

ORIGINAL ARTICLE**Comparative evaluation of Beta Blocker Effectiveness in Heart Failure Patients with Preserved Ejection Fraction versus those with Reduced Ejection Fraction: An observational study**

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ABSTRACT:

Background: The present study compared the effectiveness of β -blocker therapy in HFpEF versus HFrEF by assessing symptom improvement, hospitalization rate, and mortality. **Methods:** The study conducted an observational study with 235 adult HF patients treated with β -blockers (carvedilol, metoprolol succinate, or bisoprolol), stratified into HFpEF (LVEF $\geq 50\%$, n = 120) and HFrEF (LVEF $< 40\%$, n = 115). Clinical data, echocardiographic measurements, biomarkers, and functional status were collected at baseline. Primary outcomes included HF-related hospitalizations, all-cause mortality, and NYHA class improvement. Secondary outcomes were change in LVEF, 6-minute walk distance, and BNP levels. Statistical comparisons were made using chi-square and t-tests (or nonparametric equivalents), with significance set at $p < 0.05$. **Results:** The HFpEF cohort was older (68.4 ± 9.2 vs. 64.1 ± 10.5 years, $p = 0.01$), had a lower proportion of males (45% vs. 63%, $p = 0.008$), and more hypertension (82% vs. 70%, $p = 0.04$). β -blocker usage patterns differed: carvedilol was more common in HFrEF (53% vs. 40%, $p = 0.05$), while metoprolol was more used in HFpEF (60% vs. 47%, $p = 0.06$). HF-related hospitalizations were significantly lower in HFpEF (1.4 ± 0.8 vs. 1.9 ± 1.0 per year, $p = 0.002$). All-cause mortality trended lower in HFpEF (10% vs. 18%, $p = 0.08$). Improvement in NYHA class (38% vs. 63%, $p < 0.001$) and increase in LVEF (+1.2% vs. +7.8%, $p < 0.001$) were both greater in HFrEF. Secondary outcomes similarly favored HFrEF: larger BNP decline (-42 vs. -110 pg/mL, $p < 0.001$), greater increase in 6-minute walk (22 m vs. 48 m, $p = 0.003$), and higher symptom score improvement (34% vs. 58%, $p = 0.001$). **Conclusions:** In this cohort, β -blocker therapy was associated with benefits in both HFpEF and HFrEF, but the magnitude of improvement was greater in HFrEF. While HFpEF patients had fewer hospitalizations and a trend toward lower mortality, they showed less symptomatic and functional improvement compared to HFrEF. Further randomized, adequately powered trials are warranted to clarify the role of β -blockers in HFpEF and to guide personalized treatment strategies.

Keywords: β -blocker, Hospitalization, Heart

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INTRODUCTION

Heart failure (HF) is a complex clinical syndrome characterized by impaired cardiac function, leading to inadequate tissue perfusion and congestion. It remains a leading cause of morbidity and mortality worldwide, particularly among older adults. Clinically, heart failure is categorized based on left ventricular ejection fraction (LVEF) into heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). While both forms share common symptoms such as dyspnea, fatigue, and fluid retention, they differ markedly in underlying pathophysiology, prognosis, and response to therapy.¹ β -blockers are a cornerstone of pharmacologic therapy in HFrEF, with robust evidence demonstrating their ability to reduce mortality, hospitalization, and disease progression. By attenuating sympathetic overactivation, β -blockers improve left ventricular remodeling, decrease arrhythmic risk, and enhance overall cardiac efficiency. Current guidelines strongly recommend their use in HFrEF, with multiple large-scale

randomized controlled trials confirming their survival benefit. In contrast, the effectiveness of β -blockers in HFpEF remains uncertain due to heterogeneity in patient characteristics, comorbidities, and the complex mechanisms underlying diastolic dysfunction.²⁻⁴ Several observational studies and meta-analyses have explored the role of β -blockers in HFpEF, yielding mixed results. Some studies report modest reductions in all-cause mortality, while others show little effect on hospitalization or symptom improvement. Moreover, direct comparisons of β -blocker effectiveness between HFpEF and HFrEF are limited, making it challenging to define optimal management strategies for patients with preserved LVEF.^{5, 6} Understanding these differences is crucial, given the rising prevalence of HFpEF in aging populations and the increasing burden on healthcare systems.⁶⁻⁸ This study aims to address this gap by comparing the effectiveness of β -blocker therapy in patients with HFpEF versus HFrEF. By evaluating outcomes such as symptom improvement, hospitalization rates, and mortality, the study seeks to clarify whether the

established benefits of beta blockers in HFrEF extend to those with preserved ejection fraction. The findings may inform clinical decision-making and guide more personalized treatment strategies for patients with different forms of heart failure.

MATERIALS AND METHODS

The study employed a comparative observational approach to evaluate how beta-blocker therapy performed in patients with heart failure with preserved ejection fraction (HFpEF) versus those with reduced ejection fraction (HFrEF). Adult individuals diagnosed with heart failure and already receiving beta blockers were identified from hospital records during the study period. Based on the most recent echocardiographic measurements, patients were categorized into HFpEF (EF \geq 50%) and HFrEF (EF $<$ 40%). The final sample consisted of 235 participants, including 120 with HFpEF and 115 with

HFrEF. Demographic variables, comorbid conditions, medication profiles, and baseline clinical status were extracted from electronic records. Only those receiving guideline-recommended agents—carvedilol, metoprolol succinate, or bisoprolol—were included, while cases with missing echocardiographic data, significant valvular pathology, or inconsistent follow-up were excluded. The main endpoints analyzed were changes in symptom burden, frequency of heart-failure-related hospital admissions, and overall mortality during follow-up. Secondary measures included alterations in ejection fraction, exercise capacity, and relevant cardiac biomarkers when available. Statistical comparisons between the two heart-failure groups were performed using chi-square tests for categorical parameters and t-tests or appropriate non-parametric methods for continuous variables, with a p-value $<$ 0.05 considered statistically significant.

RESULTS

Table 1: Baseline Characteristics of Study Participants

Variable	HFpEF (n=120)	HFrEF (n=115)	p-value
Age (years), mean \pm SD	68.4 \pm 9.2	64.1 \pm 10.5	0.010*
Male (%)	54 (45%)	72 (63%)	0.008*
Hypertension (%)	98 (82%)	81 (70%)	0.040*
Diabetes Mellitus (%)	51 (43%)	49 (43%)	0.95
Baseline EF (%)	56.3 \pm 4.1	32.5 \pm 5.8	0.001*
Beta blocker used: Carvedilol (%)	48 (40%)	61 (53%)	0.922
Beta blocker used: Metoprolol (%)	72 (60%)	54 (47%)	

Table 2: Primary Outcomes

Outcome	HFpEF (n=120)	HFrEF (n=115)	p-value
HF-related hospitalizations (per year)	1.4 \pm 0.8	1.9 \pm 1.0	0.002*
All-cause mortality (%)	12 (10%)	21 (18%)	0.081*
Improvement in NYHA class (%)	46 (38%)	72 (63%)	$<$ 0.001*
Change in EF (%)	+1.2 \pm 2.1	+7.8 \pm 4.5	$<$ 0.001*

Table 3: Secondary Outcomes

Secondary Variable	HFpEF	HFrEF	p-value
Change in BNP (pg/mL)	-42 \pm 60	-110 \pm 95	$<$ 0.001*
6-minute walk distance (m)	+22 \pm 30	+48 \pm 35	0.0031*
Symptom score improvement (%)	34%	58%	0.0012*

DISCUSSION

Heart failure remains a major global health burden, with its clinical presentation broadly categorized into heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF). Although both conditions share similar symptoms and risk factors, their underlying pathophysiology and therapeutic responses differ significantly. Beta blockers are a cornerstone of treatment in HFrEF, with well-established benefits in reducing mortality and hospitalizations; however, their effectiveness in HFpEF remains less certain and continues to be a subject of clinical debate. With the rising prevalence of HFpEF, particularly among older adults and individuals with multiple comorbidities, it

is increasingly important to determine whether beta blockers confer benefits similar to those observed in HFrEF. Clarifying this could help optimize treatment strategies, reduce adverse outcomes, and guide clinicians in tailoring therapy to the unique needs of patients with different forms of heart failure. Furthermore, understanding the comparative effectiveness of beta blockers may inform future guideline recommendations and support evidence-based decision-making in clinical practice.⁹⁻¹²

In our study, the baseline characteristics of participants showed that patients with HFpEF (n=120) were older on average than those with HFrEF (n=115) (68.4 \pm 9.2 vs. 64.1 \pm 10.5 years, p=0.01), and the proportion of males was lower in the HFpEF group

(45% vs. 63%, $p=0.008$). Hypertension was more common among HFpEF patients (82% vs. 70%, $p=0.04$), while diabetes mellitus prevalence was similar in both groups (43%, $p=0.95$). Baseline ejection fraction differed significantly ($56.3 \pm 4.1\%$ for HFpEF vs. $32.5 \pm 5.8\%$ for HFrEF, $p<0.001$). Carvedilol use was slightly higher in the HFrEF group (53% vs. 40%, $p=0.05$), whereas metoprolol use was more common in HFpEF patients (60% vs. 47%, $p=0.06$). Regarding primary outcomes, HF-related hospitalizations per year were lower in HFpEF compared to HFrEF (1.4 ± 0.8 vs. 1.9 ± 1.0 , $p=0.002$), and all-cause mortality was numerically lower in HFpEF (10% vs. 18%, $p=0.08$). Improvement in NYHA class was greater among HFrEF patients (63% vs. 38%, $p<0.001$), and the change in ejection fraction showed a larger increase in HFrEF ($+7.8 \pm 4.5\%$ vs. $+1.2 \pm 2.1\%$, $p<0.001$). For secondary outcomes, HFrEF patients experienced greater reductions in BNP levels (-110 ± 95 vs. -42 ± 60 pg/mL, $p<0.001$), larger improvement in 6-minute walk distance ($+48 \pm 35$ vs. $+22 \pm 30$ m, $p=0.003$), and higher symptom score improvement (58% vs. 34%).

Previous studies have explored the impact of beta blockers in HFpEF and HFrEF populations. In a propensity score-matched cohort study using the Swedish Heart Failure Registry, 19,083 patients with HFpEF were evaluated for the association of β -blocker use with outcomes. Among 8,244 matched patients, β -blockers were associated with a modest reduction in all-cause mortality (HR 0.93; 95% CI 0.86–0.996; $P = 0.04$) but not with the composite outcome of mortality or HF hospitalization (HR 0.98; 95% CI 0.92–1.04; $P = 0.46$). In contrast, β -blockers in HFrEF were linked to significant reductions in both mortality and composite outcomes, suggesting differential benefits across HF subtypes. Similarly, Dobre et al. studied 443 patients with advanced HF and preserved LVEF ($\geq 40\%$) and reported that β -blocker prescription at discharge was associated with a 43% relative reduction in mortality risk over a mean follow-up of 25 ± 18 months (HR 0.57, 95% CI 0.37–0.88, $p=0.01$).^{12,13} Additional evidence comes from broader population studies. In the Cardiovascular Health Study, a longitudinal cohort of adults aged ≥ 65 years, β -blocker therapy among 950 participants with new-onset CHF was associated with a 26% reduction in all-cause mortality (HR 0.74, 95% CI 0.56–0.98). Mortality risk did not differ significantly between participants with reduced ($<40\%$) and preserved ($\geq 40\%$) EF (HR 0.56 vs. 0.82; interaction $P = 0.34$). An overview of randomized β -blocker trials by Ko et al. identified small but significant increases in hypotension, dizziness, and bradycardia, while fatigue risk was negligible. Importantly, β -blocker therapy led to reductions in all-cause mortality, HF hospitalizations, and worsening HF, supporting their safe and effective use in patients with HF despite minor adverse effects.¹⁵ Collectively, these findings underscore the established benefits of beta blockers in

HFrEF and suggest potential, though less certain, advantages in HFpEF, highlighting the need for continued evaluation in this population.

CONCLUSION

In this cohort, β -blocker therapy was associated with benefits in both HFpEF and HFrEF, but the magnitude of improvement was greater in HFrEF. While HFpEF patients had fewer hospitalizations and a trend toward lower mortality, they showed less symptomatic and functional improvement compared to HFrEF. Further randomized, adequately powered trials are warranted to clarify the role of β -blockers in HFpEF and to guide personalized treatment strategies.

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