Validation of the bleeding risk scores in Japanese patients with atrial fibrillation in the era of direct oral anticoagulants

Introduction: The direct oral anticoagulants (DOACs) are prevailing for the stroke prevention of atrial fibrillation (AF). Although the incidence of the major bleeding events of DOACs is considered to be less than that of warfarin, the risk stratification for major bleeding is crucial. Several risk prediction models for major bleeding have been developed for AF patients under anticoagulants which are mostly constructed in the era of warfarin. We aimed to validate the existing risk scores, e.g. HAS-BLED score, ORBIT score and ATRIA score by using an outpatient-based contemporary registry which enrolled patients with newly diagnosed AF.

Methods: Using a prospective, multicenter Japanese registry of newly diagnosed or referred AF patients (KiCS-AF), we investigated 1,311 consecutive cases (mean age: 68.2 ± 11.0 years, 904 males [69.0%], CHADS2 score 1.5±1.2, DOAC used in 1,043 cases [79.6%]) taking oral anticoagulants and completed 2-year clinical follow-up (1.9±0.3years). The bleeding event which required hospitalization was defined as major bleeding events. Biomarkers and clinical variables which significantly contributed to predict major bleeding events were assessed by Cox-regression analysis. Validation of existing risk models (HAS-BLED score, ORBIT score and ATRIA score) was assessed using the area under the receiver operating curve (AUC).

Result: Overall, major bleeding occurred in 41 patients with annual incidence of 15.6 per 1,000 patients. The prevalence of hypertension and anemia (value of hemoglobin below 13g/dl for male, 12g/dl for female), usage of antiplatelet drug and baseline level of eGFR did not differ between patients with or without bleeding event (prevalence of hypertension: 65.9% vs. 61.3%, P=0.627, anemia: 35.0% vs. 21.9%, P=0.056, antiplatelet drug use: 4.9% vs. 2.1%, P=0.229, eGFR level: 51.5 vs. 57.8ml/min, P=0.051). Multivariate analysis revealed baseline BNP level, along with patients’ age, was the dominant predictor of these events. The predictability of each risk models for bleeding; HAS-BLED score, ORBIT score and ATRIA score was 0.665, 0.691 and 0.690 respectively (c-statistics calculated from AUC).

Conclusion: The major bleeding risk scores such as ORBIT score or ATRIA score could effectively stratify the bleeding risk also in the new era of anticoagulation therapy using DOACs.