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Evidence of Cardiac Rehabilitation for Heart Failure With Reduced Ejection Fraction in Recovery to Maintenance Phase

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Heart failure (HF) with reduced left ventricular ejection fraction (HFrEF) is typically coupled with progressive left ventricular enlargement and detrimental cardiac remodeling. The management of HFrEF is comprehensive and primarily involves pharmacologic treatment using cardioprotective agents. Cardiac rehabilitation (CR) is also strongly recommended as a treatment for HFrEF. The evidence on CR for HFrEF is accumulating. CR improves exercise tolerance, subjective symptoms caused by HF, quality of life, and rehospitalization rates. Furthermore, CR may improve all-cause mortality, although the improvement might not be evident in the short term (<1 year) but could potentially become more apparent over a longer period. In the upcoming era of super-aging and advancements in information and communications technology, CR for HFrEF will also require updating. Further research on exercise therapy will require a comprehensive evaluation of the quality and nature of exercise and whether CR would be conducted in a home-based or remote setting; these studies should include older adults, and the findings have the potential to revolutionize the field of CR.

Key Words: Cardiac rehabilitation; Exercise; Heart failure; Heart failure with reduced ejection fraction

Heart failure (HF) is a syndrome in which dyspnea, fatigue, and edema occur as a result of cardiac dysfunction and leads to decreased exercise tolerance.[1] HF may present as HF with reduced left ventricular ejection fraction (HFrEF), characterized by a left ventricular ejection fraction of ≤40%, or HF with preserved left ventricular ejection fraction (HFpEF). Specifically, HFrEF is typically coupled with progressive left ventricular enlargement and detrimental cardiac remodeling. The management of HFrEF is comprehensive and primarily involves pharmacologic treatment using cardioprotective agents such as a β-blocker along with either an angiotensin receptor-neprilysin inhibitor, an angiotensin receptor blocker, or an angiotensin-converting enzyme inhibitor as foundational therapy. Additionally, mineralocorticoid receptor antagonists and sodium-glucose cotransporter 2 (SGLT2) inhibitors are recommended for patients who continue to experience symptoms. Ivabradine or vericiguat, soluble guanylate cyclase stimulators, can be added to the treatment of high-risk patients with HFrEF.[2] Dietary and exercise therapies are also administered.

Cardiac rehabilitation (CR) for HFrEF is a Class I recommendation in the JCS/JACR 2021 guidelines on the rehabilitation in patients with cardiovascular disease; the active introduction of CR is strongly advised and has been proven to be efficacious for treatment of HFrEF.[3] CR for HFrEF improves prognosis,[4,5] exercise capacity, and quality of life,[6] and notably, reduces the risk of all-cause rehospitalization[7] and rehospitalization for HF.[5,7] In HFrEF, reduced exercise capacity is primarily due to peripheral factors including loss of skeletal muscle mass, metabolic disturbances, reduced vasodilatation, and an amplified ergoreceptor reflex.[8] Enhancements in exercise capacity in patients undergoing CR are largely attributable to improvements in peripheral function.[9]

It has been suggested that CR has the greatest impact in the long term (>1 year) and may improve all-cause mortality, but has limited short-term efficacy (within 1 year).[7] Comprehensive CR increases long-term survival and reduces the rate of rehospitalization for HF in patients with chronic HF.[5] Moreover, CR improves left ventricular reverse remodeling, autonomic dysfunction, and vascular endothelial function in patients with HF.[10]

CR, primarily exercise therapy for HFrEF, has the potential to significantly impact life expectancy.[4] While some reports suggest that CR may not significantly alter all-cause mortality or prevent HF hospitalization,[11] CR does engender positive changes in quality of life and exercise tolerance, underscoring the potential for CR to significantly enhance the quality of life for patients with chronic HF. Consequently, the guidelines recommend CR for HFrEF at Recommendation Class I, Level of Evidence

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A, further supporting CR's potential benefits.

Recent studies have shown promising evidence for the CR of HFrEF. The peak oxygen uptake (peak $\dot{V}O_2$) is recommended as a measure of exercise tolerance improvement in CR.[3] Peak $\dot{V}O_2$ serves as the most effective discriminator between responders and non-responders in HFrEF patients following the training program.[12] CR also reported that 3 weeks of inpatient CR improved the metabolic exercise cardiorenal index (MECKI) of HFrEF and could be a prognostic indicator.[13] Aerobic exercise was effective in improving inflammatory markers of tumor necrosis factor-α, interleukin-6, and high-sensitivity C-reactive protein.[14] Different exercise training types effectively inhibit left ventricular pathological remodeling in patients with HFrEF.[15] With respect to efficacy, there is greater potential for high-intensity interval training to transform CR.

In contrast, HFrEF patients increased their number of steps by 25% but did not show a significant improvement in their 6-min walking distance.[16] Walking alone does not produce immediate results in exercise tolerance, even when the number of steps is increased. A recent Cochrane review states that there is no evidence of a difference in all-cause mortality between HF patients with exercise-based CR and those receiving usual care without exercise. However, exercise-based rehabilitation is likely to reduce the risk of all-cause and HF-related hospitalizations and may lead to important improvements in health-related quality of life.[17] Importantly, this review supports the promising future of exercise-based CR, which includes novel exercise methods such as home and digital support programs. There is a lack of evidence regarding CR for home-based or remote exercise programs, as well as for older adults and female patients with HFrEF, and further research is expected in the future.

In summary, the evidence on CR for HFrEF is accumulating. CR improves exercise tolerance, subjective symptoms caused by HF, quality of life, and rehospitalization rates. Furthermore, CR may improve all-cause mortality, although the improvement might not be evident in the short term (<1 year) but could potentially become more apparent over a longer period. In the coming era of super-aging, information and communications technology development, CR for HFrEF will also need to be updated. However, it is crucial to stress that further evidence should be gathered on how to implement exercise therapy such as high-intensity interval training, quality of walking, and home and remote CR, including older adults. The need for further research is urgent and the results could be transformative for the field of CR.

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None.

Disclosures

The authors declare no conflicts of interest.

Ethical Approval

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Data Availability

None.

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