Clinical features and long-term outcomes of venous thromboembolism in the warfarin era versus in the direct oral anticoagulant era

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Background/Introduction: After the introduction of direct oral anticoagulant (DOAC) for venous thromboembolism (VTE), DOAC for VTE have prevailed all over the world, which could change the daily clinical practice and clinical outcomes. However, there have been still limited data on the issue in the real world.

Purpose: We aimed to investigate demographics, practice patterns and long-term clinical outcomes in patients with VTE comparing a large observational study in the warfarin era and that in the DOAC era.

Methods: The COMMAND VTE Registry-1 (enrolled 3,027 VTE patients among 29 centers between January 2010 and August 2014 in the warfarin era) and Registry-2 (enrolled 5,197 VTE patients among 31 centers between January 2015 and August 2020 in the DOAC era) are the series of a multicenter observational study in Japan enrolling consecutive patients with acute symptomatic VTE.

Results: Patients characteristics were comparable in most of aspects between the groups, whereas prevalence of active cancer was higher in the Registry-2 (Registry-1: 23% vs. Registry-2: 29%, P<0.001). As for oral anticoagulation therapy, 88% (2,676/3,027) of patients were treated with warfarin in the Registry-1 and 79% (4,128/5,197) of patients were treated with DOAC in the Registry-2. The proportion of patients admitted to the hospital was lower in the Registry-2 (80% vs. 69%, P<0.001). The discontinuation rate of anticoagulation therapy was significantly higher in the Registry-2 (42.8% vs. 9.5%, Log rank P=0.02), which remained significant even after adjusting the confounders (adjusted hazard ratio [HR]: 0.78 (0.65-0.93), P=0.006). There was no significant difference in the cumulative incidence of major bleeding between the groups (12.1% vs. 13.7%, Log-rank P=0.26), which remained insignificant even after adjusting the confounders (adjusted HR: 1.03 (0.89-1.20), P=0.67). After stratifying a total cohort into sub-groups according to the risk classification of recurrent VTE in the current guidelines (major transient risk factors, minor transient risk factors, unprovoked, non-malignant persistent risk factors, and active cancer), the risks of recurrent VTE and major bleeding were significantly lower in the Registry-2 among active cancer group (recurrent VTE: 17.7% vs. 10.1% at 5-year, Log rank P<0.001, major bleeding: 26.6% vs 20.4% at 5-year, Log rank P=0.04), while those were not significantly different between the groups among other sub-groups.

Conclusion: In the current series of large real-world VTE registries, there seemed to be a significant risk reduction of recurrent VTE in the DOAC era compared with in the warfarin era, while there was no sign of increased risk of major bleeding in the DOAC era.