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Editorial

Prognostic Impact of LVEF Recovery in Young Adults With Acute Heart Failure

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▸ See the article "Prognostic Implications of Left-Ventricular Function Changes in Young Acute Heart Failure Patients" in volume 7 on page 162.

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Heart failure in young adults is becoming increasingly recognized as a public health crisis with profound implications for long-term cardiovascular morbidity and mortality.[1,2] Recent epidemiological data from France reveal that 4.7% of incident heart failure cases occur in patients aged 18–50 years, with an alarming upward trajectory particularly among young men whose incidence rate has increased from 0.51% to 0.59% during the years 2013–2018.[3] A most concerning mortality trend shows a staggering 906.3% increase in heart failure-related deaths among adults <45 years in recent decades, fundamentally challenging our perception of heart failure as predominantly a disease of aging.[4]

The prognosis for young patients with heart failure remains particularly concerning. Unlike their older counterparts, who may have competing mortality risks, young adults face decades of potential disease burden with substantial socioeconomic implications.[5] The absence of age-related comorbidities that may otherwise limit life expectancy makes heart failure the primary determinant of long-term survival and quality of life. Young patients often present with more aggressive disease phenotypes, including higher rates of nonischemic cardiomyopathy and inflammatory etiologies, which may be less responsive to conventional therapies.[6] The psychological burden of chronic disease diagnosis at a young age, combined with potential impacts on career development, family planning, and social functioning, creates a unique constellation of challenges that extend far beyond traditional cardiovascular endpoints.[7] Medical adherence over extended periods becomes crucial, as suboptimal therapy during the critical early recovery phase may result in irreversible myocardial remodeling and permanent functional impairment.[8,9]

In this issue of the *International Journal of Heart Failure*, Kim et al.[10] present a multicenter Korean study of 437 patients under 50 years with acute heart failure that provides essential insights into left ventricular recovery patterns in this population. This investigation represents one of the largest focused analyses of young patients with heart failure, drawing from a comprehensive registry of 5,626 patients across 10 university hospitals spanning 2011–2014. The study's rigorous methodology, including a systematic 1-year echocardiographic follow-up and comprehensive clinical outcome assessment, offers unprecedented clarity regarding the trajectory of left ventricular function recovery.

The observation that 14.6% of young patients failed to demonstrate improved left ventricular ejection fraction (LVEF) at 1 year is particularly striking when viewed alongside the marked mortality disparity. Patients with unimproved LVEF experienced a 32.8% mortality rate compared to only 9.4% among those with improved function, a more than 3-fold difference that highlights the critical importance of achieving left ventricular recovery. These mortality rates are notably higher than those typically reported in mixed-age heart failure populations, suggesting that young patients with persistent ventricular dysfunction may have a particularly high-risk phenotype that requires aggressive therapeutic intervention.

Most clinically actionable is the identification of angiotensin-converting enzyme (ACE) inhibitor use at discharge as an independent predictor of LVEF improvement, associated with a remarkable 63% reduction in risk of failure to improve ventricular function (odds ratio, 0.37; 95% confidence interval, 0.171–0.786). This finding is particularly significant given that ACE inhibitor prescription rates are suboptimal, with only 42.4% of the improved LVEF group and 21.9% of the non-improved group receiving these medications at discharge. The magnitude of this association suggests that optimization of neurohormonal blockade at the critical transition from inpatient to outpatient care may represent a most efficacious intervention to promote ventricular recovery.

A particularly noteworthy methodological strength of this study is the use of a 10% LVEF improvement threshold to define recovery based on established guidelines and research, indicating that such improvement is associated with better prognosis. This evidence-based classification system provides clinically meaningful stratification beyond arbitrary cut-off points. The investigators also employed restricted cubic spline analysis with natural cubic splines and 3 degrees of freedom to model the continuous association between ΔLVEF and mortality risk, revealing a sophisticated dose-response relationship that reaches optimal benefit around +30% to +40% LVEF improvement.

Although these findings provide valuable insights, certain important limitations warrant further consideration. The exclusion of 200 patients (31.4%) owing to missing 1-year echocardiographic follow-up data introduced a potential selection bias, particularly concerning whether those lost to follow-up experienced adverse events that precluded repeat imaging. Although baseline comparisons between included and excluded patients showed broadly comparable profiles, the potential for non-random attrition affecting study validity cannot be excluded. The heterogeneous etiologies within the unimproved LVEF group, ranging from ischemic to inflammatory causes, may have influenced outcomes independent of ventricular function trajectory, and specific heart failure etiologies were not directly adjusted for in the multivariable model. Additionally, the study period (2011–2014) predates widespread adoption of newer heart failure therapies including angiotensin receptor-neprilysin inhibitors (ARNIs) and sodium-glucose cotransporter-2 inhibitor (SGLT2i), limiting generalizability to contemporary practice patterns where these agents have demonstrated substantial benefits.

Several essential research directions emerge from these findings (**Table 1**). First, investigating the efficacy of contemporary heart failure therapies including ARNI and SGLT2i in young adults represents a high priority, given limited young adult representation in pivotal trials. Second, etiology-specific studies are needed to understand whether recovery patterns differ across ischemic, hypertrophic, restrictive, inflammatory, and idiopathic cardiomyopathy subtypes. Third, long-term follow-up studies are essential to characterize outcomes in patients facing decades of disease burden. Additionally, biomarker development and prevention strategies warrant investigation given the growing incidence in this population.

Table 1. Priority research areas for heart failure in young adults

Research priority	Specific focus areas	Rationale
Contemporary therapies	• ARNI efficacy in patients <50 years • SGLT2i outcomes in young adults • Combination therapy optimization	• Current evidence from pre-2015 era • Limited young adult representation in trials
Etiology-specific studies	• Recovery patterns by cardiomyopathy subtype • Therapeutic response differences • Genetic vs. acquired causes	• Heterogeneous outcomes may reflect underlying etiology differences
Long-term follow-up studies	• >10-year cardiovascular outcomes • Quality of life trajectories • Socioeconomic impact assessment	• Young patients face decades of disease burden with limited data
Biomarker development	• Recovery prediction markers • Treatment response indicators • Risk stratification tools	• Need for personalized treatment approaches in young adults
Prevention strategies	• Early detection methods • Lifestyle intervention efficacy • Genetic screening programs	• Growing incidence requires preventive approaches

ARNI = angiotensin receptor-neprilysin inhibitor; SGLT2i = sodium-glucose cotransporter-2 inhibitor.

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This study provides compelling evidence that young adults with heart failure represent a distinct population requiring specialized attention to LVEF recovery patterns. The dramatic 3-fold mortality difference between patients with improved and unimproved ventricular function highlights the critical importance of achieving LVEF recovery. Identifying optimal medical treatment as a modifiable predictor offers immediate opportunities to improve outcomes through evidence-based discharge protocols. As heart failure increasingly affects younger populations, understanding LVEF recovery determinants are essential to ensure that patients who may face decades of disease burden receive specialized care.

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