

## HEART FAILURE

# Improvement of LVEF in patients with HF is linked to better prognosis

“patients with HF ... [who] show improvement in their LVEF have an excellent prognosis, including lower mortality”

Current heart failure (HF) guidelines acknowledge the existence of a distinct subgroup of patients with HF and preserved left ventricular ejection fraction (HFpEF) who had a history of reduced left ventricular ejection fraction (LVEF), but this subgroup has not been well characterized. Findings by Kalogeropoulos and colleagues published in *JAMA Cardiology* now show that patients with HF and improved or recovered ejection fraction (HFrecEF) have a different clinical course to patients with HFpEF or HF and reduced left ventricular ejection fraction (HFrefEF), and might need to be assessed independently in clinical studies.

Important structural and clinical differences are thought to exist between patients with HFpEF and HFrefEF, and these differences are likely to have implications on treatment and outcomes. A new subset of patients with HF with partially or fully recovered LVEF is thought to be clinically distinct from patients with HFpEF and HFrefEF, and reports have suggested that these patients might have improved outcomes. “One out of six outpatients with HF receiving

care at Emory Healthcare belong to this subgroup, yet data on outcomes for these patients are very limited,” explains Andreas Kalogeropoulos, lead author of the study.

In this retrospective, single-centre, cohort study, the medical records of 2,507 adult outpatients diagnosed with HF between January 2012 and April 2012 were assessed. HFrefEF was defined as LVEF  $\leq 40\%$  regardless of previous LVEF evaluations, HFpEF was defined as current and all preceding assessments of LVEF  $> 40\%$ , and HFrecEF was defined as current LVEF  $> 40\%$  but previous reports of LVEF  $\leq 40\%$ . Mortality, hospitalization rates, and composite end points were evaluated.

Among the 2,166 patients who were included in the analysis, 816 (37.7%) were classified as having preserved LVEF at inception. Of these 816 patients, 466 (57.1%) were classified as having HFpEF as they had no history of reduced LVEF, whereas 350 had previous reports of LVEF  $\leq 40\%$ , and were classified as having HFrecEF. The remaining 1,350 (62.3%) patients were diagnosed with HFrefEF. Patients with

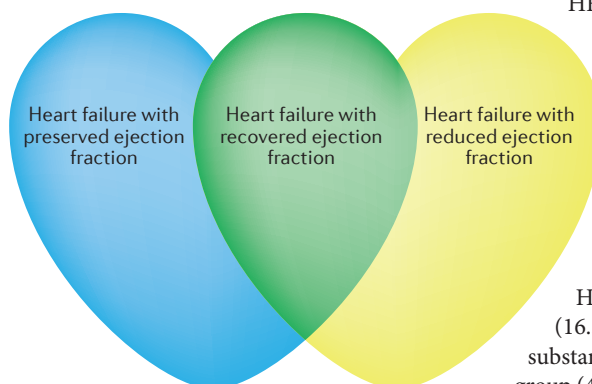
HFrecEF were younger, and less likely to have coronary heart disease and diabetes mellitus, compared with patients with HFpEF. After a median follow-up period of 3 years, age-adjusted and sex-adjusted mortality was not significantly different between the HFrefEF and HFpEF groups (16.3% vs 13.2%), but was substantially lower in the HFrecEF group (4.8%;  $P < 0.001$  vs HFrefEF

or HFpEF). Furthermore, compared with those with HFrefEF or HFpEF, patients with HFrecEF had fewer all-cause hospitalizations (adjusted rate ratio (RR) 0.71,  $P = 0.007$ ), cardiovascular hospitalizations (RR 0.50,  $P < 0.001$ ), and HF-related hospitalizations (RR 0.48,  $P = 0.002$ ).

According to Kalogeropoulos, this study is “the largest study to date showing that patients with HF presenting with low LVEF who respond well to therapy and show improvement in their LVEF have an excellent prognosis, including lower mortality and fewer hospitalizations”. The group is currently assessing the implications of these findings on therapy, including whether to down-scale the number or dose of drugs to reduce treatment burden in patients with HFrecEF.

In an accompanying editorial, Jane Wilcox and Clyde Yancy explain that these findings pave the way to better understand the capacity of the myocardium to recover, given that “reverse left ventricular remodelling is the only surrogate marker shown to be predictive of improved outcome in HFrefEF”. They conclude that “now is the time to recognize recovery as a clinical reality for patients with HFrefEF and to begin deliberate pursuit of the underlying mechanisms and future clinical considerations”.

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**ORIGINAL ARTICLE** Kalogeropoulos, A. P. et al. Characteristics and outcomes of adult outpatients with heart failure and improved or recovered ejection fraction. *JAMA Cardiol.* <http://dx.doi.org/10.1001/jamacardio.2016.1325> (2016)  
**FURTHER READING** Borlaug, B. A. The pathophysiology of heart failure with preserved ejection fraction. *Nat. Rev. Cardiol.* **11**, 507–515 (2014)