

Underutilization of Anticoagulant for Venous Thromboembolism Prophylaxis in Three Hospitals in Jakarta

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ABSTRAK

Tujuan: menilai penggunaan antikoagulan dan implementasi pedoman internasional mengenai profilaksis tromboemboli vena (TEV) pada pasien rawat inap dengan penyakit medik akut di Jakarta, Indonesia. **Metode:** studi multisenter, observasional, dengan mendata pasien terdiagnosis penyakit medik akut dan kondisi medis lainnya yang berisiko TEV dan menjalani imobilisasi sedikitnya 3 hari. **Hasil:** dari total 401 pasien, hanya 46.9% yang menerima antikoagulan, terdiri atas: unfractionated heparin (64.4%), fondaparinux (11.7%), enoxaparin (9.6%), warfarin (3.7%), dan kombinasi antikoagulan (10.6%). Profilaksis TEV dengan metoda fisik dan mekanik digunakan pada 81.3% pasien baik tunggal atau dikombinasi dengan antikoagulan. Selama rawat inap, TEV didapatkan pada 3.2% pasien. Dari 13 pasien, 10 pasien (2.5%) mengalami TEV di tungkai bawah dan 3 pasien (0.75%) diduga mengalami emboli paru. Rujukan internasional utama yang digunakan adalah AHA/ASA 2007 (47.4%), diikuti oleh ACCP 2008 (21.7%). **Kesimpulan:** studi ini menunjukkan penggunaan profilaksis antikoagulan yang kurang. Thromboprofilaksis mekanik baik tunggal atau kombinasi dengan antikoagulan merupakan yang tersering digunakan. Unfractionated heparin paling sering dipilih sebagai profilaksis TEV. Rujukan tata laksana yang lebih sering digunakan adalah AHA/ASA 2007. Profilaksis TEV pada pasien dengan penyakit medik akut perlu ditingkatkan.

Kata kunci: thromboemboli vena (TEV), profilaksis, pendataan, rawat inap bukan operasi.

ABSTRACT

Aim: to assess the current use of anticoagulants and implementation of International Guidelines in venous thromboembolism (VTE) prophylaxis in hospitalized patients with acute medical illnesses in Jakarta, Indonesia.

Methods: a multicenter, prospective, disease registry, recruiting patients diagnosed as acutely ill medical diseases and other medical conditions at risk of VTE, with in-hospital immobilization for at least 3 days. **Results:** of 401 patients, 46.9% received anticoagulants which included unfractionated heparin (64.4%), fondaparinux (11.7%), enoxaparin (9.6%), warfarin (3.7%), and combination of anticoagulants (10.6%). VTE prophylaxis using physical and mechanical method was used in 81.3% of patients, either as a single modality or in combination with anticoagulants. During hospitalization, VTE were found in 3.2% patients; 10 patients (2.5%) had lower limb events and 3 patients (0.75%) had a suspected pulmonary embolism. The main reference international guidelines used were AHA/ASA 2007 (47.4%), followed by ACCP 2008 (21.7%). **Conclusion:** the study showed underutilization of prophylaxis anticoagulants in which mechanical thromboprophylaxis either alone or combination with anticoagulants was the most commonly used. Unfractionated heparin was the preferable choice. The most commonly used guideline was AHA/ASA 2007. VTE thromboprophylaxis in medically ill patients needs to be encouraged.

Key words: venous thromboembolism (VTE), prophylaxis, registry, non-surgery hospitalization.

INTRODUCTION

Venous thromboembolism (VTE) is commonly found at autopsy in patients who received medical treatment and died in the hospital. Prophylaxis of VTE has been less extensively studied in medical patients than in surgical patients, and the use of thromboprophylaxis is uncommon in medical patients. Even though primary prophylaxis of VTE was not standardized therapy in Indonesia, this prophylaxis has been implemented in orthopedic surgery since year 2000 while some clinicians were doing secondary prophylaxis of VTE. At least 3 large randomized clinical trials have demonstrated the efficacy and safety of VTE prophylaxis in the medical setting. These studies used enoxaparin (MEDENOX)¹, dalteparin (PREVENT)², and fondaparinux (ARTEMIS)³ compared to placebo in acutely ill medical patients hospitalized with heart failure, respiratory failure, infectious disease or inflammatory disease. All studies showed a significant reduction in the rate of VTE, while the rate of major bleeding events was comparable to placebo. These results support the evidence-based recommendations for thromboprophylaxis in this clinical setting.

The benefits of these 3 studies should be translated into general practice. To facilitate its implementation, the medical practitioners should be able to readily identify suitable patients who would gain most from prophylaxis with these anticoagulants and implement

the best treatment protocols according to evidence-based and International Guidelines. MEDENOX, PREVENT, and ARTEMIS studies demonstrated the benefits of anticoagulants for acutely ill medical patients to prevent incidence of VTE. International Guidelines (AHA/ASA⁴, ACCP⁵, ESO⁶, IUA⁷) recommended the use of anticoagulants for thromboprophylaxis in acutely ill medical patients. In Indonesia, there is lack of data on the use of anticoagulants in this group of patients. We presumed that even though all doctors had known about the guidelines of anticoagulant prophylaxis, not all doctors followed the guidelines properly. Besides, we predicted as well that there was underutilization of anticoagulant prophylaxis or the guidelines were not applied optimally. This study would provide data on the appropriate use of anticoagulants, International Guidelines implementation, demographic data and risk factors of patients in the prevention of VTE within real clinical settings in Jakarta, Indonesia.

The primary objectives were to assess current use of anticoagulants oral or intravenous for VTE prophylaxis in hospitalized patients with acute medical illnesses and other medical conditions at risk of VTE, to assess the underutilization and inappropriate use of anticoagulant prophylaxis, and to assess International Guidelines implementation in VTE prophylaxis in Jakarta, Indonesia. The secondary objectives were to obtain demographic data of acutely ill medical patients who are at risk of VTE events in Jakarta,

and to assess VTE prophylaxis method other than anticoagulants used in these patients.

METHODS

Study Design

A multicenter, prospective, disease registry. The study protocol was approved by the Ethics Committee of the Medical Faculty, University of Indonesia.

Patients

Inclusion criteria were 40 years of age and older, with a diagnosis of acutely ill medical disease or other medical condition at risk of VTE, such as acute heart failure (NYHA class III / IV), acute respiratory infection, acute infective disease (CNS, Hematology), acute myocardial infarction, acute ischemic stroke, paraparesis/hemiparesis, malignancy. Patients were hospitalized for at least 6 days and were immobilized for at least 3 days. Patients who participated in other clinical study were excluded. Written informed consents were obtained from the patients before participation in the study.

Treatment

This was an observational study, therefore no specific treatment was recommended. Data were collected based on physician's daily practices without any intervention or scheduled visit. This study was performed without interfering with the patient's routine management. There were no study tests or clinical interventions performed. If there was any adverse event (AE) or serious adverse event (SAE) during visit, physician would report this AE or SAE to the pharmaceutical company manufacturing the product through the Spontaneous Reporting Procedure.

Statistical Analysis

Numerical variables were summarized using mean and standard deviation, while frequencies and percentages are reported for nominal variables. These descriptive statistics were planned to describe the baseline characteristics of subjects, including risk factors, the choice of anticoagulants, the reference guidelines, other treatments given, and VTE disease found. No comparison analysis was made.

RESULTS

Characteristics of Patients

A total of 401 patients were recruited from 18 participating physicians in 7 centers from December 2009 until November 2011. Characteristics of patients are shown in **Table 1**.

Table 1. Characteristics of patients (N=401)

Characteristics	Mean (SD*)
Age (years)	58.1 (10.96)
Weight (kg)	57.7 (12.40)
BMI (kg/m ²)	22.0 (4.47)
Systolic BP (mmHg)	130.0 (26.18)
Diastolic BP (mmHg)	78.0 (14.87)
Heart Rate (bpm)	89.0 (15.4)
Respiratory Rate (time/min)	22.0 (4.77)
Hospital Stay (days)	18.4 (17.27)
Duration of anticoagulant use (days)	10.0 (17.73)
Male, n (%)	248 (61.8)
Female, n (%)	153 (38.2)
Patients at discharge, n (%)	
- Died	74 (18.0)
- Alive	327 (82.0)

Risk Factors

Majority of the patients had prolonged immobilization as risk factor, it was 77.6% (311 patients). Most of the patients (80.6%) had at least 1 risk factor. Only 19.2% had 2 risk factors or more as shown in **Table 2**.

Table 2. Risk factors in baseline characteristics of patients (N=401)

Risk Factors	N (%)
Prolonged immobilization (>72 hrs)	311 (77.6)
History of malignancy	67 (16.7)
Obesity	45 (11.2)
Age >75 years	30 (7.5)
Trombophilia	11 (2.7)
History of VTE	7 (1.8)
Dehydration	2 (0.5)
Nephrotic syndrome	2 (0.5)
Varicose vein	1 (0.3)
At least 1 risk factor	323 (80.6)
≥2 risk factors	77 (19.2)
No data	1 (0.2)

Methods of VTE Prophylaxis Used

Methods of VTE prophylaxis used in this study were mechanical thrombophylaxis (40.1%), pharmacological thrombophylaxis (5.7%), combination of mechanical and pharmacologic thrombophylaxis (41.1%), others (0.5%), and no documented prophylaxis (12.5%) as shown in **Figure 1**. The majority of VTE prophylaxis methods used in patients in this study was mechanical method or physiotherapy (326 of 401 patients (81.3%)), either used as a single method or in combination with pharmacological thrombophylaxis.

Current Use of Anticoagulants in Hospitals in Jakarta

From the total of 401 patients, 188 patients (46.9%) received prophylaxis anticoagulants, and 213 patients (53.1%) did not. **Figure 2** shows the reasons for not using anticoagulants

resulting in underutilization of anticoagulant prophylaxis, in which 37 of 213 patients (17.5%) were contraindicated, 22 patients (10.4%) were concerned for bleeding, 99 patients (46.2%) had no anticoagulant indication (based on the doctors' opinion despite strong indication of anticoagulant prophylaxis in patients with >6 days bedridden), 45 patients (21.2%) for cost reasons, and 10 patients (4.7%) for other reasons.

Initial Choice of Anticoagulant

Table 3 shows the initial choice of anticoagulants as VTE prophylaxis. Initial choice of anticoagulants among the 188 patients were unfractionated heparin (UFH) in 121 patients (64.4%), low molecular weight heparin (enoxaparin) in 18 patients (9.6%), synthetic pentasaccharide (fondaparinux) in 22 patients (11.7%), oral anticoagulant (warfarin) in 7 patients (3.7%), and more than 1 anticoagulants in 20 patients (10.6%).

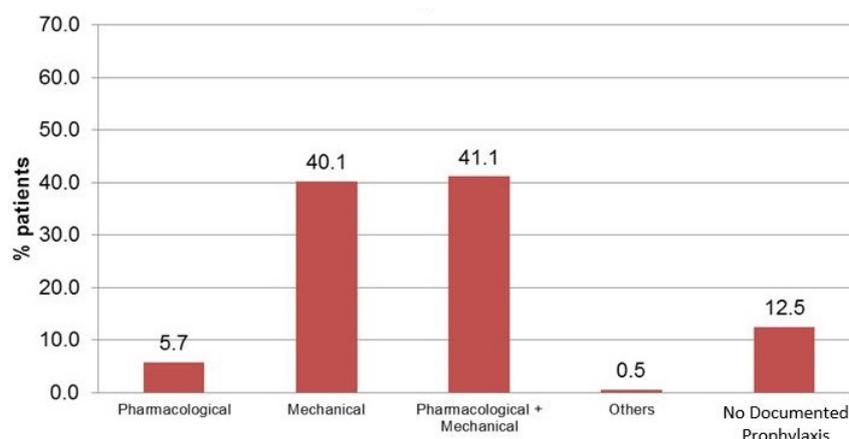


Figure 1. Methods of VTE prophylaxis used in this study

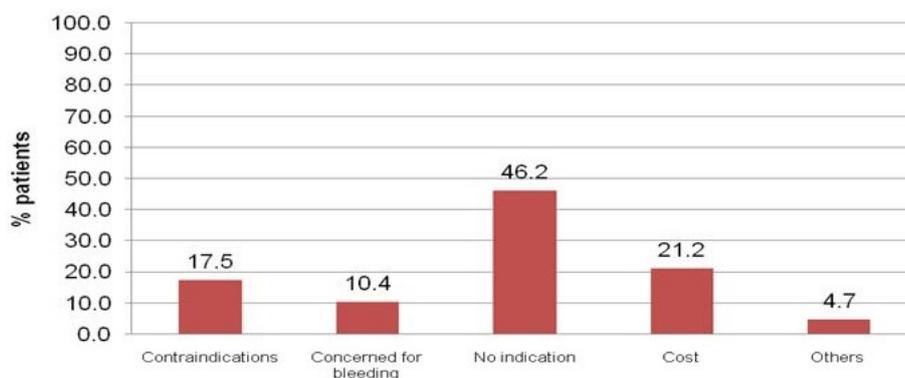


Figure 2. Reasons for not using anticoagulants

Table 3. Initial choice of anticoagulants as VTE prophylaxis (N=188)

Anticoagulant	n (%)
UFH	121 (64.4)
Fondaparinux	22 (11.7)
Enoxaparin	18 (9.6)
Warfarin	7 (3.7)
More than 1*	20 (10.6)

*enoxaparin, UFH (9); enoxaparin, warfarin (1); enoxaparin, fondaparinux (3); enoxaparin, UFH, warfarin (1); UFH, warfarin (5); UFH, fondaparinux (1)

Signs or Symptoms of VTE

Signs or symptoms of VTE were found during hospitalization in 13 patients among the total of 401 patients (3.2%), deep vein thrombosis (DVT) at lower limbs were found in 11 patients (edema in 2 patients, edema and pain in 2 patients, and edema, pain, red skin and changes in skin temperature in 7 patients), and suspected pulmonary embolism was found in 2 patients (apnea in 1 patient, dyspnea and quick breathing in 1 patient). In one patient, both local and general signs and symptoms of VTE were found.

In 13 patients with VTE, the median of length of stay in hospital is 20 days with range 2-103, the detail of the patient's length of stay and site can be found in **Table 4**.

Among these 13 patients, 10 patients received UFH, 1 patient received fondaparinux, 1 patient received enoxaparin and warfarin, 1 patient did not receive anticoagulant and 10 patients were on mechanical VTE prophylaxis.

One patient who did not receive anticoagulant is patient with hepatic fibrosis, massive ascites, and hepatic encephalopathy, therefore the patient was considered to be contraindicated to anticoagulant. The patient then died due to suspected pulmonary embolism, since the patient showed sign or symptom of apnea, despite on mechanical VTE prophylaxis.

In the meantime, 12 patients who received VTE prophylaxis anticoagulant, 5 patients died from their underlying diseases. Six of those 12 patients with signs or symptoms of VTE had underwent duplex ultrasound examination which showed venous thrombus in 2 patients, 1 patient with vein valve insufficiency, and no observed

venous thrombus in 3 patients. The other 6 patients did not undergo duplex ultrasound examination due to various reasons (the signs of thrombosis were already clear in 1 patient, patients were treated directly in 2 patients, unconsciousness in 1 patient, the ultrasound has been performed previously in 1 patient, and no data in 1 patient).

Bleeding Complications

The rate of major bleeding during anticoagulant treatment in this group (188 patients) was 2.1% (4 patients), 3 patients received UFH and 1 patient received LMWH, while the rate of minor bleeding in gum, skin and gaster was 0.5% (1 patient) each, with 8.5% hematuria (16 patients), and 0.5% (1 patient) had decreased hemoglobin without any bleeding, and another 0.5% (1 patient) had prolonged APTT (> 3 x control).

Current International Guidelines Used

Figure 3 shows the reference International Guidelines used in prescribing anticoagulant prophylaxis in this study. They were AHA/ASA 2007 in 190 patients (47.4%), for which anticoagulants were used in 118 patients and not used in 72 patients, followed by ACCP 2008 in 87 patients (21.7%), where anticoagulants were used in 45 patients and not used in 42 patients. AHA/ASA 2007 and ACCP 2008 combination was used in 98 patients (24.4%), in which anticoagulants were used in 21 patients and not used in 77 patients. Whereas ESO 2008 was used in 24 patients (6.0%), and IUA 2006 in only 1 patient (0.2%).

DISCUSSION

Current Use of Anticoagulants in Hospitals in Jakarta

In this study, the risk factors in baseline characteristics of patients referred to MEDENOX study, which were immobilization and acute infection, while others factors were age, malignancy, previous history of VTE, and obesity.¹ There were some additional risk factors which were thrombophilia, varicose vein, pregnancy/postpartum⁸, nephrotic syndrome⁹, and dehydration.¹⁰ Meanwhile, thrombocytosis, previously considered as a risk factor for VTE,

Table 4. List of patients with VTE

Site	Length of stay in hospital (days)	Sex	Age	Anticoagulant	Mechanical thrombophylaxis	Underlying diseases
Hematology	11	Female	53	UFH 25000 U/24 hours	Yes	Deep vein thrombosis lower extremities, cellulitis, abscess, type 2 diabetes mellitus
Hematology	22	Male	60	UFH 20000 U/24 hours	Yes	Irreversible shock, sepsis, hospital associated pneumonia, prostate adenocarcinoma, type 2 diabetes mellitus
Hematology	34	Female	47	UFH 3x5000 U	No	Lymphoma malignum
Hematology	18	Male	42	UFH 20000 U/24 hours, warfarin 1x2 mg	Yes	Complete fracture simphisis ramus superior inferior
Hematology	23	Female	45	UFH 20000 U/24 hours	Yes	Breast cancer stage IV
Hematology	103	Male	45	UFH 10000 U/24 hours	Yes	Non ST elevation myocardial infarction, chronic kidney disease on hemodialysis, hypertension, deep vein thrombosis
Neurology	58	Male	68	Fondaparinux 1x2.5 mg	Yes	Hypertension grade I, glaucoma ocular dextra and sinistra, hypokalemia, suspect peripheral arterial disease
Neurology	20	Male	51	UFH 10000 U/24 hours	Yes	Deep vein thrombosis, congestive heart failure fc III-IV, peripheral arterial disease, cardiogenic shock
Neurology	32	Female	44	UFH 20000 U/24 hours	Yes	Suspect thrombosis, deep vein thrombosis left leg, coronary arterial disease
Cardiology	4	Male	54	-	Yes	Hepatic cirrhosis, pulmonary embolism
Cardiology	6	Female	53	UFH 10000 U/24 hours, warfarin 1x2 mg	No	Pulmonary embolism, pulmonary tuberculosis, type 2 diabetes mellitus
Others	11	Male	60	Enoxaparin 1x0.4 cc, warfarin 1x2 mg	No	Type 2 diabetes mellitus, hypertension, deep vein thrombosis
Others	2	Male	67	UFH 10000 U/24 hours, warfarin 1x1 tab	Yes	Deep vein thrombosis, diabetic neuropathy, bilateral CVC, type 2 diabetes

was excluded from analysis due to no established supporting data. This finding is somewhat different to MEDENOX study which found that most patients (>50%) had at least 2 risk factors.

Use of Anticoagulants and VTE

In this study, 46.9% patients received prophylaxis anticoagulants, and 53.1% patients did not. Among those who did not receive

anticoagulants, the most frequent reason was no anticoagulant indication in about half of them (46.2%). This was contradictory to the eligibility criteria of patients entering this study with VTE prophylaxis. The other reasons were cost, contraindications, concerned for bleeding and others as shown in **Figure 2**.

Physicians identified that 46.2% of 213

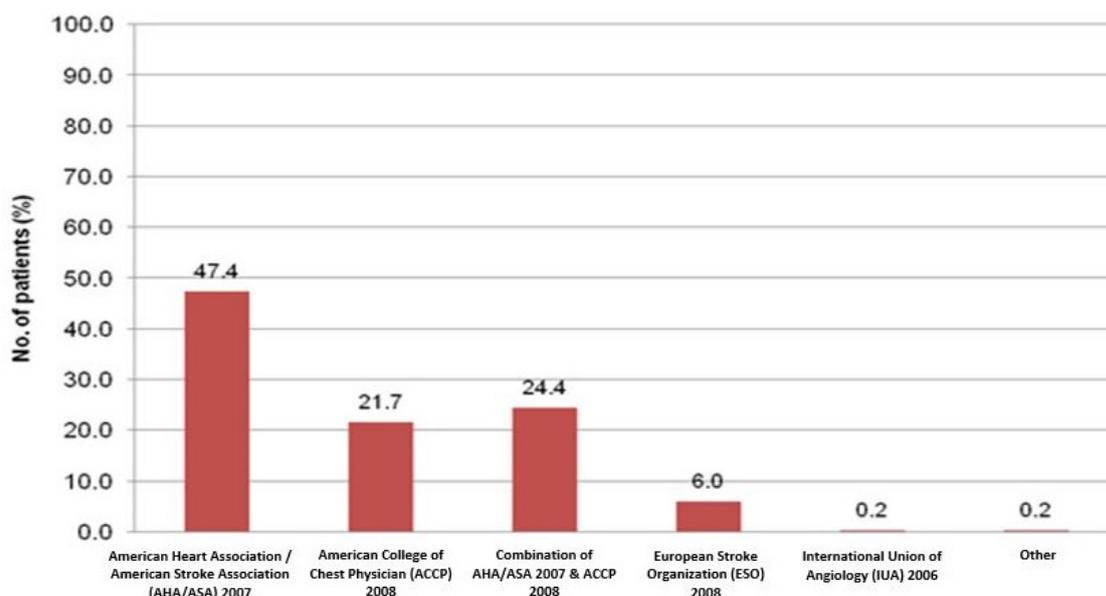


Figure 3. Reference international guidelines used in this study

Table 5. Minor bleeding complications

Minor Bleeding	N (%)
Gum	1 (0.5)
Skin	1 (0.5)
Gaster	1 (0.5)
Hematuria	16 (8.5)
Decreased Hemoglobin without bleeding	1 (0.5)
Prolonged APTT	1 (0.5)

patients had no anticoagulant indication and did not use anticoagulants to the patients. This finding represents lack of compliance of physician to start with anticoagulant prophylaxis as mentioned in reference guidelines.

VTE incidence in this study was lower than those in other studies. Patients in the other studies (MEDENOX, ARTEMIS, PREVENT) had higher risk of VTE on the whole (10.19% in MEDENOX, 8.07% in ARTEMIS, 3.84% in PREVENT) because the proportion of VTE risk factors such as age (73 years in MEDENOX, 74.7 years in ARTEMIS, 68.5 years in PREVENT, 58.1 years in this study), history of VTE (9.44% in MEDENOX, 4.59% in ARTEMIS, 3.86% in PREVENT, 1.8% in this study), obesity (20.15% in MEDENOX, 30.37% in PREVENT, 11.2% in this study), and varicose vein (25.32% in MEDENOX, 27.63% in PREVENT, 0.3% in

this study).¹⁻³ Table 6 shows the comparison of characteristics of previous studies with this study.

The description of incidence VTE (based on signs and symptoms) and types of prophylaxis is shown in Table 7. We did not conduct analysis of VTE prophylaxis and VTE incidence in our study since the study was not designed to compare the incidence and also because of group population imbalance especially the types of prophylaxis given to the subjects.

Initial Choice of Anticoagulants as VTE Prophylaxis

Most of the physicians chose UFH as VTE prophylaxis in this study because of safety concern. Among 138 patients receiving UFH (either alone or in combination therapy), the main reason for choosing UFH was controllable administration in 107 patients (78%). The other reason was its low cost in 53 patients (39%). The main reason for choosing enoxaparin among 32 patients was its practical use in 27 patients (84%), followed by its safety in 9 patients (28%). The main reason for choosing fondaparinux was patient request in 22 of 26 patients (85%), while for warfarin, it was more practical (oral use) in 5 of 8 patients (63%).

Methods of VTE prophylaxis used in this study were mechanical thrombophylaxis, pharmacological thrombophylaxis, and

combination of mechanical and pharmacologic thromboprophylaxis, and others. Mechanical thromboprophylaxis as a sole prophylaxis measure was used only in cases of contraindications to the anticoagulants and in cases of high risk of bleeding. In the latter cases, mechanical thromboprophylaxis was used until the bleeding risk has decreased and at this time anticoagulants is substituted for or added to the mechanical thromboprophylaxis. In the absence of contraindications, a combination of mechanical and pharmacologic thromboprophylaxis is suggested.^{4,7}

Despite of lower risk condition, patients receiving anticoagulants in this study, had a similar incidence of VTE as in MEDENOX and Artemis studies (4.8 % Vs 5.5% and 5.6%). It should be noted that the use of mechanical thromboprophylaxis in this study was high (81.3%), while it is use in MEDENOX and Artemis studies was depended on the usual practice at each center but the extant was not specified. The low prescription of anticoagulants by the prescribing physicians, but the high use of mechanical thromboprophylaxis in this study

revealed that there was a great need for VTE prophylaxis, which was actually realized by the physicians, but they were reluctant to use anticoagulants, primarily because of concern for bleeding, and not because there was no indication.^{1,3}

Bleeding Complication

Even there was a major and minor bleeding there was no patients reported died despite of the bleeding complications. It seems that the use of anticoagulant did not raise significant safety concern, since five (5) patients died due the underlying disease as we mention above.

Implementation of International Guidelines on VTE Prophylaxis in Jakarta

As previously described, there are 4 (four) international guidelines used on VTE prophylaxis: ACCP 2008, AHA/ASA 2007, ESO 2008 and IUA 2006. AHA/ASA 2007 was the most frequent of international guideline used (47.4%, **Figure 3**) in this study.

However, despite anticoagulant is recommended in the guidelines, around half of the patients (49.06%) were given anticoagulant. This

Table 6. Comparison of VTE prophylaxis studies

	MEDENOX	PREVENT	ARTEMIS	TROPHY
Design	RCT, multicenter, in 9 countries	RCT, multicenter, in 26 countries	RCT, multicenter, in 8 countries	Multicenter, prospective, registry study
Subjects	AIM patients, >40 years, hospitalization of ≥6 days	AIM patients, aged ≥40 years, hospitalization of ≥4 days	AIM patients, ≥60 years, hospitalization of ≥4 days	AIM patients, ≥40 years, hospitalized ≥6 days
Prophylaxis	20 mg or 40 mg of enoxaparin	5000 IU of dalteparin	2.5 mg of fondaparinux	Various regimens
Outcomes	Lower VTE incidence in group receiving 40 mg of enoxaparin (5.5%) than placebo (14.9%).	Lower VTE incidence in group receiving prophylaxis (2.77%) than placebo (4.96%).	Lower VTE incidence in group receiving prophylaxis (5.6%) than placebo (10.5%).	Thirteen patients (3.2%) of 401 patients had signs or symptoms of VTE

RCT: randomized controlled trial; AIM: acutely ill medical

Table 7. VTE incidence and types of prophylaxis

	Mechanical prophylaxis	Medical prophylaxis	Mechanical and medical prophylaxis	No prophylaxis	Total
VTE	1	4	8	0	13
Non VTE	159	21	162	46	388
Total	160	25	170	46	401

Table 8. Comparison of guideline implementation

	Languasco et al (2011)	TROPHY
Subject	310 prescriptions of medical general-ward admitted patients	401 acutely ill medical patients, aged ≥ 40 years, hospitalized for ≥ 6 days, immobilized for ≥ 3 days
Result	265 subjects (85.5%) received thromboprophylaxis, 188 subjects (60.6%) of these 265 subjects received appropriate prophylaxis according to the institutional guidelines, according to ACCP 2004	188 subjects (46.9%) received prophylaxis anticoagulants

reflects underutilization of the guidelines. Even there is strong indication to use anticoagulant, only half use the guidelines. Even if they use the recommendation only half fully follow the guidelines. Others who partially use the guidelines, due to many reasons.

According to ESO and IUA Guidelines, use of anticoagulants in ischemic stroke is not recommended, due to the benefit of the anticoagulants are counterbalanced by the intracranial hemorrhage. In this setting, as in hemorrhagic stroke, mechanical thromboprophylaxis is recommended.^{6,7}

Languasco et al.¹¹ found that underuse and inappropriate VTE prophylaxis in Argentina. They found that 85.5% of the subjects received medical prophylaxis but only 60.6% of the subjects received appropriate prophylaxis. VTE prophylaxis coverage (46.9%) in our study is lower than this study.¹¹

The summary of a anticoagulant treatment according to several International guidelines for VTE prophylaxis in medical ill patients is shown in **Table 9**.

Unfortunately, there are no available regional guidelines either in Asia or South East Asia, as well as national guidelines.

Table 9. Summary of anticoagulant treatment according to selected international guidelines for VTE prophylaxis in medically ill patients

	AHA/ASA 2007*	ACCP 2008	ESO 2008*	IUA 2006+
Indication for thromboprophylaxis				
Condition in which anticoagulant is recommended	Ischemic stroke, immobilized (seriously ill patients).	CHF; severe respiratory disease; Confined to bed and have one or more risk factors (active cancer, previous VTE, sepsis, acute neurologic disease, or inflammatory bowel disease)	Ischemic stroke patients with high risk of DVT or pulmonary embolism (e.g. due to immobilization, obesity, diabetes, previous stroke).	- Age > 40 years old with acutely medical illness and/or reduced mobility with one of morbidities : CHF class III/IV, respiratory disease, active cancer requiring therapy, acute infective disease, rheumatic disease, ischemic stroke, or acute myocardial infarction; - Acute medical illness with reduced mobility and one of the risk factors : history of VTE, malignant disease, or age over 75 years old.
Choices of Anticoagulants				
LMWH	Grade IA for all subcutaneous	Grade IA	Grade IA	Grade A (enoxaparin 40 mg od / dalteparin 5.000 U od)
LDUH	anticoagulant in general	Grade IA	Grade IA	Grade A (UFH 5.000 IU tid)
Fondaparinux		Grade IA	(not specified)	Grade B (2.5 mg daily dose)

CHF, congestive heart failure; DVT, deep vein thrombosis; LMWH: Low molecular weight heparin; LDUH, low dose unfractionated heparin

* for ischemic stroke

+ Grade A: recommendations are based on level 1 evidence from randomized controlled trials with consistent results.

Grade B: recommendations are based on level 1 evidence from randomized controlled trials with less consistent results, limited power, or other methodological problems. Grade C: recommendations are based on level 2 evidence from well-conducted observational studies with consistent results.

CONCLUSION

The present thromboprophylaxis registry in Jakarta, Indonesia, among acutely ill medical patients at risk of VTE showed underutilization of prophylaxis anticoagulant. This registry also showed underutilization of LMWH compared to UFH. AHA/ASA guideline is the most commonly used guideline for VTE prophylaxis, followed by ACCP guideline. The reasons of underutilization of anticoagulant prophylaxis were medical reasons (74.1%) which also included doctors' opinion, cost (21.2%), and other reasons (4.7%). Mechanical thromboprophylaxis either alone or in combination with pharmacological thromboprophylaxis is the most commonly used in this study population. VTE thromboprophylaxis strategy in medically ill patients needs to be improved in clinical setting.

CONFLICT OF INTEREST

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REFERENCES

1. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients (MEDENOX Study). *New Engl J Med*. 1999;341:793-800.
2. Leizorovics A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. *Circulation*. 2004;110:874-9.
3. Cohen AT, Davidson B, Gallus AS, et al. A multinational, randomized, double-blind comparison of once daily subcutaneous fondaparinux sodium with placebo for the prevention of venous thromboembolic events in acutely ill medical patients (ARTEMIS). *Blood*. 2003;102:15a.
4. Hirsh J, Guyatt G, Albers GW, et al. Executive summary: American College of Chest Physicians (ACCP) Evidence-Based Clinical Practice Guidelines. 8th ed. *Chest*. 2008;133:71S-105S.
5. Adams HP Jr, del Zoppo GJ, Alberts MJ, et al. AHA/ASA guidelines for the early management of adults with ischemic stroke. *Stroke*. 2007;38:1655-711.
6. Ringleb PA, Boussier M-G, Ford G, et al, for the European Stroke Organization (ESO) Executive Committee and the ESO Writing Committee. Guidelines for management of ischemic stroke and transient ischemic attack. *Cerebrovasc Dis*. 2008;25:457-507.
7. Nicolaides AN, Fareed J, Kakkar AK, et al. For International Union of Angiology (IUA). Prevention and treatment of venous thromboembolism international consensus statement (Guidelines according to scientific evidence). *Int Angiol*. 2006;25:101-61.
8. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. *Circulation*. 2003;107: 1-9-I-6.
9. Ismail G, Mircescu G, Ditoju AV, et al. Risk factors for predicting venous thromboembolism in patients with nephrotic syndrome: focus on haemostasis – related parameters. *Int Urol Nephrol*. 2014;46(4):787-92. PMID:24078010.
10. Prandoni P. Acquired risk factors for venous thromboembolism in medical patients. *Hematology (Am Soc Hematol Educ Program)*. 2005;458-61.
11. Languasco A, Galante M, Marin J, Soler C, Saubidet CL, Milberg M. Adherence to local guidelines for venous thromboprophylaxis: a cross-sectional study of medical inpatients in Argentina. *Thromb J*. 2011;9:18.