




Prophylaxis of Venous Thromboembolism in Patients with Infectious Disease

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Venous thromboembolism (VTE), defined as deep vein thrombosis and/or pulmonary embolism (PE), is associated with a significant disease entity in medically ill patients¹. The incidence of VTE is increasing gradually in Asia even though it is still lower than in Western countries²⁻⁴. The incidence of VTE increases sharply in the elderly⁵ of which the proportion is expected to rise more rapidly in South Korea than hitherto⁶. Moreover, recent studies showed that the recurrence rate of VTE in Korea is comparable to the rate in Western societies^{3,7}. Thus, VTE might become a big burden for national health care in near future in South Korea.

What kind of efforts are needed to minimize future risk from VTE at this moment? It is timely to focus on identifying patients at high risk of VTE in advance and applying prophylaxis, beyond treating patients diagnosed with VTE, because both physicians' and patients' awareness increased since introduction of direct oral anticoagulant in 2013. The next step would be to find out the most appropriate candidates for prevention of VTE among medically ill patients.

Who are those candidates? Many studies showed that

about 40% of the medical hospitalized patients face a moderate or high risk to develop VTE¹ during which acute infectious disease, age older than 75 years, cancer, and previous VTE history are well-known risk factors⁸. Clayton et al.⁹ showed that especially, preceding respiratory infection may increase the risk of PE or VTE in the 3 months following infection (adjusted odds ratio, 2.50; 95% confidence interval, 1.33–4.72) from a primary care general practice database. Recently, Lee et al.¹⁰ reported that infection combined with VTE increased mortality. However, there was the limitation that PE was diagnosed incidentally by conventional computed tomography in over two-thirds of the patients. That is why they could not prove the temporal and causal relationship between infection and PE.

Let us look at recent studies^{11,12}, which assessed whether thromboprophylaxis decrease the rate of VTE in medically ill patients including acute infection or respiratory disease, while the implementation of prevention programs decreased the rate of VTE in surgical¹³ and orthopedic department¹⁴. Cohen et al.¹¹ showed in the MAGELLAN trial that the patients with infection, respiratory insufficiency and two or more medical condition constituted 45.8%, 27.3%, and 30.6%, respectively, in rivaroxaban group in which extended duration of prophylaxis reduced the risk of VTE, but rivaroxaban was also associated with an increased risk of bleeding. Spyropoulos et al.¹² included in the MARINER trial patients with infectious disease (17.5%) and respiratory insufficiency (26.2%) in the rivaroxaban group versus placebo given to medical patients for 45 days after hospital discharge, in which rivaroxaban was not associated with a significant lower risk of symptomatic VTE and death due to VTE versus placebo. Spyropoulos et al.¹² estimated the risk for VTE on the basis of a modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) score of 4 or higher or a risk score of 2 or 3 plus a plasma D-dimer level of more than twice the upper limit of the normal range. Over one-third patients had IMPROVE score of 4 or higher.

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In real-life observational study, Mahlab-Guri et al.¹⁵ reported that thromboprophylaxis did not have significant effect on reducing the number of VTE events, even though the rate of patients treated for thromboprophylaxis increased from 22% at 2013 to 46% at 2018. The risk of VTE was calculated with Padua score which includes malignancy, previous VTE, obesity, elderly age, bedrest, acute infection and so on¹⁵. About 30.1% had a Padua score of 4 points or more (representing high risk of VTE), which is indication for VTE prophylaxis. In this study, 25.1% of patients had infectious disease, but there was no analysis to assess the outcome in the subgroup of patients with infectious disease¹⁵.

In clinical practice in South Korea, the proportion of patients receiving prophylaxis may be much lower than 46% although there is lack of exact data. We need to increase the rate of prophylaxis in genuine candidates with high risk of VTE (Padua score of 4 points or more). There are still controversies about the most appropriate candidates and duration for prophylaxis of VTE in medically ill patients in recent studies^{11,12,15}. We have to make our own efforts to identify candidates for VTE prophylaxis in retrospective and prospective studies in South Korea. These efforts may increase the rate of prophylaxis in adequate candidate, and after all reduce the rate of VTE in medical patients admitted with comorbidity in a super-aged Korean society before long.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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