

Incidence and Associated Factors of Deep Vein Thrombosis in Thai Surgical ICU Patients without Chemoprophylaxis: One Year Study

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Background: Deep vein thrombosis (DVT) is a major problem in the intensive care unit (ICU) patients, especially in Western countries. However, because the incidence of DVT in Asia ICU is lower, chemoprophylaxis (i.e., anticoagulant) is not routinely utilized. The aim of the present study was to identify the incidence and associated factors of DVT in Thai surgical ICU (SICU) patients without chemoprophylaxis.

Material and Method: SICU patients admitted between June 2011 and July 2012 were screened for lower extremity DVT using doppler ultrasonography. Stepwise logistic regression was performed to identify associated factors for the development of DVT.

Results: Three hundred and five patients were included in the study, 174 were male (57%) and 131 were female (43%), with ages ranged from 15 to 99 years (mean 62.8 years). Eleven patients had DVT identified (DVT rate 3.6%), two of these had symptomatic pulmonary embolisms. The associated factors for the development of DVT were prior history of venous thromboembolism ($p < 0.001$, OR 34.3, 95% CI 14.6-80.5), orthopedics group ($p < 0.001$, OR 27.2, 95% CI 5.2-142.1), and female ($p = 0.034$, OR 14.3, 95% CI 1.7-102.5).

Conclusion: The incidence of DVT in Thai SICU patients was 3.6%. Further study is required to identify method and effectiveness of DVT prophylaxis in Asian ICU patients.

Keywords: Deep Vein Thrombosis, ICU, Doppler Ultrasonography

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Deep vein thrombosis (DVT) in the intensive care unit (ICU) is a major health care problem in Western populations⁽¹⁾. The incidence of DVT in ICU patients in the Western countries is high, especially in patients not receiving chemoprophylaxis (i.e., anticoagulant administration); which ranges from 13 to 31%⁽²⁻⁵⁾. The use of chemoprophylaxis has been shown to reduce the incidence of DVT in ICU population; therefore, chemoprophylaxis has been accepted as a standard of care in ICU patients^(1,3-5). In contrast, the reported incidence of DVT in the Asian ICU patients without chemoprophylaxis is lower, ranges from 10.5 to 19%⁽⁶⁻⁸⁾. Since there is no randomized trial on DVT chemoprophylaxis in the Asian ICU patients, the role of anticoagulant administration in this group of patients remains unclear.

Hence, DVT chemoprophylaxis is not routinely utilized in the authors' institution. The objective of the present study is to identify the incidence and associated factors of DVT in our surgical ICU (SICU) patients, to whom chemoprophylaxis was not given.

Material and Method

Between June 2011 and July 2012, we routinely screened SICU patients at King Chulalongkorn Memorial Hospital, a 1,400-bed university hospital in Bangkok, Thailand; for DVT with doppler ultrasonography (SSD-4000SV, Aloka, Japan). The authors retrospectively reviewed the SICU patient' data during this period. Patients younger than 15 year-old, pregnant patients, and foreign (non-Thai) patients were excluded from the study. The doppler ultrasonography (DUS) examination was performed within five days after SICU admission and was repeated every 14 days. All DUS examinations were performed by a single surgeon and an intensivist trained in ultrasonography course, all positive results were reviewed with a

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radiologist. Bilateral lower extremities were examined with a high-frequency linear array probe starting at the groin (for the common femoral vein), down to the thigh (for the superficial femoral vein), and to the popliteal fossa (for the popliteal vein). The main criterion for DVT diagnosis was the absence of venous compressibility. The adjuncts criteria for DVT diagnosis included the presence of thrombus, the decrease of flow, and the absence of augmentation upon calf squeezing. As mentioned above, the authors did not use DVT chemoprophylaxis in our SICU. Furthermore, sequential compressive devices (SCD) were not routinely utilized and the use of the SCD was decided based on the primary surgical team. Once DVT was detected, SCD would be discontinued from the affected limb and the appropriate anticoagulant therapy would be initiated. The study was approved by our Institutional Review Board.

SICU patients were classified into eight groups comprising General Surgery, Hepatobiliary-Pancreatic Surgery, Vascular Surgery, Colorectal Surgery, Urology, Trauma, Orthopedics, and Miscellaneous (e.g. plastic surgery, head and neck surgery). Data collections included demographic data, patient groups, initial Sequential Organ Failure Assessment (SOFA) score, venous thromboembolism (VTE) risk factors (i.e., prior history of VTE, malignancy, major surgery, trauma, obesity, spinal cord injury, and hypercoagulable state), the presence of lower extremity edema, the use of SCD, the presence of pulmonary embolism (PE), ICU days, ventilator days, and DVT diagnoses. Obesity was defined as body mass index (BMI) ≥ 25 . The primary outcome of the present study was the incidence of DVT. The factors contributing to DVT analyzed in the present study were age, sex, diagnostic groups, VTE risk factors, the presence of lower extremity edema, the use of SCD, ICU days, and ventilator days. Statistical analysis was done by the Window SPSS program version 17.0 (SPSS Inc., Chicago, IL, USA) with the statistical significance set at $p < 0.05$. Univariate analysis was performed with the Fisher's exact test for comparison of categorical variables, and the Student's t-test for comparison of continuous variables. Multivariable analysis of the associated factors of DVT was performed by a stepwise regression model.

Results

Excluding one foreign patient and one pediatric patient (age 13), 305 consecutive Thai adult patients admitted to our SICU between June 2011 and July 2012 were screened for lower extremity DVT with

bedside DUS. One hundred seventy four patients were male (57%) and 131 patients were female (43%), whose ages ranged from 15 to 99 years (mean 62.8 years). The BMI ranged from 13 to 67 (mean 23.2). Ninety-three patients had BMI ≥ 25 (30.5%), however, only two of these were in the DVT group. The univariate analysis of clinical factors associated with DVT is shown in Table 1. None of these 305 patients had hypercoagulable states identified. DVT were detected in 11 patients (1 male and 10 female), resulting in the DVT rate of 3.6%. Of these 11 DVT patients, six had lower extremity edema (symptomatic DVT rate of 54.5%). The characteristics of 11 DVT patients are shown in the Attachment Table. Among 11 DVT patients, two had pulmonary embolism (PE) with clinical hypoxemia that were diagnosed by computed tomography pulmonary angiography, resulting in the PE rate of 0.7%. Fifty patients were admitted in the SICU for more than 14 days, two of these had DVT on the first DUS. Of the remaining 48 patients without DVT on the first DUS, we did not detect any new DVT formation on the repeated DUS.

Patient groups were presented in Table 2. The Fisher's exact test identified only orthopedics group to be significantly associated with DVT ($p = 0.02$). The result of stepwise regression analysis showed that prior history of VTE ($p < 0.001$, OR 34.3, 95% CI 14.6-80.5), orthopedics group ($p < 0.001$, OR 27.2, 95% CI 5.2-142.1), and female sex ($p = 0.034$, OR 14.3, 95% CI 1.7-102.5) were independent factors for the development of DVT (Table 3).

Overall mortality rate in the present study was 6.6% (twenty patients), two were in the DVT group (mortality rate 18.2%) and 18 were in non-DVT group (mortality rate 6.1%). The most common cause of death was sepsis with multiple organ failure (17 patients, 85%), followed by myocardial infarction (1 patient), end stage heart disease (1 patient), and poor graft function after liver transplantation (1 patient).

Discussion

The incidence of DVT in the authors' SICU was 3.6%, which is lower than the previous studies in Asia (10.5-19%)⁽⁶⁻⁸⁾ and in Western countries (13-31%)⁽²⁻⁵⁾. Three randomized controlled trials demonstrated that chemoprophylaxis reduced the incidence of DVT in the ICU from 13-31% to 11-15%⁽³⁻⁵⁾. However, there is no trial studying the effectiveness of chemoprophylaxis in ICU patients in Asian countries. Furthermore, there are risks of bleeding complications (6-8%) and heparin-induced

Table 1. Univariate analysis of clinical factors associated with DVT in SICU patients

Factors	Total (n = 305)	DVT (n = 11)	No DVT (n = 294)	<i>p</i> -value
Sex				0.001
Male	174 (57%)	1	173	
Female	131 (43%)	10	121	
SOFA (mean ± SD)	4.5±3.9	5.6±4.0	4.5±3.9	0.338
Major Surgery	274	11	263	0.391
History of VTE	5	4	1	<0.001
Malignancy	140	7	133	0.356
Trauma	37	1	36	0.606
Spinal cord injury	2	0	2	0.929
Head injury	6	0	6	0.801
Leg edema	32	6	26	<0.001
SCD use	25	1	24	0.616
ICU days (mean ± SD)	8.3±11.1	8.1±9.3	8.3±11.1	0.954
Ventilator days (mean ± SD)	6.3±11.1	6.0±9.6	6.3±11.1	0.922

DVT = deep vein thrombosis; SICU = surgical intensive care unit; SOFA = sequential organ failure assessment scores; VTE = venous thromboembolism; SCD = sequential compressive devices

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.

Table 2. Patient groups according to the admitting diagnosis

Group	Total (n = 305) n (%)	DVT (n = 11) n (%)	No DVT (n = 294) n (%)	<i>p</i> -value
General*	77 (25.2)	3 (27.3)	74 (25.2)	0.99
Colorectal	54 (17.7)	2 (18.2)	52 (17.7)	0.99
Vascular	38 (12.5)	1 (9.1)	37 (12.6)	0.99
Hepatobiliary-pancreatic	64 (21.0)	2 (18.2)	62 (21.1)	0.99
Trauma	30 (9.8)	0	30 (10.2)	0.40
Urology	20 (6.6)	0	20 (6.8)	0.63
Orthopedics	7 (2.3)	2 (18.2)	5 (1.7)	0.02
Miscellaneous	15 (4.9)	1 (9.1)	14 (4.8)	0.99

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

* General Surgery group included abdominal wall surgery and gastrointestinal tract surgery other than colorectal and hepatobiliary-pancreatic surgery.

Table 3. Independent associated factors of DVT in SICU patients

Step	Variable	Adjusted OR (95% CI)	<i>p</i> -value	R ²
1	History of VTE	34.3 (14.6-80.5)	<0.001	0.277
2	Orthopedics group	27.2 (5.2-142.1)	<0.001	0.322
3	Sex	14.3 (1.7-102.5)	0.034	0.330

Stepwise regression: variables included in model were age, sex, orthopedics group, history of VTE, and the presence of lower extremity edema.

thrombocytopenia (0.2-2.6%) associated with chemoprophylaxis^(5,9-11). Hence, the role of chemoprophylaxis for Asian ICU patients remains unclear.

The low rates of DVT (3.6%) and PE (0.7%) observed in the present study reflected the low incidence of VTE in Asian ICU patients as compared

Attachment Table. Characteristics of 11 SICU patients with DVT

Patients' No.	Sex	Age (years)	SOFA score	Group/diagnosis	Operations	Risk factors	Leg edema	SCD	VTE diagnosis	Outcome/cause of death
1	F	79	12	Vascular/ Chronic arterial occlusion left foot Post cardiac arrest	Left transmetatarsal amputation	Major surgery	No	No	DVT at left proximal SFV	Death/ sepsis with MOF
2	M	78	2	General/ Esophageal carcinoma	Esophagectomy	Malignancy Major surgery	No	No	DVT at left distal SFV	Alive
3	F	52	4	Colorectal/ Colonic obstruction Cervical carcinoma	Colostomy	Malignancy Major surgery Prior VTE	Yes	No	DVT at left distal SFV	Alive
4	F	55	13	Miscellaneous/ Necrotizing fasciitis both legs Cervical carcinoma	Debridement	Malignancy Major surgery	Yes	No	DVT at bilateral proximal SFV	Death/ sepsis with MOF
5	F	77	3	Orthopedics/ Spondylosis	Posterior fusion	Major surgery Obesity (BMI = 32)	Yes	No	DVT at left SFV to PV PE at right PA	Alive
6	F	48	7	Hepatobiliary-pancreatic/ Large caudate lobe hemangioma Received activated factor VII	Left hepatectomy Caudate lobe resection	Major surgery	No	Yes	DVT at right proximal SFV	Alive
7	F	99	2	Orthopedics/ Fracture left femur (fall) History of colonic carcinoma	Fracture fixation	Malignancy Major surgery Trauma	Yes	No	DVT at left proximal SFV	Alive
8	F	66	2	General/ Distal esophageal carcinoma	Esophagogastrectomy	Malignancy Major surgery	No	No	DVT at right distal SFV	Alive
9	F	64	3	Colorectal/ Cervical carcinoma Radiation proctitis	Pelvic exenteration	Malignancy Major surgery Prior VTE	Yes	No	DVT at left CFV	Alive
10	F	81	7	General/ Jejunal perforation Cervical carcinoma	Small bowel resection	Malignancy Major surgery Prior VTE	No	No	DVT at left CFV to SFV Bilateral small PE	Alive
11	F	82	7	Hepatobiliary-pancreatic/ Pancreatic carcinoma	Whipple's operation	Malignancy Major surgery Prior VTE	Yes	No	DVT at left CFV	Alive

SOFA = sequential organ failure assessment; SCD = sequential compressive devices; VTE = venous thromboembolism; CFV = common femoral vein; SFV = superficial femoral vein; PV = popliteal vein; DVT = deep vein thrombosis; PE = pulmonary embolism; PA = pulmonary artery; MOF = multiple organ failure; M = male; F = female; BMI = body mass index

to the Western populations. This correlates well with a review by White et al, which showed that Asians have a three to five fold lower incidence of symptomatic VTE than African-Americans, Hispanics and Caucasians⁽¹²⁾. The reasons for less VTE in Asians remain unclear, one possible hypothesis is that inactivation of coagulation and fibrinolysis are more effective in Asians^(12,13). Nevertheless, variation of DVT screening methods among the studies makes comparison difficult. The authors used DUS as a screening tool like several studies. Although we did not detect any new DVT formation among the 48 patients who had repeated DUS, our screening interval (every 14 days) was much longer than other studies (3-7 days)^(4,7,8). Furthermore, we did not examine the calf veins and iliac veins for DVT due to the technical limitations. This may have resulted in under diagnosis of DVT, since a significant proportion of DVT (up to 60%) has been reported to occur at the calf level⁽¹⁴⁾. Therefore, we may have underestimated the DVT rate in this study. The treatment of calf vein DVT is not standardized, but Sharpe et al demonstrated that in high risk trauma patients, some calf vein DVT propagated to an above knee location (4.7%) and resulted in PE (1.2%) when not anticoagulated⁽¹⁵⁾.

The use of DUS for DVT screening performed by non-radiologist physicians (emergency physicians and intensivists) has been reported by some investigators, demonstrating good accuracy rates (95-98%)^(16,17). These studies used the same criteria for DVT diagnosis as the present study, i.e. the absence of venous compressibility, the presence of thrombus, the decrease of flow, and the absence of augmentation upon calf squeezing. In our experience, DUS for DVT screening is not difficult to interpret and takes about 5 minutes per case if performed by a trained physician. Hence, intensivists should include a routine DVT screening using DUS to identify the incidence of DVT and the effectiveness of VTE prophylactic methods in each ICU, especially in countries where the method of VTE prophylaxis has not yet been standardized.

The risk factors of DVT in the ICU varied among the studies. The present study identified only prior history of VTE, orthopedics group, and female sex to be independent factors for the development of DVT. The association between sex and the development of DVT is unclear since some studies showed an equal distribution of DVT among male and female patients^(6,8), while the others demonstrated the presence of DVT to be male predominance^(3,7). In contrast, the strong association between orthopedics patients and the

development of DVT demonstrated in the present study corresponds well with several studies that showed high rates of DVT in Asian orthopedics patients without chemoprophylaxis (8-62%)^(10,18-21). Nonetheless, a recent meta-analysis on the rate of postoperative VTE in Asian orthopedic patients without chemoprophylaxis demonstrated low DVT rates (8.7% after total knee arthroplasty and 9.6% after hip surgery) as compared to Western studies (over 20%)⁽²²⁾. Thus, the role of chemoprophylaxis in Asian orthopedics patients also remains unclear and further study on this subject is needed. The recent study in critically ill trauma patients who were contraindicated to chemoprophylaxis also showed that past medical history of VTE and extremity fractures were independent predictors for VTE (overall VTE rate 7%), which were in agreement with the present study⁽²³⁾.

Conclusion

The incidence of DVT in Thai SICU patients without chemoprophylaxis was low (3.6%). Routine DVT screening should be performed to identify the development and the rate of DVT in every ICU. The method and effectiveness of DVT prophylaxis in Asian ICU patients remain unclear and further study is required.

What is already known in this topic?

Deep vein thrombosis (DVT) in the intensive care unit (ICU) is a major health care problem in Western populations. The incidence of DVT in ICU patients in the Western countries is high especially in patients not receiving chemoprophylaxis, ranges from 13 to 31%. The use of chemoprophylaxis has been shown to reduce the incidence of DVT in ICU population; hence, chemoprophylaxis has been accepted as a standard of care in ICU patients. In contrast, the reported incidence of DVT in the Asian ICU patients without chemoprophylaxis is lower, ranges from 10.5 to 19%. Since there is no randomized trial on DVT chemoprophylaxis in the Asian ICU patients, the role of anticoagulant administration in this group of patients remains unclear.

What this study adds?

The present study demonstrated that the incidence of DVT in Thai Surgical ICU was low (3.6%), even without chemoprophylaxis. The independent factors for the development of DVT included prior history of VTE, orthopedics group, and female sex. The method and effectiveness of DVT prophylaxis in

Asian ICU patients remain unclear and further study is required.

Potential conflicts of interest

None.

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อุบัติการณ์และปัจจัยที่เกี่ยวข้องกับการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูศัลยกรรมที่ไม่ได้รับยาป้องกันการเกิดลิ่มเลือดอุดตัน: การศึกษาในระยะเวลา 1 ปี

ศุภฤกษ์ ปรีชาบุษย์, มนตร์รวี ทุมโฆสิต, สุวิทย์ ศรีอัมภพร, พสุรเชษฐ์ สมร, รัฐพลี ภาคอรธ, สุกัญญา ศรีอัมภพร, กฤตยา กฤตยาภิรม

ภูมิหลัง: การเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูเป็นปัญหาสำคัญที่พบบ่อยในประเทศตะวันตก อย่างไรก็ตามอุบัติการณ์การเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูในเอเซียนั้นน้อยกว่าประเทศตะวันตก และการให้ยาป้องกันการเกิดลิ่มเลือดอุดตันยังไม่ได้ความนิยมแพร่หลาย จุดประสงค์ของการศึกษานี้เพื่อหาอุบัติการณ์และปัจจัยที่เกี่ยวข้องกับการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูศัลยกรรมที่ไม่ได้รับยาป้องกันการเกิดลิ่มเลือดอุดตัน

วัตถุประสงค์และวิธีการ: ผู้นิพนธ์ทำการทบทวนประวัติของผู้ป่วยไอซียูศัลยกรรมที่เข้ารับการรักษาตั้งแต่ เดือนมิถุนายน พ.ศ. 2554 ถึง กรกฎาคม พ.ศ. 2555 ซึ่งผู้ป่วยทุกรายได้รับการตรวจคัดกรองภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของขาโดยใช้เครื่องตรวจหลอดเลือดด้วยคลื่นเสียงความถี่สูง และผู้นิพนธ์ได้ใช้วิธีคำนวณทางสถิติเพื่อหาตัวทำนายการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาด้วย

ผลการศึกษา: มีผู้ป่วยทั้งหมด 305 ราย ในการศึกษาเป็นชาย 174 ราย และหญิง 131 ราย อายุเฉลี่ย 62.8 ปี พบว่ามีผู้ป่วย 11 ราย มีภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของขา (อุบัติการณ์การเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขา 3.6%) และมีผู้ป่วยสองรายที่มีภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของขาพร้อมด้วย ปัจจัยที่เกี่ยวข้องกับการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขา ได้แก่ การมีประวัติลิ่มเลือดอุดตันในหลอดเลือดดำมาก่อน ผู้ป่วยศัลยกรรมกระดูก และผู้ป่วยเพศหญิง

สรุป: อุตการณ์การเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูศัลยกรรมเท่ากับ 3.6% ผู้นิพนธ์มีความเห็นว่าควรจะมีการศึกษาเพิ่มเติมเพื่อที่จะหาแนวทางป้องกันการเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยไอซียูศัลยกรรมในประเทศเอเซีย ซึ่งน่าจะแตกต่างจากประเทศตะวันตกซึ่งพบอุบัติการณ์การเกิดลิ่มเลือดอุดตันในหลอดเลือดดำของขาสูงกว่า
