Acta Cardiol Sin 2021;37:215–216
Reply Letter
doi: 10.6515/ACS.202103_37(2).20210120A

Management of Venous Thromboembolisms: Part II. The Consensus for Pulmonary Embolism and Updates

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Key Words: Cancer • Thrombophilia • Venous thromboembolism

THE AUTHORS REPLY

Venous thromboembolism (VTE), despite less commonly perceived in Taiwan, poses dreadful complications if not managed appropriately. Over the past 4 years, we committed to increase the physicians' awareness towards, streamline the diagnosis of, and standardize the treatment strategies for VTE in Taiwan by publishing two consensus documents in this area.[1,2] Each document discussed the different aspect of VTE and intended to provide the clinicians with the contemporary evidence-supported science as broad as possible when completed. Although there is universal pathogenesis underpinning VTE — interrupted blood flow, injured blood vessels, and disturbed blood coagulation — it is a far more complex disorder in which genetic and environmental factors interact. In consequence, we were not able to cover all VTE nor generalize our recommendations to every patient with VTE within these two documents.

Several genetic tendencies for VTE have been identified, and they differ in their ethnic distribution, among which deficiency of either protein C or S, which is believed to be severe thrombophilias, is more common in Taiwan compared to Western countries.[3] It might seem reasonable to explore those genetic predispositions in those who have VTE as physicians' nature to prevent its recurrence. However, their impact on the risk of recurrent VTE is still highly debated. The odds of VTE associated with inherited thrombophilias were overestimated as a result of selection and gene-gene or gene-environment interactions in prior studies.[4] And multiple risk factors (most often acquired ones) are a prerequisite for developing thrombosis instead of standalone thrombophilia.[5] Currently, major guidelines discourage universal screening for inherited thrombophilias unless that involve with decision making (e.g. adjusting anticoagulation), recurrent and unprovoked VTE, or an unusual presentation. On contrary, antiphospholipid antibody syndrome is characterized by the exceptionally high risk of recurrent VTE and/or arterial thrombosis even when anticoagulation is extended.[6] While Dr. Chang raised his concerns on how testing for inherited thrombophilias has been frequently but inappropriately taken outside research in patients with VTE, he also reminded us of another critical issue about timing for testing should we decide to proceed. We must keep in mind that direct oral anticoagulants, as well as heparin and vitamin K antagonists, interfere laboratory measurement of protein C and S and lupus antibodies.[7] It can be elusive to interrupt anticoagulation treatment for thrombophilia testing in every patient or at all times. Therefore, those results are better scrutinized under good clinical context and preferably with helps from our hematology colleagues.

Drs. Shao and Lin recapitulated the recent advancement in cancer associated thrombosis (CAT). We agree with their view that direct oral anticoagulants can improve the treatment for CAT and are preferrable in most

Received: January 18, 2021 Accepted: January 20, 2021
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patients at low risk of bleeding. Despite that, their use for primary prevention in patients with cancer who are at high risk of thrombosis is not yet justified. In addition, their illustrations regarding individualizing treatment according to the site of cancer, associated conditions of the patient, and potential pharmacological interactions with other treatment are much appreciated as there is certainly no one-size-fits-all agent (or strategy) for CAT and for overall VTE. Meanwhile, we like to clarify here that our meta-analysis of four recent clinical trials comparing direct oral anticoagulants with dalteparin used tabular data to estimate the effect sizes (*relative risk*) along with the confidence intervals.[8] The mathematics behind those estimates is different from the Cox hazards model used in the SELECT-D study publication.

VTE manifests as a multifactorial disease. We were hindered by the paucity of systematic information about thrombophilias and cancer in our patient population with VTE when completing those two documents. Nevertheless, we believe it is the prime time to amalgamate our colleagues from cardiovascular medicine, hemato-oncology, and rheumatology into a VTE research consortium in Taiwan. With that, the outputs can truly feed back into making recommendations more appropriate and relevant to our local practice.

DISCLOSURE

Kang-Ling Wang reports honoraria from Bayer, Boehringer Ingelheim, Daiichi-Sankyo, Novartis, and Pfizer.

Pao-Hsien Chu has no relevant conflict of interest.

FUNDING SOURCES

None.

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