HHS Public Access
Author manuscript
Trends Cardiovasc Med. Author manuscript; available in PMC 2018 August 01.

Published in final edited form as:
Trends Cardiovasc Med. 2017 August ; 27(6): 420–425. doi:10.1016/j.tcm.2017.02.005.

The role of cardiac rehabilitation in patients with heart disease ☆

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Abstract

Cardiac rehabilitation is a valuable treatment for patients with a broad spectrum of cardiac disease. Current guidelines support its use in patients after acute coronary syndrome, coronary artery bypass grafting, coronary stent placement, valve surgery, and stable chronic systolic heart failure. Its use in these conditions is supported by a robust body of research demonstrating improved clinical outcomes. Despite this evidence, cardiac rehabilitation referral and attendance remains low and interventions to increase its use need to be developed.

Keywords

Cardiac rehabilitation; Cardiovascular disease

Introduction

Cardiac rehabilitation (CR) has evolved from exercise only into a comprehensive program that also addresses other cardiovascular disease risk factors and provides education and social support [1]. CR classically consists of three phases. Phase I refers to inpatient rehabilitation during the index hospitalization. Due to the increasingly shorter durations of hospital stay, phase I CR has become less formalized. Phase II refers to physician supervised, outpatient monitored physical activity during the 4 months after discharge. Patients usually undergo up to 36 sessions in a graduated exercise program. Thereafter, patients may continue into phase III, which is an enduring unmonitored exercise program. CR programs also provide nutritional, psychological and smoking cessation counseling, as well as lipid and blood pressure management. Medicare and most insurance carriers provide coverage for this service after acute coronary syndrome, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), valve surgery, and chronic stable heart failure with reduced ejection fraction (HFrEF) [2]. The American Heart Association (AHA) and American College of Cardiology (ACC) consider CR a Class I indication for these conditions [3,4].

☆Paul D. Thompson, MD: no relevant conflicts.

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The exercise prescription at CR centers optimally starts with a pre-exercise-training, symptom limited, exercise tolerance test. Thereafter, workouts typically consist of a brief warm up period, followed by supervised individualized aerobic exercise, and a brief cool down phase. The aerobic exercise consists of 20–60 min workouts 3–5 days a week at 50–80% of maximal exercise capacity [1]. Relatively recent data suggest that high intensity interval training (HIIT) produces larger and more rapid increases in exercise capacity [5–7]. A trial of 27 patients with stable ischemic cardiomyopathy randomized to either moderate continuous training at 70% of their max predicted heart rate or to HUT at 95% peak heart rate or to a exercise-advise-only control group demonstrated a 46 vs 14% ($p < 0.001$) increase in peak oxygen consumption (VO_{2MAX}) in the HUT vs continuous training group [5]. Higher VO2MAX has been associated with lower mortality rates in patients with coronary artery disease (CAD) [8]. HUT also improved endothelial function, reversed left ventricular remodeling, and increased ejection fraction more than continuous training [5]. Similar superior improvements have been noted in other studies [6,7]. Yet it should not be forgotten that the favorable meta-analyses of CR showing reductions in total mortality and rehospitalizations were based upon the utilization of moderate intensity exercise [9].

The role of exercise training

Many of the benefits of CR are derived from exercise training. Exercise training increases VO_{2MAX} and endurance capacity or the ability to maintain physical activity for extended periods of time [5]. Exercise training has multiple other potentially beneficial effects including improving endothelial function [5,10], myocardial flow reserve [11] reducing smoking, body weight, blood lipids, and blood pressure [12]. Exercise training has even been shown to reduce the progression of coronary atherosclerosis in patients with known CAD [11].

CR also reduces depression and anxiety and increases quality of life in cardiac patients [13]. Depression is associated with higher mortality, up to fourfold higher in one study of depressed cardiac patients [14]. Depression symptoms and mortality decreased by 63% and 73% among depressed patients after CR compared to non-participants ($p < 0.001$) [14].

Coronary artery disease (CAD)

CAD is the most common referral diagnosis to CR centers. Exercise training or CR in patients with CAD increases exercise tolerance and quality of life [5,6,15–17], decreases angina [18],ischemia [19], subsequent hospitalizations [15,17], and mortality [9,15].

The AHA/ACC recommends the referral of patients after myocardial infarction (MI) or coronary revascularization and those with stable angina to CR [4] because multiple meta-analysis have demonstrated that CR reduces mortality in patients with CAD [9,15,20,21]. A meta-analysis of 63 randomized clinical trials dating from 1974 through 2014 including 14,486 patients documented that CR, compared to no-exercise control reduced cardiovascular mortality (10.4 vs 7.6%, CI 0.64–0.86, number needed to treat (NNT): 37) in patients with CAD. Hospital admissions were also reduced at one year (31 vs 26%, CI 0.70–

0.96, NNT: 22). Health related quality of life increased and the cost of health care resources decreased [15].

CR benefits patients with CAD regardless of the referral diagnosis. Exercise training has long been known to reduce symptoms in patients with angina pectoris and CR may be as effective as PCI at least in the short term. Selected male patients with stable angina (n = 101) randomized to PCI or CR demonstrated increased exercise capacity and reduced coronary events at 12 months in the CR vs control group [17]. Exercise training was associated with a higher event free survival (88% vs 70%, p= 0.023), increased VO_{2MAX} (+ 16%, p < 0.001), and lower cost ($3429 vs $6956 Canadian currency).

CR also benefits patients after emergent, urgent or elective PCI. Patients (n=2395) referred to CR after emergent (32%), urgent (42%), or elective (26%) PCI and followed for a mean of 6.3 years experienced a 46% relative reduction in all-cause mortality (CI 0.41–0.71, NNT: 34) (Fig. 1) [22]. This was independent of age, sex, or PCI setting (elective vs non-elective). Recurrent MI and repeat PCI, however, were not different between the groups. Similarly, 118 patients randomized to CR or usual care after PCI increased their VO_{2MAX} (+ 26%, p < 0.001) and quality of life (+ 26.8%, p=0.001) and experienced lower rates of cardiac events (11.9 vs 32.2%, p=0.008), and hospital readmissions rates (18.6 vs 46%, p< 0.001) after six months. The rate of angiographic restenosis was similar, but the CR patients had less stenosis (29.7%, p=0.045) and less evidence of myocardial ischemia by nuclear imaging (19%, p < 0.001), although this study did precede the widespread use of drug eluting stents [19].

CR has been evaluated extensively in patients referred after acute MI. A meta-analysis of 36 randomized control trials including 6111 patients after MI demonstrated a 36% reduction in cardiac deaths (confidence interval (CI) 0.46–0.88), 26% reduction in total mortality (CI 0.85–0.95), and a 47% reduction in reinfarction (CI 0.38–0.76) [12].

CR also reduces cardiac events, hospital readmissions and mortality after CABG. An observational trial of 846 patients after CABG, 69% of whom attended CR, evaluated after a mean follow-up of 9 years reported a 46% relative risk reduction (RRR) and 12.7% absolute risk reduction of all-cause mortality with a number needed to treat of 8 (CI 0.40–0.74) [23]. These findings were independent of age, sex, prior myocardial infarction, or diabetes. Another observational study of 3975 patients after CABG demonstrated an all-cause mortality reduction of 20% with phase 1 CR and 40% with phase 2 CR [24]. Both studies used the propensity score matching method to account for inherent selection bias.

Despite the clear benefit of CR to patients with CAD, referral rates and rates of participation remain low. In one study, whereas 62% of patients above age 65 were referred to CR after MI, only 33% of these attended one session [25]. Rates are even lower among women and minorities [26]. The reasons for low referral rates are not clear, but include transportation problems, lack of insurance, financial need to return to work, and other barriers. It is also noted that many physicians underestimate the value of exercise training, risk management and psychosocial support in CAD patients and without physician referral, participation is unlikely [27].

Valvular heart disease

The evidence supporting CR for CAD patients is robust, whereas there are less data on CR for patients after valve surgery. An attempt to perform a meta-analysis of randomized, controlled trials of CR after valve surgery found only 2 trials worthy of inclusion. There was an increase in exercise capacity with CR (standard mean difference: −0.47 kJ, CI −0.81−0.13) [28], but too few participants (N = 148) to evaluate other outcomes. A retrospective review of patients participating in CR after valve surgery observed an increase in quality of life, which is congruent with an increase in VO_{2MAX} ($r=0.62$, $p < 0.05$) [29].

Data on transcatheter aortic valve replacement (TAVR) and CR have been limited to observational trials demonstrating increased exercise capacity and quality of life [30,31]. A pilot trial [32] randomized 30 TAVR patients to eight weeks of supervised endurance and resistance exercise training or standard care. Average VO_{2MAX} increased 3.7 ml/min/kg (p=0.007) more in the exercise vs. control group. Muscle strength and quality of life (+16.8%, p = 0.009) also increased more in the exercise trained group compared to control.

Heart failure

Medicare initiated coverage of CR for patients with HFrEF in 2014. Patients are eligible for coverage if they have stable heart failure with a left ventricular ejection fraction (LVEF) < 35% and New York Heart Association (NYHA) class II to IV symptoms despite at least 6 weeks of appropriate medical management [33].

The exercise training meta-analysis of trials in patients with chronic heart failure or ExTraMatch study provided evidence that exercise training benefits patients with heart failure [34]. HFrEF patients randomized to exercise experienced a 45% reduction in mortality (CI − 8 to 54%, p=0.015). Only 17 patients needed to be treated for 2 years to save a life. The combined endpoint of death or hospital admissions also decreased 38% in the exercise training group (hazard ratio (HR) 0.72, CI 0.56–0.93) (Fig. 2).

Medicare approval for CR reimbursement, however, was primarily based on the results of HF-ACTION or the Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training study. This trial randomized 2331 patients to exercise training or standard therapy [35]. Exercise training reduced the primary endpoint, all cause mortality or hospitalization, by 11% (p=0.03) after adjustment for the prespecified baseline confounders of atrial fibrillation/flutter, psychological depression, ejection fraction, and exercise capacity (Fig. 3). The secondary endpoint of CV mortality or CHF hospitalizations was also reduced by 9% (p = 0.03) after adjustment for baseline variables. Three-year mortality was similar in the two arms of the study. This trial has been strongly criticized because the increase in VO_{2max} was only 4% among the exercise training participants.

There are few studies that have examined the effect of exercise training in patients with ventricular assist devices. The REHAB-VAD or Cardiac Rehabilitation Improves Functional Capacity and Patient -Reported Health Status in Patients With Continuous Flow Left Ventricular Assist Devices trial demonstrated increased functional capacity and health status in 21 subjects randomized to CR versus usual care. The CR group experienced increases in quality of life (30%, p=0.018) and treadmill time (27%, p=0.001) compared to control. The CR group also improved VO_{2max} by 10% (p=0.007). Six minute walk, ventilatory threshold, submaximal exercise heart rate, and heart rate at one minute of recovery also only improved within the CR group.

Patients with heart failure with preserved ejection fraction (HFpEF) comprise an increasing proportion of the HF population. CR for this patient population is not presently reimbursed by third party payers or endorsed by clinical guidelines. An exercise training study of 54 patients with cardiomyopathy randomized to exercise training vs control demonstrated a reduction in left ventricular diastolic stiffness in the exercise training group suggesting that CR improves diastolic function [36]. A trial of 64 patients with HFpEF and NYHA class II-III symptoms randomized to exercise training or control, (Ex-DHF or Exercise Training in Diastolic Heart Failure) demonstrated that exercise training improves both quality of life and exercise capacity in patients with HFpEF [37].VO_{2MAX} increased by 21% ($p < 0.001$) and the mean decrease in E/e' was 3.2 ($p < 0.001$) in the exercise trained group. Subjects who decreased E/e' experienced a 38% increase of VO_{2max} and a 50% improvement of in their physical functioning.

Cardiac transplant

Cardiac transplant patients represent a small portion of those referred for cardiac rehabilitation, but these patients are typically profoundly deconditioned due to their pre transplant severe heart failure, prolonged hospital course, and side effects of immunologic therapies. Additionally, the heart is initially denervated in cardiac transplant patients reducing their physiologic response to exercise. Peak VO_2 in patients post cardiac transplant recipients is reportedly 70% less than age matched controls [38].

In 1988, a trial assessed the effectiveness of a two-year exercise program in 36 orthotopic cardiac transplant patients [38].VO_{2max} increased 27%, $p < 0.001$ with exercise training. Similarly, a trial of 27 cardiac transplant recipients randomized to CR also noted a 4.4 ml/kg/min (49%) increase in VO_{2max} at 6 months with exercise training vs a 1.9 ml/kg/min (18%) increase in the control group ($p = 0.01$) [39].

Challenges and future directions

Available data and guidelines strongly support the role of comprehensive CR in patients with heart disease. Patients benefit from decreased mortality, morbidity, disability, and increased quality of life. CR patients also benefit from reduced hospitalizations, an increasingly important measure as healthcare moves towards a capitated environment. Despite this, only 14% of patients after AMI and 31% in patients after CABG participate in CR [40]. Future studies should focus on how to include more cardiac patients in CR. Indeed, The Centers for Disease Control and Medicare have teamed up to expand CR participation as part of the "Million Hearts" program [41]. Efforts are needed to overcome the social, economic, and practice behaviors to referral, enrollment, and adherence to CR such that the clinical benefits are attained. In view of a geographic non-availability of CR programs for some patients, hybrid home CR programs are also being developed [41]. Studies are also needed to evaluate the utility of CR in patients after valve surgery and TAVR as well as in patients with HFpEF.

Conclusions

CR is a valuable treatment for a broad spectrum of patients with heart disease. It use is supported by a robust body of research demonstrating improvements in cardiopulmonary fitness, psychological factors, and quality of life and reductions in morbidity and mortality. It is also an excellent strategy for reducing hospital readmissions. Despite this evidence, the value of CR is underappreciated and underutilized by many clinicians to the detriment of patient outcomes.

Acknowledgments

Disclosures: Sean R. McMahon, MD: None. Philip A. Ades, MD: supported in part by Center of Biomedical Research Excellence Award P20GM103644 from the National Institute of General Medical Sciences.

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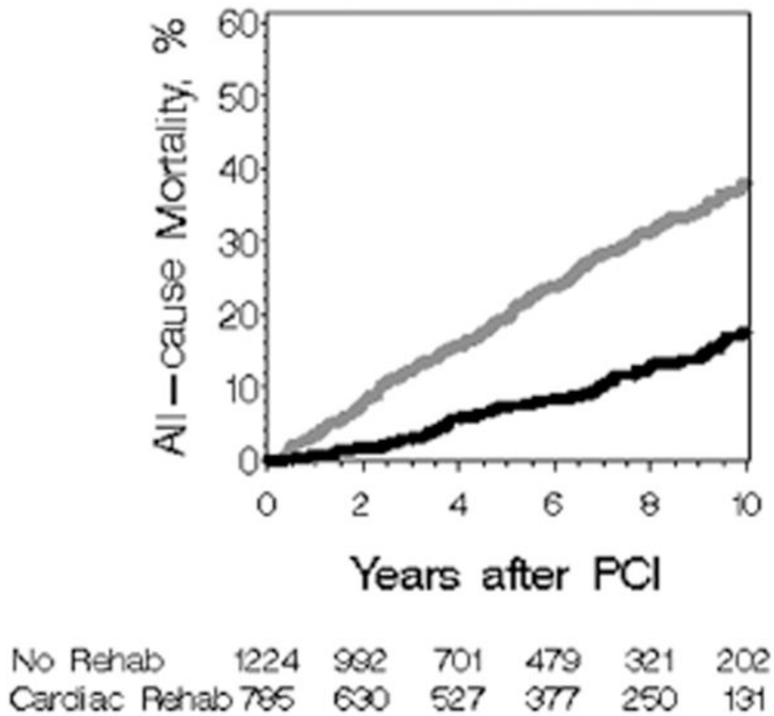

Fig. 1.

Effect of cardiac rehabilitation on mortality after percutaneous intervention. (Kaplan-Meier curve showing the association between cardiac rehabilitation (dark line) and all-cause mortality in patients after elective (26%), urgent (42%), or emergent (32%) percutaneous coronary intervention. Reproduced from [22].)

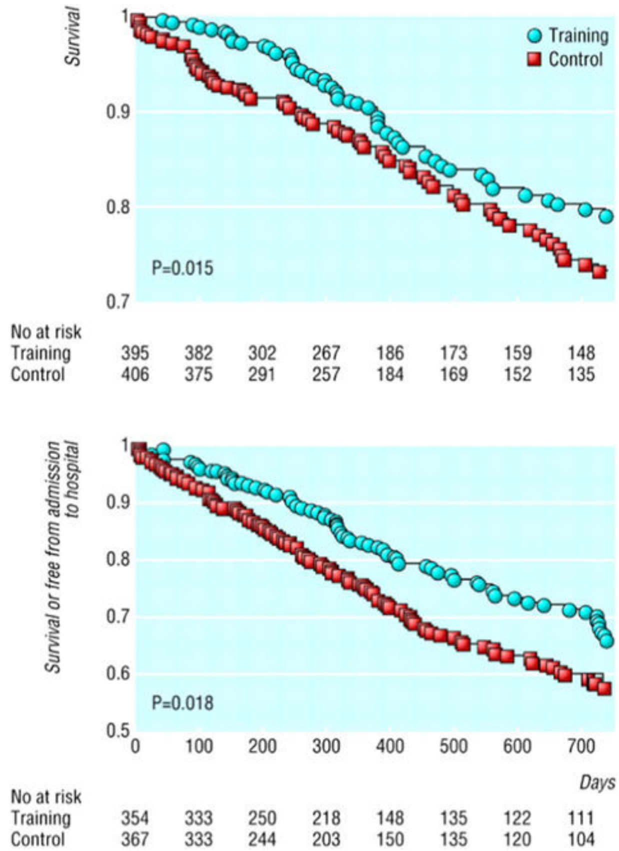

Fig. 2.

Exercise training and survival/survival or free from hospital admission in patients with chronic heart failure. (Kaplan-Meier curves demonstrating the relationship between exercise training and survival (top) and survival or free from hospital admission. Reproduced from [34].)

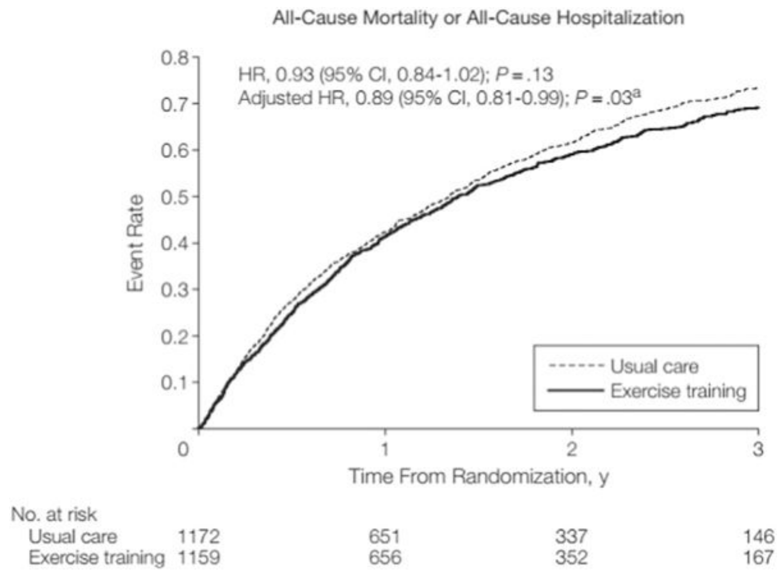

Fig. 3.

Time to All-Cause Mortality or All-Cause Hospitalization in heart failure patients. (All-cause mortality or all-cause hospitalization after adjustment for key prognostic factors. From the HF-ACTION Randomized Controlled Trial. Reproduced from [35].)