**The feasibility of early chemical thromboprophylaxis in traumatic brain injury patients admitted to a trauma ICU.**

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## Introduction

Trauma is a disease process that occurs because of man's interaction with other people and the environment. Trauma is the leading cause of non-natural death, a significant cause of permanent disability, with the economically active population group most affected (1,2). Traumatic brain injury (TBI) characterises a major source of trauma-related mortality and is a leading cause of permanent disability in the young population (3). Traumatic brain injury commonly occurs in the background of polytrauma and remains a major obstacle in improving trauma outcomes. Mortality is directly attributable to TBI in up to one-third of patients who die after multiple injuries (4).

Traumatic brain injury ranges in severity from mild to severe, with mild injury causing a headache and severe injury being fatal. In most cases, there is radiologic proof that intracranial haemorrhage is present in all TBI patients, referring to subarachnoid haemorrhage (SAH), subdural haematoma (SDH), extradural haematoma (EDH), contusions, or intracerebral haemorrhage (ICH) (5-6). These lesions, SAH, SDH, EDH, etc. are characterised by an increased risk of haemorrhage progression. The incidence of coagulopathy is higher in patients with TBI than in the general trauma population, especially in those with penetrating injury. Patients with TBI are at an increased risk of pulmonary embolism (PE) (7). The incidence of venous thromboembolism (VTE) ranges between 20 and 32%, with some studies reporting figures as high as 54% (8-10). These polytrauma patients with TBI are usually admitted to Intensive Care Units (ICU) (8). In addition to trauma-related coagulopathy, TBI increases the risk of coagulopathy, and its presence is a poor prognostic factor (10,11). Coagulopathy follows a course from hypercoagulable to hypocoagulable state, as shown in disseminated intravascular coagulation (DIC).

Deep vein thrombosis (DVT) prophylaxis, chemical thromboprophylaxis is used in combination with mechanical devices, namely the pneumatic compression devices. There is an increased risk of coagulopathy and worsening intracranial haemorrhage despite using these mechanisms, namely chemical thromboprophylaxis and mechanical compression devices (12). Although worsening of intracranial haemorrhage complication sounds catastrophic, TBI stabilise with time (13). In addition to compression devices, chemical prophylaxis may be initiated if the TBI is stable, and the benefits outweigh the risk of ICH (12,14). There is no clear evidence to support recommendations regarding the preferred drug, dose, or the timing of chemical thromboprophylaxis (15). Chemical thromboprophylaxis in patients who have sustained TBI is initiated either early within 72hours or late after 72hours once a repeat computer tomography of the brain (CTB) (15,16).

Polytrauma patients are particularly at an increased risk of developing VTE compared to the general trauma population. The risk factors are prolonged hospitalisation, significant injury severity, concurrent moderate-to-severe injuries in other organ systems, and old age. The incidence of VTE in these patients is high despite pharmacologic and mechanical prophylaxis. Certain associated injuries in polytrauma patients preclude the initiation of chemical thromboprophylaxis to avoid the risk of causing uncontrollable haemorrhage from the injured organ systems. In addition to bleeding

from the injuries, polytrauma may cause significant coagulopathy, which itself is a contraindication to initiation of chemical thromboprophylaxis (15-17).

The mainstay of treatment for VTE is anticoagulation. The most widely used agent is the low molecular weight heparin like enoxaparin; this is also the agent of choice at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Its use in TBI is based on its efficacy and non-invasive means of reducing VTE; however, in TBI patients it may lead to iatrogenic worsening of intracranial bleeding due to a combination of haemorrhage itself and thrombocytopenia and cause neurological deterioration (18). Progression of haemorrhagic TBI or haemorrhage from other injuries is a severe adverse event that makes it challenging to start chemical thromboprophylaxis (18,19). Clinicians are usually confronted with the dilemma of balancing the risk of haemorrhage due to chemical thromboprophylaxis *versus* thromboembolic sequelae associated with withholding chemical thromboprophylaxis (19).

Venous thromboembolism refers to DVT and pulmonary embolus. A pulmonary embolus may lead to hypoxia, haemodynamic instability, and cardiac arrest, which could worsen injury in TBI patients and worsen the patient's prognosis (19,20). Deep vein thrombosis is diagnosed by compression Doppler Ultrasound and other modalities of the lower limbs, which are usually done over trifurcation of deep calf veins, proximal and distal popliteal veins, and femoral areas. Pulmonary embolus is confirmed with a contrast spiral CT scan of the chest and lungs (20).

Retrospective, observational studies have shown that early initiation of pharmacologic VTE prophylaxis within 72 hours is more effective than after 72 hours and may not affect safety (20). However, studies show limited evidence on chemical VTE prophylaxis after TBI to suggest a treatment regimen, initiation, dose, and treatment period (21-22). Mesa Galan *et al.* (2016) suggested that initiation of chemical thromboprophylaxis within 72 hours after trauma may provide greater effectiveness in VTE prevention after TBI when there is no haemorrhage progression at 24 hours after admission, following a repeat CTB scan.

There is limited evidence to confirm the safety of initiation of VTE prophylaxis in patients with TBI. It is unclear whether earlier initiation of VTE prophylaxis results in a meaningful reduction of VTE rates or whether this confers the risk of delayed ICH (17). The Trauma Brain Foundation Guideline (2016) for the management of severe TBI cites level lll evidence for using low molecular weight heparin or low dose unfractionated heparin in combination with mechanical prophylaxis. The guideline, however, does not provide a recommendation with respect to which subgroups of TBI patients might benefit from early chemical thrombo-prophylaxis and the preferred agent, timing of administration and dose. The practice at CMJAH Trauma ICU is to initiate chemical thromboprophylaxis after obtaining a repeat CT, with proven clinical improvement, a stable or improvement injury compared with the index CT. Therefore, this study aims to determine the feasibility to initiate early chemical prophylaxis in our clinical setting. It further aims to identify the subgroups of TBI patients which may benefit from early chemical thromboprophylaxis based on CT findings.

## Study Design and Methodology

### Study design

This is a retrospective study, with data collection from the MediBank Resuscitation Forms, Picture archiving and communication system (PACS) records of the Department of Radiology, National Health Laboratory Service results (NHLS), clinical records of TBI patients admitted to the Trauma ICU at CMJAH in South Africa.

### Types of patients involved

Traumatic brain injury patients admitted and treated in the Trauma ICU during the study period from 01 January 2017 to 31 December 2018, who met the study inclusion criteria: being older than 18 years of age, had a repeat CT scan of the brain, and a complete MediBank Resuscitation Form were included in the study. Patients with incomplete data despite meeting the above criteria and those with delayed referral to CMJAH of more than 24hours, were excluded from the study.

### Types of data collected

Patient information such as age and gender were collected from the Medibank Resus Forms. Mechanism of injury, brain injuries sustained, and other organ injuries were collected from the Medibank Resus Forms and PACS records. Patient physiological characteristics, including Glasgow Coma Scale (GCS) upon arrival at the Trauma Unit. The Glasgow Coma Scale (GCS) of 8/15 or less was considered severe, and a GCS of more than 9/15 was considered mild and moderate. Emergency department blood pressure, evidence of hypothermia and acid-base status, were recorded. The patients' need for blood and blood product transfusion status, admission CT and the repeat CT scan of the brain were also collected. Injuries sustained and Injury Severity Score (ISS) were also documented. Blood results including the platelet levels were collected from the NHLS database system. Development of clinical DVT or pulmonary embolus was recorded. Data on 28-day mortality was also recorded.

### Statistical analysis

Analysis was done with the assistance of the Statistics Hub of the Department of Surgery, University of the Witwatersrand. The STATA Statistics/Data Analysis version 16.0 (StataCorp, Special Edition College Station, Texas), using descriptive statistics, was used to summarise most of our data. Statistical difference between comparable groups was calculated using Pearson's Chi-square test for categorical variables as appropriate. The Fisher's exact test was used for continuous variables, such as repeat CTB, initiation of chemical thromboprophylaxis, etc. A p-value $< 0.05$ was considered to be statistically significant.

### Ethics approval and study permission

Ethics approval was obtained from the Human Research Ethics Committee (HREC) (medical) of University of the Witwatersrand, clearance number: M200345. Permission to collect patient data and access to MediBank Resus Forms and patient records was obtained from the office of the CEO and Trauma Surgery Unit at CMJAH.

## Results

Hundred and thirty-two patients with TBI were admitted to a Trauma ICU during the study period and were included in the study. (Table 1.) The average age of participants was 33.8 years (19 to 61) (SD ± 9.17). Only 12, 12% (16/132) of the study subjects were females, male. 68.18% (n=90) patients had severe GCS, 17.78% (n=16/90) were patients who had worsening injuries, 31.82% (n=42) had mild to moderate head injuries as classified on GCS, 4.76% (2/42) patients were patients with worsening features (P=0.056, not statistically significant). The worsening group had an average systolic blood pressure of 140mmHg (SD 33.34) (P=0.889, not statistically significant). The average initial pulse on arrival in the hospital was 95 beats per minute (b/m), (49 to 164b/m) in the non-worsening group, versus 99.3b/m (59 to 147) in the worsening group (P=0.551 not statistically significant). The average pH values were 7.314 (range) in the non-worsening group and 7.285 (range) in the worsening group (P=0.118 not statistically significant). The average base deficit was -5.6 in the non-worsening group and -6.6 in the worsening group (P-0.255 not statistically significant). The mean lactate was 3.8 in the non-worsening group and 4.8 in the worsening group (P=0.212). The mean initial platelets (Plt) on arrival were 210 (mean=215) in the non-worsening group and 213 (mean=211.3) in the worsening group (P=0.876 not statistically significant). The average Plt at 48 hours were 148 (mean=164.8) and 138 (mean=145.2) respectively (P=0.369 not statistically significant).

Eighty percent of patients in the study group as shown in Table 1 did not require a blood transfusion, while 19.70% (n=26) of patients required blood transfusions. Only 19.23% (5/26) were patients from the worsening group, and 80.77% (21) were from the non-worsening group (P=0.350 not statistically significant).

The mean injury severity score (ISS) in the non-worsening group was 19.25 and 21.72 in the worsening group (Table 1). (P-0.299 not statistically significant)

Hundred and twenty-six (95.45%) patients were alive at 28days, 9.5% (12/126) of those were in the worsening group (see Table 1). Six patients (4.55%) died, 66.67% (4) were from the worsening group and 33.33% (2) from the non-worsening group (P=0.003 statistically significant). All patients who died were males. One patient was from the group that received chemical thromboprophylaxis within 24 hours of admission, two patients were from those that received chemical thromboprophylaxis in 48 hours, and three patients were from the group that received chemical thromboprophylaxis at least 72 hours after admission (P=0.565 not statistically significant).

Table 1. Patient characteristics and physiology.

| Demographic parameters | | Total N=132 | Non-worsening features n=114 | Worsening features n=18 | P-value |
|---|---|---|---|---|---|
| Age(years) | | 132 | 33.73 (±9.37) | 34.06 (±7.99) | |
| Gender | Male | 116 (87.88%) | 99 (85.34%) | 17 (14.66) | 0.696 |
| | Female | 16 (12.12%) | 15 (93.75%) | 1 (6.25%) | 0.696 |
| GCS | ≤9 | 90(68.18%) | 74(82.22%) | 16(17.78%) | 0.033 |
| | >9 | 42(31.82%) | 40(95.24%) | 2(4.76%) | 0.033 |
| Blood Pressure | Systolic | 137.39 (±31.59) | 136.96 (±31.44) | 140.17 (±33.34) | 0.889 |
| | Diastolic | 86.55 (±27.74) | 86.24 (±27.89) | 88.56 (±27.44) | 0.827 |
| Pulse | | 95.70 (±22.81) | 95.14 (±22.10) | 99.28 (±23.74) | 0.551 |
| Platelets | Initial | 214.65 (±83.40) | 215.15 (±84.51) | 211 (±78.20) | 0.876 |
| | 48hours | 162.11 (±64.82) | 164.81 (±66.65) | 145.17 (±50.08) | 0.369 |
| pH | - | 7.310 (±0.105) | 7.314 (±0.11) | 7.284 (±0.09) | 0.118 |
| Lactate | - | 4.05 (±2.61) | 3.94 (±2.57) | 4.79 (±2.86) | 0.212 |
| BE/D | - | -5.68 (±5.27) | -5.53 (±5.34) | -6.61 (±4.83) | 0.255 |
| Need for transfusion | Blood/ products | 26(19.70%) | 21(80.77%) | 5(19.27%) | 0.350 |
| ISS | - | 19.59 (±7.80) | 19.25 (±7.67) | 21.72 (±8.46) | 0.303 |
| Mortality | 28day | 6(4.54%) | 2(33.33%) | 4(66.67%) | 0.003 |

BP-blood pressure in mmHg, Plt-platelets. GCS=Glasgow coma scale, BE/D=base excess/deficit, ISS-injury severity score.

Table 2: Mechanism of injury (MOI), CT findings and initiation of Clexane.

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|---|---|---|---|---|---|
| Mechanism of injury | RTA | 67(55.83%) | 59 (88.06%) | 8 (11.94%) | 0.695 |
| | Assault | 30(25%) | 27(90.00%) | 3(10.00%) | 0.695 |
| | FFH | 16(13.33%) | 13(81.25%) | 3(18.75%) | 0.695 |
| | GSW | 7(5.30%) | 7(100%) | 0(0.00%) | 0.695 |
| CT Findings | SAH | 46(34.85%) | 40(86.96%) | 6(13.04%) | 0.909 |
| | EDH | 26(19.70%) | 23(88.46%) | 3(11.54%) | 0.909 |
| | SDH | 41(31.06%) | 34(82.93%) | 7(17.07%) | 0.909 |
| | ICH | 19(14.39%) | 17(89.47%) | 2(10.53%) | 0.909 |
| Time to repeat CT | 24hours | 11(9.09%) | 9(81.82%) | 2(11.54%) | 0.081 |
| | 48hrs | 49(40.50%) | 38(77.55%) | 11(22.45%) | 0.081 |
| | ±72hours | 61(50.41%) | 56(91.80%) | 5(8.20%) | 0.081 |
| Initiation of enoxaparin | 24hours | 18(13.64%) | 16(88.89%) | 2(11.11%) | 0.544 |
| | 48hourrs | 28(21.21%) | 24(85.71%) | 4(14.29%) | 0.544 |
| | ±72hours | 86(65.15%) | 74(86.04%) | 12(13.95%) | 0.544 |

SAH-subarachnoid haemorrhage, EDH-extradural haematoma, subdural haematoma. CT-computer tomography. RTA-road traffic accident, FFH-fall from height.

As shown in Table 2 above: Most of the patients, 50.76% (n=67), were involved in road traffic-related accidents (RTA), 22.73% (n=30) were victims of interpersonal violence through various methods of assault, 12.12% (n=16) fell from various heights, and only 5.30% (n=7) of the patients were victims of gun-related violence. The commonest injuries identified on the index CT brain scans were SAH, EDH, SDH & ICH. Out of these bleeds, SAH (34.85%, n=46) and SDH (31.06%, n=41) were the highest numbers of injuries, respectively. On getting a repeat CTB, 8.33% (n=11) participants had a repeat CTB within 24hours of admission, 40.50% (n=54) had a repeat CTB between 24 and 48hours of admission, and 50.41% (67) had a repeat CTB between 48 and 72hours of admission. Eighteen (13.64%) had worsening features on repeat CTB (P=0.909). Eleven (8.33%) patients did not have a repeat CT scan of the brain, the reason being delays in getting the scan, and those 11 patients had clinically neurological improvement anyway. They were then started on chemical thromboprophylaxis without any obvious adverse events. Eighty-six (65.2%) patients had initiation of chemical thromboprophylaxis at least 72hours after admission, of these, 14% (n=12/86) were those with worsening features on a repeat CTB (P-0.081). Forty-six (34.85%) had chemical thromboprophylaxis between 24hours (n=18) and 48hours (n=28), six (13.04%) of those patients were in the group with worsening features on a repeat CTB (P=0.000). In patients (n=18) with worsening features, 50% (n=9) had new-onset bleeding, and the other 50% (n=9) had progression of the index injuries (P=0.000).

Associated injuries (Table 3), 13.64% (n=18) of patients had significant long bone fractures. Out of those, 27.78% (n=5/18) were in the worsening group (P=0.169), 9.85% (n=13) of patients had

significant chest trauma, while 84.62% (n=11/13) patients had no worsening features on the repeat CTB, and only 15.38% (n=2/13) patients were from the worsening group. Many patients had minor injuries or no significant injuries at all (P=0.607). Thirteen patients had significant intra-abdominal injuries; however, only 2/13 were from the group with worsening features, the rest had minor, or no injuries at all (P=1.000), 5.30% (n=7) of patients had significant pelvis injuries, and all were from the non-worsening group (P=0.855). Those patients in the non-worsening group had major associated injuries. As noted, only 1 (0.88%) patient had a major injury to the neck, and that patient was in the non-worsening group (P=0.136).

Table 3: Injuries in patients without worsening injuries, followed by Injuries in patients with worsening injuries.

| Organ injury | Neck | Chest | Abdomen | Pelvis | Long bone |
|---|---|---|---|---|---|
| none | 97(88.89%) | 51(83.61%) | 83(86.46%) | 97(85.09%) | 85(87.63%) |
| Negligible | 16(72.73%) | 52(89.66%) | 20(86.96%) | 10(90.91%) | 16(94.12%) |
| Severe | 1(100%) | 11(84.62%) | 11(84.62%) | 7(100%) | 13(72.22%) |
| Worsening group | | | | | |
| None | 12(11.01%) | 10(16.39%) | 13(13.54%) | 17(14.91%) | 12(12.37%) |
| Negligible | 6(27.27%) | 6(10.34%) | 3(13.04%) | 1(9.09%) | 1(5.88%) |
| Severe | 0 | 2(15.38%) | 2(15.38%) | 0 | 5(27.78%) |
| P-value | 0.136 | 0.607 | 1.000 | 0.855 | 0.169 |

**Discussion**.

The study shows most patients were young, under 50 years of age. This confirms that trauma remains a common disease of the young and fit patients in our settings, as much as it is throughout the world (18). The majority of patients in this study are male. This is in keeping with the rest of the world, as it was also observed by Matsushima and his colleagues, 2021 (24). Mechanisms of injuries range from interpersonal injuries, RTA, to violent/accidental falls (19). RTA remains the highest contributor to injuries. This is a trend throughout the world. The spectrum of injuries in the study matches those observed locally and internationally (24). It is noteworthy that in South Africa the burden on injuries is due to interpersonal violence, such as assault with sharp objects, yet the study demonstrated a higher number of ICU admissions due to blunt injuries (25). This may be due to several factors, the study focussed on TBI admissions, without any comparison with penetrating injuries. Most penetrating injuries do not involve the head. It may also be due to factors such as rapid urbanisation, increase in vehicles on the road, as well as the fact that most penetrating injuries are managed in a trauma high care or general ward (25, 26). Patterns injuries and weapons used differ per province, rural provinces still see Axe related injuries, whereas urban provinces see gun short wounds (26)

The role of an initial and a repeat CT brain is well established in the management of TBI (19). All patients received an index CT scan upon arrival in the trauma emergency area. Getting a repeat CTB varied in intervals from 24 to 72hours, 49 patients (40%) had their repeat CT at least 48hrs.

Delays in getting a repeat CTB were excessive in some cases, mainly due to the limited availability of CT scan machines. There are no dedicated trauma surgery scans in our settings. All emergency scan investigations are done on one, at most, two CT scan machines at any given time. It is worth noting that 8.33% of our patients did not have a repeat CT brain due to time delays because of resource constraints. This is not unknown in a low middle-income country like ours, with as little as 14% of the GDP spent on healthcare services (27). While waiting for the repeat scan, they had clinical improvement of their neurology, and appropriate chemical thromboprophylaxis was administered. Resource constraints play a huge role; this differs from first-world countries where a repeat CT can be obtained as early as 12hours after presentation to a health care facility (13).

Clinically CMJAH Trauma ICU initiates chemical thromboprophylaxis post a repeat CT. Currently, there is no international guideline or consensus on the strict timing for the initiation of chemical thromboprophylaxis. The trauma brain foundation and other studies that were commissioned to validate the TBF guidelines do not give clear indications on the initiation of chemical thromboprophylaxis. Even centres with easy access to CT scans have not yet come up with clear guidelines for initiating chemical thromboprophylaxis (12,13). They advocate for an individualised approach to initiation of prophylactic therapy, patients are evaluated, and appropriate treatment is given to the right patient. All TBI patients are placed on pneumatic mechanical thromboprophylaxis unless factors are precluding the placement of such devices (28). This is also practised in our settings.

Some studies posit that it is safe to initiate chemical thromboprophylaxis within 72hours of sustaining a traumatic brain injury, especially in patients at low risk of progression of intracranial bleeding (12,13). These patients must have a confirmed stable injury on the repeat CT brain. This shows that repeat CT brain findings are a major determining factor in the initiation of chemical thromboprophylaxis in these patients. The study confirms our institutional practice to administer chemical prophylaxis when the CT scan does not reveal the expansion of the bleeding. This practice is in keeping with international standards (12). Patients who had worsening injuries on repeat CTB (13.64%) were given chemical thromboprophylaxis on a case-by-case basis, based on their clinical improvement, and a third CTB. In some patients, chemical thromboprophylaxis was started at least 168 hours after the injury. Two-thirds of patients in our study had severe GCS, but only (N=16) 17.78% had worsening features on a repeat CT of the brain, such as new-onset bleeding or progression of the index bleeding. In total, most of our patients (82.22%) did not have worsening features.

Our data did not show any correlation between the severity of TBI, the physiology status of the patients or the patient's neurological status, and worsening injury. Platelets play an essential role in haemostasis after trauma. A drop in platelet count is associated with an increase in the progression of post-traumatic intracranial bleeding (19,20). Our patients didn’t have a significant drop in their platelet count. However, we did not analyse the platelet functionality due to inconsistent use of thromboelastogram.

It is well known that in TBI polytrauma patients, coagulopathy is associated with intracranial bleeding progression; the majority of our study population did not have progression of their injuries (19). The patients in our study had an overall higher ISS, which the literature associated with a worse outcome (6). In our study, however, even with a high ISS, the presence of other associated injuries was not associated with a poor outcome or even increased 28-day mortality. Crawford AM et al. (2019)

suggested that most severe chest traumas are associated with significant concomitant injuries, such as TBI and are prone to developing PE. Only thirteen of our patients, 2 (15.38%) from the worsening group and 11(84.62%) from the non-worsening group, had associated chest injury.

Our patient mortality at 28-days was 4.55% (n=6). The low mortality rate may be influenced by an objective trauma system, which involves a good pre-hospital system and prompt in-hospital resuscitation and ICU care (19,28). The in-patient mortality was higher in the worsening group; this was also observed by Matsushima K *et al*. 2021 (24). Two patients were from the non-worsening group, and four were from the worsening group. Of note is that the two non-worsening patients had initiation of chemical thromboprophylaxis at 72 hours, and one required blood transfusion. However, we cannot conclusively attribute the deaths to VTE. Three patients from the worsening group had a repeat CTB at 48hours, and all four had initiations of chemical thromboprophylaxis post the CTB. The one patient had initiation of chemical thromboprophylaxis within 24 hours of admission to the ICU; whether this was the cause of death is unknown. Males had higher death rates than females, especially in the 24–54 years age group (21). All the patients who died in our study were males. None of the females had mortality as an adverse outcome; this is in keeping with the available literature that the male gender is associated with worse injuries and outcomes (29).

From our study, most patients did not worsen; even those who had worsening features on a repeat CT scan improved in ICU. This may be multifactorial, and it could be that many patients are young and have a good physiological reserve or that the trauma system in our town is working well (1). With this in mind, and comparing the available literature, a repeat CTB scan seems to be the only parameter that we can use to guide the initiation of chemical thromboprophylaxis. There are no studies that considered other parameters that could preclude the initiation of chemical thromboprophylaxis. As such, we have no direct reference point. Regarding other associated injuries (severe or minor) other than bleeding, no recent major studies reported them as a contra-indication to chemical thromboprophylaxis. This is because associated injuries are managed with damage control surgery, with precise and early haemorrhage control. They are mentioned as factors contributing to morbidity and, in certain studies, as factors affecting mortality (20).

Some institutions recommend initiation of chemical thromboprophylaxis by 48hours, based on their body of evidence. However, they also report that clinical judgement on the risk *versus* benefits of initiation of chemical thromboprophylaxis is essential. It is said that low molecular weight heparin is not associated with the progression of intracranial haemorrhage (22). This speaks to our findings that many patients can be initiated on chemical thromboprophylaxis by 48hours. This is supported by our report that we had favourable outcomes for most patients. However, this should be preceded by a repeat CTB and clinical judgement on the patient's neurology. Currently, there are no randomised control trials or multicentre studies to guide the initiation of chemical thromboprophylaxis. The available data is from institutions with a varying number of patients in their studies. There is a need for local and regional development of protocols in conjunction with available resources and practices (20).

**Limitations and strengths**

It is a retrospective study at a single centre. We couldn't add and analyze a thromboelastogram (TEG) as a variable because it was not done on every patient entered in the study. Whereas it is possible that unmeasured confounding factors may be at play, it is possible that a significant part of the TBI-associated effect is due to the TBI itself and not due to confounding factors (23). The study relied on clinical evaluation and surveillance for DVT and only requesting further evaluation if there was further suspicion. It is possible that minor clinically insignificant VTE were missed. However, there may be a selection bias in those initiated within 24 hours; these may be patients with mild

injury and good physiology The study was cost-effective, and it can help formulate a hypothesis for future prospective and multi-institutional studies.

## Conclusion

The results of the study do not show any statistically significant difference in the rate of worsening of intracranial bleeding if chemical thromboprophylaxis is initiated at 24 hours vs 72hours. It was therefore feasible to initiate early chemical prophylaxis for head injury cases at our institution. No specific bleed identified on CTB was noted to be unique in prohibiting initiation of early chemical thromboprophylaxis. However, the data is promising, and there is a need for active surveillance of PE/DVTs in TBI patients. There must be a consistent use of TEG. A prospective, multicentre study with higher study numbers is required to establish local practice guidelines on this subject.

## Conflict of Interest

None.

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