

# Cardiac Rehabilitation in Heart Failure: Looking Further Ahead



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**Disclosure:** The authors have declared no conflicts of interest.

**Received:** 11.06.19

**Accepted:** 12.09.19

**Keywords:** Cardiac rehabilitation (CR), cardiac rehabilitation programmes, coronary heart disease, heart failure (HF).

**Citation:** EMJ Cardiol. 2019;7[1]:84-87.

## ABSTRACT

Heart failure (HF) is associated with significant morbidity and mortality. Despite major advances in the treatment of HF, there are still important unmet needs among this patient population. Cardiac rehabilitation has a central role in cardiovascular prevention and for overall disease management, and can have an important impact among HF patients. The authors present a brief overview on the current role of cardiac rehabilitation among HF patients in a contemporary setting and discuss some areas of future research in the context of this intervention.

## INTRODUCTION

Cardiac rehabilitation (CR) programmes play a pivotal role in the cardiovascular continuum, being of paramount importance in the management of several pathological processes.<sup>1-3</sup> Exercise, one of the pillars of this intervention, can have profound interactions with the cardiovascular system.<sup>2,4</sup>

Additionally, contemporary CR programmes have evolved into comprehensive frameworks designed to provide an integrative approach to the individual patient, encompassing not only exercise training, but several other interventions on a multidisciplinary setting.<sup>1,5</sup> Over the last few decades, a wealth of data have shown the beneficial effects of CR, on both outcomes, such as mortality, and different measures of functional capacity and quality of life, especially in individuals with coronary heart disease,<sup>2,3,6,7</sup> attesting to its relevance.

## MAIN BODY

Heart failure (HF) presents a major and growing challenge, having an important prevalence among several world regions and being associated with substantial morbidity, mortality, and healthcare costs.<sup>8,9</sup> Whilst there have been significant improvements in the management of this syndrome, in regards to pharmacological and device-based treatments there are still important unmet needs in this patient population.<sup>8,10</sup>

Importantly, and especially for HF with a preserved ejection fraction, this syndrome can also be associated with several changes affecting the musculoskeletal, respiratory, and peripheral vascular systems; therefore, exercise training could be particularly pertinent.<sup>2,10,11</sup> In addition, the ample scope of CR also makes this intervention attractive given the overall clustering of cardiovascular risk that can be present in these individuals.<sup>1,2,5,8</sup> As such, there has been considerable interest in the role of CR programmes among HF patients.<sup>8,12,13</sup>

In this regard, several studies have been designed to assess the potential impact of CR programmes.<sup>14-16</sup> Importantly, data on this matter should be reviewed while taking into consideration both study designs and the protean nature of this entity (as expressed by patient and programme characteristics). The HF-ACTION trial, including 2,331 patients with HF and a reduced ejection fraction, showed that an exercise training programme, although safe, was not associated with a significant reduction in all-cause mortality or hospitalisations.<sup>17</sup> However, when adjusting for highly prognostic covariates, including cardiopulmonary exercise test duration, left ventricular ejection fraction, history of atrial fibrillation/flutter, Beck Depression Inventory II score, and HF aetiology, there were significant reductions on all-cause mortality or hospitalisations.<sup>17</sup> Remarkably, and as previously discussed, these data should take possible limitations relating to the patient population studied, the design of the programme, background therapy, and the blinding status into consideration.<sup>17,18</sup> Indeed, the type of exercise training modality should be highlighted, as this can lead to discrepant results in terms of different CR programmes.<sup>19</sup> In this regard, though high-intensity interval training has shown promising results,<sup>19,20</sup> a recent multicentre study (the SMARTeX Heart Failure Study) compared the effects of a supervised programme of high-intensity interval training or moderate continuous training among patients with HF and a reduced ejection fraction, and this study did not show significant differences in terms of aerobic capacity or left ventricular remodelling.<sup>21</sup> However, before generalisation of results, it should be mentioned that the differences in training intensity between groups partly overlapped (being less than intended).<sup>21</sup> Additionally, in HF with a preserved

ejection fraction, a pilot study appeared promising for high-intensity interval training in terms of both peak oxygen consumption and diastolic function parameters.<sup>22</sup> Interestingly, and showcasing the multisystemic nature of the HF syndrome, other modalities of exercise training such as those relating to the inspiratory muscles seem of potential relevance.<sup>23</sup> Given the present data, further research appears justified in order to ascertain the optimal strategy for HF patients with a reduced, as well as preserved, ejection fraction.<sup>13,22,24</sup>

Another issue worth mentioning relates to the timing of the CR intervention.<sup>12,25</sup> A recent Cochrane review showed that in the context of HF, CR can be of importance in the reduction of hospitalisations, as well as providing improvements in quality of life.<sup>14</sup> In the present meta-analysis, the authors reported no reduction in mortality, but an improvement could be present in long-term interventions.<sup>14</sup> This notion was previously described in the seminal study by Belardinelli et al.,<sup>25</sup> in which a 10-year CR programme among HF patients (with an ejection fraction <40% at baseline) was associated with significant improvements in terms of functional capacity, left ventricular ejection fraction, and cardiac mortality. The most recent Cochrane meta-analysis also reported improvements on quality of life measures,<sup>14</sup> a finding which has also been recently reported in an article by Taylor et al.<sup>15</sup> in the context of the ExTraMATCH II collaboration. Additionally, the latter analysis, which addressed individual patient data from 13 trials, encompassing a total of 3,990 patients, also reported significant improvements in exercise capacity.<sup>15</sup> Though these results should be interpreted in light of possible biases, as elegantly discussed by the authors and featured in the comparison of the results for the effect on mortality and hospitalisations with the Cochrane review, they reinforce the prominent role of CR among HF patients.<sup>12,14,16,26,27</sup> Notably, it should be stressed that despite the present data, CR uptake remains a challenge,<sup>1,28</sup> especially among older individuals, female patients, and those with more comorbidities.<sup>28</sup> As such, strategies to improve patient participation, specifically in these subgroups, are an area of growing clinical importance.<sup>1,28</sup>

New data aiming to ascertain the role of CR programmes among less-studied groups of patients are also emerging. Although data is limited, a recent position paper by the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), described that in patients with left ventricular assist devices, CR appears a promising therapy.<sup>29,30</sup> Future research should allow further refinements on the impact of this intervention among left ventricular assist devices recipients.<sup>30,31</sup> Another rapidly expanding area of investigation concerns the possible role of exercise and CR programmes in the mitigation of cardiotoxicity associated with cancer treatments.<sup>32</sup> Again, preliminary data showed this strategy to be feasible,<sup>33-35</sup> with a recent study showing that a supervised exercise programme was able to attenuate functional decline during anthracycline chemotherapy among women with

early stage breast cancer.<sup>33</sup> Larger studies are needed to address the potential impact of this approach, namely in terms of overall mortality and morbidity, as well as the optimal timing and programme duration.<sup>35</sup>

## CONCLUSION

Given the present data and the growing complexity associated with HF, the role of CR remains of ample significance, as highlighted in the Class I recommendation for these programmes by the ESC.<sup>1</sup> As contemporary patient care evolves into an era of evermore personalised medicine, the broad scope of this time-tested intervention remains central in order to provide a holistic approach to this challenging patient population.

## References

- Piepoli MF et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*. 2016;37(29):2315-81.
- Fontes-Carvalho R et al. "The effect of exercise training in systolic and diastolic function", Watson RR et al. (eds), *Lifestyle in Heart Health and Disease* (2018), London: Academic Press, pp. 153-62.
- Rauch B et al. The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized and non-randomized studies - The Cardiac Rehabilitation Outcome Study (CROS). *Eur J Prev Cardiol*. 2016;23:1914-39.
- Vilela EM et al. High-sensitivity troponin after running - A systematic review. *Neth J Med*. 2014;72(1):5-9.
- Sandesara PB et al. Cardiac rehabilitation and risk reduction: Time to "rebrand and reinvigorate." *J Am Coll Cardiol*. 2015;65:389-95.
- Anderson L et al. Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis. *J Am Coll Cardiol*. 2016;67(1):1-12.
- Vilela EM et al. Different outcomes of a cardiac rehabilitation programme in functional parameters among myocardial infarction survivors according to ejection fraction. *Neth Heart J*. 2019;27(7-8):347-53.
- Ponikowski P et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37(27):2129-200.
- Conrad N et al. Temporal trends and patterns in heart failure incidence: A population-based study of 4 million individuals. *Lancet*. 2018;391(10120):572-80.
- Del Buono MG et al. Exercise intolerance in patients with heart failure: JACC state-of-the-art review. *J Am Coll Cardiol*. 2019;73(17):2209-25.
- Kitzman DW et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: A randomized, controlled, single-blind trial. *J Am Coll Cardiol*. 2013;62(7):584-92.
- La Rovere MT et al. Role and efficacy of cardiac rehabilitation in patients with heart failure. *Monaldi Arch Chest Dis*. 2019;89(1):69-72.
- Suchy C et al. Optimising exercise training in prevention and treatment of diastolic heart failure (OptimEx-CLIN): Rationale and design of a prospective, randomised, controlled trial. *Eur J Prev Cardiol*. 2014;21(2 Suppl):18-25.
- Long L et al. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database Syst Rev*. 2019;1:CD003331.
- Taylor RS et al. Impact of exercise rehabilitation on exercise capacity and quality-of-life in heart failure: Individual participant meta-analysis. *J Am Coll Cardiol*. 2019;73(12):1430-43.
- Taylor RS et al. Impact of exercise-based cardiac rehabilitation in patients with heart failure (EXTraMATCH II) on mortality and hospitalisation: An individual patient data meta-analysis of randomised trials. *Eur J Heart Fail*. 2018;20(12):1735-43.
- O'Connor CM et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA*. 2009;301(14):1439-50.
- Tabet JY et al. Benefits of exercise training in chronic heart failure. *Arch Cardiovasc Dis*. 2009;102(10):721-30.
- Cornelis J et al. Comparing exercise training modalities in heart failure: A systematic review and meta-analysis. *Int J Cardiol*. 2016;221:867-76.
- Wisløff U et al. High-intensity interval training to maximize cardiac benefits of exercise training? *Exerc Sport Sci Rev*. 2009;37(3):139-46.

21. Ellingsen Ø et al. High-intensity interval training in patients with heart failure with reduced ejection fraction. *Circulation*. 2017;135(9):839-49.
22. Angadi SS et al. High-intensity interval training vs. moderate-intensity continuous exercise training in heart failure with preserved ejection fraction: A pilot study. *J Appl Physiol* (1985). 2015;119(6):753-8.
23. Adamopoulos S et al. Combined aerobic/inspiratory muscle training vs. aerobic training in patients with chronic heart failure: The Vent-HeFT trial: A European prospective multicentre randomized trial. *Eur J Heart Fail*. 2014;16(5):574-82.
24. Ballesta García I et al. [High-intensity interval training dosage for heart failure and coronary artery disease cardiac rehabilitation. A systematic review and meta-analysis]. *Rev Esp Cardiol (Engl Ed)*. 2019;72(3):233-43. (In Spanish).
25. Belardinelli R et al. 10-year exercise training in chronic heart failure: A randomized controlled trial. *J Am Coll Cardiol*. 2012;60(16):1521-8.
26. Patel HC, Kaye DM. Exercise training in heart failure: A long way to go yet. *Eur J Heart Fail*. 2018;20(12):1744-5.
27. Lavie CJ et al. Bringing cardiac rehabilitation and exercise training to a higher level in heart failure. *J Am Coll Cardiol*. 2019;73(12):1444-6.
28. Golwala H et al. Temporal trends and factors associated with cardiac rehabilitation referral among patients hospitalized with heart failure: Findings from get with the guidelines - Heart Failure Registry. *J Am Coll Cardiol*. 2015;66(8):917-26.
29. Bachmann JM et al. Association of cardiac rehabilitation with decreased hospitalizations and mortality after ventricular assist device implantation. *JACC Heart Fail*. 2018;6(2):130-9.
30. Adamopoulos S et al. Exercise training in patients with ventricular assist devices: A review of the evidence and practical advice. A position paper from the Committee on Exercise Physiology and Training and the Committee of Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2019;21(1):3-13.
31. Bobenko A et al. Exercise training in patients with a left ventricular assist device (Ex-VAD): Rationale and design of a multicentre, prospective, assessor-blinded, randomized, controlled trial. *Eur J Heart Fail*. 2019;21(9):1152-9.
32. Scott JM et al. Exercise therapy and cardiovascular toxicity in cancer. *Circulation*. 2018;137(11):1176-91.
33. Howden EJ et al. Exercise as a diagnostic and therapeutic tool for the prevention of cardiovascular dysfunction in breast cancer patients. *Eur J Prev Cardiol*. 2019;26(3):305-15.
34. Kirkham AA et al. The effect of an aerobic exercise bout 24 h prior to each doxorubicin treatment for breast cancer on markers of cardiotoxicity and treatment symptoms: A RCT. *Breast Cancer Res Treat*. 2018;167(3):719-29.
35. Squires RW et al. Exercise training and cardiovascular health in cancer patients. *Curr Oncol Rep*. 2018;20(3):27.

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