Clinical impact of moderate to severe left atrial enlargement in Korean patients with non-valvular atrial fibrillation: Data from the COmparison study of Drugs for symptom control and complication prEvention of AF (CODE-AF) registry

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**Introduction:** Left atrial enlargement (LAE) is associated with adverse cardiovascular events. The clinical implications of LAE based on left atrial volume index (LAVI) have not been evaluated in Korean patients with non-valvular atrial fibrillation (NVAF). We investigated the clinical outcomes based on presence and degree of LAE in Korean NVAF patients.

**Methods:** A total of 5,688 NVAF patients enrolled in the COmparison study of Drugs for symptom control and complication prEvention of AF (CODE-AF) registry were evaluated (mean age 67.3 years, 64.2% male). Degree of LAE was classified based on the LAVI (mild, ≥ 34 mL/m²; moderate, ≥ 42 mL/m²; severe, ≥ 48 mL/m²). The primary outcome of interest of the current study was the rate of stroke or systemic embolism (SSE) during follow-up.

**Result:** The mean LAVI in the overall population was 46.9 ± 23.7 mL/m² and LAE was diagnosed in 3724 (65.5%) patients (mild, 15.7%; moderate, 12.5%; severe, 37.3%). Clinical covariables associated with moderate to severe LAE were age, male sex, diabetes, peripheral artery disease, valvular heart disease, chronic kidney disease, presence of an intracardiac device, prior AF ablation, persistent or permanent AF, left ventricular ejection fraction, and E/e’ ratio. Compared to patients with no or mild LAE, patients with moderate to severe LAE had significantly higher rates of SSE (2.1% vs. 1.2%, P = 0.004) and bleeding (6.5% vs. 5.5%, P = 0.040) at 2-years of follow-up. The presence of moderate to severe LAE was associated with higher risk of SSE in univariable (HR 1.98, 95% CI 1.25-3.15, P = 0.004) and multivariable (HR 1.72, 95% CI 1.07-2.78, P = 0.026) models. In patients with moderate to severe LAE who were prescribed regular anticoagulation (n = 4036, 68.8%), SSE rates among patients receiving non-vitamin K oral anticoagulants (NOAC) were significantly lower than in patients receiving warfarin (3.7% vs. 1.6%, P = 0.008), but no significant difference in SSE occurrence was observed among patients with no or mild LAE who were prescribed anticoagulation (P = 0.600).

**Conclusion:** Moderate to severe LAE was associated with higher incidence of SSE among patients with NVAF. The beneficial effect of NOAC over warfarin was prominent only in patients with moderate to severe LAE.