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Editorial

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Beta-Blockers in Heart Failure with Preserved Ejection Fraction: Could Their Use Be Vindicated as an Acceptable Option in the Future Treatment Guideline?

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▸ See the article "Beta-Blockers in Patients with Heart Failure with Preserved Ejection Fraction: Results from The Korea Acute Heart Failure (KorAHF) Registry" in volume 49 on page on page 238.

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The beneficial effects of beta-blockers (BBs) in heart failure with reduced ejection fraction (HFrEF) are established, because the efficacy of BB for reduction of mortality in patients with HFrEF has been proven in various randomized trials so far.[1-5] However, it is still debatable to use BB for reduction of mortality and hospitalization in patients with heart failure with preserved ejection fraction (HFpEF). Unfortunately, there is no single most reliable agent to improve the prognosis of HFpEF in the current treatment guideline.[6] In addition, the heterogenous pathophysiology of HFpEF has hindered researchers from developing an effective therapeutic strategy in HFpEF.

In this edition of the journal, Kim et al.[7] investigated the effect of BB in patients with HFpEF in a large domestic acute heart failure (HF) cohort. The authors made every effort to analyze the Korean Acute Heart Failure registry, one of the largest observational HF studies, using propensity score matching. In their study, however, use of spironolactone was greater in BB group than in no BB group (44.2% vs. 38%, p=0.006) even after adjusting confounding using propensity score matching. In the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial,[8] HFpEF patients with mineralocorticoid receptor antagonist (MRA) showed no significant difference in overall mortality, but MRA group was superior in patients diagnosed with elevated brain natriuretic peptide level and in those from America. We cannot easily rule out the potential influence of spironolactone, an MRA on the primary outcome of mortality. Nevertheless, A post-hoc analysis using the data from the TOPCAT trial[9] showed that BB use in HFpEF was associated with increased composite cardiovascular events, including all-cause death, hospitalization for HF, and major cardiovascular events. This result was attenuated only in patients with previous myocardial infarction. Moreover, in the study of Kim et al.[7] there were only 23% of patients with ischemic etiology. Then what would be the true reason of beneficial effect of BB in this study? Taken together, it may be noticeable that the results of BB study in HFpEF patients need careful interpretation considering co-administered medications and concomitant coronary artery disease (CAD).

In addition, left ventricular ejection fraction (LVEF) criteria of HFpEF also play an important role in the assessment of efficacy of BB. In a recent study of Cleland et al.,[10] BB was not effective in reducing mortality in HF patients with LVEF ≥50%. However, it was effective in reducing cardiovascular death in HF patients with LVEF 40–49%. Although ischemic etiology was attributed to the 90% of patients with LVEF 40–49%, patients with LVEF ≥50% also had comparable 86% of ischemic etiology in the meta-analysis of Cleland et al.[10] This suggests that CAD was not an only attributable factor. There were 5 times more patients with LVEF 40–49% (n=1,773) who could be benefitted from BB than those with LVEF 50% (n=314) in the study of Kim et al.[7] In addition to CAD and LVEF, maintaining sinus rhythm seems to be associated with the effect of BB. The mortality reduction in HFpEF patients with EF 40–49% only presented in patients with sinus rhythm.[10]

Limited data available from studies so far on the effects of BB in HFpEF patients are not consistent. Possible reasons for these conflicting results would be different definitions of HFpEF, baseline heart rate, the history of previous CAD, and the presence of atrial fibrillation. Could BB use in HFpEF be recommended in the future HF guideline? Further randomized controlled trials are warranted to investigate whether BB use is beneficial and safe in HFpEF patients. The investigation of different types of BB on HF outcomes also needed. In conclusion, caution should be exercised for physicians when interpreting future literatures about BB use in HFpEF because there could be quite a number of confounding factors due to heterogenous nature of the disease entity.

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