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Editorial: Cochrane Heart Corner

Exercise-based cardiac rehabilitation: an underused approach for management of heart failure patients☆

Rehabilitación cardiaca basada en el ejercicio: una herramienta infrautilizada en el abordaje de los pacientes con insuficiencia cardiaca

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Heart failure (HF) is a global healthcare challenge and, despite advances in therapy, is still characterised by adverse prognosis, with significant residual mortality and high hospitalisation rates.[1,2] The hallmark clinical feature of patients with HF is exercise intolerance, which limits patients' activities of daily living and is an important determinant of health-related quality of life (HRQoL) and the poor prognosis.[3,4] The pathophysiological mechanisms of exercise intolerance in HF are multifactorial, including impairments in cardiac reserve, pulmonary reserve, peripheral skeletal muscle and/or respiratory skeletal muscle, all of which can variably and meaningfully contribute to the HF syndrome.[5] Along this line, exercise training has revealed favourable effects on modification of central haemodynamic function, sympathetic tone, endothelial function, skeletal muscle function, and ventilatory efficiency in patients with HF.[5]

Previous studies have shown that exercise training in HF is safe[6] and should be a therapeutic target in HF patients[7] because of conferring beneficial effects mainly in terms of exercise capacity and HRQoL. Thus, the last European Society of Cardiology 2016 guideline on HF[8] recommends regular aerobic exercise in all patients with HF to improve functional capacity and symptoms (class I). Furthermore, evidence provided by previous Cochrane review of exercise training in 2014[9] showed that exercise training in HF with reduced ejection fraction (HFrEF) was associated with reduction in hospitalisations.

☆ This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2019, Issue 1, doi:10.1002/14651858.CD003331.pub5 (see https://www.cochranelibrary.com/ for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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Not surprisingly, current guidelines recommend regular aerobic exercise in stable patients with HFrEF to reduce the risk of HF hospitalisation as a recommendation class I. However, there remains an unmet need for evidence of survival and hospitalisation endpoints from different subgroups of HF patients such as women, older patients, patients with comorbidities and, particularly, HF with preserved ejection fraction (HFpEF).

In a recent Cochrane review of exercise training in HF (2019), Long et at.[10] evaluated the effects of exercise-based cardiac rehabilitation (CR) on mortality, hospital admission, and HRQoL of patients with HF. For this purpose, the authors included 44 trials with 5783 participants with HF (predominantly HFrEF), with a median of 6 months follow-up that compared different modalities of exercise-based CR interventions versus a no exercise control that included usual medical care. In this latest Cochrane review of exercise training in HF, Long et al. added to the previous 11 new trials with 1040 more participants with HF. After a thorough analysis evaluating the different outcomes at 2 time points (≤12 months or >12 months follow-up), Long et al. showed several key findings. First, exercise-based CR made no difference in all-cause mortality over the short term (≤12 months of follow-up): 27 trials, 28 comparisons (2596 participants): intervention 67/1302 (5.1%) vs control 75/1294 (5.8%); risk ratio (RR), 0.89; 95% confidence interval (95%CI), 0.66–1.21; $P = .47$; low-quality GRADE evidence. Exercise-based CR made no difference either over the long term (>12 months of follow-up): 6 trials/comparisons (2845 participants): intervention 244/1418 (17.2%) vs control 280/1427 (19.6%) events: RR, 0.88; 95%CI, 0.75–1.02; $P = .09$; high quality evidence. Second, CR probably reduces overall hospital admissions in the short term (≤12 months of follow-up): 21 trials, 21 comparisons (2182 participants): (intervention 180/1093 (16.5%) vs control 258/1089 (23.7%); RR, 0.70; 95%CI, 0.60–.83; $P < .001$; moderate-quality evidence, number needed to treat = 14], and may reduce HF-specific hospitalisation: 14 trials, 15 comparisons (1114 participants): intervention 40/562 (7.1%) vs control 61/552 (11.1%); RR, 0.59; 95%CI, 0.42–0.84; $P < .001$; low-quality evidence; number needed to treat = 25. Third, regardless of the HRQoL measure used, there may be clinically important improvement with exercise: 26 trials, 29 comparisons (3833 participants); standardised mean difference: −0.60; 95%CI, −0.82 to −0.39; $I^2 = 87\%$; chi-square = 215.03; $P < .001$; low-quality evidence.

The findings of this study are broadly consistent with those of the previous (2014) version of this Cochrane Review.[9] Conversely, these findings contrast with the lack of effect in all-cause or HF hospitalisations observed in the ExTraMATCH II meta-analysis of exercise training in HF (2018).[11] Compared to the previous Cochrane review,[9] the novelty in this study is the increasing number of trials using alternative modes of CR such as home- and technology-based programmes. Unfortunately, in this review[10] that additionally included 2 new trials (thus a total of 6 trials were included, $N = 639$), there was an unknown proportion of patients with HFpEF, and only 21% of the population included were women (13% in the previous 2014 Cochrane review). Regarding the mean age of the patients included in this latest review, only 13 studies ($N = 853$) reported a median age ≥65 years and only 5 studies ($N = 346$) reported a median age ≥70 years.

Overall, the results of the present review show that exercise-based CR improves HRQoL and reduces risk of hospitalisation, and these benefits appear to be consistent across different CR settings. Consequently, the findings support the recommendations provided in current clinical guidelines[8] regarding the referral of all HF patients to an exercise-based CR programme, particularly in HFrEF patients. However, despite this recommendation, less than 20% of HF patients are referred to CR programmes in Europe,[12] and less than 7% in Spain (according to R-EUReCa registry[13]).

In light of these data, exercise-based CR should be part of optimal HF management programmes, particularly in the case of HFrEF patients, in which exercise training has shown beneficial effects on prognosis and symptoms. Therefore, those results could not be extrapolated to women, older patients, and patients with HFpEF in which there is a stark need of further representation in randomised clinical trials of CR. Additionally, further robust randomised trials are needed to assess the clinical effectiveness of alternative models of exercise-based CR in patients who are unable to follow or are not compliant with centre-based CR programmes. Finally, we would like to underline that further policies to improve physician and patient awareness with regard to the benefit of exercise-based CR should be strengthened to increase CR referral among patients with HF.

Conflicts of interest

The authors declare no conflicts of interest related to this work.

REFERENCES

1. Tsao CW, Lyass A, Enserro D, et al. Temporal trends in the incidence of and mortality associated with heart failure with preserved and reduced ejection fraction. *JACC Heart Fail*. 2018;6:678–685.
2. Santas E, Valero E, Mollar A, et al. Burden of recurrent hospitalizations following an admission for acute heart failure: preserved versus reduced ejection fraction. *Rev Esp Cardiol*. 2017;70:239–246.
3. Kitzman DW, Little WC, Brubaker PH, et al. Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure. *JAMA*. 2002;288:2144–2150.
4. Palau P, Domínguez E, Núñez E, et al. Peak exercise oxygen uptake predicts recurrent admissions in heart failure with preserved ejection fraction. *Rev Esp Cardiol*. 2018;71:250–256.
5. Piña IL, Apstein CS, Balady GJ, et al. Exercise and heart failure: a statement from the American Heart Association Committee on exercise, rehabilitation, and prevention. *Circulation*. 2003;107:1210–1225.
6. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA*. 2009;301:1439–1450.
7. Fleg JL, Cooper LS, Borlaug BA, et al. Exercise training as therapy for heart failure: current status and future directions. *Circ Heart Fail*. 2015;8:209–220.
8. Ponikowski P, Voors AA, Anker SD, 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 J Heart Fail*. 2016;18:891–975.
9. Taylor RS, Sagar VA, Davies EJ, et al. Exercise-based rehabilitation for heart failure. *Cochrane Database Syst Rev*. 2014;2014:CD003331.
10. Long L, Mordi IR, Bridges C, et al. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database Syst Rev*. 2019;1:CD003331.
11. Taylor RS, Walker S, Smart NA, 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;20:1735–1743.
12. Bjarnason-Wehrens B, McGee H, Zwisler AD, et al. Cardiac rehabilitation in Europe: results from the European Cardiac Rehabilitation Inventory Survey. *Eur J Cardiovasc Prev Rehabil*. 2010;17:410–418.
13. Sociedad Española de Cardiología. Registro Español de Unidades de Rehabilitación Cardiaca. R-EUReCa. [Consultado 22 May 2020]. Disponible en: https://secardiologia.es/riesgo/cientifico/6415-registro-nacional-de-unidades-de%20rehabilitacion-cardiaca-r-eureka.