

Risk factors of recurrence and major bleeding in patients with intermediate-risk for recurrence of venous thromboembolism: from the COMMAND VTE Registry

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Background/Introduction: Patients with venous thromboembolism (VTE), including pulmonary embolism (PE), have a long-term risk of recurrence, and anticoagulation therapy is recommended for the prevention of recurrence. The latest 2019 European Society of Cardiology (ESC) guideline classified the risks of recurrence into low- (<3%/year), intermediate- (3–8%/year), and high- (>8%/year) risk, and recommended the extended anticoagulation therapy of indefinite duration for high-risk patients as well as intermediate-risk patients. However, extended anticoagulation therapy of indefinite duration for all of intermediate-risk patients have been a matter of active debate. Thus, additional risk assessment of recurrence in intermediate-risk patients might be clinically relevant in defining the optimal duration of anticoagulation therapy. Furthermore, bleeding risk during anticoagulation therapy should also be taken into consideration for optimal duration of anticoagulation therapy. However, there are limited data assessing the risk of recurrence as well as bleeding in patients with intermediate-risk for recurrence based on the classification in the latest 2019 ESC guideline.

Purpose: The current study aimed to identify the risk factors of recurrence as well as major bleeding in patients with intermediate-risk for recurrence, using a large observational database of VTE patients in Japan.

Methods: The COMMAND VTE Registry is a multicenter registry enrolling consecutive 3027 patients with acute symptomatic VTE among 29 cen-

ters in Japan. The current study population consisted of 1703 patients with intermediate-risk for recurrence. The primary outcome measure was recurrent VTE during the entire follow-up period, and the secondary outcome measures were recurrent VTE and major bleeding during anticoagulation therapy.

Results: In the multivariable Cox regression model for recurrent VTE incorporating the status of anticoagulation therapy as a time-updated covariate, off-anticoagulation therapy was strongly associated with an increased risk for recurrent VTE (HR 9.42, 95% CI 5.97–14.86). During anticoagulation therapy, the independent risk factor for recurrent VTE was thrombophilia (HR 3.58, 95% CI 1.56–7.50), while the independent risk factors for major bleeding were age ≥ 75 years (HR 2.04, 95% CI 1.36–3.07), men (HR 1.52, 95% CI 1.02–2.27), history of major bleeding (HR 3.48, 95% CI 1.82–6.14) and thrombocytopenia (HR 3.73, 95% CI 2.04–6.37).

Conclusions: Among VTE patients with intermediate-risk for recurrence, discontinuation of anticoagulation therapy was a very strong independent risk factor of recurrence during the entire follow-up period. The independent risk factors of recurrent VTE and those of major bleeding during anticoagulation therapy were different: thrombophilia for recurrent VTE, and advanced age, men, history of major bleeding, and thrombocytopenia for major bleeding.