



An Update of Anticoagulant in Venous Thromboembolism

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Introduction

Venous thromboembolism (VTE), comprised of deep vein thrombosis (DVT) and pulmonary embolism (PE), is a result of propagating thrombus formation in the vein due to either hypercoagulability, stasis, or endothelial injury. Recently, this disease warrant global awareness due to its contribution on death and chronic morbidity.¹ Global surveillance has reported the increment of VTE incidences particularly in Asia, although it is still lower than rest of the world.² Venous thromboembolism in Asia has a characteristic dominated by female gender, underweight and has main risk factors of cancer and hospitalization.² According to IDENTIA, a registry of incidence of deep vein thrombosis in medically ill patient in Indonesia, the incidence of DVT increase parallel with long duration of immobilization, obesity and cancer history.³

The clinical outcomes of VTE in Asia were reported to higher in mortality, recurrence, and progression into pulmonary embolism. These findings were congruent with data of lesser guideline directed in the management of VTE in Asia, moreover there was also lack of prophylaxis data.²

Based on those study, this paper aims to discuss about VTE prevention and therapy, focusing on anticoagulant. For the prophylaxis, this paper will discuss on cancer, hospitalization patient and in COVID 19 as an emerging global health issue.

Discussion

The classification of VTE according to its risk factor is important for planning the anticoagulant therapy.⁴ Venous thromboembolism event is divided into unprovoked and provoked. An unprovoked VTE refers to a thrombotic event that is not associated with an environmental risk factor on the contrary provoked VTE is associated with an environmental or acquired known risk factor. Risk factor itself can be transient or persistent and it is affected

recurrency and decision of anticoagulant duration. As mentioned, this paper will be focused on cancer, hospitalization and COVID-19 as the top issue related to VTE.

A. VTE anticoagulant in cancer

Since the incidence of VTE is high in cancer, mostly cancer patient is a candidate for prophylaxis anticoagulant.⁵ Here we will discuss the primary prophylaxis on cancer patient who undergo surgery and ambulatory cancer patient with systemic therapy.

In cancer patient with surgical plan, VTE prophylaxis either with low molecular weight heparin (LMWH) or Fondaparinux is recommended over unfractionated heparin (UFH) except for patient with renal impairment. In the case of extended prophylaxis is needed, LMWH is recommended to be used in this setting. VTE prophylaxis in cancer patient undergo surgery is advised to be given post-operatively rather than pre-operative to minimize the risk of bleeding.⁶ In major abdominal/pelvic surgery, extended prophylaxis for VTE is recommended.⁶

Venous thromboembolism prophylaxis in ambulatory cancer patient should be based on risk assessment by Khorana risk score and prophylaxis is recommended for moderate to high risk.

There are three stages of anticoagulant therapy for VTE in cancer patient, initial (within first week to 3 months of diagnosis), short-term (3-6 mo.), long-term (>6 mo.) and end of life. In the initial treatment direct oral anticoagulant (DOAC) or LMWH are the first line therapy. Anticoagulant is continued for short to long term depend on recurrency risk and clinical judgment with consideration of bleeding risk. In the end of life stage of cancer patient, anticoagulant is recommended to be discontinued.⁶

B. VTE in hospitalized patients

According to GARFIELD-VTE registry, hospitalization of VTE in Asia.² Prophylaxis of VTE in a hospitalized patient needs risk score assessment.

SCORING SYSTEM	POPULATION AT RISK	# OF INPUTS/ VARIABLES	OUTPUT AND RISK CATEGORY	LOWEST RISK CATEGORY	HIGHEST RISK CATEGORY	COMMENTS
CAPRINI (2005)	Surgical Patients	>30	Risk of VTE at 3 months	Lowest risk <0.7% (0 points)	Highest risk 10.7% (> 9 points)	No formal validation with original study. External validation studies in surgical outpatients (13,21,119). Meta-analysis approximately 14-fold variation in VTE risk scores (1 studies (119).
Padua Prediction Score	Medical Inpatients	11	Risk of VTE at 3 months	Lowest Risk 1.1% (<4 points)	Highest risk 3.5% (> 4 points)	Internal validation showing 12-fold variation in VTE (without prophylaxis) (125). An external validation in patients with sepsis did not find correlation with VTE risk (126).
IMPROVE Score	Medical Inpatients	7	Risk of VTE at 3 months	Lowest Risk 0.4% (0 points)	Highest risk 5.7% (> 4 points)	Validation includes 1 retrospective, 1 case-control, and 1 prospective multicenter study (128,129,130).

Figure 1. Summary of select scoring systems for predicting risk of venous thromboembolism.⁷

Padua risk score ≥ 4 or IMPROVE score ≥ 2 warrant VTE prophylaxis. Hospitalized patient which includes acute and critical-ill condition is recommended to have parenteral anticoagulant during hospitalization alone over combination with mechanical prophylaxis.⁸ unless major bleeding or high risk of bleeding. Low molecular weight heparin (LMWH) is recommended over fondaparinux and unfractionated heparin (UFH).⁸

C. VTE in COVID-19

Recent publication revealed that there is strong correlation of COVID-19 and venous thromboembolism either through direct viral immunothrombosis mechanism or indirectly via systemic inflammation-induced thrombosis. Venous thromboembolism is COVID-19 has been related to high mortality and morbidity, particularly for the occurrence of massive pulmonary embolism. Prevalence of DVT and PE related COVID-19 are 32% and 27 % respectively, it correlates with ICU admission and level of D-dimer.⁹

Problem raised whether we should give prophylaxis anticoagulant, intermediate or therapeutic anticoagulant in the absence of standard diagnostic tools. The scope of problem in this paper covers acute and critically ill hospitalized COVID-19.

According to American Society of Hematology guideline 2021, for the acute and critically-ill COVID-19 who does not have suspected or confirmed VTE, prophylactic anticoagulant is recommended over intermediate or therapeutic intensity.¹⁰ Another problem is when patient already consume anticoagulant prior to hospitalization due to COVID-19. Here is the algorithm to manage hospitalized COVID 19 with prior use of anticoagulant (Figure 2).

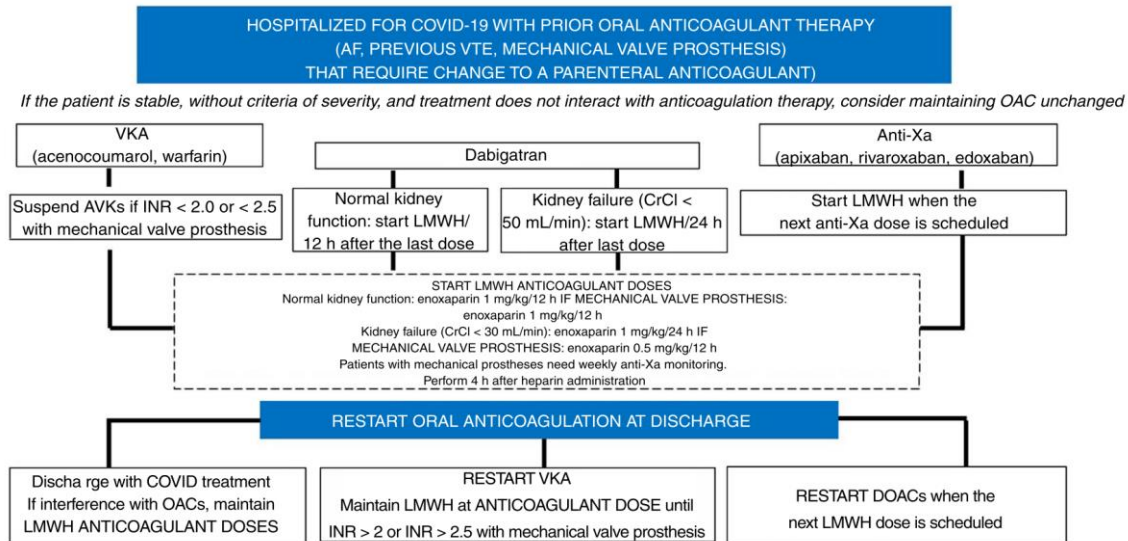


Figure 2. Antithrombotic approach to patient admitted with prior anticoagulant therapy.¹¹

Conclusions

Venous thromboembolism is a high burden disease with increasing prevalence due to many factors. Improving diagnostic strategies as well as administration of appropriate prophylaxis will reduce the incidence and complication of this disease.

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