ORIGINAL ARTICLE

Incidence and Risk Factors Associated with Venous Thromboembolism in Thai Trauma Patients

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Background: Venous thromboembolism (VTE) is a major problem in trauma patients, especially in Western countries. The incidence of VTE in Asian trauma patients is lower. Hence, chemoprophylaxis such as anticoagulation is not routinely used at the authors' institution.

Objective: To identify the incidence and risk factors of VTE in Thai trauma patients not on chemoprophylaxis.

Materials and Methods: Trauma patients admitted between September 2021, and December 2022 were screened for lower extremity deep vein thrombosis (DVT) using Doppler ultrasonography (DUS). Stepwise linear regression analysis was performed to identify factors associated with the development of VTE.

Results: Five hundred seventy-nine patients were included, of whom 396 were male (68%), and 183 were female (32%), with the mean age of 51.5 years. Nine patients had VTE, thus a VTE rate of 1.6%. Three had isolated DVT, five had isolated pulmonary embolism (PE), and one had combined DVT and PE. The risk factors for VTE were female (p=0.009, OR 10.1, 95% CI 1.8 to 56.9), spinal cord injury (p=0.015, OR 11.9, 95% CI 1.6 to 87.6), and length of stay (LOS) more than seven days (p=0.039, OR 7.5, 95% CI 1.1 to 51.1). One patient in the VTE group died of massive PE, thus the mortality rate in the VTE group was 11%.

Conclusion: The incidence of VTE in Thai trauma patients was 1.6%. Risk factors for VTE included female gender, spinal cord injury, and prolonged hospitalization. Further studies are needed to identify a subgroup of patients who would benefit from chemoprophylaxis.

Keywords: Venous thromboembolism; Trauma

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Traumatic injury is a known independent risk factor for venous thromboembolism (VTE), with underlying mechanisms attributed to venous stasis due to immobilization, venous injury, and trauma-induced hypercoagulable state[1-3]. Landmark studies from Canada showed that the incidence of VTE in trauma patients was high at 58% but could be reduced to 31% to 44% with chemoprophylaxis with heparin or low-molecular-weight heparin[4,5]. VTE chemoprophylaxis has since become the standard of care for trauma patients in Western countries[6]. The study from the United States national trauma data bank demonstrated that the incidence of VTE in trauma patients in the era of chemoprophylaxis was 1%[7]. In Asia, prior data revealed that the incidence of VTE in Asian trauma patients with selective chemoprophylaxis ranged from 0.4% to 2.8%[8-10]. The Asian guidelines recommend selective chemoprophylaxis, only when thrombotic risks outweigh bleeding risks[11]. Since the reported incidence of VTE in Asian trauma patients is lower than in Western countries, chemoprophylaxis is not routinely used. In absence of chemoprophylaxis, the authors previously reported a 3.6% incidence of VTE in surgical intensive care unit patients, of whom 10% were trauma patients[12]. The aim of the present study was to identify the incidence and risk factors for VTE in Thai trauma patients who did not receive chemoprophylaxis.

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Materials and Methods

A retrospective study was performed on trauma

Table 1. Demographic and clinical data of the 579 trauma patients

Factors	Total (n=579)	VTE (n=9)	No VTE (n=570)	p-value
Sex; n (%)				0.031*
Male	396 (68.4)	3 (33.3)	393 (68.9)	
Female	183 (31.6)	6 (66.7)	177 (31.1)	
Blood transfusion; n (%)	180 (31.1)	6 (66.7)	174 (30.5)	0.029*
Tranexamic acid; n (%)	73 (12.6)	1 (11.1)	72 (12.6)	0.683
Head injury; n (%)	317 (54.8)	4 (44.4)	313 (54.9)	0.384
Spinal cord injury; n (%)	42 (7.3)	2 (22.2)	40 (7.0)	0.134
Leg edema; n (%)	1 (0.2)	1 (11.1)	0 (0.0)	0.016*
Length of stay >7 days; n (%)	213 (36.8)	7 (77.8)	206 (36.1)	0.014*
Age ≥60 years; n (%)	226 (39.0)	5 (55.6)	221 (38.8)	0.245
BMI ≥25; n (%)	244 (42.1)	3 (33.3)	241 (42.3)	0.429
ISS; mean±SD	16.5±11.0	16.4±11.0	19.6±12.6	0.194
Mortality; n (%)	20 (3.5)	1 (11.1)	19 (3.3)	0.272

VTE=venous thromboembolism; BMI=body mass index; ISS=injury severity score; SD=standard deviation

The p-value for categorical variables were derived from Fisher's exact test, and the p-value for continuous variables were derived from Student's t test,
* Significant values ($p<0.05$)

patients admitted between September 2021, and December 2022 at King Chulalongkorn Memorial Hospital, a 1,400-bed tertiary referral university hospital in Bangkok, Thailand. Patients younger than 15-years-old, pregnant patients, and patients of non-Thai ethnicity were excluded from the study. All patients included did not receive VTE chemoprophylaxis, nevertheless, all received intermittent pneumatic compression (IPC) and a weekly deep vein thrombosis (DVT) screening with Doppler ultrasonography (DUS). Bilateral lower extremities were examined with a high-frequency linear array probe starting at the groins for the common femoral vein, down to the thighs for the superficial femoral vein, and to the popliteal fossae for the popliteal vein. The main criterion for DVT diagnosis was the absence of venous compressibility. Adjunctive criteria for DVT diagnosis included the presence of thrombus, decreased venous flow, and the absence of flow augmentation upon calf compression[10]. All positive DUS results were subsequently confirmed by radiologists. The diagnosis of pulmonary embolism (PE) was made by computed tomography pulmonary angiography (CTA) in suspected patients. If a diagnosis of VTE was made, IPC was discontinued from the affected limb and the treatment of VTE with anticoagulation would be started in the absence of contraindications.

Data collection included demographic data, injury details, and outcomes in terms of DVT and PE. Obesity was defined as a body mass index (BMI) of greater than 25, based on criteria from Japan Society for the Study of Obesity (JASSO), which may better represent obesity in the Asian population[13]. The primary outcome was the incidence of VTE, while secondary outcomes were risk factors associated with VTE. The present study was approved by the Institutional Review Board (IRB No. 0293/66). Statistical analysis was done by the IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) with statistical significance set at p-value of less than 0.05. Univariable analysis was performed with the Fisher's exact test for comparison of categorical variables, and the independent t-test for comparison of continuous variables. Multivariable analysis of factors associated with VTE risk was conducted using a stepwise linear regression model.

Results

Five hundred seventy-nine adult trauma patients admitted between September 2021, and December 2022 were identified, of which 396 were male (68%) and 183 were female (32%). The mean age was 51.5 years, with a range of 15 to 99 years. VTE was diagnosed in nine patients for a VTE rate of 1.6% (95% CI 0.4 to 30.5), of whom three had isolated DVT, five had isolated PE, and one had combined DVT/PE. Demographic and clinical data are shown in Table 1. The patients with VTE were more likely to be female, received more blood transfusions, had a higher rate of leg edema, and 78% of them had a length of stay of greater than seven days. None of the 579 patients had additional hypercoagulable states identified. The mechanisms of injury were not different between the two groups (Table 2).

Table 2. Mechanism of injuries

Groups	Total (n=579)	VTE (n=9)	No VTE (n=570)	p-value
Gun shot wound	16 (2.8)	0 (0.0)	16 (2.8)	0.776
Stab wound	25 (4.3)	0 (0.0)	25 (4.4)	0.670
Car motor vehicle accident	36 (6.2)	0 (0.0)	36 (6.3)	0.556
Pedestrian accident	23 (4.0)	1 (11.1)	22 (3.9)	0.307
Fall	199 (34.4)	4 (44.4)	195 (34.2)	0.375
Fall from height	52 (9.0)	1 (11.1)	51 (8.9)	0.574
Motorcycle	128 (22.1)	3 (33.3)	125 (21.9)	0.318
Assault	84 (14.5)	0 (0.0)	84 (14.7)	0.241
Miscellaneous	8 (1.4)	0 (0.0)	8 (1.4)	0.882

The p-value was derived from Fisher's exact test

Table 3. Characteristics of 9 trauma patients with VTE

Patients No.	Sex	Age (years)	LOS (VTE Dx)	Mechanism of injury	Diagnosis	Head injury	Spinal cord injury	Leg edema	VTE diagnosis	Outcome/ cause of death
1	F	83	10 (3)	Fall	Subarachnoid hemorrhage	Yes	No	No	DVT at left proximal SFV	Alive
2	F	39	34 (23)	Pedestrian injury	Pelvic fracture with bladder injury	No	No	No	DVT at right CFV	Alive
3	M	30	43 (8)	MCA	Spinal cord injury	No	Yes	No	Pulmonary embolism	Alive
4	F	54	53 (26)	Pedestrian injury	Subdural hemorrhage, rib fracture, and fracture both bone right leg	Yes	No	Yes	DVT at left popliteal vein	Alive
5	M	72	30 (30)	Fall from high	Neck injury with cervical spine injury	No	Yes	No	Pulmonary embolism	Death/ massive PE
6	F	85	10 (5)	Fall	Closed fracture right intertrochanter	No	No	No	Pulmonary embolism	Alive
7	F	45	32 (3)	MCA	Subarachnoid hemorrhage with multiple bone fracture	Yes	No	No	Pulmonary embolism	Alive
8	F	91	21 (8)	Fall	Closed fracture left intertrochanter	No	No	No	Pulmonary embolism	Alive
9	M	37	8 (3)	MCA	blunt traumatic aortic injury with liver injury with splenic injury with fracture right femur	No	No	No	DVT at right CFV and pulmonary embolism	Alive

VTE=venous thromboembolism; VTE Dx=days from admission to VTE diagnosis; PE=pulmonary embolism; DVT=deep vein thrombosis; LOS=length of stay; M=male; F=female; SFV=superficial femoral vein; CFV=common femoral vein; MCA=Motorcycle accident

The characteristics of the nine VTE-positive patients are shown in Table 3, all of whom sustained blunt injuries. Time to VTE diagnosis ranged from 3 to 30 days after admission, with a mean of 13 days. After the diagnosis of VTE, eight patients received therapeutic anticoagulation and recovered uneventfully. None required inferior vena cava filter placement. The only mortality from the VTE group was a 72-year-old male who had cervical spine fracture and partial spinal cord injury after a fall. He had undergone an uneventful spinal surgery and was able to walk postoperatively. DVT screenings with DUS of this patient were negative three times. However, he had a sudden cardiac arrest, from asystole, not responding to cardiopulmonary resuscitation (CPR) during a session of physical therapy on the 30-day of admission. A presumptive diagnosis of PE was made by echocardiographic findings with right ventricular enlargement and interventricular septal shift, and the patient expired after 30 minutes of CPR.

After adding and removing potential variables for VTE development, multivariable analysis using a stepwise linear regression analysis showed that female gender (p=0.009, OR 10.1, 95% CI 1.8 to 56.9), spinal cord injury (p=0.015, OR 11.9, 95% CI 1.6 to 87.6), and length of stay greater than seven days (p=0.039, OR 7.5, 95% CI 1.1 to 51.1) were independent risk factors for the development of VTE (Table 4).

The overall mortality rate in the present study was 3.5%, with 20 patients. One mortality was in the

Table 4. Independent associated factors of VTE in trauma patient

Step	Variable	Adjusted OR (95% CI)	p-value	R^2
1	Sex: female	10.1 (1.8 to 56.9)	0.009*	0.282
2	Spinal cord injury	11.9 (1.6 to 87.6)	0.015*	0.254
3	Length of stay >7 days	7.5 (1.1 to 51.1)	0.039*	0.255

OR=odds ratio; CI=confidence interval

Stepwise regression: variables included in model were blood transfusion, age, BMI, and injury severity score

* Significant values ($p<0.05$)

VTE group, thus a mortality rate of 11.1%, and 19 were in the non-VTE group, thus a mortality rate of 3.3% (p=0.272) (Table 1). The most common cause of death was severe head injury with nine patients or 45%, followed by sepsis with multiple organ failure in six patients, myocardial infarction in two patients, exsanguinations in two patients, and massive PE in one patient.

Discussion

Although VTE chemoprophylaxis has been accepted as the standard of care for trauma patients in Western countries, the role of routine chemoprophylaxis remains unclear in Asian countries given the lower VTE rate reported from the previous retrospective studies[8-10,12]. A study focusing on the association between race and the risk of VTE demonstrated a higher VTE incidence in Black and White patients, with the lowest incidence in Asians[14]. Recently, a study of VTE in isolated severe pelvic fracture patients showed that Black patients had a significantly higher VTE rate at 3.7%, followed by White patients at 2.1%, and Asians at 0.9%[15]. Furthermore, a retrospective study of 1,028 Singaporean trauma patients revealed a VTE rate of 0.5%, despite a VTE chemoprophylaxis rate of 3.2%[16]. Therefore, ethnicity may have an important role in VTE development in trauma patients. This may be partly explained by a higher incidence of thrombophilia in Blacks and Caucasians, and a more vigorous fibrinolytic activity observed in Asians[17,18].

Many risk factors of VTE in trauma have been demonstrated, including old age, lower extremity or pelvic fracture, spinal cord injury, blood transfusion, major operation, angioembolization, prolonged mechanical ventilation, and venous injury[19-23]. In the present study, the authors found that female, spinal cord injury, and prolonged hospitalization were independent risk factors associated with VTE. Theoretically, females are more prone to VTE due to their hormonal contributions to clot formation[24]. Nevertheless, a previous large retrospective study in trauma patients with 8,762 patients failed to show difference in VTE rates based on gender with 5.1% for female versus 5.4% for male (p=0.565)[25].

Recent guidelines for VTE prevention in trauma recommended chemoprophylaxis in all hospitalized trauma patients, except for fully ambulatory patients with an expected length of stay of less than 24 hours[6,26]. The chemoprophylaxis may be delayed, given at a decreased dose, or withheld in high-risk injuries such as traumatic brain, spinal cord, and solid organ injuries. Adoption of the American College of Chest Physicians guideline for VTE prophylaxis, with enoxaparin, in Thai trauma patients resulted in a 28.9% guideline adherence rate and 2.8% VTE rate[9,27]. However, the authors' institution has not adopted these guidelines due to lower VTE rates in Asians and risk of bleeding and heparin-induced thrombocytopenia associated with chemoprophylaxis[28].

There are limitations to the present study. Firstly, its retrospective nature with a homogenous population did not allow for a control group of non-Thai patients. Hence, the generalizability of the results to a wider population is limited and the effectiveness of IPC could not be evaluated. Secondly, the present study DVT screening method (DUS) could have missed calf DVTs. However, calf DVTs in trauma patients could be left untreated since it is not common at 6.8% and rarely progresses to above-knee DVT or PE at 6.9%[29]. The lack of a long-term follow-up also makes it difficult to assess the complete impact of VTE on the patients' health. Thirdly, 10% to 23% of trauma patients can develop PE without preexisting DVT[30,31] as seen in five of the present study patients. Thus, active surveillance of DVT using DUS could not prevent PE. Finally, even with a low VTE rate of 1.6%, the present study had one mortality from a massive PE in the patient with spinal cord injury. The small sample size of VTE patients, with nine cases, reduces the power and reliability of the present study's conclusion. Thus, further studies identifying a subgroup of Thai trauma patients who would benefit from VTE chemoprophylaxis is warranted.

In conclusion, the baseline incidence of VTE in Thai trauma patients even without chemoprophylaxis was low at 1.6%. Female, spinal cord injury, and prolonged hospitalization were associated risk factors for VTE identified in the present study. Further studies are required to identify a subgroup of patients who would benefit from chemoprophylaxis.

What is already known about this topic?

VTE chemoprophylaxis has been accepted as the standard of care for trauma patients in Western countries, where the studies have demonstrated a higher VTE incidence in Black and White patients compared to Asians. However, the role of routine chemoprophylaxis remains unclear in Asian countries given the lower VTE rate reported from previous retrospective studies. Therefore, VTE chemoprophylaxis remains controversial in Thai trauma patients.

What does this study add?

This study reports a low incidence of VTE in Thai trauma patients at 1.6%, even without chemoprophylaxis. The associated risk factors for VTE included female, spinal cord injury, and prolonged hospitalization.

Conflicts of interest

The authors hereby certify that there is no conflict of interest in the present study.

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