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Cardiac rehabilitation and all-causemortality in patients with heart failure: a retrospective cohort study

Cardiac rehabilitation and all-cause mortality in patients with heart failure: A retrospective cohort study

Benjamin J.R. Buckley, PhD[1*], Stephanie L. Harrison, PhD[1], Elnara Fazio-Eynullayeva, MA[2], Paula Underhill[3], Rajiv Sankaranarayanan, PhD[4], David J. Wright, MD[1], Dick H.J. Thijssen, PhD[5,6], Gregory Y.H. Lip, MD[1,7]

[1]Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom

[2]TriNetX LLC., Cambridge, MA, United States

[3]TriNetX LLC., London, United Kingdom

[4] Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool University Hospitals NHS Foundation Trust

[5]Liverpool Centre for Cardiovascular Science, Liverpool John Moores University, Liverpool, UK

[6]Research Institute for Health Science, Department of Physiology, Radboud university medical centerum, Nijmegen, The Netherlands

[7]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

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***Corresponding author**

Dr Benjamin Buckley, Liverpool Centre for Cardiovascular Science, University of Liverpool, William Henry Duncan Building, Liverpool, L7 8TX United Kingdom

Email: Benjamin.Buckley@liverpool.ac.uk.

Phone: +44 (0)151 794 2000

Abstract

Background

Despite the benefits of exercise training in the secondary prevention of cardiovascular disease, there are conflicting findings for the impact of exercise-based cardiac rehabilitation (CR) on mortality for patients with heart failure (HF).

Methods

A retrospective cohort study was conducted which utilised a global federated health research network, primarily in the United States. Patients with a diagnosis of HF were compared between those with and without an electronic medical record of CR and/or exercise programmes within 6-months of a HF diagnosis. Patients with HF undergoing exercise-based CR were propensity score matched to HF patients without exercise-based CR by age, sex, race, co-morbidities, medications, and procedures (controls). We ascertained 2-year incidence of all-cause mortality, hospitalisation, stroke, and atrial fibrillation.

Results

Following propensity score matching, a total of 40,364 patients with HF were identified. Exercise-based CR was associated with 42% lower odds of all-cause mortality (odds ratio 0.58, 95% confidence interval (CI): 0.54-0.62), 26% lower odds of hospitalisation (0.74, 95% CI 0.71-0.77), 37% lower odds of incident stroke (0.63, 95% CI 0.51-0.79), and 53% lower odds of incident atrial fibrillation (0.47, 95% CI 0.4-0.55) compared to controls, after propensity score matching. The beneficial association of CR and exercise on all-cause mortality was consistent across all subgroups, including patients with HFrEF (0.52, 95% CI 0.48-0.56) and HFpEF (0.65, 95% CI 0.60-0.71).

Conclusions

Exercise-based CR was associated with lower odds of all-cause mortality, hospitalisations, incident stroke and incident atrial fibrillation at 2-years follow-up for patients with HF (including patients with HFrEF and HFpEF).

Keywords: Cardiac rehabilitation; Heart failure; Exercise; Secondary prevention; Retrospective cohort.

Introduction

Chronic heart failure (HF) is a growing global health challenge with increasing prevalence, and an economic burden in excess of USD 100 billion per annum, which will continue to rise with an ageing, expanding, and industrialising population.(1) Unplanned hospital admissions seem to be a key driver of the economic cost of HF on healthcare systems(1) and therefore present a primary target for preventative strategies.

At the individual level, patients with HF often suffer with fatigue, dyspnoea, and exercise intolerance(2), with at least one in five patients suffering with depression.(3) Furthermore, 5-year survival after a diagnosis of HF (typically with optimal pharmaceutical treatment) is only 27%, demonstrating only modest improvements in the 21st century compared to other serious conditions, such as cancer.(4) Thus, treatment pathways that alleviate mortality and morbidity as well as hospitalisations for patients with HF are critical to improving patient quality of life and minimising the economic burden on healthcare systems.

Exercise-based cardiac rehabilitation (CR) promotes secondary prevention of cardiovascular disease and adverse events and are an essential component of routine care for patients with acute coronary syndrome and those undergoing revascularisation (e.g. coronary artery bypass graft or percutaneous coronary intervention).(5, 6) In patients with coronary heart disease, exercise-based CR has been shown to improve exercise capacity, health-related quality of life, reduce hospitalisations, and depending on the source of evidence, reduce all-cause or cardiovascular-related mortality.(7-10) However, conflicting results have been reported related to the effects of CR in patients with HF.

The most recent (2019) Cochrane review in this topic (27 studies; 2,596 participants)(11) concluded that exercise-based CR 'probably' reduced the risk of hospital admissions and may confer clinically important improvements in health-related quality of life. However, the impact of CR on all-cause mortality for patients with HF was 'negligible'. Such mortality conclusions were limited due to many included trials having a small sample size, a small number of mortality events, and typically short follow-up periods (<12-months). Analysing six studies from this Cochrane review with >12-months follow-up, however, suggested a reduction in all-cause mortality (relative risk 0.88). In addition to primary data limitations to evaluate the effect of CR on mortality in patients with HF, it has been reported that patients who are female, older, and present with HF with preserved ejection fraction (HFpEF) are under-represented in the literature.(12) This raises various questions related to whether

HF patients benefit from CR in terms of risk for mortality, and whether these benefits can be generalised across HF subtypes.

Benefitting from access to a large online database, we explored the hypothesis that exercise-based CR has protective effects in patients diagnosed with HF to reduce risks for important clinical outcomes. The aim of the present study, using a global federated health research network, was therefore to compare 2-year all-cause mortality, hospitalisations, stroke, and atrial fibrillation (AF) in patients with HF and an electronic medical record (EMR) of exercise-based CR to propensity score matched patients with HF and no EMR of exercise-based CR. In addition, we also sought to stratify results for important patient subgroups, including patients with HFpEF.

Methods

Study Design and Participants

A retrospective observational study was conducted with data provided by TriNetX, a global federated health research network with access to EMRs from participating healthcare organisations including academic medical centres, specialty physician practices, and community hospitals, predominantly in the United States. HF was identified from International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM, ICD-10-CM) codes in patient EMRs: 428.xx (Heart Failure) and I50.xx (Heart failure). Cardiac rehabilitation was identified from ICD-10-CM codes Z71.82 (Exercise counselling), HCPCS codes S9451 (Exercise classes, non-physician provider, per session) and S9472 (CR program, non-physician provider, per diem), or Current Procedural Terminology (CPT) codes 93797 (Physician or other qualified healthcare professional services for outpatient CR) and 1013171 (Physician or other qualified health care professional services for outpatient CR). Correspondingly, these exercise-based CR codes were excluded in the controls. This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.(13) As a federated network, research studies using the TriNetX research network do not require ethical approvals as no patient identifiable identification is received.

Data Collection

The TriNetX network was searched on 28th October 2020 and an anonymised dataset of patients with HF was acquired. The exercise-based CR cohort were aged ≥18 years with exercise-based CR recorded in EMRs within 6-months of a HF diagnosis. Controls were aged ≥18 years with a diagnosis of HF and no history of CR or exercise programmes in EMRs. For both the exercise-based CR cohort and controls, patients with HF were identified in EMRs from at least 2-years prior to the search date to ensure a minimum follow-up of 2-years from HF diagnosis (18-months from CR). At the time of the search, 40 participating healthcare organisations had data available for patients who met the study inclusion criteria.

Statistical Analysis

All statistical analyses were completed on the TriNetX online platform. Baseline characteristics were compared using chi-squared tests for categorical variables and independent-sample t-tests for continuous variables. Current exercise-based CR provision is typically reserved for cardiovascular patients following an acute coronary syndrome, heart failure, or those undergoing a revascularisation procedure (coronary artery bypass graft or planned percutaneous coronary intervention). Thus, propensity score matching (PSM) was used to control for these differences in the two cohorts. CR patients and controls were 1:1 PSM using logistic regression for age at HF diagnosis, sex, race, hypertensive diseases, ischaemic heart diseases, cerebrovascular diseases, diabetes mellitus, chronic kidney disease, cardiovascular procedures (e.g. cardiography, echocardiography, cardiac catheterisation, cardiac devices, electrophysiological procedures), and cardiovascular medications (e.g. beta-blockers, antiarrhythmics, diuretics, antilipemic agents, antianginals, calcium channel blockers, ACE inhibitors). These variables were chosen because they are established risk factors for HF and/or mortality or were significantly different between the two cohorts. The TriNetX platform uses 'greedy nearest-neighbour matching' with a caliper of 0.1 pooled standard deviations. Following PSM, logistic regressions produced odds ratios with 95% confidence intervals (CIs) for 2-year incidence of all-cause mortality, hospitalisation, and stroke, comparing exercise-based CR with controls. Additional sub-analyses (following PSM) were conducted to produce odds ratios with 95% CIs to stratify results by population subgroups including sex, body mass index (BMI), history of cardiovascular events, and HF subtype (HFpEF and HFrEF) on the odds of all-cause mortality between the exercise-based CR cohort and controls. Statistical significance was set at $P<0.05$.

Results

Patient characteristics

In total, 1,225,318 patients from 40 healthcare organisations had a diagnosis of HF at least 2-years before the search date with no history of CR and exercise programmes (controls) and 20,182 patients had a diagnosis of HF at least 2-years ago with an EMR of CR and/or exercise programmes within 6-months of diagnosis (CR and exercise cohort). The exercise-based CR cohort was distributed between the four large Census Bureau designated regions of the United States as follows: 4% (*n*=721) in the Northeast, 14% (*n*=2,973) in the Midwest, 45% (*n*=9,283) in the South, 29% (*n*=6,014) in the West, and 8% (*n*=1,558) were unknown. The control cohort was also distributed between the four large Census

Bureau designated regions of the United States as follows: 12% (*n*=146,045) in the Northeast, 12% (*n*=142,857) in the Midwest, 46% (*n*=564,687) in the South, 7% (*n*=88,075) in the West, 2% (*n*=19,394) non United States, and 22% (*n*=264,260) were unknown.

Compared to controls, the exercise-based CR cohort was younger, had a lower proportion of females, had a higher proportion of people identified as White and Asian, and had a higher proportion of patients with health conditions, history of cardiovascular procedures and medications. These variables were included in subsequent PSM analyses (Table 1). Table 1 also shows the characteristics of the exercise-based CR cohort and controls after 1:1 PSM. Following 1:1 PSM, there were 20,182 patients in each cohort, which were well balanced on age, sex, health conditions, and cardiovascular procedures (P>0.05). Although statistically different, patients in each cohort were well balanced following PSM for White or unknown race, hypertension, and cardiovascular medications (P<0.05).

Clinical outcomes

Before PSM and excluding patients with the outcome outside the measurement window, 2-year all-cause mortality was 9.3% (*n*=1,872 of 20,038 participants) in the exercise-based CR cohort, and 13.4% (*n*=144,521 of 1,082,155 participants) in controls (P<0.0001). Logistic regression models showed 33% lower odds of all-cause mortality (odds ratio 0.67, 95% CI: 0.64-0.70) in the exercise-based CR cohort compared to controls.

Following PSM and excluding patients with the outcome outside the measurement window, 2-year all-cause mortality was 9.2% (*n*=1,875 of 20,111 participants) in the exercise-based CR cohort and 15.1% (*n*=3,025 of 20,036 participants) in the matched controls (P<0.0001). Logistic regression models showed 42% lower odds of all-cause mortality (odds ratio 0.58, 95% CI: 0.54-0.62) in the exercise-based CR cohort compared to controls. Following PSM, exercise-based CR was also associated with 26% fewer hospitalisations (odds ratio 0.74, 95% CI 0.71-0.77), 37% lower odds of incident stroke (0.63, 95% CI 0.51-0.79), and 53% lower odds of incident AF (odds ratio 0.47, 95% CI 0.4-0.55).

Subgroup analyses

Following PSM, subgroup logistic regression analyses demonstrated that exercise-based CR was associated with lower odds for all-cause mortality compared to propensity matched controls for all included subgroups (female, male; age ≥75 years, age <75 years; BMI ≥30, BMI <30; history of stroke, no history of stroke; history of acute myocardial infarction (AMI), no history of AMI; history of AF, no history of AF; hypertensive, no history of hypertension; and HFpEF (HF with preserved ejection fraction), HFrEF (HF with reduced ejection fraction); all *P*<0.0001) (Figure 1).

Discussion

Collectively, this retrospective analysis represents the largest follow-up data set of its kind for patients with HF, strongly supporting the clinical value of CR and exercise following a HF diagnosis. We present two principal findings. Firstly, in 40,364 patients with HF, exercise-based CR was associated with 42% lower odds of all-cause mortality, 26% lower odds of hospitalisation, 37% lower odds of stroke, and 53% lower odds of incident AF compared to propensity matched controls. These findings were independent of sex, age, race, included comorbidities, and HF subtype. Secondly, this is the first study to demonstrate that exercise-based CR is associated with lower odds of mortality (35%) in patients with HFpEF compared to patients with HFpEF without exercise-based CR.

Not confined to HF patients, exercise-based CR is generally recommended (with the highest level of scientific evidence - class I) by the European Society of Cardiology (ESC),(14) the American Heart Association (AHA) and the American College of Cardiology (ACC).(15) These global recommendations are supported by studies that find CR-related improvements in exercise capacity, health-related quality of life, and reductions in hospital admissions.(7-9) Findings related to all-cause mortality, however, are less clear. In contrast to earlier Cochrane meta-analyses,(7, 8) the most recent Cochrane systematic review and meta-analysis of 63 studies (14,846 participants)(9) did not observe a statistically significant reduction in all-cause mortality following exercise-based CR in coronary heart disease patients compared to no-exercise controls. In agreement with this observation, the most recent Cochrane review of randomised controlled trials, which compared CR to no exercise for patients with HF (27 studies; 2,596 participants) concluded that CR appears to have no impact on mortality in the short term (<12-months follow-up).(11) Such conclusions were likely limited due to a small number of events (<300) and a short follow-up time period, in addition to an overall low-quality of evidence. Indeed, our study included >20,000 individuals with HF undergoing CR and a follow-up of 2 years, which represents the largest of its kind. Our finding of lower mortality in HF patients undergoing CR supports some previous high-quality studies (when aggregated) that evaluated the effect of CR on mortality using trials with >12-months follow-up.(11) To further support this, another systematic review found no short-term effects on mortality (<6-months).(16) The authors estimated an additional ~10,000 participants would be needed to be statistically powered to evaluate the effect of CR on mortality for patients with HF. It is also possible that the included randomised controlled trials recruited relatively healthy patients (i.e. typically middle-aged males with no comorbidities),(11) which may attenuate the perceived effectiveness of CR in this population.(17)

Some individual trials have found a positive effect of CR on mortality in HF patients. For example, in a multi-centre randomised controlled trial of >2,300 patients with HFrEF, O'Connor et al(18) demonstrated a significant 11% reduction in all-cause mortality or hospitalisation readmission at 2.5-year follow-up with CR compared to controls, after adjustment for baseline characteristics. Similarly, Mudge et al(19) found a significantly lower all-cause mortality with exercise-based CR (3 events of 140 participants) compared to no exercise control (10 events of 138 participants), although with a small number of events, caution is warranted when interpreting such findings. When the results of Mudge et al. were stratified by patients with HFrEF and HFpEF, death and readmission rates were higher in patients with HFpEF compared to patients with HFrEF (OR: 1.99; 95% CI: 1.02 to 3.88; P=0.04). However, there was no statistically significant effect of the intervention for patients with HFpEF.(19) This highlights the need for ongoing research efforts to improve outcomes in this challenging population.

Patients with HFpEF are an especially important cardiovascular subpopulation to focus on, particularly because there is a scarcity of effective treatment options.(20) Our results are the first to suggest exercise-based CR is associated with lower odds of all-cause mortality in patients with HFpEF.(21) These encouraging findings in 18,485 patients with HFpEF are strongly supportive of the need for future investigation, including randomised controlled trials powered to investigate mortality and hospitalisations, such as the EX-DHF Trial.(22)

Although some evidence favours exercise-based CR following an acute stroke,(23) the association of CR with incident stroke in patients with HF has not been previously investigated. In the present study, exercise-based CR was associated with significantly lower odds of incident stroke (37%) compared to propensity matched controls. As the effect of exercise-based CR on incident stroke in cardiovascular populations is largely unknown, future prospective research is needed. We also found significantly lower odds of incident AF in patients with HF following exercise-based CR compared to propensity matched controls. This is aligned with our previous work that demonstrated CR was associated with lower odds of mortality and lower odds of disease progression in patients with AF (*studies under review*).

Hospitalisation is an important outcome when considering both patient and healthcare burden, especially for HF patients who demonstrate high rehospitalisation rates. The present study shows that exercise-based CR was associated with 26% lower odds of hospitalisation compared to propensity matched controls. This is largely aligned with previous research findings.(11, 16, 18, 24, 25) Despite recent reductions for in-hospital and 30-day mortality for patients with HF, rehospitalisation rates seem to have increased.(26) Given the heterogeneity of readmission triggers for patients with HF, a better focus on preventive strategies to reduce hospitalisation is needed.(27) In this regard, exercise-based CR presents a promising secondary prevention strategy for reduced mortality, hospitalisation, and secondary cardiovascular events in patients with HF.

Alarmingly, given that of 1,245,500 patients with HF, only 1.6% (n=20,182) were referred to an exercise-based CR programme within 6-months of diagnosis, there is urgent need for improved awareness and referral. Indeed, based on the present study's findings, significant improvements in mortality, hospitalisation, and cardiovascular comorbidity may be realised in patients with HF who undergo an exercise-based CR programme. Improved uptake of such programmes could therefore have substantial impact on patient health and healthcare burden.

The benefit of CR for patients with HF may be explained through improvements in cardiorespiratory fitness. As such, it has been proposed that cardiorespiratory fitness may be a suitable surrogate end point for the treatment effect of CR on mortality in patients with HF.(28, 29) Indeed, an improvement of 5% in predicted cardiorespiratory fitness was associated with a corresponding 10% reduction in risk of cardiac hospitalisation or all-cause mortality during 2.5-years of follow-up.(17) The mechanisms behind the improvement in cardiorespiratory fitness are likely to be a combined improvement in central cardiac output, peripheral oxygen extraction, skeletal muscle function,(30, 31) and vascular function/structure.(32) More specifically in patients with HFpEF, exercise training has been shown to improve exercise capacity and quality of life, associated with atrial reverse remodelling and improved left ventricular diastolic function.(33)

Limitations

Given the problematic limitations of existing (and likely subsequent) randomised controlled trials to evaluate the effectiveness of CR on all-cause mortality in patients with HF, alternative research methods such as applied in the present study are warranted. Such real-world data can supplement our understanding of the impact of CR on important clinical endpoints (e.g. all-cause mortality) in cardiovascular subpopulations such as HFpEF, by including comparatively larger cohorts, higher event rates, and samples that are more likely representative of the population. Nevertheless, a number of limitations are noteworthy. First, the data were collected from health care organization EMR databases and some co-morbidities may be underreported, and race was not available for all participants. Indeed, recording of ICD codes in administrative datasets may vary by factors such as age, number of comorbidities, severity of illness, length of hospitalisation, and whether in-hospital death occurred.(34) In particular, an EMR of CR and exercise does not necessarily provide information as to whether a participant attended, the intervention type and dose, or intervention adherence – this is an important limitation to this type of data. Nor do we have patient physical activity levels following the intervention, which would be an interesting outcome. We could also not determine the influence of attending different healthcare organizations due to data privacy restrictions. In addition, outcomes which occurred outside of the TriNetX network are not well captured. Second, the data were largely from multiple healthcare organizations in the United States but may not be representative of the wider population and the generalisability of the results beyond this cohort is therefore unclear. Third, other HF subsets such as patients with acute decompensated HF, left ventricular assist devices (LVAD), or those with transplants were not adequately represented. Fourth, HF aetiology information was not available for this dataset and future research should investigate how different aetiologies may influence outcomes. Finally, residual confounding may have impacted our results, including lifestyle factors and socioeconomic status, and quality of care, which were not available from EMRs.

Conclusion

Using a global federated health research network, we found that participation in exercise-based CR in 40,364 patients with HF were associated with lower odds of all-cause mortality, hospitalisation, incident stroke, and incident AF at 2-years follow-up. Importantly, the survival benefit associated with exercise-based CR was observed in all patient subgroups, including patients with HFrEF and HFpEF, which has not been previously demonstrated. Given that the majority of patients with HF do not have access to CR programmes, findings of the present study provide the largest supporting evidence to date that exercise-based CR should be made available to patients with HF.

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BJRB contributed to the conception or design of the work. BJRB contributed to the acquisition, analysis, and interpretation of data for the work. BJRB drafted the manuscript. SLH, EFE, PU, RS, DJW, DHJT, and GYHL critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Table 1. Baseline characteristics %(*n*)* of the HF populations with and without exercise-based CR, before and after propensity score matching.

	Initial populations			Propensity score matched populations		
	HF without CR (n=1,225,318)	HF with CR (n=20,549)	*P*-value	HF without CR (n=20,182)	HF with CR (n=20,182)	*P*-value
Age (years) at diagnoses; mean (SD)	67.6 (16.1)	64.5 (13.9)	<0.001	64.7 (14.1)	64.4 (13.5)	0.382
Female	48.9 (587,100)	36.8 (7,428)	<0.001	36.7 (7,412)	36.8 (7,427)	0.877
Race[a]						
White	69.5 (834,697)	73.5 (14,842)	<0.001	75.8 (15,302)	73.5 (14,841)	<0.001
Black or African American	17 (204,097)	16.9 (3,404)	0.624	16.2 (3,274)	16.9 (3,404)	0.082
Asian	1.6 (19,200)	2.1 (418)	<0.001	1.9 (382)	2.1 (416)	0.224
Unknown	11.6 (138,724)	6.6 (1,337)	<0.001	5.5 (1,101)	6.6 (1,337)	<0.001
Hypertensive diseases	31.3 (375,380)	77.4 (15,320)	<0.001	78.4 (15,811)	77.4 (15,622)	0.023
Ischaemic heart diseases	16.1 (193,531)	75.6 (15,320)	<0.001	75.4 (15,216)	75.9 (15,314)	0.256
Cerebrovascular diseases	5.7 (68,249)	19.2 (3,871)	<0.001	18.9 (3,814)	19.2 (3,870)	0.478
Diabetes Mellitus	16.1 (193,039)	41.6 (8,403)	<0.001	41.7 (8,416)	41.6 (8,399)	0.864
Chronic Kidney Disease	8.8 (105,797)	28.6 (5,781)	<0.001	29.1 (5,866)	28.6 (5,776)	0.323
Cardiovascular Procedures[b]	27.1 (325, 026)	86.4 (17,446)	<0.001	85.8 (17,322)	86.4 (17,440)	0.089
Cardiovascular Medications[c]	29.5 (353,958)	83.7 (16,905)	<0.001	84.8 (17,121)	83.7 (16,899)	0.002

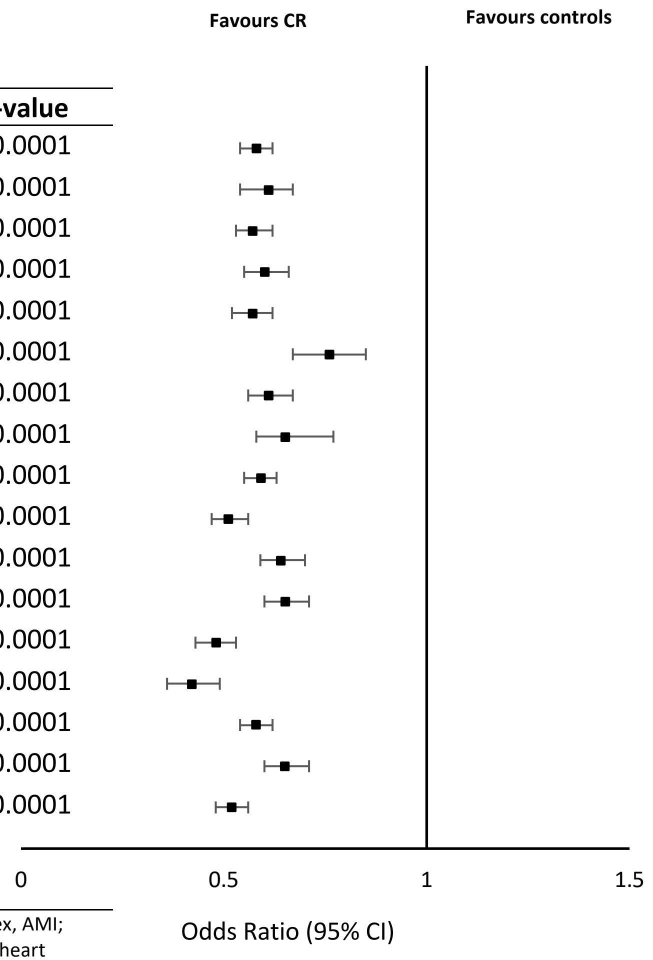
*Values are % (n) unless otherwise stated. Baseline characteristics were compared using a chi-squared test for categorical variables and an independent-sample t-test for continuous variables. [a]Data are taken from structured fields in the electronic medical record systems of the participating healthcare organizations, therefore, there may be regional or country-specific differences in how race categories are defined. [b]Cardiovascular procedures include cardiography, echocardiography, catheterization, cardiac devices, electrophysiological procedures.
[c]Cardiovascular medications include beta-blockers, antiarrhythmics, diuretics, lipid lowering agents, antianginals, calcium channel blockers, ACE inhibitors. HF; heart failure, CR; cardiac rehabilitation, SD; standard deviation.

Table 2. Major adverse events at 2-year follow-up from HF diagnosis; comparing HF patients who received exercise-based CR (*n*=20,182) to propensity matched HF patients who received usual care only (*n*=20,182).

Major adverse events	% of events	Odds Ratio	95% CI	*P*-value
All-cause mortality	9.3 vs 15.2	0.58	0.54-0.62	<0.0001
Hospitalisation	40.4 vs 47.8	0.74	0.71-0.77	<0.0001
Incident stroke*	0.7 vs 1.2	0.63	0.51-0.79	<0.0001
Incident AF[#]	2.2 vs 4.5	0.47	0.4-0.55	<0.0001

HF; heart failure, 95% CI; 95% confidence interval, CR; cardiac rehabilitation, AF; atrial fibrillation.
*Subsample of patients with no history of stroke before HF diagnosis (*n*=34,756).
[#]Subsample of patients with no history of AF before HF diagnosis (*n*=21,006).

Subgroup	Participants (n)	Odds Ratio	95% CI	*P*-value
Total cohort	40,364	0.58	0.54-0.62	<0.0001
Female	14,772	0.61	0.54-0.67	<0.0001
Male	25,391	0.57	0.53-0.62	<0.0001
Aged ≥75 years	15,419	0.6	0.55-0.66	<0.0001
Aged <75 years	25,174	0.57	0.52-0.62	<0.0001
BMI ≥30	12,370	0.76	0.67-0.85	<0.0001
BMI <30	13,498	0.61	0.56-0.67	<0.0001
History of stroke	6,040	0.65	0.58-0.77	<0.0001
No history of stroke	34,328	0.59	0.55-0.63	<0.0001
History of AMI	18,440	0.51	0.47-0.56	<0.0001
No history of AMI	21,922	0.64	0.59-0.7	<0.0001
History of AF	19,444	0.65	0.6-0.71	<0.0001
No history of AF	20,138	0.48	0.43-0.53	<0.0001
SBP ≥140 mmHg	7,404	0.42	0.36-0.49	<0.0001
SBP <140 mmHg	26,216	0.58	0.54-0.62	<0.0001
HFpEF	18,485	0.65	0.6-0.71	<0.0001
HFrEF	20,140	0.52	0.48-0.56	<0.0001



CR; cardiac rehabilitation, HF; heart failure, AF; atrial fibrillation, 95% CI; 95% confidence interval, BMI; body mass index, AMI; acute myocardial infarction, SBP; systolic blood pressure, HFpEF; heart failure with preserved ejection fraction, HFrEF; heart failure with reduced ejection fraction.

Figure 1. Subgroup-specific odds ratios for all-cause mortality during 2-year follow-up from HF diagnosis; comparing HF patients who received exercise-based CR to propensity-matched HF patients who received usual care only (controls).