Impact of body mass index on real-world outcomes of rivaroxaban treatment in Japanese patients with nonvalvular atrial fibrillation

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**Introduction**: Direct oral anticoagulants (DOACs) are widely used for patients with non-valvular atrial fibrillation (NVAF) to reduce the risk of stroke and systemic embolism. However, there is limited evidence regarding the safety and effectiveness of DOACs in patients with low or high body mass index (BMI) in the real world. Xarelto post-authorization safety and effectiveness study in Japanese patients with atrial fibrillation (XAPASS) is a prospective observational post-marketing surveillance study mandated by the Japanese authority. It aims to examine safety and effectiveness of rivaroxaban in clinical practice. This sub-analysis examined relationships between BMI and clinical outcomes among NVAF patients enrolled in the XAPASS.

**Methods**: One year follow-up data of 9578 patients in the XAPASS were analyzed to evaluate safety and effectiveness profile in relation to 4 BMI categories (kg/m²): underweight (<18.5), normal (18.5 to <25), overweight (25 to <30), and obese (30≤). Kaplan-Meier analysis was performed to compare outcomes of major bleeding and a composite outcome of stroke/non-central nervous system (non-CNS) systemic embolism (SE)/myocardial infarction (MI). Multivariable Cox regression analysis was used to investigate associations between the BMI categories and clinical outcomes. Details of all-cause mortality were also examined.

**Result**: Of 9578 NVAF patients treated with rivaroxaban, 542 (5.7%), 4410 (46.0%), 2167 (22.6%), and 499 (5.2%) were identified as underweight, normal, overweight, and obese patients, respectively. Kaplan-Meier analysis showed that major bleeding incidence of underweight, overweight, and obese patients were comparable compared with that of normal patients (hazard ratio (HR) 1.15; 95% confidence interval (CI) 0.57-2.30, HR 0.92; 95% CI 0.61-1.40, HR 0.88; 95% CI 0.40-1.91, for underweight, overweight, and obese, respectively). Only underweight, not overweight and obese patients, had higher incidence of stroke/non-CNS SE/MI compared with that of normal patients (HR 2.11; 95% CI 1.20-3.70, HR 1.06; 95% CI 0.69-1.61, HR 0.97; 95% CI 0.44-2.12, for underweight, overweight, and obese, respectively). Multivariable analysis identified no independent associations between the BMI categories and stroke/non-CNS SE/MI. Underweight patients had higher incidence of all-cause mortality,
with rates of 10.66, 1.91, 1.76, and 0.93 events per 100 patient-years for underweight, normal, overweight, and obese patients, respectively. Representative causes of death in the underweight patients were cardiac disorders, cancer, and respiratory disorders.

**Conclusion**: BMI was not independently associated with safety and efficacy outcomes of NVAF patients. However, careful management of NVAF and comorbidities may be required for underweight patients as this sub-analysis showed high incidence of thromboembolic event and all-cause mortality in this population.