Prevention of cardioembolic stroke and systemic embolism (SE) in patients with atrial fibrillation (AF) is of significance importance in the super-aging Japanese society, and therefore appropriate risk assessment and the following sufficient anticoagulation treatment are encouraged. The CHADS₂ or CHA₂DS₂-VASc score has been used as a risk stratification scheme for non-valvular AF (NVAF) patients worldwide. In Europe and the United States, the CHA₂DS₂-VASc score is recommended (Figure 1), whereas in Japan and Canada, the modified risk scheme based on the CHADS₂ score is used. Female sex is not included as a risk in the Japanese or Canadian guidelines. Importantly, neither CHADS₂ nor CHA₂DS₂-VASc includes body weight or related factors, because it is uncertain whether body weight itself is a risk factor for thromboembolic events in NVAF patients.

In this issue of the Journal, Hamatani et al address this important issue by analyzing data from the Fushimi AF Registry, a community-based Japanese prospective cohort. Patients with low body weight (LBW: ≤50 kg) showed a higher risk profile and a higher incidence of stroke/SE, but no difference in the incidence of major bleeding compared with those over 50 kg using multivariate and propensity score matching analyses. Although there have been several studies investigating the effect of obesity or overweight on the outcome for AF patients in Caucasian populations, the influence of LBW or low body mass index (BMI) has not been evaluated, because patients with low BMI (<18.5 kg/m²) have been excluded from such studies. Furthermore, their conflicting results suggest that it is still uncertain whether obesity or overweight is a risk factor for thromboembolic events in AF patients. In an Asian population, Wang et al showed that underweight AF patients (BMI <18.5 kg/m²) had a higher rate of cardiovascular mortality than either overweight or obese AF patients (BMI ≥24 kg/m²).
mainly due to heart failure. However, the incidence of stroke in their population was not associated with BMI. Accordingly, the report by Hamatani et al provides the first evidence that LBW is associated with the highly increased incidence of thromboembolic events observed in NVAF patients. It should be noted that patients with high BW (>60 kg) are not at a high risk for thromboembolic events in this population.

Most interestingly, LBW showed the highest hazard ratio for thromboembolic events among the risk factors of CHADS2: risk score, anticoagulants, female sex, vascular disease, and renal dysfunction (Figure 2). This intriguing finding raises the possibility that LBW should be adopted as a novel risk factor into risk stratification schemes (Figure 1). Clearly, the results need to be confirmed in other independent datasets and/or the pooled data of the Shinken Database, J-RHYTHM Registry, and Fushimi AF Registry, all of which are Japanese AF cohorts. Also, the predictive value of a risk stratification scheme including LBW for thromboembolic events should be compared with present schemes such as the CHADS2 or CHA2DS2-VASc score, and be evaluated by statistical methods such as c-statistic and net reclassification improvement.

The LBW group had a higher mean age (almost 80 years old) and more female patients than the non-LBW group. Moreover, there was a significant difference in the incidence of thromboembolic events between the LBW and non-LBW groups for patients ≥75 years old (P<0.01), whereas no significant difference was found for patients <75 years old (P=0.08). Although multivariate analysis and propensity score-matching analysis showed that LBW was an independent determinant, the possibility of interactions among age, sex, and BW cannot be completely excluded. Lack of BW data for 10.9% of the study patients may also limit the conclusions of the study. Moreover, underlying mechanisms by which LBW is associated with a higher risk for thromboembolic events are largely unknown. Nonetheless, Hamatani et al provide clinically useful and noteworthy information for risk stratification of thromboembolic events in Japanese NVAF patients and generate some important exploratory results that should stimulate further studies.

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References