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Editorial

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Heart Failure With Preserved Ejection Fraction and Atrial Fibrillation: Are Beta-Blockers Still Relevant?

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▸ See the article "Differences in the Effects of Beta-Blockers Depending on Heart Rate at Discharge in Patients With Heart Failure With Preserved Ejection Fraction and Atrial Fibrillation" in volume 6 on page 119.

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While the efficacy of beta-blockers (BBs) in patients with heart failure (HF) with reduced ejection fraction is well-established,[1-3] the evidence supporting their use in patients with heart failure with preserved ejection fraction (HFpEF) is limited. Conceptually, heart rate (HR) reduction is believed to benefit patients as it increases ventricular filling time.[4] However, numerous studies have failed to demonstrate the benefits of HR reduction in patients with HFpEF.[5,6] Conversely, chronotropic incompetence is considered a major pathophysiologic mechanism in HFpEF,[7] and BBs can worsen symptoms and exercise capacity. Moreover, there is evidence that increasing HR through atrial pacing in an HFpEF population can reduce left ventricular end-diastolic filling pressure.[8] Furthermore, BBs in HFpEF can worsen exercise capacity, which can be reversed after withdrawing BBs.[9,10]

The effects of BBs on clinical outcomes in patients with HFpEF remain unclear. One major factor contributing to this uncertainty is the lack of large-scale, randomized controlled trials targeting patients with HFpEF treated with BBs. In the Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors With Heart Failure (SENIORS) trial, approximately 36% of enrolled patients had left ventricular ejection fraction (LVEF) greater than 35%, and post-hoc analysis suggested a potential association between nebivolol use and improved LVEF.[11] However, many of these patients met the HF category of mildly reduced LVEF, limiting the findings' applicability to true HFpEF populations and failing to demonstrate improved clinical outcome. A meta-analysis of patients with LVEF greater than 40% also found no evidence that BBs improved clinical outcomes.[12]

Atrial fibrillation (AF) is common in HFpEF, and doubles the risk of mortality, serving as a poor prognostic marker.[13] However, few studies have explored the efficacy of BBs in patients with HFpEF and AF. In this issue of the *International Journal of Heart Failure*, Kim et al.[14] analyzed 687 patients from the Korean Acute Heart Failure (KorAHF) registry, who were hospitalized with acute HF and presented with LVEF ≥50% and concomitant AF. The study divided patients into high and low HR groups based on a median heart rate of 75 bpm and analyzed outcomes based on BBs prescription at discharge. While no difference was observed in the low HR group, the high HR group showed notably reduced rehospitalization events with BB use. Although studies on BBs in HFpEF with AF are scarce, some retrospective studies have reported improved clinical outcome with BBs.[15,16]

The strength of the study is the highlight of the differential effects of BBs based on HR in patients with AF. A prior study using KorAHF registry demonstrated reduced rehospitalization risk in patients with HFpEF and AF,[17] and the current study may suggest a potential mechanism and specific subgroup among the HFpEF and AF population regarding BBs benefit. The finding that BBs use reduced HF rehospitalization in patients with high HR suggests that tachycardia may be an important mechanism of HF worsening in this population. Another interesting aspect in this study is that among patients with low HR, HR was inversely correlated with increased rehospitalization risk with BBs, possibly due to bradycardia or exaggerated chronotropic incompetence, consistent with previous studies.

The limitations of this study include, change in more than 40% of BB prescriptions after discharge, lack of consistent benefit in long-term period, and missing data on rhythm control strategy. According to recent findings from the Early Treatment of Atrial Fibrillation for Stroke Prevention Trial (EAST-AFNET 4), the presence of rhythm control therapies could be a major confounding factor.[18] Nevertheless, maintaining an appropriate HR range in patients with HFpEF with AF underscores the importance of managing this comorbid condition effectively. Recent analyses of the Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure (DELIVER) trial suggested a potential beneficial role of BBs in the specific clinical scenario of AF in HFpEF.[19] Future large-scale prospective studies and meta-analyses are warranted to validate potential roles of BBs and the adequate range of HR for these specific patients with HFpEF and AF.

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