

## Adverse outcomes after worsening renal function in patients with atrial fibrillation: the Fushimi AF Registry

H. Ogawa<sup>1</sup>, Y. An<sup>1</sup>, S. Ikeda<sup>1</sup>, Y. Aono<sup>1</sup>, K. Doi<sup>1</sup>, Y. Hamatani<sup>1</sup>, A. Fujino<sup>1</sup>, M. Ishii<sup>1</sup>, M. Iguchi<sup>1</sup>, N. Masunaga<sup>1</sup>, M. Esato<sup>2</sup>, H. Wada<sup>1</sup>, K. Hasegawa<sup>1</sup>, M. Abe<sup>1</sup>, M. Akao<sup>1</sup>

<sup>1</sup>Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; <sup>2</sup>Ogaki Tokushukai Hospital, Ogaki, Japan  
On behalf of The Fushimi AF Registry investigators

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**Background:** Patients with atrial fibrillation (AF) commonly coexist with chronic kidney disease (CKD). Non-vitamin K antagonist oral anticoagulants (NOAC) are recommended for stroke prevention in patients with non-valvular atrial fibrillation (AF), and worsening renal function (WRF) as well as CKD is an important issue in using NOAC. However, little is known about the clinical outcomes of patients after WRF.

**Purpose:** We aimed to investigate outcomes after WRF in AF patients.

**Methods:** The Fushimi AF Registry is a community-based prospective survey of the AF patients in our city. Follow-up data including prescription status were available for 4,441 patients. Of them, 1,890 patients who have baseline and at least 1 follow-up creatinine clearance (CrCl) measurements, estimated by the Cockcroft-Gault formula, were analyzed in the present study. WRF was defined as a decrease of  $\geq 20\%$  from baseline CrCl measurement at any time point during follow-up. We evaluated demographics and outcomes after WRF in AF patients.

**Results:** During the median follow-up period of 2,194 days, mean CrCl decrease of 2.2 ml/min/year was observed and WRF occurred in 981 patients (51.9%). Patients with WRF were significantly more often female (with vs. without WRF; 40.3% vs. 35.4%;  $p=0.03$ ), older (73.4 vs. 71.1 years of

age;  $p<0.01$ ), more often paroxysmal type (49.9% vs. 47.1%;  $p<0.01$ ), and more likely to have prior stroke (17.9% vs. 12.7%;  $p<0.01$ ), heart failure (30.8% vs. 24.8%;  $p<0.01$ ), diabetes (31.7% vs. 27.1%;  $p=0.03$ ), and coronary artery disease (19.9% vs. 12.1%;  $p<0.01$ ) than those without WRF. Co-existing of CKD and mean CrCl at baseline were comparable (37.4% vs. 36.9%;  $p=0.82$ , 65.3 vs. 63.5 ml/min;  $p=0.66$ , respectively). Mean CHA2DS2-VASc score was significantly higher in WRF patients (3.55 vs. 3.03;  $p<0.01$ ). On landmark analysis, all-cause mortality occurred in 135 patients (8.6 /100 person-years) after WRF and 82 patients (1.7 /100 person-years) without WRF, with an adjusted hazard ratio (HR) of 6.33 (95% confidence interval [CI], 4.33–9.50;  $p<0.01$ ), adjusted by sex, age, body weight, serum creatinine, type of AF, oral anticoagulant prescription and comorbidities. Stroke or systemic embolism occurred in 45 patients after WRF (3.0 /100 person-years) and 78 (1.7 /100 person-years) patients without WRF (adjusted HR 1.60 [95% CI, 1.04–2.49;  $p=0.03$ ]) (Figure).

**Conclusions:** AF patients after WRF had higher incidence of various adverse events.

