Impact of proteinuria on cardiovascular outcomes in Japanese diabetic patients with atrial fibrillation: the Fushimi AF Registry

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Background: Previous studies have suggested that proteinuria is independently associated with clinical outcomes in diabetic patients, irrespective of the presence of renal dysfunction. However, data regarding the impact of proteinuria on clinical outcomes in diabetic patients with atrial fibrillation (AF) are limited.

Methods: The Fushimi AF Registry is a community-based prospective survey of AF patients in our city in Japan. Follow-up data were available in 4,454 patients, and 634 diabetic patients with available data of proteinuria and estimated glomerular filtration rate (eGFR) were examined. We compared the clinical background and outcomes between patients with proteinuria (n=251) and those without (n=383). Then, we divided the patients into 4 subgroups according to the presence of proteinuria and renal dysfunction, and compared the clinical outcomes between groups; group 1 (without proteinuria, eGFR =60 ml/min/1.73 m²; n=203), group 2 (with proteinuria, eGFR =60; n=96), group 3 (without proteinuria, eGFR <60; n=180), group 4 (with proteinuria, eGFR <60; n=155).

Results: Age was comparable between patients with or without proteinuria. Patients with proteinuria had higher prevalences of previous heart failure (HF), stroke/systemic embolism, hypertension and renal dysfunction. The prevalences of previous myocardial infarction, and major bleeding were similar between two groups. During the median follow-up of 1,505 days, the incidence rates of HF hospitalization (4.1/100 person-years vs. 2.5/100 person-years; p<0.01) and cardiovascular death (1.8/100 person-years vs. 0.4/100 person-years; p<0.01) were higher in patients with proteinuria. When we divided patients into 4 subgroups, the incidences of HF hospitalization (group 1: 1.8/100 person-years vs. group 2: 3.4/100 person-years vs. group 3: 3.8/100 person-years vs. group 4: 4.9/100 person-years; p<0.01) and cardiovascular death (group 1: 0.3/100 person-years vs. group 2: 1.8/100 person-years vs. group 3: 0.5/100 person-years vs. group 4: 2.2/100 person-years; p<0.01) tended to be higher in not only group 3 and group 4 but also group 2 than group 1 (Figure). Multivariate Cox proportional hazards regression analysis including female gender, age (=75 years), hypertension, pre-existing HF, renal dysfunction (eGFR <60), low left ventricular ejection fraction (<40%) and proteinuria revealed that proteinuria was an independent determinant of both of HF hospitalization (adjusted hazard ratio [HR]: 1.57, 95% confidence interval [CI]: 1.05-2.34) and cardiovascular death (HR: 3.76, 95% CI: 1.59-8.88).

Conclusion: In Japanese diabetic patients with AF, proteinuria was associated with higher incidences of HF hospitalization and cardiovascular death, irrespective of the presence of renal dysfunction.
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