Clinical long-term outcomes in fragile patients with venous thromboembolism receiving direct oral anticoagulant: From the COMMAND VTE Registry-2

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Background: In patient with venous thromboembolism (VTE), assessment of risk of the opposing complications, major bleeding and recurrent VTE, is clinically imperative to determine the duration of anticoagulation therapy. Patients with VTE and fragility (age ≥75 years, creatinine clearance level ≤50 ml/min, and/or body weight ≤50 kg) are reportedly at increased risk of bleeding complications associated with anticoagulant. However, there is lack of real-world data with respect to bleeding risk in fragile patients with VTE receiving direct oral anticoagulant (DOAC).

Purpose: The current study aimed to assess the relationship between fragility and long-term outcomes in such patients.

Methods: The COMMAND VTE Registry-2 is a multicenter registry enrolling 5,197 consecutive acute symptomatic VTE patients among 31 centers in Japan between January 2015 and August 2020. The current study population consisted of 3,928 patients with treatment with DOAC and available data of body weight and serum creatine level, who were divided into a fragile group (N=2,136, 45.6%) and a non-fragile group (N=1,792, 54.4%). The primary outcomes were major bleeding and recurrent VTE.

Results: In the entire study population, the mean age was 68±15 years, 59% was women, and mean body weight, body mass index, creatinine clearance level were 59.2±14.1 kg, 23.4±4.4 kg/m², and 67.8 (49.1-94.2) ml/min, respectively. The fragile group showed a higher proportion of female and higher prevalence of several comorbidities including hypertension and history of stroke than the non-fragile group, while there was not statistically difference in diabetes mellitus, liver cirrhosis, autoimmune disorder, active cancer, history of VTE, history of major bleeding, and transient VTE risk factor between the two groups. As for laboratory test, the fragile group showed higher prevalence of anemia. The fragile group more often received off-label doses of DOAC, while discontinuation of anticoagulation therapy was not statistically different between the two groups. There was a significantly difference in the cumulative 5-year incidence of major bleeding between the two groups but not in the cumulative 5-year incidence of recurrent VTE (the fragile group, 15.0% vs the non-fragile group, 11.1%, P = 0.049; and 9.6% vs 8.9%, P = 0.38, respectively). However, after adjusting for potential confounders, the excess risk of the fragile group relative to the non-fragile group was not statistically significant for major bleeding or recurrent VTE (adjusted HR 1.09, 95%CI 0.87-1.37, P = 0.47 and adjusted HR 1.06, 95%CI 0.80-1.41, P = 0.67, respectively).

Conclusions: In the multivariate analysis with data from the current large-scale observational study, there was not statistically significant association between the fragility and major bleeding or recurrent VTE in patient receiving DOAC.