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Impacts of mineralocorticoid receptor antagonists on mortality in heart failure patients with beta-blockers

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Introduction: Mineralocorticoid receptor antagonists (MRA) is an important drug for patients with heart failure with reduced ejection fraction (HFrEF). Although beneficial impacts of MRA on the patient’s survival have been shown from landmark trials, Japanese registry data did not consistently support it. Beta-blockers have a key role for MRA to provide beneficial effects. In these Japanese studies β-blockers might not be used enough to make MRA work.

Purpose: To examine impacts of MRA on mortality of the Japanese HFrEF patients treated with β-blockers.

Methods: Of all consecutive patients who were hospitalized in the university hospital because of HF between 2002 and 2010, 144 patients with left ventricular EF (LVEF) =35% who were introduced β-blockers in the hospital were analysed (age 60.1±15.0 years, male 78%, LVEF 27.0±5.9 %). Follow-up period was 3-years. Primary and secondary end points were all-cause death and cardiac death respectively. Data were collected from medical records. In order to examine impacts of MRA, Kaplan-Meier survival curve analysis and Cox regression analysis were performed.

Results: A prescription rate of MRA among the HFrEF patients increased from 45% in 2002 to 78% in 2010. All of MRA at baseline were spironolactone and mean daily dosage was 28.5±13.2 mg. Mean daily dosage of β-blockers was 8.8±8.6 mg in the carvedilol equivalent dosage. Patients treated with MRA (n=86) were likely to have higher NYHA class III or IV (56% vs. 41%), lower LVEF (27% vs. 29%) and lower systolic blood pressure (114 vs. 120 mmHg) compared with patients without MRA (n=58). Dosage of loop diuretics in patients with MRA was higher than that in patients without MRA (31.2 mg vs. 19.8 mg in the furosemide equivalent dose, p<0.01) at baseline, but no significant differences were observed at the end of follow-up (32.5 mg vs. 24.4 mg). After the follow-up, all-cause mortality in patients without MRA was significantly higher than patients with MRA (13% vs. 2.7%, p=0.03 by log-rank test). In the Cox regression analysis after adjustment for NYHA class, systolic blood pressure and loop diuretics, the absence of MRA remained to predict higher all-cause mortality (hazard ratio=0.18, 95% confidence interval=0.04 to 0.94). Meanwhile, no significant difference was observed in cardiac death (p = 0.17) between the two groups.

Conclusions: One of the MRA, spironolactone, reduces all-cause mortality among Japanese HFrEF patients treated with β-blockers. Our finding emphasizes an importance of β-blockers under the MRA treatment in HFrEF patients.