Venous Thromboembolism Prophylaxis and The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) Score in Medical Illness Patients

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Abstract

Objective: To describe applicability of The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) score to implement venous thromboembolism prophylaxis in patients with medical illness in Hasan Sadikin General Hospital Bandung.

Methods: This study was descriptive, cross-sectional research from database was performed on December 2018. Inclusion criteria in this study were all patients hospitalized in Department of Internal Medicine, Hasan Sadikin General Hospital in November 2018 with medical illness, which is patients with medical condition involves a more systemic, pharmaceutical approach to treatment. Exclusion criteria were surgical disease, which is requires some form of intervention such as surgery, also patients with incomplete medical record were excluded.

Results: There were 162 patients (56% male and 44% female). Median age were higher in males compared to females (53 [18–76] vs. 49 [18–85]) years. Low-risk (score <2), medium-risk (score 2 – 3), and high-risk (score >4) for IMPROVE venous thromboembolism score were 77.2%, 17.3%, and 5.6% respectively.). Low-risk (score <7) and high-risk (score >7) for IMPROVE bleeding score were 75.9% and 24.1% respectively. Medical thromboprophylaxis were given to 14.8% patients, with 91.7% and 8.3% of the patients received unfractionated heparin (UFH) and low-molecular weight heparin (LMWH) respectively. Thromboprophylaxis was given in 88.9% of high-risk patients for venous thromboembolism. There were 18.7% patients with low-risk and 2.6% with high-risk for bleeding that received prophylaxis.

Conclusion: The majority of inpatients treated with thromboprophylaxis had low-risk for both thromboembolism and bleeding. The rate of thromboprophylaxis usage was still low; with the most frequently used thromboprophylaxis agent was UFH. Most of high-risk patients for venous thromboembolism received thromboprophylaxis.

Keywords: Bleeding risk, IMPROVE score, thromboembolism risk, thromboprophylaxis

Introduction

Venous thromboembolism is characterized with venous thrombosis, frequently occurring in the lower extremities. Several cases of venous thrombosis may cause embolization, particularly to lungs. The emboli may cause partial or complete obstruction of pulmonary arteries or its branches.[1]

Predisposing factors of venous thrombosis may be defined using Virchow triad, consisting of: stasis of blood flow, hypercoagulability, and endothelial injury. Stasis of blood flow may be caused by several conditions, such as immobilization, bed rest, congestive heart failure, and previous history of venous

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thrombosis. Hypercoagulability may be found in patients with history of malignancy, anticardiolipin antibody, nephrotic syndrome, essential thrombocytosis, estrogen therapy, heparin usage (heparin-induced thrombocytopenia), inflammatory bowel disease, paroxysmal nocturnal hemoglobinuria, disseminated intravascular coagulation, and deficiency of several proteins (such as protein C, protein S, and antithrombin III). Endothelial injury may occur due to trauma or internal bleeding.[2]

Annual incidence of venous thromboembolism in Europe and United States were approximately 50/100,000 persons per year. Genetic variability may be noted, with lower incidence were found in Asian and Hispanic population compared to Caucasians, African Americans, Latino, and Asia-Pacific populations. No significant incidence between both sexes were noted. Increasing trend in incidence of lung emboli were noted, with annual incidence rate of lung emboli of 1 in 1000 persons in United States. Pulmonary emboli occurs in 60–80% cases of venous thromboembolism, 50% of which cases were asymptomatic. Lung emboli is one of the most frequent cause of death, ranking 3rd and casing about 650,000 mortalities each year.[3-6]

Approximately 100,000 and 300,000 deaths related to venous thromboembolism were reported annually in United States and Europe, respectively. Venous thromboembolism related mortalities may be prevented by using thromboprophylaxis medications. No consensus regarding the dosage of the medication has been reached, due to the risk of bleeding as a possible side effect of thromboprophylaxis medications.[7] The IMPROVE (International Medical Prevention Registry on Venous Thromboembolism) predictive score was designed to assesses the risk of VTE in hospitalized medical patients. IMPROVE scores may be utilized to assess the risk of thromboembolism and bleeding.[8] This study aims to assess the risk factors associated with venous thromboembolism and bleeding according to IMPROVE scores and administration of thromboprophylaxis medications of inpatients with medical illness in Department of Internal Medicine , Hasan Sadikin General Hospital.

Table 1 IMPROVE score for Thromboembolism[8]

Parameter	Score
History of thromboembolism	3
Thrombophilia	2
Paralysis of lower extremities	2
Malignancy	2
Immobilization ≥7 days	1
History of admittance to intensive care unit	1
Age >60 years	1

Methods

The descriptive, cross-sectional study was performed on December 2018. Data were collected from database of inpatients hospitalized with medical illness in Department of Internal Medicine Dr. Hasan Sadikin General Hospital Bandung. Inclusion criteria in this study were all patients hospitalized in November 2018 with medical illness, which is patients with medical condition involves a more systemic, pharmaceutical approach to treatment. Exclusion criteria were surgical disease, which is requires some form of intervention such as surgery, also patients with incompleted medical record were excluded. Several variables included in this study are as described below.

Risk for venous thromboembolism,

Table 2 IMPROVE Score for Bleeding[8]

Parameter	Score
Previous history of gastroduodenal ulcer	4.5
History of bleeding (last 3 months)	4
Platelet count <50x10^9 /L	4
Previous history of hepatic failure (INR>1.5)	2.5
History of admittance to intensive care unit	2.5
History of central venous catheter insertion	2
Rheumatic diseases	2
History of malignancy	2
Male sex	1
Age 40–84 vs ≥ 85 years	1.5 vs 3.5
Glomerular filtration rate 30-59 vs <30	1 vs 2.5

categorized according to IMPROVE score: low risk (score <2), moderate risk (score 2–3), and high risk (score ≥4) (Table1).

Risk for bleeding, categorized according to IMPROVE score: low risk (score <7) and high risk (score ≥7) (Table 2).

Thromboprophylaxis refers to administration of anticoagulants, specifically unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) during the period of hospitalization.

Descriptive statistics were used in presenting the results. Median, mean, and percentage were used as descriptive statistics in describing the patients with risk of venous thromboembolism and bleeding.

Table 3 Subjects Characteristics

Characteristics	Total (n=162)
Sex, n (%)	
Male	91 (56)
Female	71 (44)
Age (years)	
Median (range)	51 (18–85)
VTE risk, n (%)	
Low risk	125 (77,2)
Moderate risk	28 (17,3)
High risk	9 (5,5)
Bleeding risk, n (%)	
Low risk	123 (75,9)
High risk	39 (24,1)
Thromboprophylaxis, n (%)	
UFH	22 (13,6)
LMWH	2 (1,2)
No thromboprophylaxis	138 (85,2)
VTE risk with thromboprophylaxis, n (%)	
Low risk	0 (0)
Moderate risk	16 (57,1)
High risk	8 (88,9)
Bleeding risk with thromboprophylaxis, n (%)	
Low risk	23 (18,7)
High risk	1 (2.6)

Results

Total participants from database who fulfilled inclusion were 162 patients, with distribution of 56% males and 44% females. Male patients were older compared to female patients (Median 53 [18–76] vs 49 [18–85]) years. Risk of thromboembolism was assessed using IMPROVE score: 77.2% low risk patients (scores <2); 17.3% moderate risk patients (score 2–3); and 5.6% high risk patients (scores ≥4). Risk of bleeding was assessed using IMPROVE score: 75.9% low risk patients (scores <7) and 24.1% high risk patients (scores ≥7). Thromboprophylaxis medications were given to 14.8% of the patients included in the study. The medications given were unfractionated heparin (UFH) in 91.7% patients and low-molecular weight heparin (LMWH) in 8.3% patients.

Patients with low risk for venous thromboembolism did not receive thromboprophylaxis. There were 57.1% medium risk and 88.9% of high risk patients for venous thromboembolism that received thromboprophylaxis medications. There were 17.8% low risk and 2.6% medium risk patients for bleeding that received thromboprophylaxis medications. Subject's characteristics were described in Table 3.

From 37 patients with venous thromboembolism, the majority of these patients had previous history of malignancy. There were 27 (73%) patients with previous history of malignancy and 10 (27%) patients with previous history of prolonged immobilization. The majority of the patients with previous history of malignancy had received thromboprophylaxis: 22 (81.5%) patients received thromboprophylaxis and 5 (18.5%) patients did not receive thromboprophylaxis. On subjects with previous history of prolonged immobilization, 2 (20%) patients had received thromboprophylaxis and 8 (80%) patients did not receive thromboprophylaxis.

There were 3 high risk patients for bleeding: 2 (66.7%) of the patients had not received thromboprophylaxis and 1 (33.3%) patient had received thromboprophylaxis. The patient that was given thromboprophylaxis had previous history of malignancy.

Discussion

International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) score was formulated in order to assess the risk of venous thromboembolism and bleeding. The

score had listed 7 risk factors in assessing the risk of venous thromboembolism: previous history of venous thromboembolism; thrombophilia; paralysis of lower extremities; previous history of malignancy; prolonged immobilization (≥7 days); and previous history of admittance in intensive care unit (in patients aged >60 years). There are three risk stratifications in thromboembolism risk: low risk (score <2), moderate risk (score 2–3), and high risk (score ≥4). Assessment of risk for bleeding utilize 13 risk factors to be examined on the patient: previous history of gastroduodenal ulcers; previous history of bleeding in the last 3 months; platelet count $<50x10^9$/L; previous history of hepatic failure; previous history of admittance in intensive care unit ; previous history of central venous catheter insertion; previous history of rheumatic diseases; previous history of malignancy; age; sex; and glomerular filtration rate. The risk is further stratified into low risk (score <7) and high risk (score ≥7). Patients with moderate risk for thromboembolism (score >2) and low risk for bleeding (score <7) are recommended to be given thromboprophylaxis medication in order to prevent emboli formation. In patients with high risk of bleeding (score ≥7), mechanical thromboprophylaxis is recommended in order to reduce the risk of emboli formation.[9]

IMPROVE scoring system has been routinely utilized in 12 countries: Australia, Brazil, Canada, Colombia, France, Germany, Italy, Japan, Spain, England, United States, and Venezuela. Previously, a multicenter study conducted in 52 hospitals from the 12 aforementioned counties were performed during the period of July 2002–September 2006, with total of 15,156 individuals diagnosed with venous thromboembolism; 3,410 of subjects in United States and 11,746 in other countries. The patients' age range were 52–79 years old with median of 68 years old; the majority of the patients were females (50.6% vs. 49.4%). Compared to the previous study, this study had lower median (51 years old) and range for age (18 – 85 years old). The patients in our study were predominantly male (56% vs. 44%).[10,11]

In this study, 22.8% of patients had high risk for venous thromboembolism with 64.9% of the patients had received medication (UFH or LMWH) for thromboprophylaxis. In comparison with other studies, less number of patients were at high risk for thromboembolism despite the higher rate of thromboprophylaxis medication. In other study, 52% patients in United States and 43% patients in other countries had moderate to high risk for venous thromboembolism. There were 7,640 (50%) patients that had received either medical or mechanical thromboprophylaxis. There were 33% patients in United States and 47% patients in other countries that had received UFH or LMWH as thromboprophylaxis. The study had suggested several factors that may be associated with lower usage of thromboprophylaxis, notably the lack of awareness regarding thromboprophylaxis usage, lack of thromboprophylaxis algorithms in the said institution, and risk of bleeding that may occur during thromboprophylaxis procedure.[10-12]

Other countries, in contrast, had preferred the usage of LMWH compared to UFH (82.1% vs. 17.9%). Overall, higher usage of LMWH was found in the study compared to the UFH usage (74.8% vs. 25.2%). In our study, the vast majority of the patients were treated with UFH (91.7% vs. 8.35). The choice for medical thromboprophylaxis were similar with studies from United States, which UFH usage was preferred compared to LMWH in thromboprophylaxis. Costs in utilizing LMWH was not significantly different compared to usage of UFH, thus, LMWH may be safer that UFH, particularly in minimizing the risk of heparin induced thrombocytopenia (HIT).[10-14]

In this study, there were 75.9% patients with low risk (score <7) and 24.1% patients with high risk (score ≥7) for bleeding. In comparison, a retrospective study consisted of 12,082 subjects from Academic Health System in United States during the period of October 1, 2012–July 31, 2014, had found the majority (81% vs. 19%) of the patients had low risk of bleeding. Other study had noted that 90.3% of patient had low risk for bleeding and 9.7% had high risk for bleeding. The results of these studies concur with our study, that the majority of the patients in Hasan Sadikin General Hospital had low risk for bleeding.[7]

According the previous study from Academic Health System, bleeding had occurred on 2.6% patients with venous thromboembolism, with 1.8% patients had major bleeding (defined as bleeding that cause decrease of hemoglobin ≥2 g/dL or may require 2 units of blood transfusion). Major bleeding may occur as intracranial, intraocular, adrenal gland, and/or pericardial hemorrhage. In other studies, 3.2% of patients had suffered from bleeding after thromboprophylaxis therapy, with 1.2% of these patients had suffer from major bleeding.[7] In contrast, no cases of bleeding

after thromboprophylaxis therapy were found on our patients.

In this study there were 162 subjects with mean age 51 years old. Most of subjects were male (56% vs. 44%). There were 22.8% of patients had high risk for venous thromboembolism with 64.9% of the patients had received medication (UFH or LMWH) for thromboprophylaxis. There were 75.9% patients with low risk (score <7) and 24.1% patients with high risk (score ≥7) for bleeding. The majority of inpatients had low risk for both venous thromboembolism and bleeding. The administration of thromboprophylaxis is still uncommonly performed, only given in 14.8% subjects. Thromboprophylaxis was given in 88.9% of high risk patients for venous thromboembolism .The majority of patients with high risk of venous thromboembolism received UFH as thromboprophylaxis medication.

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