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Original Article

Venous thromboembolism prophylaxis in operative traumatic brain injury

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ABSTRACT

Background: Venous thromboembolism (VTE) is a significant complication in patients with traumatic brain injury (TBI), but the optimal timing of pharmacological prophylaxis in operative cases remains controversial.

Methods: This retrospective study aimed to describe the timing of pharmacological prophylaxis initiation in operative TBI cases, stratified by surgery type, and to report the frequency of worsening postoperative intracranial pathology.

Results: Data from 90 surgical TBI patients were analyzed, revealing that 87.8% received VTE pharmacological prophylaxis at a mean of 85 hours postsurgery. The timing of initiation varied by procedure, with burr holes having the earliest start at a mean of 66 h. Craniotomy and decompressive craniectomy had the longest delay, with means of 116 and 109 h, respectively. Worsening intracranial pathology occurred in 5.6% of patients, with only one case occurring after VTE pharmacological prophylaxis initiation. The overall VTE rate was 3.3%.

Conclusion: These findings suggest that initiating VTE pharmacological prophylaxis between 3 and 5 days postsurgery may be safe in operative TBI patients, with the timing dependent on the procedure's invasiveness. The low frequencies of worsening intracranial pathology and VTE support the safety of these proposed timeframes. However, the study's limitations, including its single-center retrospective nature and lack of a standardized protocol, necessitate further research to confirm these findings and establish evidence-based guidelines for VTE pharmacological prophylaxis in operative TBI patients.

Keywords: Pharmacological prophylaxis, Timing, Traumatic brain injury, Venous thromboembolism, Chemoprophylaxis

INTRODUCTION

Venous thromboembolism (VTE) incidence in traumatic brain injury (TBI) patients ranges from 20% to 30%.[11,17,21] Recommendations for optimal timing of VTE pharmacological prophylaxis, especially in operative cases, vary. Enoxaparin has shown efficacy in reducing VTE risk in trauma patients, with a 30% reduction in all deep vein thrombosis (DVT) cases, a 58% reduction in proximal-vein thrombosis, and an overall reduction of 31%.[12] In TBI, the major concern is the risk of worsening intracranial pathology due to VTE pharmacological prophylaxis. This study aims to report the timing of pharmacological prophylaxis initiation in operative TBI cases,

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stratified by surgery type, and the frequency of worsening postoperative pathology.

MATERIALS AND METHODS

The Institutional Review Board (IRB) was consulted, and a consent waiver was granted because the study posed minimal risk to participants. Despite the waiver of consent, all data were anonymized and securely stored to ensure participants' privacy and confidentiality were rigorously protected throughout the study. After IRB approval, we conducted a retrospective review of an urban Level II Trauma Center's trauma registry from May 2018 to February 2020.

Variables included demographics, Glasgow coma scale (GCS), TBI severity, injury severity score (ISS), total length of stay (LOS), intensive care unit (ICU) LOS, duration of mechanical ventilation, primary neurosurgical diagnosis, postsurgical computed tomography (CT) at 6, 24, and 72 h, post-VTE CT if obtained, and type of neurosurgical intervention. We recorded the number of patients receiving VTE pharmacological prophylaxis, timing of prophylaxis initiation, frequency of return to the OR for worsening intracranial pathology, surveillance Doppler ultrasound (US), and VTE events. Reasons for not receiving pharmacological prophylaxis were also noted. Exclusion criteria were pediatric patients, LOS under 24 h, and non-operative TBI cases. Data were analyzed descriptively using means with standard deviations and medians with interquartile ranges (IQRs).

RESULTS

During the study period, 483 TBI patients were admitted. The cohort included 90 (18.6%) surgical cases, with a mean age of 66 (standard deviation [SD] ± 16.3) years and 67 (74.4%) male patients. The median GCS was 14 (IQR 6.75), and the median ISS was 25 (IQR 8). Among the patients, 52 (57.8%) had mild TBI, 23 (25.6%) had severe TBI, and 15 (16.7%) had moderate TBI. Patients had a mean ICU LOS of 7.9 (SD ± 8.4) days and a mean duration of mechanical ventilation of 9.9 (SD ± 10) days. The overall mean hospital stay was 21.3 (SD ± 33) days. The most common diagnosis was an acute or acute-on-chronic subdural hematoma (SDH) in 77 (85.6%) patients. Other diagnoses included epidural hematoma (5, 5.6%), brain contusions (4, 4.4%), traumatic subarachnoid hemorrhages (2, 2.2%), concussion (1, 1.1%), and diffuse brain edema (1, 1.1%).

Follow-up CT scans were obtained in 72 (80%), 65 (72.2%), and 60 (66.7%) patients at 6, 24, and 72 h after the immediate postoperative CT, respectively. Of these, 58/72 (80.6%), 59/65 (90.8%), and 57/60 (95%) studies were reported as "stable" within the same time frame. The most common procedure was burr-hole surgery, performed in 41 (45.6%) patients. In the total cohort, 79 (87.8%) patients received VTE pharmacological prophylaxis at a mean of 85 (SD ± 111) hours after surgery. The procedures with the longest time between surgery and initiation of pharmacological prophylaxis were craniotomy and decompressive craniectomy, with mean times of 116 (SD ± 180) and 109 (SD ± 46) hours, respectively. Table 1 summarizes the type of surgery, the number of patients who received VTE pharmacological prophylaxis, and the mean timing between surgery and initiation of prophylaxis.

In total, 11 patients (12.2%) did not receive pharmacological prophylaxis. Incomplete chart documentation for the reason not to start VTE prophylaxis was observed in 3/11 (27.3%) patients. CT after VTE prophylaxis initiation was obtained in 51/90 (56.7%) patients, with 48/51 (94.1%) reported as stable. Five (5.6%) patients required a return to the OR due to worsening intracranial pathology; 4 (4.4%) before and 1 (1.1%) after initiation of VTE pharmacological prophylaxis. Surveillance lower extremity venous US imaging was performed in 35 (38.9%) patients. The frequency of VTE was 3 (3.3%) patients from the total cohort of surgical patients.

DISCUSSION

VTE pharmacological prophylaxis in patients undergoing craniotomy for intracranial pathology has been studied previously.[2,10,20,22,24,25] Reducing VTE incidence with pharmacological prophylaxis in neurosurgical patients remains a key goal. A meta-analysis reported a 21.5% VTE rate in patients without prophylaxis, while the frequency of intracranial hemorrhage associated with prophylaxis ranges from 1.5% to 3%.[2,9,13,16]

VTE pharmacological prophylaxis in TBI remains debated, with limited descriptions of practices in exclusively operative cases. Delays in prophylaxis beyond 4 days postinjury increase VTE risk in TBI.[5,23] Based on the American College of Surgeons Trauma Quality Improvement Program guidelines, surgical patients, particularly those undergoing craniotomy and intracranial pressure (ICP) monitor placement, are classified as "high-risk" for intracranial bleeding progression.[5] Strategies for "high-risk" patients include using a retrievable inferior vena cava filter, surveillance duplex US, or initiating pharmacological prophylaxis after confirming stability on CT in patients with an ICP monitor or postcraniotomy.[5]

In non-surgical patients, the Berne-Norwood criteria recommend starting pharmacological prophylaxis after a stable head CT is demonstrated in patients with a low to moderate risk of expansion.[5] This timeframe is set within 24 h for low-risk patients and 72 h for moderate-risk patients.[3] Brain imaging after VTE prophylaxis initiation is not routinely performed;[14] in our series, it was obtained in 56.7% of patients. Over 94% of these CTs were reported as stable postprophylaxis, a lower frequency compared to other series, such as Kim *et al*., who

Table 1: Patients stratified by procedures and pharmacological prophylaxis.

Type of surgery	Total (%)	VTE prophylaxis		Time from surgery to prophylaxis (hours)			
		Yes (*n*=79) (%)	No (*n*=11) (%)	Mean	SD	Min	Max
Burr holes	41 (45.6)	36 (87.8)	5 (12.2)	66	23	40	155
Craniotomy	25 (27.8)	22 (88)	3 (12)	116	180	44	906
Decompressive craniectomy and ICP monitoring	8 (8.9)	8 (100)	-	84	33	57	160
Decompressive craniectomy	6 (6.7)	5 (83.3)	1 (16.7)	109	46	39	150
Craniotomy and ICP monitoring	5 (5.6)	5 (100)	-	78	24	54	112
Bolt/EVD for ICP monitoring	4 (4.4)	2 (50)	2 (50)	74	6	69	79
Burr hole and ICP monitoring	1 (1.1)	1 (100)	-	-	-	-	-

VTE: Venous thromboembolism, ICP: Intracranial pressure, EVD: External ventricular drainage, NA: Not applicable, SD: Standard deviation, Min: Minimum, Max: Maximum

obtained CT after prophylaxis in 88% of cases.[15] Our rationale for obtaining a CT included changes in the neurological exam during acute hospitalization, assessing stability after removing intracranial devices or if acute blood was observed on CT before initiating VTE pharmacological prophylaxis. The 94% stability on CT without further intervention supports the safety of pharmacological prophylaxis post-CT at 72 h. Most cases involved acute or acute-on-chronic SDHs. However, we aim to describe the outcomes of all surgical interventions in neurotrauma. Most of our cases involved burr holes, which require less exposure to the subdural space and associated vasculature. The average time to start pharmacological prophylaxis was 66 h in the burr-hole patients, less than other procedures ranging from 74 h for ICP monitoring placement to 116 h observed in craniotomies. It has been reported that patients with ICP monitoring experience longer delays in initiating VTE prophylaxis, thus increasing the potential risk for VTE.[4] Allen *et al*. found that patients with ICP monitors received VTE prophylaxis more frequently (64.3% vs. 49.4%, $P < 0.001$) but also with a longer delay in its initiation (5 vs. 4 days) compared to patients without monitoring.[4] Dengler *et al*. found a median time of 3.6 days for VTE prophylaxis initiation and an overall 12% incidence of VTE in severe TBI patients. They found no association between DVT or intracranial hemorrhage expansion with the initiation of DVT prophylaxis using either unfractionated heparin or low-molecular-weight heparin.[8] Interestingly, one might assume that more extensive and invasive surgery, such as decompressive craniectomy with concurrent implantation of an ICP monitor, would be associated with more delayed initiation of VTE prophylaxis. However, we found a mean of 109 h (4.5 days) for decompressive craniectomy alone, compared to 84 h (3.5 days) for decompressive craniectomy with concurrent ICP monitor placement, although the latter involved only eight cases.

The reported incidence of intracranial contusion expansion after TBI varies widely, with rates reaching up to 51%.[1,7,18,19] Chang *et al*. reported a 38% expansion rate for intraparenchymal hemorrhage (IPH) and identified three prognostic factors: Subarachnoid hemorrhage, larger initial hematoma size, and the presence of SDH. Subarachnoid hemorrhage was the strongest predictor, and each cm^3 increase in initial volume raised progression odds by 11%. SDH was also predictive of expansion but was the weakest of the three factors.[7] Abdel-Aziz *et al*. reported that the risk of IPH expansion was higher if pharmacological prophylaxis was started before day 3 after the trauma.[1] Recently, Byrne *et al*. found that delays in initiating chemical VTE prophylaxis increased the risk of thromboembolism by 8% for each additional day. Conversely, earlier initiation of VTE prophylaxis raised the risk of repeated neurosurgery, with each additional day of prophylaxis associated with a 28% decrease in the odds of repeated neurosurgery.[6] These timeframes and the fact that most reinterventions (4.4%) occurred without pharmacological prophylaxis suggest surgical patients may benefit from early VTE prophylaxis initiation.

Limitations

This study has several limitations. The relatively small sample size, retrospective single-center data, and lack of a standardized protocol limit the generalizability of the observed outcomes. In addition, the absence of a control arm weakens the strength of the recommendations. However, we aimed to focus exclusively on surgical patients and to present outcomes based on the type of procedure performed.

CONCLUSION

This study demonstrated that initiating VTE prophylaxis between 3 and 5 days after neurosurgical intervention in TBI patients did not increase the risk of worsening intracranial bleeding. The timing of prophylaxis initiation varied by the type and extent of surgery, with burr-hole procedures having the earliest initiation post-surgery. The low frequency of worsening intracranial pathology requiring surgical intervention after VTE prophylaxis and the low incidence of

VTE suggest that these proposed timeframes may be safe for use in this patient population.

Ethical approval

The Institutional Review Board has waived the ethical approval for this study. The approval number is STUDY-20-01889.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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