hemorrhage (BH) including diffuse axonal injury.

Additional data variables included date of initiation of chemical VTE prophylaxis and the presence or absence of VTE. As per institutional policy during this study period, all trauma patients underwent weekly screening duplex color flow ultrasound examinations of the bilateral lower extremities, regardless of clinical relevancy. We did not routinely screen for upper-extremity DVTs; rather only obtained duplex scans, if there were clinical signs warranting investigation. PE was diagnosed with chest CT angiograms only when clinically relevant. All injury types were compared and grouped into VTE and non-VTE cohorts for further comparison.

Data analyses were performed with the IBM Statistical Package for the Social Sciences software (IBM Corp Released 2013; IBM SPSS Statistics for Windows, version 22.0; Armonk, NY; IBM Corp). Discrete variables were compared using Pearson's chi-square analysis. Continuous variables were compared using a Student's *t*-test. Bivariate and multivariate logistic regression was used to analyze the data for significant predictors of VTE development. The level of statistical significance was set at 0.05. Main effect odds ratios were calculated using bivariate models. Interaction effects were calculated using multivariate models including the interaction term and the constituent main effects.

Results

Patient demographics

The mean age of the study cohort was 50 ± 21 y, mean ISS was 18 ± 9, and mean GCS was 13 ± 4. The majority were male (64%) and sustained blunt trauma (97%, Table 1). The most common mechanisms of injury were motor vehicle crashes (62%) followed by falls (26%) and gunshot wounds (3.5%, Table 2). Of the 1425 patients, 548 sustained a TBI, and 877 sustained an isolated SI with or without spinal cord compromise.